A preparative small molecule mimic of liver CYP450 enzymes in the aliphatic C—H oxidation of carbocyclic *N*-heterocycles

Supplementary Information

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I. General Methods

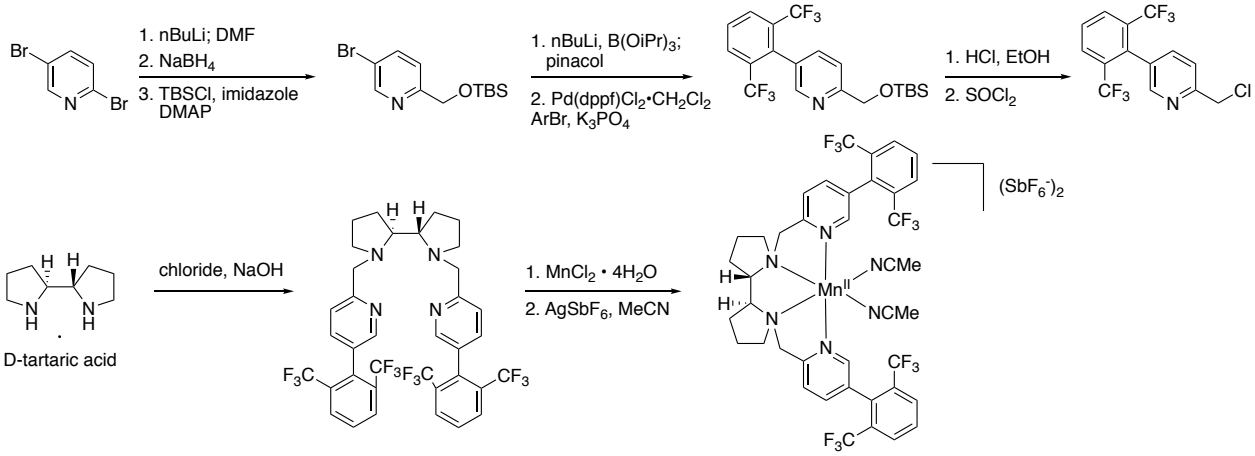
All C—H oxidations were carried out under air with magnetic stirring, with no precautions to exclude oxygen or moisture. All other reactions were performed with oven dried or flame dried glassware under inert atmosphere of dry nitrogen or argon. (*R,R*)- and (*S,S*)-Fe(PDP)[1,2] and Mn(PDP)[3,4] and Mn(CF_3-PDP)[2,3] catalyst were synthesized according to literature protocol. Mn(CF_3PDP) **1** (known as the White-Gormisky-Zhao catalyst) is commercial from Strem chemicals and the manganese chloride catalyst precursor (prior to metathesis) is commercial at J&K scientific. All catalysts were stored at 0 ºC. The catalysts were warmed to room temperature prior to use and weighed out in air. Chloroacetic acid was purchased from Sigma-Aldrich and broken into small pieces before use. H_2O_2 (50% wt. aqueous solution) was purchased from Sigma-Aldrich and used as received. $AgSbF_6$ used for catalyst metathesis was purchased from Strem Chemicals and stored and weighed in an argon atmosphere glove box to avoid light. Solvents including THF, DCM, diethyl ether, DMF, toluene and benzene were dried by passing through a bed of activated alumina (Glass Contour, Laguna Beach, CA). Triethylamine and pyridine were distilled over calcium hydride prior to use. All other commercially available reagents were purchased from common sources (e.g. Sigma-Aldrich, Strem Chemicals, Oakwood, Alfa-Aesar, TCI America, etc.) and were used as received.

Thin-layer chromatography was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV and/or staining including potassium permanganate, ceric ammonium molybdate, or phosphomolybdic acid/cerium sulfate. Flash column chromatography was performed using ZEOprep 60 ECO 43-60 micron silica gel (American International Chemical Inc.) or basic aluminum oxide, Brockmann Grade II (3% H_2O added to Brockmann grade I) or Brockmann grade III (6% H_2O added to Brockmann grade I) prepared from Alfa Asear aluminum oxide, activated, basic, Brockmann grade I, 58 angstroms, 60 mesh powder, S.A. 150 m^2/g, CAS: 1344-28-1. Medium pressure liquid chromatography was performed on a Teledyne Isco ComiFlash Rf machine using pre-packed RediSep columns.

^{1}H NMR were recorded using a Varian Unity-500 (500 MHz), Varian Unity Inova-500 (500 MHz), Carver Bruker-500 (500 MHz) and Carver Bruker-600 (600 MHz) spectrometer, using solvent as internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as: s=singlet, d=doublet, t=triplet, q=quartet, p=pentet, sxt=sextet, hept=heptet oct=octet, non=nonet, m=multiplet, br=broad, app=apparent; coupling constants in Hz; integration. Proton-decoupled ^{13}C NMR were recorded using a Varian Unity-500 (500 MHz), Carver Bruker-500 (500 MHz) and Carver Bruker-600 (600 MHz) using solvent as internal standard ($CDCl_3$ at 77.16 ppm). ^{19}F NMR were recorded using a Varian Unity-500 (470 MHz), Carver

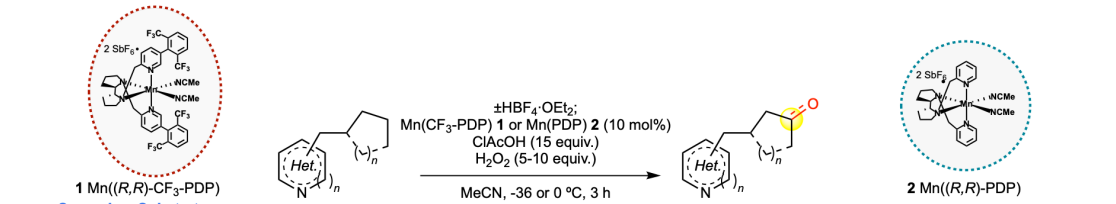
Bruker-500 (500 MHz) and Carver Bruker-600 (600 MHz) spectrometer and are reported in ppm using $CFCl_3$ (0 ppm) using external standard. Labeled solvent or ligand impurities were calculated out when reporting isolated yields. High resolution mass spectrometry (HRMS) was performed with a Waters Q-TOF Ultima spectrometer or Waters GCT Premier EI spectrometer. Optical rotations were obtained using a JASCO P2000 polarimeter (cell dimensions: 3.5 X 50 mm) and were reported as $[\alpha]_D^{T/^oC}$ concentration (c = g/100 mL, solvent).

II. Synthesis of Mn(CF$_3$-PDP) Catalyst [1]

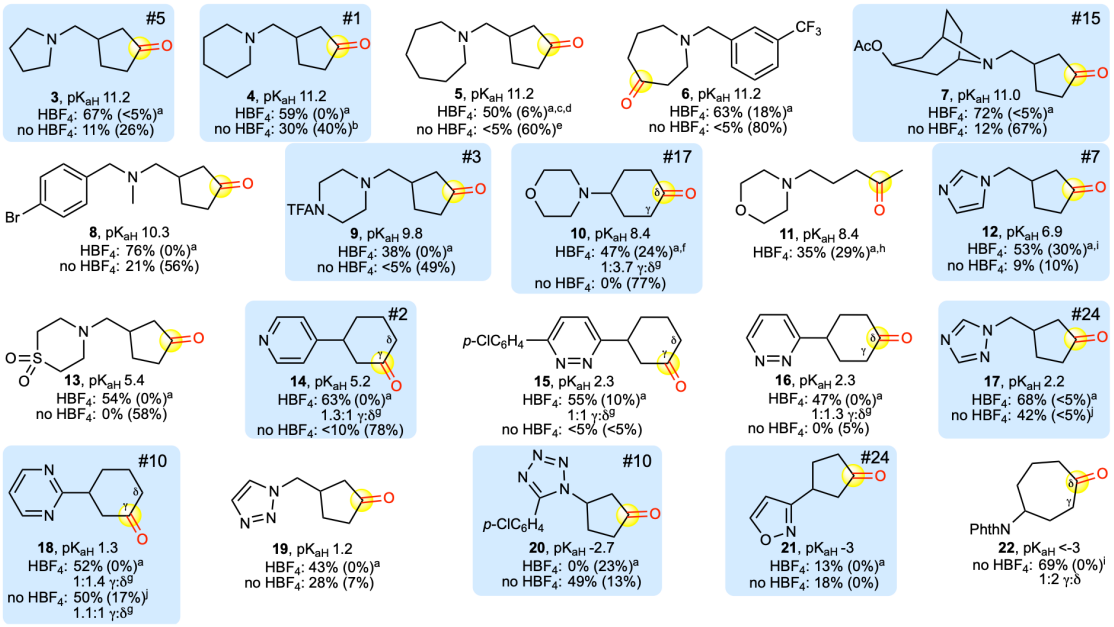


The CF_3-PDP ligand was made according to the procedure described in ref. 2. Insertion of manganese and metathesis was performed according to the procedure described in ref. 3. Mn(CF_3PDP) **1** (known as the White-Gormisky-Zhao catalyst) is commercial from Strem chemicals and the manganese chloride catalyst precursor (prior to metathesis) is commercial at J&K scientific.

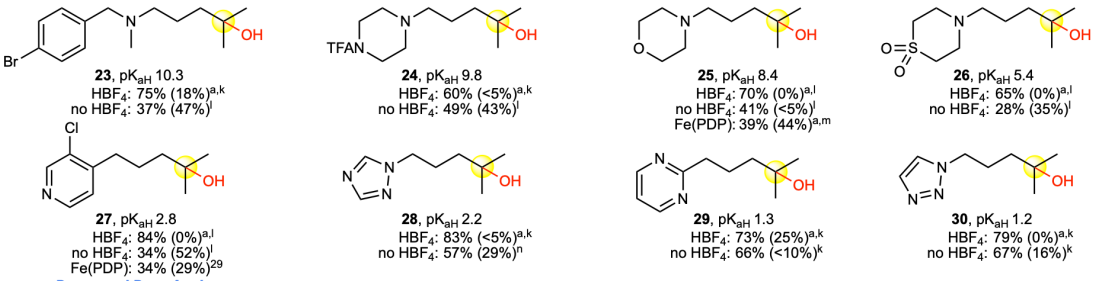
III. Supplementary Figure 1. Heterocycle Scope.



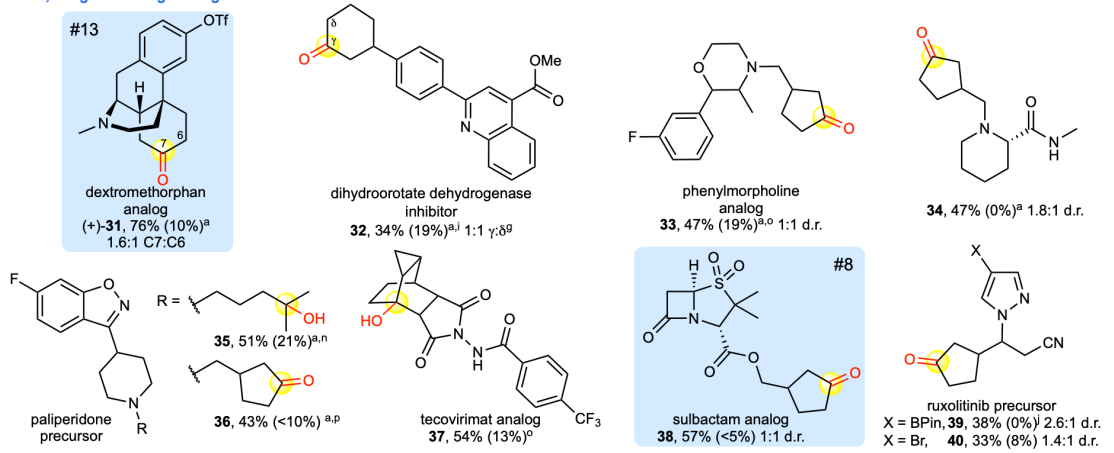
a, Secondary Substrates



b, Tertiary Substrates



c, Drugs and Drug Analogs



Isolated yields are an average of two to three experiments, major isolated site of oxidation is highlighted in yellow, and recovered starting material (RSM) is given in parentheses. Experimental pK_{aH} reported in water (see SI for references). Blue boxes with numbers indicate frequency of *N*-heterocycles in FDA approved drugs according to ref. 1. ClAcOH, chloroacetic acid. NPhth, phthalimide. General methylene oxidation with HBF_4 was done using Method A at -36 °C unless otherwise noted. General methylene oxidation without HBF_4 was done using Method B unless otherwise noted. [a]Nitrogen was HBF_4•OEt_2 protected as described in Materials and Methods. [b]Method A at 0 °C. [c]Modified Method D [2.5 mol% $Mn(CF_3$-PDP) **1**, 7.5 equiv. ClAcOH, 5 equiv. H_2O_2] at -36 °C. [d]With 20% di-oxidation. [e]Modified Method D [2.5 mol% $Mn(CF_3$-PDP) **1**, 7.5 equiv. ClAcOH, 5 equiv. H_2O_2] at 0 °C. [f]Method C [2 x 5 mol% $Mn(CF_3$-PDP) **1**] at 0 °C. [g]Ratios are statistically corrected. [h]Method C [3 x 5 mol% $Mn(CF_3$-PDP) **1**] at 0 °C. [i]Method D. [j]Method A at -36 °C. [k]Method B with Mn(PDP) **2**. [l]Method A with Mn(PDP) **2**. [m]3 x 5 mol% Fe(PDP), iterative addition protocol (ref. 21). [n]Method C [2 x 5 mol% Mn(PDP) **2**] at -36 °C. [o]Method B. [p]Method C [3 x 5 mol% $Mn(CF_3$-PDP) **1**] at -36 °C.

Preparation of Substrates and Compounds Characterization for Supplementary Figure 1

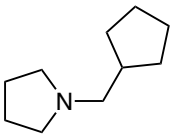
General Procedure A for *N*-Alkylation

To a flame-dried round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere was added substrate (1.0 equiv.) and DMF (0.5 M). The solution was cooled to 0 °C and NaH (1.25 equiv.) was added in one portion. The solution was stirred at 0 °C for 15 minutes and alkyl bromide or tosylate (1.1 equiv.) was added dropwise. The reaction was stirred overnight (16 h) at room temperature. The reaction was quenched by the addition of water. The aqueous layer was extracted with CH_2Cl_2 (x 3). The combined organic layer was washed with H_2O (x10), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography.

General Procedure B for *N*-Alkylation

To a round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere was added substrate (1.0 equiv.), 1,2-dichloroethane (0.1 M), aldehyde (1.1 equiv.) and acetic acid (1% v/v). The reaction solution was stirred for 30 minutes at room temperature. $NaBH(OAc)_3$ (1.2 equiv.) was added in one portion. The reaction was stirred at room temperature overnight (18 h). The reaction was quenched at room temperature by the addition of sat. aq. $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (x2). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography.

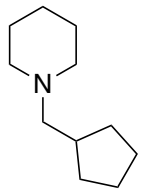
1-(cyclopentylmethyl)pyrrolidine [S1]



To a flame-dried round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere was added cyclopentylmethyl 4-methylbenzenesulfonate (1.35 g, 5.29 mmol, 1.0 equiv.) and MeCN (18 mL, 0.3 M). K_2CO_3 (1.09 g, 7.93 mmol, 1.5 equiv.) was added, followed by pyrrolidine (0.65 mL, 7.93 mmol, 1.5 equiv.). The reaction was stirred at 60 °C for 24 h. Upon completion, the reaction was concentrated under reduced pressure. The residue was dissolved in 30 mL CH_2Cl_2 and washed with 30 mL H_2O. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL) and the combined organic layers were dried with Na_2SO_4. The filtrate was concentrated under reduced pressure and purified by flash chromatography (Brockmann Grade II basic alumina) using 5% EtOAc/Hex afforded 1-(cyclopentylmethyl)pyrrolidine (**S1**) as a colorless oil (0.493 g, 3.22 mmol, 61% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.54-2.44 (m, 4H), 2.37 (d, J = 7.3 Hz, 2H), 2.02 (hept, J = 7.8 Hz, 1H), 1.82-1.72 (m, 6H), 1.64-1.47 (m, 4H), 1.25-1.13 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 62.9, 54.8, 39.6, 31.8, 25.4, 23.6. HRMS (ESI+) *m/z* calculated for $C_{10}H_{20}N$ $[M+H]^+$: 154.1590 , found: 154.1597.

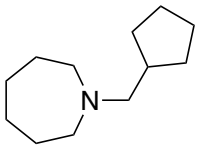
1-(cyclopentylmethyl)piperidine [S2]



According to general procedure B for *N*-alkylation, piperidine (0.5 mL, 425.8 g, 5.0 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (981.5 mg, 10.0 mmol, 2.0 equiv.), acetic acid (0.5 mL) and $NaBH(OAc)_3$ (1.27 g, 6.0 mmol, 1.2 equiv.) were reacted in 1,2-dichloroethane (50 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 5% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 1-(cyclopentylmethyl)piperidine (**S2**) as an orange oil (685.8 mg, 4.1 mmol, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 – 2.27 (m, 4H), 2.22 (d, *J* = 7.1 Hz, 2H), 2.05 (hept, *J* = 7.6 Hz, 1H), 1.79 – 1.68 (m, 2H), 1.64 – 1.45 (m, 8H), 1.40 (p, *J* = 6.2 Hz, 2H), 1.16 (dq, *J* = 11.8, 7.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 65.7, 55.1, 37.6, 31.9, 26.2, 25.4, 24.7. HRMS (ESI+) *m/z* calculated for $C_{11}H_{22}N$ $[M+H]^+$: 168.1752, found 168.1759.

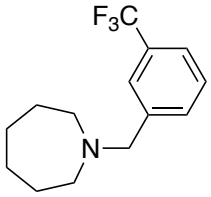
1-(cyclopentylmethyl)azepane [S3]



To a flame-dried round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere was added cyclopentylmethyl 4-methylbenzenesulfonate (1.27 g, 5.00 mmol, 1.0 equiv.) and MeCN (18 mL, 0.3 M). K_2CO_3 (1.04 g, 7.50 mmol, 1.5 equiv.) was added, followed by azepane (0.85 mL, 7.50 mmol, 1.5 equiv.). The reaction was stirred at 60 °C for 24 h. Upon completion, the reaction was concentrated under reduced pressure. The residue was dissolved in 30 mL CH_2Cl_2 and washed with 30 mL H_2O. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL) and the combined organic layers were dried with Na_2SO_4. The filtrate was concentrated under reduced pressure and purified by flash chromatography (Brockmann Grade II basic alumina) using 5% EtOAc/Hex afforded 1-(cyclopentylmethyl)azepane (**S3**) as a colorless oil (0.570 g, 3.14 mmol, 63% yield).

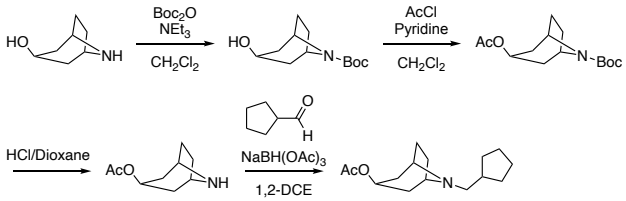
^{1}H-NMR (500 MHz, $CDCl_3$) δ 2.67-2.22 (m, 4H), 2.39 (d, J = 7.2 Hz, 2H), 2.02 (hept, J = 7.6 Hz, 1H), 1.76-1.69 (m, 2H), 1.65-1.45 (m, 12H), 1.21-1.14 (m, 2H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 63.6, 55.7, 38.4, 31.6, 28.0, 27.4, 25.4. HRMS (ESI+) *m/z* calculated for $C_{12}H_{24}N$ $[M+H]^+$: 182.1903 , found: 182.1912.

1-(3-(trifluoromethyl)benzyl)azepane [S4]

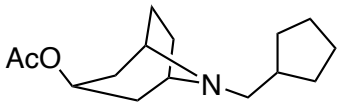


To a flame-dried round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere was added 1-(bromomethyl)-3-(trifluoromethyl)benzene (1.20 g, 5.00 mmol, 1.0 equiv.) and MeCN (18 mL, 0.3 M). K_2CO_3 (1.04 g, 7.50 mmol, 1.5 equiv.) was added, followed by azepane (0.85 mL, 7.50 mmol, 1.5 equiv.). The reaction was stirred at 60 °C for 24 h. Upon completion, the reaction was concentrated under reduced pressure. The residue was dissolved in 30 mL CH_2Cl_2 and washed with 30 mL H_2O. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL) and the combined organic layers were dried with Na_2SO_4. The filtrate was concentrated under reduced pressure and purified by flash chromatography (35 mm fritted glass column, Brockmann Grade II basic alumina) using 2% EtOAc/Hex afforded 1-(3-(trifluoromethyl)benzyl)azepane (**S4**) as a colorless oil (1.16 g, 4.52 mmol, 90% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 7.7 Hz, 1H), 3.68 (s, 2H), 2.62 (m, 4H), 1.63 (m, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 141.5, 132.1, 130.6 (q, J = 31.8 Hz), 128.7, 125.4 (q, J = 3.8 Hz), 124.5 (q, J = 272.2 Hz), 123.7 (q, J = 3.9 Hz), 62.4, 55.8, 28.4, 27.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ − 62.5. HRMS (ESI+) *m/z* calculated for $C_{14}H_{19}F_3N^+$ $[M+H]^+$: 258.1464, found: 258.1471.



(1*R*,3*r*,5*S*)-8-(cyclopentylmethyl)-8-azabicyclo[3.2.1]octan-3-yl acetate [S5]



To a flame-dried round bottom flask was added nortropine (2.54 g, 20.00 mmol, 1.00 equiv.) and this was dissolved in CH_2Cl_2 (35 mL). NEt_3 (4.05 g, 5.57 mL, 40.00 mmol, 2.00 equiv.) was added, followed by Boc_2O (5.24 g, 24.00 mmol, 1.20 equiv.) in one portion, and this was left to stir for 16 hours. The resultant solution was washed with sat. citric acid, water, and brine. The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to yield *tert*-butyl (1*R*,3*r*,5*S*)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate (4.55 g, 20.00 mmol, 100% yield) as a white solid. This was carried forward without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.19-4.11 (m, 3H), 2.16-2.06 (m, 4H), 1.96-1.89 (m, 2H), 1.72-1.67 (m, 2H), 1.45 (s, 9H).

To a flame-dried round bottom flask was added *tert*-butyl (1*R*,3*r*,5*S*)-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate (4.91 g, 21.56 mmol, 1.00 equiv.) and this was dissolved in CH_2Cl_2 (40 mL). The solution was cooled to 0 ºC, followed by the addition of pyridine (3.41 g, 3.47 mL, 43.14

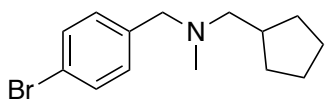
mmol, 2.00 equiv.) and AcCl (2.71 g, 2.46 mL, 34.50 mmol, 1.60 equiv.). The reaction was allowed to warm to room temperature over 6 hours, after which it was diluted with CH_2Cl_2 (50 mL) and washed with H_2O (2x100 mL) and brine (100 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to yield a crude residue which was purified via chromatography (35 mm fritted glass column, 125 mL SiO_2) using 20% EtOAc/hexanes as eluant afforded *tert*-butyl (1*R*,3*r*,5*S*)-3-acetoxy-8-azabicyclo[3.2.1]octane-8-carboxylate (5.11 g, 18.89 mmol, 88% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.07 (t, *J* = 5.2 Hz, 1H), 4.18(br s, 2H), 2.11 (d, *J* = 14.1 Hz, 2H), 2.05 (s, 3H), 2.01-1.92 (m, 4H), 1.72 (d, *J* = 15.0 Hz, 2H), 1.46 (s, 9H).

To a solution of *tert*-butyl (1*R*,3*r*,5*S*)-3-acetoxy-8-azabicyclo[3.2.1]octane-8-carboxylate (5.11 g, 18.98 mmol, 1.0 equiv.) in 1,4-dioxane (20 mL) was added HCl (4.0 M in dioxane, 47 mL, 189.98 mmol, 10.00 equiv.) and this was allowed to stir at room temperature overnight. The resultant solution was concentrated under reduced pressure resulting in a crude solid which was washed with ice cold diethyl ether to yield the hydrochloride salt of (1*R*,3*r*,5*S*)-8-azabicyclo[3.2.1]octan-3-yl acetate (3.90 g, 18.98 mmol, 100% yield) as an off-white powder which was carried forward without further purification.

(1*R*,3*r*,5*S*)-8-azabicyclo[3.2.1]octan-3-yl acetate hydrochloride salt (411.0 mg, 2.00 mmol, 1.00 equiv.) was suspended in CH_2Cl_2 (10 mL) and transferred to a separatory funnel. K_2CO_3 (0.3 M aq., 10 mL, 3.00 mmol, 1.50 equiv.) was added, and this was shaken vigorously. The layers were separated and the aqueous layer was further washed with CH_2Cl_2 (2x10 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to yield the free base of (1*R*,3*r*,5*S*)-8-azabicyclo[3.2.1]octan-3-yl acetate. This was dissolved in 1,2-DCE (20 mL), and cyclopentanecarbaldehyde (236.0 mg, 2.40 mmol, 1.20 equiv.) was added, followed by $NaBH(OAc)_3$ (636.0 mg, 3.00 mmol, 1.50 equiv.). This was allowed to stir at room temperature for 24 hours. The resulting suspension was transferred to a separatory funnel and washed with sat. $NaHCO_3$ (20 mL). The layers were separated and the aqueous layer was further washed with CH_2Cl_2 (2x30 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to yield a crude residue which was purified via chromatography (35 mm fritted glass column, 100 mL Brockmann Grade II basic alumina) using 5% EtOAc/Hex as gradient afforded (1*R*,3*r*,5*S*)-8-(cyclopentylmethyl)-8-azabicyclo[3.2.1]octan-3-yl acetate (**S5**) as a colorless liquid (351.9 mg, 1.40 mmol, 58% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.96 (t, *J* = 5.4 Hz, 1H), 3.14 (br s, 2H), 2.24 (d, *J* = 7.2 Hz, 2H), 2.10-2.04 (m, 2H), 2.03 (s, 3H), 1.92 (sept, *J* = 7.6 Hz, 1H), 1.90-1.87 (m, 4H), 1.77-1.71 (m, 2H), 1.64 (d, *J* = 14.0 Hz, 2H), 1.60-1.47 (m, 4H), 1.22-1.16 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 68.5, 58.5, 58.3, 39.8, 36.5, 31.5, 26.3, 25.3, 21.8. HRMS (ESI+) *m/z* calculated for $C_{15}H_{26}NO_2^+$ $[M+H]^+$: 252.1958, found: 252.1960.

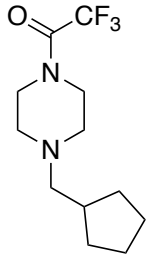
***N*-(4-bromobenzyl)-1-cyclopentyl-*N*-methylmethanamine [S6]**



According to general procedure B for *N*-alkylation, (4-bromobenzyl)methylamine (1.67 g, 8.33 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (1.23 g, 12.5 mmol, 1.5 equiv.), acetic acid (0.83 mL) and $NaBH(OAc)_3$ (1.94 g, 9.2 mmol, 1.1 equiv.) were reacted in 1,2-dichloroethane (83 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% EtOAc/hexanes gradient as eluent afforded *N*-(4-bromobenzyl)-1-cyclopentyl-*N*-methylmethanamine (**S6**) as a pale yellow oil (881.3 mg, 3.12 mmol, 37% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.40 (m, 2H), 7.23 – 7.17 (m, 2H), 3.41 (s, 2H), 2.23 (d, J = 7.5 Hz, 2H), 2.17 (s, 3H), 2.10 (hept, J = 7.5 Hz, 1H), 1.79 – 1.70 (m, 2H), 1.60 – 1.46 (m, 4H), 1.23 – 1.13 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9, 131.3, 130.7, 120.6, 63.5, 62.1, 42.8, 37.9, 31.2, 25.3. HRMS (ESI+) *m/z* calculated for $C_{14}H_{21}NBr$ $[M+H]^+$: 282.0857, found 282.0858.

1-(4-(cyclopentylmethyl)piperazin-1-yl)-2,2,2-trifluoroethan-1-one [S7]



According to general procedure B for N-alkylation, *tert*-butyl piperazine-1-carboxylate (1.86 g, 10.0 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (2.16 g, 22.0 mmol, 2.2 equiv.), acetic acid (1.0 mL) and $NaBH(OAc)_3$ (2.54 g, 12.0 mmol, 1.2 equiv.) were reacted in 1,2-dichloroethane (100 mL). The crude material was purified by flash column chromatography on silica (45 mm fritted glass column, 250 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% → 25% → 30% → 35% EtOAc/hexanes gradient as eluent afforded *tert*-butyl 4-(cyclopentylmethyl)piperazine-1-carboxylate as a pale yellow oil (2.05 g, 7.64 mmol, 76% yield).

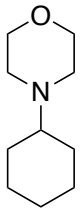
To a round bottom flask equipped with stir bar was added *tert*-butyl 4-(cyclopentylmethyl)piperazine-1-carboxylate (1.05 g, 3.9 mmol, 1.0 equiv.) and HCl in dioxane (4 M, 1.98 mL, 7.9 mmol, 2.0 equiv.). The reaction was stirred open to air overnight (16 h). The residue was dissolved in CH_2Cl_2 and washed with saturated aqueous K_2CO_3. The organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo* to afford 1-(cyclopentylmethyl)piperazine. The crude material was taken onto the next step without further purification. ***Important Note:*** *1-(cyclopentylmethyl)piperazine readily forms the carbamic acid upon sitting under an atmosphere of air at room temperature. Material was moved forward immediately to the next step.*

To a round bottom flask equipped with stir bar under N_2 atmosphere was added 1-(cyclopentylmethyl)piperazine (656.3 mg, 3.9 mmol, 1.0 equiv.) and CH_2Cl_2 (17.6 mL, 0.22 M). Et_3N (0.65 mL, 4.7 mmol, 1.2 equiv.) and trifluoroacetic anhydride (0.65 mL, 4.7 mmol, 1.2 equiv.) were added and the reaction was stirred at room temperature overnight (16 h). The reaction was quenched with H_2O and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was dried with Na_2SO_4, filtered and

concentrated in vacuo. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% → 25% → 30% → 35% EtOAc/hexanes gradient as eluent afforded 1-(4-(cyclopentylmethyl)piperazin-1-yl)-2,2,2-trifluoroethan-1-one (**S7**) as a pale yellow oil (209.6 mg, 0.79 mmol, 20% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.67 (t, *J* = 5.1 Hz, 2H), 3.59 (t, *J* = 5.0 Hz, 2H), 2.50 – 2.44 (m, 4H), 2.27 (d, *J* = 7.5 Hz, 2H), 2.10 – 2.00 (m, 1H), 1.78 – 1.69 (m, 2H), 1.64 – 1.48 (m, 4H), 1.24 – 1.14 (m, 2H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 155.5 (q, *J* = 35.6 Hz), 116.6 (q, *J* = 288.0 Hz), 64.2, 53.5, 52.8, 46.0, 43.6, 37.1, 31.3, 25.3. ^{19}F-NMR (471 MHz, $CDCl_3$) δ -68.8. HRMS (ESI+) *m/z* calculated for $C_{12}H_{20}N_2OF_3$ $[M+H]^+$: 265.1528, found 265.1524.

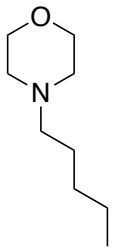
4-cyclohexylmorpholine [S8]



To a round bottom flask equipped with a magnetic stir bar was added 4-(cyclohex-1-en-1-yl)morpholine (1.68 mL, 1.67 g, 10.0 mmol, 1.0 equiv.), EtOH (237 mL, 0.04 M) and Pd/C (53.2 mg, 0.5 mmol, 5 mol%). The flask was sealed with a rubber septum, purged with hydrogen and stirred under a hydrogen balloon (1 atm) at room temperature until the reaction was complete by TLC (18 h). The reaction was filtered through celite using MeOH as the eluent and concentrated *in vacuo* to afford 4-cyclohexylmorpholine (**S8**) as a colorless oil (527 mg, 3.11 mmol, 31% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 – 3.68 (m, 4H), 2.60 – 2.49 (m, 4H), 2.17 (tt, *J* = 10.5, 3.4 Hz, 1H), 1.92 – 1.84 (m, 2H), 1.84 – 1.74 (m, 2H), 1.67 – 1.58 (m, 1H), 1.30 – 1.05 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 67.6, 63.9, 49.9, 29.1, 26.4, 25.9. HRMS (ESI+) *m/z* calculated for $C_{10}H_{20}NO$ 170.1545, found 170.1537.

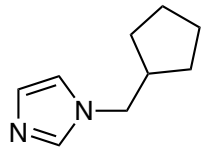
4-pentylmorpholine [S9]



According to general procedure A for *N*-alkylation, morpholine (0.44 mL, 435.6 mg, 5.0 mmol, 1.0 equiv.), NaH (150.0 mg, 6.25 mmol, 1.25 equiv.) and 1-bromopentane (0.68 mL, 830.7 mg, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 5% →10% MeOH/CH_2Cl_2 gradient as eluent afforded 4-pentylmorpholine (**S9**) as a pale yellow oil (583.9 mg, 3.71 mmol, 74% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 – 3.68 (m, 4H), 2.47 – 2.38 (m, 4H), 2.36 – 2.27 (m, 2H), 1.52 – 1.44 (m, 2H), 1.37 – 1.23 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 67.2, 59.4, 54.0, 29.9, 26.4, 22.8, 14.2. HRMS (ESI+) *m/z* calculated for $C_9H_{20}NO$ 158.1545, found 158.1544.

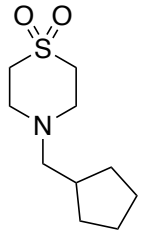
1-(cyclopentylmethyl)-1*H*-imidazole [S10]



According to general procedure A for N-alkylation, imidazole (340.4 mg, 5.0 mmol, 1.0 equiv.), NaH (167.0 mg, 6.25 mmol, 1.25 equiv.) and cyclopentylmethyl 4-methylbenzenesulfonate (1.40 g, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude product was purified by flash column chromatography on silica (30 mm fritted glass column, 150 mL SiO_2) using 2% MeOH/CH_2Cl_2 afforded 1-(cyclopentylmethyl)-1*H*-imidazole (**S10**) as a pale yellow oil (673.0 mg, 4.48 mmol, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.03 (s, 1H), 6.90 (s, 1H), 3.83 (d, J = 7.4 Hz, 2H), 2.26 (hept, J = 7.7 Hz, 1H), 1.74-1.52 (m, 6H), 1.22-1.16 (m, 2H) . ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.3, 129.4, 119.1, 52.0, 41.5, 30.5, 25.0. HRMS (ESI+) *m/z* calculated for $C_9H_{15}N_2$ $[M+H]^+$: 151.1230 , found: 151.1235.

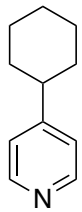
4-(cyclopentylmethyl)thiomorpholine 1,1-dioxide [S11]



According to general procedure B for *N*-alkylation, thiomorpholine 1,1-dioxide (1.08 g, 8.0 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (1.47 g, 15.0 mmol, 1.9 equiv.), acetic acid (0.8 mL) and $NaBH(OAc)_3$ (2.54 g, 12.0 mmol, 1.5 equiv.) were reacted in 1,2-dichloroethane (80 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% → 25% → 30% → 35% EtOAc/hexanes gradient as eluent afforded 4-(cyclopentylmethyl)thiomorpholine 1,1-dioxide (**S11**) as a white solid (1.44 g, 6.6 mmol, 83% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.07 – 3.01 (m, 4H), 3.01 – 2.95 (m, 4H), 2.39 (dd, *J* = 7.5, 1.3 Hz, 2H), 2.01 (hept, *J* = 7.6 Hz, 1H), 1.79 – 1.67 (m, 2H), 1.65 – 1.48 (m, 4H), 1.25 – 1.12 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 62.6, 51.5, 51.1, 37.7, 31.2, 25.2. HRMS (ESI+) *m/z* calculated for $C_{10}H_{20}NO_2S$ $[M+H]^+$: 218.1215, found 218.1205.

4-cyclohexylpyridine [S12]

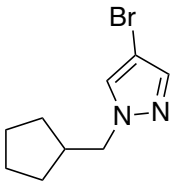


Prepared according to a published procedure.[5] To a flame dried 3-neck round bottom flask was added *i*-Pr_2NH (3.3 mL, 23.3 mmol, 1.55 equiv.) in THF (65 mL, 0.36 M). The solution was cooled to -78 °C and *n*-BuLi (1.6 M in hexanes, 14.1 mL, 22.5 mmol, 1.5 equiv.) was added dropwise. After 10 minutes, the solution was warmed to 0 °C and stirred for a further 20 minutes. The solution was again cooled to -78 °C and 4-picoline (1.46 mL, 15.0 mmol, 1.0 equiv.) in THF (9.8 mL) was added dropwise. The reaction was stirred at -78 °C for 1 h then, 1,5-dibromopentane (2.0 mL, 15.0 mmol, 1.0 equiv.) in THF (6.5 mL) was added dropwise. After stirring at -78 °C for 1 h, the reaction was warmed to room temperature and stirred at room temperature overnight. The reaction was quenched with aq. sat. NH_4Cl and the organic layer was separated. The aqueous layer was extracted with EtOAc (3

x 50 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 20% EtOAc/hexanes as eluent afforded 4-cyclohexylpyridine (**S12**) as a pale yellow oil (348.0 mg, 2.16 mmol, 14% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 – 8.45 (m, 2H), 7.15 – 7.06 (m, 2H), 2.54 – 2.42 (m, 1H), 1.91 – 1.81 (m, 4H), 1.80 – 1.72 (m, 1H), 1.47 – 1.33 (m, 4H), 1.33 – 1.19 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 149.9, 122.5, 44.0, 33.7, 26.7, 26.1. HRMS (ESI+) *m/z* calculated for $C_{11}H_{16}N$ $[M+H]^+$: 162.1283, found 162.1275.

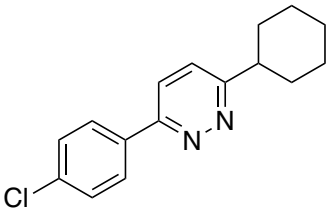
4-bromo-1-(cyclopentylmethyl)-1*H*-pyrazole [S13]



According to general procedure A for *N*-alkylation, 4-bromo-1H-pyrazole (294.0 mg, 2.0 mmol, 1.0 equiv.), NaH (58.0 mg, 2.4 mmol, 1.2 equiv.) and cyclopentylmethyl 4-methylbenzenesulfonate (560 mg, 2.2 mmol, 1.1 equiv.) were reacted in DMF (4 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% EtOAc/hexanes gradient as eluent afforded 4-bromo-1-(cyclopentylmethyl)-1*H*-pyrazole (**S13**) as a colorless oil (55.9 mg, 0.24 mmol, 12% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.38 (s, 1H), 3.99 (d, J = 7.5 Hz, 2H), 2.38 (hept, J = 7.7 Hz, 1H), 1.75 – 1.67 (m, 2H), 1.66 – 1.60 (m, 2H), 1.60 – 1.51 (m, 2H), 1.28 – 1.18 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.5, 129.2, 92.7, 57.8, 40.8, 30.3, 25.1. HRMS (ESI+) *m/z* calculated for $C_9H_{14}N_2Br$ $[M+H]^+$: 229.0340, found 229.0338.

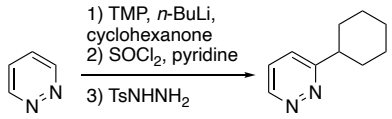
3-(4-chlorophenyl)-6-cyclohexylpyridazine [S14]



Prepared according to a published procedure.[6] To a flame-dried 100 mL round bottom flask with a stir bar was added Pd-PEPPSI-IPr (18.1 mg, 0.027 mmol, 1 mol%) and 3-chloro-6-(4-chlorophenyl)pyridazine (600.0 mg, 2.67 mmol, 1.0 equiv.) and toluene (10.7 mL, 4.0 M). The solution was cooled to 0 °C and a THF solution of cyclohexylzinc(II) bromide (1.2 equiv.) was added via syringe. The reaction was stirred at room temperature for 3 hours. The reaction mixture was quenched with 1M aq. HCl and extracted with ethyl acetate (3 x 30 mL). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (30 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% → 6% ethyl acetate/hexanes gradient as eluent afforded 3-(4-chlorophenyl)-6-cyclohexylpyridazine (**S14**) as a white solid (279.5 mg, 1.0 mmol, 38% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.7 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 1H), 2.99 (app. t, *J* = 11.9, 3.1 Hz, 1H), 2.04 (d, *J* = 12.8 Hz, 2H), 1.94 – 1.87 (m, 2H), 1.83 – 1.76 (m, 1H), 1.63 (app. q, *J* = 12.8, 2.8 Hz, 2H), 1.47 (app. q, *J* = 12.9, 3.1 Hz, 2H), 1.38 – 1.27 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 156.4, 136.1, 135.1, 129.3, 128.2, 125.5, 123.9, 44.6, 32.8, 26.5, 26.1. HRMS (ESI+) *m/z* calculated for $C_{16}H_{18}N_2Cl$ $[M+H]^+$: 273.1159, found 273.1164.

3-cyclohexylpyridazine [S15]



To a flame-dried round bottom flask was added 2,2,6,6-tetramethylpiperidine (6.95 mL, 41.2 mmol, 1.1 equiv.). The flask was cooled to -78 ºC was added *n*-BuLi (1.6 M in hexanes, 25.8 mL, 41.2 mmol, 1.1 equiv.) was added dropwise. The solution was stirred at -78 ºC for 30 minutes before being transferred via canula into a solution of pyridazine (2.7 mL, 37.5 mmol, 1.0 equiv.) in THF (221 mL, 0.17 M). The solution was stirred at -78 ºC for 1 hour before a solution of cyclohexanone (4.3 mL, 41.2 mmol, 1.1 equiv.) in THF (68 mL, 0.55 M) was added dropwise. The reaction was stirred at -78 ºC for 5 hours. The reaction was quenched with aq. sat. NH_4Cl. After being allowed to warm to room temperature, the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (45 mm fritted glass column, 250 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 1-(pyridazin-3-yl)cyclohexan-1-ol as a brown solid (3.48 g, 19.5 mmol, 52% yield).

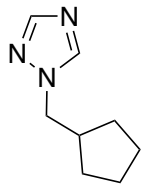
To a solution of 1-(pyridazin-3-yl)cyclohexan-1-ol (3.0 g, 16.8 mmol, 1.0 equiv.) in pyridine (37 mL, 0.45 M) at 0 ºC was added thionyl chloride (6.1 mL, 84.2 mmol, 5.0 equiv.) dropwise. The solution was stirred at 0 ºC for 30 minutes at which time it was poured CAREFULLY into ice water. The pH was adjusted to 10 with 3 M NaOH and the solution was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with 10% citric acid, dried with Na_2SO_4, filtered and concentrated *in vacuo* to afford 3-(cyclohex-1-en-1-yl)pyridazine as a dark brown oil. The crude material was taken on to the next step without further purification.

To a solution of 3-(cyclohex-1-en-1-yl)pyridazine (1.46 g, 9.12 mmol, 1.0 equiv.) in toluene (51 mL, 0.18 M) was added *p*-tosylsulfonyl hydrazide (3.4 mL, 18.24 mmol, 2.0 equiv.) and triethylamine (3.8 mL, 27.4 mmol, 3.0 equiv.) and the reaction was heated to 100 ºC overnight. After cooling to room temperature, the reaction was quenched with water and the organic layer was separated. The aqueous layer was extracted with CH2Cl2 (3 x 50 mL). The combined organic layers were dried with Na2SO4,

filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (30 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 10% → 20% → 30% → 40% → 50% ethyl acetate/hexanes gradient afforded 3-cyclohexylpyridazine (**S15**) as a brown oil (102.4 mg, 0.63 mmol, 7% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.38 (dd, *J* = 8.5, 4.8 Hz, 1H), 7.32 (dd, *J* = 8.5, 1.7 Hz, 1H), 2.96 (tt, *J* = 12.0, 3.5 Hz, 1H), 2.04 – 1.96 (m, 2H), 1.93 – 1.84 (m, 2H), 1.82 – 1.74 (m, 1H), 1.58 (qd, *J* = 12.5, 3.3 Hz, 3H), 1.45 (qt, *J* = 12.9, 3.4 Hz, 2H), 1.36 – 1.23 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 149.8, 126.6, 124.8, 45.1, 32.8, 26.5, 26.0. HRMS (ESI+) *m/z* calculated for $C_{10}H_{15}N_2$ $[M+H]^+$: 163.1235, found 163.1240.

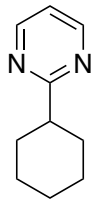
1-(cyclopentylmethyl)-1*H*-1,2,4-triazole [S16]



According to general procedure A for *N*-alkylation, 1,2,4-triazole (345.4 mg, 5.0 mmol, 1.0 equiv.), NaH (150.0 mg, 6.25 mmol, 1.25 equiv.) and cyclopentylmethyl 4-methylbenzenesulfonate (1.40 g, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude product was purified by flash column chromatography on silica (30 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2→ 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 1-(cyclopentylmethyl)-1*H*-1,2,4-triazole (**S16**) as a pale yellow oil (371.5 mg, 2.46 mmol, 49% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.91 (s, 1H), 4.08 (d, *J* = 7.5 Hz, 2H), 2.49 – 2.39 (m, 1H), 1.79 – 1.53 (m, 6H), 1.30 – 1.18 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.9, 142.9, 54.7, 40.3, 30.4, 25.6. HRMS (ESI+) *m/z* calculated for $C_8H_{14}N_3$ $[M+H]^+$: 152.1188, found 152.1183.

2-cyclohexylpyrimidine [S17]



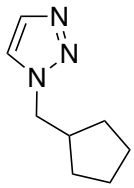
To a 3-neck round bottom flask equipped with a reflux condenser, was added magnesium turnings (632.0 mg, 26.0 mmol, 2.6 equiv.). The flask was flame dried under vacuum and cooled under N_2 before THF (25 mL) was added. The flask was heated with a heat gun to maintain reflux while bromocyclohexane (2.7 mL, 3.6 g, 22.0 mmol, 2.2 equiv.) in THF (8 mL) was added dropwise. Following addition, the reaction was stirred at room temperature for 2 h to afford cyclohexylmagnesium bromide.

To a separate flame dried 3-neck round bottom flask equipped with a reflux condenser was added $NiCl_2$(dpe) (792.0 mg, 1.5 mmol, 15 mol%), 2-bromopyrimidine (1.6 g, 10.0 mmol, 1.0 equiv.) and diethyl ether (19 mL) and the mixture was cooled to 0 °C. Cyclohexylmagnesium bromide was added via cannula over 10 minutes. The reaction was heated to 70 °C for 20 h. The reaction was cooled to room temperature and quenched with 1 M HCl (30 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 x 50 mL). The combined organic layer was washed with water, dried over

Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 5% → 10% → 15% → 20% EtOAc/hexanes gradient as eluent afforded 2-cyclohexylpyrimidine (**S17**) as a colorless oil (297.8 mg, 1.8 mmol, 18% yield).

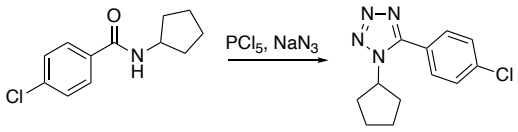
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.9 Hz, 2H), 7.09 (t, *J* = 4.9 Hz, 1H), 2.88 (tt, *J* = 11.9, 3.5 Hz, 1H), 2.04 – 1.97 (m, 2H), 1.85 (dt, *J* = 12.9, 3.3 Hz, 2H), 1.78 – 1.70 (m, 1H), 1.62 (qd, *J* = 12.5, 3.4 Hz, 2H), 1.41 (qt, *J* = 12.6, 3.1 Hz, 2H), 1.31 (tt, *J* = 12.7, 3.4 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 174.9, 157.1, 118.6, 47.7, 32.1, 26.4, 26.1. HRMS (ESI+) *m/z* calculated for $C_{10}H_{15}N_2$ 163.1235, found 163.1231.

1-(cyclopentylmethyl)-1*H*-1,2,3-triazole [S18]

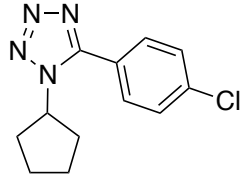


According to general procedure A for *N*-alkylation, 1,2,3-triazole (345.4 mg, 5.0 mmol, 1.0 equiv.), NaH (150.0 mg, 6.25 mmol, 1.25 equiv.) and cyclopentylmethyl 4-methylbenzenesulfonate (1.40 g, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude product was purified by flash column chromatography on silica (30 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2→ 1% → 2% MeOH/CH_2Cl_2 gradient as eluent afforded 1-(cyclopentylmethyl)-1*H*-1,2,3-triazole (**S18**) as a white solid (254.2 mg, 1.68 mmol, 34% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (app. s, 1H), 7.54 (app. s, 1H), 4.30 (d, *J* = 7.2 Hz, 2H), 2.43 (hept, *J* = 7.7 Hz, 1H), 1.77 – 1.68 (m, 2H), 1.68 – 1.62 (m, 2H), 1.62 – 1.52 (m, 2H), 1.34 – 1.22 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.8, 123.4, 55.0, 40.8, 30.4, 25.1. HRMS (ESI+) *m/z* calculated for $C_8H_{14}N_3$ $[M+H]^+$: 152.1188, found 152.1182.



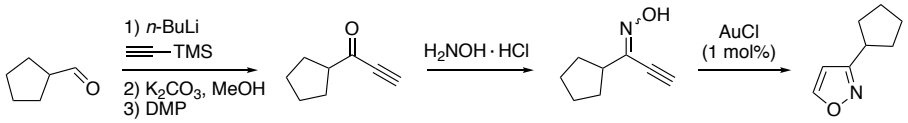
5-(4-chlorophenyl)-1-cyclopentyl-1*H*-tetrazole [S19]



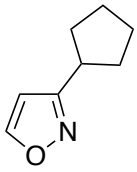
To a flame dried round bottom flask equipped with reflux condenser was added 4-chloro-*N*-cyclopentylbenzamide (1.57 g, 7.0 mmol, 1.0 equiv.) and CH_2Cl_2 (34 mL, 0.2 M). PCl_5 (1.46 g, 7.0 mmol, 1.0 equiv.) was added and the reaction was refluxed for 2 h. The reaction was cooled to room temperature and sodium azide (455.1 mg, 7.0 mmol, 1.0 equiv.) was added. The reaction was stirred at room temperature for 48 h. The reaction was poured into sat. aq. $NaHCO_3$ and extracted with CH_2Cl_2 (3 x 50 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 10% EtOAc/hexanes as eluent

afforded 5-(4-chlorophenyl)-1-cyclopentyl-1*H*-tetrazole (**S19**) as a white solid (584.6 mg, 2.35 mmol, 34% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.57 – 7.53 (m, 2H), 4.82 (app p, *J* = 6.4 Hz, 1H), 2.25 – 2.15 (m, 4H), 2.13 – 2.02 (m, 2H), 1.81 – 1.70 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 137.7, 130.4, 129.8, 123.1, 59.8, 34.1, 24.8. HRMS (ESI+) *m/z* calculated for $C_{12}H_{14}N_4Cl$ $[M+H]^+$: 249.0907, found 249.0910.



3-cyclopentylisoxazole [S20]



In a flame dried round bottom flask under N_2 was added trimethylsilylacetylene (3.1 mL, 2.16 g, 22.0 mmol, 1.1 equiv.) and THF (66 mL, 0.3 M). The reaction was cooled to -78 °C. *n*-BuLi (1.6 M in hexanes, 13.1 mL, 21.0 mmol, 1.05 equiv.) was added dropwise and the mixture was stirred at -78 °C for 1 h. Cyclopentanecarbaldehyde (1.96 g, 20.0 mmol, 1.0 equiv.) was added at -78 °C and the reaction was stirred for an additional 30 min. at -78 °C and then warmed to room temperature over 30 min. The reaction was quenched with water (80 mL) and the aqueous layer was extracted with diethyl ether (3 x 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was dissolved in MeOH (66 mL, 0.3 M). Potassium carbonate (8.3 g, 60.0 mmol, 3.0 equiv.) was added and the reaction was stirred open to air for 2 h. The reaction was filtered through a pad of Celite, using CH_2Cl_2 as eluent. The filtrate was washed sequentially with sat. aq. NH_4Cl solution and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was dissolved in CH_2Cl_2 (100 mL, 0.2 M) and cooled to 0 °C. Dess-Martin periodinane (9.34 g, 22.0 mmol, 1.1 equiv.) was added and the reaction was stirred at room temperature for 4 h. Upon completion, as monitored by TLC, the reaction was filtered through a pad of Celite, using CH_2Cl_2 as eluent. The filtrate was washed sequentially with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% EtOAc/hexanes gradient as eluent afforded 1-cyclopentylprop-2-yn-1-one (692.2 mg, 5.7 mmol, 28% yield over 3 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.20 (s, 1H), 3.03 – 2.91 (m, 1H), 2.02 – 1.84 (m, 4H), 1.78 – 1.57 (m, 4H).

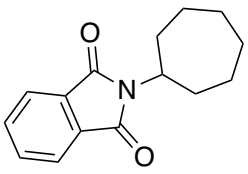
To a solution of 1-cyclopentylprop-2-yn-1-one (692.2 mg, 5.7 mmol, 1.0 equiv.) in MeOH (16 mL, 0.35 M) was added hydroxylamine hydrochloride (787.3 mg, 11.3 mmol, 2.0 equiv.), sodium sulfate (1.61 g, 11.3 mmol, 2.0 equiv.) and pyridine (1.7 mL, 1.66 g, 21.0 mmol, 3.7 equiv.) and the reaction was stirred

at room temperature for 30 minutes. The reaction was quenched with water (50 mL) and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% EtOAc/hexanes gradient as eluent afforded 1-cyclopentylprop-2-yn-1-one oxime (400.7 mg, 2.9 mmol, 52% yield) as an approximately 1:1 mixture of *E*:*Z*-oxime (Only the *Z*-isomer will cyclize in the following step). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (br s, 1H), 3.61 (s, 0.5H), 3.45 (p, *J* = 8.1 Hz, 0.4H), 3.00 (s, 0.4H), 2.81 (p, *J* = 8.0 Hz, 0.5H), 1.96 – 1.82 (m, 2H), 1.79 – 1.54 (m, 6H).

Prepared according to a reported procedure.[7] To a solution of 1-cyclopentylprop-2-yn-1-one oxime (400.7 mg, 2.9 mmol, 1.0 equiv.) in CH_2Cl_2 (58 mL, 0.05 M) was added gold(I) chloride (6.8 mg, 0.03 mmol, 1.0 mol%). The reaction was stirred at 30 °C for 30 minutes before being concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 5% EtOAc/hexanes gradient as eluent afforded 3-cyclopentylisoxazole (**S20**) as a colorless oil (194.2 mg, 1.42 mmol, 49% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 – 8.28 (m, 1H), 6.18 (d, *J* = 1.6 Hz, 1H), 3.19 (p, *J* = 8.0 Hz, 1H), 2.14 – 2.01 (m, 2H), 1.83 – 1.74 (m, 2H), 1.74 – 1.64 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 158.1, 103.0, 36.9, 32.6, 25.5. HRMS (ESI+) *m/z* calculated for $C_8H_{12}NO$ $[M+H]^+$: 138.0919, found 138.0914.

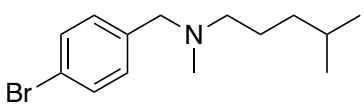
2-cycloheptylisoindoline-1,3-dione [S21]



Prepared according to a reported procedure.[8] To a stirred solution of cycloheptanol (0.6 mL, 571.0 mg, 5.0 mmol, 1.0 equiv.), triphenylphosphine (1.41 g, 5.4 mmol, 1.075 equiv.) and phthalimide (809 mg, 5.5 mmol, 1.1 equiv.) in THF (19 mL, 0.26 M) was added diisopropyl azodicarboxylate (1.0 mL, 1.06 g, 5.25 mmol, 1.05 equiv.) under N_2 atmosphere at room temperature. After 4 h, the solvent was removed *in vacuo* and the residue was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% → 6% EtOAc/hexanes gradient as eluent afforded 2-cycloheptylisoindoline-1,3-dione (**S21**) as a white solid (881.2 mg, 3.6 mmol, 72%).

Spectral data in agreement with those previously reported in the literature.[8]

***N*-(4-bromobenzyl)-*N*,4-dimethylpentan-1-amine [S22]**

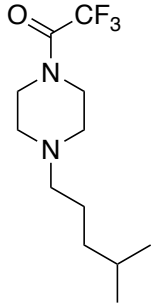


According to general procedure B for *N*-alkylation, (4-bromobenzyl)methylamine (0.8 mL, 800.3 mg, 4.0 mmol, 1.0 equiv.), 4-methylpentanal (801.2 g, 8.0 mmol, 2.0 equiv.), acetic acid (0.4 mL) and $NaBH(OAc)_3$ (1.02 g, 4.8 mmol,

1.2 equiv.) were reacted in 1,2-dichloroethane (40 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% EtOAc/hexanes gradient as eluent afforded *N*-(4-bromobenzyl)-*N*,4-dimethylpentan-1-amine (**S22**) as a colorless oil (983.4 mg, 3.46 mmol, 86% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (app d, *J* = 8.4 Hz, 2H), 7.19 (app d, *J* = 8.1 Hz, 2H), 3.42 (s, 2H), 2.32 (app t, *J* = 7.5 Hz, 2H), 2.16 (s, 3H), 1.57 – 1.44 (m, 3H), 1.20 – 1.14 (m, 2H), 0.88 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.7, 131.4, 130.8, 120.7, 61.8, 58.0, 42.4, 36.8, 28.1, 25.4, 22.8. HRMS (ESI+) *m/z* calculated for $C_{14}H_{23}NBr$ $[M+H]^+$: 284.1014, found 284.1006.

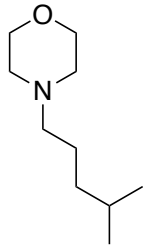
2,2,2-trifluoro-1-(4-(4-methylpentyl)piperazin-1-yl)ethan-1-one [S23]



According to general procedure B for *N*-alkylation, 2,2,2-trifluoro-1-(piperazin-1-yl)ethan-1-one (2.73 g, 15.0 mmol, 1.0 equiv.), 4-methylpentanal (2.0 g, 20.0 mmol, 1.3 equiv.), acetic acid (1.5 mL) and $NaBH(OAc)_3$ (3.81 g, 18.0 mmol, 1.2 equiv.) were reacted in 1,2-dichloroethane (150 mL). The crude material was purified by flash column chromatography on silica (45 mm fritted glass column, 250 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% EtOAc/hexanes gradient as eluent afforded 2,2,2-trifluoro-1-(4-(4-methylpentyl)piperazin-1-yl)ethan-1-one (**S23**) as a colorless oil (455.4 mg, 1.71 mmol, 11% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.69 (app t, *J* = 5.1 Hz, 2H), 3.61 (app t, *J* = 4.9 Hz, 2H), 2.48 (app t, *J* = 5.0 Hz, 4H), 2.34 (t, *J* = 7.7 Hz, 2H), 1.59 – 1.43 (m, 3H), 1.22 – 1.14 (m, 2H), 0.88 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5 (q, *J* = 35.5 Hz), 116.6 (q, *J* = 288.0 Hz), 58.7, 53.2, 52.6, 45.9, 43.5, 36.7, 28.1, 24.7, 22.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ -68.80. HRMS (ESI+) *m/z* calculated for $C_{12}H_{22}N_2O_2F_3$ $[M+H]^+$: 267.1684, found 267.1693.

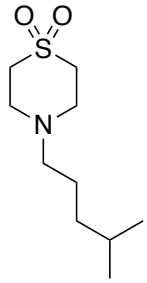
4-(4-methylpentyl)morpholine [S24]



According to general procedure A for *N*-alkylation, morpholine (0.49 mL, 496.5 mg, 5.7 mmol, 1.0 equiv.), NaH (171.1 mg, 7.13 mmol, 1.25 equiv.) and 4-methylpentyl 4-methylbenzenesulfonate (1.62 g, 6.3 mmol, 1.1 equiv.) were reacted in DMF (11.4 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(4-methylpentyl)morpholine (**S24**) as a pale yellow oil (778.0 mg, 4.54 mmol, 80% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 3.74 – 3.65 (m, 4H), 2.55 – 2.39 (m, 4H), 2.39 – 2.25 (m, 2H), 1.64 – 1.46 (m, 3H), 1.24 – 1.17 (m, 2H), 0.91 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 67.6, 60.5, 54.8, 37.9, 29.1, 25.0, 23.0. HRMS (ESI+) *m/z* calculated for $C_{10}H_{22}NO$ 172.1701, found 172.1698.

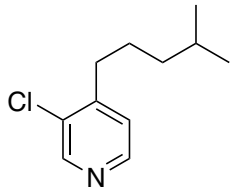
4-(4-methylpentyl)thiomorpholine-1,1-dioxide [S25]



According to general procedure A for *N*-alkylation, thiomorpholine 1,1-dioxide (675.9 mg, 5.0 mmol, 1.0 equiv.), NaH (150.0 mg, 6.25 mmol, 1.25 equiv.) and 4-methylpentyl-4-methylbenzenesulfonate (1.4 g, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 2% → 3% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(4-methylpentyl)thiomorpholine-1,1-dioxide (**S25**) as a pale yellow oil (706.4 mg, 3.22 mmol, 64% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.09 – 3.02 (m, 4H), 3.01 – 2.94 (m, 4H), 2.51 – 2.43 (m, 2H), 1.53 (hept, J = 6.7 Hz, 1H), 1.50 – 1.42 (m, 2H), 1.21 – 1.12 (m, 2H), 0.88 (d, 6H, J = 6.6 Hz). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 57.5, 51.6, 50.9, 36.6, 28.0, 25.1, 22.7. HRMS (ESI+) *m/z* calculated for $C_{10}H_{22}NO_2S$ $[M+H]^+$: 220.1371, found 220.1362.

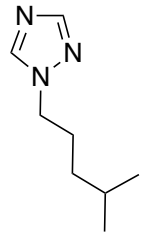
3-chloro-4-(4-methylpentyl)pyridine [S26]



Prepared according to a reported procedure.[9] A flame-dried 100 mL round bottom flask was charged with diisopropylamine (0.9 mL, 6.4 mmol, 1.16 equiv.) and THF (2.5 mL, 2.2 M). The mixture was cooled to -78 °C and *n*-butyllithium (4.0 mL, 6.3 mmol, 1.15 equiv., 1.6 M in Hexanes) was added dropwise via syringe. The reaction mixture was stirred at -78 °C for 15 minutes and 0 °C for 5 minutes. The mixture was cooled back down to -78 °C, upon which 3-chloro-4-methylpyridine (0.6 mL, 5.5 mmol, 1.0 equiv.) was added dropwise. The mixture was further stirred for 1 hour, at which time 1-bromo-3-methylbutane (0.7 mL, 6.1 mmol, 1.1 equiv.) was added. The mixture was stirred for an additional 5 minutes at -78 °C and was then allowed to warm to ambient temperature and stirred overnight. The reaction was quenched with water (0.5 mL) and the mixture was passed through a silica plug (50 mL) and flushed with EtOAc (300 mL). The filtrate was concentrated *in vacuo*. The residue was further purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 10% → 20% → 25% EtOAc/hexanes gradient afforded 3-chloro-4-(4-methylpentyl)pyridine (**S26**) as a colorless oil (684.0 mg, 3.46 mmol, 63% yield).

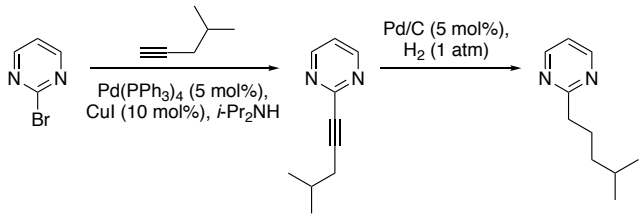
Spectral data in agreement with those previously reported in the literature.[9]

1-(4-methylpentyl)-1*H*-1,2,4-triazole [S27]

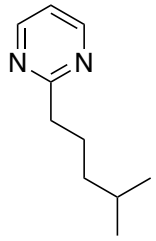


According to general procedure A for *N*-alkylation, 1,2,4-triazole (345.4 mg, 5.0 mmol, 1.0 equiv.), NaH (150.0 mg, 6.25 mmol, 1.25 equiv.) and 4-methylpentyl-4-methylbenzenesulfonate (1.41 g, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 2% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 1-(4-methylpentyl)-1*H*-1,2,4-triazole (**S27**) as a pale yellow oil (612.8 mg, 4.00 mmol, 80% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.92 (s, 1H), 4.13 (td, *J* = 7.2, 2.4 Hz, 2H), 1.91 – 1.82 (m, 2H), 1.60 – 1.51 (m, 1H), 1.20 – 1.12 (m, 2H), 0.92 – 0.81 (m, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 152.0, 142.9, 50.1, 35.7, 27.8, 27.7, 22.5. HRMS (ESI+) *m/z* calculated for $C_8H_{16}N_3$ $[M+H]^+$: 154.1344, found 154.1344.



2-(4-methylpentyl)pyrimidine [S28]



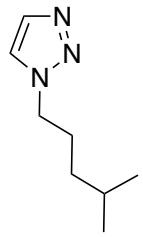
To a flame dried round bottom flask was added 2-bromopyrimidine (1.3 g, 8.0 mmol, 1.0 equiv.), $Pd(PPh_3)_4$ (462.2 mg, 0.4 mmol, 5 mol%) and copper(I) iodide (152.4 mg, 0.8 mmol, 10 mol%). The flask was evacuated and backfilled with N_2 (x3). *i*-Pr_2NH (16 mL, 0.5 M) was added via syringe, followed by 4-methyl-1-pentyne (1.9 mL, 1.3 g, 16.0 mmol, 2.0 equiv.). The rubber septum was quickly replaced with a yellow polyethylene cap and secured with electrical tape. The reaction was heated to 60 °C overnight (11 h), at which time it was allowed to cool to room temperature and quenched with water (20 mL). The reaction was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 5% → 10% → 15% → 30% EtOAc/hexanes gradient as eluent afforded 2-(4-methylpent-1-yn-1-yl)pyrimidine as a colorless oil (1.20 g, 7.5 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.9 Hz, 2H), 7.19 (t, *J* = 4.9 Hz, 1H), 2.35 (d, *J* = 6.7 Hz, 2H), 1.98 (hept, *J* = 6.7 Hz, 1H), 1.05 (d, *J* = 6.6 Hz, 6H).

To a round bottom flask equipped with a magnetic stir bar was added 2-(4-methylpent-1-yn-1-yl)pyrimidine (425.9 mg, 2.66 mmol, 1.0 equiv.), EtOH (53 mL, 0.04 M) and Pd/C (14 mg, 0.13 mmol, 5 mol%). The flask was sealed with a rubber septum, purged with hydrogen and stirred under a hydrogen

balloon (1 atm) at room temperature until the reaction was complete by TLC (18 h). The reaction was filtered through celite using MeOH as the eluent and concentrated *in vacuo* to afford 2-(4-methylpentyl)pyrimidine (**S28**) as a colorless oil (362.1 mg, 2.20 mmol, 83% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.68 – 8.60 (m, 2H), 7.09 (app t, *J* = 5.0 Hz, 1H), 2.92 (app t, *J* = 7.8, 2H), 1.86 – 1.75 (m, 2H), 1.57 (app non, *J* = 6.7 Hz, 1H), 1.30 – 1.20 (m, 2H), 0.88 – 0.84 (m, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 171.8, 157.1, 118.4, 40.0, 38.8, 28.0, 26.8, 22.7. HRMS (ESI+) *m/z* calculated for $C_{10}H_{17}N_2$ 165.1392, found 165.1387.

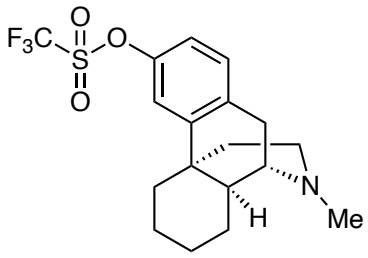
1-(4-methylpentyl)-1*H*-1,2,3-triazole [S29]



According to general procedure A for *N*-alkylation, 1,2,3-triazole (345.4 mg, 5.0 mmol, 1.0 equiv.), NaH (150.0 mg, 6.25 mmol, 1.25 equiv.) and 4-methylpentyl-4-methylbenzenesulfonate (1.41 g, 5.5 mmol, 1.1 equiv.) were reacted in DMF (10 mL). The crude material was purified by CombiFlash on silica (40 g) using 20% → 30% → 40% → 50% EtOAc/hexanes gradient as eluent afforded 1-(4-methylpentyl)-1*H*-1,2,3-triazole (**S29**) as a pale yellow oil (312.1 mg, 2.037 mmol, 41% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.53 (s, 1H), 4.35 (t, *J* = 7.3 Hz, 2H), 1.94 – 1.84 (m, 2H), 1.56 (hept, *J* = 6.7 Hz, 1H), 1.23 – 1.15 (m, 2H), 0.87 (d, *J* = 6.7 Hz, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 133.8, 123.2, 50.5, 35.6, 28.4, 27.7, 22.5. HRMS (ESI+) *m/z* calculated for $C_8H_{16}N_3$ $[M+H]^+$: 154.1344, found 154.1348.

(4bS,8aS,9S)-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-yl trifluoromethanesulfonate [S30]



Prepared according to a reported procedure.[9] Dextromethorphan (1.36g, 5.00 mmol, 1.00 equiv.) was added to a round bottom flask equipped with a magnetic stir bar. HBr (11.0 mL, 48% wt. in H_2O) was added and the reaction was refluxed for 24 hours. Upon cooling to room temperature, the reaction mixture was poured onto ice, and the resultant solution was basified to pH = 10. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined layers were dried with Na_2SO_4, filtered and concentrated to afford (4bS,8aS,9S)-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol as a beige solid (1.12 g, 4.35 mmol, 87% yield). No further purification was required.

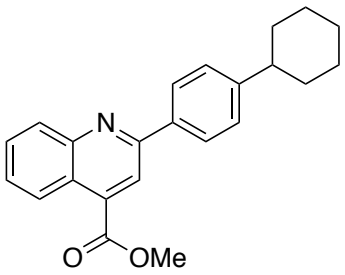
Spectral data in agreement with those previously reported in the literature.[9]

To a round bottom flask was added (4bS,8aS,9S)-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-ol (515.0 mg, 2.00 mmol, 1.00 equiv.) and CH_2Cl_2 (15 mL, 0.13 M). NEt_3

(4.05 g, 5.57 mL, 40.0 mmol, 20.0 equiv.) was added and the mixture was cooled to 0 °C. $PhNTf_2$ (629.0 mg, 0.639 mL, 5.22 mmol, 1.20 equiv.) was added in one portion and the reaction was allowed to warm to rt overnight. The resulting solution was diluted with CH_2Cl_2 (50 mL) and washed with 1 M NaOH (3 x 50 mL) and brine (50 mL). The combined layers were dried with Na_2SO_4, dried, and concentrated under reduced pressure. The crude product was purified via chromatography (35 mm fritted glass column, 75 mL SiO_2) using 7.5% MeOH/CH_2Cl_2 to afford (4bS,8aS,9S)-11-methyl-6,7,8,8a,9,10-hexahydro-5H-9,4b-(epiminoethano)phenanthren-3-yl trifluoromethanesulfonate (**S30**) as a yellow oil (483.5 mg, 1.24 mmol, 62% yield).

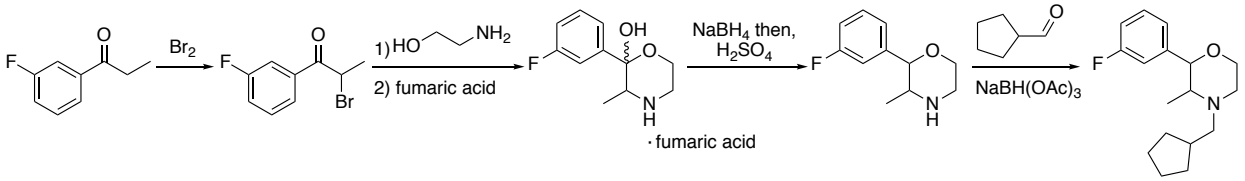
Spectral data in agreement with those previously reported in the literature.[9]

Methyl 2-(4-cyclohexylphenyl)quinoline-4-carboxylate [S31]

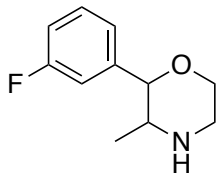


To a solution of 2-(4-cyclohexylphenyl)quinoline-4-carboxylic acid[10] (1.0 g, 3.0 mmol, 1.0 equiv.) in DMF (10 mL, 0.3 M) was added cesium carbonate (1.2 g, 3.6 mmol, 1.2 equiv.) and methyl iodide (0.4 mL, 851.6 mg, 6.0 mmol, 2.0 equiv.). The reaction was stirred at room temperature overnight (16 h). The reaction was diluted with EtOAc and washed with brine (8 x 50 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% EtOAc/hexanes gradient as eluent afforded methyl 2-(4-cyclohexylphenyl)quinoline-4-carboxylate (**S31**) as an off white solid (332.9 mg, 0.96 mmol, 32% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 8.6 Hz, 1H), 8.39 (s, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.3 Hz, 2H), 7.76 (ddt, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.61 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 2H), 4.08 (s, 3H), 2.65 – 2.56 (m, 1H), 1.98 – 1.84 (m, 4H), 1.83 – 1.74 (m, 1H), 1.54 – 1.38 (m, 4H), 1.36 – 1.24 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 157.0, 150.2, 149.4, 136.6, 135.6, 130.4, 130.0, 127.7, 127.6, 127.6, 125.5, 124.0, 120.5, 52.9, 44.6, 34.5, 27.0, 26.3. HRMS (ESI+) *m/z* calculated for $C_{23}H_{24}NO_2$ $[M+H]^+$: 346.1807, found 346.1795.



2-(3-fluorophenyl)-3-methylmorpholine [S32]



Prepared according to a reported procedure.[11] To a round bottom flask was added 1-(3-fluorophenyl)propan-1-one (3.04 g, 20.0 mmol, 1.0 equiv.) and CH_2Cl_2 (34 mL, 0.6 M). Bromine (1.0 mL, 3.2 g, 20.0 mmol, 1.0 equiv.) was added dropwise and the reaction was allowed to stir at room temperature overnight. The reaction was washed with water (4 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford 2-bromo-1-(3-fluorophenyl)propan-1-one as a yellow oil (4.6 g, 19.9 mmol, 99% yield). The crude material was taken onto the next step without further purification.

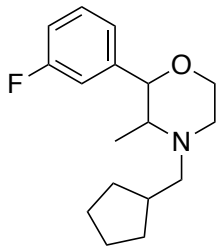
To a round bottom flask was added 2-bromo-1-(3-fluorophenyl)propan-1-one (4.6 g, 19.9 mmol, 1.0 equiv.), MeCN (50 mL, 0.4 M) and ethanolamine (2.41 mL, 2.44 g, 40.0 mmol, 2.0 equiv.) and the reaction was heated to 40 °C for 6 h. After cooling to room temperature overnight, the reaction was concentrated *in vacuo*. The residue was taken up in EtOAc (30 mL), washed with sat. aq. $NaHCO_3$ (3 x 50 mL) and brine (2 x 50 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (40 g) using 100% CH_2Cl_2 → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 2-(3-fluorophenyl)-3-methylmorpholin-2-ol as a pale orange solid (2.0 g, 9.4 mmol, 47% yield). The free base was dissolved in MeOH (14 mL) and fumaric acid (1.1 g, 9.4 mmol, 1.0 equiv.) was added. The mixture was stirred open to air for 30 minutes before being concentrated *in vacuo* and recrystallized from MeOH/EtOAc affording 2-(3-fluorophenyl)-3-methylmorpholin-2-ol fumarate salt as a white solid (949.4 mg, 2.9 mmol, 31% yield).

A solution of 2-(3-fluorophenyl)-3-methylmorpholin-2-ol fumarate salt (949.4 mg, 2.9 mmol, 1.0 equiv.) in 1:1 EtOH:H_2O (7.3 mL) was cooled to 0 °C. A solution of sodium borohydride (439.0 mg, 11.6 mmol, 4.0 equiv.) in water (5 mL) was added dropwise. The reaction was allowed to warm to room temperature and stirred overnight. The following morning, the reaction was cooled to 0 °C and concentrated HCl (4.2 mL) was added dropwise. The ethanol was removed under reduced pressure. The crude mixture was diluted with water, cooled to 0 °C, made basic by adding 40% aq. NaOH (tested with litmus paper) and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 and added dropwise to 4.2 mL of concentrated H_2SO_4 at 0 °C and stirred overnight. The following morning, the reaction was poured into ice water, the layers were separated and the aqueous layer was cooled to 0 °C. The aqueous layer was made basic with 40% aq. NaOH (tested with litmus paper) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford 2-(3-fluorophenyl)-3-methylmorpholine (**S32**) as a colorless oil (546.7 mg, 2.8 mmol, 97% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 7.33 (td, J = 8.0, 5.9 Hz, 1H), 7.16 – 7.11 (m, 1H), 7.11 – 7.06 (m, 1H), 7.05 – 6.99 (m, 1H), 4.83 (br s, 1H), 3.98 (d, J = 9.1 Hz, 1H), 3.92 (ddd, J = 11.5, 3.6, 1.2 Hz, 1H), 3.66 (td, J = 11.7, 2.6 Hz, 1H), 3.03 (ddd, J = 12.8, 11.9, 3.5 Hz, 1H), 2.87 (ddd, J = 12.8, 2.6, 1.2 Hz, 1H),

2.73 (dq, *J* = 9.0, 6.5 Hz, 1H), 0.79 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, CD_3OD) δ 164.0 (d, 244.6 Hz), 143.9 (d, *J* = 7.2 Hz), 130.9 (d, 8.2 Hz), 124.6 (d, *J* = 2.9 Hz), 115.8 (d, *J* = 21.3 Hz), 115.2 (d, *J* = 21.9 Hz), 86.2 (d, *J* = 1.7 Hz), 68.5, 57.0, 46.8, 17.8. ^{19}F NMR (471 Hz, CD_3OD) δ -115.0. HRMS (ESI+) *m/z* calculated for $C_{11}H_{15}NOF$ $[M+H]^+$: 196.1138, found 196.1131.

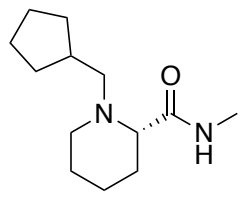
4-(cyclopentylmethyl)-2-(3-fluorophenyl)-3-methylmorpholine [S33]



According to general procedure B for *N*-alkylation, 2-(3-fluorophenyl)-3-methylmorpholine (**S32**) (545.0 g, 2.8 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (549.6 mg, 5.6 mmol, 2.0 equiv.), AcOH (0.3 mL) and $NaBH(OAc)_3$ (653.0 mg, 3.1 mmol, 1.1 equiv.) were reacted in 1,2-dichlorethane (30 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(cyclopentylmethyl)-2-(3-fluorophenyl)-3-methylmorpholine (**S33**) as a white solid (463.0 mg, 1.7 mmol, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 1H), 7.14 – 7.10 (m, 1H), 7.10 – 7.05 (m, 1H), 7.01 – 6.95 (m, 1H), 4.10 (d, *J* = 8.9 Hz, 1H), 3.96 (ddd, *J* = 11.2, 3.5, 1.7 Hz, 1H), 3.82 (td, *J* = 11.4, 2.4 Hz, 1H), 2.93 (dt, *J* = 11.8, 2.1 Hz, 1H), 2.67 (dd, *J* = 12.6, 9.3 Hz, 1H), 2.48 (td, *J* = 11.7, 3.4 Hz, 1H), 2.35 (dq, *J* = 8.9, 6.2 Hz, 1H), 2.20 (dd, *J* = 12.6, 5.1 Hz, 1H), 2.15 – 2.05 (m, 1H), 1.85 – 1.73 (m, 2H), 1.67 – 1.51 (m, 4H), 1.36 – 1.25 (m, 1H), 1.19 – 1.10 (m, 1H), 0.85 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9 (d, *J* = 245.7 Hz), 143.2 (d, *J* = 7.1 Hz), 129.8 (d, *J* = 8.2 Hz), 124.0 (d, *J* = 2.8 Hz), 115.0 (d, *J* = 21.2 Hz), 115.0 (d, *J* = 21.6 Hz), 84.6 (d, *J* = 1.8 Hz), 67.4, 61.4, 59.5, 52.6, 37.4, 31.7, 31.6, 25.2 (overlapping carbon), 15.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.3. HRMS (ESI+) *m/z* calculated for $C_{17}H_{25}NOF$ $[M+H]^+$: 278.1920, found 278.1913.

(*S*)-1-(cyclopentylmethyl)-*N*-methylpiperidine-2-carboxamide [S34]



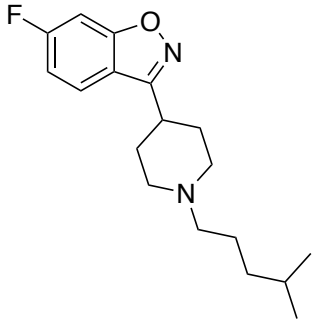
To a round bottom flask equipped with stir bar was added methyl (*S*)-piperidine-2-carboxylate (1.43 g, 10.0 mmol, 1.0 equiv.) and methylamine (40 wt% in H_2O, 40 mL). The reaction was stirred overnight (16 h) at room temperature and then concentrated *in vacuo* to afford (*S*)-*N*-methylpiperadine-2-carboxamide. The crude material was taken onto the next step without further purification.

According to general procedure B for *N*-alkylation, (*S*)-*N*-methylpiperadine-2-carboxamide (1.42 g, 10.0 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (2.16 g, 22.0 mmol, 2.2 equiv.), acetic acid (1.0 mL) and $NaBH(OAc)_3$ (2.54 g, 12.0 mmol, 1.2 equiv.) were reacted in 1,2-dichloroethane (100 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL

SiO_2) using 100% CH_2Cl_2 → 5% MeOH/CH_2Cl_2 gradient as eluent afforded (*S*)-1-(cyclopentylmethyl)-*N*-methylpiperidine-2-carboxamide (**S34**) as a pale yellow solid (351.1 mg, 1.56 mmol, 16% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.73 (br s, 1H), 3.15 – 3.07 (m, 1H), 2.81 (d, *J* = 5.0 Hz, 3H), 2.65 (dd, *J* = 10.2, 3.2 Hz, 1H), 2.33 – 2.23 (m, 1H), 2.18 – 2.02 (m, 2H), 1.98 – 1.86 (m, 2H), (1.82 – 1.34 (m, 9H), 1.30 – 1.19 (m, 2H), 1.19 – 1.00 (m, 2H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 175.8, 68.5, 62.5, 51.7, 37.6, 31.3, 31.1, 30.3, 25.7, 25.1, 25.0, 24.8, 23.6. HRMS (ESI+) *m/z* calculated for $C_{13}H_{25}N_2O$ $[M+H]^+$: 225.1967, found 225.1957. $[\alpha]_D^{23}$ = –49.3824 (c = 0.68, $CHCl_3$).

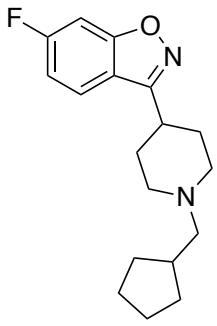
6-fluoro-3-(1-(4-methylpentyl)piperidin-4-yl)benzo[*d*]isoxazole [S35]



According to general procedure B for *N*-alkylation, *N*-6-fluoro-3-(4-piperidinyl)benziosoxazole (2.20 g, 10.0 mmol, 1.0 equiv.), 4-methylpentanal (3.00 g, 30.0 mmol, 3.0 equiv.), AcOH (1.0 mL) and $NaBH(OAc)_3$ (2.54 g, 12.0 mmol, 1.2 equiv.) were reacted in 1,2-dichloroethane (100 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 6-fluoro-3-(1-(4-methylpentyl)piperidin-4-yl)benzo[*d*]isoxazole (**S35**) as a white solid (2.83 g, 9.3 mmol, 93% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.23 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.04 (td, *J* = 8.9, 2.1 Hz, 1H), 3.15 – 3.05 (m, 3H), 2.43 – 2.34 (m, 2H), 2.21 – 2.01 (m, 6H), 1.61 – 1.50 (m, 3H), 1.23 – 1.15 (m, 2H), 0.89 (d, *J* = 6.6 Hz, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 164.2 (d, *J* = 250.5 Hz), 164.0 (d, *J* = 13.6 Hz), 161.2, 122.8 (d, *J* = 11.1 Hz), 117.44, 112.4 (d, *J* = 25.3 Hz), 97.6 (d, *J* = 26.7 Hz), 59.5, 53.7, 37.0, 34.8, 30.6, 28.2, 24.9, 22.8. ^{19}F-NMR (471 MHz, $CDCl_3$) δ -109.7. HRMS (ESI+) *m/z* calculated for $C_{18}H_{26}N_2OF$ $[M+H]^+$: 305.2029, found 305.2028.

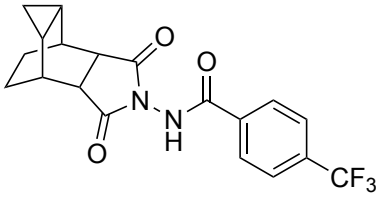
3-(1-(cyclopentylmethyl)piperidin-4-yl)-6-fluorobenzo[*d*]isoxazole [S36]



According to general procedure B for *N*-alkylation, *N*-6-fluoro-3-(4-piperidinyl)benziosoxazole (1.1 g, 10.0 mmol, 1.0 equiv.), cyclopentanecarbaldehyde (1.47 g, 15.0 mmol, 1.9 equiv.), AcOH (0.5 mL) and $NaBH(OAc)_3$ (1.6 g, 7.5 mmol, 1.5 equiv.) were reacted in 1,2-dichlorethane (50 mL). The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 3-(1-(cyclopentylmethyl)piperidin-4-yl)-6-fluorobenzo[*d*]isoxazole (**S36**) as a pale yellow solid (1.08 g, 3.6 mmol, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.23 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.05 (td, *J* = 8.9, 2.2 Hz, 1H), 3.09 – 3.00 (m, 3H), 2.32 (d, *J* = 7.3 Hz, 2H), 2.15 – 1.98 (m, 7H), 1.83 – 1.72 (m, 2H), 1.67 – 1.48 (m, 4H), 1.28 – 1.17 (m, 2H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 164.2 (d, *J* = 250.4 Hz), 164.0 (d, *J* = 13.6 Hz), 161.5, 122.8 (d, *J* = 11.1 Hz), 117.5, 112.4 (d, *J* = 25.3 Hz), 97.5 (d, *J* = 26.7 Hz), 65.0, 54.1, 37.6, 34.9, 31.7, 30.8, 25.4. ^{19}F-NMR (471 MHz, $CDCl_3$) δ -109.9. HRMS (ESI+) *m/z* calculated for $C_{18}H_{24}N_2OF$ $[M+H]^+$: 303.1873, found 303.1863.

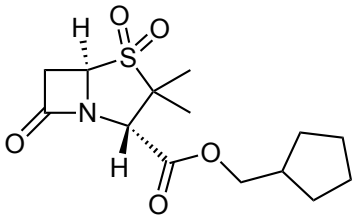
_N_-(1,3-dioxooctahydro-4,6-ethanocyclopropa[*f*]isoindol-2(1*H*)-yl)-4-(trifluoromethyl)benzamide [S37]



Prepared according to a reported procedure.[12] To a round bottom flask equipped with a reflux condenser was added hexahydro-4,6-ethanocyclopropa[*f*]isoindole-1,3(2*H*,3a*H*)-dione (937.0 mg, 4.9 mmol, 1.0 equiv.), 4-(trifluoromethyl) benzoic acid hydrazide (1.05 g, 5.1 mmol, 1.05 equiv.) and EtOH (62 mL, 0.08 M). The mixture was heated to reflux for 4 hours. The reaction was cooled to room temperature and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 50% EtOAc/hexanes as eluent afforded *N*-(1,3-dioxooctahydro-4,6-ethanocyclopropa[*f*]isoindol-2(1*H*)-yl)-4-(trifluoromethyl)benzamide (**S37**) as a white solid as a mixture of rotomers (946.5 mg, 2.50 mmol, 51% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.35 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 8.3 Hz, 2H), 3.25 (app. s, 0.6 H), 3.19 (app. s, 1.5 H), 2.40 (s, 2H), 1.47 (d, *J* = 9.8 Hz, 1H), 1.29 (d, *J* = 9.9 Hz, 0.5H), 1.21 (app. d, *J* = 9.1 Hz, 1.5H), 1.18 – 1.07 (m, 3H), 0.85 – 0.78 (m, 1H), 0.54 (app. q, *J* = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6)) δ 176.3 (176.0), 164.0 (163.6), 134.8, 132.4 (q, *J* = 31.9 Hz), 128.8 (128.6), 125.9, 125.8 (q, *J* = 4.0 Hz), 123.8 (q, *J* = 272.7 Hz), 42.8 (42.8), 27.2 (27.2), 18.8 (19.0), 13.9 (14.0), 5.4 (5.5). ^{19}F NMR (471 MHz, DMSO-d_6) δ -61.53, -61.54. HRMS (ESI+) *m/z* calculated for $C_{19}H_{18}N_2O_3F_3$ $[M+H]^+$: 397.1270, found 379.1268.

Cyclopentylmethyl (2S,5R)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide [S38]

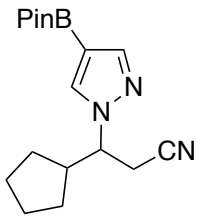


To a flame-dried round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere was added sulbactam (466.0 mg, 2.00 mmol, 1.00 equiv.) and CH_2Cl_2 (20 mL, 0.1 M). DMAP (24.0 mg, 0.20 mmol, 0.10 equiv.), and cyclopentane methanol (200.0 mg, 2.00 mmol, 1.00 equiv.) were added, followed by dropwise addition of DIC (252.0 mg, 2.00 mmol, 1.00 equiv.). This was allowed

to stir at room temperature overnight. The resulting mixture was filtered over celite and concentrated under reduced pressure. The crude residue was purified via chromatography (35 mm fritted glass column, 100 mL SiO_2) using 20% EtOAc/Hex as eluent to afford cyclopentylmethyl (2S,5R)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (**S38**) as a white solid (472.8 mg, 1.50 mmol, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.61 (dd, *J* = 4.3, 2.1 Hz, 1H), 4.39 (s, 1H), 4.10 (m, 2H), 3.49 (dd, *J* = 16.2, 4.2 Hz, 1H), 3.44 (dd, *J* = 16.1 Hz, 2.0 Hz, 1H), 2.24 (hept, *J* = 7.6 Hz, 1H), 1.79 (m, 2H), 1.62 (s, 3H), 1.68-1.54 (m, 5H), 1.42 (s, 3H), 1.25 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 167.2, 70.7, 63.5, 62.8, 61.3, 38.4, 29.7, 29.5, 25.5, 20.6, 18.7. HRMS (ESI+) *m/z* calculated for $C_{14}H_{22}NO_5S^+$ $[M+H]^+$: 316.1213, found: 316.1224. $[\alpha]_D^{23}$ = +171.6094 (c = 0.5, $CHCl_3$).

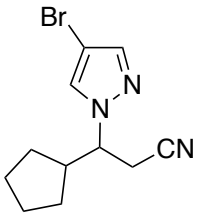
3-cyclopentyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl)propanenitrile [S39]



Prepared according to a reported procedure.[13] To a round bottom flask equipped with a reflux condenser was added 3-cyclopentylacrylonitrile (533.0 mg, 4.4 mmol, 1.3 equiv.), 4-pyrazoleboronic acid pinacol ester (918.5 mg, 3.4 mmol, 1.0 equiv.), 1,8-diazabicycloundec-7-ene (DBU, 1.1 mL, 1.1 g, 7.1 mmol, 2.1 equiv.) and MeCN (16 mL, 0.2 M). The mixture was heated to reflux for 24 hours. The reaction was cooled to room temperature and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% → 25% → 30% EtOAc/hexanes gradient as eluent afforded 3-cyclopentyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl)propanenitrile (**S39**) as a white solid (846.8 g, 2.7 mmol, 79% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.77 (s, 1H), 4.15 (ddd, *J* = 9.9, 8.7, 3.9 Hz, 1H), 3.05 (dd, *J* = 16.9, 8.6 Hz, 1H), 2.87 (dd, *J* = 16.9, 3.9 Hz, 1H), 2.57 – 2.44 (m, 1H), 1.91 (dtd, *J* = 11.9, 7.5, 3.9 Hz, 1H), 1.76 – 1.41 (m, 5H), 1.32 (s, 12H), 1.29 – 1.19 (m, 1H), 1.19 – 1.08 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.4, 136.3, 117.0, 83.5, 63.8, 44.6, 30.3, 30.1, 25.5, 25.0, 25.0, 24.9, 23.7. HRMS (ESI+) *m/z* calculated for $C_{17}H_{27}N_3O_2Br$ $[M+H]^+$: 316.2196, found 316.2192.

3-(4-bromo-1*H*-pyrazol-1-yl)-3-cyclopentylpropanenitrile [S40]



Prepared according to a reported procedure.[13] To a round bottom flask equipped with a reflux condenser was added 3-cyclopentylacrylonitrile (980.0 mg, 8.1 mmol, 1.3 equiv.), 4-bromopyrazole (913.5 mg, 6.2 mmol, 1.0 equiv.), 1,8-diazabicycloundec-7-ene (DBU, 1.96 mL, 2.0 g, 13.1 mmol, 2.1 equiv.) and MeCN (29 mL, 0.2 M). The mixture was heated to reflux for 24 hours. The reaction was cooled to room temperature and concentrated

in vacuo. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% EtOAc/hexanes gradient as eluent afforded 3-(4-bromo-1*H*-pyrazol-1-yl)-3-cyclopentylpropanenitrile (**S40**) as a white solid (1.47 g, 5.5 mmol, 88% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.51 (s, 1H), 4.11 (ddd, *J* = 10.2, 8.5, 3.9 Hz, 1H), 3.02 (dd, *J* = 17.0, 8.5 Hz, 1H), 2.85 (dd, *J* = 17.0, 3.9 Hz, 1H), 2.47 (app. sxt., *J* = 7.5 Hz, 1H), 1.96 – 1.86 (m, 1H), 1.76 – 1.44 (m, 5H), 1.28 – 1.18 (m, 1H), 1.18 – 1.08 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.8, 129.4, 116.8, 93.4, 64.4, 44.4, 30.2, 30.0, 25.5, 24.9, 23.6. HRMS (ESI+) *m/z* calculated for $C_{11}H_{15}N_3Br$ $[M+H]^+$: 268.0449, found 268.0441.

General Oxidation Procedures

General Oxidation Procedure when using HBF_4 Protonation:

Method A: Slow Catalyst Addition Protocol

This protocol was used for HBF_4 protected substrates or when Method B gave low conversion. This procedure was adapted from ref. 3. A 40 mL vial was charged with substrate (0.3 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.) and a stir bar. MeCN (0.6 mL, 0.5 M) was added along the wall to ensure all compounds were washed beneath the solvent level and the vial was sealed with a screw cap fitted with a PTFE/Silicone septum. The vial was cooled to -36 ºC with 1,2-dichloroethane/dry ice bath or to 0 ºC with ice/water bath. A 1.0 mL syringe was filled with a solution of the catalyst (0.03 mmol, 10 mol%) in MeCN (0.375 mL, 0.083 M). A few drops of this solution was added to the reaction. A 10 mL syringe was filled with a solution of H_2O_2 (for methylene oxidation: 204 mg, 3.0 mmol, 10.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich; for tertiary oxidation: 102 mg, 1.5 mmol, 5.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich) in MeCN (3.75 mL, 0.4 M). Both syringes were fitted with 25G needles and loaded in a syringe pump resulting in a simultaneous addition of catalyst and oxidant solutions over 3 hours while the reaction vial was maintained at the corresponding temperature (1.25 mL/h addition rate set for the H_2O_2 syringe; 0.125 mL/h for the catalyst syringe). Upon completion, the reaction mixture was concentrated to a minimum amount of solvent. The residue was dissolved in ~20 mL DCM and washed with 20 mL sat. $NaHCO_3$ solution (CAUTION: CO_2 was released) to remove $ClCH_2CO_2H$. The aqueous layer was extracted with DCM (2 x 15 mL) and the combined organic layer was dried with Na_2SO_4. The filtrate was concentrated and purified by flash chromatography on silica gel.

General Oxidation Procedure for non-HBF_4 Protonated Substrates:

Method B: Single Catalyst Addition Protocol

This protocol was used for non-HBF_4 protected substrates or tertiary substrates. This procedure was adapted from ref. 3. A 40 mL vial was charged with substrate (0.3 mmol, 1.0 equiv.), catalyst (0.03 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.) and a stir bar. MeCN (0.6 mL, 0.5 M) was added along the wall to ensure all compounds were washed beneath the solvent level and the vial was sealed with a screw cap fitted with a PTFE/Silicone septum. The vial was cooled to -36 ºC with 1,2-dichloroethane/dry ice bath or 0 ºC with an ice/water bath. A separate solution of H_2O_2 (for methylene oxidation: 204 mg, 3.0 mmol, 10.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich; for tertiary oxidation: 102 mg, 1.5 mmol, 5.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich) in MeCN (3.75 mL, 0.4 M) was loaded into a 10 mL syringe fitted with a 25G needle and was added dropwise to the stirring reaction over 3 hours *via* a syringe pump (1.25 mL/h addition rate) while the reaction vial was

maintained at the corresponding temperature. Upon completion, the reaction mixture was concentrated to a minimum amount of solvent. The residue was dissolved in ~20 mL DCM and washed with 20 mL sat. $NaHCO_3$ solution (CAUTION: CO_2 was released) to remove $ClCH_2CO_2H$. The aqueous layer was extracted with DCM (2 x 15 mL) and the combined organic layer was dried with Na_2SO_4. The filtrate was concentrated and purified by flash chromatography on silica gel.

Method C: Iterative Catalyst Addition Protocol

This protocol was used when Method B gave low conversion and method A gave low recovered starting material. This procedure was adapted from ref. 3. A 40 mL vial was charged with substrate (0.3 mmol, 1.0 equiv.), catalyst (0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.) and a stir bar. MeCN (0.6 mL, 0.5 M) was added along the wall to ensure all compounds were washed beneath the solvent level and the vial was sealed with a screw cap fitted with a PTFE/Silicone septum. The vial was cooled to -36 ºC with dry ice/1,2-dichloroethane bath or 0 ºC with an ice/water bath. A separate solution of H_2O_2 (for methylene oxidation: 204 mg, 3.0 mmol, 10.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich; for tertiary oxidation: 102 mg, 1.5 mmol, 5.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich) in MeCN (3.75 mL, 0.4 M) was loaded into a 10 mL syringe fitted with a 25G needle and was added dropwise to the stirring reaction over 3 hours *via* a syringe pump (1.25 mL/h addition rate) while the reaction vial was maintained at the corresponding temperature. At 1.5 hours, an additional 5 mol% catalyst (0.015 mmol in 0.1 mL MeCN) was added dropwise to the reaction. Upon completion, the reaction mixture was concentrated to a minimum amount of solvent. The residue was dissolved in ~20 mL DCM and washed with 20 mL sat. $NaHCO_3$ solution (CAUTION: CO_2 was released) to remove $ClCH_2CO_2H$. The aqueous layer was extracted with DCM (2 x 15 mL) and the combined organic layer was dried with Na_2SO_4. The filtrate was concentrated and purified by flash chromatography on silica gel.

Method D: Lower Catalyst Loading Protocol

A 40 mL vial was charged with substrate (0.3 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (107 mg, 1.13 mmol, 3.75 equiv.) and a stir bar. MeCN (1.0 mL, 0.3 M) was added along the wall to ensure all compounds were washed beneath the solvent level and the vial was sealed with a screw cap fitted with a PTFE/Silicone septum. The vial was cooled to 0 ºC with an ice/water bath. A 1.0 mL syringe was filled with a solution of the catalyst (0.0075 mmol, 2.5 mol%) in MeCN (0.625 mL). A few drops of this solution were added to the reaction. A 10 mL syringe was filled with a solution of H_2O_2 (51 mg, 0.75 mmol, 2.5 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich) in MeCN (6.25 mL). Both syringes were fitted with 25G needles and loaded in a syringe pump resulting in a simultaneous addition of catalyst and oxidant solutions over 3 hours while the reaction vial was maintained at 0 ºC (2.083 mL/h addition rate set for the H_2O_2

syringe; 0.208 mL/h for the catalyst syringe). Upon completion, the reaction mixture was concentrated to a minimum amount of solvent. The residue was dissolved in ~20 mL DCM and washed with 20 mL sat. $NaHCO_3$ solution (CAUTION: CO_2 was released) to remove $ClCH_2CO_2H$. The aqueous layer was extracted with DCM (2 x 15 mL) and the combined organic layer was dried with Na_2SO_4. The filtrate was concentrated and purified by flash chromatography on silica gel.

General procedure for the HBF_4•OEt_2 protection[9]

This procedure was adapted from ref. 9. To a flame dried 40 mL vial with a magnetic stir bar was added substrate (0.3 mmol, 1.0 equiv.) and anhydrous CH_2Cl_2 (1.2 mL, 0.25 M). The vial was flushed with a N_2 stream and then cooled to 0 ºC. HBF_4•OEt_2 (45.5 µL, 1.1 equiv.) was added dropwise *via* syringe and the reaction was allowed to stir at 0 ºC for 30 minutes then warmed to room temperature and stirred for an additional 1 h. The reaction was concentrated *in vacuo* and left on high vacuum overnight (12-24 h). Resultant HBF_4 salt were used as substrates following the corresponding oxidation protocol described above.

General Procedure for HBF_4 Deprotection

This procedure was adapted from ref. 9. Upon completion, the reaction was warmed to room temperature and concentrated *in vacuo* to a minimum amount of solvent. The reaction was diluted with DCM (10 mL), basified with 3 M NaOH (10 mL) and stirred vigorously for 20 minutes. The resulting solution was poured into 3 M NaOH (30 mL) and extracted with DCM (3 x 20 mL). The combined organic layer was washed with brine (1 x 60 mL) then dried with Na_2SO_4. The filtrate was concentrated and purified by flash column chromatography on silica gel.

A Guide to Choosing Oxidation Conditions

Tertiary Oxidation with and without HBF_4 Protection: Tertiary oxidation is generally a more facile reaction, thus lower temperature (-36 ºC) is generally sufficient to afford good yields of tertiary oxidation. Start with Method B: Single Catalyst Addition Protocol at -36 ºC. If the conversion of starting material is low under Method B, try Method A: Slow Catalyst Addition Protocol at -36 ºC. If the mass balance is low under Method A, try Method C: Iterative Catalyst Addition Protocol at -36 ºC.

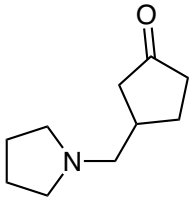
Secondary oxidation is a more challenging reaction than tertiary oxidation and often requires more forcing conditions. Thus, -36 ºC may be used when using more forcing catalyst addition protocol Method A. However, moving to less forcing addition protocols such as Method B and C, no reactivity is observed unless the reaction is performed at 0 ºC.

Secondary Oxidation with HBF_4 Protection: Start with Method A: Slow Catalyst Addition Protocol at -36 ºC. If the conversion of starting material is low under Method A, try Method B: Single Catalyst Addition Protocol at 0 ºC. If conversion is still low under Method B, try Method A: Slow Catalyst Addition Protocol at 0 ºC. If the mass balance is low under Method A at 0 ºC, try Method C: Iterative Catalyst Addition Protocol at 0 ºC.

Secondary Oxidation without HBF_4 Protection: Start with Method B: Single Catalyst Addition Protocol at 0 ºC. If the conversion of starting material is low under Method B, try Method A: Slow Catalyst Addition Protocol at -36 ºC. If the conversion of starting material is still low under Method A at -36 ºC, try Method A: Slow Catalyst Addition Protocol at 0 ºC. If the mass balance is low under Method A try Method C: Iterative Catalyst Addition Protocol at 0 ºC.

C—H Oxidation of Substrates and Products Characterization for Supplementary Figure 1

3-(pyrrolidin-1-ylmethyl)cyclopentan-1-one [3]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)pyrrolidine (**S1**) (46.0 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S1•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 25% EtOAc/Hex as eluent afforded 3-(pyrrolidin-1-ylmethyl)cyclopentan-1-one (**3**) as a pale yellow oil.

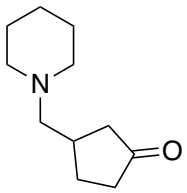
Run 1: (31.3 mg, 0.187 mmol, 66% yield), <5% rsm. **Run 2:** (36.0 mg, 0.201 mmol, 67% yield), <5% rsm. **Run 3:** (34.1 mg, 0.204 mmol, 68% yield), <5% rsm. **Average: 67% yield ± 1.0%, <5% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 1-(cyclopentylmethyl)pyrrolidine (**S1**) (46.0 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.030 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 75 mL Brockmann Grade 3 basic alumina) using 25% EtOAc/Hex as eluent afforded 3-(pyrrolidin-1-ylmethyl)cyclopentan-1-one (**3**) as a pale yellow oil.

Run 1: (6.6 mg, 0.039 mmol, 13% yield), (13.3 mg, 0.087 mmol, 29% rsm). **Run 2:** (4.0 mg, 0.023 mmol, 8% yield), (10.6 mg, 0.069 mmol, 23% rsm). **Average: 10.5% yield ± 3.5%, 26% rsm ± 4.2%.**

^1H NMR (500 MHz, $CDCl_3$) δ 2.54-2.43 (m, 6H), 2.43-2.33 (m, 2H), 2.32-2.23 (m, 1H), 2.19-2.08 (m, 2H), 1.95-1.87 (m, 1H), 1.80-1.72 (m, 4H), 1.65-1.55 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.6, 61.7, 54.7, 44.3, 38.2, 36.7, 28.1, 23.6. HRMS (ESI+) *m/z* calculated for $C_{10}H_{18}NO$ $[M+H]^+$: 168.1383, found: 168.1392.

3-(piperidin-1-ylmethyl)cyclopentan-1-one [4]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)piperidine (**S2**) (50.2 mg, 0.300 mmol, 1.0 equiv.), was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S2•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann Grade II basic Al_2O_3) using 10% → 20% → 30% EtOAc/Hexanes gradient as eluent afforded 3-(piperidin-1-ylmethyl)cyclopentan-1-one (**4**) as a colorless oil.

Run 1: (33.2 mg, 0.183 mmol, 61.0% yield), 0% rsm. **Run 2:** (32.8 mg, 0.181 mmol, 60.3% yield), 0% rsm. **Run 3:** (30.1 mg, 0.166 mmol, 55.3% yield), 0% rsm. **Average: 58.9% yield ± 3.1%, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 1-(cyclopentylmethyl)piperidine (**S2**) (50.2 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at 0 °C with an ice/water bath. . The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann Grade II basic Al_2O_3) using 10% → 20% → 30% EtOAc/Hexanes gradient as eluent afforded 3-(piperidin-1-ylmethyl)cyclopentan-1-one (**4**) as a colorless oil.

Run 1: (17.6 mg, 0.097 mmol, 32.4% yield), (20.6 mg, 0.123 mmol, 41.0% rsm). **Run 2:** (14.7 mg, 0.081 mmol, 27.0% yield), (19.3 mg, 0.115 mmol, 38.5% rsm). **Average: 29.7% yield, 39.8% rsm.**

Alternate conditions:

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 1-(cyclopentylmethyl)piperidine (**S2**) (50.2 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann Grade II basic Al_2O_3) using 10% → 20% → 30% EtOAc/Hexanes gradient as eluent afforded 3-(piperidin-1-ylmethyl)cyclopentan-1-one (**4**) as a colorless oil.

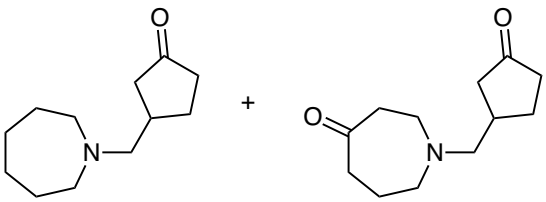
Yield: (3.6 mg, 0.020 mmol, 6.6% yield), (33.6 mg, 0.201 mmol, 66.9% rsm).

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 1-(cyclopentylmethyl)piperidine (**S2**) (50.2 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann Grade II basic Al_2O_3) using 10% → 20% → 30% EtOAc/Hexanes gradient as eluent afforded 3-(piperidin-1-ylmethyl)cyclopentan-1-one (**4**) as a colorless oil.

Run 1: (11.5 mg, 0.063 mmol, 21.1% yield), (20.7 mg, 0.124 mmol, 41.2% rsm). **Run 2:** (14.8 mg, 0.082 mmol, 27.2% yield), (22.1 mg, 0.132 mmol, 44.0% rsm). **Average: 24.2% yield, 42.6% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.61 – 2.22 (m, 9H), 2.20 – 2.09 (m, 2H), 1.94 (dd, *J* = 18.1, 8.8 Hz, 1H), 1.67 – 1.51 (m, 5H), 1.48 – 1.35 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.8, 64.3, 55.1, 44.3, 38.1, 34.7, 28.1, 26.0, 24.5. HRMS (ESI+) *m/z* calculated for $C_{11}H_{20}NO$ $[M+H]^+$: 182.1545, found 182.1547.

3-(azepan-1-ylmethyl)cyclopentan-1-one [5] and 1-((3-oxocyclopentyl)methyl)azepan-4-one [S41]



5 **S41**

With HBF_4 Protection (Entry 4): According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)azepane (**S3**) (54.0 mg, 0.300 mmol, 1.0 equiv.) was protected with HBF_4.OEt_2 (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to a modified version of **General Method D: Lower Catalyst Loading Protocol:** the resultant **S3•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (212.7 mg, 2.3 mmol, 7.5 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (10.2 mg, 0.075 mmol, 2.5 mol%), H_2O_2 (50 wt% in H_2O, 102.0 mg, 1.5 mmol, 5.0 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant, 0.625 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex → 30% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded 3-(azepan-1-ylmethyl)cyclopentan-1-one (**5**) as a colorless oil and 1-((3-oxocyclopentyl)methyl)azepan-4-one (**S41**) as a colorless oil.

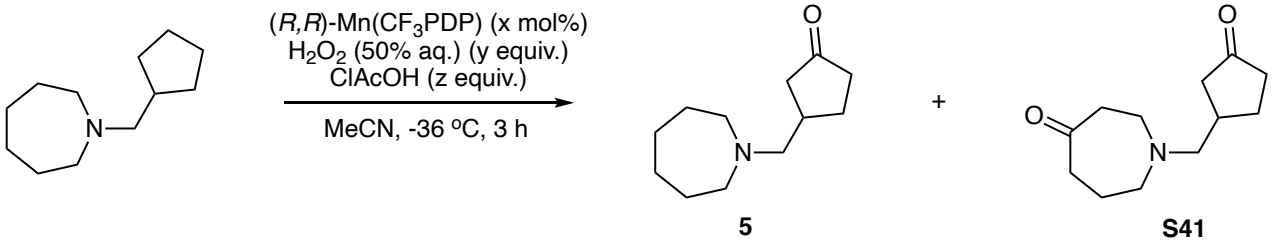
Run 1: (**5**, 29.5 mg, 0.152 mmol, 51% yield), (**S41**, 12.1 mg, 0.057 mmol, 19% yield), (4.1 mg, 0.023 mmol, 7.5% rsm). **Run 2:** (**5**, 28.7 mg, 0.147 mmol, 49% yield), (**S41**, 13.4 mg, 0.064 mmol, 21% yield), (2.3 mg, 0.013 mmol, 4.3% rsm). **Run 3:** (**5**, 29.2 mg, 0.149 mmol, 50% yield), (**S41**, 12.9 mg, 0.062

mmol, 21% yield), (4.1 mg, 0.023 mmol, 7.5% rsm). **Average: 50% yield of 5 ± 0.8%, 20% yield of S41 ±1.0%, 5.8% rsm ± 1.6%.**

Without HBF_4 Protection (Entry 5): The oxidation was carried out according to a modified version of **General Method D: Lower Catalyst Loading Protocol:** 1-(cyclopentylmethyl)azepane (**S3**) (54.0 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (212.7 mg, 2.3 mmol, 7.5 equiv.), (*S,S*)-Mn(CF_3PDP) catalyst **1** (10.2 mg, 0.0075 mmol, 2.5 mol%), H_2O_2 (50 wt% in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant, 0.625 mL with catalyst). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex → 30% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded afforded trace product and recovered starting material.

Run 1: <5% yield **5**, <5% yield **S41**, (33.5 mg, 0.186 mmol, 62% rsm). **Run 2:** <5% yield **5**, <5% yield **S41**, (31.9 mg, 0.174 mmol, 58% rsm). **Average: <5% yield of 5, <5% bb yield of S41, 60% rsm ± 2.8%.**

Optimization:



entry	x (mol %)	y (eq.)	z (eq.)	yield (%)[a]			
				rsm	**% yield 5**	**% yield S41**	**Ratio 5:S41**
1	10.0	10.0	15	<5%	30%	40%	1:1.3
2	5.0	5.0	7.5	9%	51%	21%	2.4:1
3	2.5	2.5	3.75	18%	46%	9%	5.1:1
4	2.5	5.0	7.5	6%	50%	20%	2.5:1
5[b]	2.5	7.5	5.0	60%	<5%	<5%	N/A

[a]Isolation yields [b]At 0 °C without HBF_4 protection.

Entry 1: With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)azepane (**S3**) (54.0 mg, 0.300 mmol, 1.0 equiv.) was protected with HBF_4.OEt_2 (45 µL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method A: Slow Catalyst Addition Protocol:** the resultant **S3•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.6 mg, 0.030 mmol, 10.0

mol%), H_2O_2 (50 wt% in H_2O, 204.0 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.375 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex → 30% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded 3-(azepan-1-ylmethyl)cyclopentan-1-one (**5**) as a colorless oil and 1-((3-oxocyclopentyl)methyl)azepan-4-one (**S41**) as a colorless oil.

Run 1: (**5**, 18.7 mg, 0.096 mmol, 32% yield), (**S41**, 23.2 mg, 0.111 mmol, 37% yield), <5% rsm. **Run 2:** (**5**, 16.4 mg, 0.084 mmol, 28% yield), (**S41**, 27.0 mg, 0.129 mmol, 43% yield), <5% rsm. **Average: 30% yield of 5 ± 2.8%, 40% yield of S41 ± 4.2%, <5% rsm.**

Entry 2: With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)azepane (**S3**) (54.0 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to a modified version of **General Method A: Slow Catalyst Addition Protocol:** the resultant **S3•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (212.7 mg, 2.3 mmol, 7.5 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5.0 mol%), H_2O_2 (50 wt% in H_2O, 102.0 mg, 1.5 mmol, 5.0 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant, 0.625 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex → 30% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded 3-(azepan-1-ylmethyl)cyclopentan-1-one (**5**) as a colorless oil and 1-((3-oxocyclopentyl)methyl)azepan-4-one (**S41**) as a colorless oil.

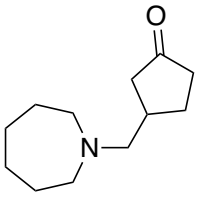
Run 1: (**5**, 29.2 mg, 0.150 mmol, 50% yield), (**S41**, 11.3 mg, 0.054 mmol, 18% yield), (5.3 mg, 0.030 mmol, 10% rsm). **Run 2:** (**5**, 30.2 mg, 0.154 mmol, 52% yield), (**S41**, 14.4 mg, 0.069 mmol, 23% yield), (4.3 mg, 0.024 mmol, 8% rsm). **Average: 51% yield of 5 ± 1.1%, 21% yield of S41 ± 3.5%, 9% rsm ± 1.3%.**

Entry 3: With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)azepane (**S3**) (54.0 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method D: Lower Catalyst Loading Protocol:** the resultant **S3•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (106.0 mg, 1.12 mmol, 3.75 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (10.2 mg, 0.0075 mmol, 2.5 mol%), H_2O_2 (50 wt% in H_2O, 51.0 mg, 0.75 mmol, 2.5 equiv.), MeCN (1.0 mL in 40 mL vial,

6.25 mL with oxidant, 0.625 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex → 30% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded 3-(azepan-1-ylmethyl)cyclopentan-1-one (**5**) as a colorless oil and 1-((3-oxocyclopentyl)methyl)azepan-4-one (**S41**) as a colorless oil.

Run 1: (**5**, 26.9 mg, 0.138 mmol, 46% yield), (**S41**, 4.8 mg, 0.023 mmol, 8% yield), (8.7 mg, 0.049 mmol, 16% rsm). **Run 2:** (**5**, 27.3 mg, 0.140 mmol, 47% yield), (**S41**, 6.9 mg, 0.033 mmol, 11% yield), (10.0 mg, 0.057 mmol, 19% rsm). **Average: 46% yield of 5 ± 0.42%, 9% yield of S41 ± 2.5%, 18% rsm ± 1.9%.**

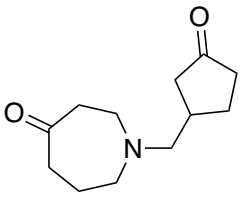
3-(azepan-1-ylmethyl)cyclopentan-1-one [5]



^{1}H NMR (500 MHz, $CDCl_3$) δ 2.73-2.71 (m, 4H), 2.63-2.53 (m, 2H), 2.48-2.35 (m, 2H), 2.29-2.22 (m, 1H), 2.18-2.08 (m, 2H), 1.94 (dd, *J* = 17.9, 9 Hz, 1H), 1.67-1.54 (m, 9H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 220.2, 62.9, 55.9, 44.1, 38.1, 35.9, 28.4, 27.7, 27.3. HRMS (ESI+) *m/z* calculated for $C_{12}H_{22}NO$ $[M+H]^+$: 196.1696, found: 196.1706.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

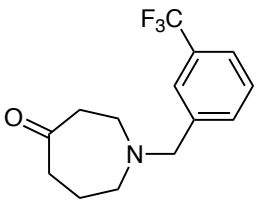
1-((3-oxocyclopentyl)methyl)azepan-4-one [S41]



^{1}H NMR (500 MHz, $CDCl_3$) δ 2.79 (t, *J* = 5.9 Hz, 2H), 2.75 (t, *J* = 4.8 Hz, 2H), 2.61 (t, *J* = 5.3 Hz, 2H), 2.63-2.59 (m, 2H), 2.54-2.47 (m, 4H), 2.45-2.33 (m, 2H), 2.31-2.23 (m, 1H), 2.21-2.08 (m, 2H), 1.97-1.89 (m, 1H), 1.84-1.79 (m, 2H), 1.67-1.57 (m, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 219.4, 213.3, 62.6, 58.4, 51.1, 44.3, 43.8, 42.9, 37.9, 35.5, 27.6, 24.1. HRMS (ESI+) *m/z* calculated for $C_{12}H_{20}NO_2$ $[M+H]^+$: 210.1489, found: 210.1494.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

1-(3-(trifluoromethyl)benzyl)azepan-4-one [6]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(3-(trifluoromethyl)benzyl)azepane (**S4**) (77.0 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S4•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg,

3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex as eluent afforded 1-(3-(trifluoromethyl)benzyl)azepan-4-one (**6**) as a pale yellow oil.

Run 1: (50.4 mg, 0.186 mmol, 62% yield), (12.3 mg, 0.047 mmol, 16% rsm). **Run 2:** (52.9 mg, 0.195 mmol, 65% yield), (13.5 mg, 0.053 mmol, 18% rsm). **Run 3:** (51.4 mg, 0.190 mmol, 63% yield), (15.2 mg, 0.059 mmol, 20% rsm). **Average: 63.3% yield ± 1.5%, 18.0% rsm ± 2%, .**

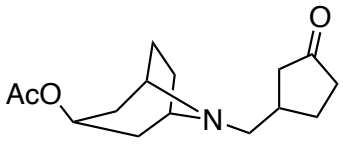
Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 1-(3-(trifluoromethyl)benzyl)azepane (**S4**) (46.0 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.030 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (35 mm fritted glass column, 75 mL Brockmann Grade II basic alumina) using 10% EtOAc/Hex as eluent afforded trace product and recovered starting material.

Run 1: 0.2 mmol scale, <5% yield, (40.0 mg, 0.154 mmol, 77% rsm). **Run 2:** 0.2 mmol scale, <5% yield, (42.6 mg, 0.176 mmol, 82% rsm). **Average: <5% yield, 80% rsm ± 3.5%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.52-7.48 (m, 2H), 7.44 (t, J = 7.7 Hz, 1H), 3.70 (s, 2H), 2.74-2.70 (m, 4H), 2.61-2.57 (m, 2H), 2.55-2.52 (m, 2H), 1.86-1.82 (m, 2H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 213.4, 140.2, 132.0, 130.9 (q, J = 32.0 Hz), 129.0, 125.4 (q, J = 4.3 Hz), 124.3 (q, *J* = 272.9 Hz), 124.2 (q, J = 3.9 Hz), 62.3, 58.1, 50.8, 44.4, 43.0, 24.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ −62.5. HRMS (ESI+) *m/z* calculated for $C_{14}H_{17}F_3NO^+$ $[M+H]^+$: 272.1257, found: 272.1265.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

(1*R*,3*r*,5*S*)-8-((3-oxocyclopentyl)methyl)-8-azabicyclo[3.2.1]octan-3-yl acetate [7]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, (1*R*,3*r*,5*S*)-8-(cyclopentylmethyl)-8-azabicyclo[3.2.1]octan-3-yl acetate (**S5**) (50.3 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S5•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (237 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.50 mL with oxidant, 0.25 mL with catalyst). The reaction was run at -36

°C with a 1,2-dichloroethane/dry ice bath. The reaction was concentrated under reduced pressure and the crude residue was diluted with CH_2Cl_2. The solution was washed with sat. $NaHCO_3$ (20 mL) and the aqueous layer was further washed with CH_2Cl_2 (2x20 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Flash column chromatography on silica (35 mm fritted glass column, 100 mL Brockmann Grade II basic alumina) using 25% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded (1*R*,3*r*,5*S*)-8-((3-oxocyclopentyl)methyl)-8-azabicyclo[3.2.1]octan-3-yl acetate (**7**) as a pale yellow oil.

Run 1: (40.1 mg, 0.151 mmol, 74% yield), <5% rsm. **Run 2:** (37.7 mg, 0.142 mmol, 71% yield), <5% rsm. **Run 3:** (37.9 mg, 0.143 mmol, 72% yield), <5% rsm. **Average: 72% yield ± 1.5%, <5% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: (1*R*,3*r*,5*S*)-8-(cyclopentylmethyl)-8-azabicyclo[3.2.1]octan-3-yl acetate (**S5**) (50.3 mg, 0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (237 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.50 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (35 mm fritted glass column, 100 mL Brockmann Grade II basic alumina) using 25% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded (1*R*,3*r*,5*S*)-8-((3-oxocyclopentyl)methyl)-8-azabicyclo[3.2.1]octan-3-yl acetate (**7**) as a pale yellow oil.

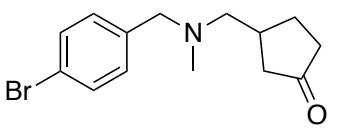
Run 1: (5.3 mg, 0.020 mmol, 10.0% yield), (33.1 mg, 0.132 mmol, 66% rsm). **Run 2:** (7.4 mg, 0.028 mmol, 14.0%), (33.6 mg, 0.134 mmol, 67% rsm). **Average: 12% yield ± 2.8%, 67% rsm ± 0.7%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.91 (t, *J* = 5.5 Hz, 1H), 3.10 (br s, 2H), 2.38-2.20 (m, 5H), 2.14-2.03 (m, 4H), 1.98 (s, 3H), 1.97-1.85 (m, 5H), 1.65-1.59 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.7, 170.4, 67.9, 59.1, 59.0, 57.4, 43.7, 38.0, 36.7, 36.6, 36.5, 27.5, 26.2, 26.1, 21.6.

HRMS (ESI+) *m/z* calculated for $C_{15}H_{24}NO_3^+$ $[M+H]^+$: 266.1751, found: 266.1754.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

3-(((4-bromobenzyl)(methyl)amino)methyl)cyclopentan-1-one [8]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4*N*-(4-bromobenzyl)-1-cyclopentyl-*N*-methylmethanamine (**S6**) (84.7 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S6•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3-PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with

oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% hexanes → 10% → 20% → 30% → 40% → 50% EtOAc/hexanes gradient as eluent afforded 3-(((4-bromobenzyl)(methyl)amino)methyl)cyclopentan-1-one (**8**) as yellow oil.

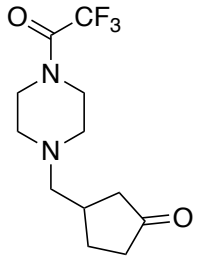
Run 1: (70.5 mg, 0.238 mmol, 79.3% yield), 0% rsm. **Run 2:** (67.8 mg, 0.229 mmol, 76.3% yield), 0% rsm. **Run 3:** (65.4 mg, 0.221 mmol, 73.6% yield), 0% rsm. **Average: 76.4% yield ± 2.9%, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 4*N*-(4-bromobenzyl)-1-cyclopentyl-*N*-methylmethanamine (**S6**) (56.4 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.1 mg, 0.02 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) 100% hexanes → 10% → 20% → 30% → 40% → 50% EtOAc/hexanes gradient as eluent afforded 3-(((4-bromobenzyl)(methyl)amino)methyl)cyclopentan-1-one (**8**) as yellow oil.

Run 1: (14.0 mg, 0.047 mmol, 23.6% yield), (29.1 mg, 0.103 mmol, 51.2% rsm). **Run 2:** (11.3 mg, 0.038 mmol, 19.1% yield), (34.2 mg, 0.121 mmol, 60.6% rsm). **Average: 21.4% yield, 55.9% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 2H), 7.22 – 7.15 (m, 2H), 3.43 (s, 2H), 2.52 – 2.30 (m, 4H), 2.20 (s, 3H), 2.27 – 2.10 (m, 3H), 1.89 (dd, *J* = 18.1, 8.6 Hz, 1H), 1.64 – 1.53 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.6, 138.4, 131.5, 130.6, 120.9, 62.2, 62.2, 43.9, 42.7, 37.9, 35.2, 27.5. HRMS (ESI+) *m/z* calculated for $C_{14}H_{19}NOBr$ $[M+H]^+$: 296.0650, found 296.0648.

3-((4-(2,2,2-trifluoroacetyl)piperazin-1-yl)methyl)cyclopentan-1-one [9]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(4-(cyclopentylmethyl)piperazin-1-yl)-2,2,2-trifluoroethan-1-one (**S7**) (79.3 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 µL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S7•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 50% → 60% → 70%

→ 80% → 100% EtOAc/hexanes gradient as eluent afforded 3-((4-(2,2,2-trifluoroacetyl)piperazin-1-yl)methyl)cyclopentan-1-one (**9**) as a pale yellow oil.

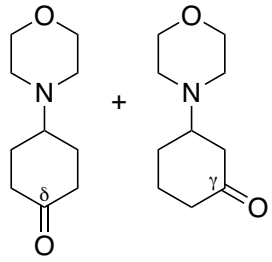
Run 1: (30.8 mg, 0.111 mmol, 36.9% yield), 0% rsm. **Run 2:** (32.0 mg, 0.115 mmol, 38.3% yield), 0% rsm. **Run 3:** (33.4 mg, 0.120 mmol, 40.0% yield), 0% rsm. **Average: 38.4% yield ± 1.6%, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 1-(4-(cyclopentylmethyl)piperazin-1-yl)-2,2,2-trifluoroethan-1-one (**S7**) (52.9 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.1 mg, 0.02 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% hexanes → 10% → 20% → 30% → 40% → 50% EtOAc/hexanes gradient as eluent afforded trace product and recovered starting material.

Run 1: <5% yield, (26.2 mg, 0.099 mmol, 49.6% rsm). **Run 2:** <5% yield, (25.0 mg, 0.095 mmol, 47.3% rsm). **Average: <5% yield, 48.5% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (t, *J* = 5.1 Hz, 2H), 3.60 (t, *J* = 5.0 Hz, 2H), 2.56 – 2.33 (m, 8H), 2.33 – 2.24 (m, 1H), 2.23 – 2.08 (m, 2H), 1.95 (dd, *J* = 18.2, 8.1 Hz, 1H), 1.70 – 1.58 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 218.9, 155.5 (q, *J* = 35.7 Hz), 116.6 (q, *J* = 288.0 Hz), 63.0, 53.5, 52.8, 45.9, 43.7, 43.4, 37.8, 34.4, 27.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ -68.8. HRMS (ESI+) *m/z* calculated for $C_{12}H_{18}N_2O_2F_3$ $[M+H]^+$: 279.1320, found 279.1316.

4-morpholinocyclohexan-1-one [10a] and 3-morpholinocyclohexan-1-one [10b]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-cyclohexylmorpholine (**S8**) (50.8 mg, 0.300 mmol, 1.0 equiv.) was protected with HBF_4.OEt_2 (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method C: Iterative Catalyst Addition Protocol:** the resultant **S8•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*S,S*)-Mn(CF_3PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%), H_2O_2 (50 wt% in H_2O, 204.0 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 °C with an ice/water bath. A further addition of (*S,S*)-Mn(CF_3-PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction at 1.5 hours. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2

→ 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 4-morpholinocyclohexan-1-one (4-ketone, **10a**) as a colorless oil and 3-morpholinocyclohexan-1-one (3-ketone, **10b**) as a colorless oil.

Run 1: (17.2 mg, 0.094 mmol, 31.3% yield of δ-ketone **10a**), (9.3 mg, 0.051 mmol, 16.9% yield of γ-ketone **10b**), (48.2% overall yield, 3.7:1 δ:γ ratio), (17.2 mg, 0.102 mmol, 33.9% rsm). **Run 2:** (15.2 mg, 0.083 mmol, 27.6% yield of δ-ketone **10a**), (8.4 mg, 0.046 mmol, 15.3% yield of γ-ketone **10b**), (42.9% overall yield, 3.6:1 δ:γ ratio), (8.6 mg, 0.051 mmol, 16.9% rsm). **Run 3:** (17.8 mg, 0.097 mmol, 32.3% yield of δ-ketone **10a**), (9.2 mg, 0.050 mmol, 16.7% yield of γ-ketone **10b**), (49.0% overall yield, 3.9:1 δ:γ ratio), (10.2 mg, 0.060 mmol, 20.1% rsm). **Average: 46.7% yield ± 3.3%, 3.7:1 δ:γ ketone ratio, 23.6% rsm ± 9.0%.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 4-cyclohexylmorpholine (**S8**) (50.8 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204.0 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% MeOH/CH_2Cl_2 gradient as eluent afforded only recovered starting material as a colorless oil.

Run 1: 0% yield, (40.4 mg, 0.237 mmol, 79.6% rsm). **Run 2:** 0% yield, (37.8 mg, 0.223 mmol, 74.4% rsm). **Average: 0% yield, 77.0% rsm.**

Alternate conditions:

With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-cyclohexylmorpholine (**S8**) (50.8 mg, 0.300 mmol, 1.0 equiv.) was protected with HBF_4.OEt_2 (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S8•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 4-morpholinocyclohexan-1-one (4-ketone, **10a**) as a colorless oil and 3-morpholinocyclohexan-1-one (3-ketone, **10b**) as a colorless oil.

Yield: (12.5 mg, 0.068 mmol, 22.7% yield of δ-ketone **10a**), (4.3 mg, 0.023 mmol, 7.8% yield of γ-ketone **10b**), (30.5% overall yield, 2.9:1 δ:γ ratio), (5.5 mg, 0.032 mmol, 10.8% rsm).

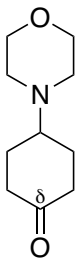
With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-cyclohexylmorpholine (**S8**) (50.8 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method B: Single Catalyst Addition Protocol:** the resultant **S8•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*S,S*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204.0 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 °C with an ice/water bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 4-morpholinocyclohexan-1-one (4-ketone, **10a**) as a colorless oil and 3-morpholinocyclohexan-1-one (3-ketone, **10b**) as a colorless oil.

Yield: (13.2 mg, 0.072 mmol, 24.0% yield of δ-ketone **10a**), (8.3 mg, 0.045 mmol, 15.1% yield of γ-ketone **10b**), (39.1% overall yield, 3.2:1 δ:γ ratio), (19.7 mg, 0.116 mmol, 38.8% rsm).

With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-cyclohexylmorpholine (**S8**) (50.8 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S8•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at 0 °C with an ice/water bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 4-morpholinocyclohexan-1-one (4-ketone, **10a**) as a colorless oil.

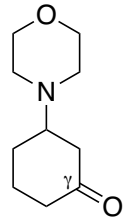
Yield: (11.8 mg, 0.064 mmol, 21.4% yield of δ-ketone **10a**), (0% yield of γ-ketone **10b**), (21.4% overall yield), 0% rsm.

4-morpholinocyclohexan-1-one [10a]



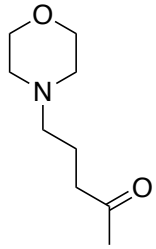
^1H NMR (500 MHz, $CDCl_3$) δ 3.77 – 3.67 (m, 4H), 2.62 – 2.53 (m, 5H), 2.48 (dt, *J* = 14.7, 5.8 Hz, 2H), 2.33 – 2.23 (m, 2H), 2.08 – 1.96 (m, 2H), 1.91 – 1.80 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.1, 67.4, 60.3, 50.2, 38.8, 27.9. HRMS (ESI+) *m/z* calculated for $C_{10}H_{18}NO_2$ $[M+H]^+$: 184.1338, found 184.1339.

3-morpholinocyclohexan-1-one [10b]



^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (t, *J* = 4.7 Hz, 4H), 2.66 (tt, *J* = 10.2, 3.6 Hz, 1H), 2.61 – 2.48 (m, 5H), 2.42 – 2.31 (m, 2H), 2.31 – 2.22 (m, 1H), 2.12 – 2.03 (m, 1H), 2.04 – 1.96 (m, 1H), 1.75 – 1.52 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.6, 67.3, 63.5, 49.7, 44.5, 41.4, 28.0, 22.4. HRMS (ESI+) *m/z* calculated for $C_{10}H_{18}NO_2$ $[M+H]^+$: 184.1338, found 184.1333.

5-morpholinopentan-2-one [11]

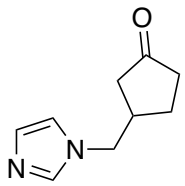


According to the **general procedure for HBF_4•OEt_2 protection**, 4-pentylmorpholine (**S9**) (47.2 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method C: Iterative Catalyst Addition Protocol**: the resultant **S9•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3-PDP) **1** (20.3 mg, 0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 °C with an ice/water bath. A further addition of (*S,S*)-Mn(CF_3-PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction at 1 hour. A further addition of (*S,S*)-Mn(CF_3-PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction at 2 hours. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 4% MeOH/CH_2Cl_2 as eluent afforded 5-morpholinopentan-2-one (**11**) as a pale yellow oil.

Run 1: (16.8 mg, 0.098 mmol, 32.7% yield), (13.1 mg, 0.083 mmol, 27.7% rsm). **Run 2:** (17.2 mg, 0.100 mmol, 33.6%), (13.4 mg, 0.085 mmol, 28.3% rsm). **Run 3:** (19.8 mg, 0.116 mmol, 38.5% yield), (15.1 mg, 0.096 mmol, 31.9% rsm). **Average: 34.9% yield ± 3.1%, 29.3% rsm ± 2.3%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (t, *J* = 4.7 Hz, 4H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.41 (app. t, *J* = 4.7 Hz, 4H), 2.31 (t, *J* = 7.1 Hz, 2H), 2.15 (s, 3H), 1.76 (p, *J* = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.7, 67.1, 58.2, 53.8, 41.5, 30.3, 20.9. HRMS (ESI+) *m/z* calculated for $C_9H_{18}NO_2$ $[M+H]^+$: 172.1338 found 172.1330.

3-((1*H*-imidazol-1-yl)methyl)cyclopentan-1-one [12]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)-1*H*-imidazole (**S10**) (44.8 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition**

Protocol: The resultant **S10•HBF$_4$** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF$_3$PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), ClCH$_2$CO$_2$H (425 mg, 4.5 mmol, 15.0 equiv.), H$_2$O$_2$ (50% wt. in H$_2$O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF$_4$ Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 75 mL SiO$_2$) using 5% MeOH/CH$_2$Cl$_2$ as eluent afforded 3-((1*H*-imidazol-1-yl)methyl)cyclopentane-1-one (**12**) as a pale yellow oil.

Run 1: (25.6 mg, 0.156 mmol, 52% yield), <5% rsm. **Run 2:** (25.4 mg, 0.156 mmol, 52% yield), <5% rsm. **Run 3:** (27.0 mg, 0.164 mmol, 54.7% yield), <5% rsm. **Average: 53% yield ± 1.7%, <5% rsm.**

Lower catalyst loading: : According to **General Method D: Lower Catalyst Loading Protocol:** the resultant **S10•HBF$_4$** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF$_3$PDP) **1** (10.6 mg, 0.0075 mmol, 2.5 mol%), ClCH$_2$CO$_2$H (106 mg, 1.13 mmol, 3.75 equiv.), H$_2$O$_2$ (50% wt. in H$_2$O, 51 mg, 0.75 mmol, 2.5 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant, 0.625 mL MeCN with catalyst). The reaction was run at 0 °C with an ice/water bath. The reaction was worked up according to the **General Procedure for HBF$_4$ Deprotection.** Flash chromatography on silica (35 mm fritted glass column, 75 mL SiO$_2$) using 5% MeOH/CH$_2$Cl$_2$ as eluent afforded 3-((1*H*-imidazol-1-yl)methyl)cyclopentane-1-one (**12**) as a pale yellow oil.

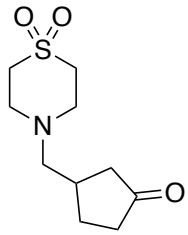
Run 1: (26.1 mg, 0.159 mmol, 53% yield), (14.4 mg, 0.096 mmol, 32% rsm). **Run 2:** (26.6 mg, 0.162 mmol, 54% yield), (14.4 mg, 0.096 mmol, 32% rsm). **Run 3:** (25.6 mg, 0.156 mmol, 52% yield), (12.2 mg, 0.081 mmol, 27% rsm). **Average 53.0% yield ± 1%, 30.3% rsm ± 2.9%**

Without HBF$_4$ Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 1-(cyclopentylmethyl)-1*H*-imidazole (**S10**) (44.8 mg, 0.300 mmol, 1.0 equiv.), ClCH$_2$CO$_2$H (425 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF$_3$PDP) catalyst **1** (40.7 mg, 0.030 mmol, 10 mol%), H$_2$O$_2$ (50 wt% in H$_2$O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated NaHCO$_3$ and DCM as described in General Method B. Flash column chromatography on silica (35 mm fritted glass column, 75 mL SiO$_2$) using 5% MeOH/DCM as eluent afforded 3-((1*H*-imidazol-1-yl)methyl)cyclopentane-1-one (**12**) as a pale yellow oil.

Run 1: (3.9 mg, 0.024 mmol, 8% yield), 11.1% rsm. **Run 2:** (4.4 mg, 0.027 mmol, 9% yield), 9.0% rsm. **Average: 8.5% yield ± 1%, 10.1% rsm ± 1.5%.**

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45 (s, 1H), 7.04 (s, 1H), 6.89 (s, 1H), 4.02 (dd, J = 14.0, 7.0 Hz, 1H), 3.96 (dd, J = 14.0, 7.3 Hz, 1H), 2.65-2.56 (m, 1H), 2.37-2.27 (m, 2H), 2.21-2.06 (m, 2H), 1.89 (dd, J = 18.2, 10.1 Hz, 1H), 1.64-1.56 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 216.6, 137.2, 129.9, 119.1, 51.1, 42.6, 38.6, 37.9, 27.1. HRMS (ESI+) *m/z* calculated for C$_9$H$_{12}$N$_2$O [M+H]$^+$: 165.1022, found: 165.1028.

3-((1,1-dioxidothiomorpholino)methyl)cyclopentan-1-one [13]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-(cyclopentylmethyl)thiomorpholine 1,1-dioxide (**S11**) (65.2 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S11•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 3-((1,1-dioxidothiomorpholino)methyl)cyclopentan-1-one (**13**) as a colorless oil.

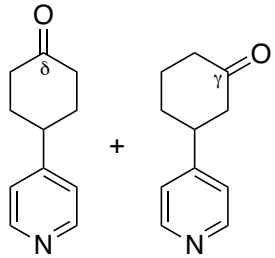
Run 1: (38.4 mg, 0.166 mmol, 55.3% yield), 0% rsm. **Run 2:** (38.8 mg, 0.168 mmol, 55.9% yield), 0% rsm. **Run 3:** (35.9 mg, 0.155 mmol, 51.7% yield), 0% rsm. **Average: 54.3% yield ± 2.3%, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 4-(cyclopentylmethyl)thiomorpholine 1,1-dioxide (**S11**) (46.3 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.1 mg, 0.02 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% MeOH/CH_2Cl_2 gradient as eluent afforded only recovered starting material as a colorless oil.

Run 1: 0% yield, (24.4 mg, 0.112 mmol, 56.1% rsm). **Run 2:** 0% yield, (27.6 mg, 0.119 mmol, 59.7% rsm). **Average: 0% yield, 57.9% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.10 – 2.93 (m, 8H), 2.61 – 2.46 (m, 2H), 2.46 – 2.08 (m, 5H), 1.92 (dd, *J* = 17.4, 7.9 Hz, 1H), 1.67 – 1.55 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 218.5, 61.6, 51.4, 51.2, 43.5, 37.7, 34.9, 27.4. HRMS (ESI+) *m/z* calculated for $C_{10}H_{18}NO_3S$ $[M+H]^+$: 232.1007, found 232.1009.

4-(pyridin-4-yl)cyclohexan-1-one [14a] and 3-(pyridin-4-yl)cyclohexan-1-one [14b]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-cyclohexylpyridine (**S12**) (48.4 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S12•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(pyridin-4-yl)cyclohexan-1-one (minor, **14a**) and 3-(pyridin-4-yl)cyclohexan-1-one (major, **14b**) as a mixture as a yellow oil.

Run 1: (34.7 mg, 0.198 mmol, 66.0% yield, 1.3:1 γ:δ), 0% rsm. **Run 2:** (32.1 mg, 0.183 mmol, 61.0%, 1.3:1 γ:δ), 0% rsm. **Run 3:** (32.3 mg, 0.184 mmol, 61.4% yield, 1.4:1 γ:δ), (7.7 mg, 0.050 mmol, 16.8% rsm). **Average: 62.8% yield ± 2.8%, 1.3:1 γ:δ, 0% rsm.**

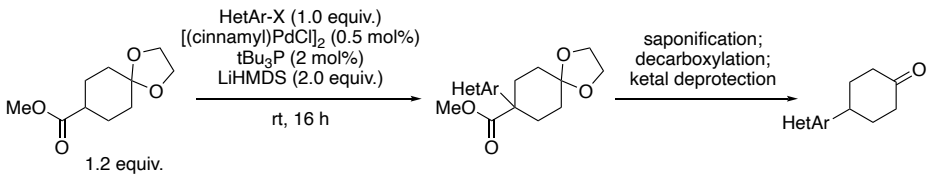
Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 4-cyclohexylpyridine (**S12**) (48.4 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) 100% CH_2Cl_2 → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded trace product and recovered starting material as a colorless oil.

Run 1: <10% yield, (35.3 mg, 0.219 mmol, 73.0% rsm). **Run 2:** <10% yield, (40.2 mg, 0.249 mmol, 83.1% rsm). **Average: <10% yield, 78.1% rsm.**

Spectral data in agreement with those previously reported in the literature.[14,15]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.56 – 8.46 (m, 2H), 7.14 (d, *J* = 5.1 Hz, 0.72H), 7.11 (d, *J* = 5.1 Hz, 1.24H), 3.03 – 2.93 (m, 1H), 2.59 – 2.51 (m, 0.67H), 2.51 – 2.40 (m, 2.62H), 2.40 – 2.30 (m, 0.73H), 2.24 – 2.16 (m, 0.65H), 2.16 – 2.01 (m, 1.47H), 1.96 – 1.69 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.0 (δ-product), 209.8, 153.5 (δ-product), 152.9, 150.1 (δ-product), 150.0, 122.2 (δ-product), 122.0, 47.7, 43.8, 41.9 (δ-product), 41.1, 41.0, 33.0 (δ-product), 31.9, 25.3. HRMS (ESI+) *m/z* calculated for $C_{11}H_{14}NO$ $[M+H]^+$: 176.1075, found 176.1070.

Previous Route:[14]

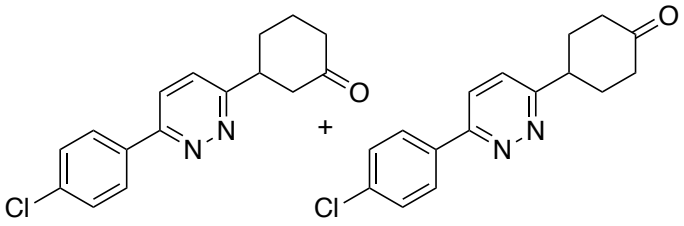


Oxidation of 4-bromo-1-(cyclopentylmethyl)-1*H*-pyrazole [S13]

With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-bromo-1-(cyclopentylmethyl)-1*H*-pyrazole (**S13**) (45.8 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S13•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. No product or recovered starting material was observed by TLC.

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 4-bromo-1-(cyclopentylmethyl)-1*H*-pyrazole (**S13**) (45.8 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.1 mg, 0.02 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. No product or recovered starting material was observed by TLC.

3-(6-(4-chlorophenyl)pyridazin-3-yl)cyclohexan-1-one [15a] and 4-(6-(4-chlorophenyl)pyridazin-3-yl)cyclohexan-1-one [15b]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 3-(4-chlorophenyl)-6-cyclohexylpyridazine (**S14**) (54.6 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S14•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3-PDP) **1** (27.1 mg, 0.02 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The

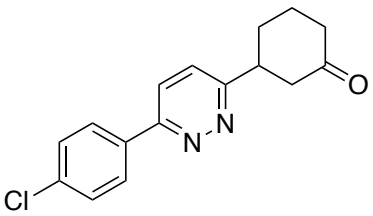
reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% → 40% → 50% → 60% ethyl acetate/hexanes gradient as eluent afforded 3-(6-(4-chlorophenyl)pyridazin-3-yl)cyclohexan-1-one (**15a**) as a white solid and 4-(6-(4-chlorophenyl)pyridazin-3-yl)cyclohexan-1-one (**15b**) as a white solid.

Run 1: (21.3 mg, 0.074 mmol, 37.1% yield of C3 ketone **15a**), (9.8 mg, 0.034 mmol, 17.0% yield of C4 ketone **15b**), (54.1% overall yield, 1.1:1 C3:C4 ratio), (6.6 mg, 0.024 mmol, 12.1% rsm). **Run 2:** (21.2 mg, 0.074 mmol, 37.0% yield of C3 ketone **15a**), (10.3 mg, 0.036 mmol, 18.0% yield of C4 ketone **15b**), (55.0% overall yield, 1:1 C3:C4 ratio), (3.0 mg, 0.011 mmol, 5.5% rsm). **Run 3:** (21.0 mg, 0.073 mmol, 36.6% yield of C3 ketone **15a**), (10.3 mg, 0.036 mmol, 18.0% yield of C4 ketone **15b**), (54.6% overall yield, 1:1 C3:C4 ratio), (6.0 mg, 0.022 mmol, 11.0% rsm). **Average: 54.6% yield ± 0.5%, 1:1 γ:δ ratio, 9.5% rsm ± 3.5%.**

Without HBF_4: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 3-(4-chlorophenyl)-6-cyclohexylpyridazine (**S14**) (54.6 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.1 mg, 0.02 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% → 40% → 50% → 60% ethyl acetate/hexanes gradient as eluent afforded no desired product or recovered starting material.

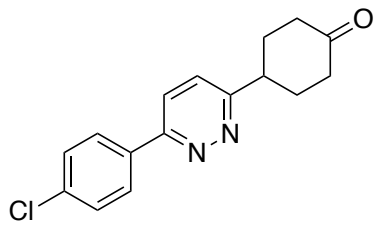
Run 1: <5% yield, <5% rsm. **Run 2:** <5% yield, <5% rsm. **Average: <5% yield, <5% rsm.**

3-(6-(4-chlorophenyl)pyridazin-3-yl)cyclohexan-1-one [15a]



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 1H), 3.37 (tt, *J* = 11.7, 3.8 Hz, 1H), 2.96 (app. t, *J* = 13.2 Hz, 1H), 2.73 – 2.67 (m, 1H), 2.53 – 2.41 (m, 2H), 2.24 – 2.19 (m, 2H), 2.16 – 2.06 (m, 1H), 1.90 – 1.79 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.4, 163.0, 157.0, 136.4, 134.6, 129.4, 128.3, 126.1, 124.1, 46.5, 44.8, 41.2, 31.6, 25.3. HRMS (ESI+) *m/z* calculated for $C_{16}H_{16}N_2OCl$ $[M+H]^+$: 287.0951, found 287.0955. *Site of oxidation was confirmed by ^{1}H, gCOSY, gHSQC and gHMBC NMRs.*

4-(6-(4-chlorophenyl)pyridazin-3-yl)cyclohexan-1-one [15b]



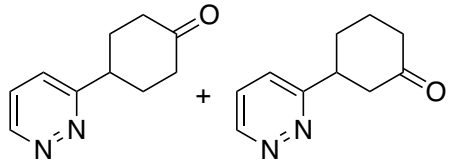
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 1H), 3.47 (tt, *J* = 11.4, 3.7 Hz, 1H), 2.64 – 2.52 (m, 4H), 2.44 – 2.36 (m, 2H), 2.20 (qd, *J* = 12.2, 5.1 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.4, 163.9, 157.0, 136.5, 134.7, 129.4, 128.3, 125.5, 124.1, 42.4, 40.8, 32.1. HRMS (ESI+) *m/z* calculated for $C_{16}H_{16}N_2OCl$ $[M+H]^+$: 287.0951, found 287.0954.

Oxidation of pyridazine N-oxide

Without HBF_4: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 6-(4-chlorophenyl)-3-cyclohexylpyridazine 1-oxide (56.6 mg, 0.196 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (277.8 mg, 2.94 mmol, 15.0 equiv.), (*S,S*)-Mn(CF_3PDP) catalyst **1** (26.6 mg, 0.0196 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 133 mg, 1.96 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. The crude reaction mixture was run through a silica plug with 100% ethyl acetate as eluent to remove metal impurities. The crude mixture was analyzed by quantitative ^{1}H NMR analysis with mesitylene added as internal standard.

Yield: 20% rsm.

4-(pyridazin-3-yl)cyclohexan-1-one [16a] and 3-(pyridazin-3-yl)cyclohexan-1-one [16b]



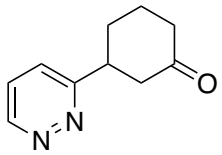
With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 3-cyclohexylpyridazine (**S15**) (32.4 mg, 0.200 mmol, 1.0 equiv.) was protected with HBF_4.OEt_2 (30 µL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S15•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3-PDP) **1** (27.1 mg, 0.02 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 1% → 2% → 3% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(pyridazin-3-yl)cyclohexan-1-one (**16a**) and 3-(pyridazin-3-yl)cyclohexan-1-one (**16b**) as a pale yellow oil.

Run 1: (16.3 mg, 0.092 mmol, 46.2% yield, 1.3:1 C4:C3), 0% rsm. **Run 2 (0.29 mmol scale):** (24.4 mg, 0.138 mmol, 47.7% yield, 1.3:1 C4:C3), 0% rsm. **Average: 47.0% yield 1.3:1 δ:γ, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 3-cyclohexylpyridazine (**S15**) (31.4 mg, 0.194 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3-PDP) **1** (26.3 mg, 0.019 mmol, 10 mol%), $ClCH_2CO_2H$ (275 mg, 2.91 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 132 mg, 1.94 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.43 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. The crude reaction mixture was run through a silica plug with 100% ethyl acetate as eluent to remove metal impurities. The crude mixture was analyzed by quantitative ^1H NMR analysis with mesitylene added as internal standard.

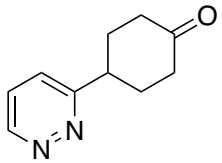
Run 1: no desired product, 6% rsm. **Run 2 (0.161 mmol scale):** no desired product, 4% rsm. **Average: 0% yield, 5% rsm.**

3-(pyridazin-3-yl)cyclohexan-1-one [16a]



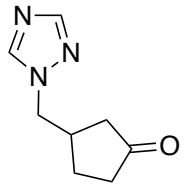
^1H NMR (500 MHz, $CDCl_3$) δ 9.10 (dd, *J* = 5.0, 1.6 Hz, 1H), 7.44 (dd, *J* = 8.4, 4.9 Hz, 1H), 7.33 (dd, *J* = 8.5, 1.7 Hz, 1H), 3.33 (tt, *J* = 11.6, 4.0 Hz, 1H), 2.94 (app. t, *J* = 12.0 Hz, 1H), 2.72 – 2.64 (m, 1H), 2.54 – 2.39 (m, 2H), 2.25 – 2.05 (m, 3H), 1.90 – 1.77 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.4, 164.5, 150.3, 126.9, 125.4, 46.6, 45.3, 41.2, 31.6, 25.4. HRMS (ESI+) *m/z* calculated for $C_{10}H_{13}N_2O$ $[M+H]^+$: 177.1028, found 177.1033.

4-(pyridazin-3-yl)cyclohexan-1-one [16b]



^1H NMR (500 MHz, $CDCl_3$) δ 9.11 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.45 (dd, *J* = 8.5, 4.8 Hz, 1H), 7.39 (dd, *J* = 8.5, 1.7 Hz, 1H), 3.45 (tt, *J* = 11.6, 3.6 Hz, 1H), 2.64 – 2.50 (m, 4H), 2.42 – 2.32 (m, 2H), 2.22 – 2.10 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.3, 165.4, 150.3, 126.9, 124.8, 42.9, 40.9, 32.2. HRMS (ESI+) *m/z* calculated for $C_{10}H_{13}N_2O$ $[M+H]^+$: 177.1028, found 177.1030.

3-((1*H*-1,2,4-triazol-1-yl)methyl)cyclopentan-1-one [17]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)-1*H*-1,2,4-triazole (**S16**) (45.4 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S16•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3-PDP) **1** (40.7 mg, 0.03 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted

glass column, 30 mL SiO_2) using 2% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 3-((1*H*-1,2,4-triazol-1-yl)methyl)cyclopentan-1-one (**17**) as a colorless oil.

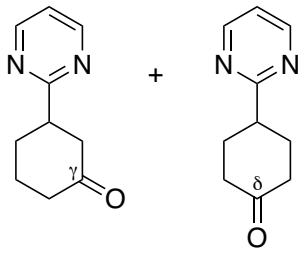
Run 1: (33.1 mg, 0.200 mmol, 66.8% yield), <5% rsm. **Run 2:** (34.3 mg, 0.208 mmol, 69.2%), <5% rsm. **Run 3 (0.288 mmol scale):** (31.7 mg, 0.192 mmol, 66.6% yield), <5% rsm. **Average: 67.5% yield ± 1.4%, <5% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 1-(cyclopentylmethyl)-1*H*-1,2,4-triazole (**S16**) (45.4 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3-PDP) **1** (40.7 mg, 0.03 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 3-((1*H*-1,2,4-triazol-1-yl)methyl)cyclopentan-1-one (**17**) as a colorless oil.

Run 1: (20.5 mg, 0.124 mmol, 41.4%), <5% rsm. **Run 2:** (21.4 mg, 0.130 mmol, 43.2% yield), <5% rsm. **Average: 42.3% yield, <5% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.88 (s, 1H), 4.25 – 4.14 (m, 2H), 2.83 – 2.69 (m, 1H), 2.36 – 2.21 (m, 2H), 2.19 – 2.02 (m, 2H), 1.92 (dd, *J* = 18.3, 10.0 Hz, 1H), 1.66 – 1.54 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 216.5, 152.2, 143.2, 53.3, 42.4, 37.9, 37.3, 26.8. HRMS (ESI+) *m/z* calculated for $C_8H_{12}N_3O$ $[M+H]^+$: 166.0980, found 166.0974.

3-(pyrimidin-2-yl)cyclohexan-1-one [18a] and 4-(pyrimidin-2-yl)cyclohexan-1-one [18b]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 2-cyclohexylpyrimidine (**S17**) (48.6 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S17•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 20% → 30% → 40% → 50% → 60% → 70% → 80% EtOAc/Hexanes gradient as eluent afforded 3-(pyrimidin-2-yl)cyclohexan-1-one (**18a**) as a colorless oil and 4-(pyrimidin-2-yl)cyclohexan-1-one (**18b**) as a colorless oil.

Run 1: (15.9 mg, 0.090 mmol, 30.1% yield of γ-ketone **18a**), (11.3 mg, 0.064 mmol, 21.4% yield of δ-ketone **18b**), (51.5% overall yield, 1:1.4 γ:δ), 0% rsm. **Run 2:** (15.6 mg, 0.089 mmol, 29.5% yield of γ-ketone **18a**), (10.4 mg, 0.059 mmol, 19.7% yield of δ-ketone **18b**), (49.2% overall yield, 1:1.3 γ:δ), 0% rsm. **Run 3:** (16.5 mg, 0.094 mmol, 31.2% yield of γ-ketone **18a**), (12.2 mg, 0.069 mmol, 23.1% yield of δ-ketone **18b**), (54.3% overall yield, 1:1.5 γ:δ), 0% rsm. **Average: 51.7% yield ± 2.6%, 1:1.4 γ:δ, 0% rsm.**

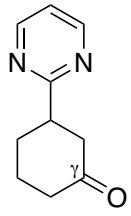
Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 2-cyclohexylpyrimidine (**S17**) (48.6 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. . The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 20% → 30% → 40% → 50% → 60% → 70% → 80% EtOAc/Hexanes gradient as eluent afforded 3-(pyrimidin-2-yl)cyclohexan-1-one (**18a**) as a colorless oil and 4-(pyrimidin-2-yl)cyclohexan-1-one (**18b**) as a colorless oil.

Run 1: (19.4 mg, 0.110 mmol, 36.7% yield of γ-ketone **18a**), (8.1 mg, 0.046 mmol, 15.3% yield of δ-ketone **18b**), (52.0% overall yield, 1.2:1 γ:δ), (11.4 mg, 0.070 mmol, 23.4% rsm). **Run 2:** (17.8 mg, 0.101 mmol, 33.7% yield of γ-ketone **18a**), (9.9 mg, 0.056 mmol, 18.7% yield of δ-ketone **18b**), (52.4% overall yield, 1:1.1 γ:δ), (9.3 mg, 0.057 mmol, 19.1% rsm). **Run 3:** (17.6 mg, 0.100 mmol, 33.3% yield of γ-ketone **18a**), (6.8 mg, 0.039 mmol, 12.9% yield of δ-ketone **18b**), (46.2% overall yield, 1.3:1 γ:δ), (4.0 mg, 0.025 mmol, 8.2% rsm). **Average: 50.2% yield ± 3.5%, 1.1:1 γ:δ**, **16.9% rsm ± 7.8%.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 2-cyclohexylpyrimidine (**S17**) (48.6 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 20% → 30% → 40% → 50% → 60% → 70% → 80% EtOAc/Hexanes gradient as eluent afforded 3-(pyrimidin-2-yl)cyclohexan-1-one (**18a**) as a colorless oil and 4-(pyrimidin-2-yl)cyclohexan-1-one (**18b**) as a colorless oil.

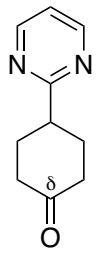
Yield: (14.6 mg, 0.083 mmol, 27.6% yield of γ-ketone **18a**), (8.4 mg, 0.048 mmol, 15.9% yield of δ-ketone **18b**), (43.5% overall yield, 1:1.2 γ:δ), 0% rsm.

3-(pyrimidin-2-yl)cyclohexan-1-one [18a]



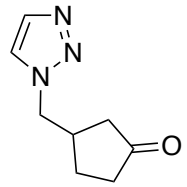
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.9 Hz, 2H), 7.15 (t, *J* = 4.9 Hz, 1H), 3.40 (tt, *J* = 10.9, 4.2 Hz, 1H), 2.85 (dd, *J* = 14.5, 11.2 Hz, 1H), 2.68 – 2.60 (m, 1H), 2.49 – 2.34 (m, 2H), 2.23 – 2.15 (m, 1H), 2.13 – 2.03 (m, 1H), 2.02 – 1.91 (m, 1H), 1.91 – 1.74 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.0, 171.8, 157.3, 119.1, 47.3, 45.6, 41.3, 30.9, 24.9. HRMS (ESI+) *m/z* calculated for $C_{10}H_{13}N_2O$ $[M+H]^+$: 177.1028, found 177.1021.

4-(pyrimidin-2-yl)cyclohexan-1-one [18b]



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 2H), 7.16 (t, *J* = 4.8 Hz, 1H), 3.39 – 3.32 (m, 1H), 2.57 – 2.44 (m, 4H), 2.40 – 2.29 (m, 2H), 2.24 – 2.12 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.2, 172.4, 157.2, 119.0, 44.9, 40.6, 31.3. HRMS (ESI+) *m/z* calculated for $C_{10}H_{13}N_2O$ $[M+H]^+$: 177.1028, found 177.1023.

3-((1*H*-1,2,3-triazol-1-yl)methyl)cyclopentan-1-one [19]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(cyclopentylmethyl)-1*H*-1,2,3-triazole (**S18**) (45.4 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S18•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3-PDP) **1** (40.7 mg, 0.03 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 3-((1*H*-1,2,3-triazol-1-yl)methyl)cyclopentan-1-one (**19**) as a colorless oil.

Run 1: (22.4 mg, 0.136 mmol, 45.2% yield), 0% rsm. **Run 2:** (20.1 mg, 0.122 mmol, 40.6%), 0% rsm. **Run 3:** (21.6 mg, 0.131 mmol, 43.6% yield), 0% rsm. **Average: 43.1% yield ± 2.3%, 0% rsm .**

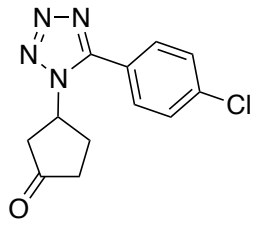
Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 1-(cyclopentylmethyl)-1*H*-1,2,3-triazole (**S18**) (45.4 mg, 0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm

fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 3-((1*H*-1,2,3-triazol-1-yl)methyl)cyclopentan-1-one (**19**) as a colorless oil.

Run 1: (13.2 mg, 0.080 mmol, 26.6% yield), (2.9 mg, 0.019 mmol, 6.4% rsm). **Run 2 (0.264 mmol scale):** (13.1 mg, 0.079 mmol, 30.0%), (2.6 mg, 0.017 mmol, 6.5% rsm). **Average: 28.3% yield, 6.5% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (app s, 1H), 7.56 (app s, 1H), 4.47 (d, *J* = 7.1 Hz, 2H), 2.89 – 2.77 (m, 1H), 2.44 – 2.27 (m, 2H), 2.26 – 2.11 (m, 2H), 2.00 (dd, *J* = 18.3, 10.1 Hz, 1H), 1.75 – 1.65 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 216.4, 134.1, 123.7, 54.0, 42.6, 38.0, 37.9, 27.0. HRMS (ESI+) *m/z* calculated for $C_8H_{12}N_3O$ $[M+H]^+$: 166.0980, found 166.0974.

3-(5-(4-chlorophenyl)-1*H*-tetrazol-1-yl)cyclopentan-1-one [20]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 5-(4-chlorophenyl)-1-cyclopentyl-1*H*-tetrazole (**S19**) (48.7 mg, 0.200 mmol, 1.0 equiv.) was protected with HBF_4.OEt_2 (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S19•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3-PDP) **1** (27.1 mg, 0.02 mmol, 10 mol%), $ClCH_2CO_2H$ (283,5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 15% → 20% → 25% → 30% EtOAc/hexanes as eluent afforded only recovered starting material.

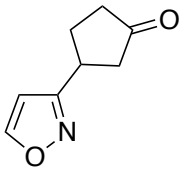
Run 1: 0% yield, (11.2 mg, 0.045 mmol, 22.5% rsm). **Run 2:** 0% yield, (12.1 mg, 0.049 mmol, 24.3% rsm). **Average: 0% yield, 23.4% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 5-(4-chlorophenyl)-1-cyclopentyl-1*H*-tetrazole (**S19**) (74.6 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 15% → 20% → 25% → 30% EtOAc/hexanes as eluent afforded 3-(5-(4-chlorophenyl)-1*H*-tetrazol-1-yl)cyclopentan-1-one (**20**) as a white solid.

Run 1: (37.7 mg, 0.144 mmol, 47.8% yield), (9.4 mg, 0.038 mmol, 12.6% rsm). **Run 2:** (38.2 mg, 0.146 mmol, 48.7%), (11.2 mg, 0.045 mmol, 15.0% rsm). **Run 3:** (40.8 mg, 0.155 mmol, 51.8% yield), (9.1 mg, 0.037 mmol, 12.2% rsm). **Average: 49.4% yield ± 2.1%, 13.2% rsm ± 1.5%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.55 (m, 4H), 5.20 (app p, *J* = 6.1 Hz, 1H), 2.90 (dd, *J* = 18.6, 5.5 Hz, 1H), 2.85 – 2.75 (m, 2H), 2.59 (td, *J* = 8.0, 6.1 Hz, 2H), 2.46 – 2.37 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.3, 153.5, 138.3, 130.3, 130.1, 122.2, 55.8, 44.8, 36.5, 30.5. HRMS (ESI+) *m/z* calculated for $C_{12}H_{12}N_4OCl$ $[M+H]^+$: 263.0700, found 263.0705.

3-(isoxazol-3-yl)cyclopentan-1-one [21]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 3-cyclopentylisoxazole (**S20**) (41.2 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S20•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3-PDP) **1** (20.3 mg, 0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 10% → 20% → 30% → 40% → 50% EtOAc/hexanes as eluent afforded 3-(isoxazol-3-yl)cyclopentan-1-one (**21**) as a colorless oil.

Run 1: (5.6 mg, 0.037 mmol, 12.3% yield), 0% rsm. **Run 2:** (6.2 mg, 0.041 mmol, 13.7%), 0% rsm. **Average: 13.0% yield, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 3-cyclopentylisoxazole (**S20**) (41.2 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (20.3 mg, 0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 10% → 20% → 30% → 40% → 50% EtOAc/hexanes as eluent afforded 3-(isoxazol-3-yl)cyclopentan-1-one (**21**) as a colorless oil.

Run 1: (7.3 mg, 0.048 mmol, 16.0% yield), 0% rsm. **Run 2:** (9.1 mg, 0.06 mmol, 20.0%), 0% rsm. **Run 3:** (8.2 mg, 0.054 mmol, 18.0% yield), 0% rsm. **Average: 18.0% yield ± 2.0%, 0% rsm.**

Lower Catalyst Loading: According to **General Method D,** 3-cyclopentylisoxazole (**S20**) (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (7.1 mg, 0.005 mmol, 2.5 mol%), $ClCH_2CO_2H$ (70.7 mg, 0.75 mmol,

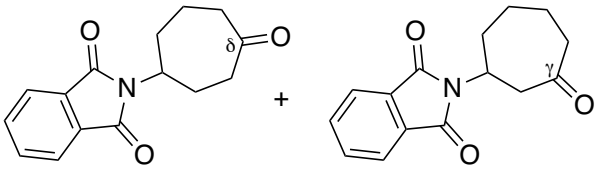
3.75 equiv.), H_2O_2 (50% wt. in H_2O, 34 mg, 0.5 mmol, 2.5 equiv.), MeCN (0.66 mL in 40 mL vial, 4.16 mL with oxidant, 0.416 mL MeCN with catalyst). The reaction was run at 0 °C with an ice/water bath. The reaction mixture was concentrated under reduced pressure and purified via flash chromatography on silica (35 mm fritted glass column, 75 mL SiO_2) using 10% → 25% → 35% → 45% → 55% → 65% EtOAc/Hex gradient as eluent afforded 3-(isoxazol-3-yl)cyclopentan-1-one (**21**) as a colorless oil.

Run 1: (6.0 mg, 0.04 mmol, 20% yield), 0% rsm.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, *J* = 1.7 Hz, 1H), 6.26 (d, *J* = 1.7 Hz, 1H), 3.59 (app p, *J* = 9.1 Hz, 1H), 2.67 (dd, *J* = 18.7, 7.6 Hz, 1H), 2.52 – 2.39 (m, 3H), 2.36 – 2.25 (m, 1H), 2.11 (dq, *J* = 12.9, 9.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 216.9, 164.4, 159.0, 103.0, 43.6, 38.0, 34.0, 29.1.

HRMS (ESI+) *m/z* calculated for $C_8H_{10}NO_2$ $[M+H]^+$: 152.0712, found 152.0710.

2-(4-oxocycloheptyl)isoindoline-1,3-dione [22a] and 2-(3-oxocycloheptyl)isoindoline-1,3-dione [22b]



Without HBF_4 Protection: The reaction was run with **General Method D: Lower Catalyst Loading Protocol**: 2-cycloheptylisoindoline-1,3-dione (**S21**) (73.0 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (10.2 mg, 0.0075 mmol, 2.5 mol%), $ClCH_2CO_2H$ (106.3 mg, 1.13 mmol, 3.75 equiv.), H_2O_2 (50% wt. in H_2O, 51 mg, 0.75 mmol, 2.5 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant, 0.625 mL with catalyst). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method D. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 100% hexanes → 10% → 20% → 30% EtOAc/hexanes as eluent afforded 2-(4-oxocycloheptyl)isoindoline-1,3-dione (**22a**) as a white solid and 2-(3-oxocycloheptyl)isoindoline-1,3-dione (**22b**) as a white solid.

Run 1: (52.9 mg, 0.206 mmol, 68.5% yield, 2:1 δ:γ), 0% rsm. **Run 2:** (52.3 mg, 0.203 mmol, 67.7%, 2:1 δ:γ), 0% rsm. **Run 3:** (55.6 mg, 0.216 mmol, 72.0% yield, 2:1 δ:γ), 0% rsm. **Average: 69.4% yield ± 2.3%, 2:1 δ:γ, 0% rsm.** Regioisomer ratio determined by quantitative ^{13}C NMR.

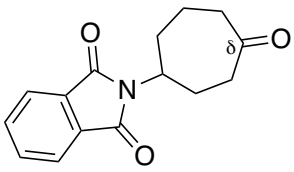
Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 2-cycloheptylisoindoline-1,3-dione (**S21**) (73.0 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.03 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 100% hexanes → 10% → 20% → 30% → 50%

EtOAc/hexanes as eluent afforded 2-(4-oxocycloheptyl)isoindoline-1,3-dione (**22a**) and 2-(3-oxocycloheptyl)isoindoline-1,3-dione (**22b**) as a white solid and 2-(3,6-dioxocycloheptyl)isoindoline-1,3-dione as a white solid.

Yield: (16.8 mg, 0.065 mmol, 21.7% yield mono-oxidized products, 4.4:1 δ:γ), (7.0 mg, 0.026 mmol, 8.6% di-oxidized product), 0% rsm.

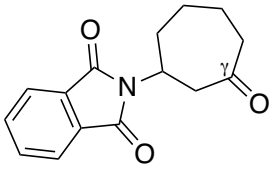
Spectral data in agreement with those previously reported in the literature.[8]

2-(4-oxocycloheptyl)isoindoline-1,3-dione [22a]



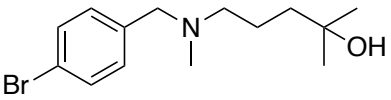
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H), 4.29 – 4.21 (m, 1H), 2.65 – 2.51 (m, 5H), 2.35 (app. q, *J* = 12.1 Hz, 1H), 2.04 – 1.95 (m, 2H), 1.94 – 1.85 (m, 1H), 1.75 – 1.64 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 213.3, 168.0, 134.1, 131.9, 123.3, 53.6, 43.4, 40.9, 34.0, 28.4, 22.1.

2-(3-oxocycloheptyl)isoindoline-1,3-dione [22b]



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 4.47 (tt, *J* = 11.9, 2.7 Hz, 1H), 3.64 (dd, *J* = 14.9, 12.2 Hz, 1H), 2.66 – 2.58 (m, 1H), 2.59 – 2.50 (m, 2H), 2.44 – 2.36 (m, 1H), 2.10 – 2.02 (m, 1H), 2.02 – 1.94 (m, 2H), 1.78 – 1.68 (m, 1H), 1.57 – 1.47 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.8, 167.8, 134.2, 131.9, 123.4, 48.2, 48.1, 44.1, 35.5, 27.8, 23.8.

5-((4-bromobenzyl)(methyl)amino)-2-methylpentan-2-ol [23]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, *N*-(4-bromobenzyl)-*N*,4-dimethylpentan-1-amine (**S22**) (56.8 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol:** the resultant **S22•HBF_4** (0.200 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (18.6 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 68 mg, 1.0 mmol, 5.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 4% → 6% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 5-((4-bromobenzyl)(methyl)amino)-2-methylpentan-2-ol (**23**) as a colorless oil.

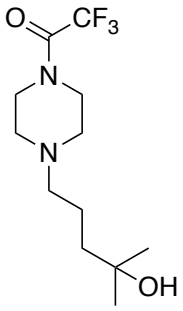
Run 1: (45.2 mg, 0.151 mmol, 75.3% yield), (12.4 mg, 0.044 mmol, 21.8% rsm). **Run 2:** (47.0 mg, 0.157 mmol, 78.3% yield), (10.4 mg, 0.037 mmol, 18.3% rsm). **Run 3:** (43.2 mg, 0.144 mmol, 72.0% yield), (8.3 mg, 0.029 mmol, 14.6% rsm). **Average: 75.2% yield ± 3.2%, 18.2% rsm ± 3.6%.**

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: *N*-(4-bromobenzyl)-*N*,4-dimethylpentan-1-amine (**S22**) (56.8 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*S,S*)-Mn(PDP) catalyst **2** (18.6 mg, 0.020 mmol, 10 mol%), H_2O_2 (50% wt. in H_2O, 68 mg, 1.0 mmol, 5.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) 2% → 4% → 6% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 5-((4-bromobenzyl)(methyl)amino)-2-methylpentan-2-ol (**23**) as a colorless oil.

Run 1: (21.1 mg, 0.070 mmol, 35.1% yield), (26.0 mg, 0.091 mmol, 45.7% rsm). **Run 2:** (23.2 mg, 0.077 mmol, 38.6% yield), (27.9 mg, 0.098 mmol, 49.1% rsm). **Average: 36.9% yield, 47.4% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 4.75 (br s, 1H), 3.46 (s, 2H), 2.42 (t, *J* = 6.0 Hz, 2H), 2.13 (s, 3H), 1.66 (p, *J* = 6.4 Hz, 2H), 1.58 (app t, *J* = 6.3 Hz, 2H), 1.21 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.0, 131.6, 131.0, 121.2, 69.3, 61.9, 58.7, 42.8, 41.6, 29.9, 22.1. HRMS (ESI+) *m/z* calculated for $C_{14}H_{23}NOBr$ $[M+H]^+$: 300.0963, found 300.0954.

2,2,2-trifluoro-1-(4-(4-hydroxy-4-methylpentyl)piperazin-1-yl)ethan-1-one [24]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 2,2,2-trifluoro-1-(4-(4-methylpentyl)piperazin-1-yl)ethan-1-one (**S23**) (53.3 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol:** the resultant **S23•HBF_4** (0.200 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (18.6 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 68 mg, 1.0 mmol, 5.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 2,2,2-trifluoro-1-(4-(4-hydroxy-4-methylpentyl)piperazin-1-yl)ethan-1-one (**24**) as a pale yellow oil.

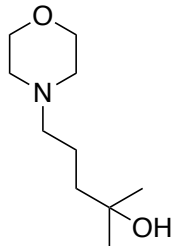
Run 1: (33.3 mg, 0.118 mmol, 59.0% yield), <5% rsm. **Run 2:** (33.1 mg, 0.117 mmol, 58.6% yield), <5% rsm. **Run 3:** (34.9 mg, 0.124 mmol, 61.8% yield), <5% rsm. **Average: 59.8% yield ± 1.7%, <5% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 2,2,2-trifluoro-1-(4-(4-methylpentyl)piperazin-1-yl)ethan-1-one (**S23**) (53.3 mg, 0.200 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (18.6 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 68 mg, 1.0 mmol, 5.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 2,2,2-trifluoro-1-(4-(4-hydroxy-4-methylpentyl)piperazin-1-yl)ethan-1-one (**24**) as a pale yellow oil.

Run 1: (27.3 mg, 0.097 mmol, 48.4% yield), (25.5 mg, 0.096 mmol, 47.9% rsm). **Run 2:** (27.9 mg, 0.099 mmol, 49.4% yield), (20.6 mg, 0.077 mmol, 38.7% rsm). **Average: 48.9% yield, 43.3% rsm.**

^1H NMR (500 MHz, $CDCl_3$) δ 4.30 (br. s, 1H), 3.68 (app t, J = 5.1 Hz, 2H), 3.60 (app t, J = 5.0 Hz, 2H), 2.52 (app t, J = 5.1 Hz, 4H), 2.40 (t, J = 6.1 Hz, 2H), 1.67 – 1.52 (m, 4H), 1.18 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5 (q, J = 35.8 Hz), 116.5 (q, J = 287.9 Hz), 69.5, 58.9, 53.0, 52.4, 45.5, 43.1, 42.6, 29.7, 21.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -68.9. HRMS (ESI+) *m/z* calculated for $C_{12}H_{22}N_2O_2F_3$ $[M+H]^+$: 283.1633, found 283.1630.

2-methyl-5-morpholinopentan-2-ol [25]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-(4-methylpentyl)morpholine (**S24**) (51.4 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S24•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann grade II basic Al_2O_3) using 40% → 80% → 100% EtOAc/hexanes → 10% MeOH/EtOAc gradient as eluent afforded 2-methyl-5-morpholinopentan-2-ol (**25**) as a pale yellow oil.

Run 1: (38.8 mg, 0.207 mmol, 69.1% yield), 0% rsm. **Run 2:** (39.3 mg, 0.210 mmol, 69.9%), 0% rsm. **Run 3:** (39.9 mg, 0.213 mmol, 71.0% yield), 0% rsm. **Average: 70.0% yield ± 1.0%, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 4-(4-methylpentyl)morpholine (**S24**) (51.4 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9

mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann grade II basic Al_2O_3) using 40% → 80% → 100% EtOAc/hexanes → 10% MeOH/EtOAc gradient as eluent afforded 2-methyl-5-morpholinopentan-2-ol (**25**) as a pale yellow oil.

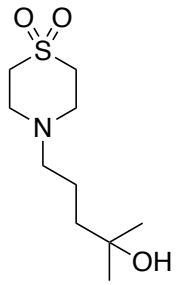
Run 1: (21.7 mg, 0.116 mmol, 38.6% yield), <5% rsm. **Run 2:** (24.0 mg, 0.128 mmol, 42.7%), <5% rsm. **Average: 40.7% yield, <5% rsm.**

With Fe(PDP): According to the **general procedure for HBF_4•OEt_2 protection**, 4-(4-methylpentyl)morpholine (**S24**) (51.4 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was conducted according to the iterative addition protocol.[9] A 40 mL vial was charged with **S24•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Fe(PDP) catalyst (14.0 mg, 0.015 mmol, 0.05 equiv.), CH_3COOH (9.0 mg, 0.15 mmol, 0.5 equiv.), MeCN (0.45 mL) and a stir bar. The vial was stirred vigorously and a solution of H_2O_2 (50% wt. in H_2O, 24.5 mg, 1.2 equiv.) in MeCN (3.75 mL) was added dropwise over 60-75 seconds. The reaction was allowed to stir for 10 minutes at room temperature before a second batch of catalyst (14.0 mg, 0.015 mmol, 0.05 equiv.) and AcOH (9.0 mg, 0.15 mmol, 0.5 equiv.) dissolved in 0.3 mL MeCN was added *via* pipette. This was followed by a solution of H_2O_2 (50 wt%, 24.5 mg, 1.2 equiv.) in MeCN (3.75 mL) over 60-75 seconds. After another 10 minutes a third batch of catalyst and H_2O_2 was added in the same manner. The third addition was allowed to stir for 10 minutes for a total reaction time of 30 minutes. **Significant decrease in yield was observed when the peroxide solution was added rapidly.** Upon completion, the reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on alumina (15 mm fritted glass column, 20 mL Brockmann grade II basic Al_2O_3) using 40% → 80% → 100% EtOAc/hexanes → 10% MeOH/EtOAc gradient as eluent afforded 2-methyl-5-morpholinopentan-2-ol (**25**) as a pale yellow oil.

Run 1: (19.9 mg, 0.106 mmol, 35.4 % yield), (25.2 mg, 0.147 mmol, 49.0% rsm). **Run 2:** (24.4 mg, 0.130 mmol, 43.4 % yield), (20.1 mg, 0.117 mmol, 39.1% rsm). **Average: 39.4% yield, 44.1% rsm.**

^{1}H NMR (500 MHz, CD_3OD) δ 3.73 – 3.66 (m, 4H), 2.56 – 2.43 (m, 4H), 2.40 – 2.29 (m, 2H), 1.66 – 1.57 (m, 2H), 1.53 – 1.45 (m, 2H), 1.19 (s, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 71.0, 67.6, 60.7, 54.7, 42.7, 29.3, 22.1. HRMS (ESI+) *m/z* calculated for $C_{10}H_{22}NO_2$ $[M+H]^+$: 188.1651, found 188.1644.

4-(4-hydroxy-4-methylpentyl)thiomorpholine-1,1-dioxide [26]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 4-(4-methylpentyl)thiomorpholine-1,1-dioxide (**S25**) (61.6 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S25•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(4-hydroxy-4-methylpentyl)thiomorpholine-1,1-dioxide (**26**) as a pale yellow oil.

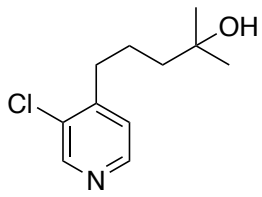
Run 1: (46.2 mg, 0.196 mmol, 65.4% yield), 0% rsm. **Run 2:** (46.4 mg, 0.197 mmol, 65.7% yield), 0% rsm. **Run 3:** (44.3 mg, 0.188 mmol, 62.7% yield), 0% rsm. **Average: 64.6% yield ± 1.7%, 0% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 4-(4-methylpentyl)thiomorpholine-1,1-dioxide (**S25**) (61.6 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 4-(4-hydroxy-4-methylpentyl)thiomorpholine-1,1-dioxide (**26**) as a pale yellow oil.

Run 1: (19.3 mg, 0.082 mmol, 27.3% yield), (26.1 mg, 0.119 mmol, 39.7% rsm). **Run 2:** (19.8 mg, 0.084 mmol, 28.0% yield), (19.2 mg, 0.088 mmol, 29.2% rsm). **Average: 27.7% yield, 34.5% rsm.**

^1H NMR (500 MHz, $CDCl_3$) δ 3.10 – 3.03 (m, 4H), 3.03 – 2.98 (m, 4H), 2.97 (br. s, 1H), 2.52 (t, J = 6.6 Hz, 2H), 1.64 – 1.56 (m, 2H), 1.56 – 1.50 (m, 2H), 1.20 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 70.1, 57.8, 51.3, 50.9, 42.0, 29.7, 22.1. HRMS (ESI+) *m/z* calculated for $C_{10}H_{22}NO_3S$ $[M+H]^+$: 236.1320, found 236.1314.

5-(3-chloropyridin-4-yl)-2-methylpentan-2-ol [27]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 3-chloro-4-(4-methylpentyl)pyridine (**S26**) (59.3 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst**

Addition Protocol: the resultant **S26•HBF$_4$** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF$_4$ Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 5-(3-chloropyridin-4-yl)-2-methylpentan-2-ol (**27**) as a colorless oil.

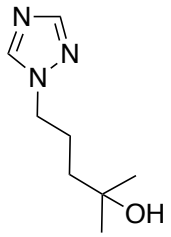
Run 1: (54.9 mg, 0.257 mmol, 85.6% yield), 0% rsm. **Run 2:** (54.0 mg, 0.253 mmol, 84.2%), 0% rsm. **Run 3:** (52.7 mg, 0.247 mmol, 82.2% yield), 0% rsm. **Average: 84.0% yield ± 1.7%, 0% rsm.**

Without HBF$_4$ Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 3-chloro-4-(4-methylpentyl)pyridine (**S26**) (59.3 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. . The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded 5-(3-chloropyridin-4-yl)-2-methylpentan-2-ol (**27**) as a colorless oil.

Run 1: (21.2 mg, 0.099 mmol, 33.1% yield), (31.4 mg, 0.159 mmol, 52.9% rsm). **Run 2:** (22.7 mg, 0.106 mmol, 35.4%), (30.5 mg, 0.154 mmol, 51.4% rsm). **Average: 34.3% yield, 52.2% rsm.**

Spectral data in agreement with those previously reported in the literature.[9]

2-methyl-5-(1*H*-1,2,4-triazol-1-yl)pentan-2-ol [28]



With HBF$_4$ Protection: According to the **general procedure for HBF$_4$•OEt$_2$ protection**, 1-(4-methylpentyl)-1*H*-1,2,4-triazole (**S27**) (46.0 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol**: the resultant **S27•HBF$_4$** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF$_4$ Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 2-methyl-5-(1*H*-1,2,4-triazol-1-yl)pentan-2-ol (**28**) as a colorless oil.

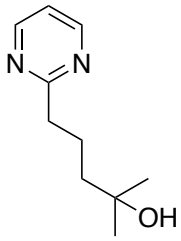
Run 1: (41.9 mg, 0.248 mmol, 82.5% yield), <5% rsm. **Run 2:** (41.9 mg, 0.248 mmol, 82.5%), <5% rsm. **Run 3:** (42.4 mg, 0.251 mmol, 83.5%), <10% rsm. **Average: 82.8% yield ± 0.6%, <5% rsm.**

Without HBF_4 Protection: The reaction was run with **General Method C: Iterative Catalyst Addition Protocol**: 1-(4-methylpentyl)-1*H*-1,2,4-triazole (**S27**) (46.0 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (14.0 mg, 0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. A further addition of (*S,S*)-Mn(PDP) **2** (14.0 mg, 0.015 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction at 1.5 hours. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method D. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 2-methyl-5-(1*H*-1,2,4-triazol-1-yl)pentan-2-ol (**28**) as a colorless oil.

Run 1: (27.7 mg, 0.164 mmol, 54.6% yield), (16.3 mg, 0.106 mmol, 35.5% rsm). **Run 2:** (30.9 mg, 0.183 mmol, 60.9%), (11.8 mg, 0.077 mmol, 25.7% rsm). **Run 3:** (27.7 mg, 0.164 mmol, 54.6% yield), (11.8 mg, 0.077 mmol, 25.7% rsm). **Average: 56.7% yield ± 3.6%, 29.0% rsm ± 5.7%.**

^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.91 (s, 1H), 4.19 (t, *J* = 7.1 Hz, 2H), 2.03 – 1.93 (m, 2H), 1.83 (br. s, 1H), 1.47 – 1.39 (m, 2H), 1.20 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.9, 143.0, 70.5, 50.1, 40.1, 29.5, 25.0. HRMS (ESI+) *m/z* calculated for $C_8H_{16}N_3O$ $[M+H]^+$: 170.1293, found 170.1293.

2-methyl-5-(pyrimidin-2-yl)pentan-2-ol [29]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 2-(4-methylpentyl)pyrimidine (**S28**) (49.3 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 µL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol**: the resultant **S28•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 2-methyl-5-(pyrimidin-2-yl)pentan-2-ol (**29**) as a colorless oil.

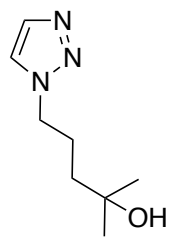
Run 1: (40.5 mg, 0.225 mmol, 74.9% yield), (11.5 mg, 0.070 mmol, 23.3% rsm). **Run 2:** (39.0 mg, 0.216 mmol, 72.1% yield), (12.6 mg, 0.077 mmol, 25.6% rsm). **Run 3:** (38.3 mg, 0.212 mmol, 70.8% yield), (12.6 mg, 0.077 mmol, 25.6% rsm). **Average: 72.6% yield ± 2.1%, 24.8% rsm ± 1.3%.**

Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 2-(4-methylpentyl)pyrimidine (**S28**) (49.3 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (14.0 mg, 0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% → 10% MeOH/CH_2Cl_2 gradient as eluent afforded 2-methyl-5-(pyrimidin-2-yl)pentan-2-ol (**29**) as a colorless oil.

Run 1: (35.9 mg, 0.199 mmol, 66.4% yield), <10% rsm. **Run 2:** (35.8 mg, 0.199 mmol, 66.2% yield), <10% rsm. **Average: 66.3% yield, <10% rsm.**

^1H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, J = 4.9 Hz, 2H), 7.12 (t, J = 4.9 Hz, 1H), 2.98 (t, J = 7.6 Hz, 2H), 1.98 – 1.85 (m, 2H), 1.79 (br s, 1H), 1.63 – 1.50 (m, 2H), 1.21 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 157.1, 118.6, 71.0, 43.3, 39.7, 29.4, 23.4. HRMS (ESI+) *m/z* calculated for $C_{10}H_{17}N_2O$ $[M+H]^+$: 181.1341, found 181.1339.

2-methyl-5-(1*H*-1,2,3-triazol-1-yl)pentan-2-ol [30]



With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(4-methylpentyl)-1*H*-1,2,3-triazole (**S29**) (46.0 mg, 0.300 mmol, 1.0 equiv.), was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol**: the resultant **S29•HBF_4** (0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 2-methyl-5-(1*H*-1,2,3-triazol-1-yl)pentan-2-ol (**30**) as a colorless oil.

Run 1: (41.8 mg, 0.247 mmol, 82.3% yield), 0% rsm. **Run 2:** (39.3 mg, 0.232 mmol, 77.4%), 0% rsm. **Run 3:** (38.5 mg, 0.228 mmol, 75.8% yield), 0% rsm. **Average: 78.5% yield ± 3.4%, 0% rsm.**

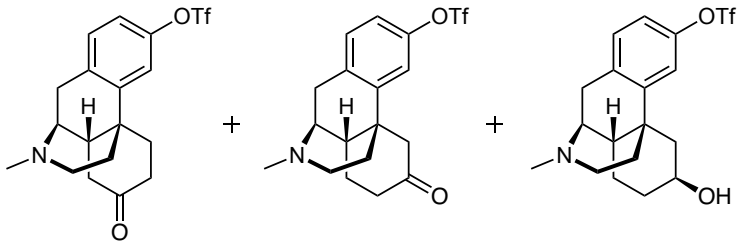
Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 1-(4-methylpentyl)-1*H*-1,2,3-triazole (**S29**) (46.0 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(PDP) **2** (27.9 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 102 mg, 1.5 mmol, 5.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL

saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded 2-methyl-5-(1*H*-1,2,3-triazol-1-yl)pentan-2-ol (**30**) as a colorless oil.

Run 1: (33.5 mg, 0.198 mmol, 66.0% yield), (6.8 mg, 0.044 mmol, 14.8% rsm). **Run 2:** (33.9 mg, 0.200 mmol, 66.8%), (7.0 mg, 0.046 mmol, 15.2% rsm). **Run 3:** (34.8 mg, 0.206 mmol, 68.5% yield), (7.7 mg, 0.050 mmol, 16.8% rsm). **Average: 67.1% yield ± 1.3%, 15.6% rsm ± 1.1%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.55 (s, 1H), 4.36 (t, *J* = 7.3 Hz, 2H), 2.34 (br s, 1H), 2.04 – 1.92 (m, 2H), 1.47 – 1.38 (m, 2H), 1.16 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.7, 123.4, 70.2, 50.5, 40.1, 29.4, 25.4. HRMS (ESI+) *m/z* calculated for $C_8H_{16}N_3O$ $[M+H]^+$: 170.1293, found 170.1295.

3-(OTf)-Dextromethorphan *C*-7 Ketone [31a], 3-(OTf) Dextromethorphan *C*-6 Ketone [31b], and 3-(OTf) Dextromethorphan C-6 α-Alcohol [31c]



31a **31b** **31c**

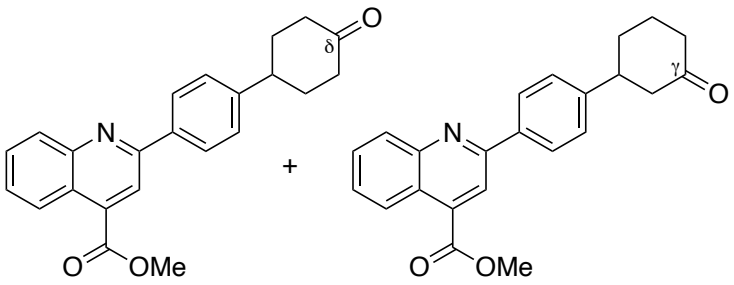
According to the **general procedure for HBF_4•OEt_2 protection**, 3-(OTf) Dextromethorphan (**S30**) (77.9 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S30•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.2 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography (35 mm fritted glass column, 75 mL Brockmann Grade III basic alumina) using 25% (200 mL) → 50% (100 mL) → 60% (50 mL) → 70% (50 mL) → 80% (50 mL) → 90% (50 mL) → 100% (200 mL) EtOAc/hexanes gradient → 10% MeOH/EtOAc (200 mL) as eluent afforded 3-(OTf)-Dextromethorphan *C*-7 Ketone (**31a**), 3-(OTf) Dextromethorphan *C*-6 Ketone (**31b**), and 3-(OTf) Dextromethorphan *C*-6 α-Alcohol (**31c**) all as yellow oils.

Run 1: (40.1 mg, 0.099 mmol, 49.7% yield of **31a**), (11.2 mg, 0.028 mmol, 13.8% yield of **31b**), (15.4 mg, 0.037 mmol, 18.4% yield of **31c**), (81.9% overall yield), (5.6 mg, 0.014 mmol, 7.0% rsm). **Run 2:** (37.2 mg, 0.092 mmol, 46.1% yield of **31a**), (9.9 mg, 0.025 mmol, 12.3% yield of **31b**), (14.3 mg, 0.035 mmol, 17.6% yield of **31c**), (76.0% overall yield), (8.8 mg, 0.023 mmol, 11.4% rsm). **Run 3** (0.160 mmol): (27.7 mg, 0.069 mmol, 43.2% yield of **31a**), (7.2 mg, 0.018 mmol, 11.2% yield of **31b**), (10.4 mg, 0.25 mmol, 16.0% yield of **31c**), (70.4% overall yield), (8.8 mg, 0.020 mmol, 12.6% rsm). **Average: 46%**

yield of 31a ± 3.3%, 12% yield of 31b ± 1.3%, 17% yield of 31c ± 1.2%, 76.1% overall yield ± 5.8%, 10.3% rsm ± 2.9%.

Spectral data in agreement with those previously reported in the literature.[9]

Methyl 2-(4-(4-oxocyclohexyl)phenyl)quinoline-4-carboxylate [32a] and methyl 2-(4-(3-oxocyclohexyl)phenyl)quinoline-4-carboxylate [32b]



According to the **general procedure for HBF_4•OEt_2 protection**, methyl 2-(4-cyclohexylphenyl)quinoline-4-carboxylate (**S31**) (69.1 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method C: Iterative Catalyst Addition Protocol**: the resultant **S31•HBF_4** (0.200 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3PDP) **1** (13.6 mg, 0.010 mmol, 5 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 °C with an ice/water bath. A further addition of (*S,S*)-Mn(CF_3PDP) catalyst **1** (13.6 mg, 0.010 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction at 1.5 hours. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 15% → 20% → 30% EtOAc/hexanes gradient as eluent afforded a mixture of methyl 2-(4-(4-oxocyclohexyl)phenyl)quinoline-4-carboxylate (**32a**) and methyl 2-(4-(3-oxocyclohexyl)phenyl)quinoline-4-carboxylate (**32b**) as a white solid.

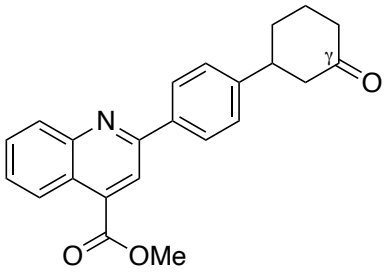
Run 1: (13.9 mg, 0.039 mmol, 19.3% yield), <5% rsm. **Run 2:** (14.5 mg, 0.040 mmol, 20.2% yield), <5% rsm. **Run 3:** (16.0 mg, 0.045 mmol, 22.3% yield), <5% rsm. **Average: 20.6% yield ± 1.6%, <5% rsm.**

Lower catalyst loading: According to **General Method D,** the resultant **S31•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (10.6 mg, 0.0075 mmol, 2.5 mol%), $ClCH_2CO_2H$ (106 mg, 1.13 mmol, 3.75 equiv.), H_2O_2 (50% wt. in H_2O, 51 mg, 0.75 mmol, 2.5 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant, 0.625 mL MeCN with catalyst). The reaction was run at 0 °C with an ice/water bath. The resultant mixture was concentrated to ~ 1 mL and diluted with CH_2Cl_2 (10 mL) and washed with 1.5 M K_2CO_3 (15 mL). The aqueous layer was washed with CH_2Cl_2 (2 x 20 mL), dried with Na_2SO_4, and concentrated under reduced pressure. Flash chromatography on silica (35 mm fritted glass column, 90 mL SiO_2) using 10% → 25% EtOAc/Hex as eluent afforded a mixture of methyl 2-(4-(4-oxocyclohexyl)phenyl)quinoline-4-carboxylate (**32a**) and methyl 2-(4-(3-oxocyclohexyl)phenyl)quinoline-4-carboxylate (**32b**) as a white solid.

Run 1: (38.8 mg, 0.108 mmol, 36% yield, 1:1 γ:δ), (17.6 mg, 0.051 mmol, 17% rsm). **Run 2 (0.14 mmol scale):** (15.0 mg, 0.042 mmol, 31% yield, 1:1 γ:δ), (9.8 mg, 0.029 mmol, 21% rsm). **Average: 34% yield ± 3.5%, 1:1 γ:δ, 19% rsm ± 2.8%.** Regioisomer ratio determined by ^{13}C NMR.

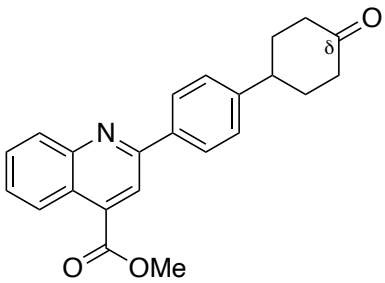
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 8.5 Hz, 1H), 8.38 (s, 1H), 8.22 (d, *J* = 7.6 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 2H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.46 – 7.35 (m, 2H), 4.07 (s, 3H), 3.16 – 3.05 (m, 0.9H), 2.69 – 2.36 (m, 3.9H), 2.32 – 2.23 (m, 0.6H), 2.22 – 2.09 (m, 1.4H), 2.06 – 1.74 (m, 2.6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.1, 210.9, 167.0, 167.0, 156.5, 156.5, 149.4, 146.7, 146.2, 137.5, 137.4, 135.8, 130.4, 130.1, 128.0, 127.9, 127.9, 127.4, 127.3, 125.6, 124.1, 120.3, 52.9, 48.9, 44.7, 42.7, 41.4, 41.3, 34.0, 32.8, 25.6. HRMS (ESI+) *m/z* calculated for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1600, found 360.1585. Regioisomers were separated by CombiFlash (12g silica column) using 100% hexanes → 20% EtOAc/hexanes gradient over 40 column volumes.

Methyl 2-(4-(3-oxocyclohexyl)phenyl)quinoline-4-carboxylate [32a]



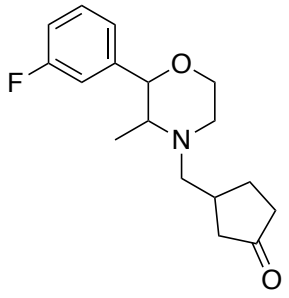
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (d, *J* = 8.6 Hz, 1H), 8.39 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 2H), 7.77 (t, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 2H), 4.08 (s, 3H), 3.11 (tt, *J* = 11.9, 3.9 Hz, 1H), 2.69 – 2.54 (m, 2H), 2.53 – 2.46 (m, 1H), 2.46 – 2.37 (m, 1H), 2.23 – 2.10 (m, 2H), 1.98 – 1.88 (m, 1H), 1.88 – 1.77 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.9, 166.8, 156.4, 148.8, 146.5, 136.9, 136.2, 130.4, 129.9, 128.2, 128.1, 127.4, 125.6, 124.1, 120.5, 53.0, 48.9, 44.7, 41.3, 32.8, 25.6. HRMS (ESI+) *m/z* calculated for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1600, found 360.1600.

Methyl 2-(4-(4-oxocyclohexyl)phenyl)quinoline-4-carboxylate [32b]



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (d, *J* = 8.4 Hz, 1H), 8.40 (s, 1H), 8.34 (br. s, 1H), 8.19 (d, *J* = 7.4 Hz, 2H), 7.80 (t, *J* = 7.4 Hz, 1H), 7.65 (t, *J* = 7.7 Hz, 1H), 7.44 (d, *J* = 7.0 Hz, 2H), 4.09 (s, 3H), 3.14 (t, *J* = 12.1 Hz, 1H), 2.61 – 2.50 (m, 4H), 2.29 (d, *J* = 12.9 Hz, 2H), 2.07 – 1.97 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.1, 167.0, 156.6, 149.4, 146.8, 137.4, 135.8, 130.4, 130.1, 128.0, 127.9, 127.5, 125.6, 124.1, 120.4, 52.9, 42.8, 41.5, 34.0, 29.9. HRMS (ESI+) *m/z* calculated for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1600, found 360.1600.

3-((2-(3-fluorophenyl)-3-methylmorpholino)methyl)cyclopentan-1-one [33]



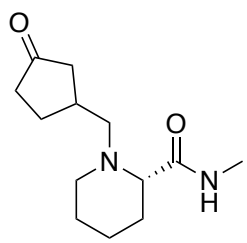
According to the **general procedure for HBF_4•OEt_2 protection**, 4-(cyclopentylmethyl)-2-(3-fluorophenyl)-3-methylmorpholine (**S33**) (83.2 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol**: the resultant **S33•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on alumina (Brockmann grade II, 15 mm fritted glass column, 30 mL Al_2O_3) using gradient 0% → 10% → 20% → 30% → 40% → 50% EtOAc/hexanes as eluent afforded 3-((2-(3-fluorophenyl)-3-methylmorpholino)methyl)cyclopentan-1-one (**33**) as a white solid.

Run 1: (41.9 mg, 0.144 mmol, 47.9% yield, 1:1 d.r.), (14.7 mg, 0.053 mmol, 17.7% rsm). **Run 2:** (39.4 mg, 0.135 mmol, 45.1% yield, 1:1 d.r.), (18.2 mg, 0.066 mmol, 21.9% rsm). **Run 3:** (42.8 mg, 0.147 mmol, 49.0% yield, 1:1 d.r.), (15.5 mg, 0.056 mmol, 18.6% rsm). **Average: 47.3% yield ± 2.0%, 1:1 d.r., 19.4% rsm ± 2.2%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 1H), 7.13 – 7.09 (m, 1H), 7.09 – 7.04 (m, 1H), 7.02 – 6.95 (m, 1H), 4.05 (app. t, *J* = 8.5 Hz, 1H), 3.99 – 3.91 (m, 1H), 3.79 (app. qd, *J* = 11.6, 2.4 Hz, 1H), 2.86 (app. t, *J* = 11.7 Hz, 1H), 2.81 – 2.73 (m, 1H), 2.56 – 2.11 (m, 8H), 2.00 (app. dd, *J* = 17.9, 8.7 Hz, 0.5H), 1.87 (app. dd, *J* = 17.9, 8.7 Hz, 0.5H), 1.76 – 1.65 (m, 0.5H), 1.63 – 1.51 (m, 0.5H), 0.83 (app. t, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.4 (219.3), 162.9 (d, *J* = 245.8 Hz), 142.9 (d, *J* = 7.2 Hz) [142.8 (d, *J* = 7.1 Hz)], 129.9 (d, *J* = 8.1 Hz) [129.9 (d, *J* = 8.1 Hz)], 124.0 (d, *J* = 3.3 Hz) [123.9 (d, *J* = 3.4 Hz)], 115.2 (d, *J* = 21.2 Hz) [115.1 (d, *J* = 22.1 Hz)], 115.0 (d, *J* = 21.7 Hz) [114.9 (d, *J* = 21.6 Hz)], 84.6 (d, *J* = 3.7 Hz), 67.2, 61.3 (61.3), 58.6 (58.2), 52.9 (52.7), 44.1 (44.0), 38.1 (37.8), 35.0 (34.9), 27.9 (27.7), 15.5 (15.4). ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.2. HRMS (ESI+) *m/z* calculated for $C_{17}H_{23}NO_2F$ $[M+H]^+$: 292.1713, found 292.1700.

Site of oxidation/formation of diastereoisomers confirmed by de novo synthesis. See page 143.

(2*S*)-*N*-methyl-1-((3-oxocyclopentyl)methyl)piperidine-2-carboxamide [34]



According to the **general procedure for HBF_4•OEt_2 protection**, (*S*)-1-(cyclopentylmethyl)-*N*-methylpiperidine-2-carboxamide (**S34**) (67.3 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S34•HBF_4** (0.300 mmol, 1.0 equiv.),

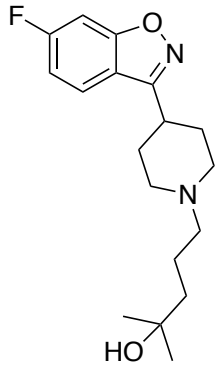
(*S,S*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2/1% NH_4OH → 2% → 4% MeOH/CH_2Cl_2/1% NH_4OH gradient as eluent afforded the crude product, which was partitioned between CH_2Cl and 1 M NaOH. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (x2). This extraction removes traces of water and NH_4OH from the column conditions. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford (2*S*)-*N*-methyl-1-((3-oxocyclopentyl)methyl)piperidine-2-carboxamide (**34**) as a colorless oil as a mixture of diastereomers.

Run 1: (36.6 mg, 0.154 mmol, 51.1% yield, 2:1 d.r.), 0% rsm. **Run 2:** (32.9 mg, 0.138 mmol, 46.0%, 1.8:1 d.r.), 0% rsm. **Run 3:** (32.0 mg, 0.134 mmol, 44.8% yield, 1.7:1 d.r.), 0% rsm. **Average: 47.3% yield ± 3.3%, 1.8:1 dr, 0% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (br. s, 0.7H), 6.46 (br. s, 0.3H), 3.11 – 3.02 (m, 1H), 2.80 (d, *J* = 5.0 Hz, 2H), 2.77 (d, *J* = 5.0 Hz, 1H), 2.70 (dd, *J* = 10.1, 3.6 Hz, 0.7H), 2.67 (dd, *J* = 10.4, 3.6 Hz, 0.3H), 2.54 – 2.04 (m, 7H), 2.04 – 1.87 (m, 2H), 1.77 (dd, *J* = 18.9, 8.5 Hz, 0.7H), 1.72 – 1.61 (m, 1H), 1.60 – 1.35 (m, 3H), 1.34 – 1.18 (m, 1.3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (218.9), 218.5, (175.2), 175.1, (68.7), 68.3, (61.4), 61.4, 51.9, (51.7), 43.8, (43.7), 38.0, (37.6), 34.7, (34.3), (30.3), 29.8, 27.8, (27.6), 25.8, (25.7), (24.9), 24.7, (23.4), 23.3. HRMS (ESI+) *m/z* calculated for $C_{13}H_{23}N_2O_2$ $[M+H]^+$: 239.1760, found 239.1755.

Site of oxidation/formation of diastereoisomers confirmed by de novo synthesis. See page 144.

5-(4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)-2-methylpentan-2-ol [35]



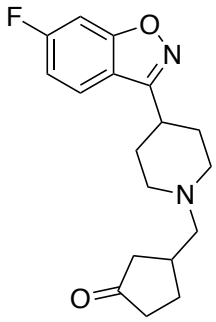
According to the **general procedure for HBF_4•OEt_2 protection**, 6-fluoro-3-(1-(4-methylpentyl)piperidin-4-yl)benzo[*d*]isoxazole (**S35**) (152.2 mg, 0.500 mmol, 1.0 equiv.) was protected with HBF_4•OEt_2 (75.5 µL, 0.550 mmol, 54 wt.%, 1.1 equiv.) in CH_2Cl_2 (2.0 mL, 0.25 M). The oxidation was carried out according to **General Method C: Iterative Catalyst Addition Protocol**: the resultant **S35•HBF_4** (0.500 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (708.7 mg, 7.5 mmol, 15.0 equiv.), (*S,S*)-Mn(PDP) catalyst **2** (23.3 mg, 0.025 mmol, 5 mol%), H_2O_2 (50% wt. in H_2O, 170 mg, 2.5 mmol, 5.0 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. A further addition of (*S,S*)-Mn(PDP) catalyst **2** (23.3 mg, 0.025 mmol, 5 mol%) in MeCN (0.2 mL) was added dropwise to the reaction at 1.5 hours. The reaction was worked up

according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 4% → 6% → 8% → 10% MeOH/CH_2Cl_2 as eluent afforded 5-(4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)-2-methylpentan-2-ol (**35**) as an off white solid.

Run 1: (84.5 mg, 0.264 mmol, 52.7% yield), (37.7 mg, 0.124 mmol, 24.8% rsm). **Run 2:** (76.5 mg, 0.239 mmol, 47.8%), (32.6 mg, 0.107 mmol, 21.4% rsm). **Run 3:** (85.3 mg, 0.266 mmol, 53.2% yield), (24.3 mg, 0.080 mmol, 16.0% rsm). **Average: 51.2% yield ± 3.0%, 20.7% rsm ± 4.4%.**

^{1}H NMR (500 MHz, CD_3OD) δ 7.91 (dd, *J* = 8.8, 5.1 Hz, 1H), 7.38 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.16 (td, *J* = 8.9, 2.1 Hz, 1H), 3.23 – 3.09 (m, 3H), 2.45 (app. t, *J* = 7.4 Hz, 2H), 2.27 (td, *J* = 11.8, 2.9 Hz, 2H), 2.17 – 1.99 (m, 4H), 1.73 – 1.63 (m, 2H), 1.55 – 1.48 (m, 2H), 1.21 (s, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ 165.8 (d, *J* = 249.2 Hz), 165.2 (d, *J* = 13.8 Hz), 162.5, 124.4 (d, *J* = 11.2 Hz), 118.5, 113.5 (d, *J* = 25.6 Hz), 98.0 (d, *J* = 27.3 Hz), 70.9, 60.5, 54.4, 42.9, 35.2, 31.1, 29.4, 22.5. ^{19}F NMR (471 MHz, CD_3OD) δ -111.7. HRMS (ESI+) *m/z* calculated for $C_{18}H_{26}N_2O_2F$ $[M+H]^+$: 321.1978, found 321.1976.

3-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)methyl)cyclopentan-1-one [36]



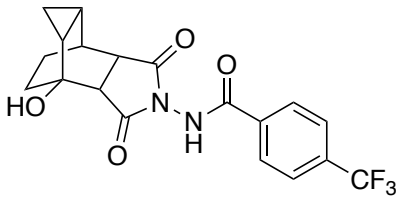
According to the **general procedure for HBF_4•OEt_2 protection**, 3-(1-(cyclopentylmethyl)piperidin-4-yl)-6-fluorobenzo[*d*]isoxazole (**S36**) (90.7 mg, 0.300 mmol, 1.0 equiv.) was protected with HBF_4•OEt_2 (45 µL, 0.330 mmol, 54 wt.%, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method C: Iterative Catalyst Addition Protocol**: the resultant **S36•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 7.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. A further addition of (*R,R*)-Mn(CF_3PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction at 1 hour. A further addition of (*R,R*)-Mn(CF_3PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%) in MeCN (0.1 mL) was added dropwise to the reaction after an additional 1 hour. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 80% → 90% → 100% EtOAc → 10% MeOH/EtOAc as eluent afforded 3-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)methyl)cyclopentan-1-one (**36**) as a pale yellow oil.

Run 1: (37.1 mg, 0.117 mmol, 39.1% yield), <10% rsm. **Run 2:** (41.3 mg, 0.131 mmol, 43.5%), <10% rsm. **Run 3:** (43.1 mg, 0.136 mmol, 45.4% yield), <10% rsm. **Average: 42.7% yield ± 3.2%, <10% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.24 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.06 (td, *J* = 8.8, 2.1 Hz, 1H), 3.15 – 2.96 (m, 3H), 2.55 – 2.37 (m, 4H), 2.37 – 1.94 (m, 10H), 1.72 – 1.60 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.6, 164.2 (d, *J* = 250.8 Hz), 164.0 (d, *J* = 13.5 Hz), 161.2, 122.7 (d, *J* = 11.1 Hz), 117.4, 112.5 (d, *J* = 25.4 Hz), 97.6 (d, *J* = 26.6 Hz), 63.6, 54.1, 53.9, 44.1, 38.0, 34.7, 30.6, 27.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ -109.6. HRMS (ESI+) *m/z* calculated for $C_{18}H_{22}N_2O_2F$ $[M+H]^+$: 317.1665, found 317.1652.

Site of oxidation confirmed by de novo synthesis. See page 146.

4-hydroxy-1,3-dioxooctahydro-4,6-ethanocyclopropa[*f*]isoindol-2(1*H*)-yl)-4-(trifluoromethyl)benzamide [37]

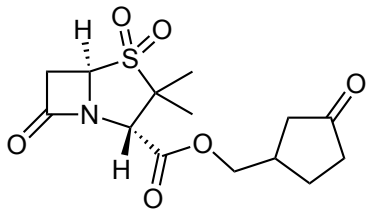


The reaction was run with **General Method B: Single Catalyst Addition Protocol**: *N*-(1,3-dioxooctahydro-4,6-ethanocyclopropa[*f*]isoindol-2(1*H*)-yl)-4-(trifluoromethyl)benzamide (**S37**) (113.5 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 30% → 40% → 50% → 60% → 70% → 80% EtOAc/hexanes as eluent afforded 4-hydroxy-1,3-dioxooctahydro-4,6-ethanocyclopropa[*f*]isoindol-2(1*H*)-yl)-4-(trifluoromethyl)benzamide (**37**) as a white solid as a mixture of rotamers.

Run 1: (64.9 mg, 0.165 mmol, 55.1% yield), (18.6 mg, 0.049 mmol, 16.4% rsm). **Run 2:** (61.0 mg, 0.155 mmol, 51.8% yield), (14.5 mg, 0.038 mmol, 12.8% rsm). **Run 3:** (64.0 mg, 0.163 mmol, 54.3% yield), (11.5 mg, 0.030 mmol, 10.1% rsm). **Average: 53.7% yield ± 1.7%, 13.1% rsm ± 3.2%.**

^{1}H NMR (500 MHz, CD_3OD) δ 8.09 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H), 3.57 – 3.41 (m, 1H), 3.26 – 3.10 (m, 1H), 2.49 – 2.41 (m, 1H), 1.89 – 1.70 (m, 1H), 1.48 – 1.37 (m, 3H), 1.26 – 1.18 (m, 1H), 1.07 – 1.00 (m, 1H), 0.70 – 0.62 (m, 1H). ^{13}C NMR (126 MHz, CD_3OD) δ 177.4, 176.2, 166.9, 136.4, 135.1 (q, *J* = 33.1 Hz), 129.7, 126.8 (q, *J* = 3.9 Hz), 125.2 (q, *J* = 271.8 Hz), 73.1, 29.1, 27.9, 21.7, 19.7, 17.7, 6.1. ^{19}F NMR (471 MHz, CD_3OD) δ -64.6. HRMS (ESI+) *m/z* calculated for $C_{19}H_{18}N_2O_4F_3$ $[M+H]^+$: 395.1219, found 395.1209.

(3-oxocyclopentyl)methyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide [38]



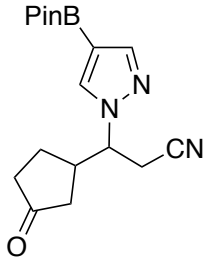
The reaction was run with **General Method B: Single Catalyst Addition Protocol:** cyclopentylmethyl (2S,5R)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (**S38**) (63.1 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283 mg, 3.00 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.0 mg, 0.020 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (35 mm fritted glass column, 75 mL SiO_2) using 40% EtOAc/Hex → 50% EtOAc/Hex gradient as eluent afforded (3-oxocyclopentyl)methyl (2*S*,5*R*)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4,4-dioxide (**38**) as a colorless oil.

Run 1: (36.2 mg, 0.110 mmol, 55% yield), <5% rsm, (d.r. 1.18:1). **Run 2:** (38.9 mg, 0.118 mmol, 59% yield), <5% rsm, (d.r. 1.13:1). **Run 3:** (36.9 mg, 0.112 mmol, 56% yield), <5% rsm, (d.r. 1.05:1). **Average: 56.6% yield ± 2.1%, <5% rsm, 1.12:1 d.r.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.61 (app. td, *J* = 4.5, 2.0 Hz, 1H), 4.38 (s, 0.5H), 4.37 (s, 0.5H), 4.23 (m, 2H), 3.49 (dd, *J* = 16.2, 4.4 Hz, 1H), 3.42 (app dt, *J* = 16.3, 2.3 Hz, 1H), 2.61 (m, 1H), 2.45-2.38 (m, 1H), 2.37-2.30 (m, 1H), 1.99-1.92 (m, 1H), 1.75-1.64 (m, 1H), 1.59 (s, 3H), 1.30 (s, 1.5H), 1.39 (s, 1.5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 217.1 (216.9), 170.9 (170.8), 167.0, 69.4 (69.2), 63.3 (63.3), 62.8 (62.7), 61.2 (61.2), 41.9 (41.7), 38.5 (38.4), 37.8 (37.6), 35.7 (35.6), 26.2, 20.5 (20.4), 18.7 (18.7). HRMS (ESI+) *m/z* calculated for $C_{14}H_{20}NO_6S^+$ $[M+H]^+$: 330.1006, found: 330.1010.

Site of oxidation confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

3-(3-oxocyclopentyl)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl)propanenitrile [39]



The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 3-cyclopentyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl)propanenitrile (**S39**) (63.0 mg, 0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at -36 ºC with a dry ice/1,2-dichloroethane bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method A. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 20% → 30% → 40% → 50% → 60% EtOAc/hexanes as eluent afforded 2 separate

diastereosiomers of 3-(3-oxocyclopentyl)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl)propanenitrile (**39**) each as a white solid.

Run 1: (6.2 mg, 0.019 mmol, 9.4% yield of 1st ketone diastereomer), (17.8 mg, 0.054 mmol, 27.0% yield of 2nd ketone diastereomer), (36.4% overall yield, 1:2.9 d.r.), 0% rsm. **Run 2:** (9.2 mg, 0.028 mmol, 14.0% yield of 1st ketone diastereomer), (17.0 mg, 0.052 mmol, 25.8% yield of 2nd ketone diastereomer), (39.8% overall yield, 1:1.8 d.r.), 0% rsm. **Run 3:** (5.9 mg, 0.018 mmol, 9.0% yield of 1st ketone diastereomer), (17.9 mg, 0.054 mmol, 27.2% yield of 2nd ketone diastereomer), (36.2% overall yield, 1:3.0 d.r.), 0% rsm. **Average: 37.5% yield ± 2.0%, 1:2.6 d.r., 0% rsm.**

First diastereoisomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.79 (s, 1H), 4.32 (td, *J* = 9.0, 4.6 Hz, 1H), 3.13 (dd, *J* = 16.9, 8.7 Hz, 1H), 2.90 (dd, *J* = 16.9, 4.6 Hz, 1H), 2.90 – 2.80 (m, 1H), 2.52 (dd, *J* = 17.9, 7.6 Hz, 1H), 2.30 (dd, *J* = 18.9, 8.4 Hz, 1H), 2.22 – 2.08 (m, 1H), 1.93 (dd, *J* = 17.9, 11.6 Hz, 1H), 1.84 – 1.75 (m, 1H), 1.64 – 1.52 (m, 1H), 1.33 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.4, 147.0, 136.8, 116.4, 83.7, 62.8, 42.1, 41.5, 38.2, 26.5, 25.0, 24.9, 23.4. HRMS (ESI+) *m/z* calculated for $C_{17}H_{25}BN_3O_3$ $[M+H]^+$: 330.1989, found 330.1975.

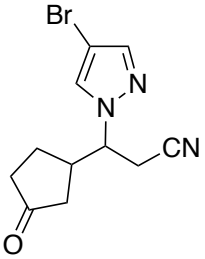
Site of oxidation confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

Second diastereoisomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.76 (s, 1H), 4.35 (td, *J* = 8.5, 4.9 Hz, 1H), 3.12 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.98 (dd, *J* = 17.0, 4.9 Hz, 1H), 2.95 – 2.86 (m, 1H), 2.37 – 2.19 (m, 3H), 2.13 (dd, *J* = 18.4, 6.9 Hz, 1H), 2.01 (dd, *J* = 17.8, 11.5 Hz, 1H), 1.67 – 1.55 (m, 1H), 1.32 (s, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.4, 146.9, 136.6, 116.5, 83.7, 62.6, 41.6, 41.5, 38.6, 26.9, 25.0, 24.9, 22.8. HRMS (ESI+) *m/z* calculated for $C_{17}H_{25}BN_3O_3$ $[M+H]^+$: 330.1989, found 330.1983.

Site of oxidation confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

3-(4-bromo-1*H*-pyrazol-1-yl)-3-(3-oxocyclopentyl)propanenitrile [40]



Without HBF_4 Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 3-(4-bromo-1*H*-pyrazol-1-yl)-3-cyclopentylpropanenitrile (**S40**) (80.4 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 20% → 30% → 40%

→ 50% → 60% EtOAc/hexanes as eluent afforded 2 diastereoisomers of 3-(4-bromo-1*H*-pyrazol-1-yl)-3-(3-oxocyclopentyl)propanenitrile (**40**) each as a white solid.

Run 1: (11.4 mg, 0.040 mmol, 13.5% yield of 1st ketone diastereomer), (15.2 mg, 0.054 mmol, 18.0% yield of 2nd ketone diastereomer), (31.5% overall yield, 1:1.3 d.r.), (12.2 mg, 0.045 mmol, 15.2% rsm). **Run 2:** (11.5 mg, 0.041 mmol, 13.6% yield of 1st ketone diastereomer), (15.5 mg, 0.055 mmol, 18.3% yield of 2nd ketone diastereomer), (31.9% overall yield, 1:1.3 d.r.), <5% rsm. **Run 3:** (12.0 mg, 0.043 mmol, 14.2% yield of 1st ketone diastereomer), (18.2 mg, 0.065 mmol, 21.5% yield of 2nd ketone diastereomer), (35.7% overall yield, 1:1.5 d.r.), <5% rsm. **Average: 33.0% yield ± 2.3%, 1:1.4 d.r., 8.4% rsm ± 5.9%.**

With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 3-(4-bromo-1*H*-pyrazol-1-yl)-3-cyclopentylpropanenitrile (**S40**) (53.6 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S40•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 20% → 30% → 40% → 50% → 60% EtOAc/hexanes as eluent afforded only recovered starting material.

Yield: 0% yield, (14.1 mg, 0.053 mmol, 26.3% rsm).

With HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, 3-(4-bromo-1*H*-pyrazol-1-yl)-3-cyclopentylpropanenitrile (**S40**) (53.6 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method B: Single Catalyst Addition Protocol**: the resultant **S40•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 20% → 30% → 40% → 50% → 60% EtOAc/hexanes as eluent afforded only recovered starting material.

Run 1: 0% yield, (35.0 mg, 0.131 mmol, 65.3% rsm). **Run 2:** 0% yield, (36.4 mg, 0.136 mmol, 67.9% rsm). **Average: 0% yield, 66.6% rsm.**

First diastereoisomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.55 (s, 1H), 4.28 (td, *J* = 9.1, 4.3 Hz, 1H), 3.09 (dd, *J* = 16.9, 8.9 Hz, 1H), 2.87 (dd, *J* = 16.9, 4.4 Hz, 1H), 2.93 – 2.79 (m, 1H), 2.51 (dd, *J* = 17.8, 7.6 Hz, 1H), 2.32 (dd, *J* = 18.9, 8.4 Hz, 1H), 2.17 (ddd, *J* = 19.6, 11.5, 9.1 Hz, 1H), 1.93 (dd, *J* = 17.7, 11.5 Hz, 1H), 1.86 – 1.77 (m, 1H), 1.62 – 1.52 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.0, 141.6, 130.0, 116.2, 93.9, 63.3, 42.0, 41.3, 38.2, 26.5, 23.3. HRMS (ESI+) *m/z* calculated for $C_{11}H_{13}N_3OBr$ $[M+H]^+$: 282.0242, found 282.0249.

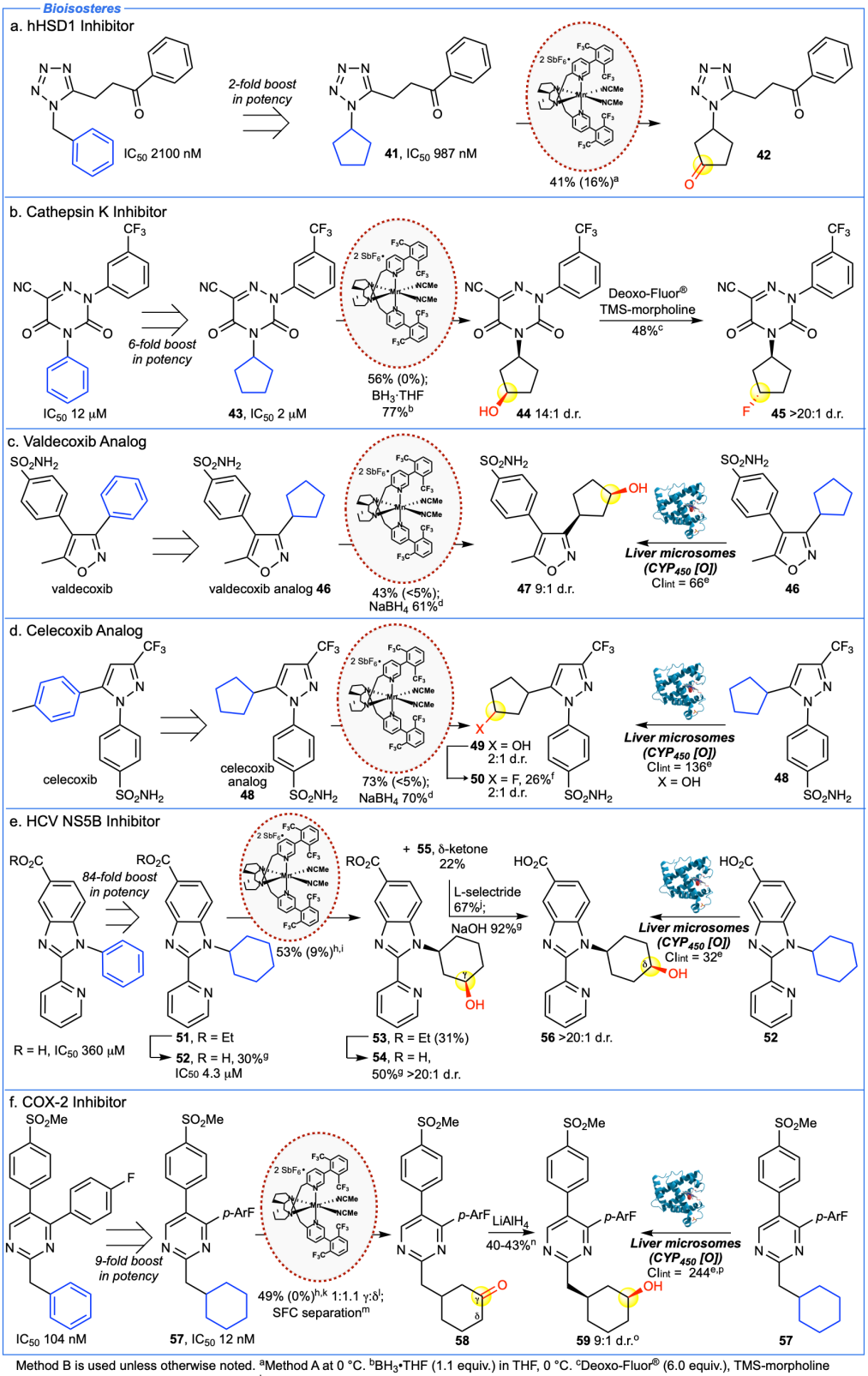
Site of oxidation confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

Second diastereoisomer

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.53 (s, 1H), 4.31 (td, *J* = 8.6, 4.6 Hz, 1H), 3.09 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.95 (dd, *J* = 17.0, 4.6 Hz, 1H), 2.92 – 2.83 (m, 1H), 2.39 – 2.21 (m, 3H), 2.14 (dd, *J* = 18.4, 7.6 Hz, 1H), 1.99 (dd, *J* = 18.3, 10.5 Hz, 1H), 1.68 – 1.54 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 215.0, 141.5, 129.7, 116.3, 94.0, 63.1, 41.6, 41.2, 38.5, 26.8, 22.7. HRMS (ESI+) *m/z* calculated for $C_{11}H_{13}N_3OBr$ $[M+H]^+$: 282.0242, found 282.0244.

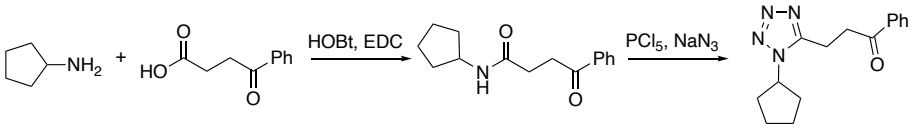
Site of oxidation confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

IV. Supplementary Figure 2. Bioisosteres

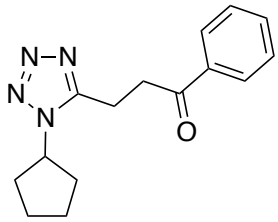


Method B is used unless otherwise noted. [a]Method A at 0 °C. [b]BH_3•THF (1.1 equiv.) in THF, 0 °C. [c]Deoxo-Fluor® (6.0 equiv.), TMS-morpholine (6.0 equiv.), refluxed in CH_2Cl_2 overnight. [d]$NaBH_4$ (1.1 equiv.) in MeOH, 0 °C. [e]Unscaled intrinsic clearance in rat liver microsome preparations, μL of compound metabolized per minute per mg of protein. For human liver microsome preparations, see SI. [f]Deoxo-Fluor® (6.0 equiv.), TMS-morpholine (6.0 equiv.), refluxed in toluene overnight. [g]2M NaOH (2.7 equiv.) in MeOH, 60 °C. [h]Nitrogen was HBF_4•OEt_2 protected. [i]Method C [3 x 5 mol% $Mn(CF_3$-PDP) **1**] at -36 °C. Starting material recycled once. [j]L-selectride® (1.0 equiv.) in THF, -78 °C. [k]Modified Method A [5 mol% $Mn(CF_3$-PDP) **1**] at -36 °C. [l]Ratios are statistically corrected. [m]Ketone regioisomers/enantiomers separated by chiral super critical fluid separation. [n]$LiAlH_4$ (1.1 equiv.) in THF, -78 °C. [o]Optical rotation based on a 9:1 mixture of diastereoisomers. [p]Unscaled intrinsic clearance in human liver microsome preparations: 223 μL/min/mg.

Preparation of Substrates and Compound Characterization for Supplementary Figure 2



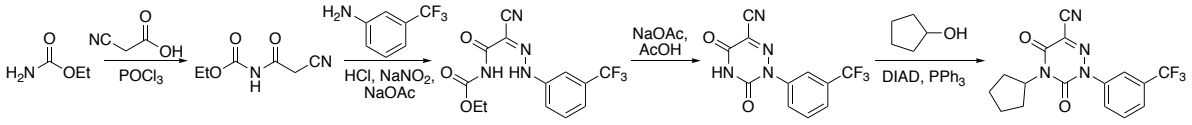
3-(1-cyclopentyl-1*H*-tetrazol-5-yl)-1-phenylpropan-1-one [41]



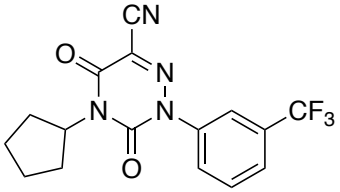
To a solution of cyclopentylamine (0.99 mL, 851.5 mg, 10.0 mmol, 1.0 equiv.) in CH_2Cl_2 (50 mL, 0.2 M) cooled to 0 °C was added diisopropyl ethylamine (0.17 mL, 129.3 mg, 1.0 mmol, 0.1 equiv.) dropwise. Next were added, in the following order: 1) 3-benzoylpropionic acid (1.78 g, 10.0 mmol, 1.0 equiv.), 2) hydroxybenzotriazole (HOBt, 20% by weight H_2O, 1.68 g, 11.0 mmol, 1.1 equiv.), and 3) 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 1.55 g, 10.0 mmol, 1.0 equiv.) and the reaction was warmed to room temperature and stirred overnight. The reaction was washed with a 1:1 volume each of sat. aq. $NaHCO_3$ solution, 10 wt% aq. citric acid and brine. Following each of the first two washes, the aqueous layer was extracted with CH_2Cl_2 (x2) and the combined organic layer was taken onto the next wash. The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide crude *N*-cyclopentyl-4-oxo-4-phenylbutanamide which was taken onto the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 2H), 7.59 – 7.54 (m, 1H), 7.50 – 7.43 (m, 2H), 5.69 (br s, 1H), 4.19 (sxt, J = 7.0 Hz, 1H), 3.36 (t, J = 6.6 Hz, 2H), 2.58 (t, J = 6.6 Hz, 2H), 2.03 – 1.92 (m, 2H), 1.76 – 1.53 (m, 4H), 1.45 – 1.31 (m, 2H).

To a flame dried round bottom flask was added *N*-cyclopentyl-4-oxo-4-phenylbutanamide (1.68 g, 6.9 mmol, 1.0 equiv.) and CH_2Cl_2 (34 mL, 0.2 M). PCl_5 (1.43 g, 6.9 mmol, 1.0 equiv.) was added and the reaction was stirred at room temperature for 15 minutes. Sodium azide (446.0 mg, 6.9 mmol, 1.0 equiv.) was added and the reaction was stirred at room temperature for 48 h. The reaction was poured into sat. aq. $NaHCO_3$ and extracted with CH_2Cl_2 (3 x 50 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 20% EtOAc/hexanes as eluent afforded 3-(1-cyclopentyl-1*H*-tetrazol-5-yl)-1-phenylpropan-1-one (**41**) as a white solid (464.6 mg, 1.72 mmol, 25% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.97 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.48 (app. t, J = 7.8 Hz, 2H), 4.90 (tt, J = 7.7, 6.0 Hz, 1H), 3.71 (t, J = 7.0 Hz, 2H), 3.24 (t, J = 6.9 Hz, 2H), 2.31 – 2.21 (m, 2H), 2.21 – 2.12 (m, 2H), 2.09 – 1.98 (m, 2H), 1.85 – 1.74 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7, 153.9, 136.3, 133.8, 128.9, 128.2, 59.0, 35.8, 33.3, 24.6, 18.0. HRMS (ESI+) *m/z* calculated for $C_{15}H_{19}N_4O$ $[M+H]^+$: 271.1559, found 271.1551.



4-cyclopentyl-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile [43]



To a flame dried round bottom flask equipped with a reflux condenser was added ethyl carbamate (1.78 g, 20.0 mmol, 1.0 equiv.), cyanoacetic acid (1.7 g, 20.0 mmol, 1.0 equiv.) and toluene (6.25 mL, 3.2 M). Phosphoryl chloride (0.97 mL, 1.6 g, 10.4 mmol, 0.52 equiv.) dissolved in DMF (0.48 mL) was added dropwise and the reaction was heated to 75 °C for 1.5 h. The reaction was cooled to room temperature, poured CAREFULLY into ice water (30 mL) and stirred for 30 minutes. The precipitate was collected by filtration, washed with water and dried to give ethyl (2-cyanoacetyl)carbamate as a pale orange solid (2.06 g, 13.2 mmol, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (br s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.04 (s, 2H), 1.33 (t, J = 7.1 Hz, 3H).

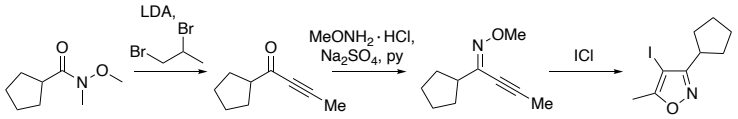
Prepared according to a reported procedure.[16] To a mixture of 3-trifluoromethylaniline (1.6 mL, 2.0 g, 12.6 mmol, 1.0 equiv.), concentrated hydrochloric acid (7.1 mL) and water (19 mL) cooled to 0 °C was added an aqueous solution of sodium nitrite (1.22 g in 9.6 mL H_2O, 17.6 mmol, 1.4 equiv.) dropwise. The reaction mixture was stirred for 30 minutes. A mixture of ethyl (2-cyanoacetyl)carbamate (2.22 g, 14.3 mmol, 1.13 equiv.) and sodium acetate (3.51 g, 42.8 mmol, 3.4 equiv.) in EtOH (63 mL) was added dropwise at 0 °C and the reaction was stirred for a further 2 h. The precipitate was collected by filtration, washed with water and dried to give ethyl (*Z*)-(2-cyano-2-(2-(3-(trifluoromethyl)phenyl)hydrazineylidene)acetyl)carbamate as an orange solid (3.72 g, 11.3 mmol, 90% ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.26 (br s, 1H), 8.45 (br s, 1H), 7.60 (t, J = 7.9 Hz, 1H), 7.57 – 7.44 (m, 3H), 4.35 (q, J = 7.1 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H).

Prepared according to a reported procedure.[16] A mixture of ethyl (*Z*)-(2-cyano-2-(2-(3-(trifluoromethyl)phenyl)hydrazineylidene)acetyl)carbamate (1.68 g, 5.1 mmol, 1.0 equiv.), sodium acetate (2.1 g, 25.6 mmol, 5.0 equiv.) and glacial acetic acid (29 mL, 0.18 M) was heated to reflux for 2 h. The reaction was cooled to room temperature, poured into water (86 mL) and stirred for 30 minutes. The precipitate was collected by filtration, washed sequentially with water (2 x 10 mL) and petroleum ether (2 x 10 mL) and dried to give 3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile as an orange solid (841.7 mg, 3.0 mmol, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.79 – 7.72 (m, 2H), 7.71 – 7.64 (m, 1H).

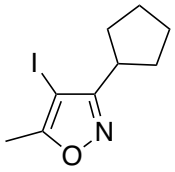
To a round bottom flask was added 3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (564.4 mg, 2.0 mmol, 1.0 equiv.), cyclopentanol (0.45 mL, 5.0 mmol, 2.5 equiv.)

and THF (40 mL, 0.05 M) and the mixture was cooled to 0 °C. A solution of DIAD (1.1 mL, 5.6 mmol, 2.8 equiv.) and triphenylphosphine (1.47 g, 5.6 mmol, 2.8 equiv.) in toluene (6.4 mL, 0.89 M) was added at once. The reaction was stirred at room temperature overnight (14 h). The reaction was concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% EtOAc/hexanes gradient as eluent afforded 4-cyclopentyl-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (**43**) as an orange solid (337.8 mg, 0.96 mmol, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (br. s, 1H), 7.79 – 7.72 (m, 2H), 7.68 – 7.62 (m, 1H), 5.27 (p, J = 8.5 Hz, 1H), 2.20 – 2.09 (m, 2H), 2.09 – 1.92 (m, 4H), 1.70 – 1.59 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.1, 146.8, 139.7, 132.0 (q, J = 33.4 Hz), 130.0, 128.6, 126.3 (q, J = 3.6 Hz), 123.4 (q, J = 272.6 Hz), 122.5 (q, J = 3.9 Hz), 111.1, 55.4, 28.3, 25.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.7. HRMS (ESI+) *m/z* calculated for $C_{16}H_{14}N_4O_2F_3$ $[M+H]^+$: 351.1069, found 351.1069.



3-cyclopentyl-4-iodo-5-methylisoxazole [S42]



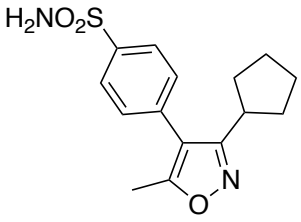
To a flame-dried round bottom flask was added diisopropylamine (9.5 mL, 68.0 mmol, 3.4 equiv.) and the flask was cooled to 0 °C. *n*-Butyl lithium (1.6 M in hexanes, 43.8 mL, 70.0 mmol, 3.5 equiv.) was added dropwise. The mixture was stirred at 0 °C for 15 minutes and then cooled to -78 °C. THF was added (50 mL, 0.4 M) followed by 1,2-dibromopropane (2.3 mL, 22.0 mmol, 1.1 equiv.) dropwise. The reaction was stirred for 30 minutes at 0 °C before being cooled to -78 °C. *N*-methoxy-*N*-methylcyclopentanecarboxamide (3.1 g, 20.0 mmol, 1.0 equiv.) was added and the reaction was allowed to warm to room temperature overnight. The mixture was cooled to 0 °C and quenched with 4 M aqueous HCl. The organic layer was separated and the aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic layer was washed with $NaHCO_3$ and brine, dried with Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% → 6% EtOAc/hexanes gradient as eluent afforded 1-cyclopentylbut-2-yn-1-one as a yellow oil (1.96 g, 14.4 mmol, 72% yield).

1-cyclopentylbut-2-yn-1-one (2.0 g, 14.4 mmol, 1.0 equiv.), methoxyamine hydrochloride (2.4 g, 28.8 mmol, 2.0 equiv.), anhydrous sodium sulfate (4.1 g, 28.8 mmol, 2.0 equiv.), pyridine (4.1 mL) and methanol (41 mL, 0.35 M) were added to a round bottom flask and the reaction was stirred at room temperature overnight. The mixture was diluted with sat. aq. NH_4Cl (50 mL) and extracted with EtOAc

(3 x 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% → 6% EtOAc/hexanes gradient as eluent afforded (*Z*)-1-cyclopentylbut-2-yn-1-one *O*-methyl oxime as a yellow oil (1.99 g, 12.0 mmol, 86% yield).

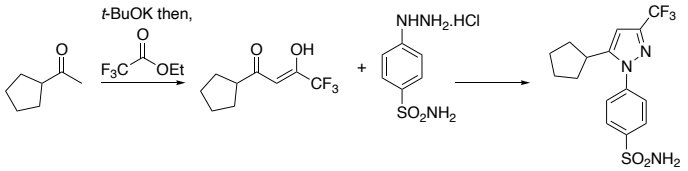
Prepared according to a reported procedure.[17] To a stirred solution of 1-cyclopentylbut-2-yn-1-one *O*-methyl oxime (774 mg, 4.68 mmol, 1.0 equiv.) in CH_2Cl_2 (47.0 mL, 0.1 M) was added iodine monochloride (1 M in CH_2Cl_2, 5.6 mL, 5.62 mmol, 1.2 equiv.) dropwise. The reaction was stirred at room temperature open to air until complete as monitored by TLC. Excess iodine monochloride was removed by washing with sat. aq. $Na_2S_2O_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo* to afford 3-cyclopentyl-4-iodo-5-methylisoxazole (**S42**) (855.9 mg, 3.088 mmol, 66% yield) which was taken onto the next step without further purification.

4-(3-cyclopentyl-5-methylisoxazol-4-yl)benzenesulfonamide [46]

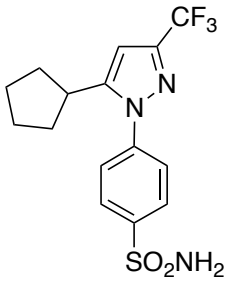


Prepared according to a reported procedure.[17] To a flame-dried round bottom flask was added benzenesulfonamide-4-boronic acid (700.0 mg, 3.50 mmol, 1.4 equiv.), potassium bicarbonate (350.0 mg, 3.50 mmol, 1.4 equiv.) and palladium(II) chloride (22.0 mg, 0.12 mmol, 5 mol%). The flask was purged and refilled with N_2 x 3. DMF and H_2O (degassed with Ar, 4:1, 20.0 mL DMF, 5.0 mL H_2O) were added, followed by 3-cyclopentyl-4-iodo-5-methylisoxazole (**S42**) (690.0 mg, 2.48 mmol, 1.0 equiv.). The flask was purged with Ar while stirring at room temperature for 5 minutes. The rubber septum was quickly replaced with a yellow polyethylene cap and secured with electrical tape. The reaction was heated to 80 °C for 2 hours. After 2 hours, the reaction was cooled to room temperature and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 20% → 30% → 40% EtOAc/hexanes gradient as eluent afforded 4-(3-cyclopentyl-5-methylisoxazol-4-yl)benzenesulfonamide (**46**) as a pale yellow solid (364.7 mg, 1.19 mmol, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 4.97 (br s, 2H), 3.03 (p, J = 7.9 Hz, 1H), 2.37 (s, 3H), 1.95 – 1.85 (m, 2H), 1.83 – 1.71 (m, 4H), 1.64 – 1.54 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 165.7, 141.1, 136.2, 130.3, 127.1, 115.3, 36.6, 32.0, 25.5, 11.6. HRMS (ESI+) *m/z* calculated for $C_{15}H_{19}N_2O_3S$ $[M+H]^+$: 307.1116, found 307.1107.



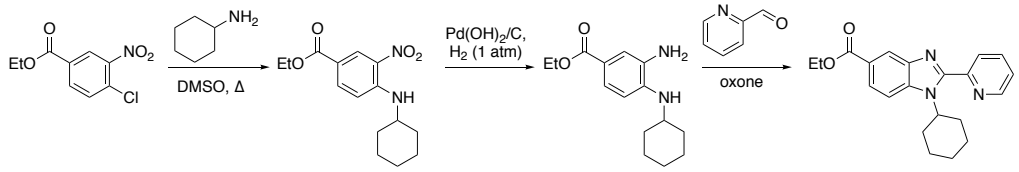
4-(5-cyclopentyl-3-(trifluoromethyl)-1*H*-pyrazole-1-yl)benzenesulfonamide [48]



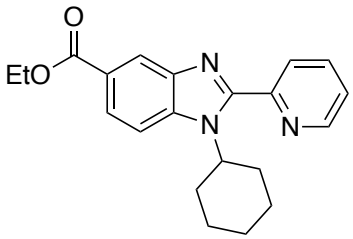
To a flame-dried round bottom flask was added 1-cyclopentyl-ethanone (999.0 mg, 8.9 mmol, 1.0 equiv.) and THF (18 mL, 0.5 M). The solution was cooled to 0 °C and *t*-BuOK (1.20 g, 10.7 mmol, 1.2 equiv.) was added in portions. After stirring at 0 °C for 30 minutes, ethyl trifluoroacetate (1.3 mL, 10.7 mmol, 1.2 equiv.) was added and the reaction mixture was allowed to stir at room temperature for 6 hours. The reaction was concentrated *in vacuo*, added to ice water and acidified with 1 M HCl to pH 6. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with H_2O (50 mL), dried with $MgSO_4$ and concentrated *in vacuo*. The solid residue was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% acetone/hexanes gradient as eluent afforded 1-cyclopentyl-4,4,4-trifluorobutane-1,3-dione (1.18 g, 5.67 mmol, 64% yield).

Prepared according to a reported procedure.[18] 4-Hydrazinylbenzenesulfonamide hydrochloride (492.1 mg, 2.2 mmol, 1.1 equiv.) was added to a stirred solution of 1-cyclopentyl-4,4,4-trifluorobutane-1,3-dione (416.4 mg, 2.0 mmol, 1.0 equiv.) in EtOH (30 mL, 0.07 M). The mixture was heated to reflux for 20 hours. The reaction was cooled to room temperature and concentrated *in vacuo*. The residue was taken up in EtOAc (20 mL), washed with H_2O (30 mL), dried with $NaSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 20% EtOAc/hexanes gradient as eluent afforded 4-(5-cyclopentyl-3-(trifluoromethyl)-1*H*-pyrazole-1-yl)benzenesulfonamide (**48**) as a white solid (533.8 mg, 1.48 mmol, 74% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 2H), 6.50 (s, 1H), 5.01 (s, 2H), 3.05 (p, *J* = 8.2 Hz, 1H), 2.04 – 1.95 (m, 2H), 1.87 – 1.73 (m, 2H), 1.69 – 1.56 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.4, 143.8 (q, *J* = 38.2 Hz), 142.8, 142.4, 127.9, 126.6, 121.3 (q, *J* = 267.0 Hz), 102.6, 36.6, 34.2, 25.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.4. HRMS (ESI+) *m/z* calculated for $C_{15}H_{17}N_3O_2F_3S$ $[M+H]^+$: 360.0994, found 360.0985.



Ethyl 1-cyclohexyl-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [51]



Prepared according to a reported procedure.[19] To a round bottom was flask was added ethyl 4-chloro-3-nitrobenzoate (1.47 g, 6.4 mmol, 1.0 equiv.), DMSO (3.7 mL, 1.7 M) and cyclohexylamine (1.54 mL, 1.33 g, 13.4 mmol, 2.1 equiv.) and the mixture was heated to 60 °C for 5 h. After cooling to room temperature, the reaction mixture was added dropwise with vigorous stirring to water (38 mL). After stirring for an additional 15 minutes, the precipitate was collected by filtration, washed with water and dried to afford ethyl 4-(cyclohexylamino)-3-nitrobenzoate as a bright yellow solid (1.62 g, 5.5 mmol, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 – 8.85 (m, 1H), 8.41 (d, *J* = 7.4 Hz, 1H), 8.02 (app. d, *J* = 9.1 Hz, 1H), 6.87 (d, *J* = 9.1 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.65 – 3.51 (m, 1H), 2.14 – 2.01 (m, 2H), 1.88 – 1.75 (m, 2H), 1.74 – 1.63 (m, 1H), 1.51 – 1.27 (m, 8H).

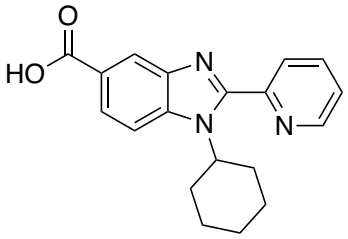
To a round bottom flask was added ethyl 4-(cyclohexylamino)-3-nitrobenzoate (1.62 g, 5.5 mmol, 1.0 equiv.), MeOH (10 mL, 0.55 M) and $Pd(OH)_2/C$ (8 mg, 0.06 mmol, 1 mol%). The flask was sealed with a rubber septum, purged with hydrogen and stirred under a hydrogen balloon (1 atm) at room temperature until the reaction was complete by TLC (3 days). The reaction was filtered through celite using MeOH as the eluent and concentrated *in vacuo* to afford ethyl 3-amino-4-(cyclohexylamino)benzoate as a dark purple solid (1.4 g, 5.5 mmol, quantitative). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.41 (d, *J* = 1.9 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.47 (br s, 3H), 3.33 (tt, *J* = 10.2, 3.8 Hz, 1H), 2.13 – 2.01 (m, 2H), 1.83 – 1.73 (m, 2H), 1.71 – 1.62 (m, 1H), 1.46 – 1.28 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.30 – 1.16 (m, 3H).

To a round bottom flask was added ethyl 3-amino-4-(cyclohexylamino)benzoate (1.2 g, 4.5 mmol, 1.0 equiv.), DMF (5.5 mL) and water (0.23 mL). 2-Pyridine carboxyaldehyde (0.53 mL, 592.3 mg, 5.5 mmol, 1.23 equiv.) was added followed by oxone (445.0 mg, 2.9 mmol, 0.65 equiv.). The reaction was stirred at room temperature for 1 h. Water (22 mL) was added and the pH of the reaction mixture was brought up to 9 by the addition of 1 M NaOH. The brown precipitate was collected by filtration, washed with water and dried. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 10% → 20% → 30% → 40% EtOAc/hexanes gradient as eluent afforded ethyl 1-cyclohexyl-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**51**) as a pale brown solid (826.0 mg, 2.4 mmol, 53% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 – 8.70 (m, 1H), 8.55 (d, *J* = 1.5 Hz, 1H), 8.23 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.99 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.87 (td, *J* = 7.8, 1.8 Hz, 1H), 7.72 (d, *J* = 8.7 Hz, 1H), 7.38 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 5.47 (tt, *J* = 12.4, 4.0 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 2.29 (qd, *J* = 12.5, 3.6 Hz, 2H), 2.15 – 2.05 (m, 2H), 2.00 – 1.91 (m, 2H), 1.84 – 1.75 (m, 1H), 1.51 – 1.29 (m, 3H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 152.6, 150.8, 148.9, 143.2, 138.2, 137.1, 125.8, 124.6,

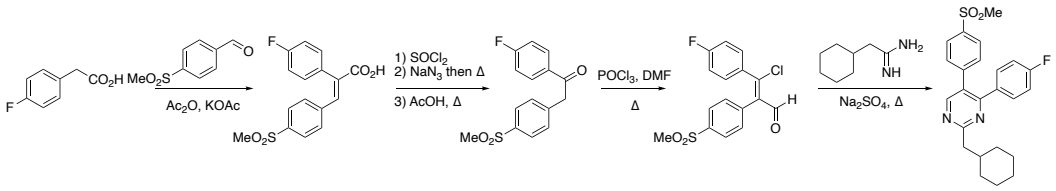
124.1, 124.0, 122.9, 112.9, 60.9, 57.3, 31.4, 26.2, 25.6, 14.5. HRMS (ESI+) *m/z* calculated for $C_{21}H_{24}N_3O_2$ $[M+H]^+$: 350.1869, found 350.1859.

1-cyclohexyl-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid [52]

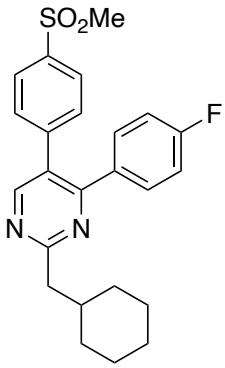


Prepared according to a reported procedure.[19] Ethyl 1-cyclohexyl-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**51**) (70.0 mg, 0.20 mmol, 1.0 equiv.) was dissolved in MeOH (0.4 mL, 0.5 M) and 2M NaOH (0.27 mL, 0.53 mmol, 2.7 equiv.) was added. The mixture was stirred at 60 °C for 2 h. MeOH was removed under reduced pressure and the residue was acidified to pH 4 with glacial acetic acid. The precipitated carboxylic acid was collected by filtration, washed with water and dried to give 1-cyclohexyl-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid (**52**) as a beige solid (19.1 mg, 0.059 mmol, 30% yield).

^{1}H NMR (500 MHz, DMSO) δ 8.78 (d, *J* = 4.9 Hz, 1H), 8.28 (s, 1H), 8.17 (d, *J* = 7.9 Hz, 1H), 8.07 – 7.96 (m, 2H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.57 (t, *J* = 6.2 Hz, 1H), 5.39 – 5.29 (m, 1H), 2.34 – 2.23 (m, 2H), 1.96 (d, *J* = 12.1 Hz, 2H), 1.88 (d, *J* = 11.8 Hz, 2H), 1.68 (d, *J* = 10.4 Hz, 1H), 1.44 – 1.30 (m, 3H). ^{13}C NMR (126 MHz, DMSO) δ 167.7, 152.1, 150.0, 149.0, 142.5, 137.6, 137.5, 125.6, 124.6, 123.8, 121.5, 113.3, 56.7, 30.9, 25.7, 23.7. HRMS (ESI+) *m/z* calculated for $C_{19}H_{20}N_3O_2$ $[M+H]^+$: 322.1556, found 322.1546.



2-(cyclohexylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidine [57]



Prepared according to a reported procedure.[20] A round bottom flask fitted with a reflux condenser was charged with 4-fluorophenyl acetic acid (2.5 g, 16.2 mmol, 1.0 equiv.), 4-(methylsulfonly)benzaldehyde (3.00 g, 16.2 mmol, 1.0 equiv.), potassium acetate (2.11 g, 21.5 mmol, 1.33 equiv.) and acetic anhydride (6.5 mL, 7.1 g, 69.2 mmol, 4.3 equiv.). The mixture was heated to 140 °C for 48 h. The reaction was cooled to room temperature, water was added (40 mL) and the mixture was treated with a solution of 10 M NaOH until pH 12 was reached, followed by conc. HCl until pH 1 was reached. The resulting mixture was extracted with CH_2Cl_2 (3 x 80 mL). The combined organic layer was extracted with 2 M NaOH (3 x 80 mL) and water (80 mL). The combined aqueous solutions were washed with CH_2Cl_2 (100 mL), then acidified with conc. HCl until pH 1 was reached, and finally extracted with CH_2Cl_2 (5 x 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and

concentrated *in vacuo*. The yellow solid was recrystallized from ethanol to afford (*E*)-2-(4-fluorophenyl)-3-(4-(methylsulfonyl)phenyl)acrylic acid and residual starting material as a white solid (1.25 g, 3.9 mmol, 24% yield).

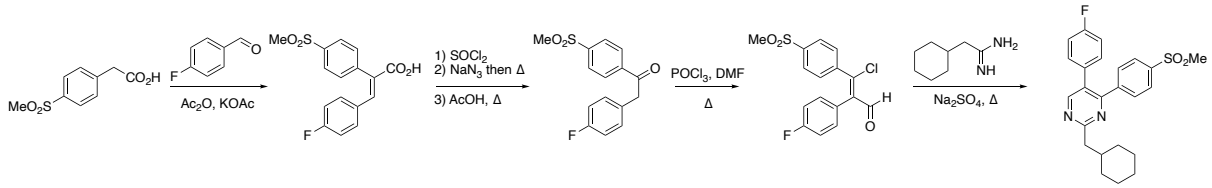
To a round bottom flask was added (*E*)-2-(4-fluorophenyl)-3-(4-(methylsulfonyl)phenyl)acrylic acid (1.0 g, 3.12 mmol, 1.0 equiv.) and dichloromethane (9.4 mL, 0.33 M). The mixture was cooled to 0 °C and oxalyl chloride (0.8 mL, 9.4 mmol, 3.0 equiv.) and DMF (2 μL, 0.03 mmol, 1 mol%) were added. The reaction was allowed to stir at room temperature overnight. The reaction mixture was concentrated *in vacuo*, dissolved in acetone (3 mL) and added dropwise to a solution of sodium azide (263.7 mg, 4.05 mmol, 1.3 equiv.) in water (3 mL) maintained at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight. The next day, the reaction was diluted with water (20 mL) and extracted with dichloromethane (3 x 20 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was dissolved in toluene (17 mL) and heated at reflux for 1.5 h, after which it was cooled to room temperature, concentrated *in vacuo*, and dissolved in 2:1 AcOH:H_2O (2.1 mL:1.0 mL). The solution was heated to reflux for 2 h, after which it was cooled to room temperature, diluted with water (6 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 → 2% EtOAc/CH_2Cl_2 → 2% MeOH/CH_2Cl_2 gradient as eluent to afford 1-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)ethan-1-one as a white solid (0.64 g, 2.2 mmol, 70% yield).

To a flame dried round bottom flask was added DMF (3.3 mL, 1.1 M) and the flask was cooled to 0 °C. Phosphoryl chloride (2.0 mL, 21.5 mmol, 6.0 equiv.) was added dropwise and the reaction was stirred at room temperature for 30 minutes. The reaction was cooled to 0 °C and 1-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)ethan-1-one (1.0 g, 3.6 mmol, 1.0 equiv.) was added. The reaction was stirred at 0 °C for a further 1 h and was then heated to 65 °C for 5 h. The reaction was cooled to room temperature and poured CAREFULLY into ice cold sat. aq. $NaHCO_3$ solution. The solution was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was washed with water (2 x 50 mL) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 10% → 20% → 30% → 40% EtOAc/hexanes gradient as eluent afforded (*Z*)-3-chloro-3-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)acrylaldehyde as a pale yellow solid (816.4 mg, 2.4 mmol, 67% yield).

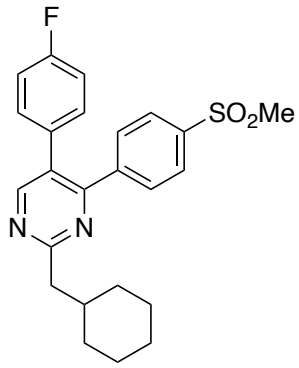
To the round bottom flask containing 2-cyclohexylacetimidamide•HCl salt (**S44**) (2.32 g, 13.1 mmol, 4.0 equiv.) was added sodium carbonate (1.75 g, 16.5 mmol, 5.0 equiv.), (*Z*)-3-chloro-3-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)acrylaldehyde (1.11 g, 3.3 mmol, 1.0 equiv.) and MeCN (22.0 mL, 0.15 M). The reaction was heated to reflux overnight (18 h), after which the reaction was cooled to room

temperature, quenched with water (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% → 30% → 40% EtOAc/hexanes gradient eluent followed by recrystallization from acetone/hexanes afforded 2-(cyclohexylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidine (**57**) as a white solid (711.5 mg, 1.68 mmol, 51% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.44 – 7.36 (m, 4H), 7.03 – 6.97 (m, 2H), 3.09 (s, 3H), 2.95 (d, J = 7.2 Hz, 2H), 2.10 – 1.99 (m, 1H), 1.79 – 1.70 (m, 4H), 1.69 – 1.63 (m, 1H), 1.34 – 1.18 (m, 3H), 1.16 – 1.06 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.7, 163.8 (d, J = 251.2 Hz), 162.5, 158.1, 142.6, 140.2, 133.2 (d, J = 3.3 Hz), 132.0 (d, J = 8.2 Hz), 130.4, 128.3, 128.1, 115.8 (d, J = 21.8 Hz), 47.2, 44.6, 38.1, 33.4, 26.5, 26.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -110.3. HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_2SF$ $[M+H]^+$: 425.1699, found 425.1697.



2-(cyclohexylmethyl)-5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidine [S43]



Prepared according to a reported procedure.[20] A round bottom flask fitted with a reflux condenser was charged with 4-(methylsulfonyl)phenyl acetic acid (2.14 g, 10.0 mmol, 1.0 equiv.), 4-fluorobenzaldehyde (1.1 mL, 1.24 g, 10.0 mmol, 1.0 equiv.), potassium acetate (1.31 g, 13.3 mmol, 1.33 equiv.) and acetic anhydride (4.0 mL, 4.4 g, 42.7 mmol, 4.3 equiv.). The mixture was heated to 140 °C for 48 h. The reaction was cooled to room temperature, water was added (40 mL) and the mixture was treated with a solution of 10 M NaOH until pH 12 was reached, followed by conc. HCl until pH 1 was reached. The resulting mixture was extracted with CH_2Cl_2 (3 x 80 mL). The combined organic layer was extracted with 2 M NaOH (3 x 80 mL) and water (80 mL). The combined aqueous solutions were washed with CH_2Cl_2 (100 mL), then acidified with conc. HCl until pH 1 was reached, and finally extracted with CH_2Cl_2 (5 x 50 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford (*E*)-3-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)acrylic acid and residual starting material as a white solid (1.80 g, 5.6 mmol, 56% yield).

To a round bottom flask equipped with a reflux condenser was added (*E*)-3-(4-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)acrylic acid (2.0 g, 6.23 mmol, 1.0 equiv.) and thionyl chloride (4.1 mL, 6.7 g,

56.1 mmol, 9.0 equiv.). The reaction was heated to reflux for 1.5 h and then stirred at room temperature for an additional 18 h. The reaction mixture was concentrated *in vacuo*, dissolved in acetone (6 mL) and added dropwise to a solution of sodium azide (445.4 mg, 6.9 mmol, 1.1 equiv.) in water (3 mL) maintained at 0 °C. The mixture was allowed to warm to room temperature, diluted with water (25 mL) and extracted with toluene (35 mL). The organic layer was washed with brine, dried over $MgSO_4$ and filtered. The filtrate was heated at reflux for 1.5 h, after which it was cooled to room temperature, concentrated *in vacuo*, and dissolved in 2:1 AcOH:H_2O (4.2 mL:2.1 mL). The solution was heated to reflux for 2 h, after which it was cooled to room temperature, diluted with water (6 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo* to afford 2-(4-fluorophenyl)-1-(4-(methylsulfonyl)phenyl)ethan-1-one as a pale yellow solid. The crude material was taken onto the next step without further purification.

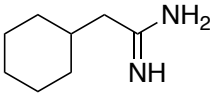
To a flame dried round bottom flask was added DMF (3.5 mL, 1.1 M) and the flask was cooled to 0 °C. Phosphoryl chloride (1.5 mL, 2.5 g, 16.0 mmol, 4.0 equiv.) was added dropwise and the reaction was stirred at room temperature for 30 minutes. The reaction was cooled to 0 °C and 2-(4-fluorophenyl)-1-(4-(methylsulfonyl)phenyl)ethan-1-one (1.17 g, 4.0 mmol, 1.0 equiv.) was added. The reaction was stirred at 0 °C for a further 1 h and was then heated to 65 °C for 5 h. The reaction was cooled to room temperature and poured CAREFULLY into ice cold sat. aq. $NaHCO_3$ solution. The solution was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was washed with water (2 x 50 mL) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 10% → 20% → 30% → 40% EtOAc/hexanes gradient as eluent afforded (*Z*)-3-chloro-2-(4-fluorophenyl)-3-(4-(methylsulfonyl)phenyl)acrylaldehyde as a pale orange solid (378.6 mg, 1.1 mmol, 28% yield).

To the round bottom flask containing 2-cyclohexylacetimidamide (**S44**) (1.26 g, 9.00 mmol, 4.5 equiv.) was added sodium carbonate (509.0 mg, 4.8 mmol, 2.4 equiv.), (*Z*)-3-chloro-2-(4-fluorophenyl)-3-(4-(methylsulfonyl)phenyl)acrylaldehyde (677.6 mg, 2.0 mmol, 1.0 equiv.) and MeCN (13.0 mL, 0.15 M). The reaction was heated to reflux overnight (18 h), after which the reaction was cooled to room temperature, quenched with water (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 5% → 10% → 15% → 20% → 30% → 40% EtOAc/hexanes gradient eluent followed by recrystallization from acetone/hexanes afforded 2-(cyclohexylmethyl)-5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidine (**S43**) as a white solid (252.8 mg, 0.60 mmol, 30% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 7.18 – 7.11 (m, 2H), 7.09 – 7.03 (m, 2H), 3.04 (s, 3H), 2.95 (d, *J* = 7.2 Hz, 2H), 2.10 – 1.98 (m, 1H), 1.79 – 1.70 (m,

4H), 1.70 – 1.64 (m, 1H), 1.34 – 1.07 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 162.9 (d, J = 249.3 Hz), 161.3, 158.6, 143.3, 141.1, 131.6 (d, J = 3.6 Hz), 131.2 (d, J = 8.2 Hz), 130.9, 129.6, 127.5, 116.4 (d, J = 21.8 Hz), 47.1, 44.6, 38.2, 33.4, 26.6, 26.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.8. HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_2SF$ $[M+H]^+$: 425.1699, found 425.1685.

2-cyclohexylacetimidamide [S44]



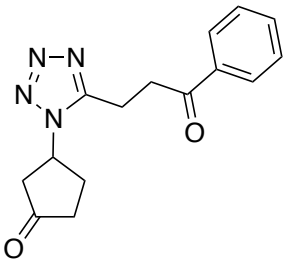
To a round bottom flask equipped with a reflux condenser was added cyclohexylmethyl 4-methylbenzenesulfonate (2.68 g, 10.0 mmol, 1.0 equiv.), sodium cyanide (980.0 mg, 20.0 mmol, 2.0 equiv.) and DMF (33 mL, 0.3 M). The reaction was heated to reflux overnight (18 h), after which it was cooled to room temperature and diluted with EtOAc. The organic layer was washed sequentially with H_2O (2 x 30 mL), sat. aq. $NaHCO_3$ solution (2 x 30 mL) and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 2% → 4% EtOAc/hexanes gradient eluent afforded 2-cyclohexylacetonitrile as a colorless oil (959.8 mg, 7.8 mmol, 78% yield).

Prepared according to a reported procedure.[21] To a suspension of ammonium chloride (535 mg, 10.0 mmol, 2.0 equiv.) in toluene (6 mL, 1.6 M) at 0 °C was added trimethylaluminium (2 M in toluene, 5 mL, 10.0 mmol, 2.0 equiv.) dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for 3 h. This reagent, $CH_3Al(Cl)NH_2$ was used directly in the next step.

A mixture of 2-cyclohexylacetonitrile (616.0 mg, 5.0 mmol, 1.0 equiv.) and $CH_3Al(Cl)NH_2$ in a sealed schlenk flask was heated to 95 °C overnight. The mixture was cooled to 0 °C and MeOH (10 mL) was added dropwise. The slurry was stirred for 1 h then filtered, washing with MeOH (100 mL). The filtrate was concentrated *in vacuo*, affording 2-cyclohexylacetimidamide•HCl salt (**S44**) as a white solid. The crude material was taken onto the next step without further purification.

C—H Oxidation of Substrates and Product Characterization for Supplementary Figure 2

3-(5-(3-oxo-3-phenylpropyl)-1*H*-tetrazol-1-yl)cyclopentan-1-one [42]



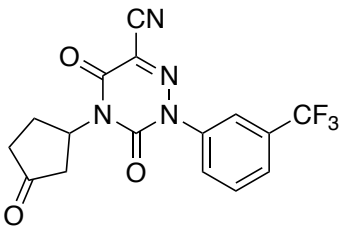
The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 3-(1-cyclopentyl-1*H*-tetrazol-5-yl)-1-phenylpropan-1-one (**41**) (81.1 mg, 0.300 mmol, 1.0 equiv), (*S,S*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 9 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 30% → 40% → 50% → 60% → 70% EtOAc/hexanes as eluent afforded 3-(5-(3-oxo-3-phenylpropyl)-1*H*-tetrazol-1-yl)cyclopentan-1-one (**42**) as a colorless oil.

Run 1: (34.7 mg, 0.122 mmol, 40.7% yield), (13.4 mg, 0.050 mmol, 16.5% rsm). **Run 2:** (34.1 mg, 0.120 mmol, 40.0%), (7.9 mg, 0.029 mmol, 9.7% rsm). **Run 3:** (36.3 mg, 0.128 mmol, 42.6% yield), (18.5 mg, 0.068 mmol, 22.8% rsm). **Average: 41.1% yield ± 1.3%, 16.3% rsm ± 6.6%.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 5.39 (p, *J* = 6.2 Hz, 1H), 3.77 – 3.64 (m, 2H), 3.32 – 3.19 (m, 2H), 2.97 – 2.84 (m, 2H), 2.80 – 2.62 (m, 2H), 2.62 – 2.51 (m, 1H), 2.51 – 2.38 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 213.2, 197.6, 154.3, 136.0, 133.9, 128.9, 128.1, 55.1, 44.5, 36.6, 36.1, 30.1, 17.7. HRMS (ESI+) *m/z* calculated for $C_{15}H_{17}N_4O_2$ $[M+H]^+$: 285.1352, found 285.1340.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

3,5-dioxo-4-(3-oxocyclopentyl)-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile [S45]



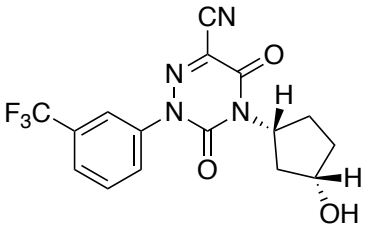
The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 4-cyclopentyl-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (**43**) (105.1 mg, 0.300 mmol, 1.0 equiv.), (*S,S*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30

mL SiO_2) using gradient 20% → 25% → 30% → 35% EtOAc/hexanes as eluent afforded (**S45**) as a white solid.

Run 1: (60.0 mg, 0.165 mmol, 54.9% yield), 0% rsm. **Run 2:** (61.7 mg, 0.169 mmol, 56.5%), 0% rsm. **Run 3 (0.2 mmol scale):** (40.3 mg, 0.111 mmol, 55.3% yield), 0% rsm. **Average: 55.6% yield ± 0.8%, 0% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (br s, 1H), 7.77 – 7.70 (m, 2H), 7.69 – 7.63 (m, 1H), 5.65 (app. p, *J* = 8.4 Hz, 1H), 2.84 (dd, *J* = 18.7, 6.5 Hz, 1H), 2.72 – 2.64 (m, 1H), 2.60 (dd, *J* = 18.7, 9.6 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.38 – 2.27 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 213.8, 153.0, 146.8, 139.4, 132.1 (q, *J* = 33.5 Hz), 130.1, 128.5, 126.5 (q, *J* = 3.6 Hz), 122.7, 123.3 (q, *J* = 272.6 Hz), 122.4 (q, *J* = 3.9 Hz), 110.8, 51.0, 40.1, 37.4, 26.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.8. HRMS (ESI+) *m/z* calculated for $C_{16}H_{12}N_4O_3F_3$ $[M+H]^+$: 365.0862, found 365.0858.

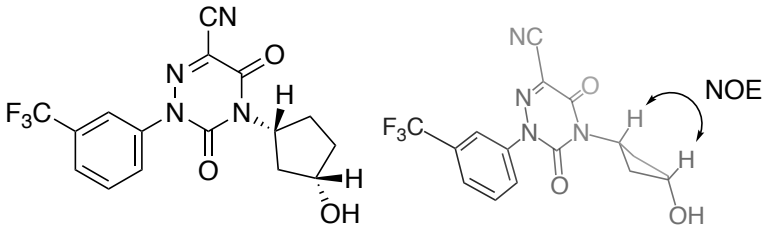
(*cis*)-4-(3-hydroxycyclopentyl)-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile [44]



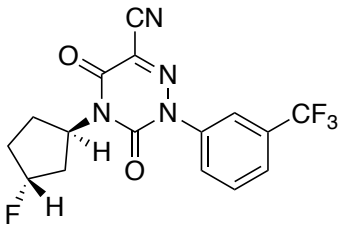
To a solution of 3,5-dioxo-4-(3-oxocyclopentyl)-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (**S45**) (212.7 mg, 0.58 mmol, 1.0 equiv.) in THF (1.9 mL, 0.3 M) was added BH_3•THF (1M in THF, 0.64 mL, 0.64 mmol, 1.1 equiv.) at 0 °C. The reaction was stirred at 0 °C for 10 minutes. The reaction was quenched by the addition of water (2 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5mL). The combined organic layer was dried with $NaSO_4$, filtered and concentrated *in vacuo*. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 30% → 35% → 40% EtOAc/hexanes as eluent afforded 4-(3-hydroxycyclopentyl)-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (**44**) as a white solid (164.3 mg, 0.449 mmol, 77.3% yield, 14:1 d.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (br. s, 1H), 7.77 – 7.74 (m, 1H), 7.74 – 7.70 (m, 1H), 7.70 – 7.64 (m, 1H), 5.41 – 5.32 (m, 1H), 4.37 – 4.29 (m, 1H), 3.41 (d, *J* = 9.5 Hz, 1H), 2.48 – 2.33 (m, 2H), 2.11 – 1.96 (m, 3H), 1.79 – 1.67 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.1, 147.0, 139.5, 132.2 (q, *J* = 33.6 Hz), 130.1, 128.6, 126.5 (q, *J* = 3.5 Hz), 123.3 (q, *J* = 272.8 Hz), 122.9, 122.5 (q, *J* = 3.9 Hz), 110.7, 73.0, 53.1, 37.7, 35.3, 25.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.8. HRMS (ESI+) *m/z* calculated for $C_{16}H_{14}N_4O_3F_3$ $[M+H]^+$: 367.1018, found 367.1003.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of ^{1}H, gCOSY, gHSQC and 1D NOE.



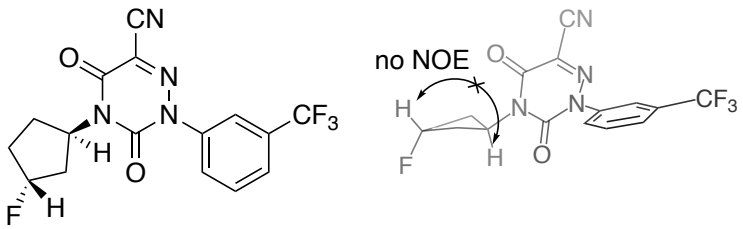
(*trans*)-4-(3-fluorocyclopentyl)-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile [45]



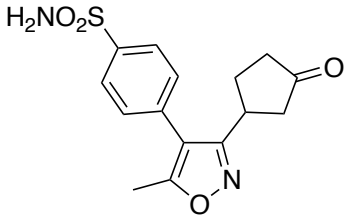
In a 3-neck round bottom flask equipped with a reflux condenser *N*-(trimethylsilyl)morpholine (209.0 mg, 1.31 mmol, 6.0 equiv.) was added dropwise to a solution of Deoxo-Fluor® (0.24 mL, 1.31 mmol, 6.0 equiv.) in CH_2Cl_2 (4.4 mL, 0.3 M) at -78 °C. The solution was stirred for 2.5 h at room temperature. The solution was then cooled to -78 °C and a solution of 4-(3-hydroxycyclopentyl)-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (**44**) (80.0 mg, 0.22 mmol, 1.0 equiv.) in CH_2Cl_2 (14.5 mL, 0.015 M) was added *via* cannula. The mixture was heated to reflux for 19 h and then concentrated *in vacuo*. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 5% → 10% → 15% EtOAc/hexanes gradient as eluent afforded 4-(3-fluorocyclopentyl)-3,5-dioxo-2-(3-(trifluoromethyl)phenyl)-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (**45**) as a pale yellow oil (38.5 mg, 0.105 mmol, 47.5% yield, >20:1 d.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.77 – 7.70 (m, 2H), 7.69 – 7.61 (m, 1H), 5.66 – 5.55 (m, 1H), 5.31 (dtd, $J_{H\text{-}F}$ = 52.8 Hz, $J_{H\text{-}H}$ = 4.1, 1.8 Hz), 2.51 – 2.21 (m, 4H), 2.17 – 2.00 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.0, 146.8, 139.6, 132.1 (q, J = 33.5 Hz), 130.1, 128.5, 126.4 (q, J = 3.6 Hz), 123.3 (q, J = 272.7 Hz), 122.8, 122.5 (q, J = 3.9 Hz), 110.9, 96.2 (d, J = 172.2 Hz), 53.2, 35.6 (d, J = 21.4 Hz), 32.7 (d, J = 20.9 Hz), 26.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.8, -173.9. HRMS (ESI+) *m/z* calculated for $C_{16}H_{13}N_4O_2F_4$ $[M+H]^+$: 369.0975, found 369.0963.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of ^{1}H and 1D NOE.



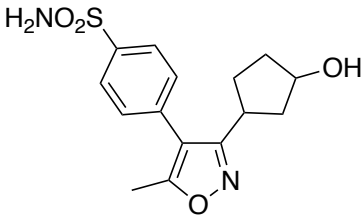
4-(5-methyl-3-(3-oxocyclopentyl)isoxazol-4-yl)benzenesulfonamide [S46]



The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 4-(3-cyclopentyl-5-methylisoxazol-4-yl)benzenesulfonamide (**46**) (61.3 mg, 0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (13.6 mg, 0.010 mmol, 5 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.50 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method A. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using gradient 30% → 40% → 50% → 60% EtOAc/hexanes as eluent afforded 4-(5-methyl-3-(3-oxocyclopentyl)isoxazol-4-yl)benzenesulfonamide (**S46**) as a white solid.

Run 1: (25.8 mg, 0.081 mmol, 40.3% yield), <5% rsm. **Run 2:** (27.0 mg, 0.084 mmol, 42.1% yield), <5% rsm. **Run 3:** (28.9 mg, 0.090 mmol, 45.1% yield), <5% rsm. **Average: 42.5% yield ± 2.4%, <5% rsm.** ^{1}H NMR (500 MHz, MeOD) δ 8.05 – 7.98 (m, 2H), 7.60 – 7.51 (m, 2H), 3.67 (app. p, *J* = 8.1 Hz, 1H), 2.53 – 2.36 (m, 2H), 2.40 (s, 3H), 2.35 – 2.17 (m, 3H), 2.09 – 2.00 (m, 1H). ^{13}C NMR (126 MHz, MeOD) δ 219.7, 168.4, 165.0, 144.6, 135.5, 131.1, 127.9, 116.7, 43.7, 38.2, 34.5, 29.2, 11.3. HRMS (ESI+) *m/z* calculated for $C_{19}H_{17}N_2O_4S$ $[M+H]^+$: 321.0909, found 321.0904.

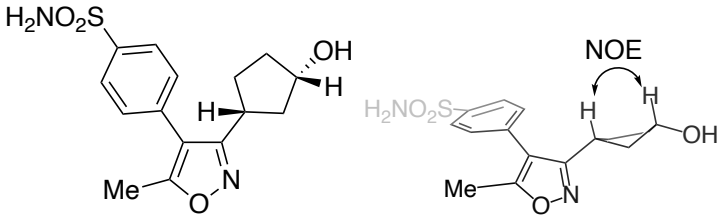
4-(3-(3-hydroxycyclopentyl)-5-methylisoxazol-4-yl)benzenesulfonamide [47]



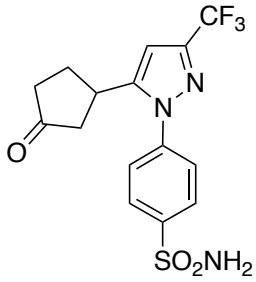
To a solution of 4-(5-methyl-3-(3-oxocyclopentyl)isoxazol-4-yl)benzenesulfonamide (**S46**) (31.6 mg, 0.10 mmol, 1.0 equiv.) in MeOH (0.33 mL, 0.3 M) was added sodium borohydride (4.1 mg, 0.11 mmol, 1.1 equiv.) at 0 °C. The reaction was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 50% → 60% → 70% → 80% EtOAc/hexanes gradient as eluent afforded 4-(3-(3-hydroxycyclopentyl)-5-methylisoxazol-4-yl)benzenesulfonamide (**47**) as a white solid as a mixture of diastereomers (19.4 mg, 0.06 mmol, 61% yield, 9:1 d.r.).

^{1}H NMR (500 MHz, CD_3OD) δ 8.03 – 7.96 (m, 2H), 7.55 – 7.47 (m, 2H), 4.34 (tt, *J* = 5.4, 2.8 Hz, 0.1H), 4.22 (qd, *J* = 6.3, 4.5 Hz, 0.9H), 3.46 (dq, *J* = 9.9, 8.1 Hz, 0.1H), 3.19 (tt, *J* = 9.1, 7.8 Hz, 0.9H), 2.38 (s, 3H), 2.23 (ddd, *J* = 13.3, 8.3, 6.5 Hz, 0.9H), 2.11 – 1.63 (m, 5.2H). ^{13}C NMR (126 MHz, CD_3OD) δ 167.9, 166.4, 144.5, 136.0, 131.2, 127.7, 116.6, (73.7), 73.6, (41.7), 41.2, 36.0, 35.6, (35.4), (35.2), (30.5), 30.0, 11.2. HRMS (ESI+) *m/z* calculated for $C_{15}H_{19}N_2O_4S$ $[M+H]^+$: 323.1066, found 323.1057.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of ^{1}H, gCOSY, gHSQC and 1D NOE.



4-(5-(3-oxocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide [S47]

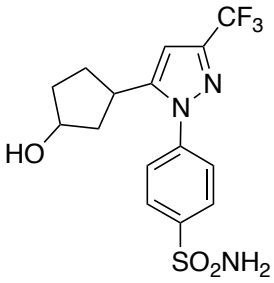


The reaction was run with **General Method B: Single Catalyst Addition Protocol**: 4-(5-cyclopentyl-3-(trifluoromethyl)-1*H*-pyrazole-1-yl)benzenesulfonamide (**48**) (107.8 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 20% → 30% → 40% → 50% → 60% EtOAc/hexanes gradient as eluent afforded 4-(5-(3-oxocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**S47**) as a white solid.

Run 1: (84.6 mg, 0.227 mmol, 75.5% yield), (4.2 mg, 0.012 mmol, 3.9% rsm). **Run 2:** (77.9 mg, 0.209 mmol, 69.6% yield), (4.7 mg, 0.013 mmol, 4.4% rsm). **Run 3:** (82.3 mg, 0.220 mmol, 73.5% yield), (2.9 mg, 0.008 mmol, 2.7% rsm). **Average: 72.9% yield ± 3.0%, 3.7% ± 0.9% rsm.**

^{1}H NMR (500 MHz, CD_3OD) δ 8.11 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H), 6.81 (s, 1H), 3.67 – 3.57 (m, 1H), 2.52 (dd, *J* = 18.5, 7.5 Hz, 1H), 2.40 – 2.29 (m, 3H), 2.28 – 2.19 (m, 1H), 2.09 – 1.97 (m, 1H). ^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ 216.0, 149.3, 144.6, 141.8 (q, *J* = 37.4 Hz), 140.7, 127.1, 126.4, 121.4 (q, *J* = 268.7 Hz), 103.2, 44.5, 37.8, 32.8, 29.6. ^{19}F NMR (471 MHz, DMSO-*d*$_6$) δ -60.8. HRMS (ESI+) *m/z* calculated for $C_{15}H_{15}N_3O_3F_3S$ $[M+H]^+$: 374.0786, found 374.0782.

4-(5-(3-hydroxycyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide [49]

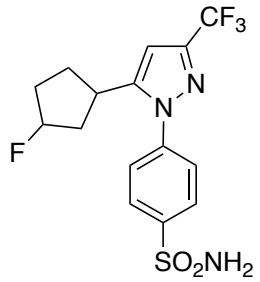


To a solution of 4-(5-(3-oxocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**S47**) (18.1 mg, 0.05 mmol, 1.0 equiv.) in MeOH (0.2 mL, 0.3 M) was added sodium borohydride (2.2 mg, 0.06 mmol, 1.1 equiv.) at 0 °C. The reaction was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL).

The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 50% → 60% → 70% → 80% EtOAc/hexanes gradient as eluent afforded 4-(5-(3-hydroxycyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**49**) as a white solid as a mixture of diastereomers (12.6 mg, 0.03 mmol, 70% yield, 2.2:1 d.r.).

^{1}H NMR (500 MHz, CD_3OD) δ 8.13 – 8.06 (m, 2H), 7.73 – 7.64 (m, 2H), 6.76 (s, 0.7H), 6.70 (s, 0.3H), 4.41 – 4.35 (m, 0.3H), 4.30 – 4.24 (m, 0.7H), 3.51 – 3.40 (m, 0.3H), 3.19 (p, *J* = 8.6 Hz, 0.7H), 2.35 – 2.26 (m, 0.7H), 2.18 – 2.05 (m, 0.7H), 2.00 – 1.94 (m, 1H), 1.93 – 1.73 (m, 2H), 1.68 – 1.56 (m, 1.4H). ^{13}C NMR (126 MHz, CD_3OD) δ 153.0, (152.5), (145.9), 145.9, (144.4 (q, *J* = 38.0 Hz)), 144.3 (q, *J* = 38.0 Hz), 143.1, (128.6), 128.6, 127.7, 122.8 (q, *J* = 268.0 Hz), 103.6, (103.2), 73.6, (73.5), (43.8), 43.4, 36.1, (35.8), 35.4, (35.3), 32.5, (32.5). ^{19}F NMR (471 MHz, CD_3OD) δ -63.83, -63.84. HRMS (ESI+) *m/z* calculated for $C_{15}H_{17}N_3O_3F_3S$ $[M+H]^+$: 376.0943, found 376.0930.

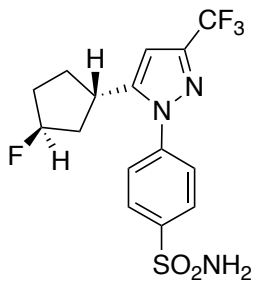
4-(5-(3-fluorocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide [50]



In a flame-dried round bottom flask, *N*-(trimethylsilyl)morpholine (85.8 mg, 0.545 mmol, 6.0 equiv.) was added dropwise to a solution of Deoxo-Fluor® (50 wt% in toluene, 0.2 mL, 0.545 mmol, 6.0 equiv.) in CH_2Cl_2 (0.3 mL, 0.3 M) at -78 °C. The solution was stirred for 2.5 h at room temperature. After 2.5 hours, a solution of 4-(5-(3-hydroxycyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**49**) (34.1 mg, 0.091 mmol, 1.0 equiv.) in toluene (6.1 mL, 0.015 M) was cooled to -78 °C and the TMS-morpholine/Deoxo-Fluor® solution was added dropwise and the mixture was heated to reflux overnight. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% → 40% EtOAc/hexanes gradient as eluent afforded *trans*-4-(5-(3-fluorocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide and *cis*-4-(5-(3-fluorocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**50**) as a pale yellow solid.

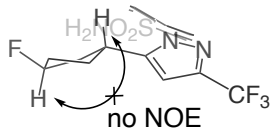
Run 1: (9.4 mg, 0.025 mmol, 27% yield, 2:1 d.r.). **Run 2 (0.095 mmol scale):** (9.1 mg, 0.024 mmol, 25% yield, 1.5:1 d.r.). **Average: 26% yield, 2:1 d.r.**

Major Diastereoisomer: *trans*-4-(5-(3-fluorocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide

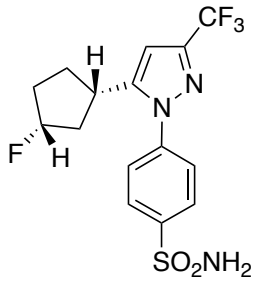


^{1}H NMR (500 MHz, CD_3OD) δ 8.16 – 8.06 (m, 2H), 7.76 – 7.66 (m, 2H), 6.74 (s, 1H), 5.19 (app. dt, $J_{H\text{-}F}$ = 53.9 Hz, $J_{H\text{-}H}$ = 4.6 Hz, 1H), 3.48 – 3.38 (m, 1H), 2.32 – 2.08 (m, 3H), 1.96 – 1.79 (m, 2H), 1.75 – 1.62 (m, 1H). ^{13}C NMR (126 MHz, CD_3OD) δ 151.6, 146.0, 144.4 (q, J = 38.0 Hz), 143.0, 128.7, 127.8, 122.8 (q, J = 268.0 Hz), 103.4 (q, J = 2.0 Hz), 96.7 (d, J = 172.1 Hz), 42.1 (d, J = 21.9 Hz), 35.4, 33.6 (d, J = 22.1 Hz), 32.1. ^{19}F NMR (471 MHz, CD_3OD) δ -63.8, -170.1. HRMS (ESI+) *m/z* calculated for $C_{15}H_{16}N_3O_2F_4S$ $[M+H]^+$: 378.0899, found 378.0882.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of ^{1}H, gHSQC and 1D NOE.

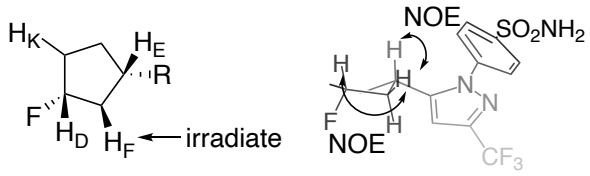


Minor Diastereoisomer: *cis*-4-(5-(3-fluorocyclopentyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide

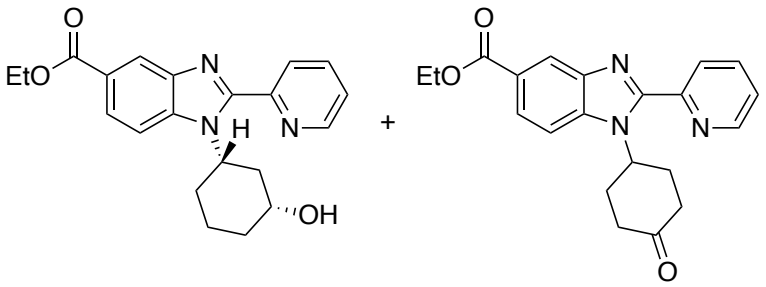


^{1}H NMR (600 MHz, CD_3OD) δ 8.14 – 8.07 (m, 2H), 7.73 – 7.66 (m, 2H), 6.71 (s, 1H), 5.14 (app. dt, $J_{H\text{-}F}$ = 54.1 Hz, $J_{H\text{-}H}$ = 4.9 Hz, 1H), 3.31 – 3.25 (m, 1H), 2.38 (dddd, J = 30.6, 15.1, 10.0, 5.3 Hz, 1H), 2.14 – 2.02 (m, 2H), 1.98 – 1.85 (m, 2H), 1.82 – 1.67 (m, 1H). ^{13}C NMR (151 MHz, CD_3OD) δ 152.6, 146.0, 144.4 (q, J = 38.1 Hz), 143.0, 128.7, 127.8, 122.8 (q, J = 268.1 Hz), 103.6, 96.8 (d, J = 172.8 Hz), 41.5 (d, J = 21.8 Hz), 35.7, 35.1 (d, J = 22.3 Hz), 32.8. ^{19}F NMR (471 MHz, CD_3OD) δ -63.9, -169.3. HRMS (ESI-) *m/z* calculated for $C_{15}H_{14}N_3O_2F_4S$ $[M-H]^-$: 376.0743, found 376.0742.

The relative stereochemistry of the minor diastereoisomer was determined based on a combination of ^{1}H, gCOSY, gHSQC and 1D NOE.



(*cis*)-Ethyl 1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [53] and Ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [55]

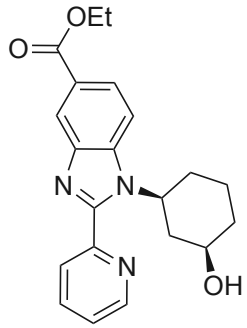


According to the **general procedure for HBF_4•OEt_2 protection**, ethyl 1-cyclohexyl-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**51**) (174.7 mg, 0.5 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (75 μL, 0.550 mmol, 1.1 equiv.) in CH_2Cl_2 (2.0 mL, 0.25 M). The oxidation was carried out according to **General Method C: Iterative Catalyst Addition Protocol**: the resultant **51•HBF_4** (0.500 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (709 mg, 7.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (33.9 mg, 0.025 mmol, 5 mol%), H_2O_2 (50% wt. in H_2O, 340 mg, 5.0 mmol, 10.0 equiv.), MeCN (1.0 mL in 40 mL vial, 6.25 mL with oxidant). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. A further addition of (*R,R*)-Mn(CF_3PDP) catalyst **1** (33.9 mg, 0.025 mmol, 5 mol%) in MeCN (0.3 mL) was added dropwise to the reaction at 1 hour. A further addition of (*R,R*)-Mn(CF_3PDP) catalyst **1** (33.9 mg, 0.025 mmol, 5 mol%) in MeCN (0.2 mL) was added dropwise to the reaction after an additional 1 hour. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. The crude mixture was purified by CombiFlash (24g silica column) using 100% hexanes → 60% EtOAc/hexanes gradient over 70 column volumes afforded (*cis*)-ethyl 1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**53**) and ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**55**) each as white solids. Recovered starting material was recycled once.

Run 1: *Cycle 1* (43.8 mg, 0.120 mmol, 24.0% γ–alcohol **53**), (20.2 mg, 0.056 mmol, 11.1% δ–ketone **55**), (64.0 mg, 0.183 mmol, 36.6% rsm). *Cycle 2* (15.8 mg, 0.043 mmol, 23.6% γ–alcohol **53**), (15.5 mg, 0.043 mmol, 23.3% δ–ketone **55**), (16.1 mg, 0.046 mmol, 25.2% rsm). *Overall* (59.6 mg, 0.163 mmol, 32.6% γ–alcohol **53**), (35.7 mg, 0.098 mmol, 19.6% δ–ketone **55**), (52.2% overall yield, 1.7:1 γ:δ ratio), (16.1 mg, 0.046 mmol, 9.2% rsm). **Run 2:** *Cycle 1* (43.1 mg, 0.118 mmol, 23.6% γ–alcohol **53**), (24.7 mg, 0.068 mmol, 13.6% δ–ketone **55**), (67.4 mg, 0.193 mmol, 38.6% rsm). *Cycle 2* (18.0 mg, 0.049 mmol, 25.5% γ–alcohol **53**), (16.6 mg, 0.046 mmol, 23.7% δ–ketone **55**), (18.0 mg, 0.052 mmol, 26.7% rsm). *Overall* (61.1 mg, 0.167 mmol, 33.4% γ–alcohol **53**), (41.3 mg, 0.114 mmol, 22.7% δ–ketone **55**), (56.1% overall yield, 1.5:1 γ:δ ratio), (18.0 mg, 0.052 mmol, 10.3% rsm). **Run 3:** *Cycle 1* (40.5 mg, 0.111 mmol, 22.2% γ–alcohol **53**), (31.4 mg, 0.086 mmol, 17.3% δ–ketone **55**), (57.5 mg, 0.165 mmol, 32.9% rsm). *Cycle 2* (10.3 mg, 0.028 mmol, 17.1% γ–alcohol **53**), (12.7 mg, 0.035 mmol, 21.1% δ–ketone **55**), (12.1 mg, 0.035 mmol, 21.0% rsm). *Overall* (50.8 mg, 0.139 mmol, 27.8% γ–alcohol **53**), (44.1 mg, 0.121 mmol, 24.3% δ–ketone **55**), (52.1% overall yield, 1.1:1 γ:δ ratio), (12.1 mg, 0.035 mmol, 6.9% rsm).

Average: 31.2% yield of γ–alcohol 53 ± 3.0%, 22.2% yield of δ–ketone 55 ± 2.4%, 53.5% overall yield with 1.4:1 γ:δ ratio, 8.8% rsm ± 1.7%.

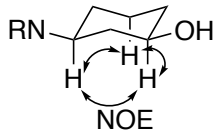
(±)-(*cis*)-Ethyl 1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [53]



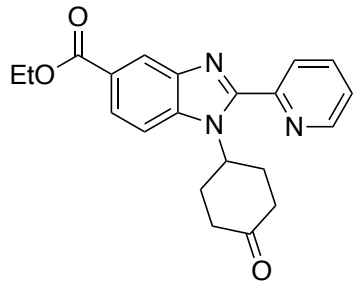
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 – 8.67 (m, 1H), 8.55 (d, *J* = 1.6 Hz, 1H), 8.30 – 8.24 (m, 1H), 8.02 – 7.96 (m, 1H), 7.91 – 7.83 (m, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.42 – 7.35 (m, 1H), 5.68 – 5.58 (m, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.85 – 3.75 (m, 1H), 2.47 – 2.38 (m, 1H), 2.34 – 2.17 (m, 2H), 2.14 – 2.08 (m, 1H), 2.08 – 1.93 (m, 2H), 1.76 (br. s, 1H), 1.54 – 1.35 (m, 2H), 1.42 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 152.2, 150.6, 148.9, 143.1, 138.1, 137.2, 125.9, 124.9, 124.3, 124.3, 122.9, 112.7, 70.0, 61.0, 54.9, 40.4, 34.9, 30.0, 22.5, 14.5. HRMS (ESI+) *m/z* calculated for $C_{21}H_{24}N_3O_3$ $[M+H]^+$: 366.1818, found 366.1810.

Site of alcohol was determined by oxidizing the alcohol to ketone, see below.

The relative stereochemistry was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.



Ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [55]



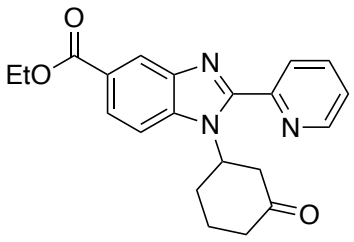
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 – 8.71 (m, 1H), 8.57 (s, 1H), 8.35 (d, *J* = 7.9 Hz, 1H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.92 (t, *J* = 7.7 Hz, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.46 – 7.40 (m, 1H), 6.22 (tt, *J* = 12.5, 4.0 Hz, 1H), 4.42 (q, *J* = 7.4 Hz, 2H), 2.88 – 2.75 (m, 2H), 2.68 – 2.57 (m, 4H), 2.49 – 2.41 (m, 2H), 1.42 (t, *J* = 7.1, 1.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.0, 167.0, 152.2, 150.6, 149.0, 143.1, 137.9, 137.4, 126.0, 125.2, 124.6, 124.5, 123.2, 112.3, 61.1, 55.1, 40.2, 30.2, 14.5. HRMS (ESI+) *m/z* calculated for $C_{21}H_{22}N_3O_3$ $[M+H]^+$: 364.1661, found 364.1651.

Oxidation of (*cis*)-ethyl 1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate

(*cis*)-Ethyl 1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**53**) (22.8 mg, 0.06 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (0.3 mL, 0.2 M) and cooled to 0 °C. Dess-Martin periodinane (29.1 mg, 0.068 mmol, 1.1 equiv.) was added and the reaction was stirred at room temperature

for 3 h. Upon completion, as monitored by TLC, the reaction was filtered through a pad of Celite, using CH_2Cl_2 as eluent. The filtrate was washed sequentially with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% hexanes → 60% ethyl acetate/hexanes gradient as eluent afforded ethyl 1-(3-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**S48**) as a white solid (10.0 mg, 0.028 mmol, 46% yield).

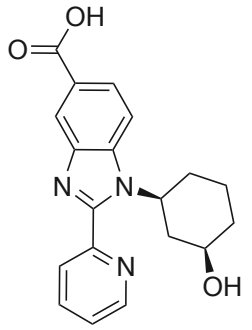
Ethyl 1-(3-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [S48]



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 – 8.65 (m, 1H), 8.58 (s, 1H), 8.34 – 8.28 (m, 1H), 8.07 – 7.99 (m, 1H), 7.92 – 7.85 (m, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.43 – 7.36 (m, 1H), 6.01 (tt, *J* = 12.7, 4.7 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.41 (app. t, *J* = 13.7 Hz, 1H), 2.89 (dd, *J* = 13.8, 4.5 Hz, 1H), 2.68 (qd, *J* = 13.0, 4.9 Hz, 1H), 2.62 – 2.54 (m, 1H), 2.54 – 2.43 (m, 1H), 2.39 – 2.32 (m, 1H), 2.28 – 2.18 (m, 1H), 1.77 (qt, *J* = 13.9, 4.0 Hz, 1H), 1.43 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.9, 167.0, 152.1, 150.3, 148.9, 143.2, 137.7, 137.4, 125.8, 125.3, 124.7, 124.5, 123.3, 111.9, 61.1, 55.5, 46.4, 40.9, 29.8, 22.6, 14.5. HRMS (ESI+) *m/z* calculated for $C_{21}H_{22}N_3O_3$ $[M+H]^+$: 364.1661, found 364.1654.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

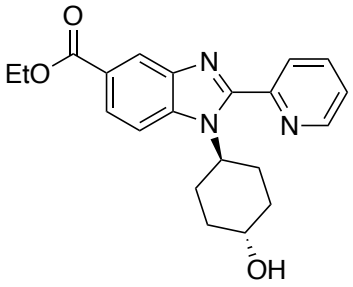
(±)-(*cis*)-1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid [54]



(±)-(*cis*)-Ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**53**) (40.0 mg, 0.109 mmol, 1.0 equiv.) was dissolved in MeOH (0.22 mL, 0.5 M) and 2M NaOH (0.15 mL, 0.291 mmol, 2.7 equiv.) was added. The mixture was stirred at 60 °C for 2 h. MeOH was removed under reduced pressure and the residue was acidified to pH 4 with glacial acetic acid. The precipitated carboxylic acid was collected by filtration, washed with water and dried to give (±)-(*cis*)-1-(3-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid (**54**) as a beige solid with 3 equiv. acetic acid (28.1 mg, 0.054 mmol, 50% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.75 (d, *J* = 4.9 Hz, 1H), 8.40 (s, 1H), 8.11 – 8.06 (m, 1H), 8.05 – 7.97 (m, 2H), 7.80 (d, *J* = 8.6 Hz, 1H), 7.56 – 7.52 (m, 1H), 5.33 – 5.23 (m, 1H), 3.69 – 3.60 (m, 1H), 2.35 – 2.24 (m, 3H), 2.06 – 1.93 (m, 2H), 1.41 (t, *J* = 9.7 Hz, 2H). ^{13}C NMR (126 MHz, CD_3OD) δ 180.2, 153.0, 151.2, 150.3, 143.5, 138.8, 137.0, 134.2, 126.8, 126.1, 125.8, 122.1, 113.2, 70.5, 56.5, 41.0, 35.4, 30.9, 24.2, 23.5. HRMS (ESI+) *m/z* calculated for $C_{19}H_{20}N_3O_3$ $[M+H]^+$: 338.1505, found 338.1516.

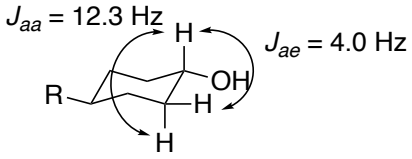
(±)-(*trans*)-ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [S49]: Reduction of ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate with $NaBH_4$



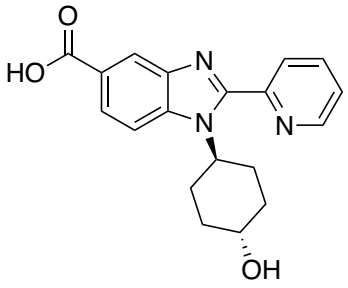
To a solution of ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**55**) (45.6 mg, 0.125 mmol, 1.0 equiv.) in EtOH (1.25 mL, 0.1 M) was added sodium borohydride (5.7 mg, 0.151 mmol, 1.2 equiv.) at 0 °C. The reaction was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% CH_2Cl_2 → 5% MeOH/CH_2Cl_2 gradient as eluent afforded (±)-(*trans*)-ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**S49**) as a white solid as a mixture of diastereoisomers (29.2 mg, 0.080 mmol, 64% yield, 9:1 d.r.).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.8 Hz, 1H), 8.54 (s, 1H), 8.24 (d, *J* = 7.9 Hz, 1H), 7.98 (d, *J* = 8.6 Hz, 1H), 7.87 (td, *J* = 7.9, 2.3 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 0.1H), 7.63 (d, *J* = 8.7 Hz, 0.9H), 7.39 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.55 (tt, *J* = 12.3, 4.0 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.20 – 4.16 (m, 0.1H), 3.84 (tt, *J* = 11.0, 4.2 Hz, 0.9H), 2.79 (qd, *J* = 13.0, 3.8 Hz, 0.2H), 2.40 (qd, *J* = 13.0, 3.4 Hz, 1.8H), 2.25 (br. s, 0.8H), 2.19 – 2.13 (m, 1.9H), 2.13 – 2.07 (m, 1.9H), 2.01 – 1.95 (m, 0.2H), 1.89 – 1.84 (m, 0.2H), 1.70 – 1.63 (m, 0.2H), 1.52 (qd, *J* = 13.0, 3.6 Hz, 1.8H), 1.41 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (167.3), 167.1, 152.5, (152.2), (150.7), 150.5, 148.9, 143.0, (142.9), (138.2), 138.0, 137.2, (137.1), 125.8, 124.8, (124.7), 124.3, 124.2, 122.9, (122.7), (113.1), 112.6, 69.8, (64.3), 61.0, (60.5), 56.2, 34.9, (32.2), (29.8), 29.0, (24.4), 14.5. HRMS (ESI+) *m/z* calculated for $C_{21}H_{24}N_3O_3$ $[M+H]^+$: 366.1818, found 366.1816.

The relative stereochemistry of the major diastereoisomer was determined by 1H, gCOSY, gHSQC and 2D NOSEY NMR.



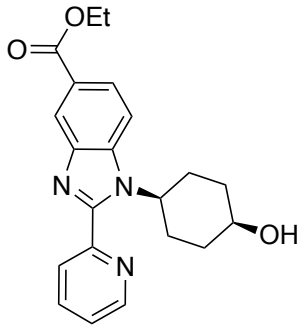
(±)-(*trans*)-1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid [S50]



(±)-(*trans*)-ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**S49**) (29.0 mg, 0.079 mmol, 1.0 equiv.) was dissolved in MeOH (0.16 mL, 0.5 M) and 2M NaOH (0.11 mL, 0.214 mmol, 2.7 equiv.) was added. The mixture was stirred at 60 °C for 2 h. MeOH was removed under reduced pressure and the residue was acidified to pH 4 with glacial acetic acid. The precipitated carboxylic acid was collected by filtration, washed with water and dried to give (±)-(*trans*)-1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid (**S50**) as a white solid with 5 equiv. acetic acid (27.7 mg, 0.043 mmol, 55% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.79 – 8.75 (m, 1H), 8.39 (s, 1H), 8.09 – 7.98 (m, 3H), 7.92 – 7.85 (m, 0.1H), 7.81 – 7.76 (m, 0.9H), 7.58 – 7.52 (m, 1H), 5.20 (app. t, *J* = 12.0 Hz, 1H), 4.10 – 4.05 (m, 0.1H), 3.85 – 3.75 (m, 0.9H), 2.81 (q, *J* = 13.2 Hz, 0.2H), 2.50 (q, *J* = 13.0 Hz, 1.8H), 2.17 – 2.00 (m, 4H), 1.68 – 1.58 (m, 0.2H), 1.42 (q, *J* = 12.7 Hz, 1.8H). ^{13}C NMR (126 MHz, CD_3OD) δ 175.4, 153.2, (153.0), 151.2, (150.4), 150.4, 143.4, 138.8, (138.8), 137.0, 133.9, 126.8, (126.7), 126.0, 125.9, (125.8), 122.1, (113.5), 113.3, 70.1, (64.9), 57.78, 35.5, (32.7), 29.9, (25.5). HRMS (ESI+) *m/z* calculated for $C_{19}H_{20}N_3O_3$ $[M+H]^+$: 338.1505, found 338.1504.

(±)-(*cis*)-ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate [S51]: Reduction of ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate with L-Selectride



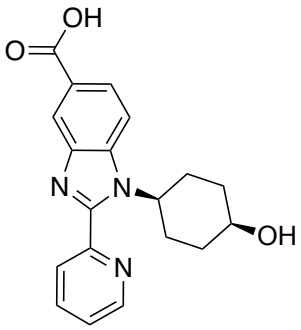
To a solution of ethyl 1-(4-oxocyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**55**) (51.4 mg, 0.141 mmol, 1.0 equiv.) in THF (2.8 mL, 0.05 M) at -78 °C was added L-Selectride® (0.946 M solution in THF, 0.15 mL, 0.141 mmol, 1.0 equiv.) dropwise. The reaction was allowed to stir at -78 °C for 30 minutes. The reaction was quenched by the addition of sat. aq. NH_4Cl (5 mL) and the mixture was allowed to warm to room temperature before being extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% CH_2Cl_2 → 5% MeOH/CH_2Cl_2 gradient as eluent afforded (±)-(*cis*)-ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**S51**) as a white solid as a single diastereoisomer (34.4 mg, 0.094 mmol, 67% yield, >20:1 d.r.).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.8 Hz, 1H), 8.55 (s, 1H), 8.27 (d, *J* = 7.9 Hz, 1H), 7.99 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.88 (td, *J* = 7.8, 1.8 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.38 (dd, *J* = 7.6, 4.8 Hz, 1H), 5.55 (tt, *J* = 12.7, 4.4 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.20 (t, *J* = 3.0 Hz, 1H), 2.80 (qd, *J* = 13.1,

3.9 Hz, 2H), 2.00 (d, *J* = 13.2 Hz, 2H), 1.95 – 1.84 (m, 2H), 1.82 – 1.70 (br. s, 1H), 1.74 – 1.64 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 152.2, 150.7, 148.9, 142.9, 138.2, 137.2, 125.9, 124.8, 124.2, 122.7, 113.1, 64.5, 61.0, 56.2, 32.2, 24.5, 14.5. HRMS (ESI+) *m/z* calculated for $C_{21}H_{24}N_3O_3$ $[M+H]^+$: 366.1818, found 366.1813.

The downfield shift of the α-OH proton and upfield shift of the ipso-OH carbon indicates that the proton is equatorial, thus the relative stereochemistry of the cyclohexyl ring is cis.[22]

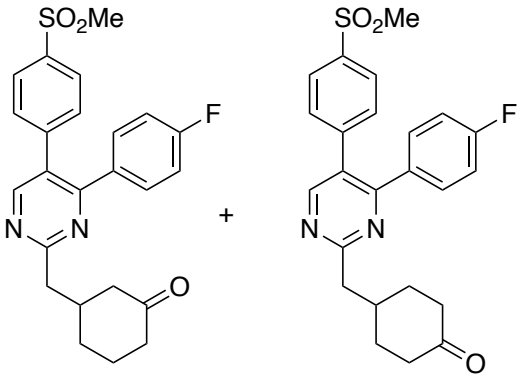
(±)-(*cis*)-1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid [56]



(±)-(*cis*)-ethyl 1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (**S51**) (26.9 mg, 0.074 mmol, 1.0 equiv.) was dissolved in MeOH (0.15 mL, 0.5 M) and 2M NaOH (0.1 mL, 0.200 mmol, 2.7 equiv.) was added. The mixture was stirred at 60 °C for 2 h. MeOH was removed under reduced pressure and the residue was acidified to pH 4 with glacial acetic acid. The precipitated carboxylic acid was collected by filtration, washed with water and dried to give (±)-(*cis*)-1-(4-hydroxycyclohexyl)-2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid (**56**) as a white solid with 10 equiv. acetic acid (22.9 mg, 0.068 mmol, 92% yield).

^{1}H NMR (600 MHz, CD_3OD) δ 8.77 (d, *J* = 4.9 Hz, 1H), 8.42 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 8.05 – 8.00 (m, 2H), 7.93 (d, *J* = 8.6 Hz, 1H), 7.58 – 7.53 (m, 1H), 5.26 (tt, *J* = 12.7, 4.3 Hz, 1H), 4.07 (t, *J* = 3.0 Hz, 1H), 2.80 (qd, *J* = 12.9, 3.8 Hz, 2H), 2.01 – 1.90 (m, 2H), 1.87 – 1.80 (m, 2H), 1.69 – 1.60 (m, 2H). ^{13}C NMR (151 MHz, CD_3OD) δ 173.0, 153.5, 151.0, 150.5, 143.4, 138.8, 137.8, 130.5, 126.8, 125.9, 125.7, 122.5, 113.9, 64.9, 57.8, 32.7, 25.5. HRMS (ES+) *m/z* calculated for $C_{19}H_{20}N_3O_3$ $[M+H]^+$: 338.1505, found 338.1504.

3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [58a] and 4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [58b]

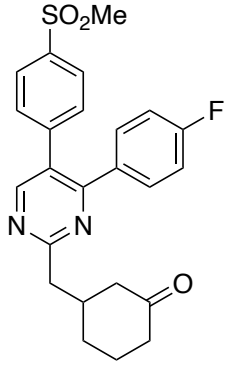


According to the **general procedure for HBF_4•OEt_2 protection**, 2-(cyclohexylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidine (**57**) (127.4 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 µL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **57•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (20.3 mg, 0.015 mmol, 5 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0

equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.25 mL with oxidant, 0.33 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 40% → 50% → 60% → 70% → 80% EtOAc/hexanes gradient as eluent afforded a mixture of 3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**58a**) and 4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**58b**) as a white solid.

Run 1: (60.8 mg, 0.139 mmol, 46.2% yield, 1.1:1 δ:γ), 0% rsm. **Run 2 (0.24 mmol scale):** (52.5 mg, 0.120 mmol, 49.9% yield, 1.1:1 δ:γ), 0% rsm. **Run 3 (0.5 mmol scale):** (109.1 mg, 0.249 mmol, 49.8% yield, 1:1 δ:γ), 0% rsm. **Average: 48.6% yield ± 2.1%, 1.1:1 δ:γ, 0% rsm.**

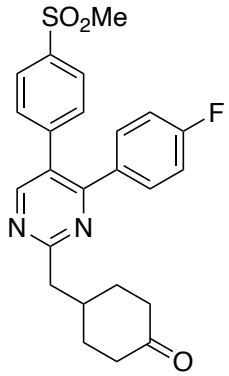
3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [58a]



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.39 – 7.35 (m, 2H), 6.99 (t, *J* = 8.6 Hz, 2H), 3.17 (dd, *J* = 13.6, 6.3 Hz, 1H), 3.09 (s, 3H), 3.01 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.62 – 2.53 (m, 1H), 2.47 – 2.36 (m, 2H), 2.32 (app. td, *J* = 13.1, 6.1 Hz, 1H), 2.23 (t, *J* = 12.5 Hz, 1H), 2.15 – 2.07 (m, 2H), 2.05 – 1.98 (m, 1H), 1.72 (qt, *J* = 12.7, 4.1 Hz, 1H), 1.56 (qd, *J* = 12.8, 3.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.4, 169.0, 163.8 (d, *J* = 251.2 Hz), 162.8, 158.3, 142.3, 140.3, 132.9 (d, *J* = 3.3 Hz), 132.0 (d, *J* = 8.7 Hz), 130.4, 128.8, 128.1, 115.9 (d, *J* = 21.8 Hz), 47.8, 46.1, 44.6, 41.4, 38.9, 31.6, 25.2. ^{19}F NMR (565 MHz, $CDCl_3$) δ -110.0. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M+H]^+$: 439.1492, found 439.1485.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [58b]



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.36 (m, 4H), 7.01 (t, *J* = 8.6 Hz, 2H), 3.09 (s, 3H), 3.09 (d, *J* = 7.2 Hz, 2H), 2.57 (ttt, *J* = 10.8, 7.1, 3.5 Hz, 1H), 2.47 – 2.35 (m, 4H), 2.17 – 2.09 (m, 2H), 1.64 (qd, *J* = 12.1, 5.0 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 211.8, 169.8, 163.8 (d, *J* = 251.2 Hz), 162.8, 158.4, 142.3, 140.3, 133.0 (d, *J* = 3.3 Hz), 132.0 (d, *J* = 8.7 Hz), 130.4, 128.7, 128.2, 115.9 (d, *J* = 21.8 Hz), 45.1, 44.6, 40.9, 36.0, 32.6. ^{19}F NMR (565 MHz, $CDCl_3$) δ -109.9. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M+H]^+$: 439.1492, found 439.1488.

On a 542 mg scale, chiral super critical fluid separation on Waters SFC afforded separation of enantiomers of 3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one and 4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one.

Injection Volume: 1.0 ml

Co-Solvent: 20% IPA + 0.2% DIPA

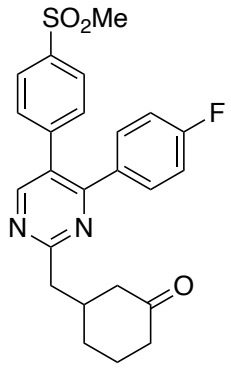
UV Wavelength: 210 nm

Concentration: 542 mg in 36 ml MeOH

Column: OJ-H, 30 x 250 mm

Flow rate: 3 mL/min

Retention times: 1.063, 1.086 and 1.086 min

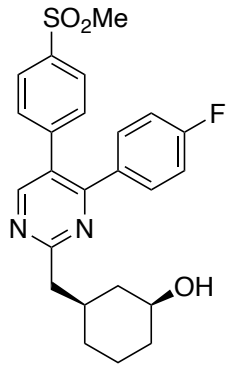


The absolute stereochemistry has not been determined.

(+)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one, **(+)-58a**: $[\alpha]_D^{23}$ = +5.1250 (c = 0.48, $CHCl_3$).

(–)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one, **(–)58a**: $[\alpha]_D^{23}$ = –5.4423 (c = 0.52, $CHCl_3$).

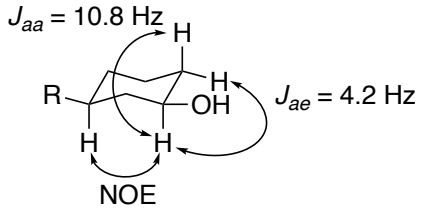
(+)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol [59a]



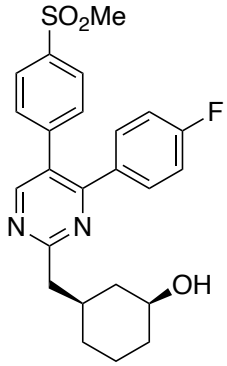
To a flame-dried round bottom flask was added (+)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [**(+)-58a**] (90.0 mg, 0.205 mmol, 1.0 equiv.) and THF (4.1 mL, 0.05 M) and the mixture was cooled to -78 °C. Lithium aluminum hydride (8.6 mg, 0.226 mmol, 1.1 equiv.) was added and the reaction was stirred at -78 °C for 2 hours. The reaction was then warmed to 0 °C and monitored by TLC. Following full conversion of the starting material (as monitored by TLC), the reaction was quenched with water and the mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded (+)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol (**59a**) as a white solid as a 9:1 mixture of diastereoisomers (38.5 mg, 0.087 mmol, 42.6% yield).

^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.64 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 2H), 7.46 – 7.38 (m, 4H), 7.04 – 6.99 (m, 2H), 4.10 – 4.05 (m, 0.1H), 3.57 (tt, *J* = 10.8, 4.2 Hz, 0.9H), 3.06 (s, 3H), 3.00 (dd, *J* = 13.4, 7.0 Hz, 0.9H), 2.94 (dd, *J* = 13.4, 7.5 Hz, 0.9H), 2.95 – 2.91 (m, 0.2H), 2.52 – 2.45 (m, 0.1H), 2.17 – 2.07 (m, 1H), 2.01 – 1.96 (m, 1H), 1.96 – 1.92 (m, 0.9H), 1.78 (dp, *J* = 13.7, 3.5 Hz, 1H), 1.74 – 1.68 (m, 1H), 1.67 – 1.48 (m, 0.7H), 1.47 – 1.40 (m, 0.2H), 1.32 (qt, *J* = 13.3, 3.6 Hz, 1H), 1.37 – 1.27 (m, 0.2H), 1.21 – 1.12 (m, 1.1H), 1.11 – 0.98 (m, 1.8H). ^{13}C NMR (151 MHz, CD_2Cl_2) δ (170.5), 170.3, 163.9 (d, *J* = 250.1 Hz), 162.6, (162.6), 158.5, (142.8), 142.8, 140.5, (140.5), 133.8 (d, *J* = 3.3 Hz), 132.4 (d, *J* = 8.7 Hz), 130.7, 128.7, (128.7), 128.2, 115.8 (d, *J* = 21.8 Hz), 70.8, (66.9), 46.8, (46.3), 44.8, 42.6, (39.8), 36.8, 36.1, (35.9), (33.6), 32.4, 24.3, (20.4). ^{19}F NMR (471 MHz, CD_2Cl_2) δ -111.7, (-110.7). $[a]_D^{22}$ = +6.2500 (c = 0.52, $CHCl_3$), (rotation based on a 9:1 mixture of diastereoisomers). HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_3FS$ $[M+H]^+$: 441.1648, found 441.1649.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.



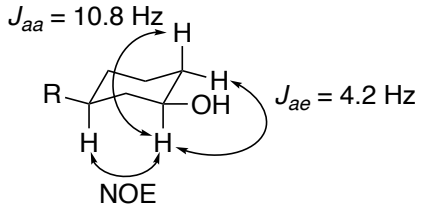
(–)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol [59b]



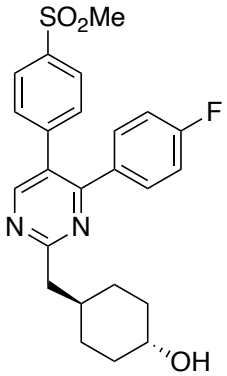
To a flame-dried round bottom flask was added (–)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [**(–)-58a**] (88.4 mg, 0.201 mmol, 1.0 equiv.) and THF (4.0 mL, 0.05 M) and the mixture was cooled to -78 °C. Lithium aluminum hydride (8.4 mg, 0.222 mmol, 1.1 equiv.) was added and the reaction was stirred at -78 °C for 2 hours. The reaction was then warmed to 0 °C and monitored by TLC. Following full conversion of the starting material (as monitored by TLC), the reaction was quenched with water and the mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded (–)-3-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol (**59b**) as a white solid as a 9:1 mixture of diastereoisomers (35.5 mg, 0.081 mmol, 40.0% yield).

^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.64 (s, 1H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.04 – 6.98 (m, 2H), 4.10 – 4.05 (m, 0.1H), 3.57 (tt, *J* = 10.8, 4.2 Hz, 0.9H), 3.06 (s, 3H), 3.00 (dd, *J* = 13.4, 7.0 Hz, 0.9H), 2.94 (dd, *J* = 13.4, 7.5 Hz, 0.9H), 2.95 – 2.91 (m, 0.2H), 2.51 – 2.44 (m, 0.1H), 2.17 – 2.07 (m, 1H), 2.01 – 1.96 (m, 1H), 1.96 – 1.91 (m, 0.9H), 1.78 (dp, *J* = 13.7, 3.5 Hz, 1H), 1.74 – 1.69 (m, 1H), 1.68 – 1.51 (m, 0.8H), 1.47 – 1.40 (m, 0.1H), 1.32 (qt, *J* = 13.2, 3.6 Hz, 1H), 1.25 – 1.21 (m, 0.1 H), 1.21 – 1.12 (m, 1.1H), 1.11 – 0.97 (m, 1.9H). ^{13}C NMR (151 MHz, CD_2Cl_2) δ (170.5), 170.3, 163.9 (d, *J* = 249.6 Hz), 162.6, (162.6), 158.5, (142.8), 142.7, 140.5, (140.5), 133.7 (d, *J* = 3.3 Hz), 132.4 (d, *J* = 8.7 Hz), 130.7, 128.7, 128.2, 115.8 (d, *J* = 21.8 Hz), 70.8, (66.9), 46.8, (46.3), 44.8, 42.6, (39.8), 36.8, 36.1, (33.6), (32.5), 32.4, 24.3, (20.4). ^{19}F NMR (471 MHz, CD_2Cl_2) δ -111.6, (-111.7). $[\alpha]_D^{22}$ = -5.4681 (c = 0.47, $CHCl_3$), (rotation based on a 9:1 mixture of diastereoisomers). HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_3FS$ $[M+H]^+$: 441.1648, found 441.1646.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.



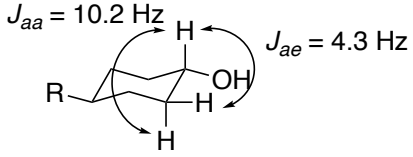
(*trans*)-4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol [S52]



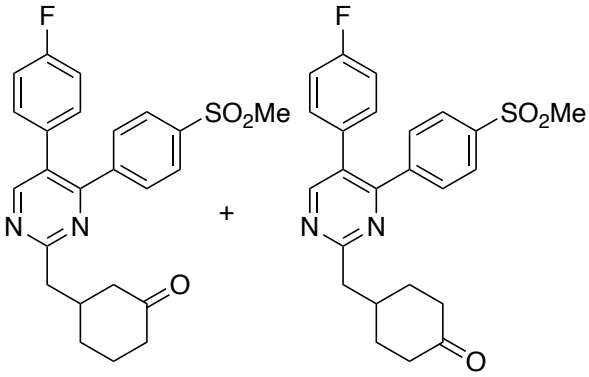
To a flame-dried round bottom flask was added 4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**58b**) (44.2 mg, 0.101 mmol, 1.0 equiv.) and THF (2.0 mL, 0.05 M) and the mixture was cooled to -78 °C. Lithium aluminum hydride (4.2 mg, 0.111 mmol, 1.1 equiv.) was added and the reaction was stirred at -78 °C for 2 hours. The reaction was then warmed to 0 °C and monitored by TLC. Following full conversion of the starting material (as monitored by TLC), the reaction was quenched with water and the mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded (*trans*)-4-((4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol (**S52**) as a white solid as a 9:1 mixture of diastereoisomers (19.7 mg, 0.045 mmol, 44.3% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.37 (m, 4H), 7.00 (app. t, *J* = 8.6 Hz, 2H), 4.00 (s, 0.1H), 3.61 (tt, *J* = 10.2, 4.3 Hz, 0.9H), 3.09 (s, 3H), 3.02 (d, *J* = 7.3 Hz, 0.2H), 2.95 (d, *J* = 7.3 Hz, 1.8H), 2.16 – 2.13 (m, 0.1H), 2.06 – 1.97 (m, 2.9H), 1.83 (d, *J* = 12.4 Hz, 2H), 1.65 – 1.55 (m, 1H), 1.31 (qd, *J* = 12.2, 3.2 Hz, 2H), 1.21 (qd, *J* = 12.7, 3.0 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (170.4), 170.3, 163.8 (d, *J* = 251.2 Hz), 162.7, (162.6), 158.1, (142.5), 142.4, 140.2, (140.2), 133.1 (d *J* = 3.3 Hz), [132.1 (d, *J* = 8.2 Hz)], 132.0 (d, *J* – 8.7 Hz), 130.4, 128.5, (128.4), 128.1, 115.9 (d, *J* = 21.8 Hz), [115.8 (d *J* = 22.3 Hz)], 70.9, (66.9), 46.2, 44.6, 37.0, (36.6), 35.5, (32.4), 31.2, (27.0). ^{19}F NMR (565 MHz, $CDCl_3$) δ -110.1, (-110.2). HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_3FS$ $[M+H]^+$: 441.1648, found 441.1646.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.



3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [S53] and 4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [S54]



According to the **general procedure for HBF_4•OEt_2 protection**, 2-(cyclohexylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidine (**S43**) (42.5 mg, 0.100 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (15 μL, 0.110 mmol, 1.1 equiv.) in CH_2Cl_2 (0.4 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **S43•HBF_4** (0.100 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (13.6 mg, 0.010 mmol, 10 mol%), $ClCH_2CO_2H$ (141.8 mg, 1.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 68 mg, 1.0 mmol, 10.0 equiv.), MeCN (0.2 mL in 40 mL vial, 1.25 mL with oxidant, 0.13 mL MeCN with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 40% → 50% → 60% → 70% → 80% EtOAc/hexanes gradient as eluent afforded a mixture of 3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one 4 (**S53**) and -((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**S54**) as a white solid.

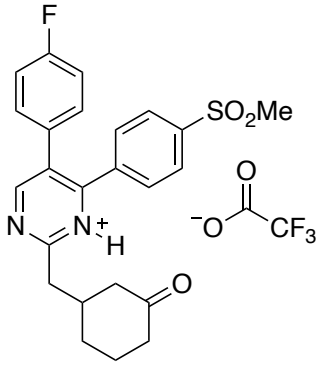
Run 1: (24.6 mg, 0.056 mmol, 56.1% yield, 1.2:1 δ:γ), 0% rsm. **Run 2:** (25.0 mg, 0.057 mmol, 57.0% yield, 1.3:1 δ:γ), 0% rsm. **Run 3:** (24.3 mg, 0.055 mmol, 55.4% yield, 1.3:1 δ:γ), 0% rsm. **Average: 56.2% yield ± 0.8%, 1.3:1 δ:γ, 0% rsm.**

Without HBF_4: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: 2-(cyclohexylmethyl)-4-(4-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)pyrimidine (**S43**) (42.5 mg, 0.100 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (13.6 mg, 0.010 mmol, 10 mol%), $ClCH_2CO_2H$ (141.8 mg, 1.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 68 mg, 1.0 mmol, 10.0 equiv.), MeCN (0.2 mL in 40 mL vial, 1.25 mL with oxidant, 0.13 mL with catalyst). The reaction was run at -36 °C with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method A. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 40% → 50% → 60% → 70% → 80% EtOAc/hexanes gradient as eluent afforded a mixture of 4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**S53**) and 3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**S54**) as a white solid.

Yield: (14.1 mg, 0.032 mmol, 32.2% yield), (5.1 mg, 0.012 mmol, 12.0% rsm).

Mixture was separated for characterization. 30 mg of mixture was separated by quantitative HPLC (Waters CSH C18 column, 5 μm, 19x100 mm, 25 mL/min flow rate). Method was performed using 30 to 65% MeCN with 0.16% TFA gradient in H_2O with 0.16% TFA over 8 minutes.

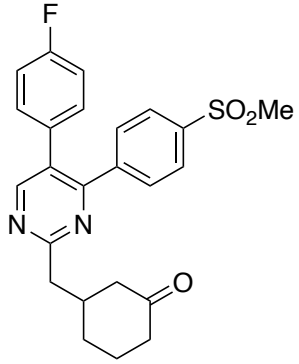
5-(4-fluorophenyl)-6-(4-(methylsulfonyl)phenyl)-2-((3-oxocyclohexyl)methyl)pyrimidin-1-ium trifluoroacetate salt



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.20 – 7.14 (m, 2H), 7.13 – 7.06 (m, 2H), 3.26 (dd, *J* = 14.0, 6.2 Hz, 1H), 3.08 (dd, *J* = 14.0, 7.8 Hz, 1H), 3.06 (s, 3H), 2.63 – 2.51 (m, 1H), 2.47 – 2.38 (m, 2H), 2.38 – 2.24 (m, 2H), 2.13 – 2.05 (m, 1H), 2.05 – 1.97 (m, 1H), 1.81 – 1.68 (m, 1H), 1.66 – 1.55 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 163.6, 163.3 (d, *J* = 250.5 Hz), 156.4, 142.0, 141.9, 131.2 (d, *J* = 8.7 Hz), 131.1, 131.0, 130.2 (d, *J* = 3.8 Hz), 127.7, 116.8 (d, *J* = 22.1 Hz), 47.0, 44.5, 44.3, 41.2, 38.4, 31.4, 24.9 (cannot see carbonyl carbon, confirmed carbonyl signal by HMBC). ^{19}F NMR (471 MHz, $CDCl_3$) δ -111.2. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M\text{-}TFA+H]^+$: 439.1492, found 439.1473.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

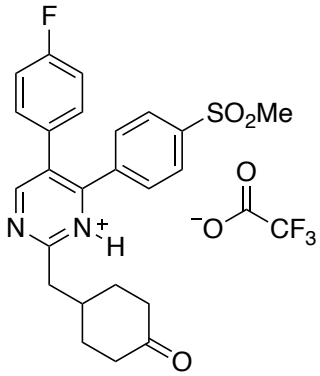
3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [S53]



5-(4-fluorophenyl)-6-(4-(methylsulfonyl)phenyl)-2-((3-oxocyclohexyl)methyl)pyrimidin-1-ium trifluoroacetate salt was made into the free base by washing with 3M NaOH and extracting with CH_2Cl_2.

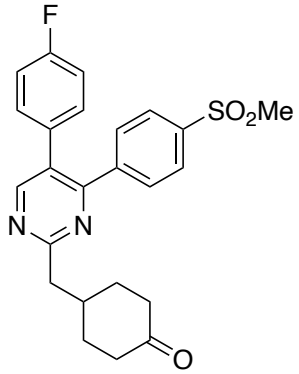
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.17 – 7.11 (m, 2H), 7.07 (app. t, *J* = 8.6 Hz, 2H), 3.17 (dd, *J* = 13.6, 6.2 Hz, 1H), 3.07 – 2.97 (m, 1H), 3.05 (s, 3H), 2.63 – 2.51 (m, 1H), 2.48 – 2.37 (m, 2H), 2.36 – 2.26 (m, 1H), 2.26 – 2.07 (m, 2H), 2.07 – 1.97 (m, 1H), 1.73 (app. qt, *J* = 12.8, 4.2 Hz, 1H), 1.64 – 1.51 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.4, 168.5, 163.0 (d, *J* = 249.6 Hz), 161.6, 158.9, 143.0, 141.3, 131.35 (d, *J* = 3.4 Hz), 131.20 (d, *J* = 8.2 Hz), 130.9, 130.1, 127.5, 116.5 (d, *J* = 22.1 Hz), 47.8, 46.0, 44.6, 41.5, 38.9, 31.6, 25.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.5. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M+H]^+$: 439.1492, found 439.1493.

5-(4-fluorophenyl)-6-(4-(methylsulfonyl)phenyl)-2-((4-oxocyclohexyl)methyl)pyrimidin-1-ium trifluoroacetate salt



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.20 – 7.14 (m, 2H), 7.13 – 7.04 (m, 2H), 3.13 (d, *J* = 7.1 Hz, 2H), 3.06 (s, 3H), 2.61 – 2.50 (m, 1H), 2.50 – 2.34 (m, 4H), 2.18 – 2.08 (m, 2H), 1.73 – 1.59 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.9, 168.2, 163.2 (d, *J* = 250.0 Hz), 162.8, 157.5, 142.4, 141.7, 131.2 (d, *J* = 8.2 Hz), 130.9, 130.9, 130.6 (unresolved doublet), 127.7, 116.7 (d, *J* = 21.6 Hz), 44.5, 44.2, 40.7, 36.1, 32.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -111.6. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M\text{-}TFA+H]^+$: 439.1492, found 439.1474.

4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [S54]



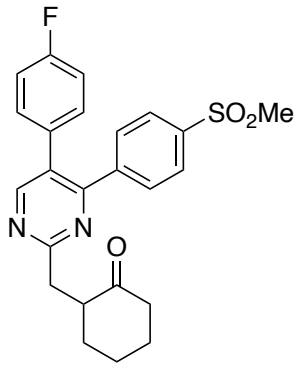
5-(4-fluorophenyl)-6-(4-(methylsulfonyl)phenyl)-2-((4-oxocyclohexyl)methyl)pyrimidin-1-ium trifluoroacetate salt was made into the free base by washing with 3M NaOH and extracting with CH_2Cl_2.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.18 – 7.11 (m, 2H), 7.07 (app. t, *J* = 8.5 Hz, 2H), 3.09 (d, *J* = 7.1 Hz, 2H), 3.05 (s, 3H), 2.61 – 2.50 (m, 1H), 2.47 – 2.34 (m, 4H), 2.17 – 2.10 (m, 2H), 1.70 – 1.58 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.7, 169.2, 163.0 (d, *J* = 249.6 Hz), 161.6, 158.9, 143.1, 141.3, 131.4 (d, *J* = 3.8 Hz), 131.2 (d, *J* = 8.2 Hz), 130.9, 130.0, 127.6,

116.5 (d, J = 21.6 Hz), 45.0, 44.5, 40.9, 36.1, 32.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.4. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M+H]^+$: 439.1492, found 439.1489.

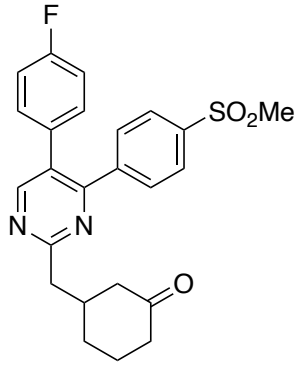
On larger 400 mg scale, initial semi-preparative HPLC separated 17 mg of 2-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one from other ketone isomers.

2-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one [S55]



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.87 (d, J = 8.1 Hz, 2H), 7.59 (d, J = 8.1 Hz, 2H), 7.13 (dd, J = 8.5, 5.3 Hz, 2H), 7.06 (app. t, J = 8.4 Hz, 2H), 3.58 (dd, J = 15.7, 7.2 Hz, 1H), 3.29 (app. sxt., J = 6.3 Hz, 1H), 3.05 (s, 3H), 2.94 (dd, J = 15.7, 6.4 Hz, 1H), 2.50 – 2.39 (m, 2H), 2.22 – 2.16 (m, 1H), 2.16 – 2.10 (m, 1H), 1.97 – 1.87 (m, 1H), 1.81 – 1.68 (m, 2H), 1.64 – 1.55 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.0, 169.0, 162.9 (d, J = 249.6 Hz), 161.4, 158.5, 143.1, 141.2, 131.5 (d, J = 3.4 Hz), 131.2 (d, J = 8.2 Hz), 130.9, 129.8, 127.5, 116.5 (d, J = 21.6 Hz), 49.4, 44.6, 42.2, 39.0, 34.2, 28.1, 25.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.6. HRMS (ESI+) *m/z* calculated for $C_{24}H_{24}N_2O_3FS$ $[M+H]^+$: 439.1492, found 439.1486.

Second chiral super critical fluid separation on Waters SFC afforded separation of enantiomers of 3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one and 4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one.
Injection Volume: 1.5 ml
Co-Solvent: 20% EtOH
UV Wavelength: 210 nm
Concentration: 316mg in 21ml MeOH
Stacked injections = 14
Column: CHIRALCEL® OJ-H, 30 x 250mm
Retention Times: 1.38, 1.38 and 1.36 min

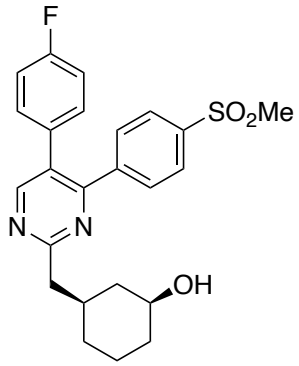


The absolute stereochemistry has not been determined.

(+)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one **S53a**: $[\alpha]_D^{23}$ = +6.0681 (c = 0.715, $CHCl_3$).

(−)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one **S53b**: $[\alpha]_D^{23}$ = –6.4679 (c = 0.52, $CHCl_3$).

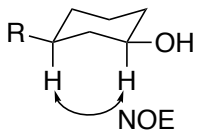
(+)-(*cis*)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol [S56]



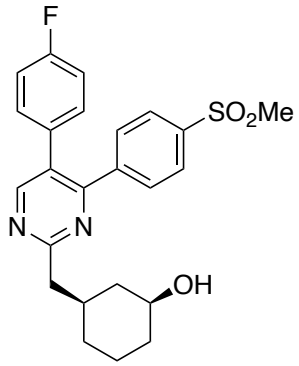
To a flame-dried round bottom flask was added (+)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**S53a**) (63.1 mg, 0.144 mmol, 1.0 equiv.) and THF (2.7 mL, 0.05 M) and the mixture was cooled to -78 °C. Lithium aluminum hydride (6.0 mg, 0.158 mmol, 1.1 equiv.) was added and the reaction was stirred at -78 °C for 2 hours. The reaction was then warmed to 0 °C and monitored by TLC. Following full conversion of the starting material (as monitored by TLC), the reaction was quenched with water and the mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded **(+)-**3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol (**S56**) as a white solid as a 9:1 mixture of diastereoisomers (59.7 mg, 0.136 mmol, 99.6% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.15 – 7.09 (m, 2H), 7.07 – 7.01 (m, 2H), 4.10 (br. s, 0.1H), 3.59 (td, *J* = 10.7, 5.2 Hz, 0.9H), 3.05 – 2.99 (m, 0.9H), 3.03 (s, 3H), 2.99 – 2.92 (m, 1.1H), 2.54 – 2.45 (m, 0.1H), 2.14 – 2.07 (m, 0.9H), 2.02 – 1.94 (m, 1.8H), 1.82 – 1.64 (m, 2.9H), 1.60 – 1.52 (m, 0.2H), 1.48 – 1.41 (m, 0.1H), 1.37 – 1.25 (m, 1H), 1.25 – 1.14 (m, 1.2H), 1.14 – 0.98 (m, 1.8H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (169.7), 169.4, 162.8 (d, *J* = 249.0 Hz), 161.4, (161.3), 158.6, (158.6) (143.2), 143.1, 141.1, (141.0), [131.5 (d, *J* = 3.3 Hz)], 131.4 (d, *J* = 3.8 Hz), 131.2 (d, *J* = 8.2 Hz), (130.8), 130.8, 129.7, (129.7), 127.5, (127.4), 116.4 (d, *J* = 21.8 Hz), [116.4 (d, *J* = 21.8 Hz)], 70.6, (66.7), 46.4, (45.9), 44.5, 42.1, (39.4), 36.6, 35.7, (33.3), (32.2), (32.2), 32.1, 24.0, (20.0). ^{19}F NMR (565 MHz, $CDCl_3$) δ -112.6, (-112.7). $[\alpha]_D^{22}$ = +4.4641 (c = 0.51, $CHCl_3$), (rotation based on a 9:1 mixture of diastereoisomers). HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_3FS$ $[M+H]^+$: 441.1648, found 441.1640.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.



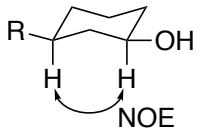
(−)-(*cis*)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol [S57]



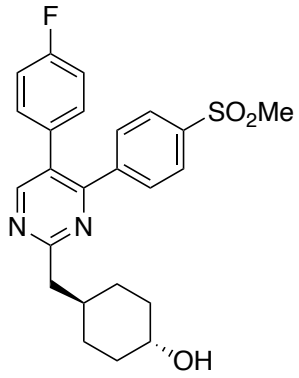
To a flame-dried round bottom flask was added (–)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**S53b**) (60.0 mg, 0.137 mmol, 1.0 equiv.) and THF (2.7 mL, 0.05 M) and the mixture was cooled to -78 °C. Lithium aluminum hydride (5.7 mg, 0.151 mmol, 1.1 equiv.) was added and the reaction was stirred at -78 °C for 2 hours. The reaction was then warmed to 0 °C and monitored by TLC. The reaction was quenched with water and the mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded (–)-3-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol (**S57**) as a white solid as a 9:1 mixture of diastereoisomers (35.1 mg, 0.797 mmol, 58% yield; 9.6 mg, 0.022 mmol, 16% rsm).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (d, *J* = 1.2 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.16 – 7.11 (m, 2H), 7.08 – 7.02 (m, 2H), 4.12 (s, 0.1H), 3.61 (tt, *J* = 10.1, 4.2 Hz, 0.9H), 3.07 – 3.01 (m, 0.9H), 3.04 (s, 3H), 2.97 (dd, *J* = 13.7, 7.6 Hz, 1.1H), 2.55 – 2.47 (m, 0.1H), 2.17 – 2.08 (m, 1H), 1.99 (t, *J* = 15.1 Hz, 1.9H), 1.80 (dt, *J* = 13.6, 3.6 Hz, 1.2H), 1.72 (d, *J* = 13.3 Hz, 1.6H), 1.32 (qt, *J* = 13.3, 3.6 Hz, 1.1H), 1.27 – 1.15 (m, 1.3H), 1.14 – 0.99 (m, 1.9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (169.6), 169.4, 162.9 (d, *J* = 249.6 Hz), 161.4, 158.6, (158.6), (143.2), 143.1, 141.1, (141.1), 131.4 (d, *J* = 3.3 Hz), 131.2 (d, *J* = 8.2 Hz), (130.9), 130.9, (129.9), 129.8, (129.7), (128.4), 127.5, (127.5), 116.4 (d, *J* = 21.8 Hz), 70.7, (66.7), 46.4, (45.9), 44.5, 42.1, (39.4), 36.6, 35.7, (33.3), (32.3), (32.2), 32.1, 24.0, (20.1). ^{19}F NMR (565 MHz, $CDCl_3$) δ -112.6, (-112.6). $[a]_D^{24}$ = -3.6393 (c = 1.22, $CHCl_3$), (rotation based on a 9:1 mixture of diastereoisomers). HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_3FS$ $[M+H]^+$: 441.1648, found 441.1648.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.



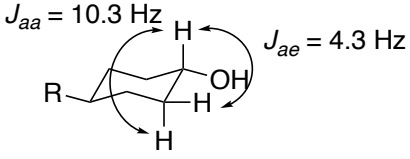
(*trans*)-4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol [S58]



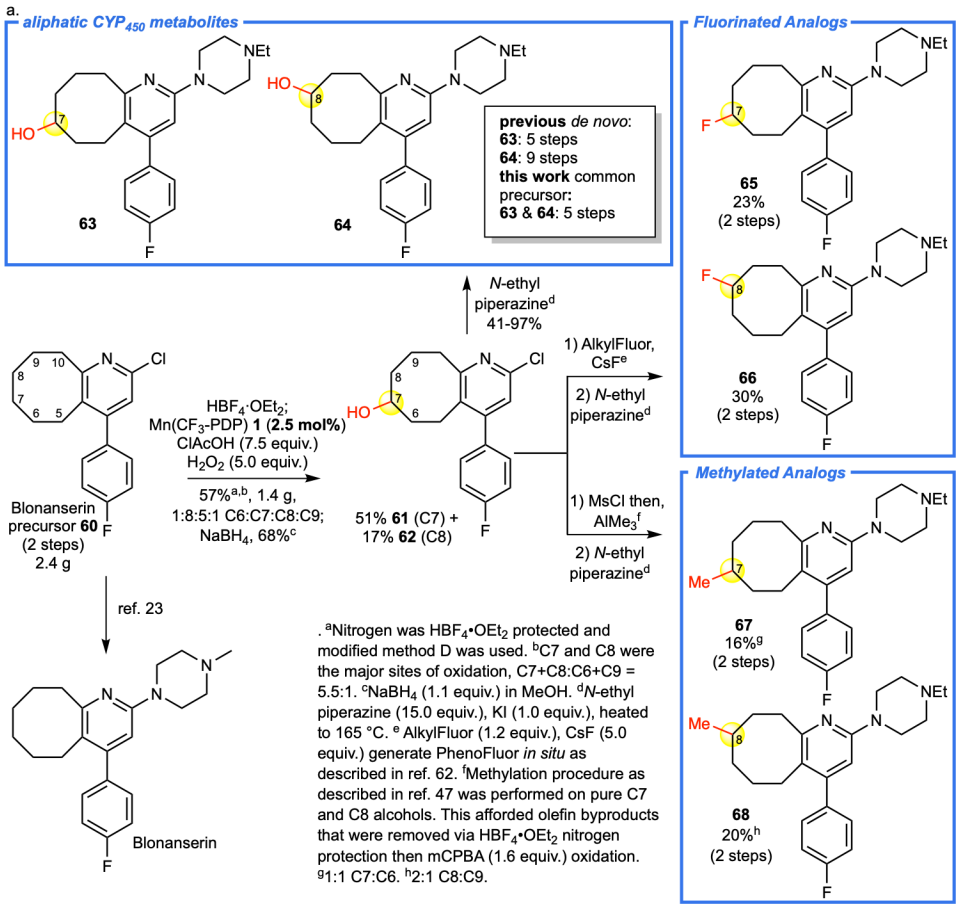
To a flame-dried round bottom flask was added 4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-one (**S54**) (55.0 mg, 0.125 mmol, 1.0 equiv.) and THF (2.5 mL, 0.05 M) and the mixture was cooled to -78 °C. Lithium aluminum hydride (5.2 mg, 0.138 mmol, 1.1 equiv.) was added and the reaction was stirred at -78 °C for 2 hours. The reaction was then warmed to 0 °C and monitored by TLC. Following full conversion of the starting material (as monitored by TLC), the reaction was quenched with water and the mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% MeOH/CH_2Cl_2 gradient as eluent afforded 4-((5-(4-fluorophenyl)-4-(4-(methylsulfonyl)phenyl)pyrimidin-2-yl)methyl)cyclohexan-1-ol (**S58**) as a white solid as a 9:1 mixture of diastereoisomers (53.1 mg, 0.121 mmol, 96.7% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.13 (dd, *J* = 8.4, 5.2 Hz, 2H), 7.05 (app. t, *J* = 8.4 Hz, 2H), 4.00 – 3.96 (m, 0.1H), 3.60 (tt, *J* = 10.3, 4.3 Hz, 0.9H), 3.03 (s, 3H), 3.01 (d, *J* = 7.3 Hz, 0.3H), 2.94 (d, *J* = 7.1 Hz, 1.7H), 2.18 – 2.05 (m, 0.2H), 2.04 – 1.95 (m, 2.8H), 1.84 – 1.79 (m, 1.8H), 1.78 – 1.64 (m, 1H), 1.64 – 1.52 (m, 0.8H), 1.34 – 1.25 (m, 1.8H), 1.24 – 1.14 (m, 1.8H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (169.8), 169.7, 162.9 (d, *J* = 249.6 Hz), 161.4, (161.3), 158.6, (143.2), 143.1, 141.1, (141.1), [131.5 (d, *J* = 3.8 Hz)], 131.4 (d, *J* = 3.3 Hz), 131.2 (d, *J* = 8.2 Hz), (130.9), 130.8, 129.7, (129.7), 127.5 (127.5), 116.4 (d, *J* = 21.3 Hz), 70.9, (66.9), 46.2, (45.7), 44.5, 37.0, (36.6), 35.5, (32.3), 31.2, (27.0). ^{19}F NMR (565 MHz, $CDCl_3$) δ -112.6, (-112.6). HRMS (ESI+) *m/z* calculated for $C_{24}H_{26}N_2O_3FS$ $[M+H]^+$: 441.1648, found 441.1648.

The relative stereochemistry of the major diastereoisomer was determined based on a combination of 1H, gCOSY, gHSQC and 2D NOSEY NMR.

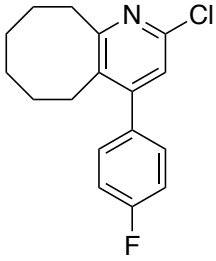


V. Supplementary Figure 3. Streamlining Metabolite Synthesis



Preparation of Substrates and Compounds Characterization for Supplementary Figure 3

2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [60]

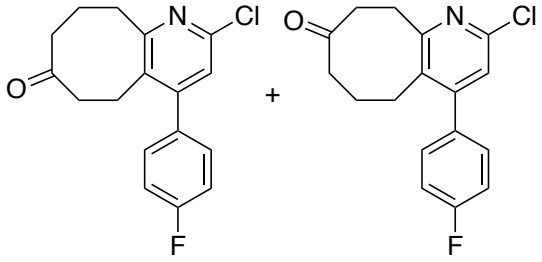


Prepared according to a reported procedure.[23] A mixture of 4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-2(1*H*)-one (1.1 g, 4.1 mmol, 1.0 equiv.) and phenyl phosphine dichloride (2.2 mL, 16.2 mmol, 4.0 equiv.) was heated to 165 °C for 4 hours. The reaction was cooled to room temperature and diluted with CH_2Cl_2 and water. The mixture was adjusted to pH 8-9 with 10% aq. NH_3. The organic layer was separated and washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 5% → 15% → 20% acetone/hexanes gradient as eluent afforded 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) as a white solid (796.5 mg, 2.75 mmol, 67% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 2H), 7.12 (t, *J* = 8.7 Hz, 2H), 6.99 (s, 1H), 3.00 (app. t, *J* = 6.3 Hz, 2H), 2.68 (app. t, *J* = 6.2 Hz, 2H), 1.88 – 1.80 (m, 2H), 1.49 – 1.40 (m, 4H), 1.40 – 1.31 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.0, 162.7 (d, *J* = 247.6 Hz), 151.9, 147.8, 135.0 (d, *J* =3.4 Hz), 132.6, 130.2 (d, *J* = 8.2 Hz), 122.9, 115.5 (d, *J* = 21.6 Hz), 35.4, 31.2, 30.7, 26.9, 26.6, 25.8. ^{19}F NMR

(471 MHz, $CDCl_3$) δ -114.2. HRMS (ESI+) *m/z* calculated for $C_{17}H_{18}NClF$ $[M+H]^+$: 290.1112, found 290.1112.

C—H Oxidation of Substrates and Product Characterization for Supplementary Figure 3

2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one [S59a] and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one [S59b]



According to the **general procedure for HBF_4•OEt_2 protection**, 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) (86.9 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method A: Slow Catalyst Addition Protocol:** the resultant **60•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (40.7 mg, 0.03 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 204.0 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 °C with a dry ice/1,2-dichloroethane bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 15% acetone/hexanes as eluent afforded a mixture of 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) as a white solid.

Run 1: (44.8 mg, 0.147 mmol, 49.2% yield, 1.7:1 rr), (3.4 mg, 0.012 mmol, 4.3% rsm). **Run 2:** (45.8 mg, 0.151 mmol, 50.3% yield, 1.8:1 rr), (4.8 mg, 0.016 mmol, 5.5% rsm). **Run 3:** (41.9 mg, 0.138 mmol, 46.0% yield, 1.7:1 rr), (5.7 mg, 0.020 mmol, 6.6% rsm). **Average: 48.5% yield ± 2.2%, 1.7:1 rr, 5.5% ± 1.2% rsm.** Regioisomer ratio determined by ^{1}H NMR.

5 mol% catalyst: According to the **general procedure for HBF_4•OEt_2 protection**, 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) (86.9 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The oxidation was carried out according to **General Method A: Slow Catalyst Addition Protocol:** the resultant **60•HBF_4** (0.300 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (20.3 mg, 0.015 mmol, 5 mol%), H_2O_2 (50 wt% in H_2O, 204.0 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 °C with a dry ice/1,2-dichloroethane bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 15% acetone/hexanes as eluent afforded a mixture of 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-

fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) as a white solid.
Run 1: (48.2 mg, 0.159 mmol, 52.9% yield, 1.7:1 rr), (18.3 mg, 0.063 mmol, 21.1% rsm). **Run 2:** (44.9 mg, 0.148 mmol, 49.3% yield, 1.5:1 rr), (23.1 mg, 0.080 mmol, 26.6% rsm). **Average: 51.1% yield, 1.6:1 rr, 23.9% rsm.** Regioisomer ratio determined by ^{1}H NMR.

2 mmol scale: According to the **general procedure for HBF_4•OEt_2 protection**, 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) (579.6 mg, 2.0 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (300.6 μL, 2.2 mmol, 1.1 equiv.) in CH_2Cl_2 (8 mL, 0.25 M). The oxidation was run with a modified **General Method A: Slow Catalyst Addition Protocol:** the resultant **60•HBF_4** (2.0 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (2.84 g, 30.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (135.5 mg, 0.010 mmol, 5 mol%), H_2O_2 (50 wt% in H_2O, 1.36 g, 20.0 mmol, 10.0 equiv.), MeCN (4 mL in 100 mL recovery flask, 25 mL with oxidant, divided into 3 equal batches and loaded into 3 50 mL syringes, 2.5 mL with catalyst, divided into 3 equal batches and loaded into 3 1 mL syringes). The reaction was run at -36 °C with a dry ice/1,2-dichloroethane bath. After each 1 hour of addition that depleted the syringes of oxidant and catalyst solutions, the next syringes (one of oxidant and one of catalyst) was loaded into the syringe pump and addition continued. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 10% → 15% acetone/hexanes as eluent afforded a mixture of 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) as a white solid.
Run 1: (313.5 mg, 1.032 mmol, 51.6% yield, 1.4:1 rr), (99.5 mg, 0.343 mmol, 17.2% rsm). **Run 2:** (294.0 mg, 0.968 mmol, 48.4% yield, 1.8:1 rr), (109.5 mg, 0.378 mmol, 18.9% rsm). **Average: 50.0% yield, 1.6:1 rr, 18.1% rsm.** Regioisomer ratio determined by ^{1}H NMR.

6 mmol scale: 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) was recrystallized from acetone prior to scale up oxidation. According to the **general procedure for HBF_4•OEt_2 protection**, 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) (1.74 g, 6.0 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (0.9 mL, 6.6 mmol, 1.1 equiv.) in CH_2Cl_2 (24 mL, 0.25 M). The oxidation was run with a modified **General Method A: Slow Catalyst Addition Protocol:** the resultant **60•HBF_4** (6.0 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (8.51 g, 90.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (406.5 mg, 0.3 mmol, 5 mol%), H_2O_2 (50 wt% in H_2O, 4.08 g, 60.0 mmol, 10.0 equiv.), MeCN (12 mL in 300 mL round bottom flask, 75 mL with oxidant, divided into two equal batches and loaded in 2 50 mL syringes and 7.5 mL with catalyst, loaded into a 10 mL syringe). Two separate syringe pumps were used: one syringe pump added oxidant (25 mL/hour) and the second syringe

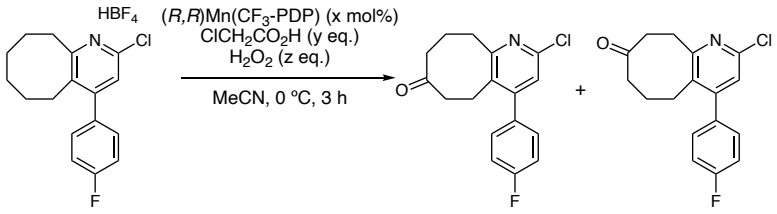
pump added catalyst (2.5 mL/hour). The reaction was run at -36 °C with a dry ice/1,2-dichloroethane bath. After 1.5 hours of addition that depleted the syringe of oxidant solution, the next syringe with oxidant solution was loaded into the syringe pump and addition continued. Upon completing of all oxidant and catalyst solutions, the reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. DO NOT concentrate the reaction to dryness. Flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 10% → 15% acetone/hexanes as eluent afforded a mixture of 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) as a white solid.

Yield: (911.1 mg, 3.00 mmol, 50.0% yield, 1.4:1 rr), (333.7 mg, 1.15 mmol, 19.2% rsm). Regioisomer ratio determined by ^{1}H NMR.

Regioisomers were assigned by taking the product, reducing to alcohol and cross-coupling to *N*-ethylpiperazine (as described in the original publication) and comparing the NMR data to the published work (see below).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 1.5H), 7.21 – 7.10 (m, 2.9H), 7.05 (s, 0.4H), 7.03 (s, 0.6H), 3.32 – 3.27 (m, 0.7H), 3.06 – 3.02 (m, 1.3H), 3.01 – 2.96 (m, 1.4H), 2.83 – 2.79 (m, 0.8H), 2.70 – 2.65 (m, 0.7H), 2.47 – 2.42 (m, 1.3H), 2.41 – 2.35 (m, 2H), 2.02 – 1.93 (m, 1.3H), 1.66 – 1.59 (m, 0.7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (213.5), 213.0, 162.8 (d, J = 248.5 Hz), [162.8 (d, J = 248.5 Hz)], 161.1, (160.4), (152.9), 152.4, 148.9, (148.6), [134.4 (d, J = 3.5 Hz)], 134.2 (d, J = 3.5 Hz), (131.4), 131.0, [130.1 (d, J = 8.1 Hz)], 130.1 (d, J = 8.2 Hz), (124.0), 123.6, 115.9 (d, J = 21.7 Hz), [115.8 (d, J = 21.7 Hz)], 47.8, (47.6), 40.5, (39.9), 36.1, (31.9), (27.7), (26.1), 25.3, 23.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ -112.9, -113.1. HRMS (ESI+) *m/z* calculated for $C_{17}H_{16}NOFCl$ $[M+H]^+$: 304.0904, found 304.0894.

Optimization for 8.3 mmol scale up:



S59a **S59b**

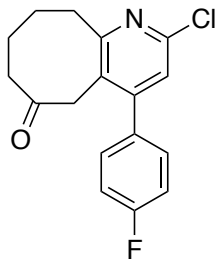
entry	x (mol %)	y (eq.)	z (eq.)	yield (%)[a]	
				rsm	**S59a**+**S59b** (**S59a**:**S59b**)
1	2.5	3.75	2.5	43	36 (1.7:1)
2	2.5	7.5	5.0	25	48 (1.6:1)
3	2.5	11.25	7.5	15	48 (1.6:1)
4[b]	2.5	7.5	5.0	48	32 (1.5:1)
5[c]	2.5	7.5	5.0	80	12 (1.9:1)

[a]Isolated yields, the ratio of regioisomers was determined by ^{1}H NMR. [b]At room temperature. [c]At -36 °C.

8.3 mmol scale: According to the **general procedure for HBF_4•OEt_2 protection**, 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**60**) (2.41 g, 8.3 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (1.25 mL, 9.13 mmol, 1.1 equiv.) in CH_2Cl_2 (33 mL, 0.25 M). The oxidation was run with a modified **Method D: Lower Catalyst Loading:** the resultant **60•HBF_4** (8.3 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (5.9 g, 62.25 mmol, 7.5 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (281.2 mg, 0.2075 mmol, 2.5 mol%), H_2O_2 (50 wt% in H_2O, 2.8 g, 41.5 mmol, 5.0 equiv.), MeCN (27 mL in 500 mL round bottom flask, 170 mL with oxidant, divided into three equal batches and loaded in 3 x 50 mL syringes and 17 mL with catalyst, loaded into a 50 mL syringe). Two separate syringe pumps were used: one syringe pump added oxidant (56.67 mL/hour) and the second syringe pump added catalyst (5.667 mL/hour). The reaction was run at 0 °C with an ice/water bath bath. Every 1.0 hour of addition that depleted the syringe of oxidant solution, the next syringe with oxidant solution was loaded into the syringe pump and addition continued. Upon completing of all oxidant and catalyst solutions, the reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. DO NOT concentrate the reaction to dryness. Flash column chromatography on silica (45 mm fritted glass column, 200 mL SiO_2) using 10% → 25% ethyl acetate/hexanes as eluent afforded a mixture of 2-chloro-4-(4- fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) as a white solid and a mixture of 2-chloro-4-(4-fluorophenyl)-7,8,9,10-tetrahydrocycloocta[*b*]pyridin-6(5*H*)-one (**S59c**) and 2-chloro-4-(4-fluorophenyl)-5,7,8,10-tetrahydrocycloocta[*b*]pyridin-9(6*H*)-one (**S59d**) as a white solid.

Run 1: (1.22 g, 4.01 mmol, 48.3% yield of **S59a**/**S59b**, 1.64:1), (220 mg, 0.725 mmol, 8.7% yield of **S59c**/**S59d**, 1.32:1), (416.2 mg, 1.44 mmol, 17.3% rsm). **Run 2:** (1.19 g, 3.92 mmol, 47.2% yield of **S59a**/**S59b**, 1.61:1), (216 mg, 0.710 mmol, 8.6% yield of **S59c**/**S59d**, 1.27:1), (454.3 mg, 1.57 mmol, 18.9% rsm). **Average: 47.8% yield of S59a/S59b, 8.7% yield of S59c/S59d, 18.1% rsm.**

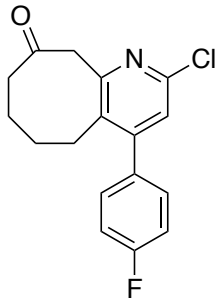
2-chloro-4-(4-fluorophenyl)-7,8,9,10-tetrahydrocycloocta[*b*]pyridin-6(5*H*)-one [S59c]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 – 7.14 (m, 4H), 7.12 (s, 1H), 3.66 (s, 2H), 3.01 – 2.95 (m, 2H), 2.38 – 2.32 (m, 2H), 2.06 – 1.97 (m, 2H), 1.87 – 1.79 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.9, 163.0 (d, J = 249.5 Hz), 162.8, 152.5, 149.7, 133.7 (d, J = 3.7 Hz), 130.6 (d, J = 8.2 Hz), 126.2, 123.2, 116.0 (d, J = 21.8 Hz), 44.5, 40.8, 35.8, 29.2, 25.9. ^{19}F NMR (470 MHz, $CDCl_3$) δ -112.8. HRMS (ESI+) *m/z* calculated for $C_{17}H_{16}NOFCl$ $[M+H]^+$: 304.0904, found 304.0901.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

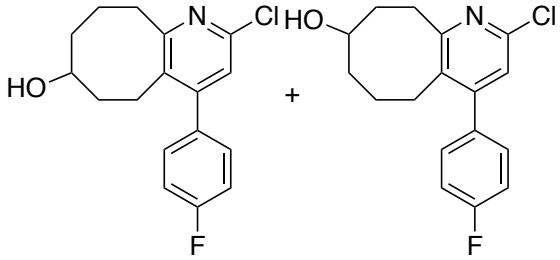
2-chloro-4-(4-fluorophenyl)-5,7,8,10-tetrahydrocycloocta[*b*]pyridin-9(6*H*)-one [S59d]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 2H), 7.18 – 7.13 (m, 2H), 7.12 (s, 1H), 4.09 (s, 2H), 2.69 – 2.63 (m, 2H), 2.47 – 2.41 (m, 2H), 1.78 – 1.70 (m, 2H), 1.61 – 1.53 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.4, 162.8 (d, J = 248.8 Hz), 155.3, 153.1, 148.4, 134.2 (d, J = 3.7 Hz), 133.0, 130.1 (d, J = 8.2 Hz), 124.5, 115.9 (d, J = 21.7 Hz), 52.4, 42.1, 29.5, 27.1, 24.5. ^{19}F NMR (470 MHz, $CDCl_3$) δ -113.4. HRMS (ESI+) *m/z* calculated for $C_{17}H_{16}NOFCl$ $[M+H]^+$: 304.0904, found 304.0902.

Site of oxidation was assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

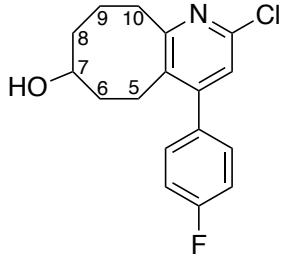
2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol [61] and 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol [62]



To a solution of 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) (496.7 mg, 1.64 mmol, 1.0 equiv.) in MeOH (5.5 mL, 0.3 M) was added sodium borohydride (68.0 mg, 1.80 mmol, 1.1 equiv.) at 0 °C. The reaction was allowed to stir at room temperature overnight. The reaction was quenched by the addition of water (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (24 g) using 100% CH_2Cl_2 → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol (**61**) as a white solid (256.5 mg, 0.84 mmol, 51% yield) and 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol (**62**) as a white solid (83.5 mg, 0.27 mmol, 17% yield).

Regioisomers were assigned by taking the product and cross-coupling to *N*-ethylpiperazine (as described in the original publication) and comparing the NMR data to the published work (see below).

2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol [61]

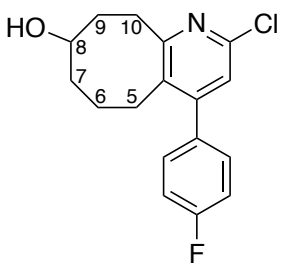


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 2H), 7.15 – 7.09 (m, 2H), 7.00 (s, 1H), 3.56 (ddd, J = 10.0, 8.3, 4.0 Hz, 1H), 3.03 – 2.91 (m, 2H), 2.77 (ddd, J = 14.2, 10.2, 3.9 Hz, 1H), 2.66 (ddd, J = 14.4, 7.6, 3.9 Hz, 1H), 2.05 – 1.94 (m, 1H), 1.88 – 1.70 (m, 3H), 1.69 – 1.57 (m, 1H), 1.56 – 1.43 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7 (d, J = 248.1 Hz), 161.9, 152.1, 148.2, 134.6 (d, J = 3.5 Hz), 132.0, 130.1 (d, J = 8.2 Hz), 123.1, 115.67 (d, J = 21.6 Hz), 72.0, 39.8, 36.9, 35.3, 26.6, 24.3. ^{19}F

NMR (471 MHz, $CDCl_3$) δ -113.4. HRMS (ESI+) *m/z* calculated for $C_{17}H_{18}NOClF$ $[M+H]^+$: 306.1061, found 306.1059.

Site of oxidation was further confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

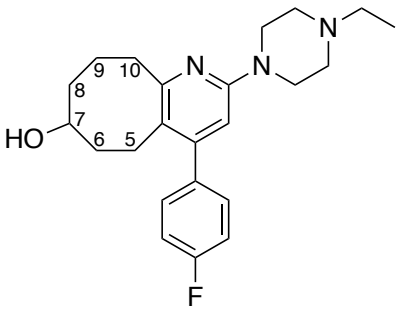
2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol [62]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 7.16 – 7.08 (m, 2H), 7.01 (s, 1H), 3.68 – 3.58 (m, 1H), 3.12 (ddd, *J* = 13.5, 10.0, 3.7 Hz, 1H), 2.95 (ddd, *J* = 13.4, 8.1, 3.7 Hz, 1H), 2.65 (t, *J* = 6.2 Hz, 2H), 2.27 – 2.17 (m, 1H), 1.82 (dddd, *J* = 13.4, 9.9, 8.1, 3.7 Hz, 1H), 1.71 – 1.43 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7 (d, *J* = 248.0 Hz), 162.0, 152.1, 148.0, 134.6 (d, *J* = 3.5 Hz), 131.8, 130.1 (d, *J* = 8.2 Hz), 123.2, 115.6 (d, *J* = 21.6 Hz)., 72.2, 39.3, 35.7, 32.1, 27.2, 27.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.5. HRMS (ESI+) *m/z* calculated for $C_{17}H_{18}NOClF$ $[M+H]^+$: 306.1061, found 306.1048.

Site of oxidation was further confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol [63]

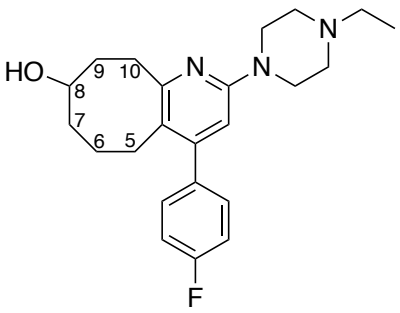


Prepared according to a reported procedure.[23] A mixture of potassium iodide (34.2 mg, 0.2 mmol, 1.0 equiv.), *N*-ethylpiperazine (397.0 μL, 359.6 mg, 3.1 mmol, 15.0 equiv.) and 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol (**61**) (63.0 mg, 0.2 mmol, 1.0 equiv.) was heated to 165 °C for 8 h. The reaction was allowed to cool to room temperature, then diluted with water and EtOAc. The mixture was stirred for 15 minutes, then the organic layer was separated. The organic layer was extracted with 1M HCl. The aqueous layer was adjusted to pH 9 with 3 M NaOH, then extracted with EtOAc (2 x 5 mL). The combined organic layer was washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on alumina (15 mm fritted glass column, 30 mL Brockmann grade II basic Al_2O_3) using 100% EtOAc as eluent afforded 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol (**63**) as a white solid (33.4 mg, 0.09 mmol, 41% yield). For biological testing, the product was further purified by recrystallization from *i*-PrOH.

^{13}C NMR data in agreement with those previously reported in the literature.[24]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 2H), 7.12 – 7.05 (m, 2H), 6.30 (s, 1H), 3.62 – 3.48 (m, 5H), 2.86 (dq, *J* = 12.8, 8.5 Hz, 2H), 2.67 (ddd, *J* = 14.2, 9.9, 3.9 Hz, 1H), 2.61 – 2.51 (m, 5H), 2.46 (q, *J* = 7.2 Hz, 2H), 1.95 (ddq, *J* = 13.1, 8.7, 4.4 Hz, 1H), 1.85 – 1.61 (m, 4H), 1.41 (tdd, *J* = 13.6, 7.5, 3.9 Hz, 1H), 1.27 – 1.20 (m, 1H), 1.13 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3 (d, *J* = 246.3 Hz), 159.0, 157.6, 150.7, 137.2 (d, *J* = 3.4 Hz), 130.2 (d, *J* = 8.0 Hz), 122.1, 115.2 (d, *J* = 21.4 Hz), 106.2, 72.6, 52.9, 52.6, 45.5, 40.5, 37.3, 35.8, 26.8, 24.0, 12.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.0. HRMS (ESI+) *m/z* calculated for $C_{23}H_{31}N_3OF$ $[M+H]^+$: 384.2451, found 384.2448.

2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol [64]

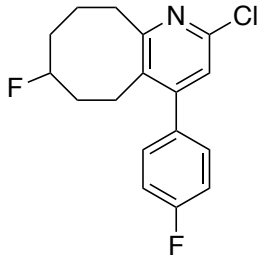


Prepared according to a reported procedure.[23] A mixture of potassium iodide (17.2 mg, 0.1 mmol, 1.0 equiv.), *N*-ethylpiperazine (397.0 μL, 359.6 mg, 3.1 mmol, 30.0 equiv.) and 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol (**62**) (31.7 mg, 0.1 mmol, 1.0 equiv.) was heated to 165 °C for 8 h. The reaction was allowed to cool to room temperature, then diluted with water and EtOAc. The mixture was stirred for 15 minutes, then the organic layer was separated. The organic layer was extracted with 1M HCl. The aqueous layer was adjusted to pH 9 with 3 M NaOH, then extracted with EtOAc (2 x 5 mL). The combined organic layer was washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on alumina (15 mm fritted glass column, 30 mL Brockmann grade II basic Al_2O_3) using 100% EtOAc as eluent afforded 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol (**64**) as a white solid (38.5 mg, 0.1 mmol, 97% yield). For biological testing, the product was further purified by recrystallization from *i*-PrOH.

^{13}C NMR data in agreement with those previously reported in the literature.[24]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 2H), 7.11 – 7.05 (m, 2H), 6.31 (s, 1H), 3.66 – 3.58 (m, 1H), 3.57 – 3.49 (m, 4H), 3.01 (ddd, *J* = 13.5, 10.0, 3.7 Hz, 1H), 2.84 (ddd, *J* = 12.7, 7.8, 3.8 Hz, 1H), 2.59 – 2.51 (m, 6H), 2.47 (q, *J* = 7.2 Hz, 2H), 2.21 (ddt, *J* = 13.7, 8.9, 3.9 Hz, 1H), 1.82 – 1.71 (m, 1H), 1.71 – 1.38 (m, 4H), 1.25 (br. s, 1H), 1.13 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3 (d, *J* = 246.3 Hz), 159.0, 157.5, 150.8, 137.2 (d, *J* = 3.3 Hz), 130.2 (d, *J* = 8.0 Hz), 122.0, 115.1 (d, *J* = 21.3 Hz), 106.4, 72.8, 52.9, 52.6, 45.6, 39.5, 36.4, 32.5, 27.9, 27.0, 12.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.1. HRMS (ESI+) *m/z* calculated for $C_{23}H_{31}N_3OF$ $[M+H]^+$: 384.2451, found 384.2452.

2-chloro-7-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [S60]

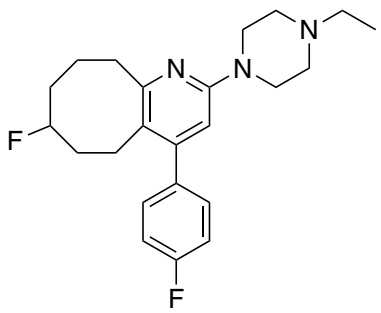


Prepared utilizing a reported procedure.[25] An oven-dried 4 mL vial was charged with cesium fluoride (dried under vacuum at 100 °C for 2 hours before use, 49.4 mg, 0.325 mmol, 5.0 equiv.) and AlkylFluor (38.6 mg, 0.078 mmol, 1.2 equiv.) and heated at 120 °C for 1 hour under vacuum. The vial was backfilled with nitrogen, and toluene (0.5 mL) was added by syringe. The mixture was heated to 100 °C with vigorous stirring until the suspension became visibly less cloudy (2 hours), indicating conversion of insoluble AlkylFluor to soluble PhenoFluor. In a separate 4 mL vial, under nitrogen, a solution of 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol (**61**) (azeotroped with benzene x3 and dried under vacuum overnight before use, 20.0 mg, 0.065 mmol, 1.0 equiv.) in toluene (0.33 mL) was prepared, and transferred to the reaction vial by syringe, rinsing with toluene (2 x 0.1 mL). The reaction was heated to 80 °C with vigorous stirring overnight. Upon completion, the reaction mixture was cooled to room temperature and filtered through pad of Celite, eluting with CH_2Cl_2 (3 x 1 mL). The filtrate was concentrated *in vacuo* and the residue was purified by CombiFlash on silica (12 g) using 100% hexanes → 6% ethyl acetate/hexanes gradient as eluent afforded 2-chloro-7-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S60**) as a white solid. A mixture of elimination side products was also isolated.

Run 1: (12.0 mg, 0.039 mmol, 59.7% yield), trace rsm. **Run 2:** (11.7 mg, 0.038 mmol, 58.5% yield), trace rsm. **Average: 59.1% yield, trace rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 2H), 7.17 – 7.12 (m, 2H), 7.03 (s, 1H), 4.42 (dtd, $J_{H\text{-}F}$ = 46.2 Hz, $J_{H\text{-}H}$ = 9.6, 4.1 Hz, 1H), 2.97 (dd, *J* = 7.6, 5.2 Hz, 2H), 2.80 (ddd, *J* = 14.3, 10.2, 3.9 Hz, 1H), 2.66 (ddd, *J* = 14.6, 7.9, 3.9 Hz, 1H), 2.14 – 1.79 (m, 4H), 1.77 – 1.61 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8 (d, *J* = 248.2 Hz), 161.5, 152.2, 148.6, 134.5 (d, *J* = 3.5 Hz), 131.5, 130.06 (d, *J* = 8.2 Hz), 123.3, 115.8 (d, *J* = 21.6 Hz), 94.2 (d, *J* = 166.4 Hz), 36.9 (d, *J* = 24.4 Hz), 35.1, 33.9 (d, *J* = 22.6 Hz), 25.5 (d, *J* = 11.1 Hz), 23.2 (d, *J* = 13.6 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.2, -162.3. HRMS (ESI+) *m/z* calculated for $C_{17}H_{17}NClF_2$ $[M+H]^+$: 308.1018, found 308.1013.

2-(4-ethylpiperazin-1-yl)-7-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [65]

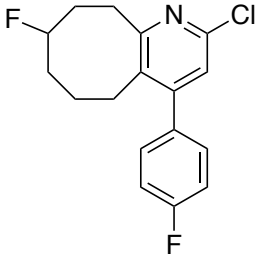


A mixture of potassium iodide (15.4 mg, 0.09 mmol, 1.0 equiv.), *N*-ethylpiperazine (177 µL, 159.9 mg, 1.4 mmol, 15.0 equiv.) and 2-chloro-7-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S60**) (28.6 mg, 0.09 mmol, 1.0 equiv.) was heated to 165 °C for 8 h. The reaction was allowed to cool to room temperature, then diluted with water and EtOAc. The mixture was stirred for 15 minutes, then the organic layer

was separated. The organic layer was extracted with 1M HCl. The aqueous layer was adjusted to pH 9 with 3 M NaOH, then extracted with EtOAc (2 x 5 mL). The combined organic layer was washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% CH_2Cl_2 → 10% MeOH/CH_2Cl_2 gradient as eluent over 80 column volumes afforded 2-(4-ethylpiperazin-1-yl)-7-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**65**) as an off-white solid (14.1 mg, 0.036 mmol, 39% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, J = 8.3, 5.4 Hz, 2H), 7.13 – 7.06 (m, 2H), 6.31 (s, 1H), 4.40 (dtd, $J_{H\text{-}F}$ = 46.5 Hz, $J_{H\text{-}H}$ = 9.7, 4.1 Hz, 1H), 3.55 (t, J = 5.2 Hz, 4H), 2.84 (t, J = 6.1 Hz, 2H), 2.69 (ddd, J = 14.5, 10.2, 4.0 Hz, 1H), 2.60 – 2.51 (m, 5H), 2.49 (q, J = 7.2 Hz, 2H), 2.05 – 1.85 (m, 3H), 1.84 – 1.67 (m, 2H), 1.64 – 1.52 (m, 1H), 1.14 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (d, J = 246.6 Hz), 158.6, 157.6, 150.8, 137.0 (d, J = 3.4 Hz), 130.1 (d, J = 8.1 Hz), 121.6, 115.3 (d, J = 21.3 Hz), 106.3, 95.2 (d, J = 164.4 Hz), 52.8, 52.6, 45.4, 37.4 (d, J = 23.5 Hz), 35.6, 34.5 (d, J = 22.5 Hz), 25.74 (d, J = 11.4 Hz), 22.8 (d, J = 14.6 Hz), 12.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.89, -160.3. HRMS (ESI+) *m/z* calculated for $C_{23}H_{30}N_3F_2$ $[M+H]^+$: 386.2408, found 386.2396.

2-chloro-8-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [S61]

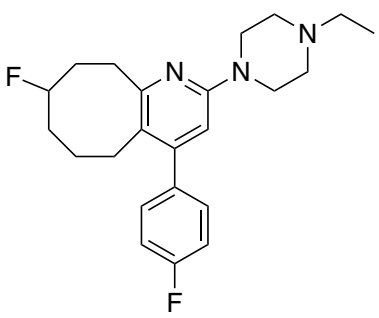


Prepared utilizing a reported procedure.[25] An oven-dried 4 mL vial was charged with cesium fluoride (dried under vacuum at 100 °C for 2 hours before use, 66.8 mg, 0.440 mmol, 5.0 equiv.) and AlkylFluor (52.2 mg, 0.106 mmol, 1.2 equiv.) and heated at 120 °C for 1 hour under vacuum. The vial was backfilled with nitrogen, and toluene (0.67 mL) was added by syringe. The mixture was heated to 100 °C with vigorous stirring until the suspension became visibly less cloudy (2 hours), indicating conversion of insoluble AlkylFluor to soluble PhenoFluor. In a separate 4 mL vial, under nitrogen, a solution of 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol (**62**) (azetroped with benzene x3 and dried under vacuum overnight before use, 26.9 mg, 0.088 mmol, 1.0 equiv.) in toluene (0.45 mL) was prepared, and transferred to the reaction vial by syringe, rinsing with toluene (2 x 0.1 mL). The reaction was heated to 80 °C with vigorous stirring overnight. Upon completion, the reaction mixture was cooled to room temperature and filtered through pad of Celite, eluting with CH_2Cl_2 (3 x 1 mL). The filtrate was concentrated *in vacuo* and the residue was purified by CombiFlash on silica (12 g) using 100% hexanes → 6% ethyl acetate/hexanes gradient as eluent afforded 2-chloro-8-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S61**) as a white solid. A mixture of elimination side products was also isolated.

Run 1: (12.6 mg, 0.041 mmol, 46.6% yield), trace rsm. **Run 2 (0.097 mmol scale):** (14.2 mg, 0.046 mmol, 47.6% yield), trace rsm. **Average: 47.1% yield.**

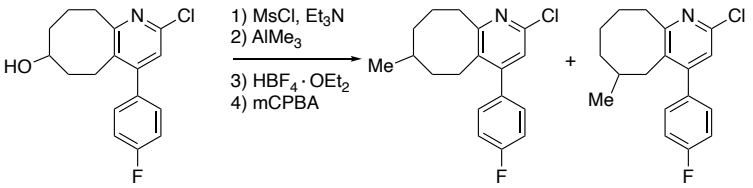
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 7.16 – 7.10 (m, 2H), 7.04 (s, 1H), 4.51 (dtd, $J_{H\text{-}F}$ = 46.3 Hz, $J_{H\text{-}H}$ = *J* = 9.4, 4.0 Hz, 1H), 3.14 (ddd, *J* = 13.5, 10.0, 3.6 Hz, 1H), 2.96 (ddd, *J* = 13.1, 8.6, 3.6 Hz, 1H), 2.73 – 2.59 (m, 2H), 2.42 – 2.29 (m, 1H), 2.10 – 1.97 (m, 1H), 1.90 – 1.74 (m, 1H), 1.72 – 1.57 (m, 2H), 1.56 – 1.44 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8 (d, *J* = 248.1 Hz), 161.5, 152.3, 148.3, 134.5 (d, *J* = 3.4 Hz), 131.41, 130.1 (d, *J* = 8.2 Hz), 123.5, 115.7 (d, *J* = 21.7 Hz), 94.2 (d, *J* = 167.6 Hz), 36.2 (d, *J* = 24.1 Hz), 32.8 (d, *J* = 22.9 Hz), 31.0 (d, *J* = 12.4 Hz), 26.9, 25.9 (d, *J* = 11.3 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.3, -164.0. HRMS (ESI+) *m/z* calculated for $C_{17}H_{17}NClF_2$ $[M+H]^+$: 308.1018, found 308.1015.

2-(4-ethylpiperazin-1-yl)-8-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [66]

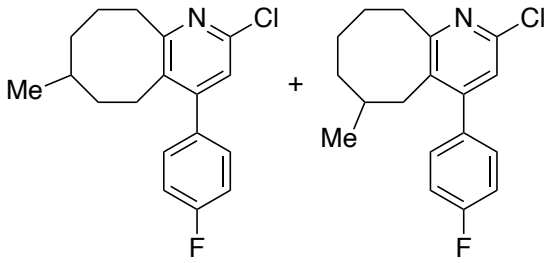


A mixture of potassium iodide (8.4 mg, 0.05 mmol, 1.0 equiv.), *N*-ethylpiperazine (100 μL, 87.9 mg, 0.77 mmol, 15.0 equiv.) and 2-chloro-8-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S61**) (15.6 mg, 0.05 mmol, 1.0 equiv.) was heated to 165 °C for 8 h. The reaction was allowed to cool to room temperature, then diluted with water and EtOAc. The mixture was stirred for 15 minutes, then the organic layer was separated. The organic layer was extracted with 1M HCl. The aqueous layer was adjusted to pH 9 with 3 M NaOH, then extracted with EtOAc (2 x 5 mL). The combined organic layer was washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% CH_2Cl_2 → 10% MeOH/CH_2Cl_2 gradient as eluent over 80 column volumes afforded 2-(4-ethylpiperazin-1-yl)-8-fluoro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**66**) as an off-white solid (12.5 mg, 0.03 mmol, 64% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 2H), 7.12 – 7.04 (m, 2H), 6.32 (s, 1H), 4.46 (dtd, $J_{H\text{-}F}$ = 46.6 Hz, $J_{H\text{-}H}$ = 9.7, 4.1 Hz, 1H), 3.55 (t, *J* = 5.0 Hz, 4H), 3.02 (ddd, *J* = 13.5, 10.1, 3.7 Hz, 1H), 2.83 (ddd, *J* = 12.7, 8.2, 3.7 Hz, 1H), 2.58 (t, *J* = 5.0 Hz, 4H), 2.55 – 2.44 (m, 4H), 2.41 – 2.29 (m, 1H), 2.03 – 1.77 (m, 2H), 1.74 – 1.62 (m, 1H), 1.58 – 1.50 (m, 1H), 1.50 – 1.39 (m, 1H), 1.14 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3 (d, *J* = 246.6 Hz), 158.5, 157.5, 150.9, 137.1 (d, *J* = 3.4 Hz), 130.1 (d, *J* = 8.1 Hz), 121.5, 115.2 (d, *J* = 21.2 Hz), 106.6, 95.2 (d, *J* = 165.2 Hz), 52.8, 52.6, 45.4, 36.3 (d, *J* = 23.9 Hz), 33.7 (d, *J* = 22.4 Hz), 31.3 (d, *J* = 13.4 Hz), 26.8, 26.7, 12.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.0, -160.5. HRMS (ESI+) *m/z* calculated for $C_{23}H_{30}N_3F_2$ $[M+H]^+$: 386.2408, found 386.2405.



2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-6-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [S62]



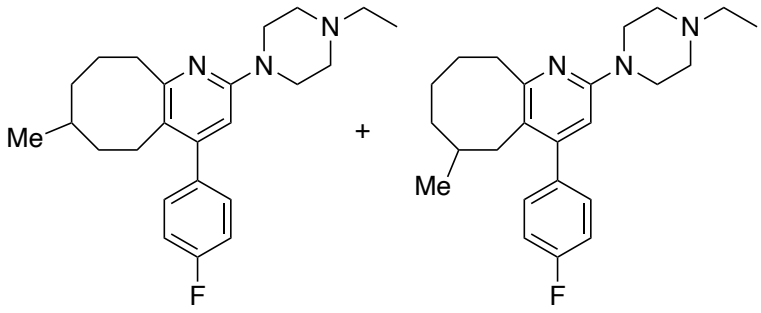
Prepared utilizing a reported procedure.[26] 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-7-ol (**61**) (94.0 mg, 0.31 mmol, 1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (1.0 mL). Methanesulfonyl chloride (28.6 μL, 42.4 mg, 0.37 mmol, 1.2 equiv.) was added, followed by triethylamine (64 μL, 46.5 mg, 0.46 mmol, 1.5 equiv.). The reaction was stirred at room temperature for 1 h, then partitioned between sat. $NaHCO_3$ and CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated *in vacuo*, then redissolved in anhydrous CH_2Cl_2 (1.0 mL) and cooled to -78 °C. Trimethylaluminum (2.0 M in hexanes, 461 μL, 0.92 mmol, 3.0 equiv.) was then added, and the reaction was stirred at -78 °C for 2 h and room temperature for 1 h. Upon completion, the mixture was diluted with CH_2Cl_2 and quenched with 1 M NaOH (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, dried with Na_2SO_4, filtered and concentrated *in vacuo*, then redissolved in anhydrous CH_2Cl_2 (1.2 mL) and cooled to 0 °C. HBF_4•OEt_2 (46 μL, 0.34 mmol, 1.1 equiv.) was added dropwise *via* syringe and the reaction was allowed to stir at 0 ºC for 30 minutes then warmed to room temperature and stirred for an additional 1 h. The reaction was concentrated *in vacuo* and left on high vacuum overnight. The resultant HBF_4 salt was dissolved in CH_2Cl_2 (0.83 mL, 0.22 M) and mCPBA (84.8 mg, 0.49 mmol, 1.6 equiv.) was added. The reaction was allowed to stir at room temperature overnight. Upon completion, 1 M NaOH was added and the reaction was stirred open to air for 15 minutes. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layer was washed with sat. Na_2SO_3, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 0% → 1% → 2% → 3% EtOAc/hexanes gradient as eluent afforded a 1:1 mixture of 2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-6-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S62**) as a white solid.

Run 1: (28.8 mg, 0.095 mmol, 30.6% yield), 0% rsm. **Run 2:** (33.0 mg, 0.109 mmol, 35.0% yield), 0% rsm. **Average: 32.8% yield, 0% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2H), 7.15 – 7.09 (m, 2H), 6.99 (s, 0.5H), 6.98 (s, 0.5H), 3.10 – 2.98 (m, 1H), 2.97 – 2.89 (m, 1H), 2.74 (ddd, *J* = 14.2, 10.2, 4.0 Hz, 0.5H), 2.65 (ddd, *J* = 14.1, 6.9, 4.1 Hz, 0.5H), 2.59 (dd, *J* = 13.9, 3.4 Hz, 0.5H), 2.42 (dd, *J* = 13.9, 10.8 Hz, 0.5H), 2.03 – 1.93 (m, 0.5H), 1.92 – 1.82 (m, 0.5H), 1.83 – 1.65 (m, 1H), 1.65 – 1.48 (m, 1H), 1.49 – 1.39 (m, 1H), 1.29 – 1.05 (m, 3H), 0.85 (d, *J* = 6.4 Hz, 1.5H), 0.76 (d, *J* = 6.8 Hz, 1.5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9, 162.7, 162.6 (d, *J* = 247.7 Hz), 162.6 (d, *J* = 247.8 Hz), 152.0, 151.8, 147.9, 147.8, 135.1 (d, *J* = 3.7 Hz), 135.0 (d, *J* = 3.5 Hz), 132.8, 132.4, 130.2 (d, *J* = 8.1 Hz), 130.2 (d, *J* = 7.9 Hz), 122.9, 122.7, 115.5 (d, *J* = 21.6 Hz), 115.5 (d, *J* = 21.6 Hz), 39.9, 36.9, 35.8, 35.3, 35.2, 34.9, 34.0, 32.3, 30.5, 29.6, 26.8, 25.4, 23.2, 22.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.7, -113.7. HRMS (ESI+) *m/z* calculated for $C_{18}H_{19}NFCl$ $[M+H]^+$: 304.1268, found 304.1265.

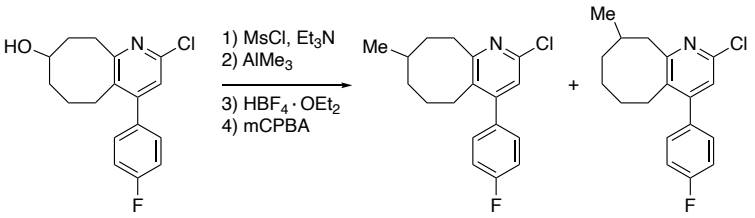
Sites of methylation were assigned based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs as well as comparison to an authentic standard of 2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine.

2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-6-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [67]

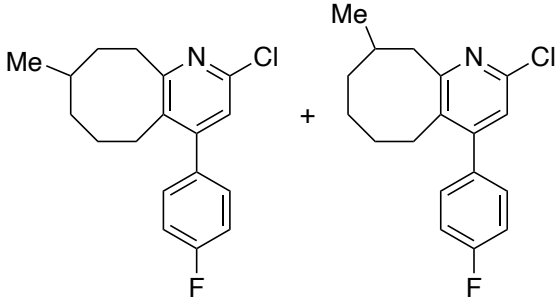


A mixture of potassium iodide (15.7 mg, 0.10 mmol, 1.0 equiv.), *N*-ethylpiperazine (181 μL, 163.3 mg, 1.43 mmol, 15.0 equiv.) and 2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-6-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S62**) (28.8 mg, 0.10 mmol, 1.0 equiv.) was heated to 165 °C for 8 h. The reaction was allowed to cool to room temperature, then diluted with water and EtOAc. The mixture was stirred for 15 minutes, then the organic layer was separated. The organic layer was extracted with 1M HCl. The aqueous layer was adjusted to pH 9 with 3 M NaOH, then extracted with EtOAc (2 x 5 mL). The combined organic layer was washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% CH_2Cl_2 → 10% MeOH/CH_2Cl_2 gradient as eluent over 80 column volumes afforded 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-6-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**67**) as a colorless oil (17.4 mg, 0.05 mmol, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.11 – 7.04 (m, 2H), 6.30 (s, 0.5H), 6.29 (s, 0.5H), 3.61 – 3.48 (m, 4H), 3.02 – 2.90 (m, 1H), 2.86 – 2.74 (m, 1H), 2.69 – 2.53 (m, 5H), 2.53 – 2.43 (m, 2H), 2.33 (dd, *J* = 14.1, 10.6 Hz, 0.5H), 1.93 (ddd, *J* = 13.1, 8.9, 3.9 Hz, 0.5H), 1.82 (ddq, *J* = 13.7, 9.0, 4.3 Hz, 0.5H), 1.75 – 1.60 (m, 1H), 1.56 (ddq, *J* = 17.0, 10.2, 4.3 Hz, 0.5H), 1.43 (dddd, *J* = 28.7, 19.1, 12.1, 5.0 Hz, 2H), 1.32 – 1.17 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.09 – 0.99 (m, 1H), 0.83 (d, *J* = 6.4 Hz, 1.5H), 0.71 (d, *J* = 6.5 Hz, 1.5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.2 (d, *J* = 245.9 Hz), 162.2 (d, *J* = 246.1 Hz), 160.0, 159.8, 157.4, 157.4, 150.7, 150.5, 137.7 (d, *J* = 3.4 Hz), 137.5 (d, *J* = 3.3 Hz), 130.3 (d, *J* = 8.0 Hz), 130.2 (d, *J* = 8.0 Hz), 123.3, 123.0, 115.1 (d, *J* = 21.3 Hz), 115.0 (d, *J* = 21.3 Hz), 106.1, 106.0, 52.8, 52.6, 45.6, 40.5, 37.0, 36.2, 35.5, 35.2, 35.0, 34.2, 32.3, 30.6, 29.7, 26.5, 25.6, 23.4, 22.8, 12.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.4, -115.4. HRMS (ESI+) *m/z* calculated for $C_{24}H_{33}N_3F$ $[M+H]^+$: 382.2659, found 382.2648.



2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-9-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [S63]



Prepared utilizing a reported procedure.[26] 2-chloro-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridin-8-ol (**62**) (94.0 mg, 0.31 mmol, 1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (1.0 mL). Methanesulfonyl chloride (28.6 μL, 42.4 mg, 0.37 mmol, 1.2 equiv.) was added, followed by triethylamine (64 μL, 46.5 mg, 0.46 mmol, 1.5 equiv.). The reaction was stirred at room temperature for 1 h, then partitioned between sat. $NaHCO_3$ and CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated *in vacuo*, then redissolved in anhydrous CH_2Cl_2 (1.0 mL) and cooled to -78 °C. Trimethylaluminum (2.0 M in hexanes, 461 μL, 0.92 mmol, 3.0 equiv.) was then added, and the reaction was stirred at -78 °C for 2 h and room temperature for 1 h. Upon completion, the mixture was diluted with CH_2Cl_2 and quenched with 1 M NaOH (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL). The organic layers were combined, dried with Na_2SO_4, filtered and concentrated *in vacuo*, then redissolved in anhydrous CH_2Cl_2 (1.2 mL) and cooled to 0 °C. HBF_4•OEt_2 (46 μL, 0.34 mmol, 1.1 equiv.) was added dropwise *via*

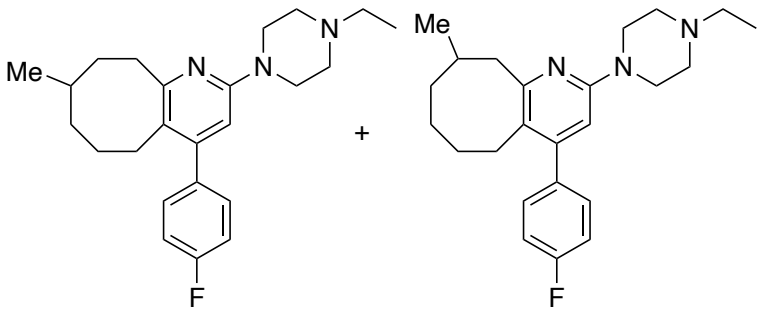
syringe and the reaction was allowed to stir at 0 ºC for 30 minutes then warmed to room temperature and stirred for an additional 1 h. The reaction was concentrated *in vacuo* and left on high vacuum overnight. The resultant HBF_4 salt was dissolved in CH_2Cl_2 (0.83 mL, 0.22 M) and mCPBA (84.8 mg, 0.49 mmol, 1.6 equiv.) was added. The reaction was allowed to stir at room temperature overnight. Upon completion, 1 M NaOH was added and the reaction was stirred open to air for 15 minutes. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layer was washed with sat. Na_2SO_3, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 0% → 1% → 2% → 3% EtOAc/hexanes gradient as eluent afforded a 2:1 mixture of 2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-9-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S63**) as a white solid.

Run 1: (40.7 mg, 0.134 mmol, 43.2% yield), 0% rsm. **Run 2:** (44.3 mg, 0.146 mmol, 47.0% yield), 0% rsm. **Average: 45.1% yield, 0% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 2H), 7.16 – 7.06 (m, 2H), 6.98 (s, 1H), 3.08 (ddd, *J* = 13.5, 10.0, 3.9 Hz, 0.7H), 2.98 – 2.87 (m, 1H), 2.81 – 2.55 (m, 2.3H), 2.02 – 1.89 (m, 1H), 1.61 – 1.50 (m, 1H), 1.50 – 1.34 (m, 2H), 1.34 – 1.10 (m, 3H), 1.06 (d, *J* = 6.7 Hz, 1H), 0.90 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1, 162.6 (d, *J* = 247.6 Hz), 162.2, 151.8, 151.8, 147.8, 147.5, 135.0 (d, *J* = 3.8 Hz), 132.6, 132.5, 130.1 (d, *J* = 8.2 Hz), 122.9, 122.8, 115.5 (d, *J* = 21.6 Hz), 42.9, 39.1, 36.1, 34.8, 34.7, 34.5, 32.9, 31.1, 30.3, 27.5, 26.9, 25.3, 23.1, 22.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.7. HRMS (ESI+) *m/z* calculated for $C_{18}H_{20}NClF$ $[M+H]^+$: 304.1268, found 304.1271.

Sites of methylation were assigned based on a combination of ^{1}H, gCOSY, gHSQC, gHMBC and TOCSY NMRs as well as comparison to an authentic standard of 2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine.

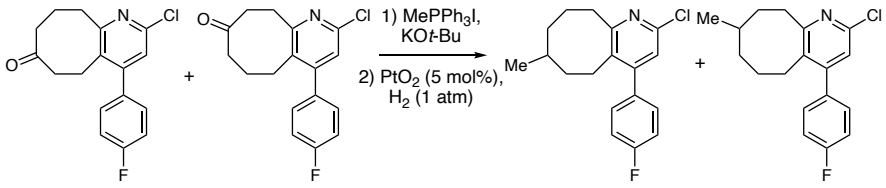
2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-9-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine [68]



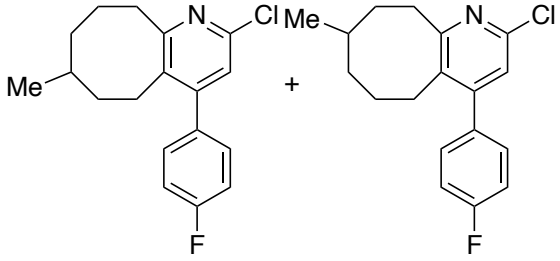
A mixture of potassium iodide (24.2 mg, 0.146 mmol, 1.0 equiv.), *N*-ethylpiperazine (280 µL, 251.2 mg, 2.2 mmol, 15.0 equiv.) and 2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-9-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**S63**) (44.3 mg, 0.146

mmol, 1.0 equiv.) was heated to 165 °C for 8 h. The reaction was allowed to cool to room temperature, then diluted with water and EtOAc. The mixture was stirred for 15 minutes, then the organic layer was separated. The organic layer was extracted with 1M HCl. The aqueous layer was adjusted to pH 9 with 3 M NaOH, then extracted with EtOAc (2 x 5 mL). The combined organic layer was washed with water, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by CombiFlash on silica (12 g) using 100% CH_2Cl_2 → 10% MeOH/CH_2Cl_2 gradient as eluent over 80 column volumes afforded 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-(4-ethylpiperazin-1-yl)-4-(4-fluorophenyl)-9-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (**68**) as a colorless oil (24.9 mg, 0.065 mmol, 45% yield).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.17 (m, 2H), 7.12 – 7.02 (m, 2H), 6.29 (br. s, 1H), 3.63 – 3.47 (m, 4H), 2.99 (ddd, *J* = 13.2, 9.9, 3.5 Hz, 1H), 2.86 – 2.75 (m, 1H), 2.65 – 2.53 (m, 5H), 2.48 (q, *J* = 7.2 Hz, 3H), 1.98 – 1.85 (m, 1H), 1.59 – 1.28 (m, 5H), 1.14 (t, *J* = 7.2 Hz, 4H), 1.05 (d, *J* = 6.8 Hz, 1H), 0.88 (d, *J* = 6.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.2 (d, *J* = 245.7 Hz), 160.2, 159.1, 157.4, 157.0, 137.6, 137.5 (d, *J* = 3.4 Hz), 130.2 (d, *J* = 7.7 Hz), 123.3, 123.1, 115.0 (d, *J* = 21.2 Hz), 106.1, 106.0, 52.9, 52.6, 45.6, 45.6, 39.3, 35.8, 35.2, 34.9, 34.5, 32.9, 31.7, 30.8, 27.2, 26.9, 25.5, 23.6, 22.9, 12.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.4, -115.4. HRMS (ESI+) *m/z* calculated for $C_{24}H_{33}N_3F$ $[M+H]^+$: 382.2659, found 382.2647.

To confirm sites of methylation, authentic standard of a mixture of 2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine and 2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[b]pyridine were synthesized from a mixture of 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[b]pyridine-7(6H)-one and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[b]pyridine-8(5H)-one.



2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine



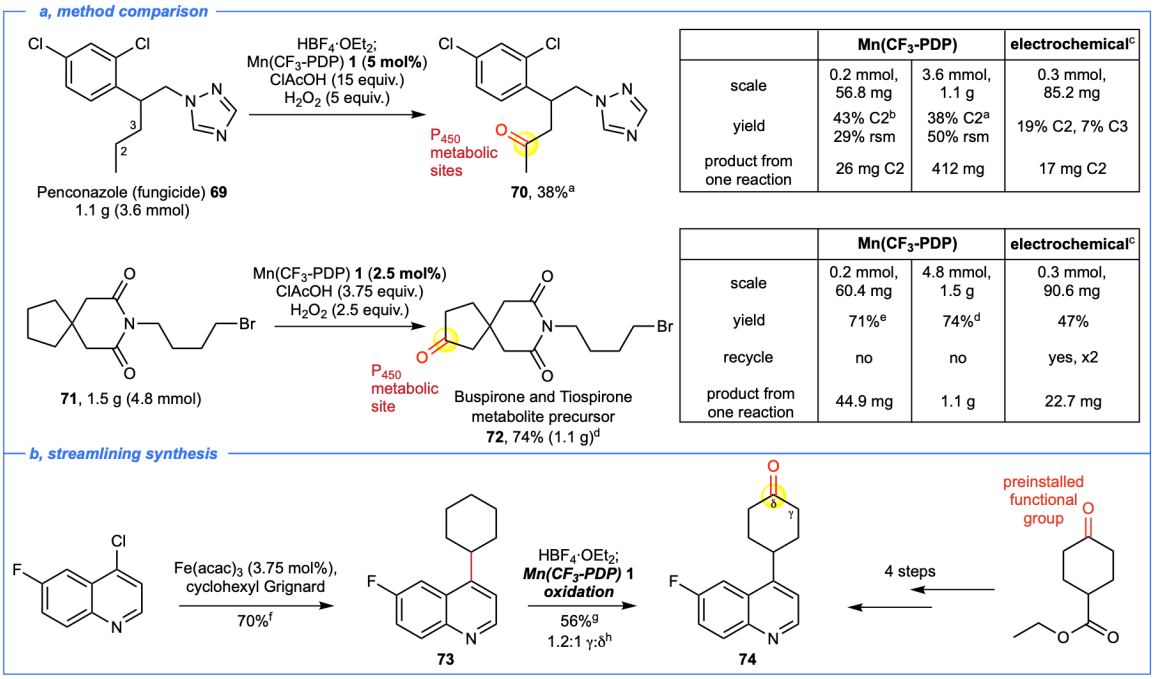
To a flame-dried round bottom flask was added methyltriphenylphosphonium iodide (95.4 mg, 0.236 mmol, 1.5 equiv.) and THF (1.0 mL, 0.16M) and the reaction was cooled to 0 °C. Potassium *tert*-butoxide (24.7 mg, 0.220 mmol, 1.4 equiv.) was added and the reaction

was stirred at room temperature for 1 hour. The mixture was cooled to 0 °C and 2-chloro-4-(4-fluorophenyl)-5,8,9,10-tetrahydrocycloocta[*b*]pyridine-7(6*H*)-one (**S59a**) and 2-chloro-4-(4-fluorophenyl)-6,7,9,10-tetrahydrocycloocta[*b*]pyridine-8(5*H*)-one (**S59b**) (47.7 mg, 0.157 mmol, 1.0 equiv.) in THF (1.0 mL) was added and the reaction was stirred at room temperature overnight. The reaction was quenched by the addition of water (20 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 2% → 4% → 6% → 8% → 10% ethyl acetate/hexanes as eluent afforded a mixture of 2-chloro-4-(4-fluorophenyl)-7-methylene-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-8-methylene-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine as a white solid (36.1 mg, 0.120 mmol, 76% yield).

To a round bottom flask under nitrogen atmosphere was added a mixture of 2-chloro-4-(4-fluorophenyl)-7-methylene-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-8-methylene-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine (36.1 mg, 0.120 mmol, 1.0 equiv.), platinum (IV) oxide (1.4 mg, 0.006 mmol, 5 mol%) and EtOH (3 mL, 0.04 M). The flask was purged with hydrogen and stirred under a hydrogen balloon (1 atm) at room temperature until the reaction was complete by ^{1}H NMR (3.5 h). The reaction was filtered through celite using CH_2Cl_2 as eluent and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% hexanes → 2% → 4% → 6% ethyl acetate/hexanes as eluent afforded a mixture of 2-chloro-4-(4-fluorophenyl)-7-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine and 2-chloro-4-(4-fluorophenyl)-8-methyl-5,6,7,8,9,10-hexahydrocycloocta[*b*]pyridine as a white solid (32.7 mg, 0.11 mmol, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 2H), 7.15 – 7.08 (m, 2H), 6.98 (s, 1H), 3.13 – 3.02 (m, 1H), 2.92 (ddd, *J* = 12.5, 8.2, 3.9 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.68 – 2.56 (m, 1H), 2.02 – 1.90 (m, 1H), 1.76 – 1.63 (m, 0.5H), 1.61 – 1.52 (m, 0.5H), 1.51 – 1.34 (m, 2H), 1.34 – 1.05 (m, 3H), 0.90 (d, *J* = 6.9 Hz, 1H), 0.84 (d, *J* = 6.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1, 162.9, 162.6 (d, *J* = 247.6 Hz), 151.8, 151.8, 147.8, 147.8, 135.0 (d, *J* = 3.8 Hz), 135.0 (d, *J* = 3.4 Hz), 132.8, 132.6, 130.2 (d, *J* = 8.2 Hz), 130.2 (d, *J* = 7.7 Hz), 122.9, 122.8, 115.5 (d, *J* = 21.6 Hz), 115.5 (d, *J* = 21.6 Hz), 39.9, 39.1, 35.8, 35.3, 34.9, 34.7, 32.9, 32.3, 30.3, 29.6, 27.5, 26.8, 25.4, 25.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.7. HRMS (ESI+) *m/z* calculated for $C_{18}H_{20}NClF$ $[M+H]^+$: 304.1268, found 304.1282.

VI. Supplementary Figure 4. Method Comparison



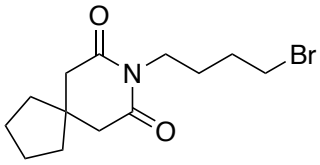
	Mn(CF3-PDP)		electrochemical[c]
scale	0.2 mmol, 56.8 mg	3.6 mmol, 1.1 g	0.3 mmol, 85.2 mg
yield	43% C2[b] 29% rsm	38% C2[a] 50% rsm	19% C2, 7% C3
product from one reaction	26 mg C2	412 mg	17 mg C2

	Mn(CF3-PDP)		electrochemical[c]
scale	0.2 mmol, 60.4 mg	4.8 mmol, 1.5 g	0.3 mmol, 90.6 mg
yield	71%[e]	74%[d]	47%
recycle	no	no	yes, x2
product from one reaction	44.9 mg	1.1 g	22.7 mg

[a]Nitrogen was HBF_4•OEt_2 protected followed by modified Method D at 0 °C. [b]Nitrogen was HBF_4•OEt_2 protected followed by Method A at 0 °C. [c]From ref. 38. [d]Method D. [e]Method B. [f]Quinoline (1.05 equiv.), $Fe(acac)_3$ (3.75 mol%) and cyclohexyl Grignard (1.0 equiv.) in THF/NMP at rt for 75 min as described in ref. 66. [g]Nitrogen was HBF_4•OEt_2 protected followed by Method A. [h]Ratios are statistically corrected.

Preparation of Substrates and Compound Characterization for Supplementary Figure 4

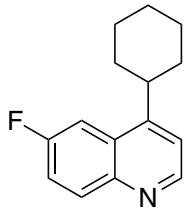
8-(4-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione [71]



Prepared according to a reported procedure.[27] To a flame dried round bottom flask fitted with a reflux condenser, was added 3,3-tetramethyleneglutarimide (836.1 mg, 5.0 mmol, 1.0 equiv.), MeCN (8.5 mL, 0.6 M), potassium carbonate (2.07 g, 15.0 mmol, 3.0 equiv.), 1,4-dibromobutane (0.66 mL, 1.19 g, 5.5 mmol, 1.1 equiv.) and potassium iodide (83.0 mg, 0.5 mmol, 10 mol%) and the solution was refluxed overnight. The reaction was cooled to room temperature and quenched with water. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% CH_2Cl_2 as eluent afforded 8-(4-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione (**71**) as a colorless oil (873.0 mg, 2.89 mmol, 58% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (t, J = 7.3 Hz, 2H), 3.40 (t, J = 6.7 Hz, 2H), 2.58 (s, 4H), 1.88 – 1.79 (m, 2H), 1.74 – 1.60 (m, 6H), 1.51 – 1.47 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 45.0, 39.6, 38.6, 37.7, 33.2, 30.3, 26.9, 24.3. HRMS (ESI+) *m/z* calculated for $C_{13}H_{21}NO_2Br$ $[M+H]^+$: 302.0756, found 302.0753.

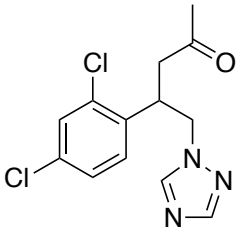
4-cyclohexyl-6-fluoroquinoline [73]



Prepared utilizing a reported procedure.[28] To a vial was added 7-fluoro-4-chloroquinoline (150.0 mg, 0.83 mmol, 1.05 equiv.) and $Fe(acac)_3$ (10.9 mg, 0.031 mmol, 3.75 mol%). The vial was sealed with a septum cap, evacuated and purged with nitrogen (x3) and the mixture was dissolved in THF (3.5 mL) and NMP (1.0 mL). The reaction mixture was treated dropwise with cyclohexylmagnesium bromide (1.4 mL of a 0.579 M solution in THF, 1.0 equiv.) at room temperature. After stirring for 75 minutes at room temperature, the reaction was quenched by adding sat. aq. NH_4Cl (5 mL) and extracted with MTBE (2 x 20 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 1% → 2% → 3% acetone/hexanes gradient as eluent afforded 4-cyclohexyl-6-fluoroquinoline (**73**) as a colorless oil. **Run 1:** (133.2 mg, 0.581 mmol, 71% yield). **Run 2:** (131.3 mg, 0.573 mmol, 69% yield). **Average: 70% yield.**

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (d, *J* = 4.6 Hz, 1H), 8.10 (dd, *J* = 9.2, 5.7 Hz, 1H), 7.67 (dd, *J* = 10.6, 2.7 Hz, 1H), 7.45 (ddd, *J* = 10.2, 6.0, 2.5 Hz, 1H), 7.28 (d, *J* = 4.6 Hz, 1H), 3.16 (tt, *J* = 8.3, 3.2 Hz, 1H), 2.04 – 1.96 (m, 2H), 1.96 – 1.89 (m, 2H), 1.88 – 1.82 (m, 1H), 1.60 – 1.47 (m, 4H), 1.39 – 1.29 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.6 (d, *J* = 246.9 Hz), 153.0 (d, *J* = 6.0 Hz), 149.8 (d, *J* = 2.7 Hz), 145.6, 132.9 (d, *J* = 9.3 Hz), 127.9 (d, *J* = 8.7 Hz), 119.1 (d, *J* = 25.6 Hz), 118.2, 106.8 (d, *J* = 22.3 Hz), 39.3, 33.5, 27.0, 26.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -113.2. HRMS (ESI+) *m/z* calculated for $C_{15}H_{17}NF$ $[M+H]^+$: 230.1345, found 230.1344.

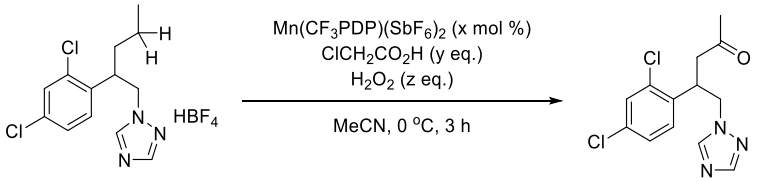
4-(2,4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)pentan-2-one [70]



0.2 mmol scale with HBF_4 Protection: According to the **general procedure for HBF_4•OEt_2 protection**, penconazole (**69**) (56.8 mg, 0.200 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (30 μL, 0.220 mmol, 1.1 equiv.) in CH_2Cl_2 (0.8 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **69•HBF_4** (0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at 0 °C with an ice/water bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% acetone/CH_2Cl_2 gradient as eluent afforded 4-(2,4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)pentan-2-one (**70**) as a colorless oil.

Run 1: (24.8 mg, 0.083 mmol, 41.6% yield), (16.7 mg, 0.059 mmol, 29.3% rsm). **Run 2:** (25.3 mg, 0.085 mmol, 42.4% yield), (14.3 mg, 0.050 mmol, 25.2% rsm). **Run 3:** (26.8 mg, 0.090 mmol, 44.9% yield), (17.9 mg, 0.063 mmol, 31.5% rsm). **Average: 43.0% yield ± 1.7%, 28.7% rsm ± 3.2%.**

Optimization for scale up oxidation:



entry	x (mol %)	y (eq.)	z (eq.)	yield (%)[a]	
				rsm (**69**)	Product (**70**)
1	2.5	3.75	2.5	55	21
2	2.5	7.5	2.5	56	25
3	2.5	7.5	5.0	67	26
4	5.0	7.5	5.0	40	36
5[b]	5.0	7.5	5.0	48	28
6	5.0	15	5.0	50	42
7	5.0	15	10	43	35

[a]Isolated yields. [b]At room temperature.

3.6 mmol scale: According to the **general procedure for HBF_4•OEt_2 protection**, 1-(2-(2,4-dichlorophenyl)pentyl)-1*H*-1,2,4-triazole (**69**) (1.08 g, 3.6 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (540 μL, 3.96 mmol, 1.1 equiv.) in CH_2Cl_2 (14.4 mL, 0.25 M). The oxidation was run with a

modified **Method D: Lower Catalyst Loading:** the resultant **69•HBF$_4$** (3.6 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (5.1 g, 54 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (243.9 mg, 0.18 mmol, 5.0 mol%), H_2O_2 (50 wt% in H_2O, 1.22 g, 18.0 mmol, 5.0 equiv.), MeCN (12 mL in 300 mL round bottom flask, 75 mL with oxidant, divided into two equal batches and loaded in 2 x 50 mL syringes and 7.5 mL with catalyst, loaded into a 10 mL syringe). Two separate syringe pumps were used: one syringe pump added oxidant (25.0 mL/hour) and the second syringe pump added catalyst (2.5 mL/hour). The reaction was run at 0 °C with an ice/water bath bath. After 1.5 hours of addition that depleted the syringe of oxidant solution, the next syringe with oxidant solution was loaded into the syringe pump and addition continued. Upon completing of all oxidant and catalyst solutions, the reaction was worked up according to the **General Procedure for HBF$_4$ Deprotection**. DO NOT concentrate the reaction to dryness. Flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 10% → 20% → 30% acetone/CH_2Cl_2 gradient as eluent afforded 4-(2,4-dichlorophenyl)-5-(1*H*-1,2,4-triazol-1-yl)pentan-2-one (**70**) as a colorless oil.

Run 1: (414 mg, 1.39 mmol, 38.5% yield), (487.9 mg, 1.72 mmol, 47.7% rsm). **Run 2:** (409 mg, 1.37 mmol, 38.1% yield), (530.9 mg, 1.87 mmol, 51.9% rsm). **Average: 38.3% yield, 49.8% rsm.**

Without HBF$_4$ Protection: The reaction was run with **General Method B: Single Catalyst Addition Protocol**: penconazole (**69**) (56.8 mg, 0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.50 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% acetone/CH_2Cl_2 gradient as eluent afforded only recovered starting material.

Yield: 0% yield, (45.7 mg, 0.161 mmol, 80.4% rsm).

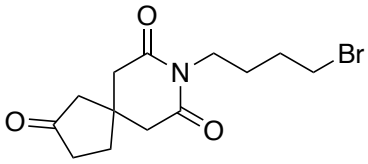
Without HBF$_4$ Protection: The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: penconazole (**69**) (56.8 mg, 0.200 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (27.1 mg, 0.020 mmol, 10 mol%), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant, 0.25 mL with catalyst). The reaction was run at 0 °C with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% acetone/CH_2Cl_2 gradient as eluent afforded only recovered starting material.

Yield: 0% yield, (47.9 mg, 0.169 mmol, 84.3% rsm).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.67 (s, 1H), 7.38 (s, 1H), 7.12 (d, *J* = 8.5, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 4.46 (dd, *J* = 14.0, 6.0 Hz, 1H), 4.40 (dd, *J* = 14.0, 5.9 Hz, 1H), 4.22 (p, *J* = 6.3 Hz, 1H),

3.04 (dd, J = 17.9, 7.7 Hz, 1H), 2.82 (dd, J = 17.9, 6.2 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.6, 152.1, 143.8, 135.9, 134.6, 134.0, 130.1, 129.4, 127.6, 51.8, 44.6, 37.4, 30.4. HRMS (ESI+) *m/z* calculated for $C_{13}H_{14}N_3OCl_2$ $[M+H]^+$: 298.0514, found 298.0517.

8-(4-bromobutyl)-8-azaspiro[4.5]decane-2,7,9-trione [72]



4.8 mmol scale: The oxidation was run with **Method D: Lower Catalyst Loading:** 8-(4-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione (**71**) (1.45 g, 4.8 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (1.7 g, 18.0 mmol, 3.75 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (162.6 mg, 0.12 mmol, 2.5 mol%), H_2O_2 (50 wt% in H_2O, 816 mg, 12.0 mmol, 2.5 equiv.), MeCN (16 mL in 300 mL round bottom flask, 100 mL with oxidant, divided into two equal batches and loaded in 2 X 50 mL syringes and 10 mL with catalyst, loaded into a 10 mL syringe). Two separate syringe pumps were used: one syringe pump added oxidant (33.33 mL/hour) and the second syringe pump added catalyst (3.333 mL/hour). The reaction was run at 0 °C with an ice/water bath bath. After 1.5 hours of addition that depleted the syringe of oxidant solution, the next syringe with oxidant solution was loaded into the syringe pump and addition continued. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method D. DO NOT concentrate the reaction to dryness. Flash column chromatography on silica (35 mm fritted glass column, 150 mL SiO_2) using 100% hexanes → 10% → 20% → 30% ethyl acetate/hexanes gradient as eluent afforded 8-(4-bromobutyl)-8-azaspiro[4.5]decane-2,7,9-trione (**72**) as a colorless oil.

Run 1: (1.09 g, 3.45 mmol, 71.8% yield), 0% rsm. **Run 2:** (1.15 g, 3.62 mmol, 75.5%), 0% rsm. **Average: 73.7% yield, 0% rsm.**

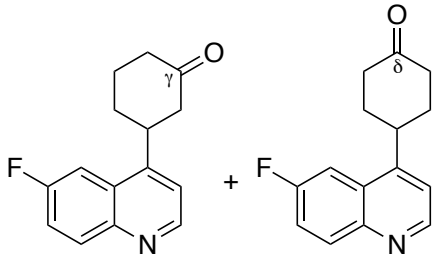
0.2 mmol scale: The reaction was run with **General Method B: Single Catalyst Addition Protocol:** 8-(4-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione (**71**) (60.4 mg, 0.200 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (283.5 mg, 3.0 mmol, 15.0 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (27.1 mg, 0.02 mmol, 10 mol%), H_2O_2 (50 wt% in H_2O, 136 mg, 2.0 mmol, 10.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.5 mL with oxidant). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 15 mL saturated $NaHCO_3$ and DCM as described in General Method B. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% hexanes → 10% → 20% → 30% ethyl acetate/hexanes gradient as eluent afforded 8-(4-bromobutyl)-8-azaspiro[4.5]decane-2,7,9-trione (**72**) as a colorless oil.

Run 1: (44.1 mg, 0.139 mmol, 69.7% yield), 0% rsm. **Run 2:** (45.2 mg, 0.143 mmol, 71.5%), 0% rsm. **Run 3:** (45.6 mg, 0.144 mmol, 72.1%), 0% rsm. **Average: 71.1% yield ± 1.2%, 0% rsm.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.79 (t, J = 7.4 Hz, 2H), 3.39 (t, J = 6.6 Hz, 2H), 2.70 (s, 4H), 2.38 (t, J = 8.0 Hz, 2H), 2.18 (s, 2H), 1.93 (t, J = 8.0 Hz, 2H), 1.83 (app. p, J = 6.8 Hz, 2H), 1.72 – 1.62 (m, 2H). ^{13}C

NMR (126 MHz, $CDCl_3$) δ 214.8, 170.6, 49.4, 43.9, 38.9, 37.0, 36.3, 33.5, 33.0, 30.2, 26.8. HRMS (ESI+) *m/z* calculated for $C_{13}H_{19}NO_3Br$ $[M+H]^+$: 316.0548, found 316.0551.

3-(6-fluoroquinolin-4-yl)cyclohexan-1-one and 4-(6-fluoroquinolin-4-yl)cyclohexan-1-one [74]



According to the **general procedure for HBF_4•OEt_2 protection**, 4-cyclohexyl-6-fluoroquinoline (**73**) (68.8 mg, 0.300 mmol, 1.0 equiv.) was protected with $HBF_4.OEt_2$ (45 μL, 0.330 mmol, 1.1 equiv.) in CH_2Cl_2 (1.2 mL, 0.25 M). The reaction was run with **General Method A: Slow Catalyst Addition Protocol**: the resultant **73•HBF_4** (0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425.3 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL with catalyst). The reaction was run at -36 °C with a dry ice/1,2-dichloroethane bath. The reaction was worked up according to the **General Procedure for HBF_4 Deprotection**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% → 30% → 40% acetone/hexanes gradient as eluent afforded 3-(6-fluoroquinolin-4-yl)cyclohexan-1-one and 4-(6-fluoroquinolin-4-yl)cyclohexan-1-one (**74**) as a colorless oil.

Run 1: (38.8 mg, 0.159 mmol, 53.2% yield, 1.2:1 γ:δ), 0% rsm. **Run 2 (0.22 mmol scale):** (31.5 mg, 0.129 mmol, 58.8% yield, 1.2:1 γ:δ), 0% rsm. **Run 3 (0.22 mmol scale):** (30.3 mg, 0.125 mmol, 56.6% yield 1.2:1 γ:δ), (15.4 mg, 0.067 mmol, 30.6% rsm). **Average: 56.2% yield ± 2.8%, 1.2:1 γ:δ, 10.2% rsm ± 17.7%.** Regioisomer ratio determined by ^{1}H NMR. Minor regioisomer for 13C NMR indicated in parentheses.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.6 Hz, 0.7H), 8.83 (d, *J* = 4.7 Hz, 0.3H), 8.17 – 8.12 (m, 1H), 7.72 (dd, *J* = 10.3, 2.8 Hz, 0.3H), 7.61 (dd, *J* = 10.3, 2.8 Hz, 0.7H), 7.54 – 7.46 (m, 1H), 7.31 (d, *J* = 4.6 Hz, 0.7H), 7.29 (d, *J* = 4.6 Hz, 0.3H), 3.75 – 3.65 (m, 1H), 2.76 – 2.54 (m, 3.3H), 2.52 – 2.43 (m, 0.7H), 2.40 – 2.33 (m, 0.6H), 2.27 – 2.15 (m, 1.4H), 2.09 – 1.89 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (209.8), 209.8, 160.8 (d, *J* = 248.0 Hz), [149.8 (d, *J* = 6.0 Hz)], [149.7 (d, *J* = 2.7 Hz)], 149.7 (d, *J* = 2.7 Hz), 149.1 (d, *J* = 5.4 Hz), 145.7, (145.7), [133.3 (d, *J* = 9.3 Hz)], 133.2 (d, *J* = 9.3 Hz), [127.6 (d, *J* = 9.3 Hz)], 127.2 (d, *J* = 8.7 Hz), 119.5 (d, *J* =25.6 Hz), [119.4 (d, *J* = 25.6 Hz)], 118.2, (118.0), 106.4 (d, *J* = 22.9 Hz), [106.4 (d, *J* = 22.3 Hz)], 47.4 (2 carbons), 41.3 (3 carbons), 39.1, (37.4), (32.8), 31.7, 25.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ -111.8, -112.1. HRMS (ESI+) *m/z* calculated for $C_{15}H_{15}NOF$ $[M+H]^+$: 244.1138, found 244.1139.

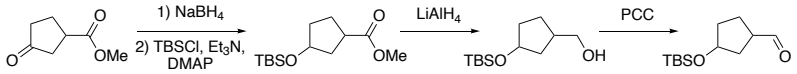
δ-ketone spectral data in agreement with those previously reported in the literature.[29]

γ-ketone confirmed based on a combination of ^{1}H, gCOSY, gHSQC and gHMBC NMRs.

VII. pK_a of Heterocycles

Heterocycle	pKa in Water	Source
Isoxazole	-3	Essentials of Heterocyclic Chemistry[30]
Tetrazole	-2.7	Handbook of Heterocyclic Chemistry Chapter 2.4[31]
1,2,3-triazole	1.2	Eur. J. Org. Chem. **2001**[32]
Pyrimidine	1.3	Essentials of Heterocyclic Chemistry[30]
1,2,4-triazole	2.2	Essentials of Heterocyclic Chemistry[30]
Pyridazine	2.3	Essentials of Heterocyclic Chemistry[30]
Pyrazole	2.5	Handbook of Heterocyclic Chemistry Chapter 2.4[31]
Pyridine	5.2	Essentials of Heterocyclic Chemistry[30]
Thiomorpholine dioxide	5.4	ChemMedChem **2007**[33]
Morpholine	8.4	Essentials of Heterocyclic Chemistry[30]
Tertiary Amine (estimated as $MeEt_2N$)	10.3	Eur. J. Org. Chem. **2019**[34]
Piperidine	11.2	Essentials of Heterocyclic Chemistry[30]

VIII. *De novo* Synthesis of Oxidized Carbocycle



3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carbaldehyde [S64]

To a solution of methyl 3-oxo cyclopentanecarboxylate (2.0 g, 14.1 mmol, 1.0 equiv.) in MeOH (24 mL, 0.59 M) cooled to 0 °C was added sodium borohydride (639.0 mg, 16.9 mmol, 1.2 equiv.) and the reaction was allowed to stir at room temperature overnight. The reaction was quenched by pouring into water (20 mL) and was extracted with diethyl ether (3 x 50 mL). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo* to afford methyl 3-hydroxycyclopentane-1-carboxylate as a pale yellow oil as a mixture of diastereomers. The crude product was used in the next step without further purification.

To a round bottom flask equipped with magnetic stir bar, under N_2 atmosphere, was added methyl 3-hydroxycyclopentane-1-carboxylate (21.1 mmol, 1.0 equiv.), *N*-methlyimidazole (5.0 mL, 63.3 mmol, 3.0 equiv.), iodine (16.0 g, 63.3 mmol, 3.0 equiv.) and CH_2Cl_2 (63 mL, 3.0 M). *tert*-Butyldimethylsilyl chloride (3.5 g, 23.2 mmol, 1.1 equiv.) was added and the reaction was stirred at room temperature until complete disappearance of the starting material by TLC analysis. At this time, the solvent was evaporated, the residue dissolved in EtOAc and washed with conc. aq. $Na_2S_2O_3$. The organic phase was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica (45 mm fritted glass column, 250 mL SiO_2) using 100% hexanes → 5% → 10% → 15% EtOAc/hexanes gradient as eluent afforded methyl 3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carboxylate as a colorless oil as a mixture of diastereomers (4.11 g, 15.9 mmol, 75% yield over 2 steps).

To a flame-dried round bottom flask was added lithium aluminum hydride (724.0 mg, 19.1 mmol, 1.2 equiv.) and THF (16 mL, 1.0 M). The flask was cooled to 0 °C and methyl 3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carboxylate (4.11 g, 15.9 mmol, 1.0 equiv.) was added dropwise. The reaction was allowed to stir at room temperature overnight. The reaction was quenched by pouring into ice/water. The mixture was filtered through a pad of Celite (CH_2Cl_2 as eluent). The organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo* to give (3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methanol as a colorless oil as a mixture of diastereomers which was taken on to the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.31 – 4.24 (m, 1H), 3.61 (dd, *J* = 10.3, 4.5 Hz, 0.4H), 3.55 (dd, *J* = 10.3, 4.5 Hz, 0.4H), 3.51 (d, *J* = 6.8 Hz, 1.2H), 2.37 (hept., *J* = 6.9 Hz, 0.7H), 2.32 – 2.25 (m, 0.4H), 1.99 – 1.84 (m, 1H), 1.84 – 1.50 (m, 3.0H), 1.50 – 1.37 (m, 1.4H), 1.33 – 1.19 (m, 1.3H), 0.89 (s, 3.7H), 0.87 (s, 5.3H), 0.07 (s, 2.2H), 0.03 (s, 3.9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (74.5), 74.1, 67.5, (66.8), 39.8, (39.7),

(39.3), 39.1, (36.2), 35.5, (26.6), 26.0, 26.0, (25.4), 18.3, (18.2), -4.6, (-4.8). HRMS (ESI+) *m/z* calculated for $C_{12}H_{27}O_2Si$ $[M+H]^+$: 231.1780, found 231.1775.

To a flame-dried round bottom flask was added (3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methanol (1.0 equiv.) and CH_2Cl_2 (0.3 M). The flask was cooled to 0 °C and pyridinum chlorochromate (1.5 equiv.) was added. The reaction was allowed to stir at room temperature overnight. The reaction was filtered through a pad of Celite/silica using CH_2Cl_2 as eluent and concentrated *in vacuo* to 3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carbaldehyde (**S64**) as a yellow oil as a mixture of diastereomers which was used in the subsequent reductive amination step without further purification.

General Procedure for Reductive Amination

To a round bottom flask equipped with a magnetic stir bar, under N_2 atmosphere ,was added substrate (1.0 equiv.), 1,2-dichloroethane (0.1 M), aldehyde (2.0 – 3.0 equiv.) and acetic acid (1% v/v). The reaction solution was stirred for 30 minutes at room temperature. $NaBH(OAc)_3$ (1.2 equiv.) was added in one portion. The reaction was stirred at room temperature overnight (18 h). The reaction was quenched at room temperature by the addition of sat. aq. $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (x 2). The combined organic layer was dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography.

General Procedure for TBS Deprotection

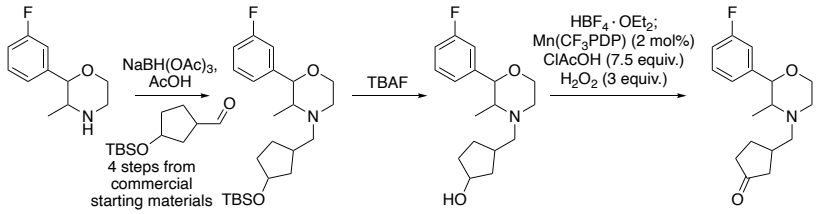
To a flame-dried round bottom flask equipped with magnetic stir bar, under N_2 atmosphere was added substrate (1.0 equiv.) and THF (1.0 M). The solution was cooled to 0 °C and TBAF (1.0 M in THF, 3.0 equiv.) was added dropwise. The reaction was stirred overnight (16 h) at room temperature. The reaction was concentrated *in vacuo* and purified by flash column chromatography.

General Procedure for Alcohol Oxidation

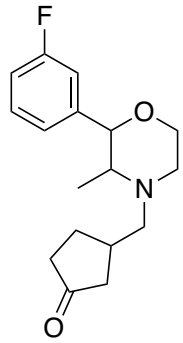
To a flame dried 40 mL vial with a magnetic stir bar was added substrate (1.0 equiv.) and anhydrous CH_2Cl_2 (0.25 M). The vial was flushed with a N_2 stream and then cooled to 0 ºC. HBF_4•OEt_2 (1.1 equiv.) was added dropwise *via* syringe and the reaction was allowed to stir at 0 ºC for 30 minutes then warmed to room temperature and stirred for an additional 1 h. The reaction was concentrated *in vacuo* and left on high vacuum overnight (12-24 h). Resultant HBF_4 salt were used as substrates for oxidation.

To the 40 mL with substrate was added $ClCH_2CO_2H$ (7.5 equiv.) and MeCN (0.5 M) was added along the wall to ensure all compounds were washed beneath the solvent level. The vial was sealed with a screw cap fitted with a PTFE/Silicone septum. The vial was cooled to -36 ºC with 1,2-dichloroethane/dry ice bath. A 1.0 mL syringe was filled with a solution of the Mn(CF_3-PDP) catalyst **1** (2 mol%) in MeCN (0.02

M). A few drops of this solution was added to the reaction. A 10 mL syringe was filled with a solution of H_2O_2 (3.0 equiv., 50% wt. in H_2O, purchased from Sigma-Aldrich) in MeCN (0.18 M). Both syringes were fitted with 25G needles and loaded in a syringe pump resulting in a simultaneous addition of catalyst and oxidant solutions over 1 hour while the reaction vial was maintained at the corresponding temperature. Upon completion, the reaction was warmed to room temperature and concentrated *in vacuo* to a minimum amount of solvent. The reaction was diluted with DCM (10 mL), basified with 3 M NaOH (10 mL) and stirred vigorously for 20 minutes. The resulting solution was poured into 3 M NaOH (30 mL) and extracted with DCM (3 x 20 mL). The combined organic layer was washed with brine (1 x 60 mL) then dried with Na_2SO_4. The filtrate was concentrated and purified by flash column chromatography on silica gel.



3-((2-(3-fluorophenyl)-3-methylmorpholino)methyl)cyclopentan-1-one [33]



According to the **general procedure for reductive amination**, 2-(3-fluorophenyl)-3-methylmorpholine (**S32**) (97.6 mg, 0.5 mmol, 1.0 equiv.), 3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carbaldehyde (**S64**) (456.8 mg, 1.0 mmol, 2.0 equiv.), AcOH (0.5 mL) and $NaBH(OAc)_3$ (127.2 mg, 0.6 mmol, 1.2 equiv.) were reacted in 1,2-dichlorethane (5 mL). The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% MeOH/CH_2Cl_2 gradient as eluent afforded 4-((3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methyl)-2-(3-fluorophenyl)-3-methylmorpholine as a pale yellow oil as a mixture of diastereomers.

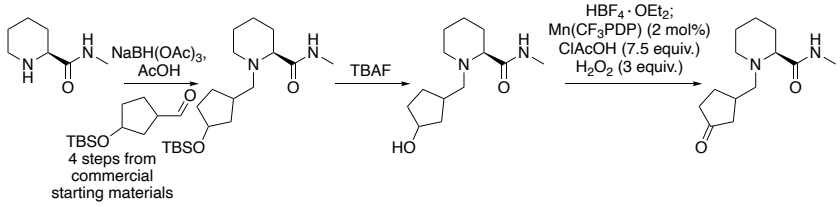
According to the **general procedure for TBS deprotection**, to 4-((3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methyl)-2-(3-fluorophenyl)-3-methylmorpholine (0.5 mmol, 1.0 equiv.) in THF (0.5 mL) was added TBAF (1.5 mL, 1.5 mmol, 3.0 equiv.). The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% → 6% MeOH/CH_2Cl_2 gradient as eluent afforded as eluent afforded 3-((2-(3-fluorophenyl)-3-methylmorpholino)methyl)cyclopentan-1-ol as a pale yellow oil as a mixture of diastereomers (69.6 mg, 0.24 mmol, 48% yield over 2 steps).

According to the **general procedure for alcohol oxidation**, 3-((2-(3-fluorophenyl)-3-methylmorpholino)methyl)cyclopentan-1-ol (29.6 mg, 0.237 mmol, 1.0 equiv.) was protected with

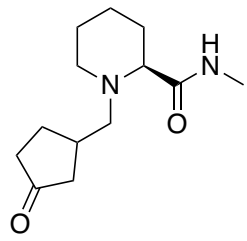
HBF_4•OEt_2 (36 μL, 0.261 mmol, 54 wt.%, 1.1 equiv.) in CH_2Cl_2 (0.95 mL, 0.25 M). The oxidation was carried out according to the **general procedure**: the resultant HBF_4 salt (0.237 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (168 mg, 1.78 mmol, 7.5 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (6.4 mg, 0.0047 mmol, 2 mol%), H_2O_2 (50% wt. in H_2O, 48 mg, 0.71 mmol, 3.0 equiv.), MeCN (0.47 mL in 40 mL vial, 2.0 mL with oxidant, 0.2 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **general procedure**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% MeOH/CH_2Cl_2 as eluent afforded 3-((2-(3-fluorophenyl)-3-methylmorpholino)meth`yl)cyclopentan-1-one (**33**) as a yellow oil (47.5 mg, 0.163 mmol, 69% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.25 (m, 1H), 7.12 – 7.08 (m, 1H), 7.08 – 7.04 (m, 1H), 7.01 – 6.95 (m, 1H), 4.05 (app. t, *J* = 8.6 Hz, 1H), 3.98 – 3.90 (m, 1H), 3.78 (app. qd, *J* = 11.6, 2.4 Hz, 1H), 2.86 (app. t, *J* = 11.6 Hz, 1H), 2.80 – 2.71 (m, 1H), 2.55 – 2.10 (m, 8H), 1.99 (app. dd, *J* = 17.2, 7.9 Hz, 0.5H), 1.86 (app. dd, *J* = 17.9, 8.6 Hz, 0.5H), 1.75 – 1.65 (m, 0.5H), 1.61 – 1.51 (m, 0.5H), 0.82 (app. t, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.3, 219.3, 162.8 (d, *J* = 246.2 Hz), 142.9 (d, *J* = 7.2 Hz), 142.8 (d, *J* = 7.2 Hz), 129.9 (d, *J* = 8.2 Hz), 129.9 (d, *J* = 8.2 Hz), 123.9 (d, *J* = 3.4 Hz), 123.9 (d, *J* = 3.4 Hz), 115.1 (d, *J* = 20.7 Hz), 115.1 (d, *J* = 21.2 Hz), 114.9 (d, *J* = 21.2 Hz), 114.9 (d, *J* = 21.6 Hz), 84.5 (d, *J* = 4.8 Hz), 84.5 (d, *J* = 4.3 Hz), 67.2, 61.3, 61.3, 58.6, 58.1, 52.8, 52.7, 44.1, 44.0, 38.1, 37.8, 35.0, 34.9, 27.9, 27.7, 15.5, 15.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.1. HRMS (ESI+) *m/z* calculated for $C_{17}H_{23}NO_2F$ $[M+H]^+$: 292.1713, found 292.1721.

Spectral data matches data from Mn(CF_3PDP) oxidation confirming site of oxidation and that Mn(CF_3PDP) oxidation forms diastereoisomers. See page 847 for spectral overlay.



(2*S*)-*N*-methyl-1-((3-oxocyclopentyl)methyl)piperidine-2-carboxamide [34]



According to the **general procedure for reductive amination**, (*S*)-*N*-methylpiperidine-2-carboxamide (71.1 mg, 0.5 mmol, 1.0 equiv.), 3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carbaldehyde (**S64**) (456.8 mg, 1.0 mmol, 2.0 equiv.), AcOH (0.5 mL) and $NaBH(OAc)_3$ (127.2 mg, 0.6 mmol, 1.2 equiv.) were reacted in 1,2-dichlorethane (5 mL). The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 5% MeOH/CH_2Cl_2 gradient as eluent afforded (2*S*)-1-((3-((*tert*-

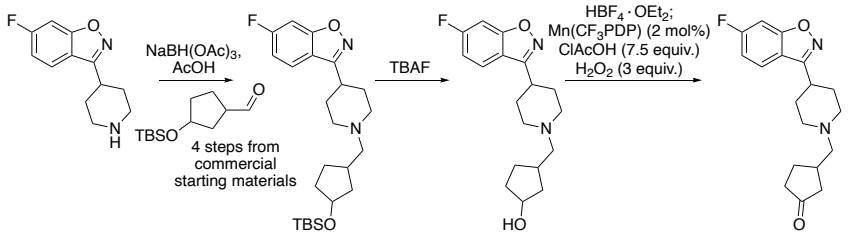
butyldimethylsilyl)oxy)cyclopentyl)methyl)-*N*-methylpiperidine-2-carboxamide as a pale yellow oil as a mixture of diastereomers.

According to the **general procedure for TBS deprotection**, to (2*S*)-1-((3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methyl)-*N*-methylpiperidine-2-carboxamide (0.5 mmol, 1.0 equiv.) in THF (0.5 mL) was added TBAF (1.5 mL, 1.5 mmol, 3.0 equiv.). The crude material was purified by flash column chromatography on alumina (15 mm fritted glass column, 30 mL Brockman Grade II alumina) using 100% EtOAc → 2% → 4% → 6% MeOH/EtOAc gradient as eluent afforded as eluent afforded (2*S*)-1-((3-hydroxycyclopentyl)methyl)-*N*-methylpiperidine-2-carboxamide as a colorless oil as a mixture of diastereomers (47.3 mg, 0.197 mmol, 39% yield over 2 steps).

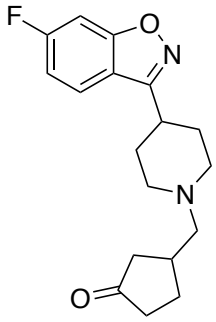
According to the **general procedure for alcohol oxidation**, (2*S*)-1-((3-hydroxycyclopentyl)methyl)-*N*-methylpiperidine-2-carboxamide (47.3 mg, 0.197 mmol, 1.0 equiv.) was protected with HBF_4•OEt_2 (30 µL, 0.217 mmol, 54 wt.%, 1.1 equiv.) in CH_2Cl_2 (0.79 mL, 0.25 M). The oxidation was carried out according to the **general procedure**: the resultant HBF_4 salt (0.197 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (140 mg, 1.48 mmol, 7.5 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (5.3 mg, 0.0040 mmol, 2 mol%), H_2O_2 (50% wt. in H_2O, 40 mg, 0.59 mmol, 3.0 equiv.), MeCN (0.4 mL in 40 mL vial, 2.0 mL with oxidant, 0.2 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **general procedure**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 1% → 2% → 3% → 4% → 5% MeOH/CH_2Cl_2 as eluent afforded (2*S*)-*N*-methyl-1-((3-oxocyclopentyl)methyl)piperidine-2-carboxamide (**34**) as a pale yellow oil (19.7 mg, 0.083 mmol, 42% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 0.5H), 6.45 (s, 0.5H), 3.06 (ddt, *J* = 12.0, 7.9, 4.2 Hz, 1H), 2.81 (d, *J* = 5.0 Hz, 1.5H), 2.77 (d, *J* = 5.0 Hz, 1.5H), 2.69 (ddd, *J* = 13.7, 10.3, 3.6 Hz, 1H), 2.55 – 2.03 (m, 7H), 2.03 – 1.86 (m, 2.8H), 1.77 (dd, *J* = 18.2, 8.8 Hz, 0.6H), 1.72 – 1.60 (m, 2H), 1.58 – 1.35 (m, 3H), 1.33 – 1.16 (m, 1.4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 218.9, 218.4, 175.2, 175.1, 68.7, 68.3, 61.4, 61.4, 51.9, 51.7, 43.8, 43.7, 38.0, 37.6, 34.7, 34.3, 30.3, 29.8, 27.8, 27.6, 25.8, 25.7, 24.9, 24.7, 23.4, 23.3. HRMS (ESI+) *m/z* calculated for $C_{13}H_{23}N_2O_2$ $[M+H]^+$: 239.1760, found 239.1763.

Spectral data matches data from Mn(CF_3PDP) oxidation confirming site of oxidation and that Mn(CF_3PDP) oxidation forms diastereoisomers. See page 851 for spectral overlay.



3-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)methyl)cyclopentan-1-one [36]



According to the **general procedure for reductive amination**, *N*-6-fluoro-3-(4-piperidinyl)benziosoxazole (110.1 mg, 0.5 mmol, 1.0 equiv.), 3-((*tert*-butyldimethylsilyl)oxy)cyclopentane-1-carbaldehyde (**S64**) (456.8 mg, 1.0 mmol, 2.0 equiv.), AcOH (0.5 mL) and $NaBH(OAc)_3$ (127.2 mg, 0.6 mmol, 1.2 equiv.) were reacted in 1,2-dichlorethane (5 mL). The crude material was purified by flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% MeOH/CH_2Cl_2 gradient as eluent afforded 3-(1-((3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methyl)piperidin-4-yl)-6-fluorobenzo[*d*]isoxazole as a pale yellow oil as a mixture of diastereomers (208.1 mg, 0.48 mmol, 96% yield).

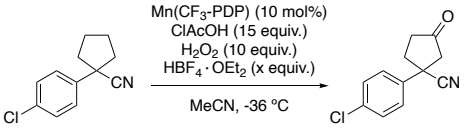
According to the **general procedure for TBS deprotection**, to 3-(1-((3-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)methyl)piperidin-4-yl)-6-fluorobenzo[*d*]isoxazole (208.1 mg, 0.48 mmol, 1.0 equiv.) in THF (0.5 mL) was added TBAF (1.5 mL, 1.5 mmol, 3.0 equiv.). The crude material was purified by flash column chromatography on alumina (15 mm fritted glass column, 30 mL Brockman Grade II alumina) using 100% ethyl acetate as eluent afforded 3-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)methyl)cyclopentan-1-ol as a pale yellow oil as a mixture of diastereomers (82.8 mg, 0.26 mmol, 54% yield).

According to the **general procedure for alcohol oxidation**, 3-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)methyl)cyclopentan-1-ol (34.6 mg, 0.109 mmol, 1.0 equiv.) was protected with HBF_4•OEt_2 (16 µL, 0.120 mmol, 54 wt.%, 1.1 equiv.) in CH_2Cl_2 (0.5 mL, 0.25 M). The oxidation was carried out according to the **general procedure**: the resultant HBF_4 salt (0.109 mmol, 1.0 equiv.), $ClCH_2CO_2H$ (77.3 mg, 0.818 mmol, 7.5 equiv.), (*R,R*)-Mn(CF_3PDP) catalyst **1** (2.95 mg, 0.0022 mmol, 2 mol%), H_2O_2 (50% wt. in H_2O, 22.2 mg, 0.327 mmol, 3.0 equiv.), MeCN (0.22 mL in 40 mL vial, 0.9 mL with oxidant, 0.09 mL with catalyst). The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up according to the **general procedure**. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 100% CH_2Cl_2 → 2% → 4% MeOH/CH_2Cl_2 as eluent afforded 3-((4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl)methyl)cyclopentan-1-one (**36**) as a pale yellow solid (15.3 mg, 0.048 mmol, 44% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.7, 5.1 Hz, 1H), 7.24 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.06 (td, *J* = 8.8, 2.2 Hz, 1H), 3.16 – 2.99 (m, 3H), 2.54 – 2.38 (m, 4H), 2.35 – 2.13 (m, 5H), 2.13 – 1.93 (m, 5H), 1.72 – 1.58 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 219.6, 164.2 (d, *J* = 250.5 Hz), 164.0 (d, *J* = 13.5 Hz), 161.2, 122.7 (d, *J* = 11.1 Hz), 117.4, 112.5 (d, *J* = 25.0 Hz), 97.6 (d, *J* = 26.9 Hz), 63.6, 54.1, 53.9, 44.1, 38.0, 34.8, 34.6, 30.6, 27.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -109.6. HRMS (ESI+) *m/z* calculated for $C_{18}H_{22}N_2O_2F$ $[M+H]^+$: 317.1665, found 317.1672.

Spectral data matches data from Mn(CF$_3$PDP) oxidation confirming site of oxidation. *See page 856 for spectral overlay.*

IX. HBF_4•OEt_2 Doping Experiments



0 equiv. HBF_4•OEt_2: The reaction was run with **General Method B: Slow Catalyst Addition Protocol**: 1-(4-chlorophenyl)cyclopentane-1-carbonitrile (61.7 mg, 0.300 mmol, 1.0 equiv.), (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.), H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.), MeCN (0.6 mL in 40 mL vial, 3.75 mL with oxidant, 0.38 mL MeCN with catalyst). The reaction was run at 0 ºC with an ice/water bath. The reaction was worked up with 9 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% acetone/hexanes as eluent afforded 1-(4-chlorophenyl)-3-oxocyclopentane-1-carbonitrile as a colorless oil.
Yield: (55.6 mg, 0.254 mmol, 84.6% yield), 0% rsm.

0.1 equiv. HBF_4•OEt_2: The reaction was run with modified **General Method B: Slow Catalyst Addition Protocol**: 1-(4-chlorophenyl)cyclopentane-1-carbonitrile (61.7 mg, 0.300 mmol, 1.0 equiv), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.) and HBF_4•OEt_2 (4.1 μL, 0.03 mmol, 0.1 equiv.) in 40 mL vial with MeCN (0.6 mL). (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%) in MeCN (3.75 mL) and H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.) in MeCN (0.38 mL) added via syringe pump over 3 hours. The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 9 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% acetone/hexanes as eluent afforded 1-(4-chlorophenyl)-3-oxocyclopentane-1-carbonitrile as a colorless oil.
Run 1: (56.3 mg, 0.257 mmol, 85.6% yield), 0% rsm. **Run 2:** (54.9 mg, 0.250 mmol, 83.6% yield), 0% rsm. **Average: 84.6% yield, 0% rsm.**

0.5 equiv. HBF_4•OEt_2: The reaction was run with modified **General Method B: Slow Catalyst Addition Protocol**: 1-(4-chlorophenyl)cyclopentane-1-carbonitrile (61.7 mg, 0.300 mmol, 1.0 equiv), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.) and HBF_4•OEt_2 (20.4 μL, 0.15 mmol, 0.5 equiv.) in 40 mL vial with MeCN (0.6 mL). (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%) in MeCN (3.75 mL) and H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.) in MeCN (0.38 mL) added via syringe pump over 3 hours. The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 9 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography

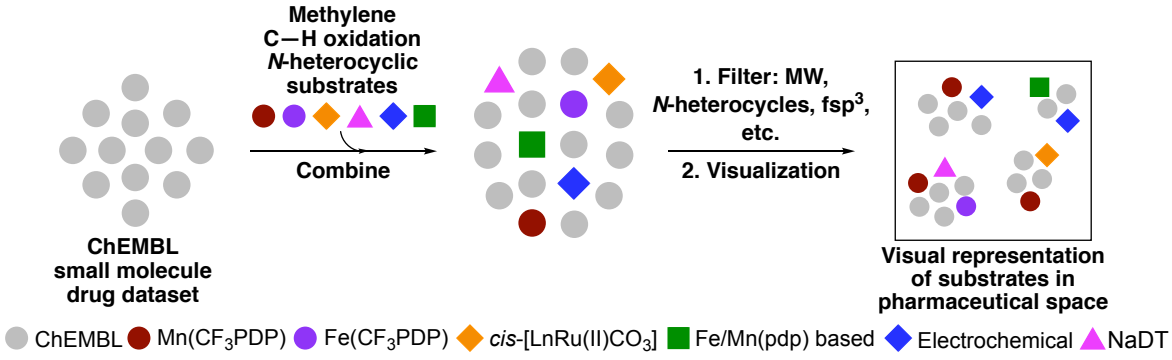
on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% acetone/hexanes as eluent afforded 1-(4-chlorophenyl)-3-oxocyclopentane-1-carbonitrile as a colorless oil.
Run 1: (37.2 mg, 0.170 mmol, 56.6% yield), (22.6 mg, 0.110 mmol, 36.7% rsm). **Run 2:** (36.9 mg, 0.168 mmol, 56.1%), (21.8 mg, 0.106 mmol, 35.4% rsm). **Average: 56.4% yield, 36.1% rsm.**

1.0 equiv. HBF_4•OEt_2: The reaction was run with modified **General Method B: Slow Catalyst Addition Protocol**: 1-(4-chlorophenyl)cyclopentane-1-carbonitrile (61.7 mg, 0.300 mmol, 1.0 equiv), $ClCH_2CO_2H$ (425 mg, 4.5 mmol, 15.0 equiv.) and HBF_4•OEt_2 (40.9 μL, 0.3 mmol, 1.0 equiv.) in 40 mL vial with MeCN (0.6 mL). (*R,R*)-Mn(CF_3PDP) **1** (40.7 mg, 0.030 mmol, 10 mol%) in MeCN (3.75 mL) and H_2O_2 (50% wt. in H_2O, 204 mg, 3.0 mmol, 10.0 equiv.) in MeCN (0.38 mL) added via syringe pump over 3 hours. The reaction was run at -36 ºC with a 1,2-dichloroethane/dry ice bath. The reaction was worked up with 9 mL saturated $NaHCO_3$ and DCM as described in General Method C. Flash column chromatography on silica (15 mm fritted glass column, 30 mL SiO_2) using 10% → 20% acetone/hexanes as eluent afforded 1-(4-chlorophenyl)-3-oxocyclopentane-1-carbonitrile as a colorless oil.
Run 1: (26.2 mg, 0.120 mmol, 39.8% yield), (27.3 mg, 0.133 mmol, 44.3% rsm). **Run 2:** (25.9 mg, 0.118 mmol, 39.4%), (28.9 mg, 0.141 mmol, 46.9% rsm). **Average: 39.6% yield, 45.6% rsm.**

Spectral data in agreement with those previously reported in the literature.[3]

X. Chemoinformatics

Workflow:



Selection of Compounds for Analysis: Representative pharmaceuticals used for chemical space analysis were obtained from the small-molecule drug dataset from ChEMBL.[35] This set of drug molecules was combined with *N*-heterocyclic substrates that demonstrated methylene oxidation with ≥15% yield with Mn(CF_3-PDP), Fe(CF_3-PDP), NaDT, electrochemical, other Fe/Mn(PDP)-based catalysts, and bis(bipyridine)-ruthenium catalyst.[2,3,8,9,36–41] The following filters were applied to all molecules: MW ≥100, MW ≤500, # Nitrogen atoms ≥1, # heterorings ≥1, # sp^3 atoms ≥4, # hydrogen bond acceptors ≤ 10, # hydrogen bond donors ≤ 5 (# of hydrogen bond donors and acceptors were chosen based on Lipinski's rule of 5).[42] Filtered substrates from the included oxidation methods are shown in **Figure S5** and **Figure S6**. This resulted in 4,499 compounds used for further analysis.

Chemical Space Analysis using UMAP: Filtered compounds were converted to their corresponding SMILES string and exported as a .csv file. For all molecules, an RDKit topological fingerprint[43] was calculated and a dimensionality reduction was conducted using Uniform Manifold Approximation and Projection (UMAP)[44] technique via a Python Script[45,46]. The following parameters were chosen: metric = jaccard, n_neighbors = 50, and min_dist = 0.005. The resultant data was exported and plotted in Excel (**Figure S8**). Alternative n_neighbor parameters were evaluated to consider the effect of weighting local versus global structure in the data (**Figures S7, S9, S10**). When n_neighbors is small (n_neighbors = 25), local structure is heavily considered (relationship between very similar points). When n_neighbors is large (n_neighbors = 100), an emphasis is placed on the overall structure of the whole dataset. Although conclusions from each of the resultant plots were similar, n_neighbors = 50 was ultimately chosen which balances both local and global structure.

Similarity Analysis: Filtered compounds were imported to DataWarrior[47] as a .sdf file. For each molecule, the PathFP fingerprint was calculated and used for further analysis. A similarity analysis was conducted which calculates a Tanimoto similarity matrix[48] between all molecules and clusters similar

molecules in a 2-dimensional area (detailed description of algorithm in ref. 47). Lines are connected between compounds which have at least 80% Tanimoto similarity (**Figure S11**).

Gradient Plot Analysis: The dataset from Chemical Space Analysis using UMAP was further parametrized using both molecular weight (MW, g/mol) and complexity (BertzCT). Molecular weight was calculated on all ChEMBL compounds in the range of 100 – 500 g/mol. BertzCT is a common complexity metric aimed to quantify the degree of topological complexness of a molecule and will be larger for more topologically complex molecules. BertzCT was calculated for all ChEMBL molecules using RDKit (see Github). The resultant gradient plots aim to describe trends in both molecular weight and complexity across chemical space (**Figures S12 and S13**).

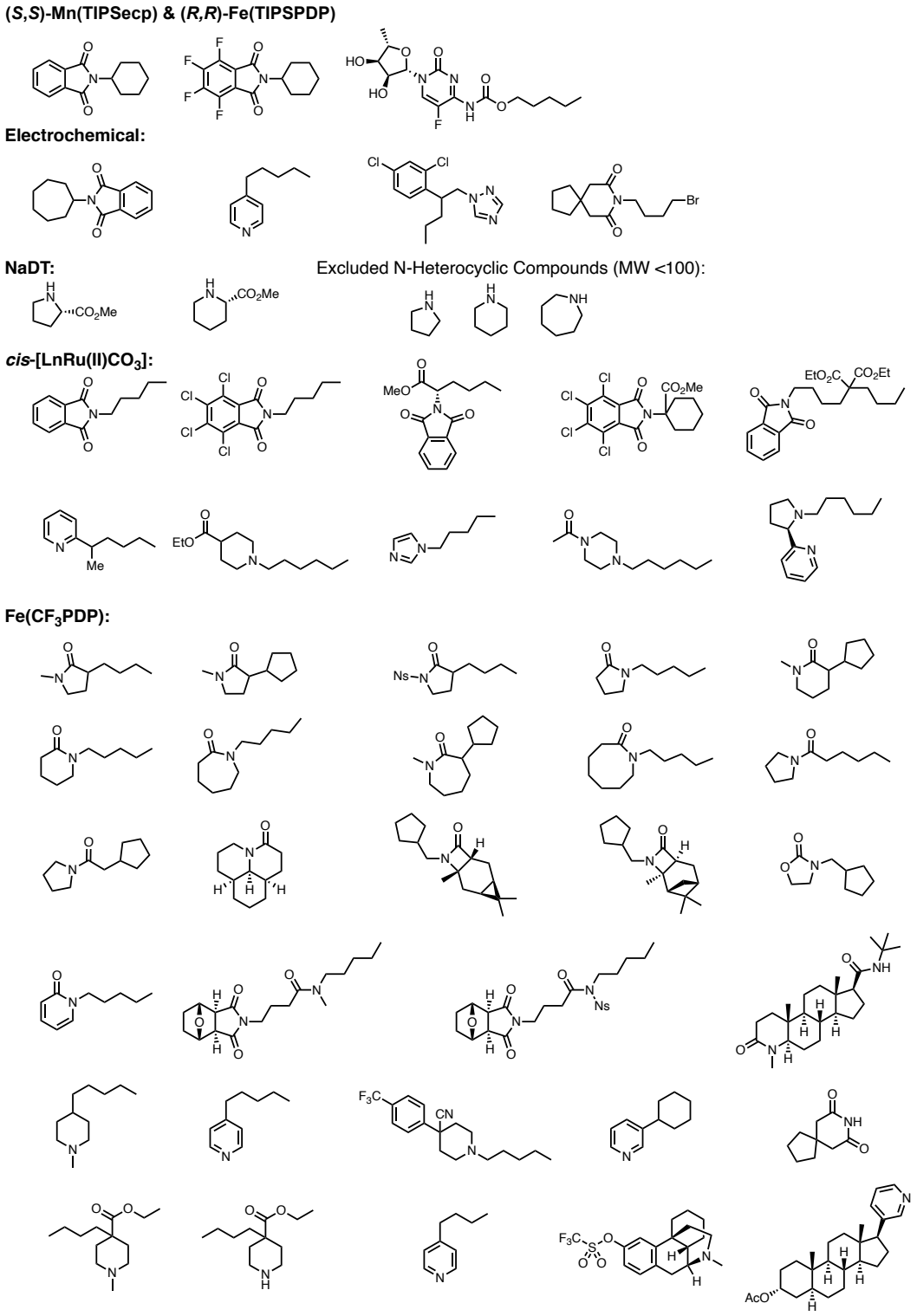


Figure S5. *N*-heterocyclic substrates demonstrated for methylene C—H oxidation prior to Mn(CF_3-PDP)

Mn(CF_3PDP):

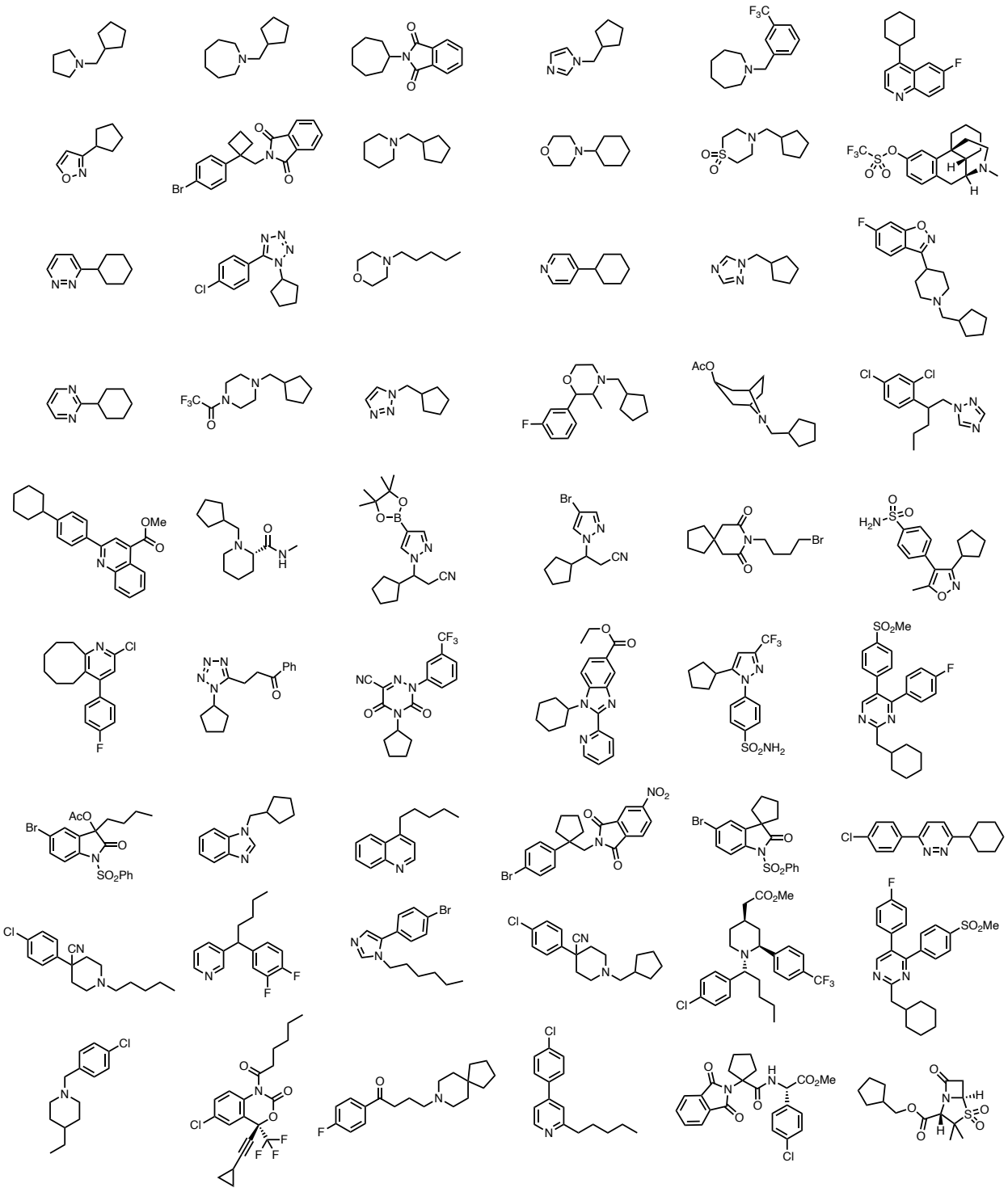


Figure S6. *N*-heterocyclic substrates demonstrated for methylene C—H oxidation using Mn(CF_3-PDP)

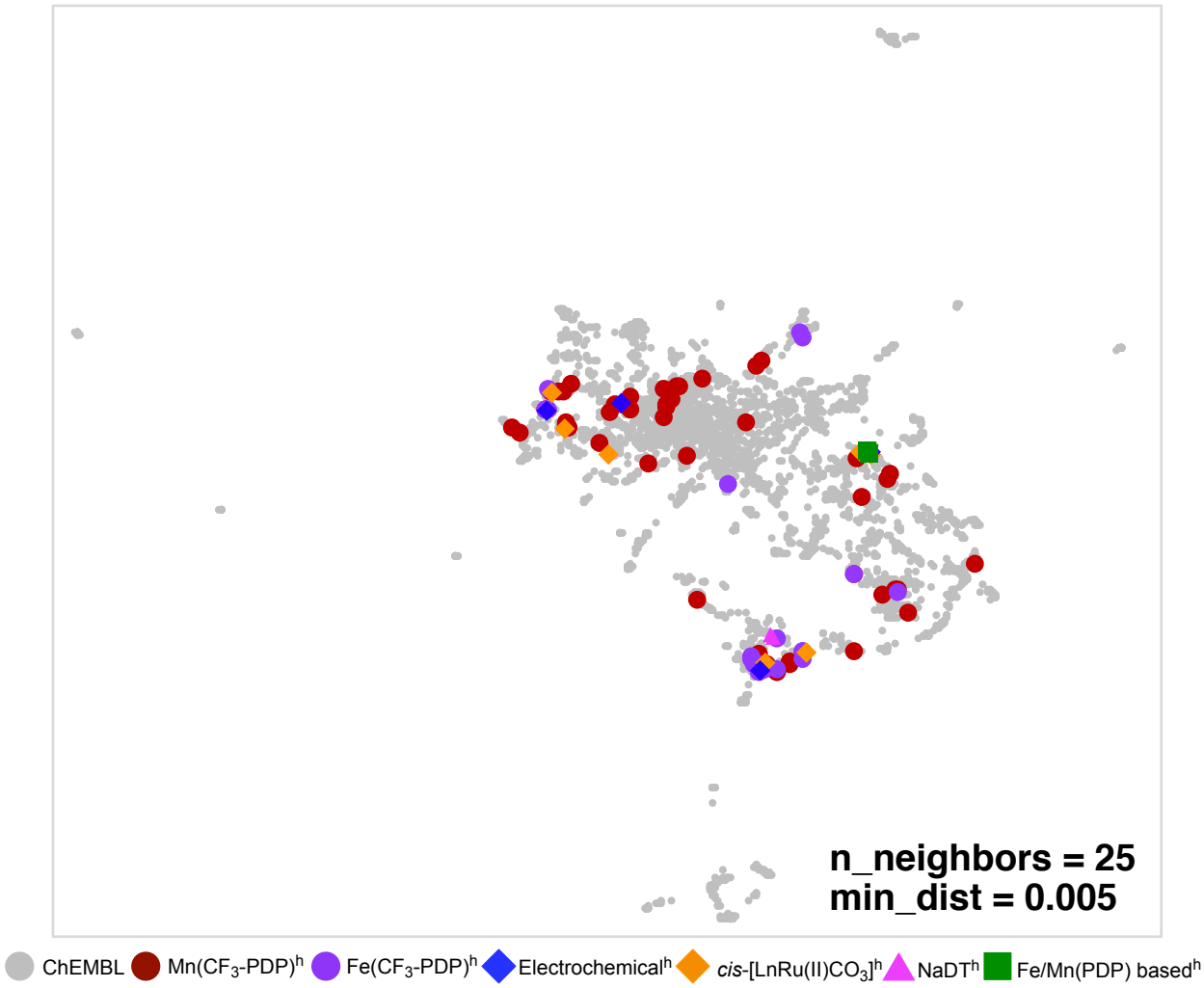


Figure S7. UMAP Projection using n_neighbors = 25, min_dist = 0.005

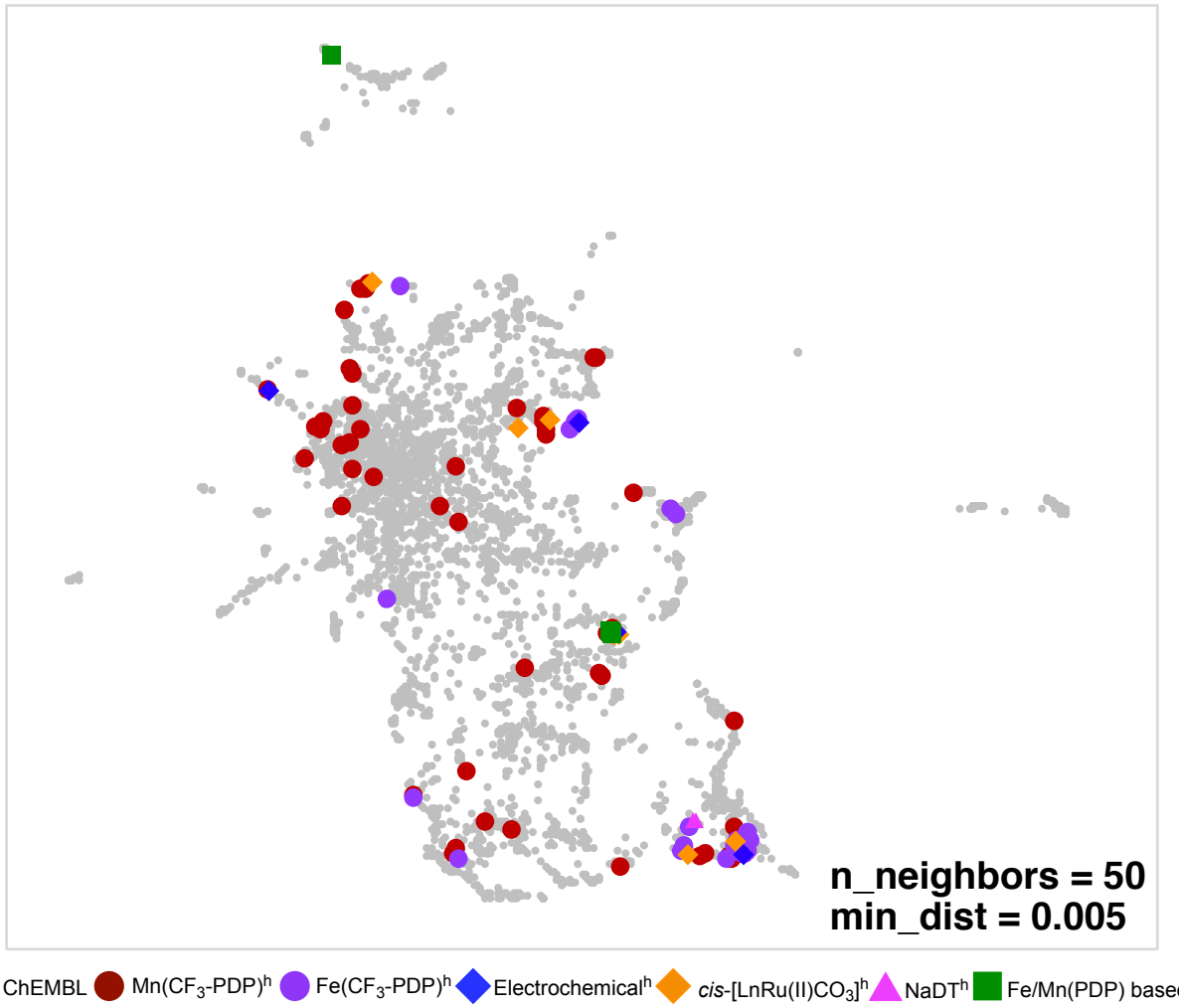


Figure S8. UMAP Projection using n_neighbors = 50, min_dist = 0.005

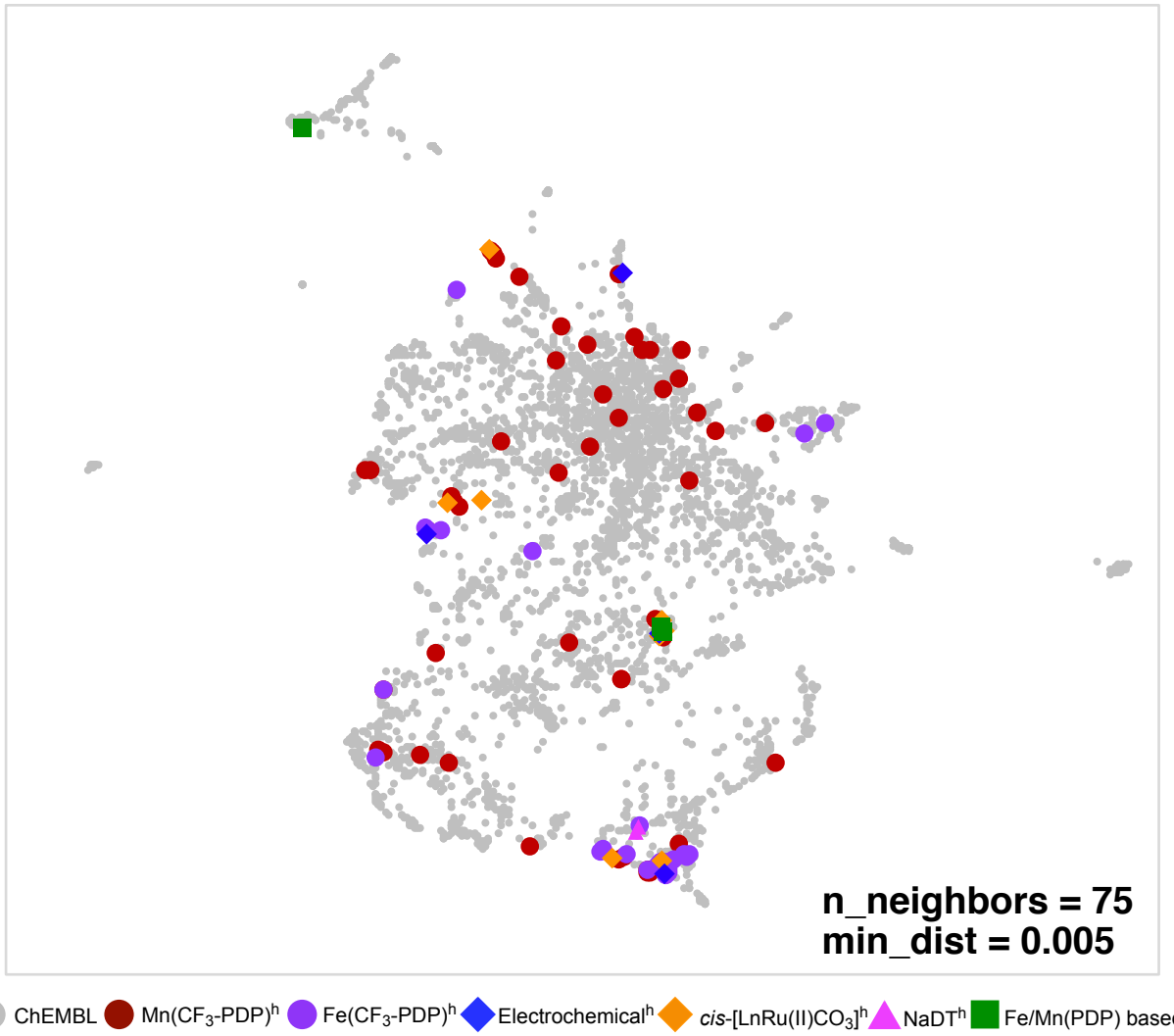


Figure S9. UMAP Projection using n_neighbors = 75, min_dist = 0.005

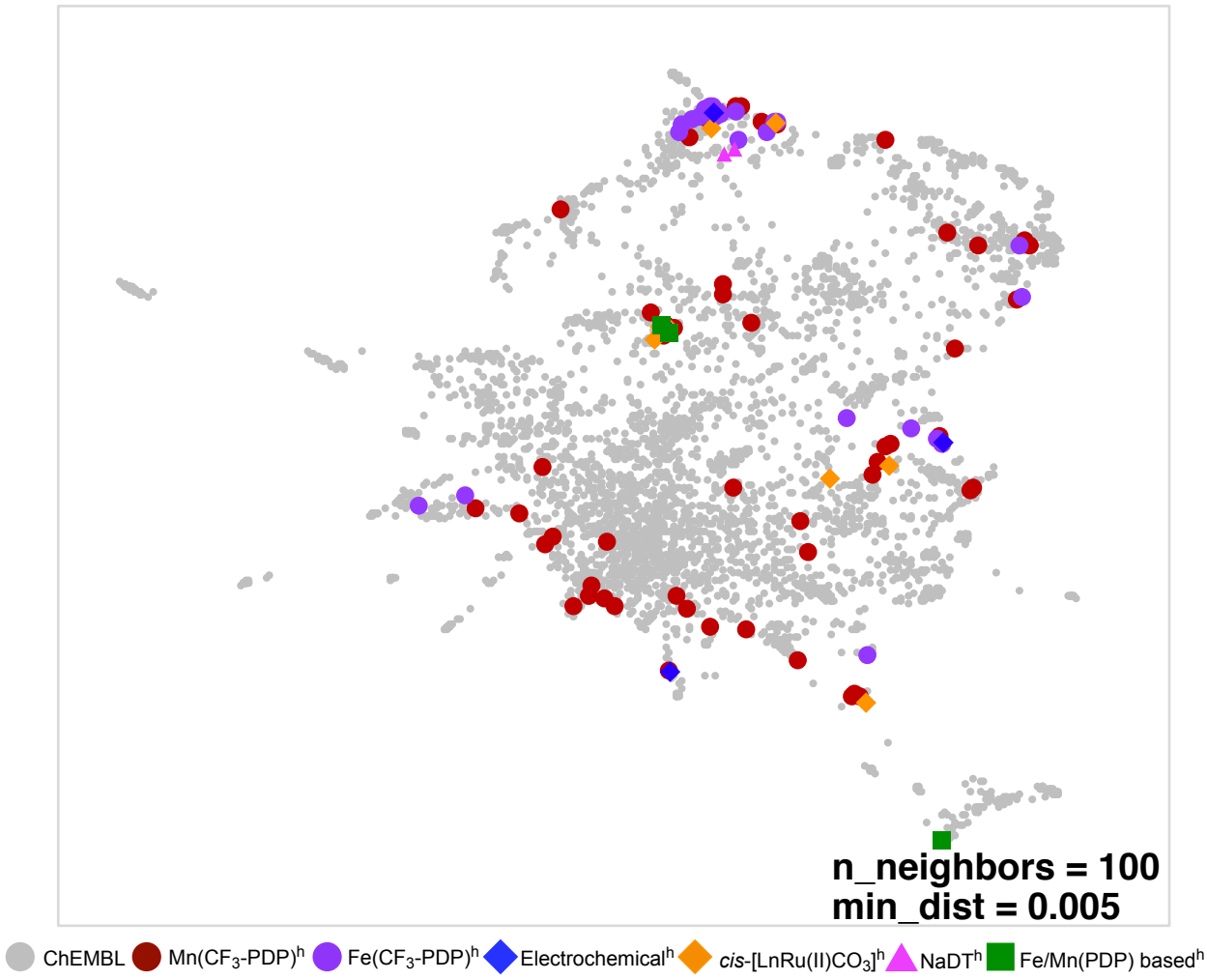


Figure S10. UMAP Projection using n_neighbors = 100, min_dist = 0.005

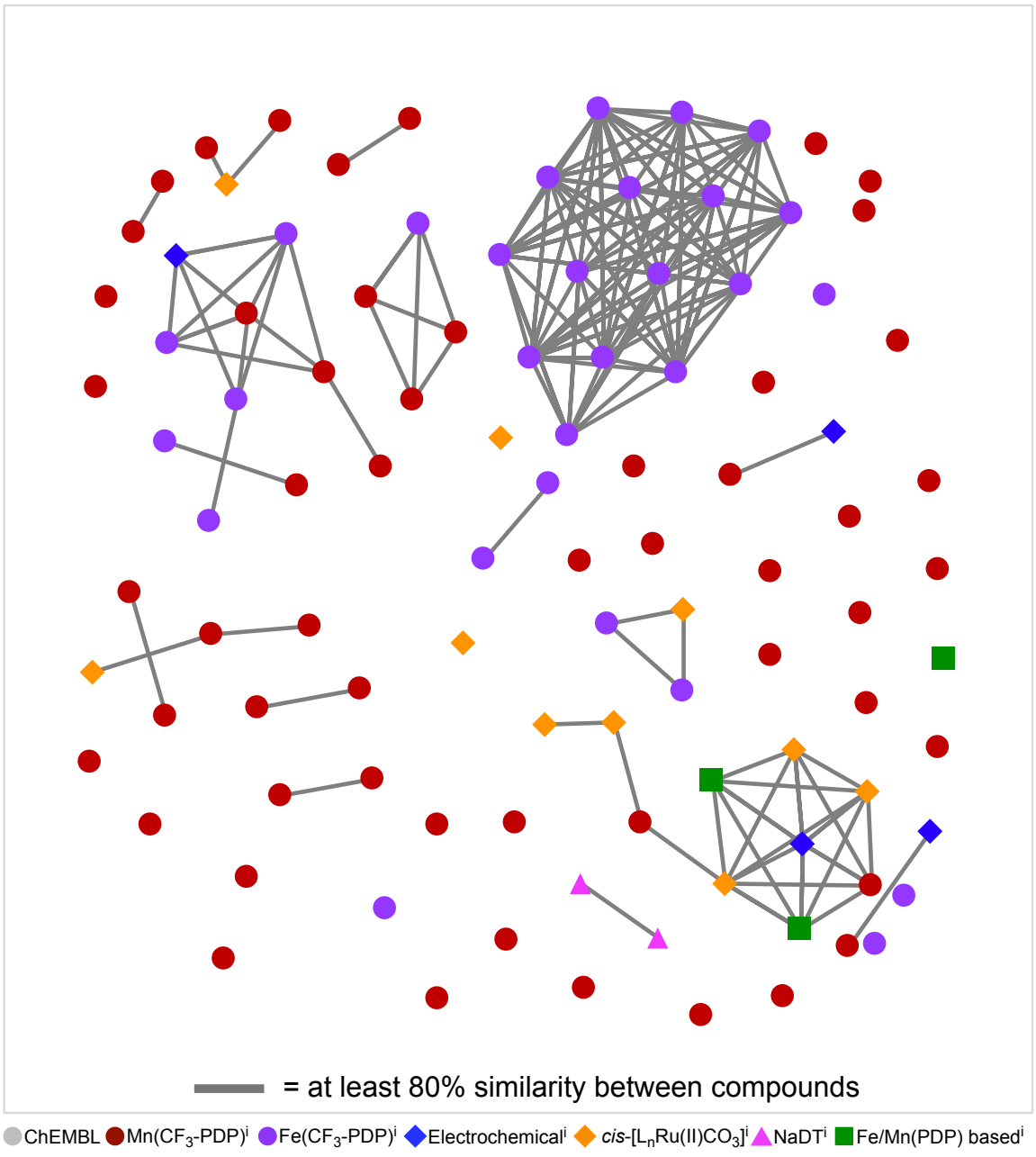


Figure S11. Similarity Analysis

Figure S12. Gradient plot analysis of chemical space using molecular weight (g/mol)

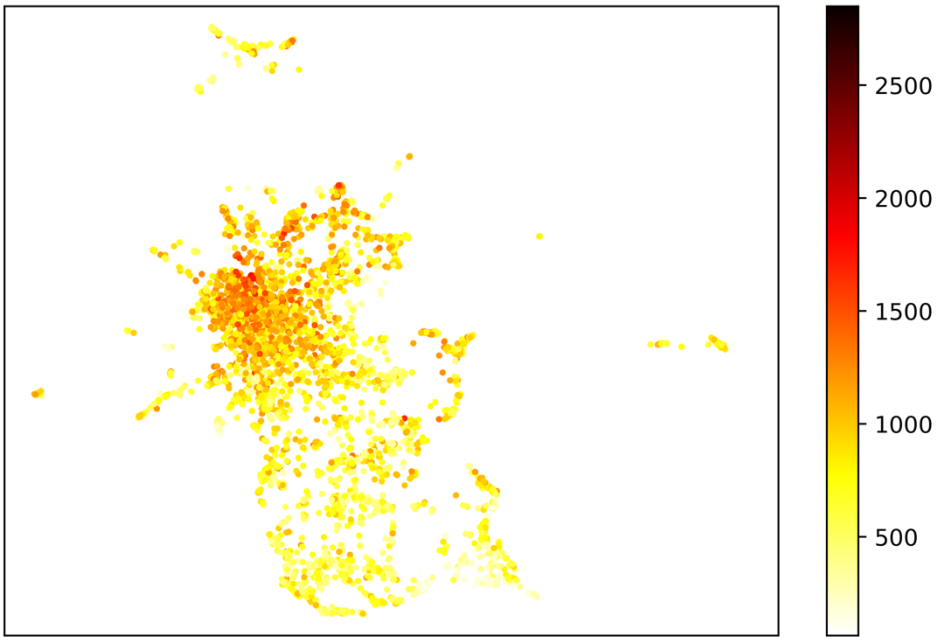


Figure S13. Gradient plot analysis of chemical space using BertzCT

XI. Biology

In vitro metabolic stability and screening metabolite identification

Incubation, data acquisition, and measurement of in vitro metabolic stability and unscaled intrinsic clearance values determined in human and rat liver microsomes were carried out by Q^2 Solutions, 5225 Exploration Drive, Indianapolis, IN 46241. Screening metabolite identification analysis was done within the Department of ADME & Discovery Toxicology, Merck & Co., Inc., Rahway, NJ, USA.

Samples were incubated at 37 °C at 0.3 µM compound in a buffer mixture consisting of 100 mM $NaPO_4$ Buffer pH 7.4 with 2 mM $MgCl_2$ and 1 mM NADPH cofactor at 0.25 mg/mL rat or human liver microsomal protein. Aliquots from the incubation samples at selected time points (0, 5, 15, 30, and 45 min) were stopped in 2 volumes of acetonitrile with 0.1% (v/v) formic acid containing internal standard Labetalol. Following mixing and centrifugation, a volume of supernatant from each stopped aliquot was diluted with 1 volume of water and subjected to LC-HRMS analysis.

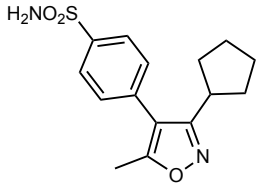
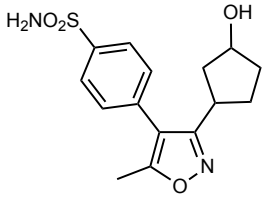
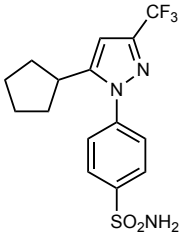
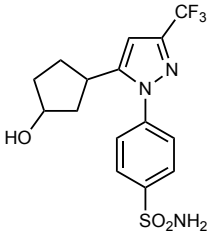
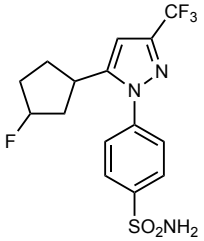
LC-HRMS analysis conducted on a Thermo Q-Exactive HF Mass Spectrometer with LEAP PAL HTS-xt DLW autosampler with Shimadzu HPLC LC-30ADvp Pumps equipped with Acquity BEH C18 1.7 µM x 100 mm LC column and mobile phases (solvent A 0.1% formic acid in water, solvent B 0.1% formic acid in acetonitrile) at 0.5 mL/min flow over a 5-min gradient. Metabolite ion inclusion lists for data dependent acquisition (Full MS / dd-MS^2 (TopN)) were generated using Mass-Metasite (version MassMetasite 4.1.9-2, Build date Oct 06, 2021, Molecular Discovery Ltd. and Lead Molecular Design SL, The Kinetic Centre, Theobald Street, Elstree, Borehamwood, Hertfordshire WD6 4PJ, United Kingdom).

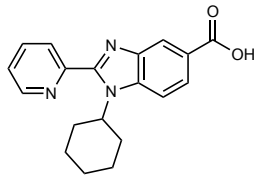
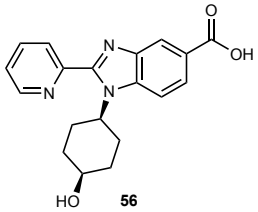
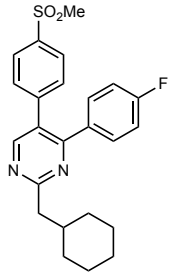
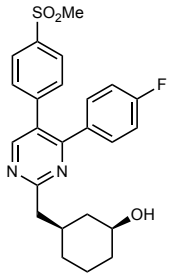
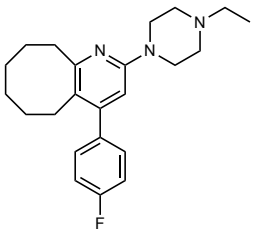
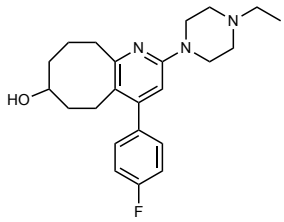
HRMS data was processed in Gubbs Mass Spec Utilities (GMSU, 265 Blue Spruce Cir, Alpharetta, GA 30005) software to then calculate % parent remaining and unscaled intrinsic clearance (Cl_{int} unscaled; units of µL/min/mg). Cl_{int} unscaled = *k*e x (µL incubation/mg microsomal protein) where *k*e is a first-order rate constant describing the disappearance of parent drug in the incubation and can be obtained from regressing the initial slope of the natural log of the analyte area/internal standard area versus time (min) profile.

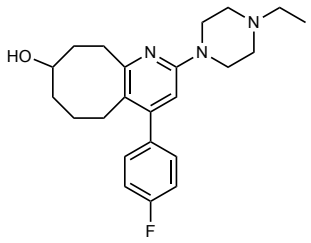
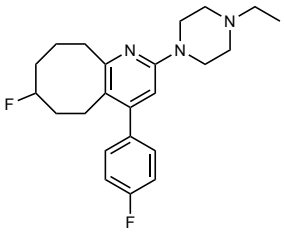
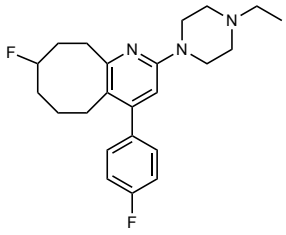
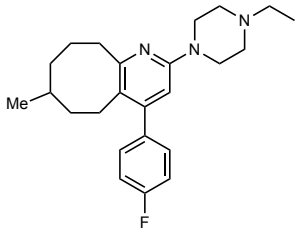
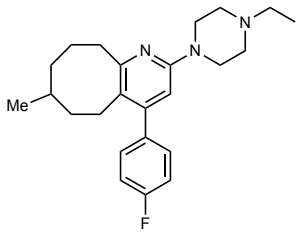
This screening (quantitative/qualitative) metabolite identification assay was used to identify primary metabolites from the same samples using raw data acquired for the in vitro unscaled intrinsic clearance determination. Metabolite identification data processing was done within the auto-batch processer of Mass-Metasite (version MassMetasite 4.2.6-1, Build date Jul 11, 2022, Molecular Discovery Ltd. And Lead Molecular Design SL, The Kinetic Centre, Theobald Street, Elstree, Borehamwood, Hertfordshire WD6 4PJ, United Kingdom). The processed data was uploaded to Oniro (version 1.3.3 or an earlier WebMetabase version, Molecular Discovery Ltd. And Lead Molecular Design SL, The Kinetic Centre,

Theobald Street, Elstree, Borehamwood, Hertfordshire WD6 4PJ, United Kingdom) where several interpretation macros were automatically executed, and metabolites were reported after analyst review.

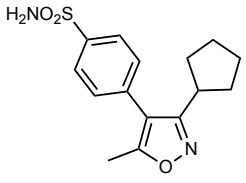
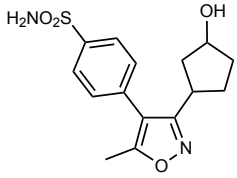
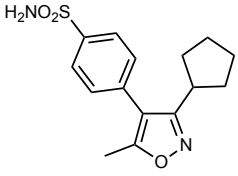
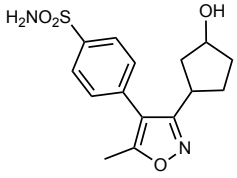
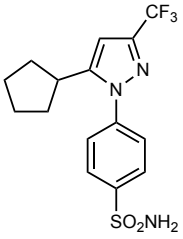
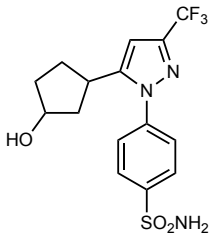
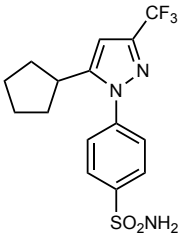
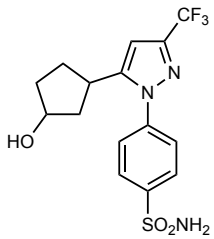
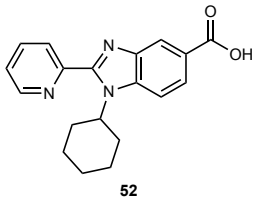
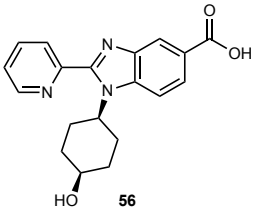
Summary of Metabolic Stability Studies

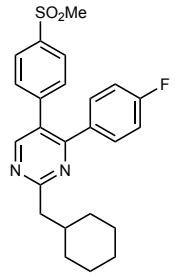
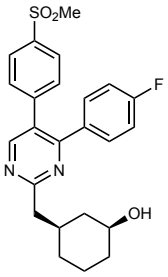
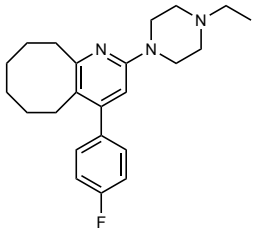
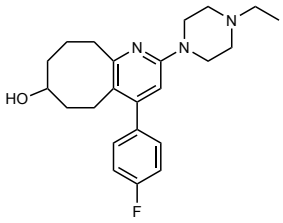
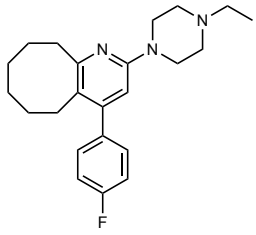
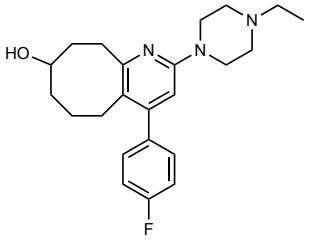
Compound	Species Microsomes	Cl_{int} unscaled (μL/min/mg)	%Parent Remaining at 45 min
 46	HUMAN	38.5	64
	RAT WISTAR HAN	66.3	47
 47	HUMAN	<20	81
	RAT WISTAR HAN	<20	94
 48	HUMAN	20.97	78
	RAT WISTAR HAN	135.96	22
 49	HUMAN	<20	93
	RAT WISTAR HAN	<20	90
 50	HUMAN	<20	111
	RAT WISTAR HAN	57.21	55
	HUMAN	<20	100

 52	RAT WISTAR HAN	32	69
 56	HUMAN	<20	96
	RAT WISTAR HAN	<20	96
 57	HUMAN	222.71	8
	RAT WISTAR HAN	244.21	6
 59	HUMAN	24.18	76
	RAT WISTAR HAN	45.88	69
 Blonanserin	HUMAN	841.9	0
	RAT WISTAR HAN	969.56	0
 63	HUMAN	156.82	17
	RAT WISTAR HAN	151.65	18
	HUMAN	189.23	12

 64	RAT WISTAR HAN	208.23	9
 65	HUMAN	949.22	0
	RAT WISTAR HAN	904.51	0
 66	HUMAN	564.27	0
	RAT WISTAR HAN	555.63	0
 67	HUMAN	916.38	0
	RAT WISTAR HAN	1119.05	0
 68	HUMAN	929	0
	RAT WISTAR HAN	1033.53	0

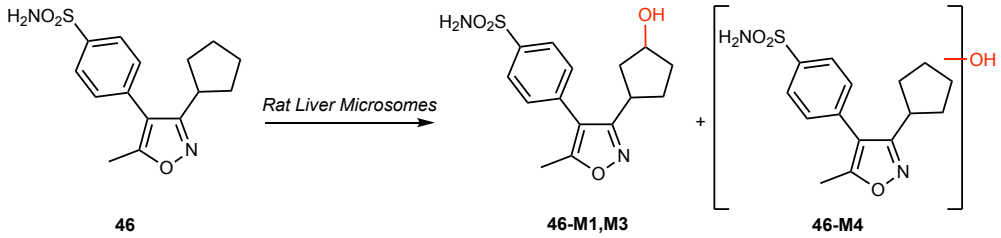
Summary of Metabolite Matching Studies with Authentic Product Standards Generated via Mn(CF_3-PDP) (1) Catalysis

Substrate	**Major metabolite*** RRT vs I.S. m/z observed	**Hydroxylated product standard from Mn(CF_3-PDP) (1) catalysis**	**Product standard** RRT vs I.S. m/z observed	**LC-MS/MS fragmentation comparison:** Major metabolite vs product standard
 **46**	**46-M1** 1.04 323.1071	 **47**	**47 (major diastereomer)** 1.04 323.1057	matches
 **46**	**46-M3** 1.07 323.1056	 **47**	**47 (minor diastereomer)** 1.07 323.1059	matches
 **48**	**48-M1** 1.19 376.0935	 **49**	**49 (major diastereomer)** 1.19 376.0935	matches
 **48**	**48-M3** 1.24 376.0937	 **49**	**49 (minor diastereomer)** 1.24 376.0933	matches
 **52**	**52-M1** 1.01 338.1503	 **56**	**56** 1.01 338.1503	matches

 57	**57-M1**** 1.30 441.1644	 59	**59** 1.30 441.1645	matches
 Blonanserin	**Blon-M4** 0.90 384.2445	 63	**63** 0.90 384.2439	matches
 Blonanserin	**Blon-M7** 0.95 384.2449	 64	**64** 0.95 384.2445	matches

*From microsomal stability studies employing rat liver microsomes
**Major metabolite also observed in incubations with human liver microsomes

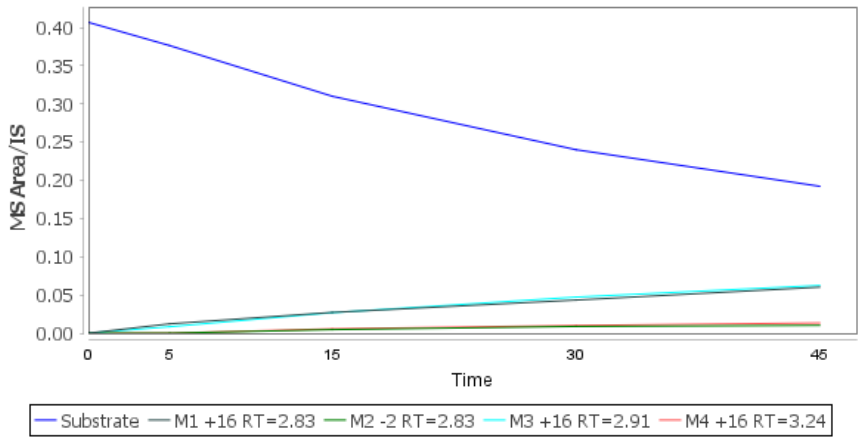
In vitro metabolic stability measurements of Compound 46 with rat liver microsomes



46 46-M1,M3 46-M4

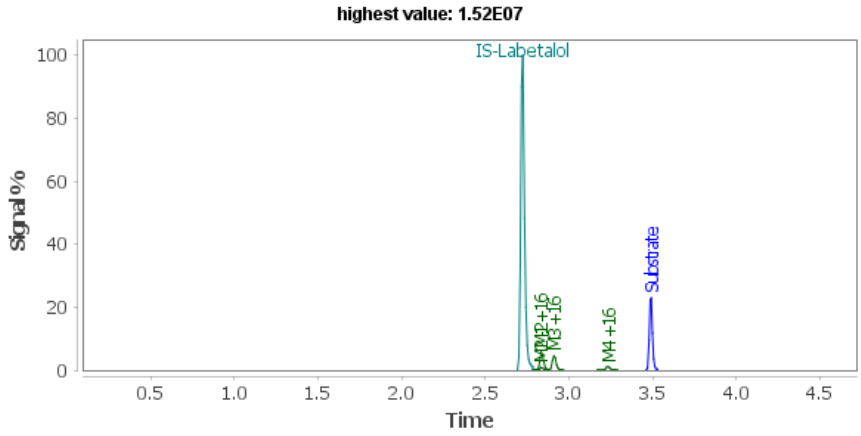
Compound **46** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **46**: Cl_{int} unscaled = 66 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample



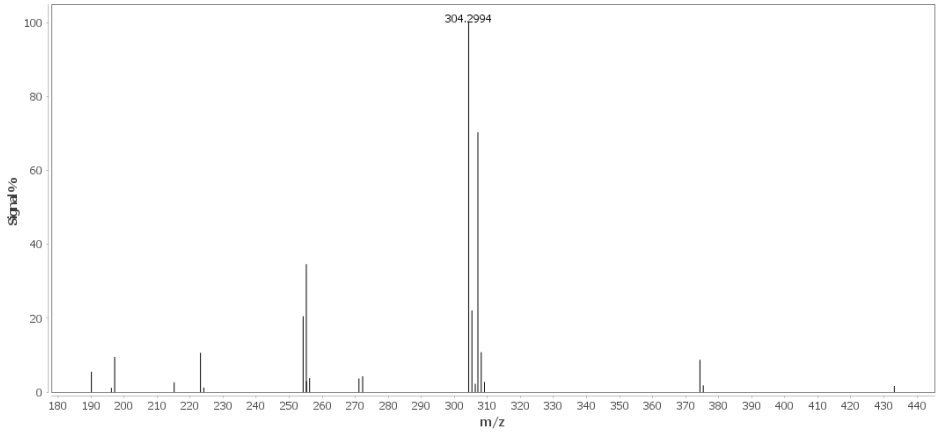
Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.72 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (46)	-	3.49	1.28	56.8	307.112	-0.29
46-M1 **46-M2**	+16 -2*	2.83	1.04	17.8 3.0	323.1071 305.0973	-3.51 -5.97
46-M3	+16	2.91	1.07	18.5	323.1056	1.19
46-M4	+16	3.24	1.19	4.0	323.1047	4.04

*In-source loss of H_2O

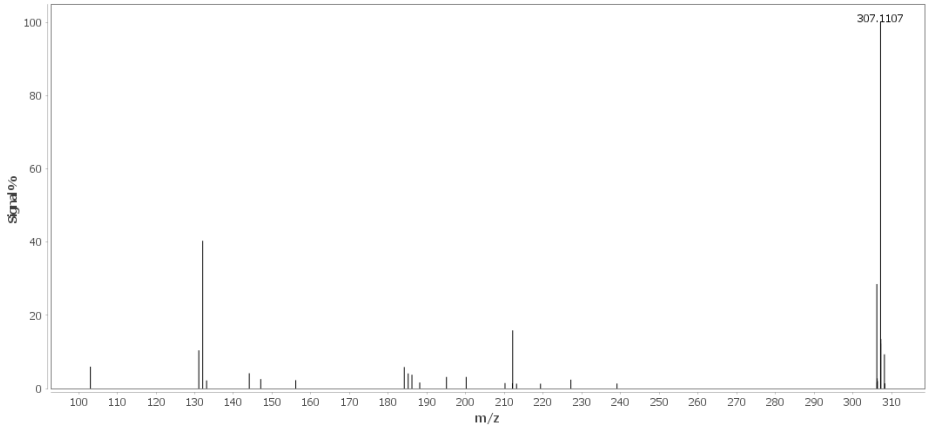
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **46**

MS (+)

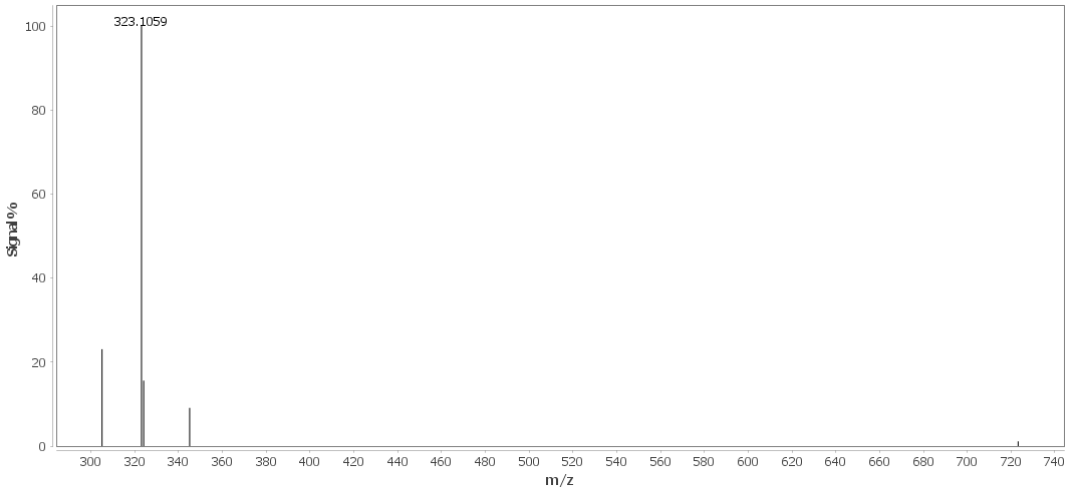


MS/MS (+)

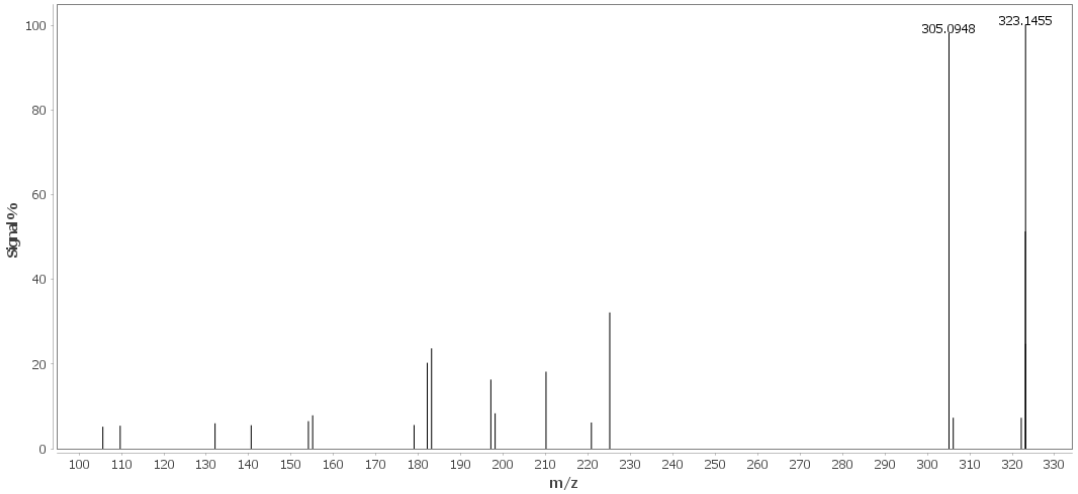


Peak #	m/z observed
1	307.1107
2	212.1062
3	200.1070
4	186.0908

Metabolite **46-M1**
MS (+)

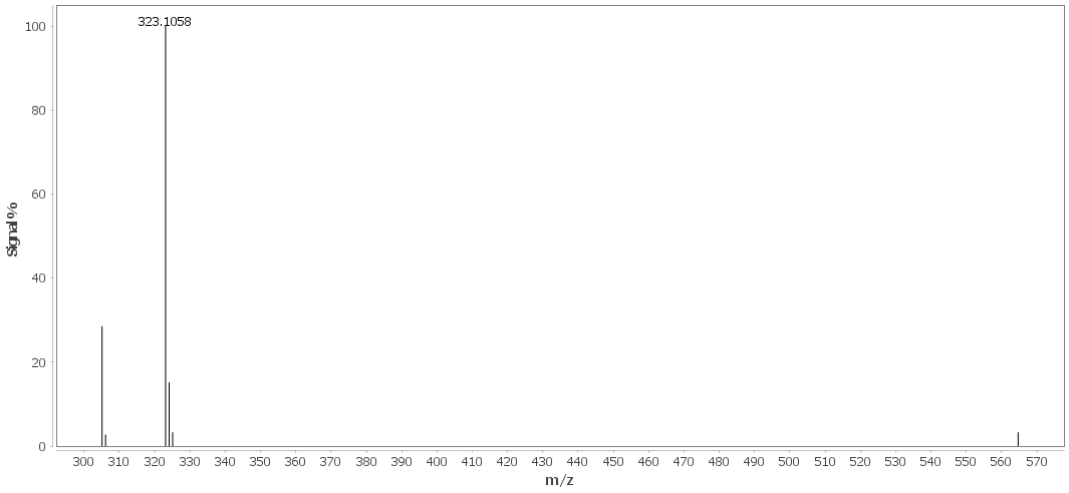


MS/MS (+)

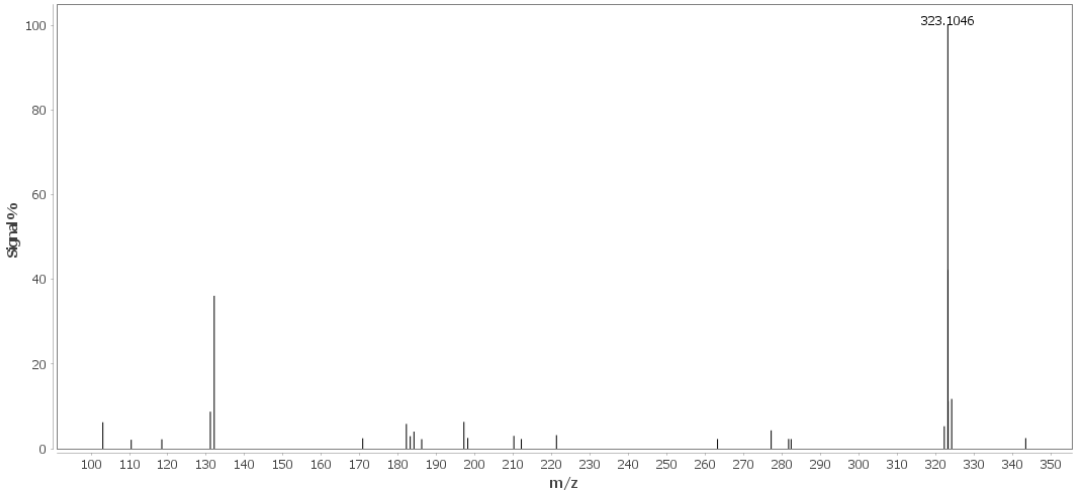


Peak #	m/z observed
1	323.1059
2	305.0965
3	225.1147
4	210.0902

Metabolite **46-M3**
MS (+)

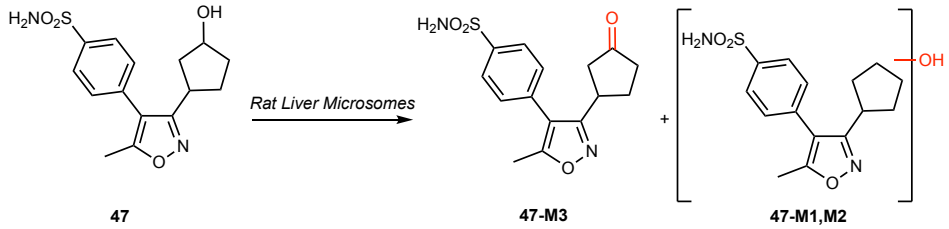


MS/MS (+)



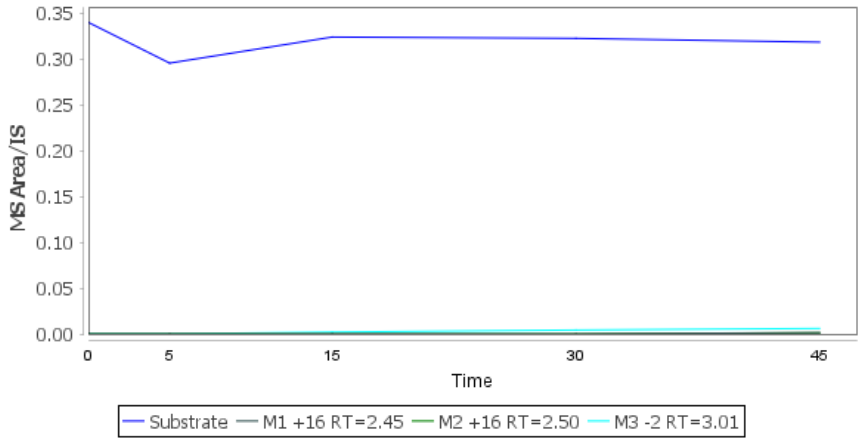
Peak #	m/z observed
1	323.1058
2	305.0951
3	210.0906
4	184.0751

In vitro metabolic stability measurements of Compound 47 with rat liver microsomes



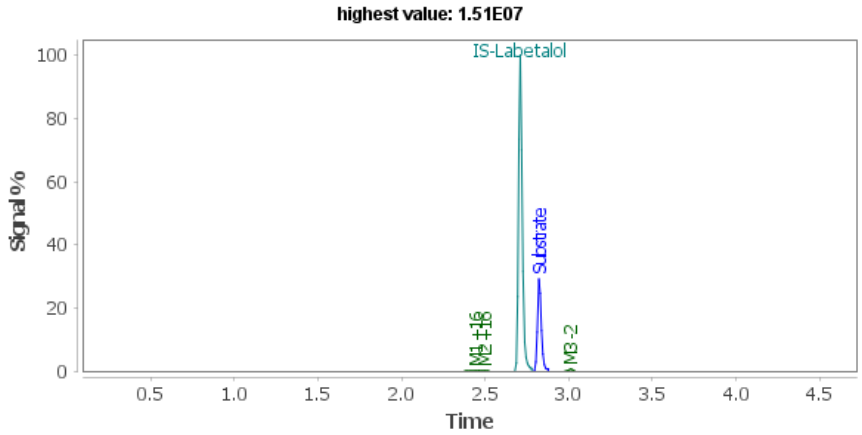
Compound **47** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **47**: Cl_{int} unscaled = <20 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

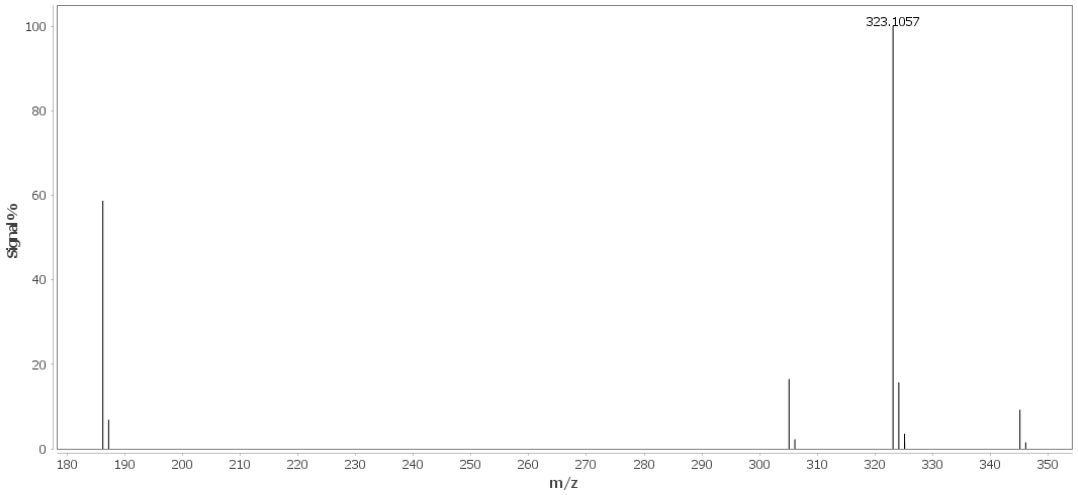


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.71 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (47)	-	2.82	1.04	97.4	323.1057	0.89
47-M1	+16	2.45	0.904	0.4	339.1029	-5.9
47-M2	+16	2.50	0.922	0.4	339.1023	-4.2
47-M3	-2	3.01	1.11	1.8	321.0901	0.7

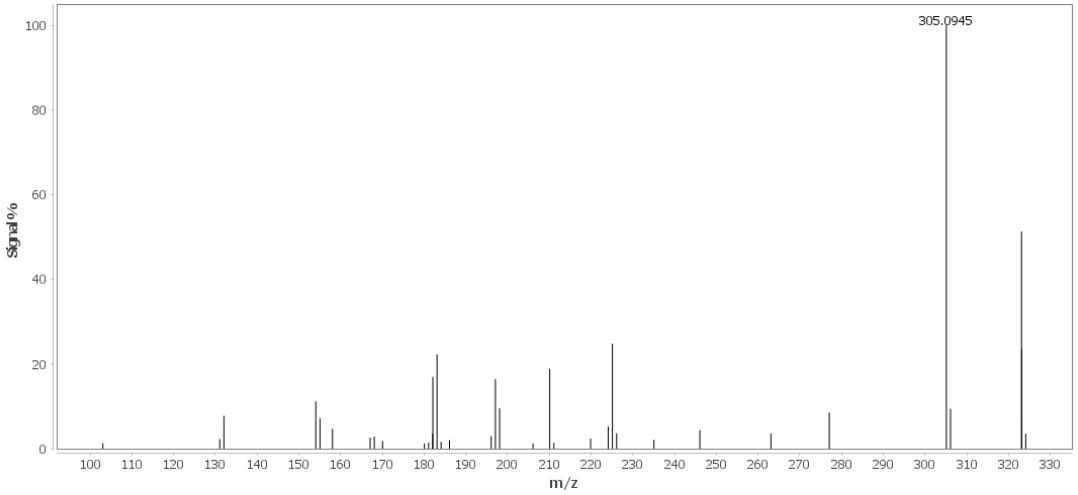
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **47**

MS (+)



MS/MS (+)

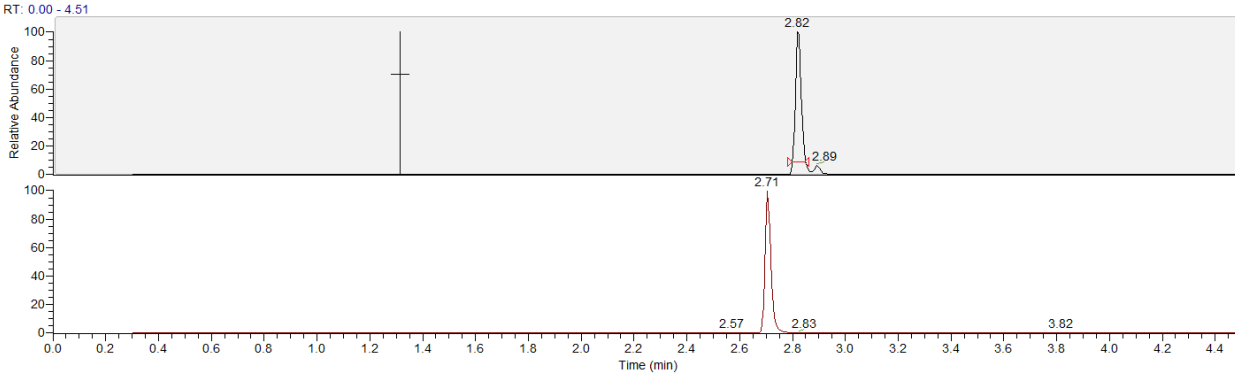


Peak #	m/z observed
1	323.1057
2	305.0945
3	225.1143
4	210.0904

No Major Observed Metabolites with LC Area% > 5.0

*Manually extracted ion chromatogram to detect major and minor diastereomers of compound **47***

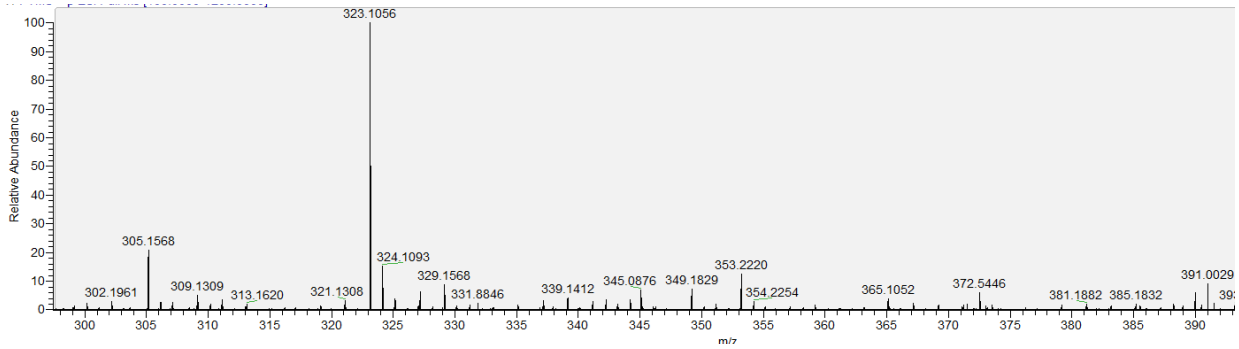
(black trace: m/z = 323.1055-323.1065; red trace: labetalol internal standard)



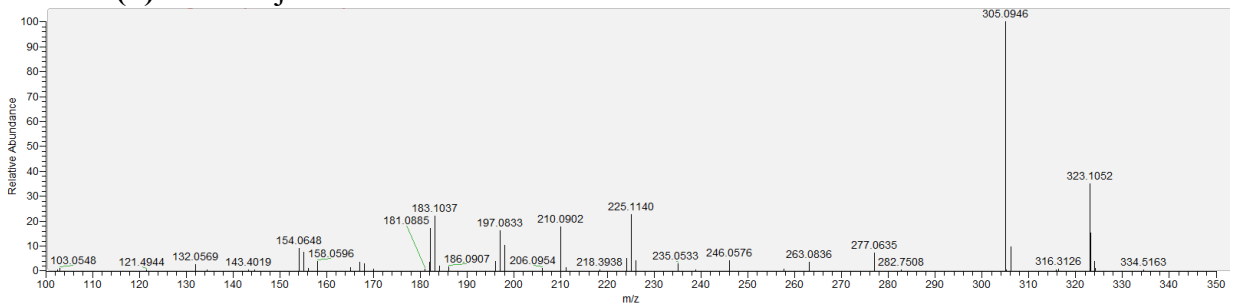
RRT of major diastereomer = 1.04

RRT of minor diastereomer = 1.07

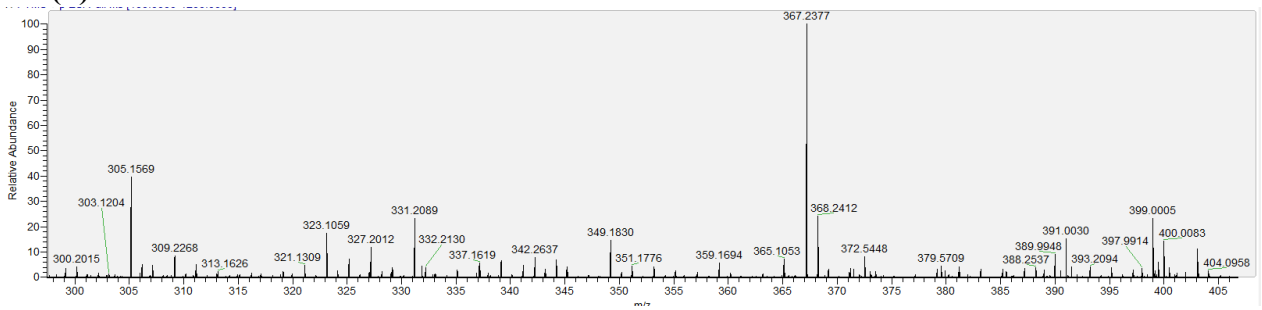
MS(+) of **47** major diastereomer



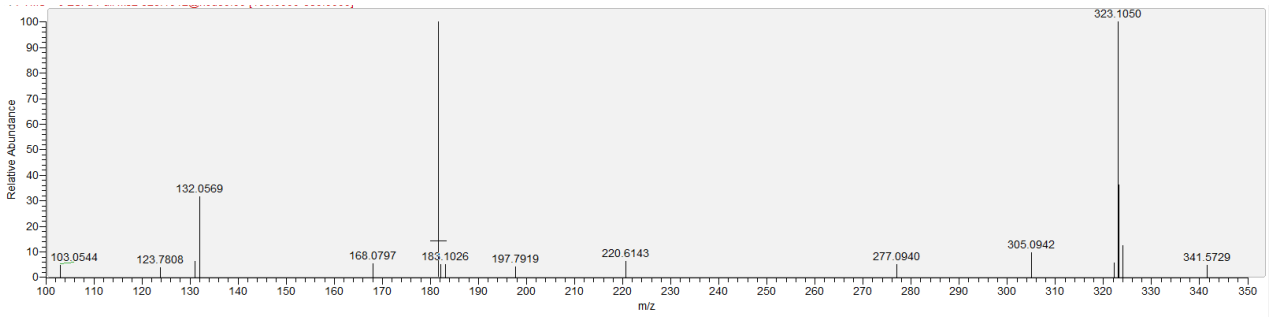
MS/MS (+) of **47** major diastereomer



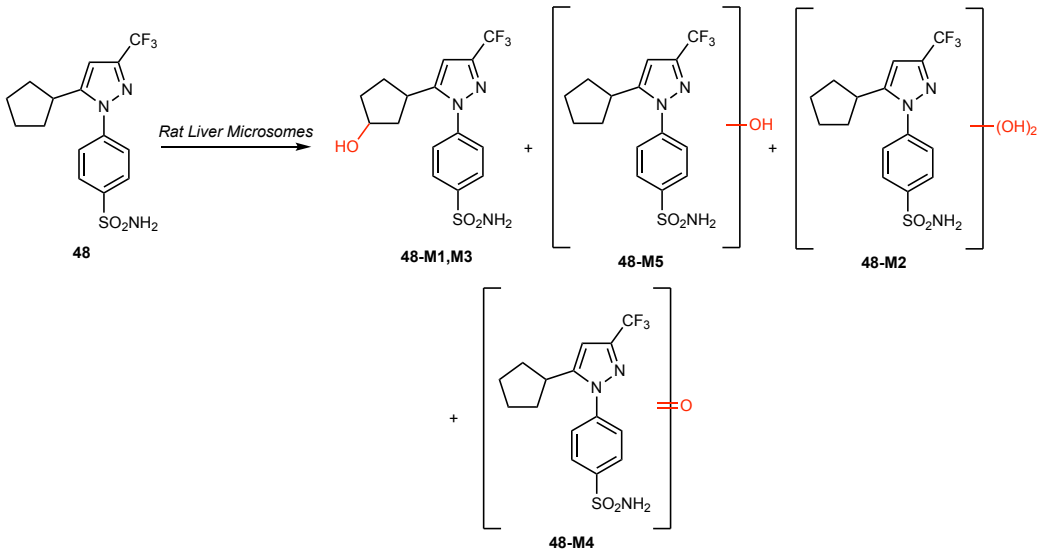
MS(+) of **47** minor diastereomer



MS/MS (+) of **47** minor diastereomer

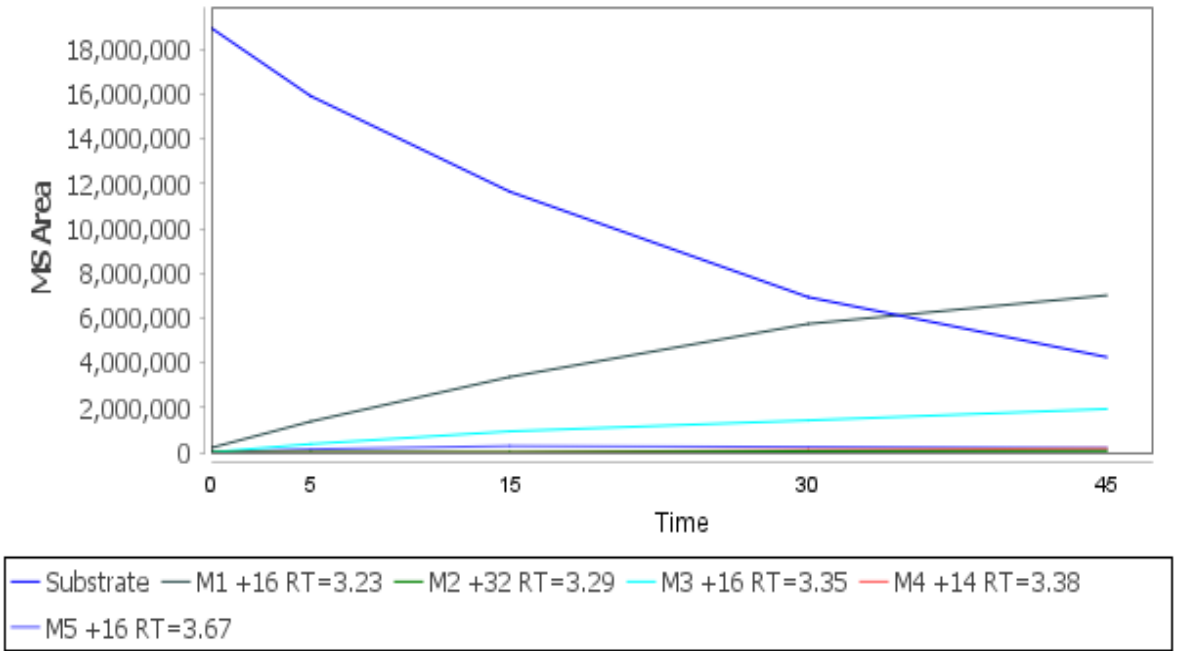


In vitro metabolic stability measurements of Compound 48 with rat liver microsomes



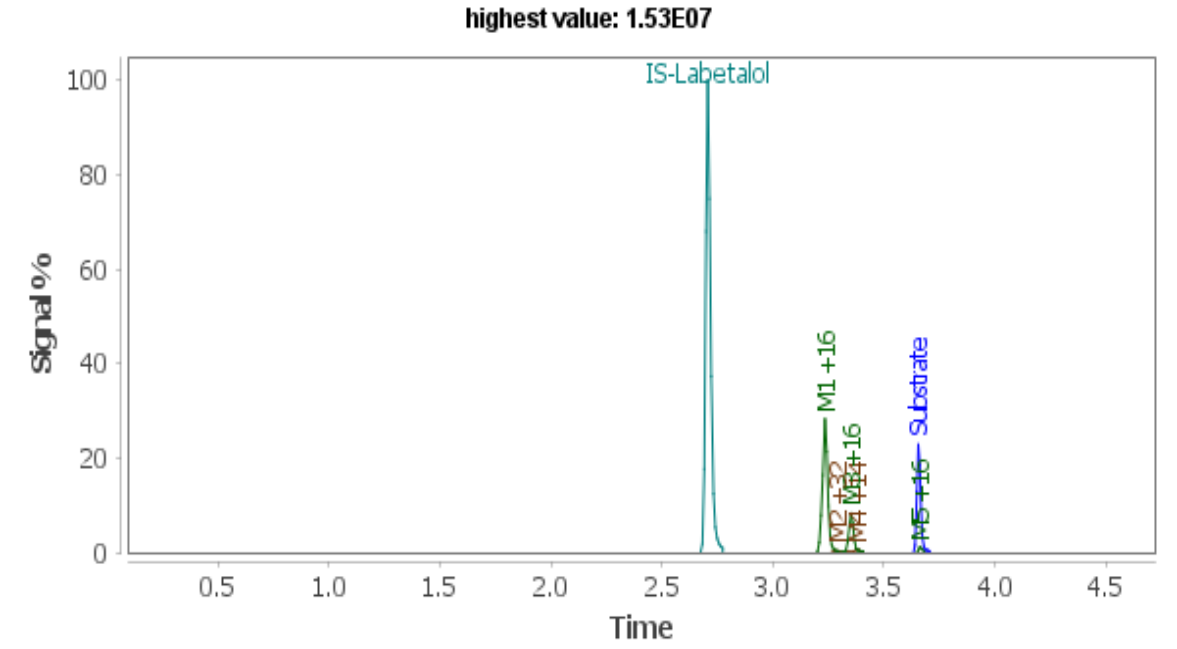
Compound **48** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **48**: Cl_{int} unscaled = 136 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample



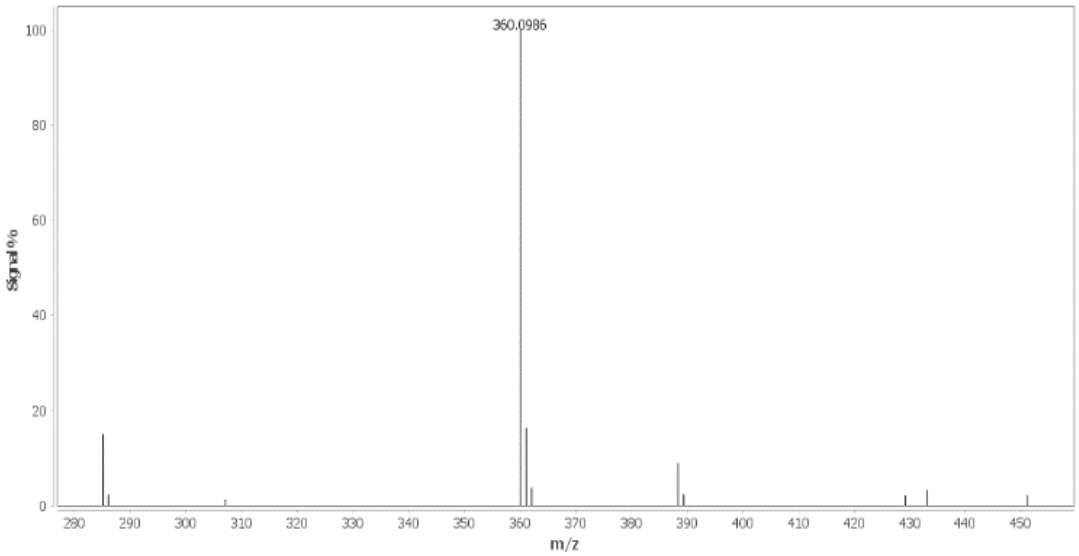
Peak Name / Mass Shift	Mass Shift	RT (min)	RRT vs I.S. 2.71 min	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (48)	-	3.65	1.35	31.2	360.0987	0.36
48-M1	+ 16	3.23	1.19	51.4	376.0935	0.55
48-M2	+ 32	3.29	1.21	1.1	392.0882	1.10
48-M3	+ 16	3.35	1.24	14.2	376.0937	-0.06

48-M4	+ 14	3.38	1.25	1.3	374.0780	0.20
48-M5	+ 16	3.66	1.35	1.4	376.0935	0.53

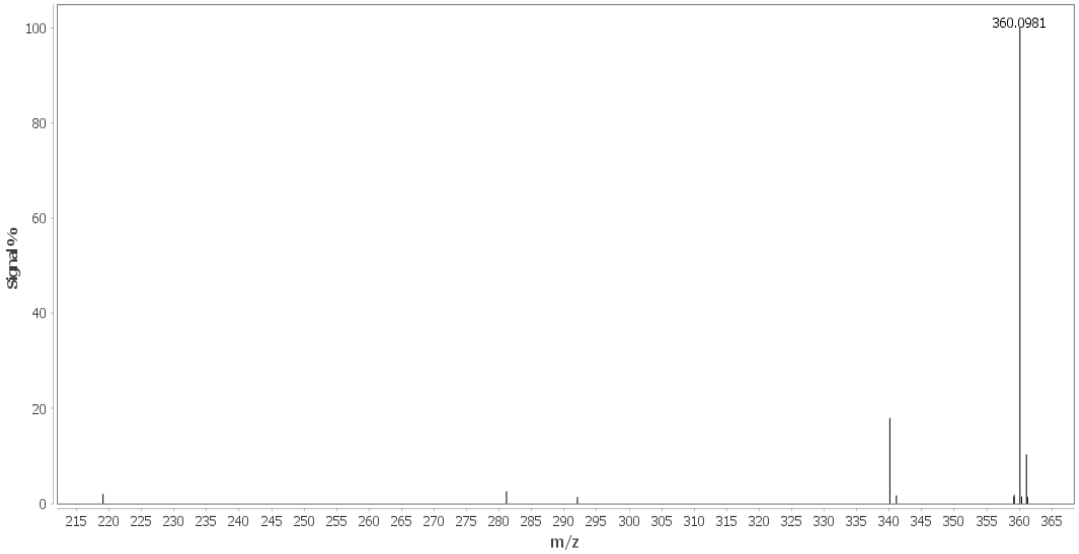
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **48**

MS (+)



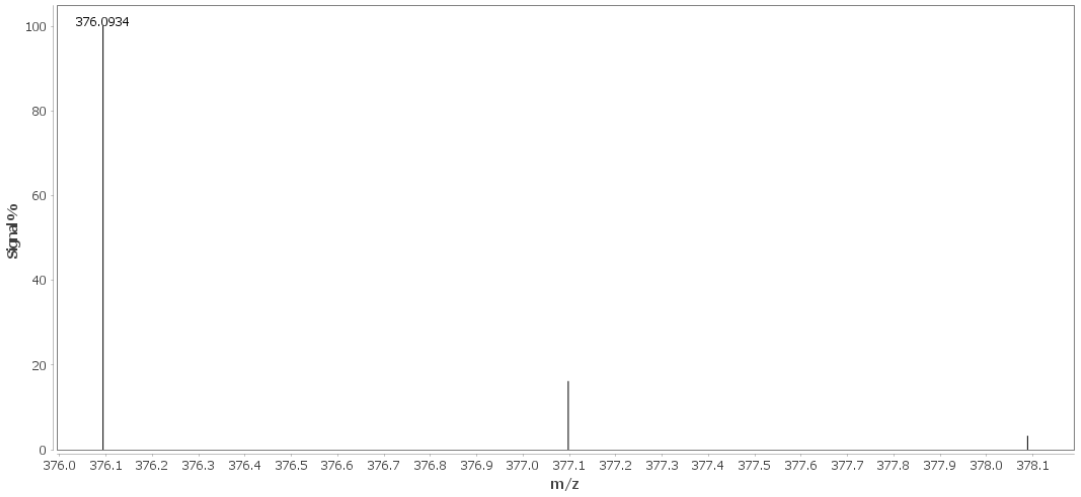
MS/MS (+)



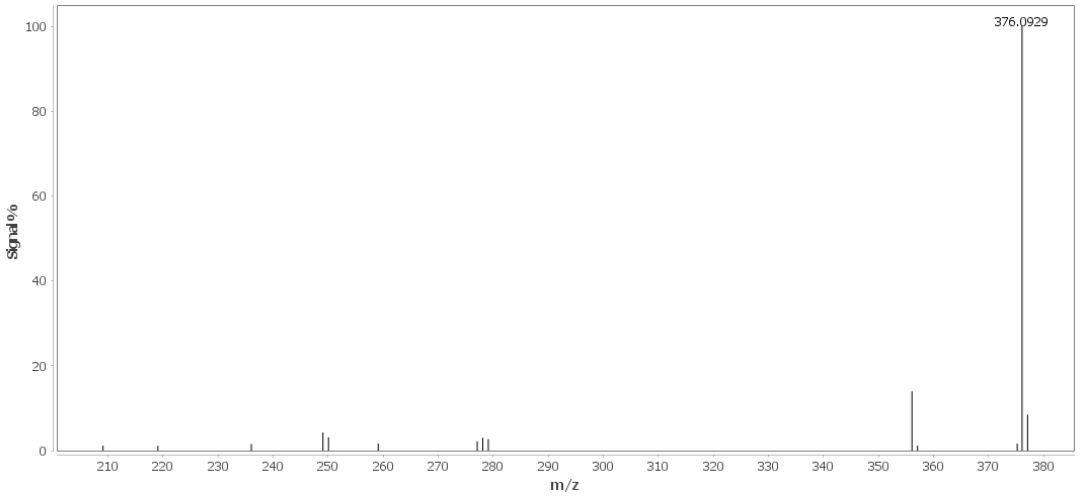
Peak #	m/z observed
1	360.0986
2	340.0919

Metabolite **48-M1**

MS (+)

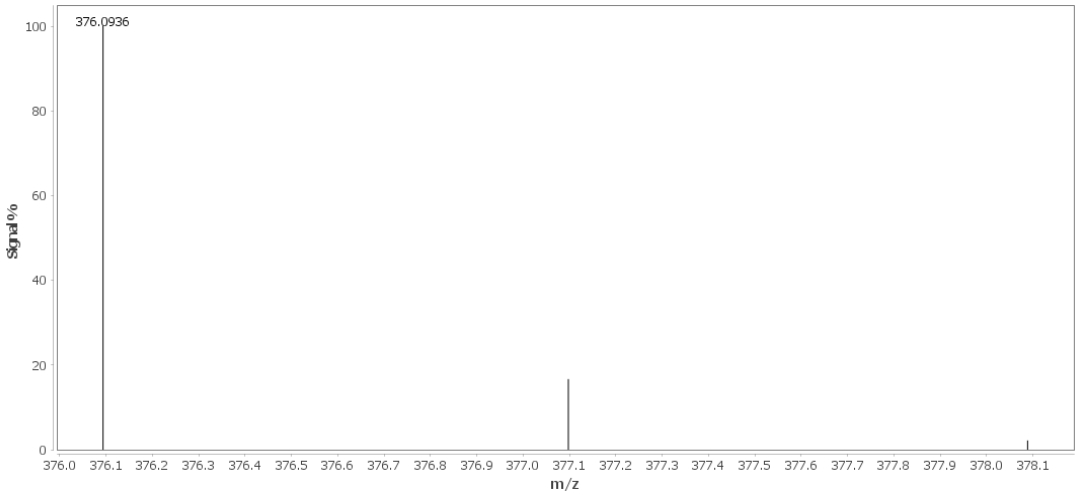


MS/MS (+)

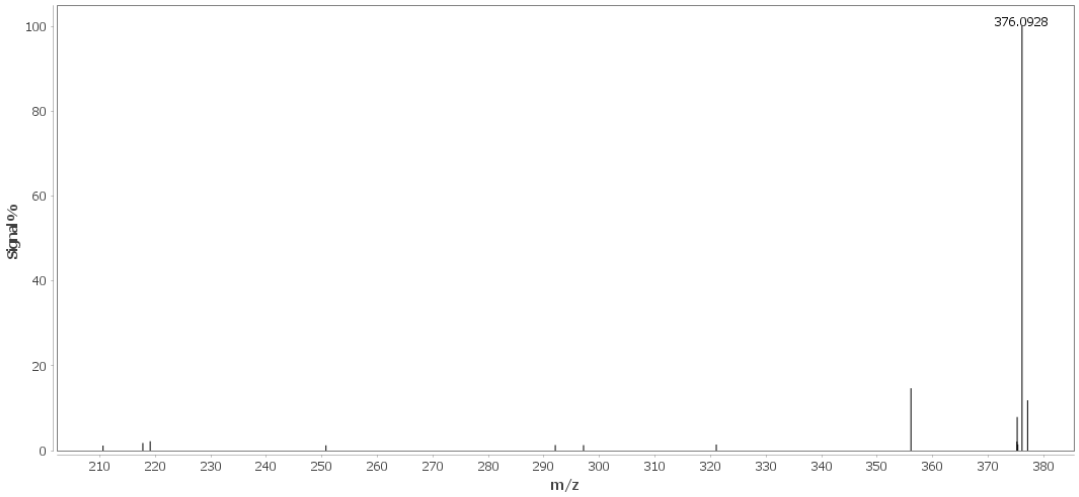


Peak #	m/z observed
1	376.0929
2	356.0868

Metabolite **48-M3**
MS (+)

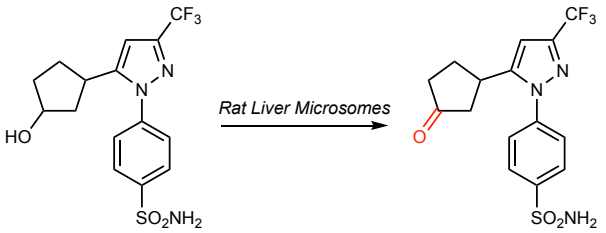


MS/MS (+)



Peak #	m/z observed
1	376.0928
2	356.0862

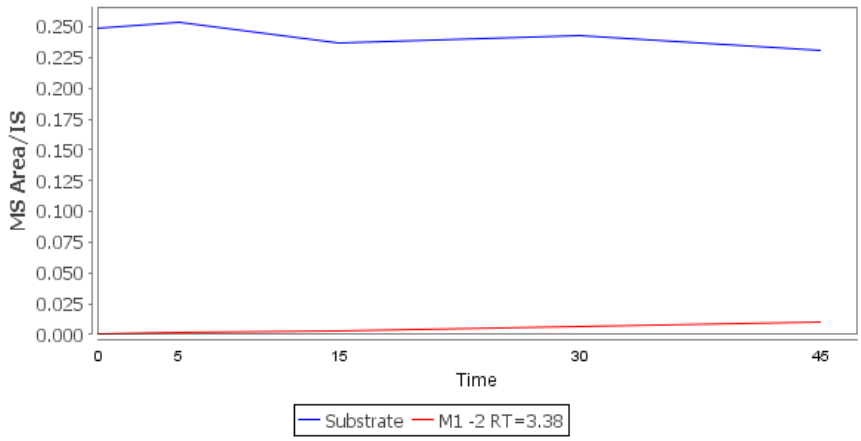
In vitro metabolic stability measurements of Compound 49 with rat liver microsomes



49 **49-M1**

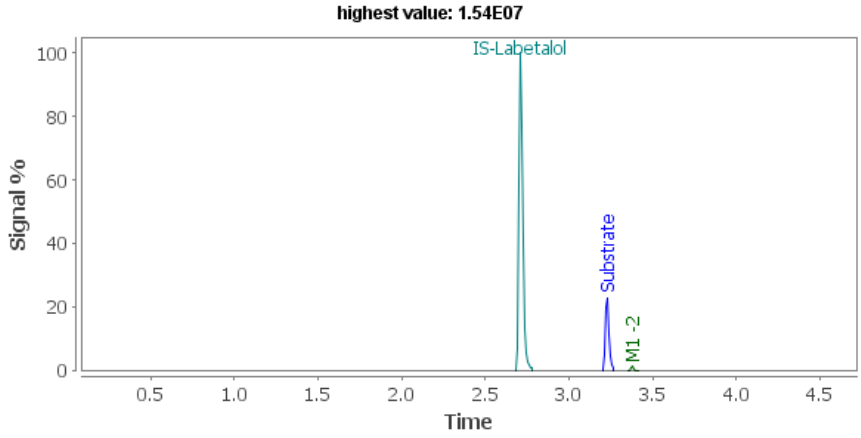
Compound **49** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **49**: Cl_{int} unscaled = <20 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

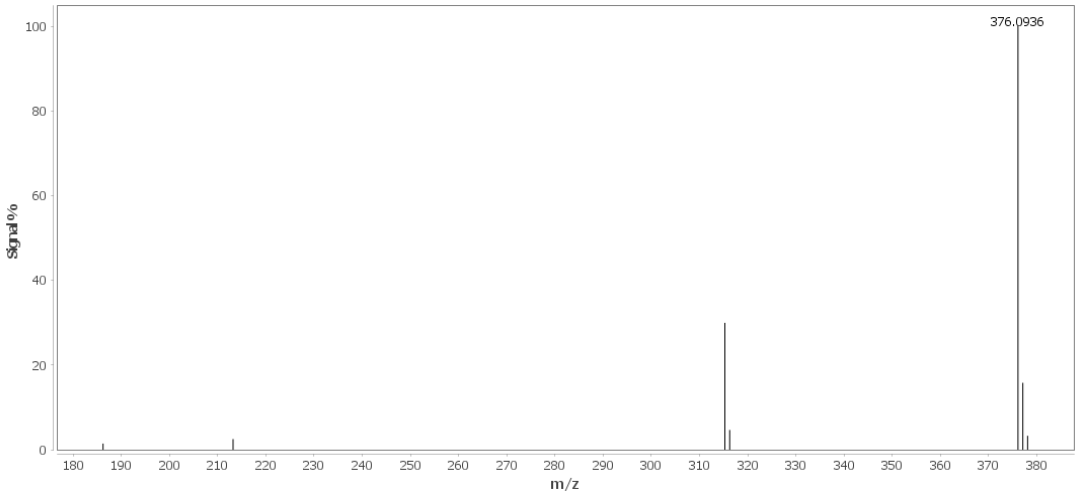


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.71 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (49)	-	3.23	1.19	95.7	376.0935	0.5
49-M1	-2	3.38	1.25	4.3	374.0779	0.5

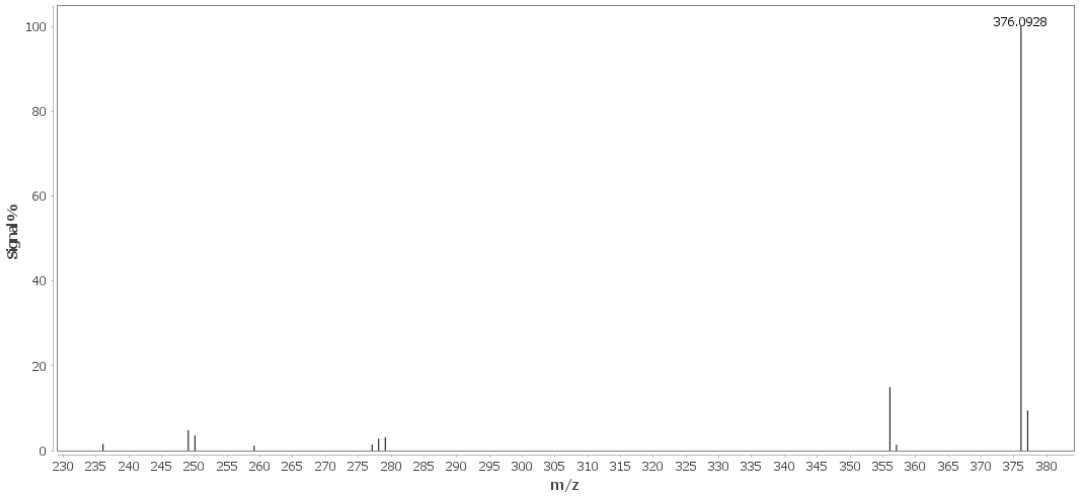
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **49**

MS (+)



MS/MS (+)

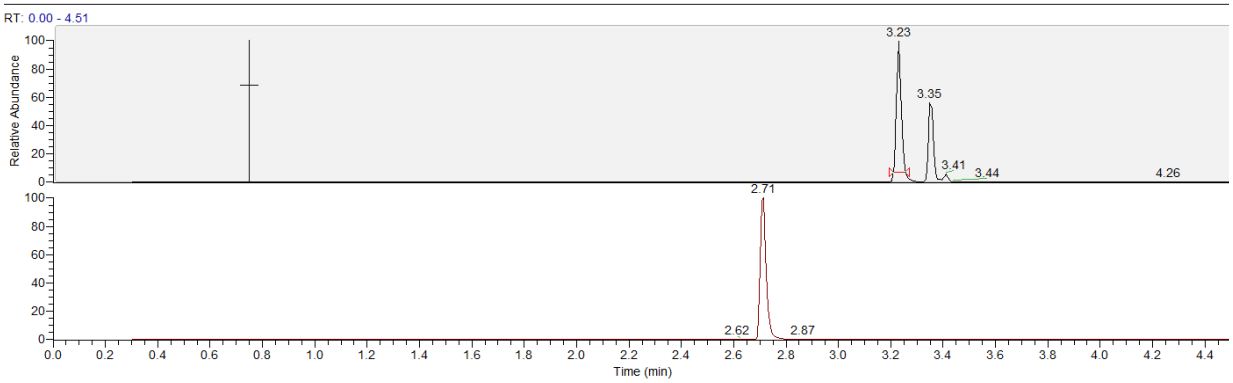


Peak #	m/z observed
1	376.0928
2	356.0865

No Major Observed Metabolites with LC Area% > 5.0

*Manually extracted ion chromatogram to detect major and minor diastereomers of compound **49***

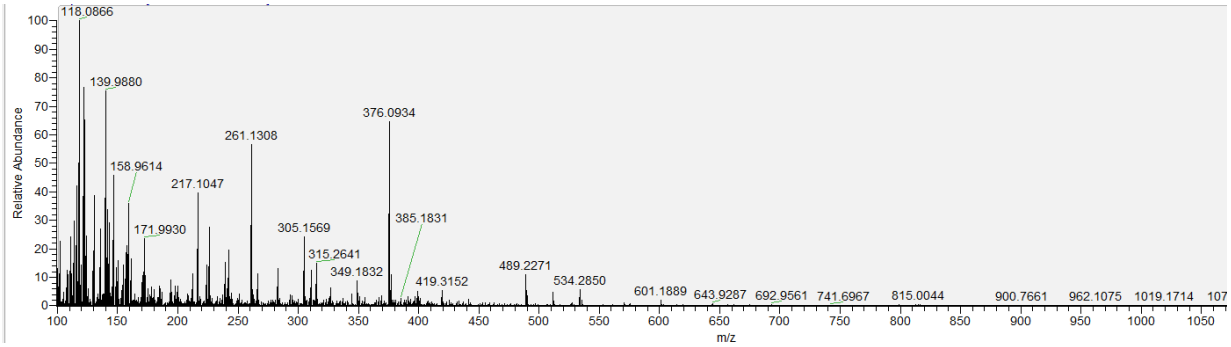
(black trace: m/z = 376.0930-376.0940; red trace: labetalol internal standard)



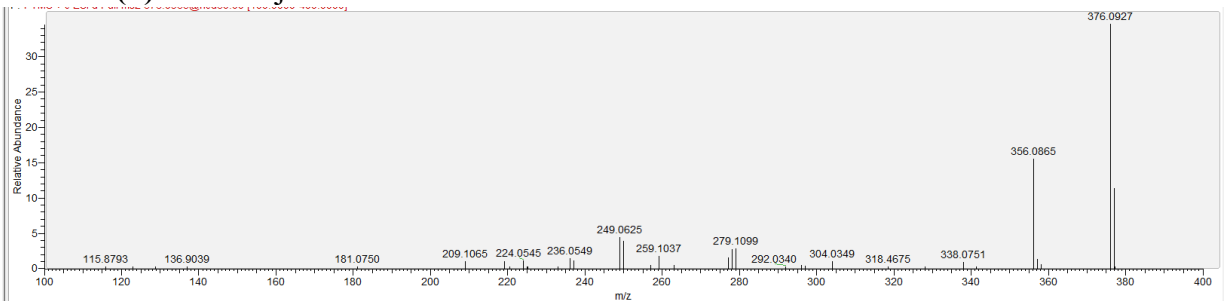
RRT of major diastereomer = 1.19

RRT of minor diastereomer = 1.24

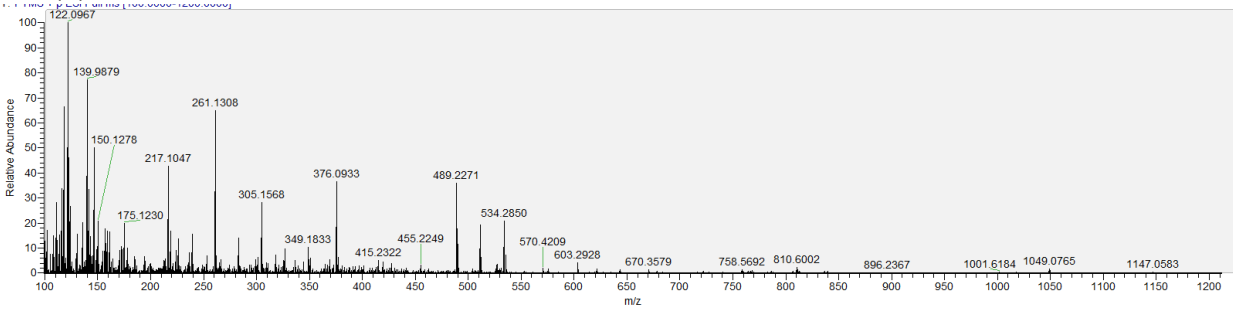
MS(+) of **49** major diastereomer



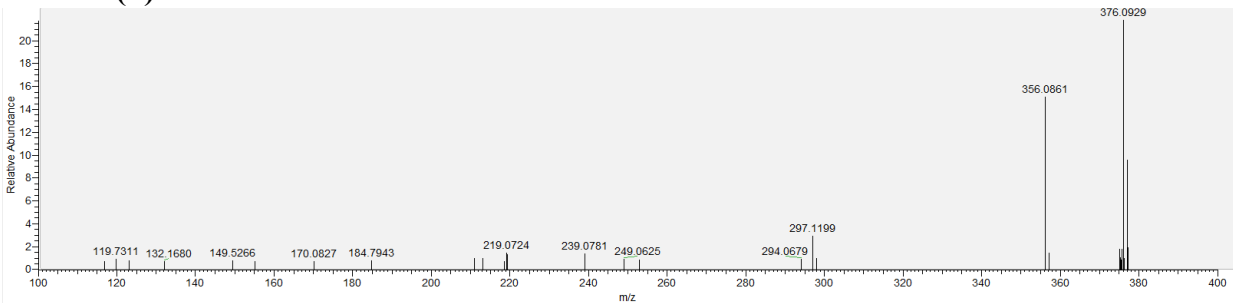
MS/MS (+) of **49** major diastereomer



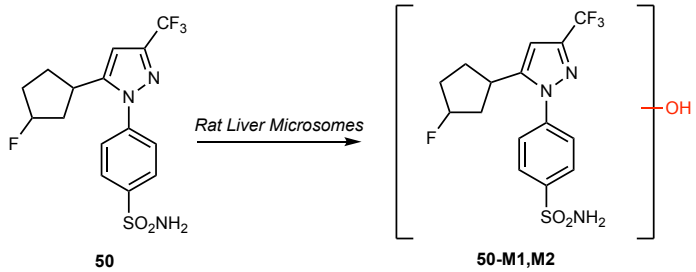
MS(+) of **49** minor diastereomer



MS/MS (+) of **49** minor diastereomer



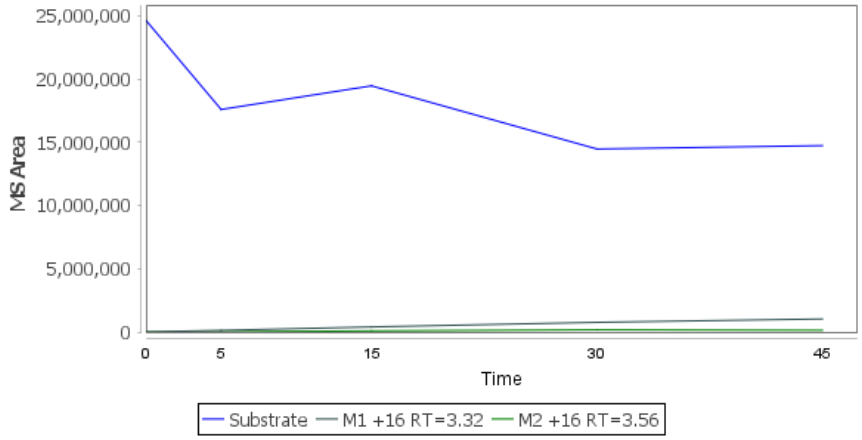
In vitro metabolic stability measurements of Compound 50 with rat liver microsomes



50 **50-M1,M2**

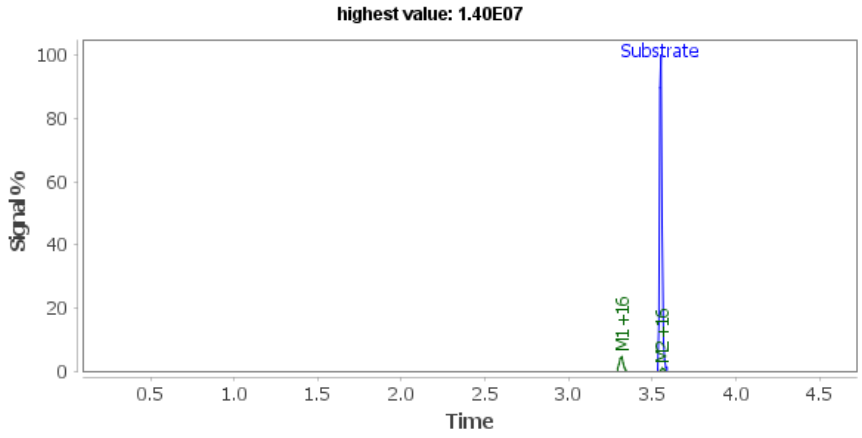
Compound **50** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **50**: Cl_{int} unscaled = 57 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

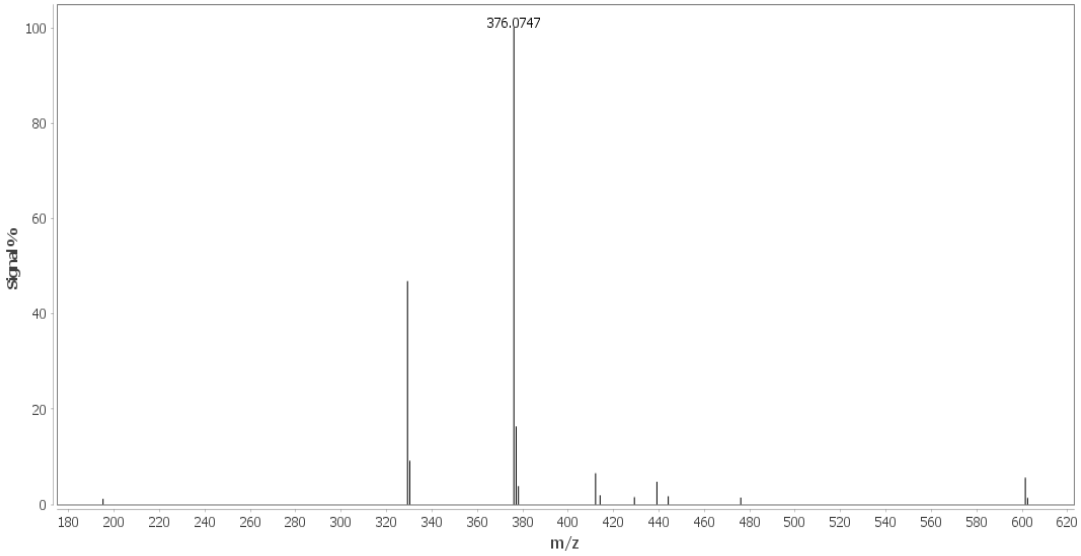


Peak Name	Mass Shift	RT (min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (50)	-	3.55	92.7	376.0745	0.3
50-M1	+16	3.52	6.5	392.0696	-0.3
50-M2	+16	3.56	0.8	392.0694	0.3

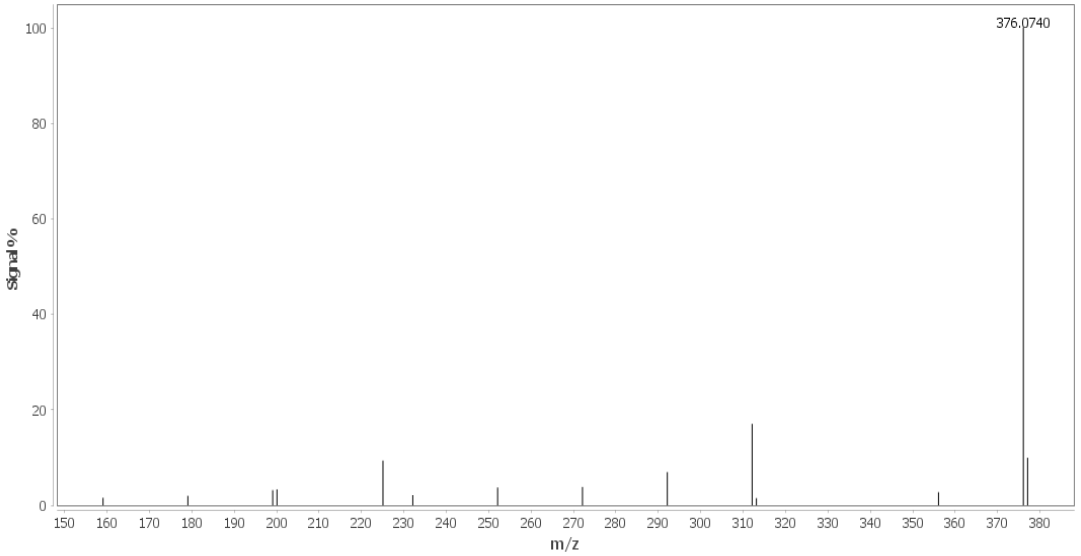
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **50**

MS (+)

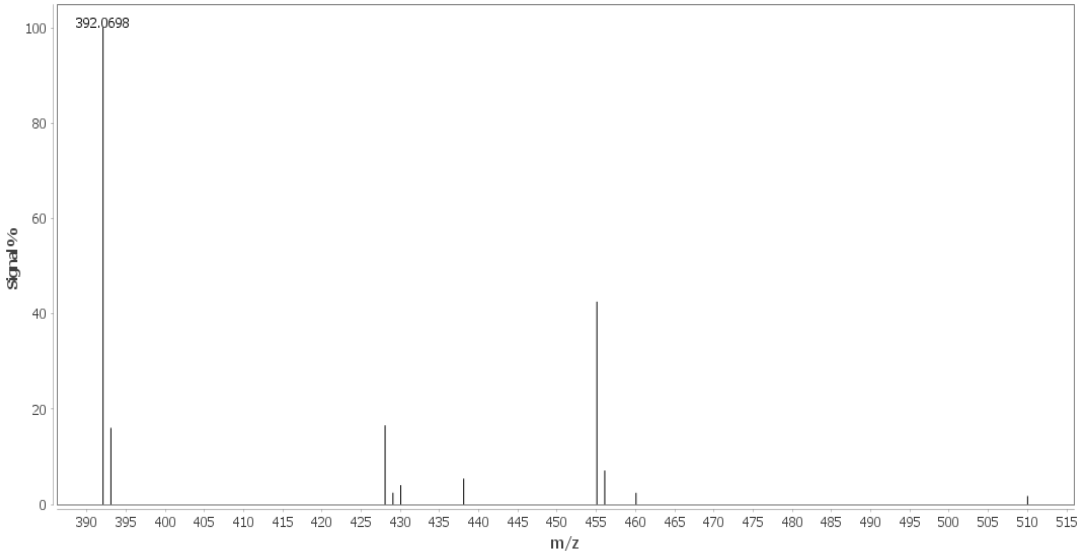


MS/MS (+)

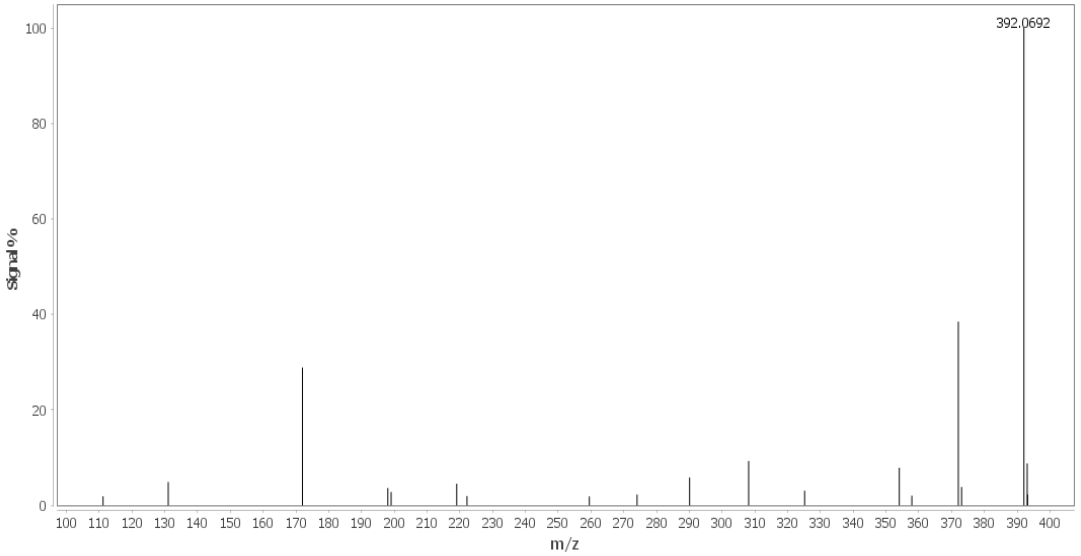


Peak #	m/z observed
1	376.0740
2	199.0479

Metabolite **50-M1**
MS (+)

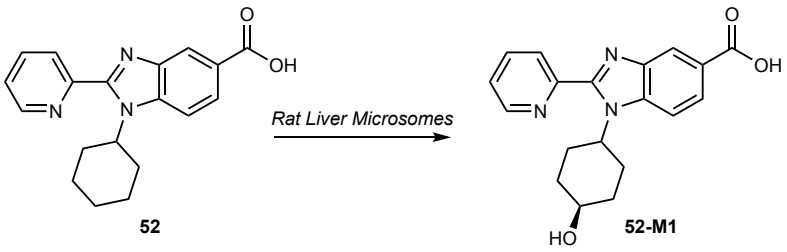


MS/MS (+)



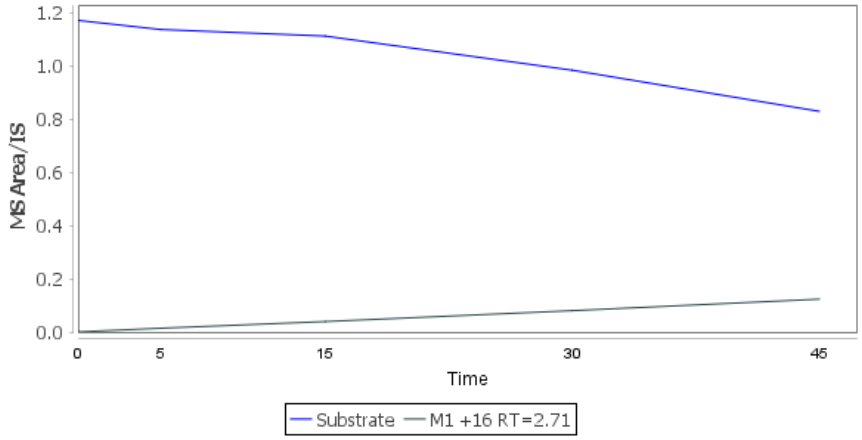
Peak #	m/z observed
1	392.0692
2	372.0634
3	354.0514
4	199.0462
5	172.0064

In vitro metabolic stability measurements of Compound 52 with rat liver microsomes



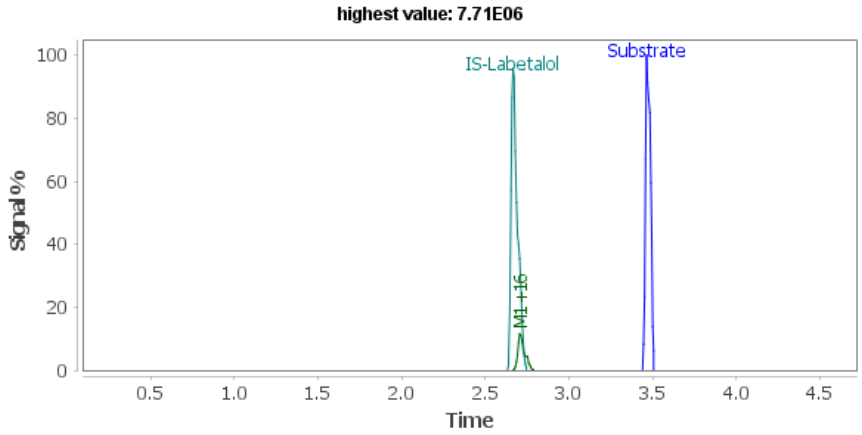
Compound **52** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **52**: Cl_{int} unscaled = 32 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample



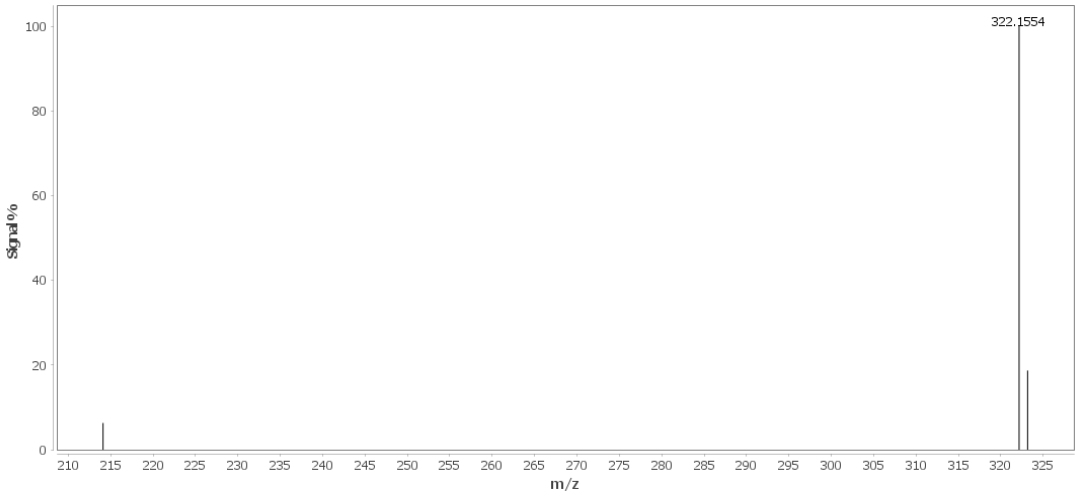
Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.67 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (52)	-	3.46	1.30	87.1	322.1553	-0.8
52-M1	+16	2.71	1.01	12.9	338.1503	-1.4

*In-source loss of H_2O

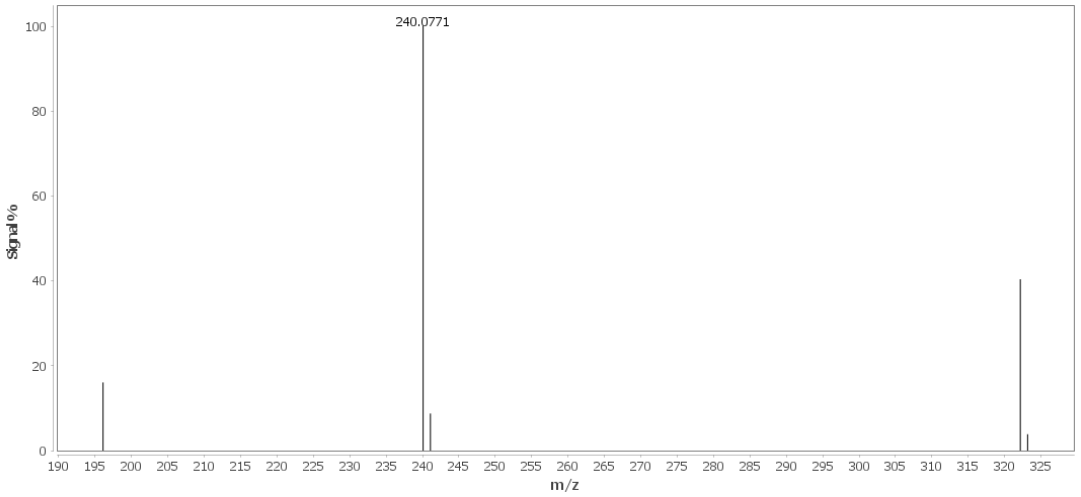
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **52**

MS (+)

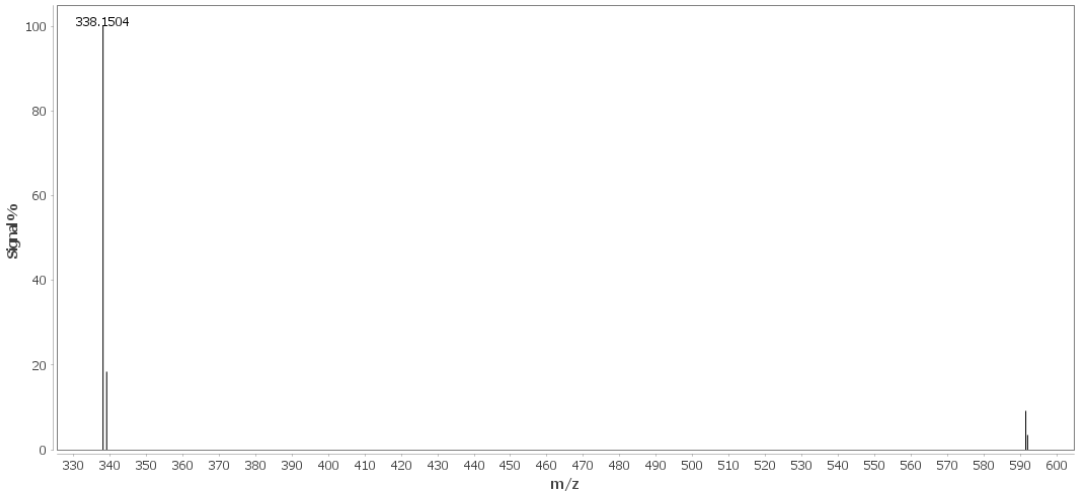


MS/MS (+)

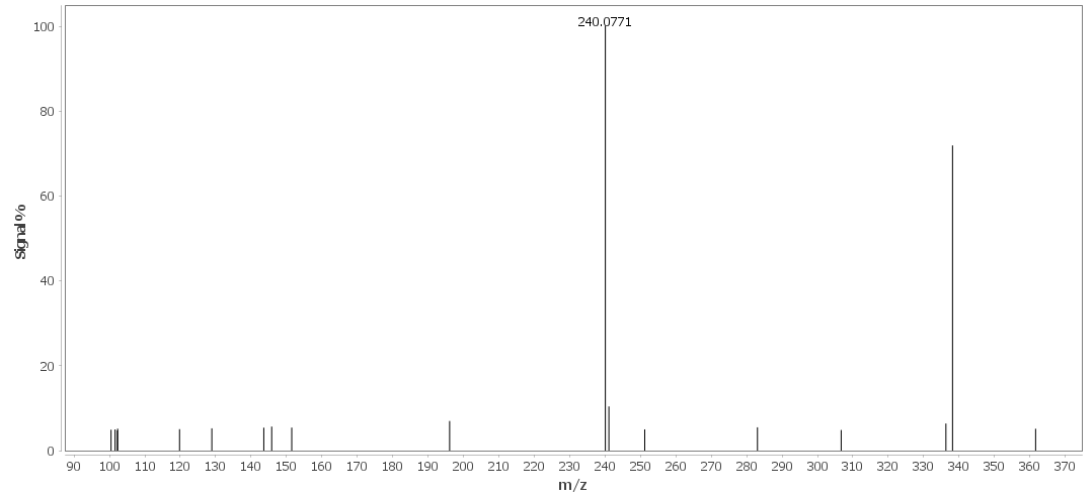


Peak #	m/z observed
1	322.1554
2	240.0771
3	196.0871

Metabolite **52-M1**
MS (+)

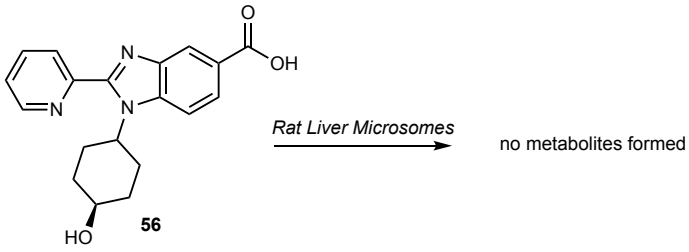


MS/MS (+)



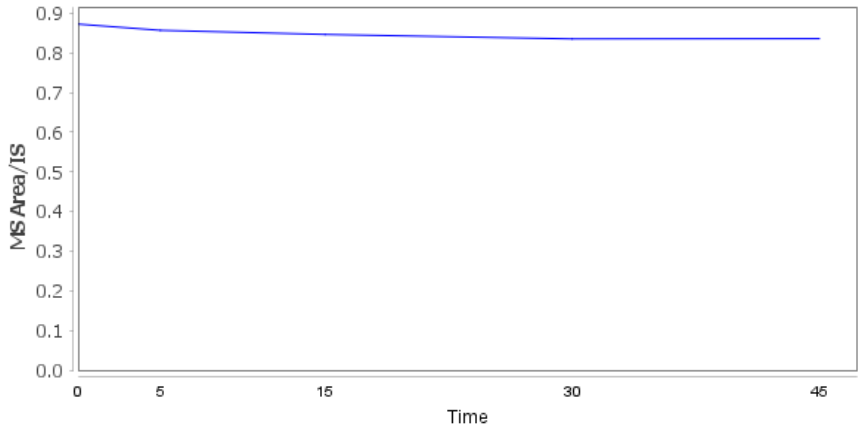
Peak #	m/z observed
1	338.1507
2	240.0771
3	196.0869

In vitro metabolic stability measurements of Compound 56 with rat liver microsomes



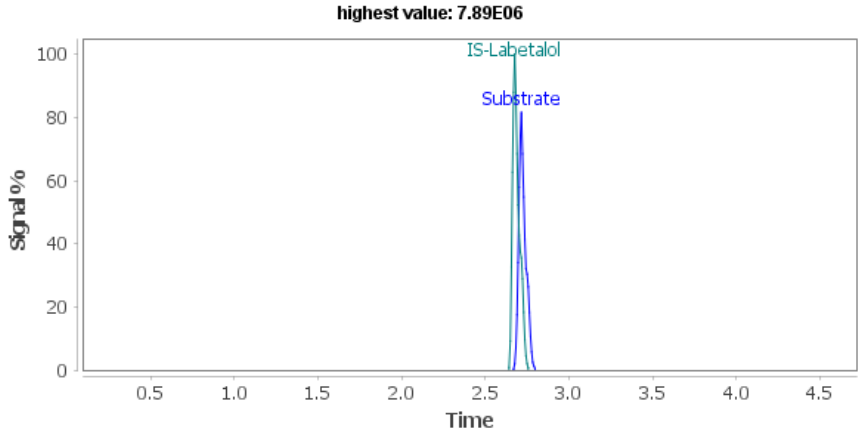
Compound **56** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



No metabolism was observed for this substrate.

Extracted ion chromatogram trace for t = 45 min sample

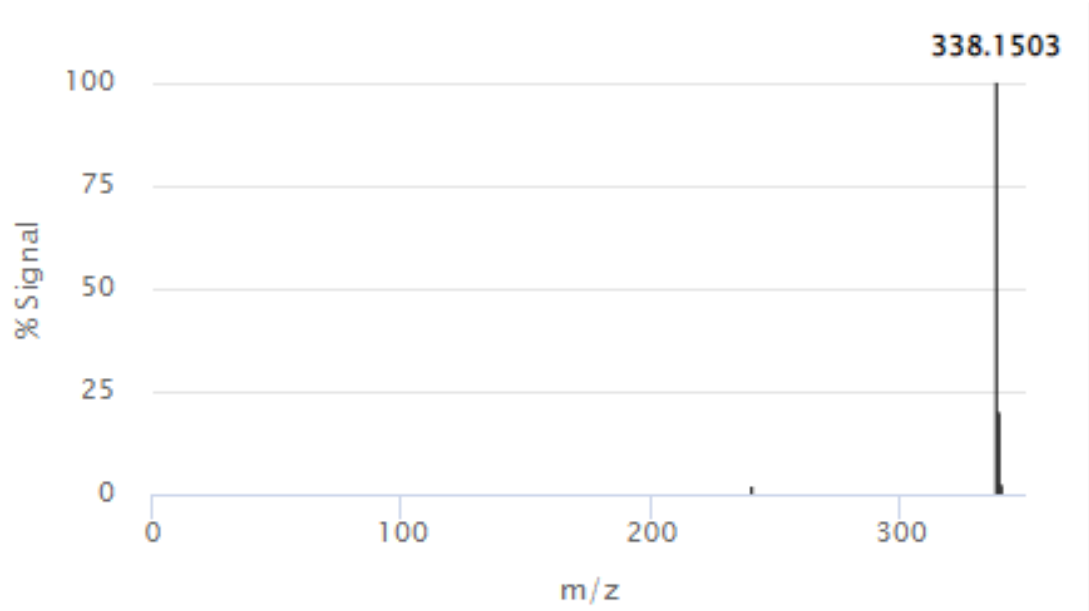


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.68 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (56)	-	2.72	1.01	100.0	338.1503	-1.1

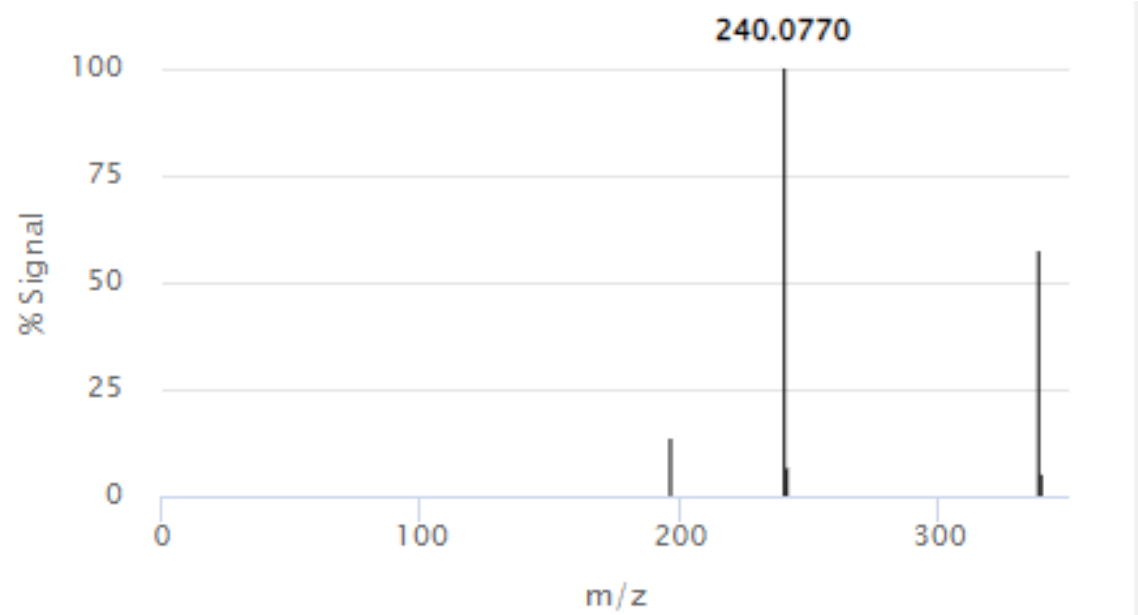
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **56**

MS (+)

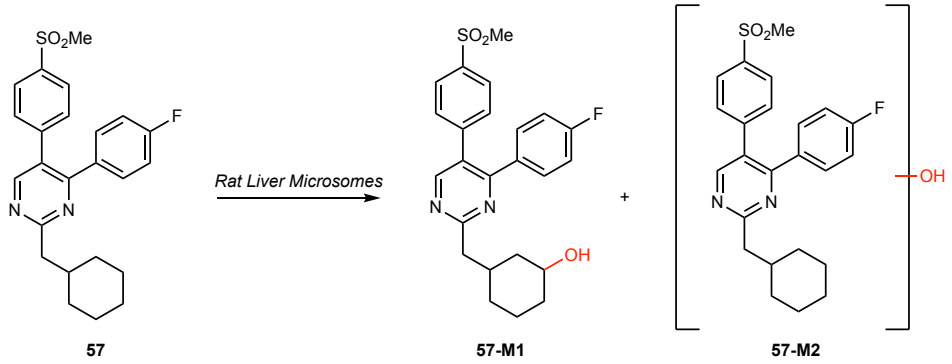


MS/MS (+)



Peak #	m/z observed
1	338.1502
2	240.0771
3	196.0871

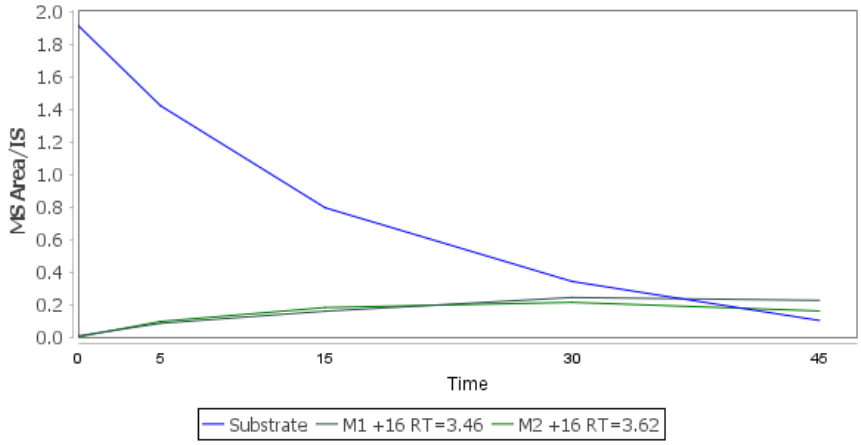
In vitro metabolic stability measurements of Compound 57 with rat liver microsomes



57 **57-M1** **57-M2**

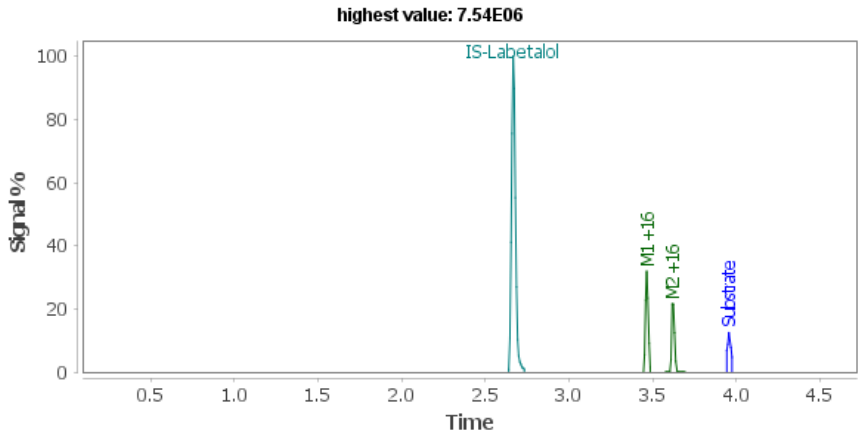
Compound **57** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **57**: Cl_{int} unscaled = 244 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

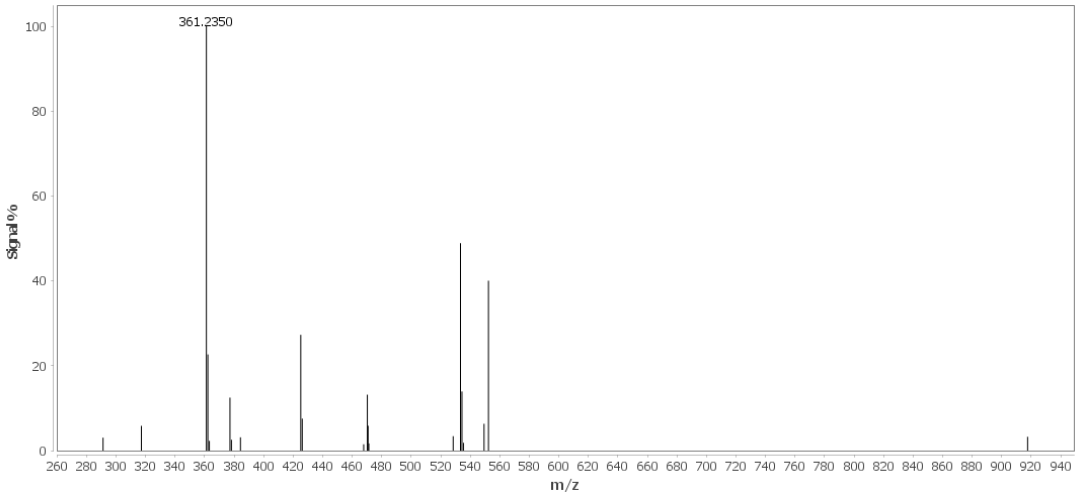


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.67 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (57)	-	3.96	1.48	20.8	425.1693	0.14
57-M1	+16	3.46	1.30	46.3	441.1644	-0.37
57-M2	+16	3.62	1.36	32.9	441.1644	-0.25

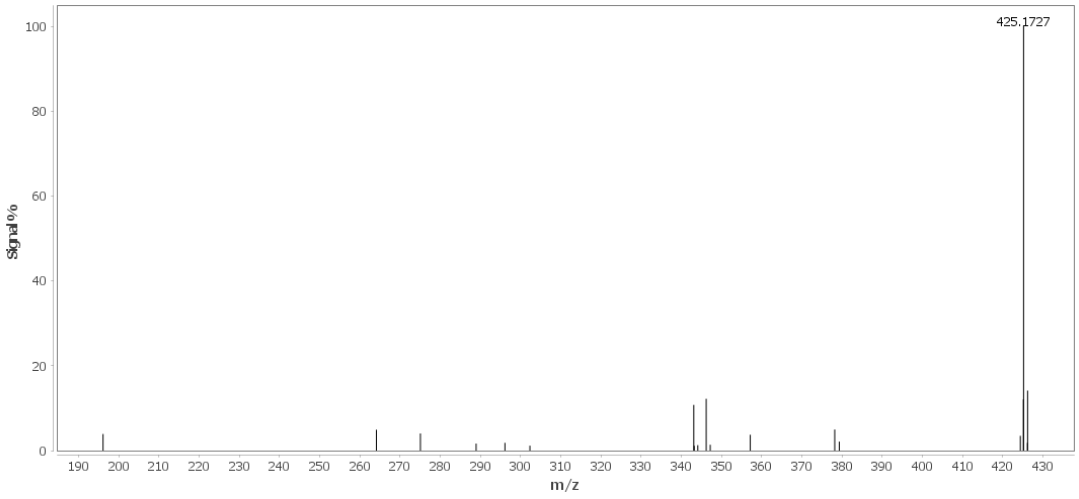
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **57**

MS (+)

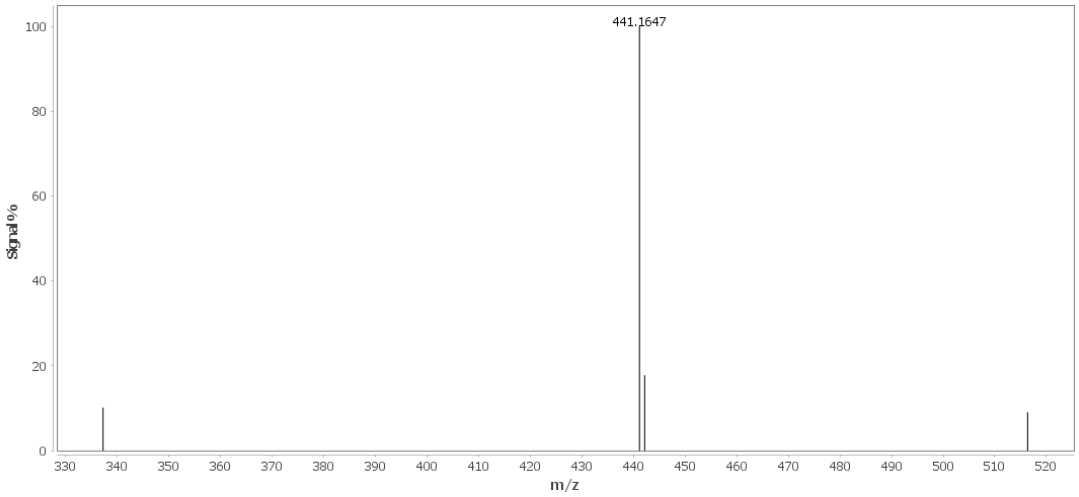


MS/MS (+)

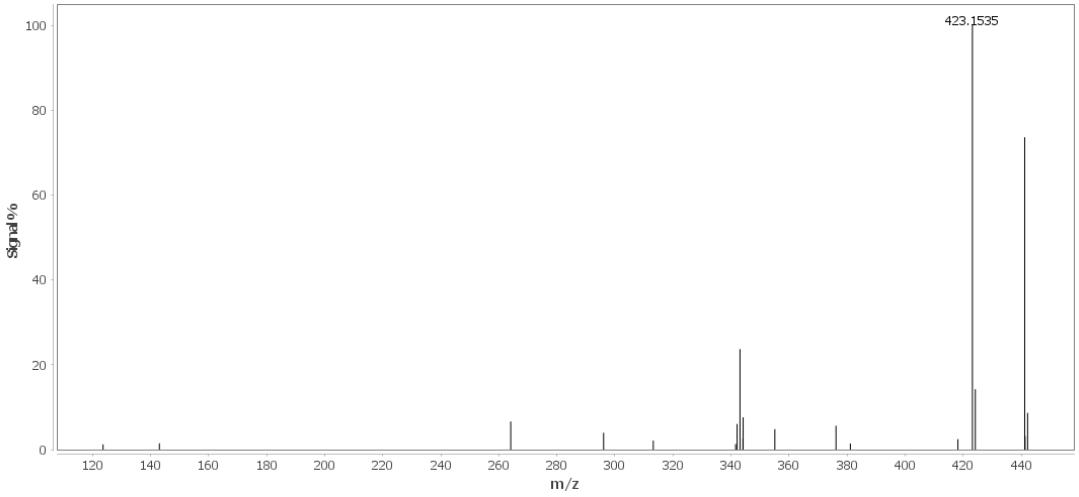


Peak #	m/z observed
1	425.1695
2	378.1739
3	346.1842
4	343.0912
5	264.1059

Metabolite **57-M1**
MS (+)

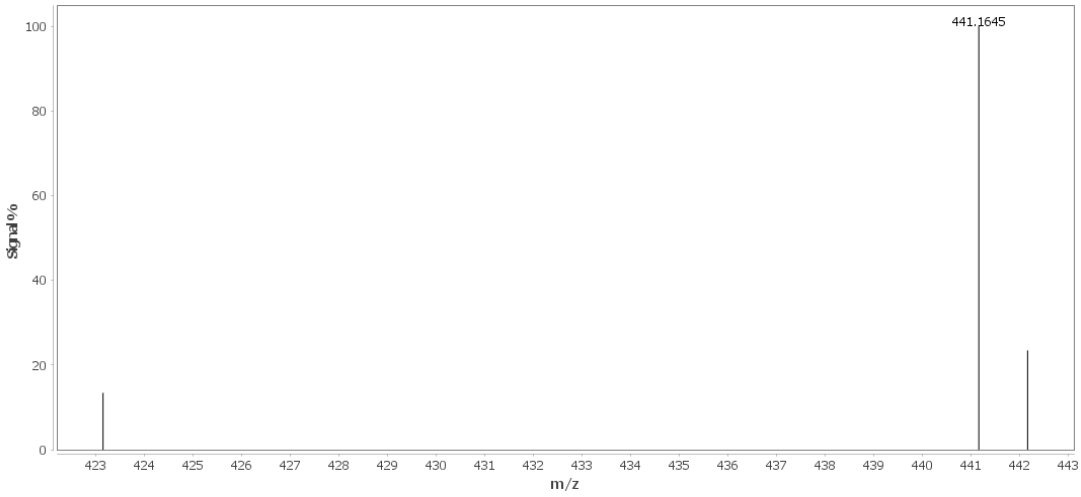


MS/MS (+)

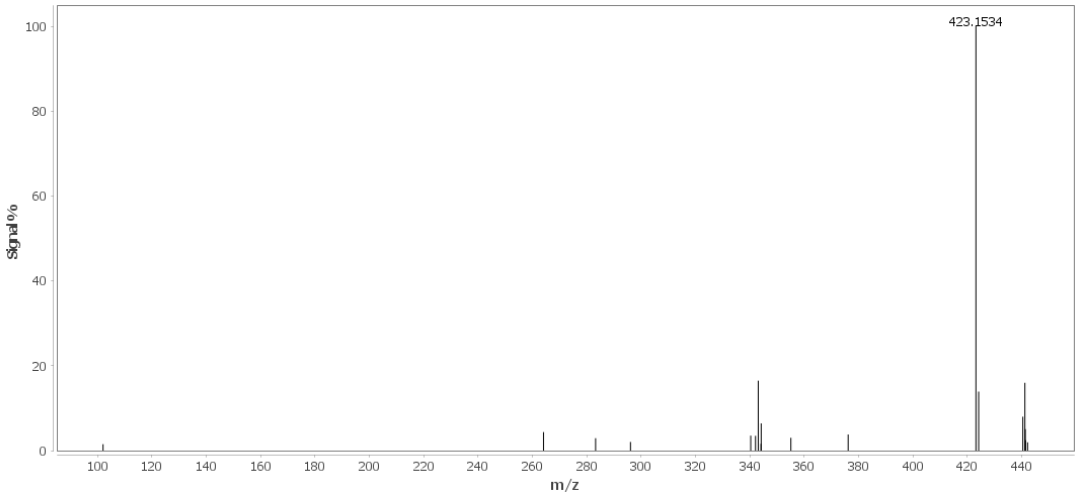


Peak #	m/z observed
1	441.1650
2	423.1535
3	376.1587
4	344.1688
5	264.1058

Metabolite **57-M2**
MS (+)

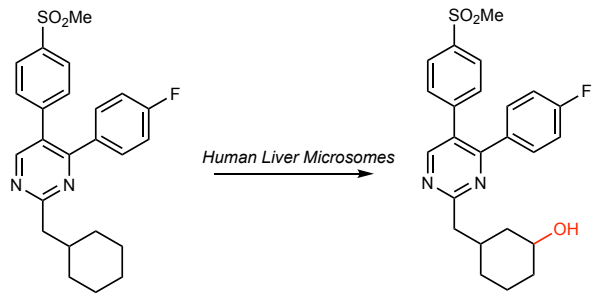


MS/MS (+)



Peak #	m/z observed
1	441.1647
2	423.1540
3	376.1596
4	344.1685
5	264.1051

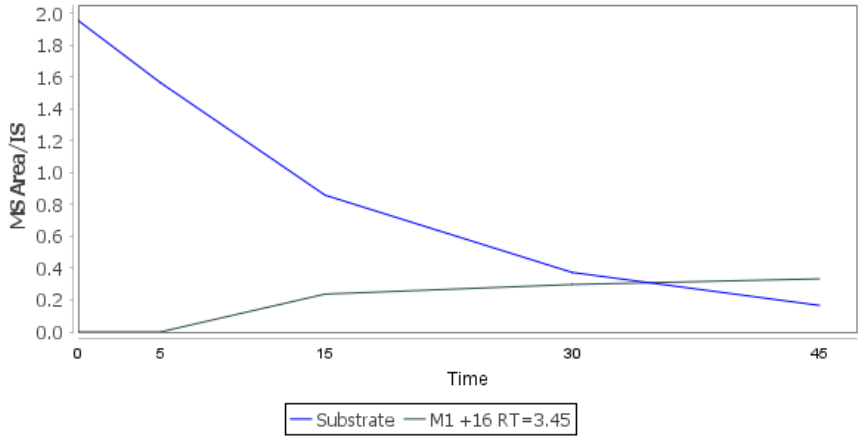
In vitro metabolic stability measurements of Compound 57 with human liver microsomes



57 **57-M1**

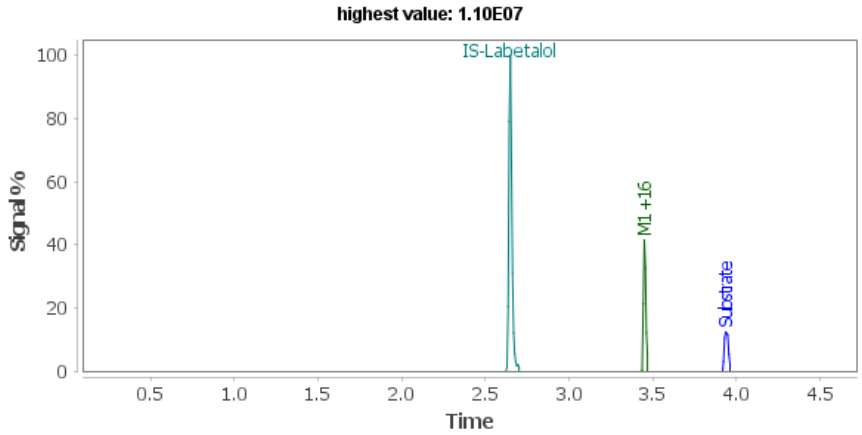
Compound **57** was treated with a preparation of human liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **57**: Cl_{int} unscaled = 223 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

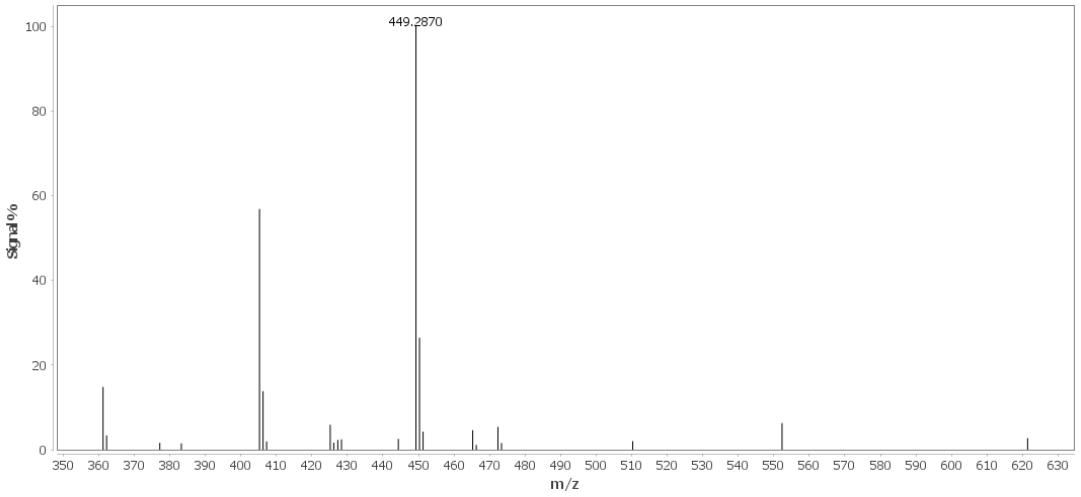


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.65 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (57)	-	3.93	1.48	33.3	425.1694	-0.07
57-M1	+16	3.45	1.30	66.7	441.1645	-0.54

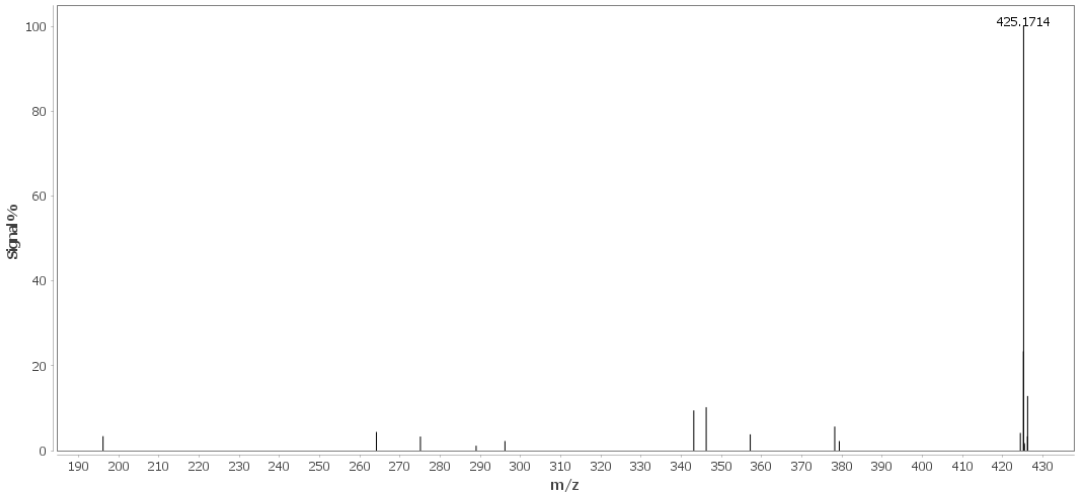
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **57**

MS (+)

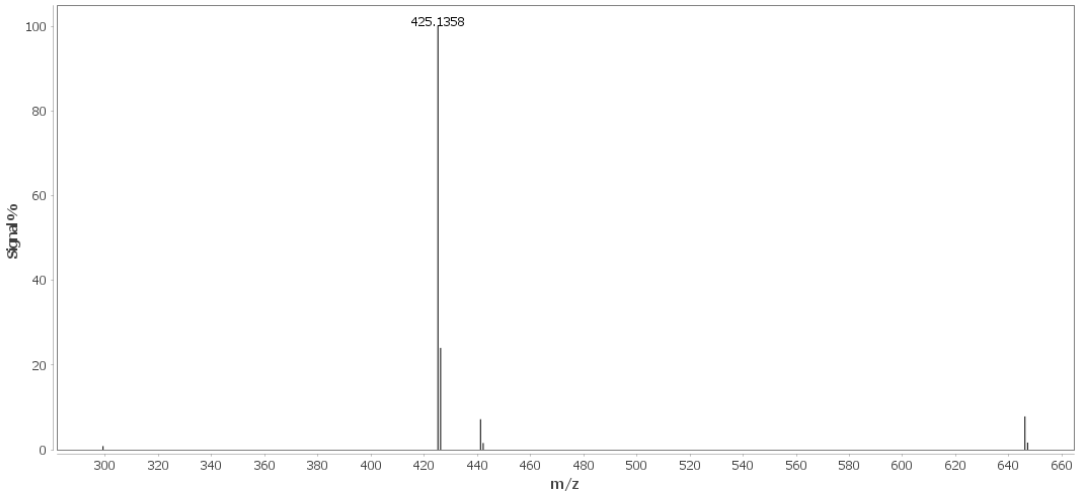


MS/MS (+)

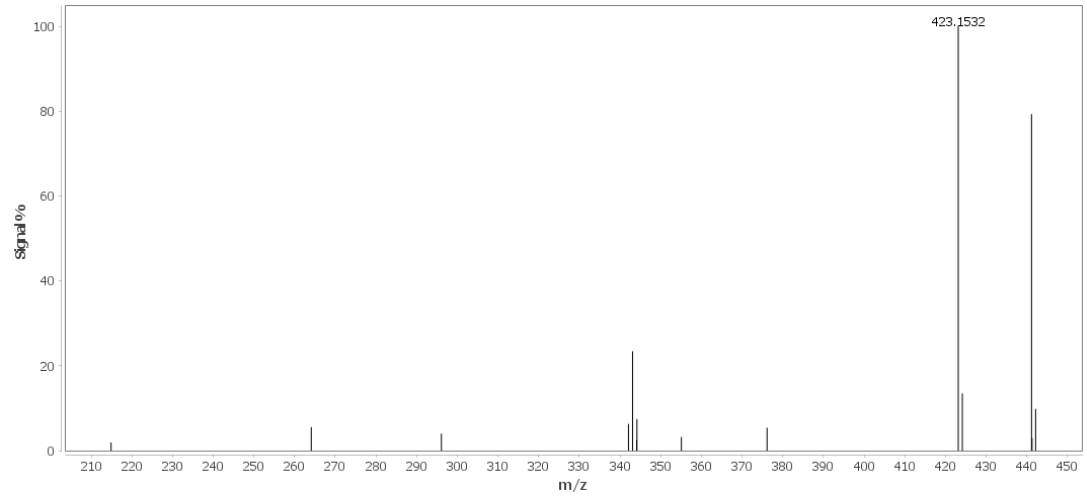


Peak #	m/z observed
1	425.1714
2	378.1733
3	346.1838
4	343.0911
5	264.1058

Metabolite **57-M1**
MS (+)

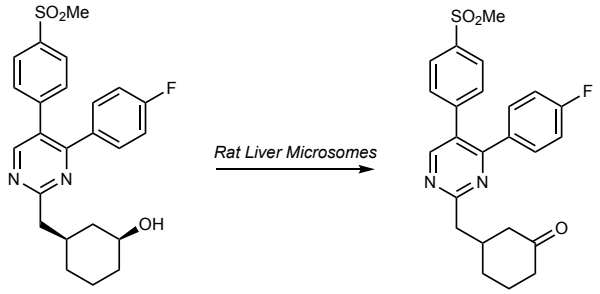


MS/MS (+)



Peak #	m/z observed
1	441.1649
2	423.1532
3	376.1571
4	344.1677
5	264.1056

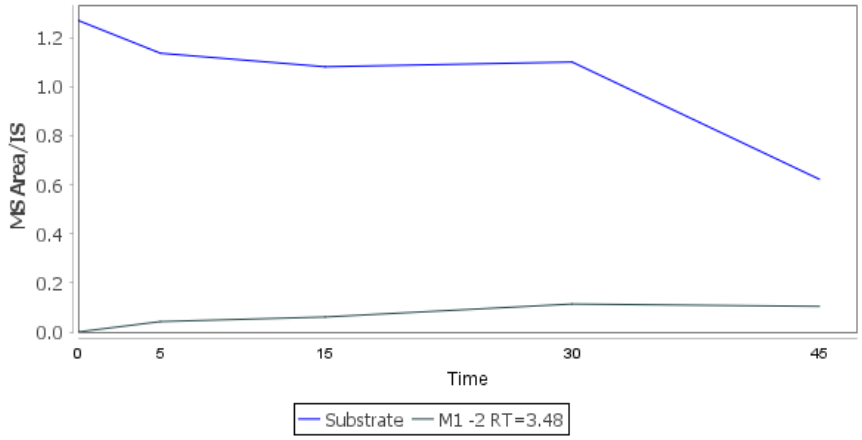
In vitro metabolic stability measurements of Compound 59 with rat liver microsomes



59 **59-M1**

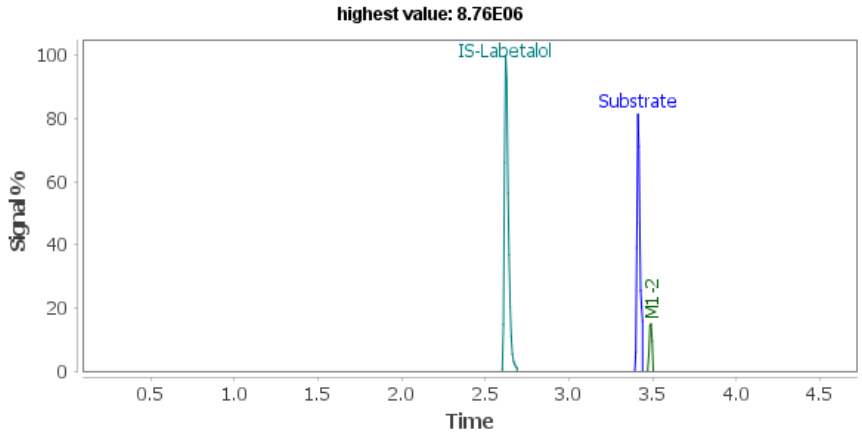
Compound **59** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **59**: Cl_{int} unscaled = 46 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

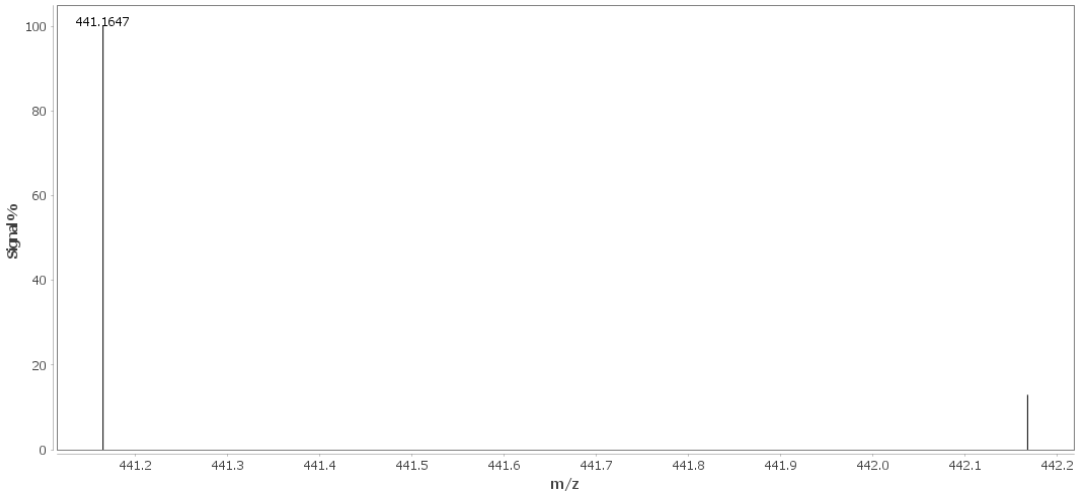


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.62 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (59)	-	3.41	1.30	85.7	441.1645	-0.45
59-M1	-2	3.49	1.33	14.3	439.1491	-1.17

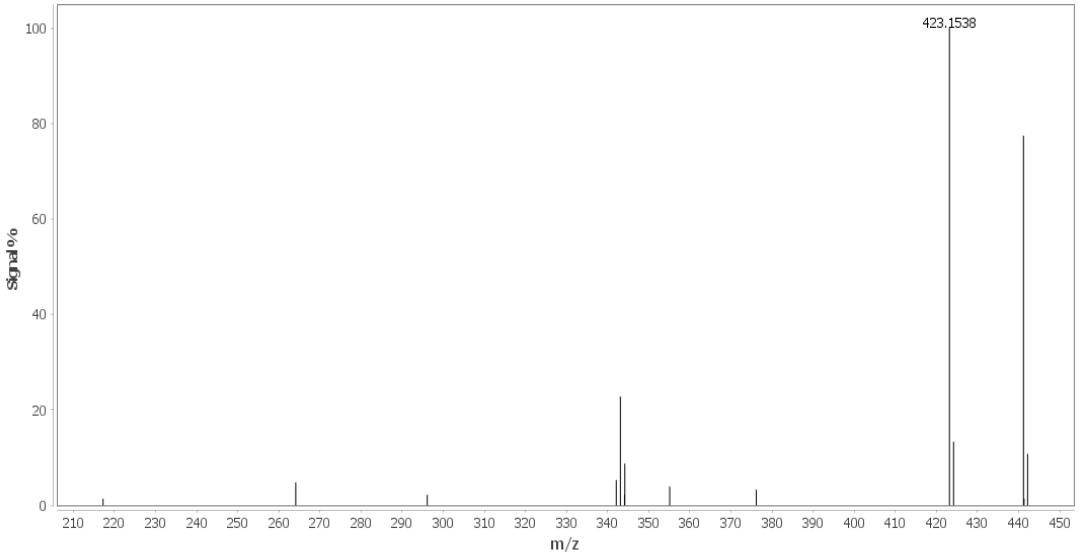
LC-MS/MS Spectra and Fragmentation of Substrate and Major Observed Metabolites (LC Area% > 5.0)

Substrate **59**

MS (+)

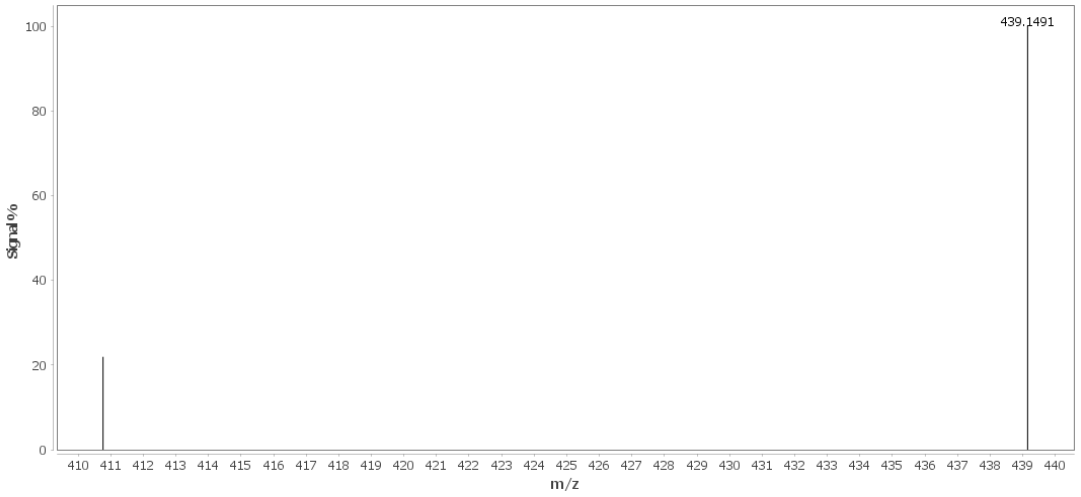


MS/MS (+)

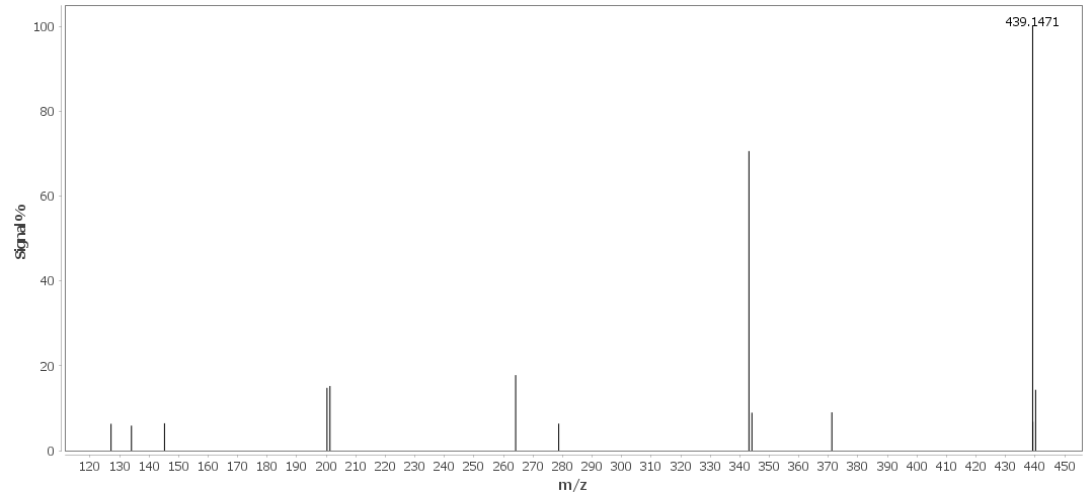


Peak #	m/z observed
1	441.1642
2	423.1538
3	343.0911
4	264.1053

Metabolite **59-M1**
MS (+)

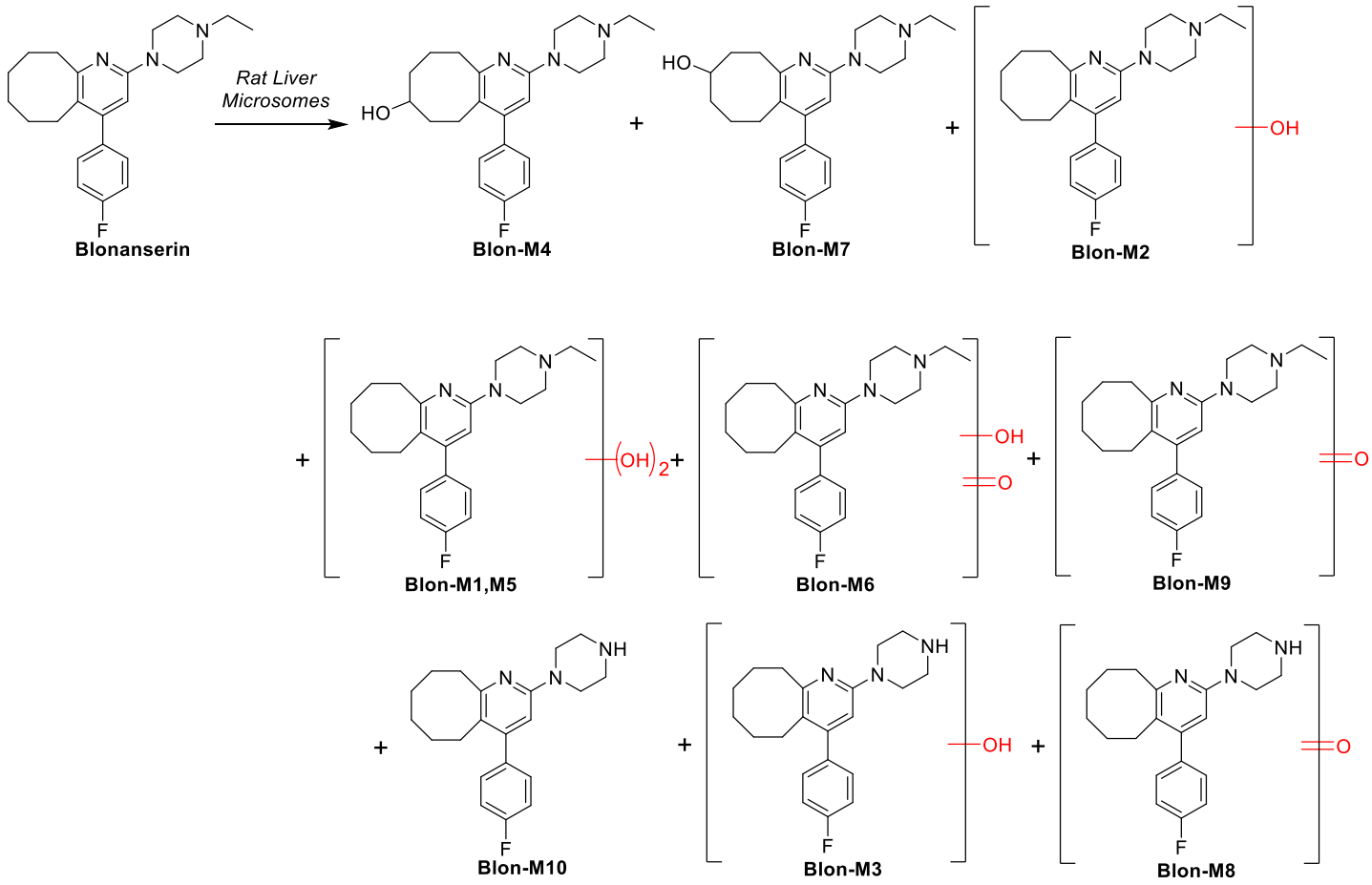


MS/MS (+)



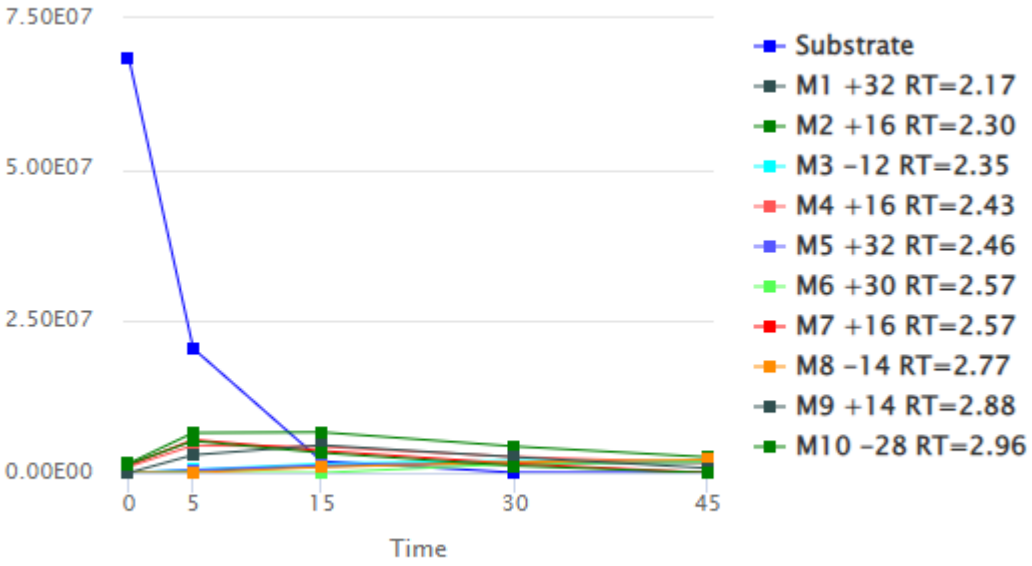
Peak #	m/z observed
1	439.1471
2	343.0904
3	264.1061

In vitro metabolic stability measurements of Blonanserin with rat liver microsomes



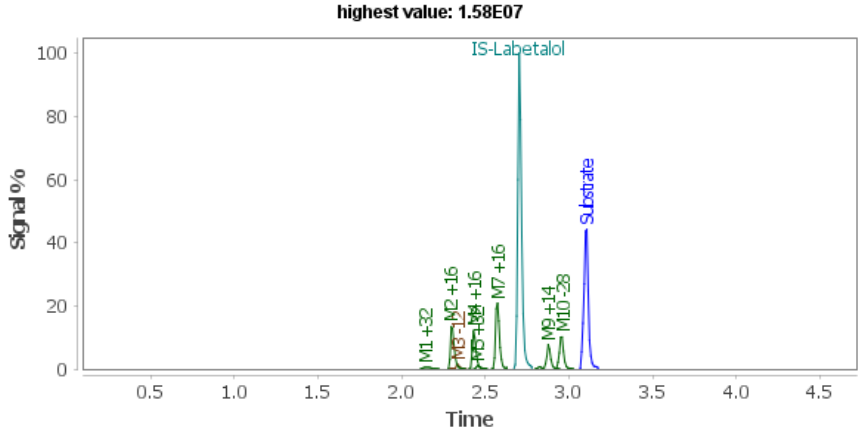
Blonanserin was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for blonanserin: Cl_{int} unscaled = 970 µL/min/mg

Extracted ion chromatogram trace for t = 5 min sample



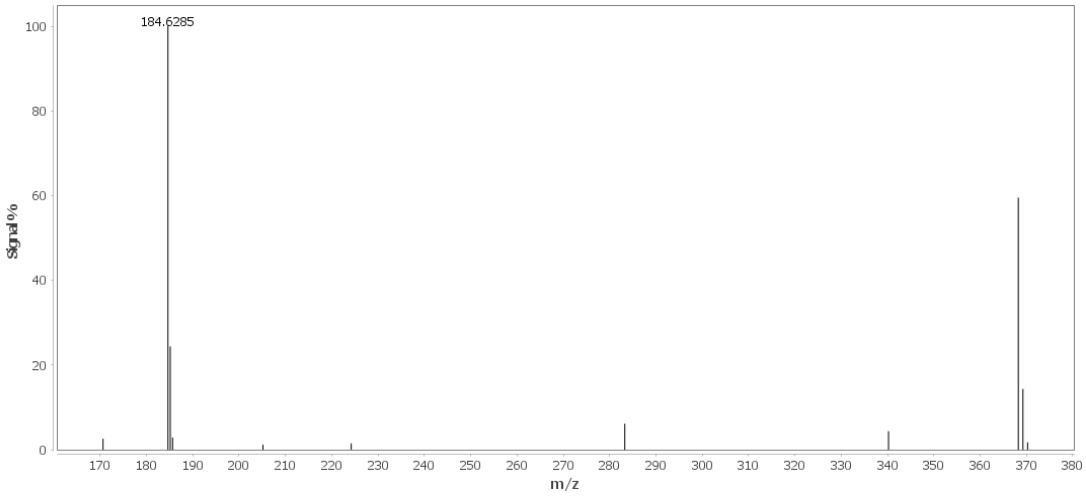
Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.70 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (Blonanserin)	-	3.11	1.15	44.1	184.6286	-0.60
Blon-M1	+32	2.14	0.79	0.6	400.2395	-0.99
Blon-M2	+16	2.30	0.85	14.2	384.2445	0.26
Blon-M3	-12	2.34	0.87	1.1	356.2135	-0.58
Blon-M4	+16	2.43	0.90	9.7	384.2445	0.19
Blon-M5	+32	2.45	0.91	1.0	400.2397	-0.50
Blon-M6	+30	2.59	0.96	-*	398.2239	-0.13
Blon-M7	+16	2.57	0.95	11.7	384.2449	-0.80
Blon-M8	-14	2.78	1.03	-**	354.1974	0.73
Blon-M9	+14	2.88	1.07	6.3	382.2290	-0.17
Blon-M10	-28	2.96	1.10	11.3	170.6129	-0.54

*Observed in t = 30 and 45 min samples only
**Observed in t = 15, 30 and 45 min samples only

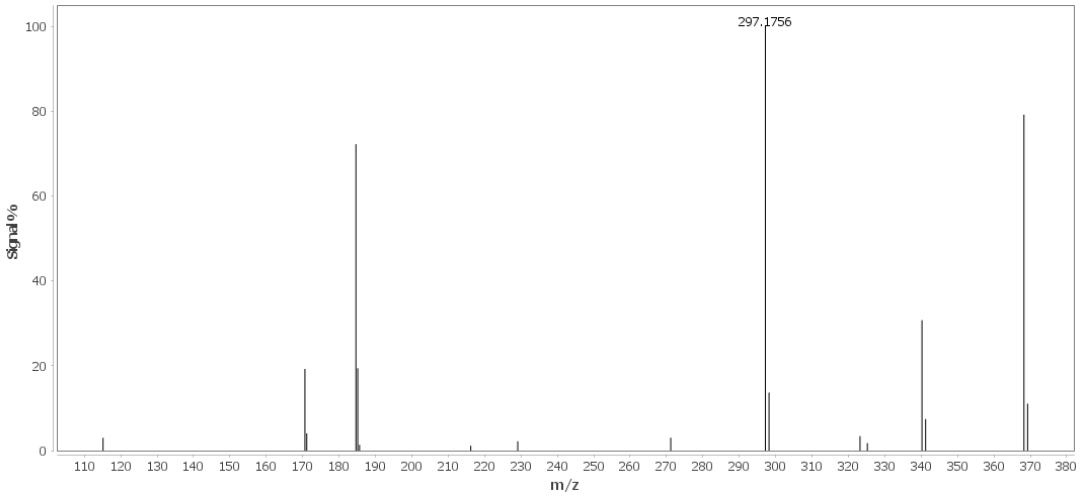
LC-MS/MS Spectra and Fragmentation of Substrate and Selected Major Observed M+16 Metabolites

Substrate **Blonanserin**

MS (+)

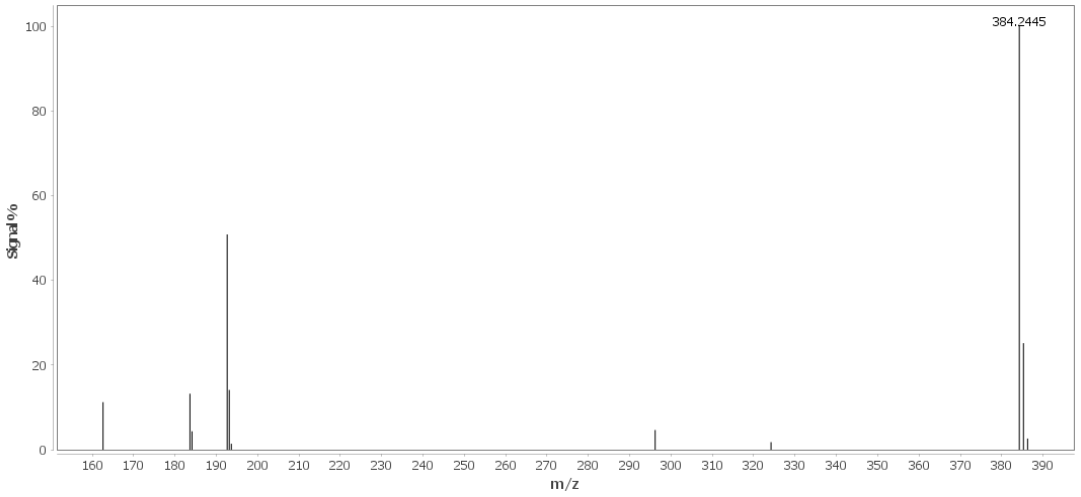


MS/MS (+)

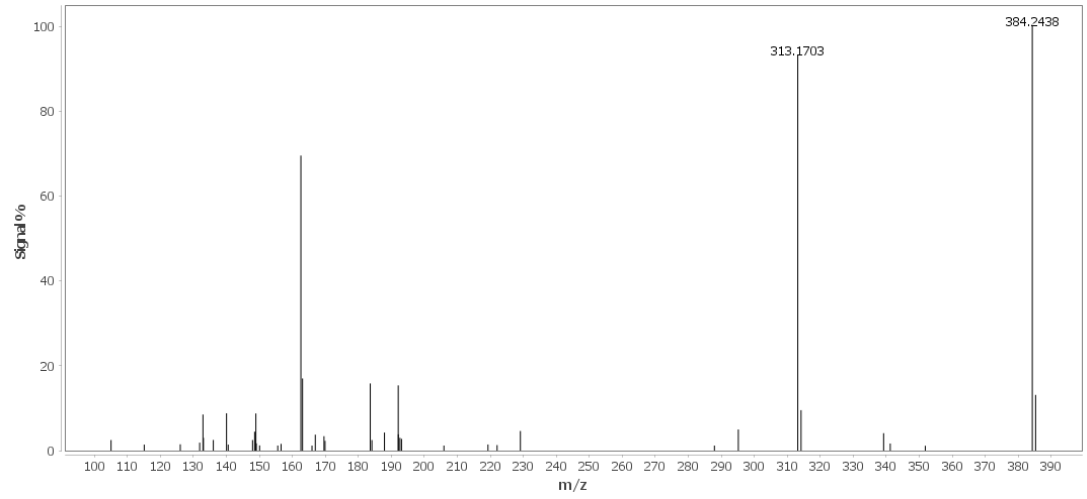


Peak #	m/z observed
1	368.2489
2	340.2174
3	297.1756
4	184.6285

Metabolite **Blon-M4**
MS (+)

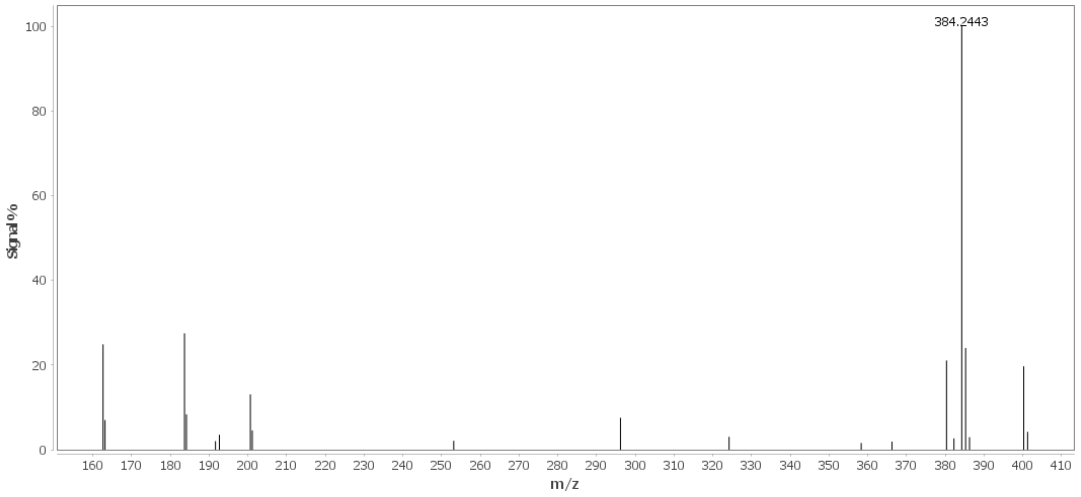


MS/MS (+)

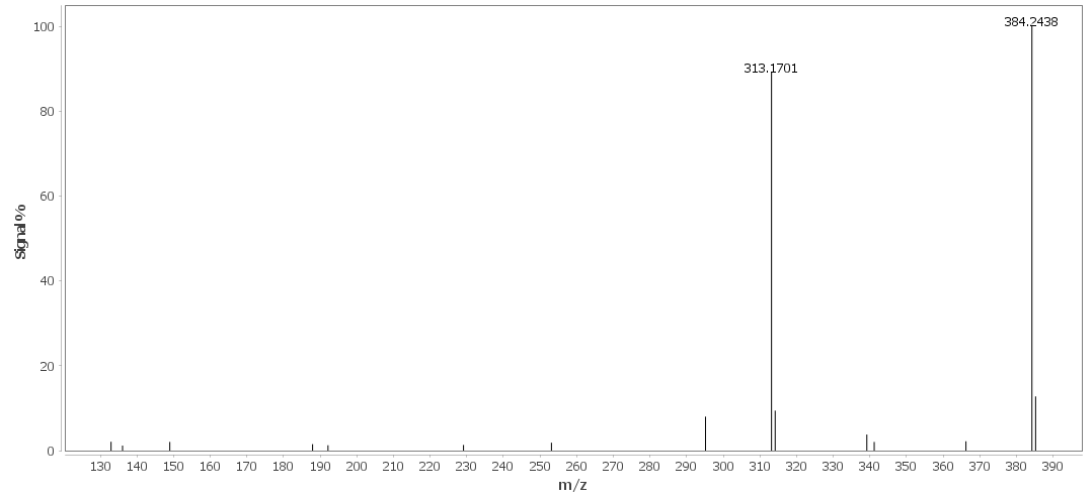


Peak #	m/z observed
1	384.2445
2	313.1703
3	192.6261
4	183.6208
5	162.5972

Metabolite **Blon-M7**
MS (+)

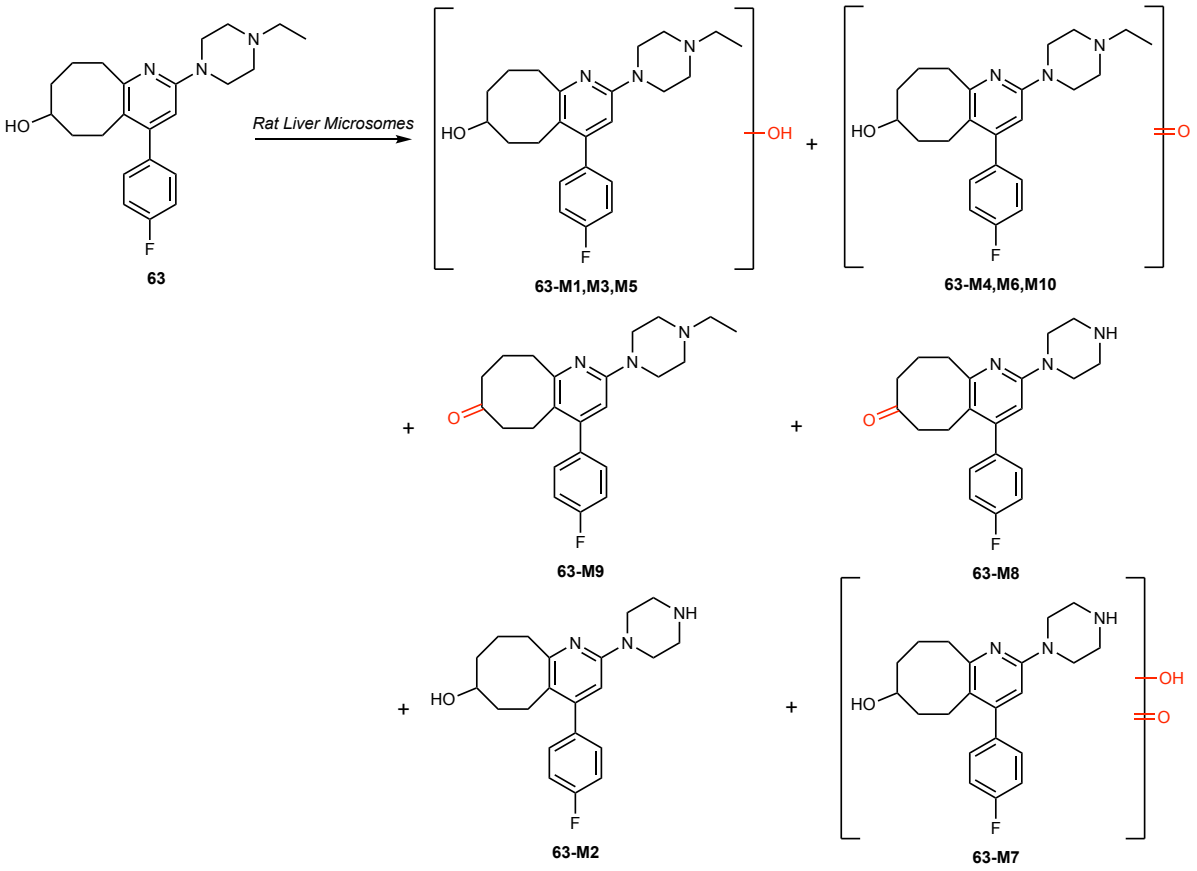


MS/MS (+)



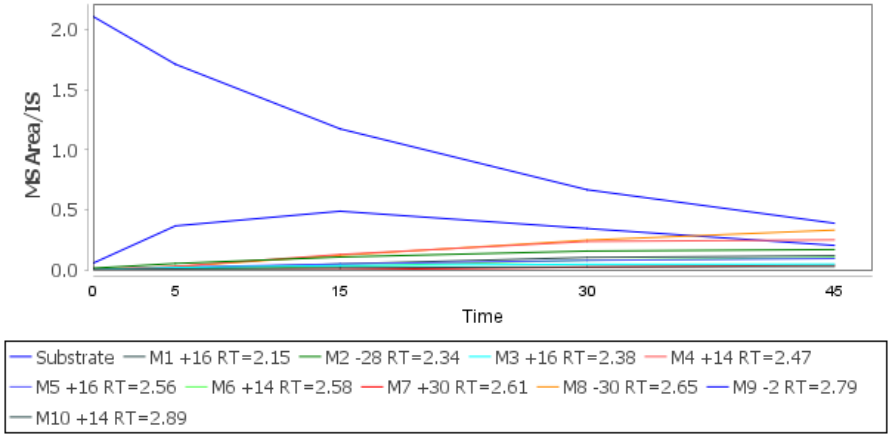
Peak #	m/z observed
1	384.2443
2	313.1701
3	295.1596

In vitro metabolic stability measurements of Compound 63 with rat liver microsomes



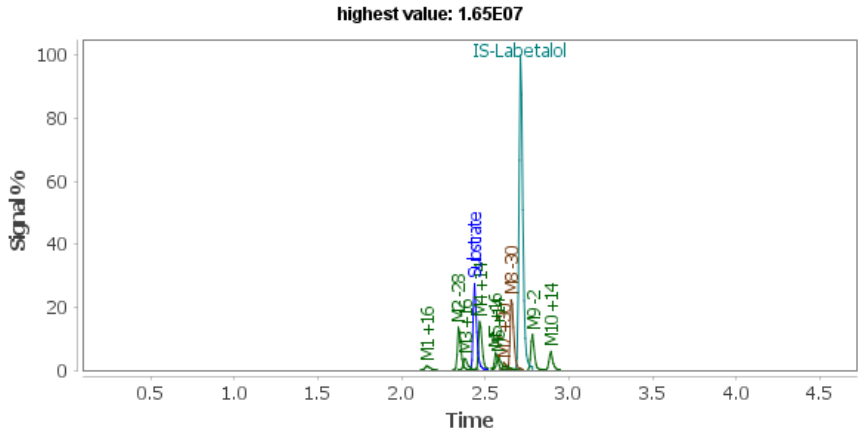
Compound **63** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **63**: Cl_{int} unscaled = 152 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

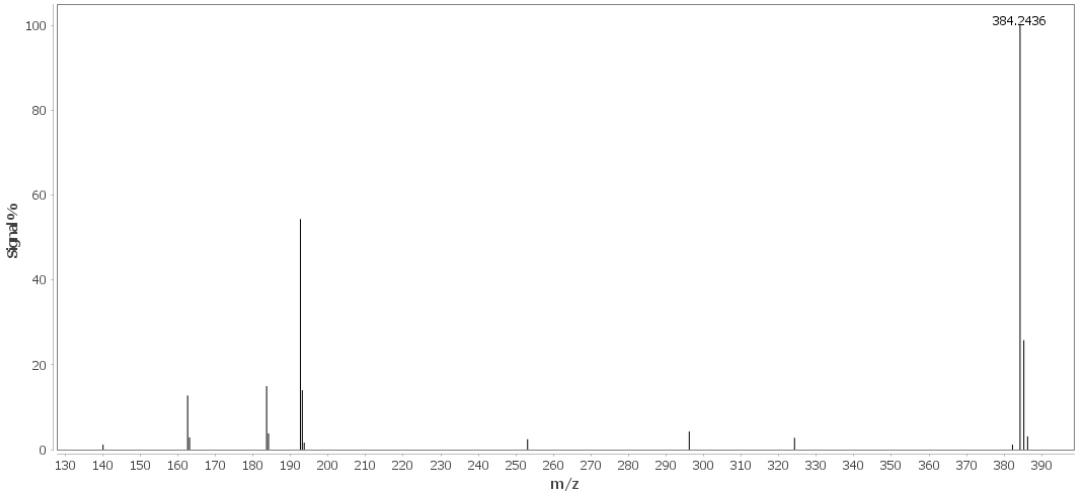


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.71 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (63)	-	2.44	0.90	22.1	384.2439	1.75
63-M1	+16	2.15	0.79	1.5	400.2391	0.84
63-M2	-28	2.34	0.86	9.6	356.2129	1.14
63-M3	+16	2.38	0.88	2.7	400.2391	0.93
63-M4	+14	2.47	0.91	14.2	398.2233	1.26
63-M5	+16	2.56	0.94	5.3	400.2391	0.74
63-M6	+14	2.58	0.95	5.8	398.2233	1.33
63-M7	+30	2.61	0.96	2.1	414.2181	1.66
63-M8	-30	2.65	0.98	18.8	354.1970	1.88
63-M9	-2	2.78	1.03	11.5	382.2283	1.66
63-M10	+14	2.89	1.07	6.6	398.2233	1.38

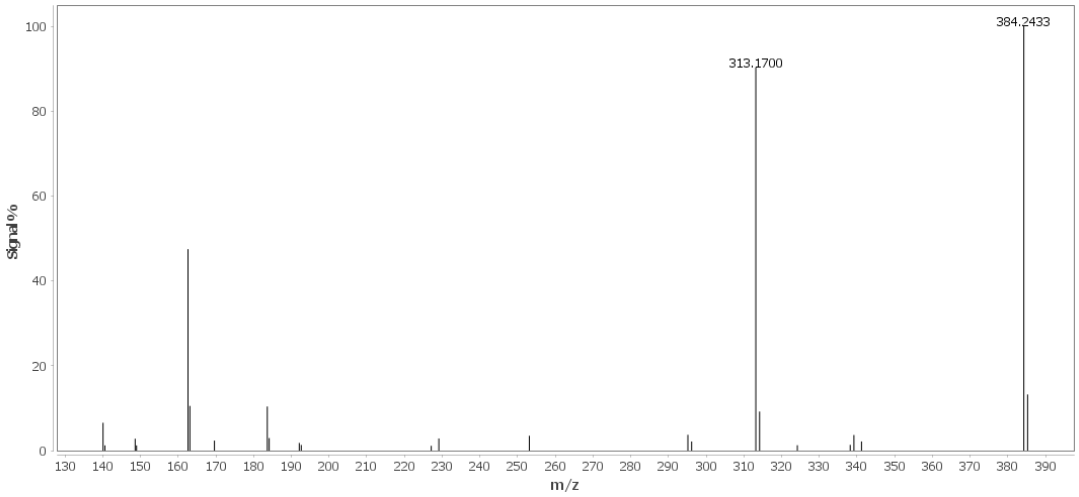
LC-MS/MS Spectra and Fragmentation of Substrate

Substrate **63**

MS (+)

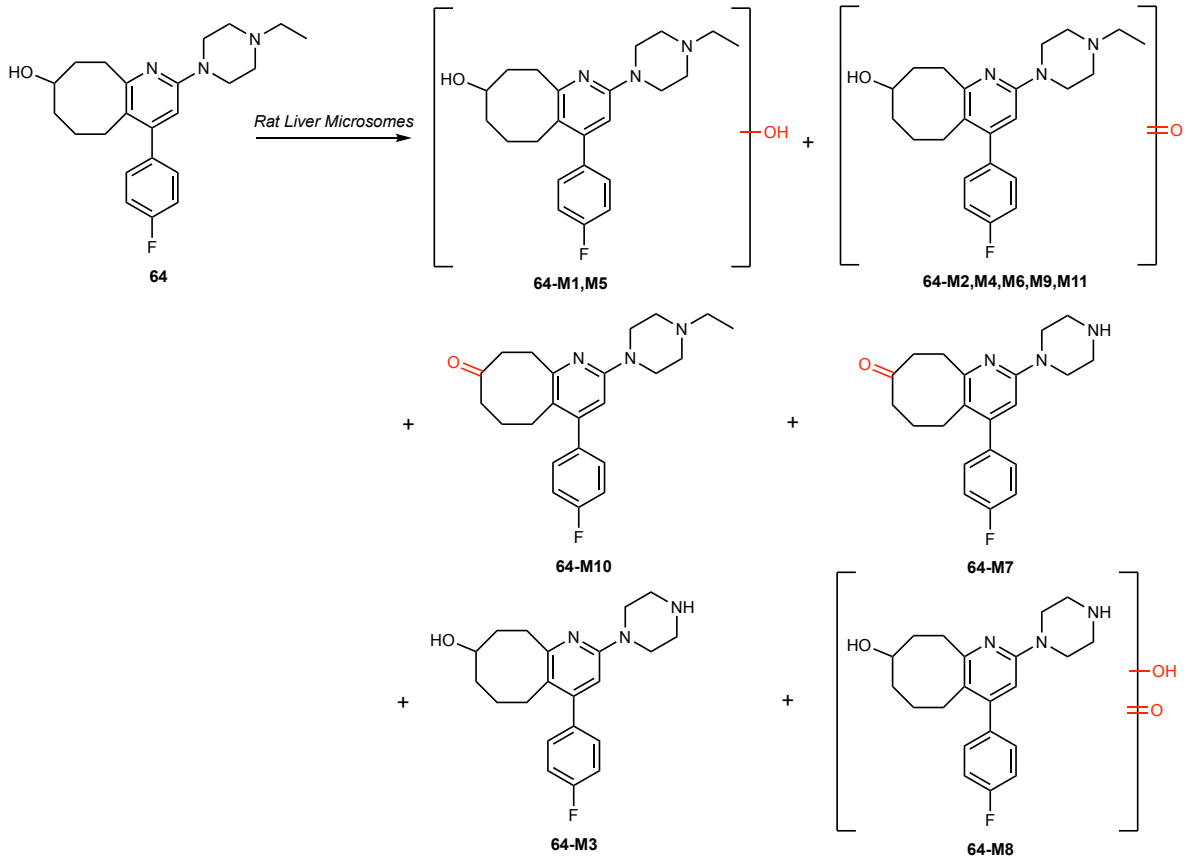


MS/MS (+)



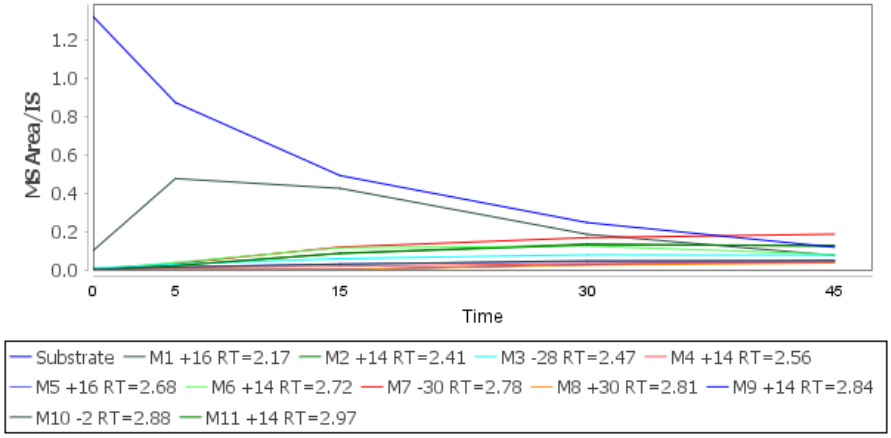
Peak #	m/z observed
1	384.2433
2	313.1700
3	192.6258
4	183.6205
5	162.5967

In vitro metabolic stability measurements of Compound 64 with rat liver microsomes



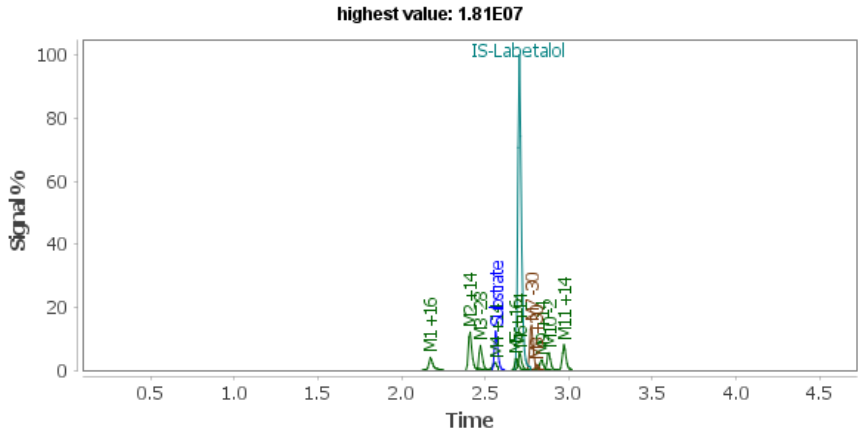
Compound **64** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **64** Cl_{int} unscaled = 208 µL/min/mg

Extracted ion chromatogram trace for t = 45 min sample

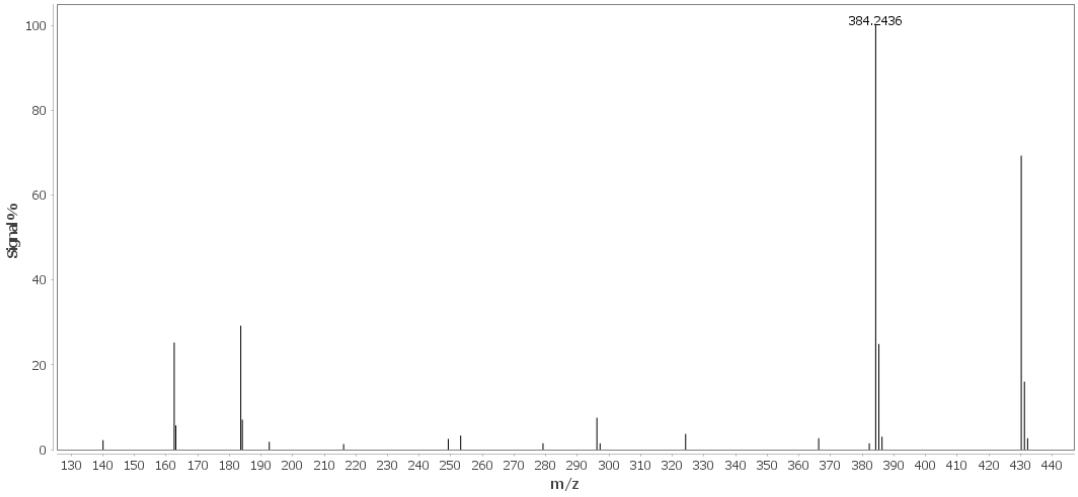


Peak Name	Mass Shift	RT (min)	RRT vs I.S. (2.70 min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (64)	-	2.56	0.95	11.8	384.2445	0.08
64-M1	+16	2.17	0.80	4.9	400.2389	1.56
64-M2	+14	2.41	0.89	12.9	398.2232	1.48
64-M3	-28	2.47	0.91	7.6	356.2127	1.46
64-M4	+14	2.56	0.95	3.9	398.2234	1.13
64-M5	+16	2.68	0.99	4.3	400.2392	0.67
64-M6	+14	2.70	1.00	8.0	398.2233	1.24
64-M7	-30	2.78	1.03	18.7	354.1970	1.80
64-M8	+30	2.81	1.04	3.5	414.2181	1.63
64-M9	+14	2.84	1.05	4.7	398.2238	1.56
64-M10	-2	2.88	1.07	7.5	382.2282	1.95
64-M11	+14	2.97	1.10	12.3	398.2231	1.82

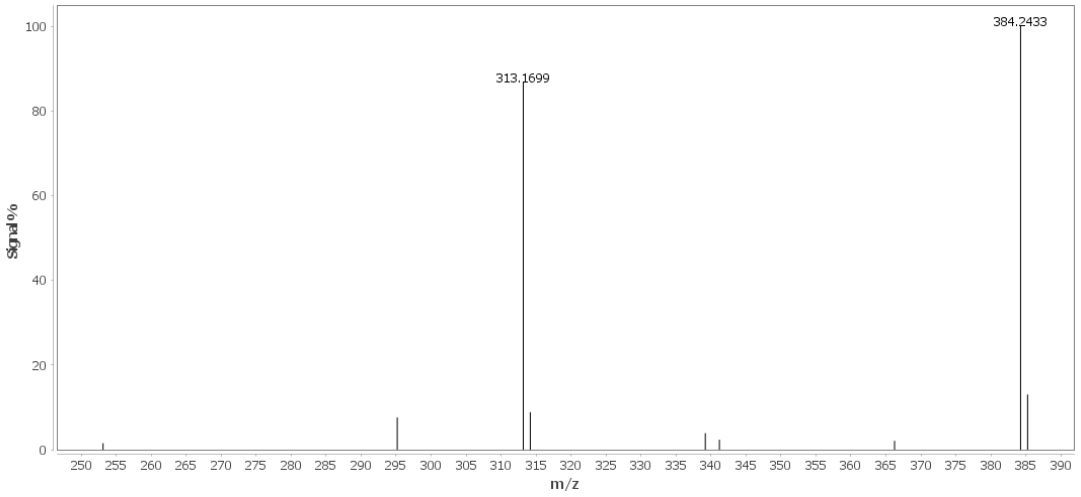
LC-MS/MS Spectra and Fragmentation of Substrate

Substrate **64**

MS (+)

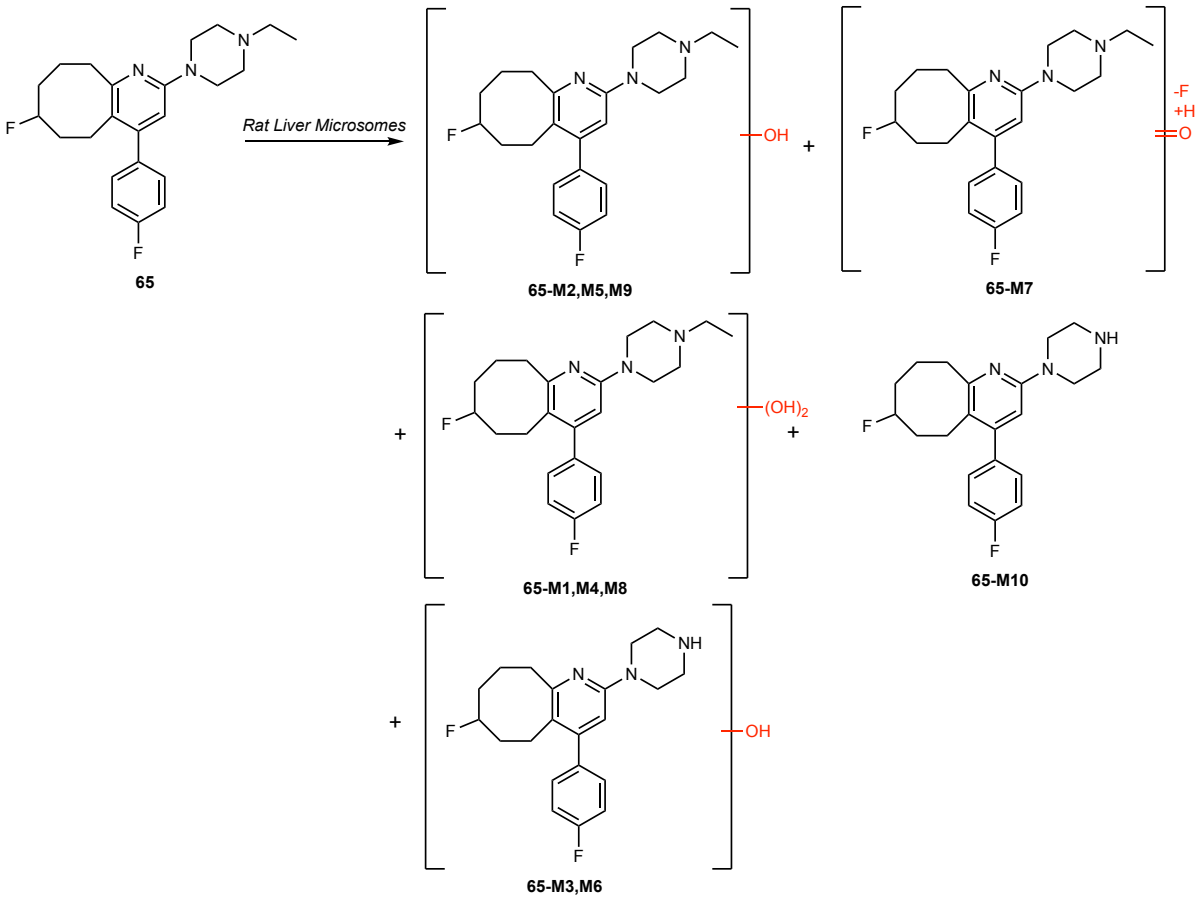


MS/MS (+)



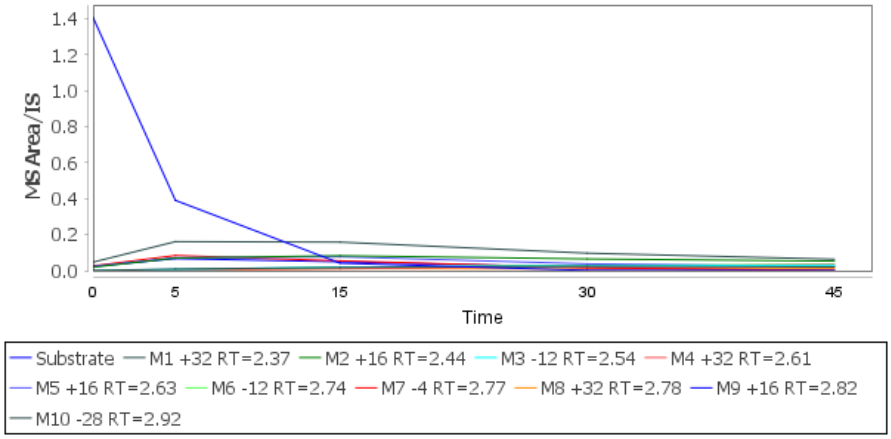
Peak #	m/z observed
1	384.2433
2	313.1699
3	295.1595

In vitro metabolic stability measurements of Compound 65 with rat liver microsomes



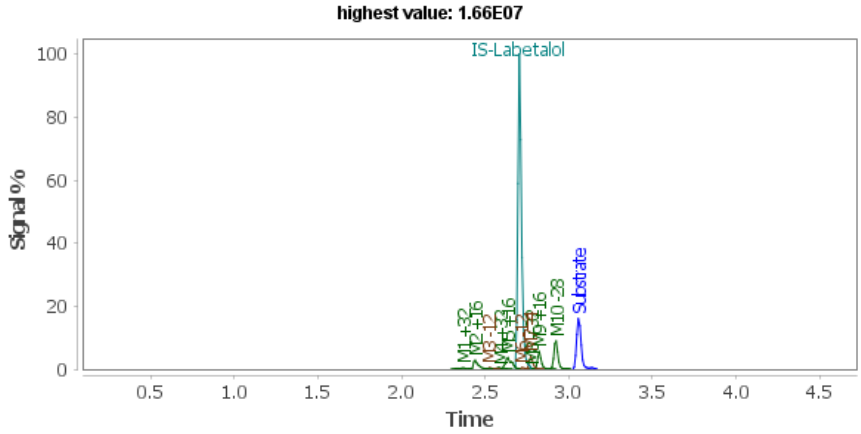
Compound **65** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



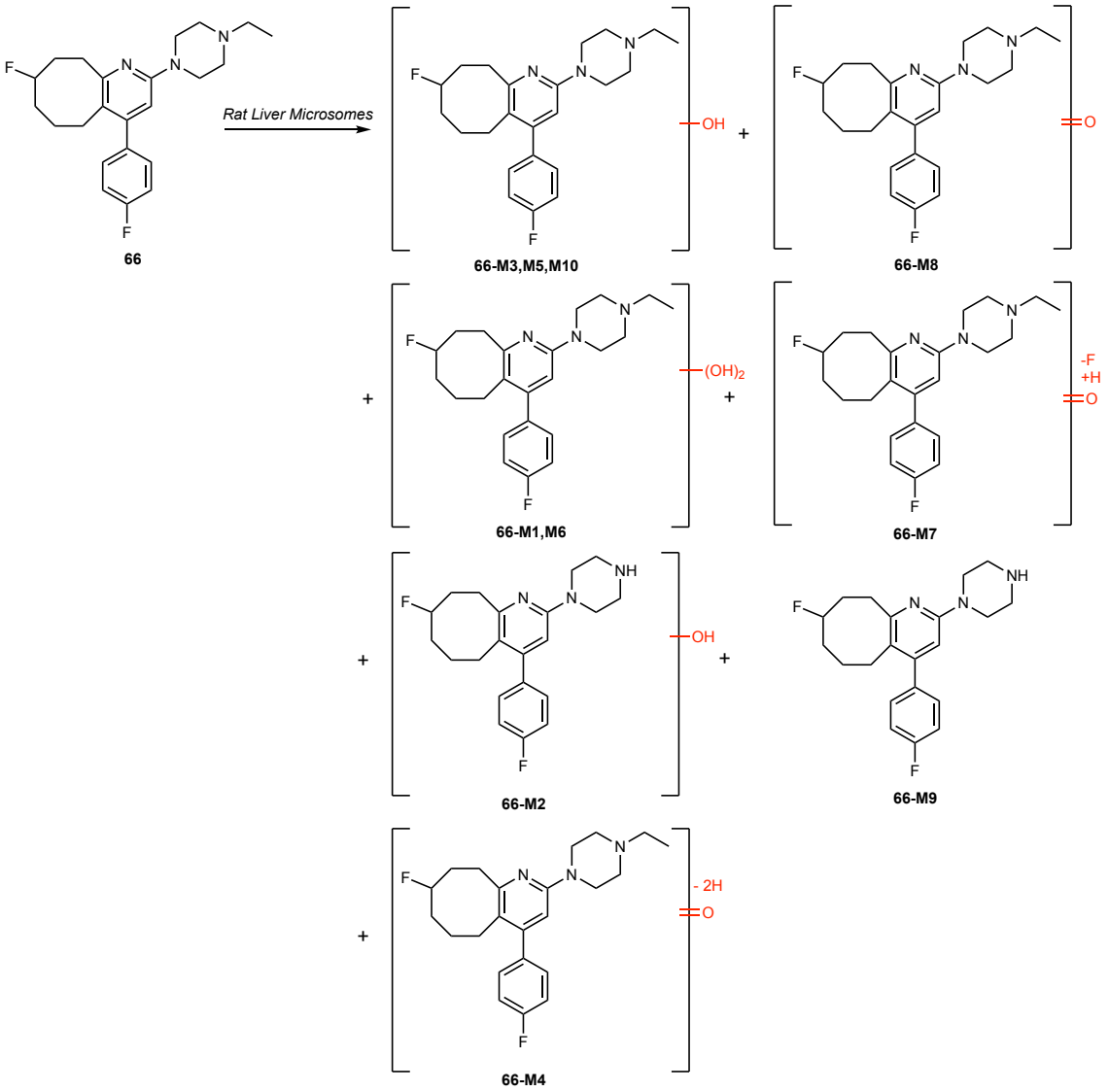
Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **65**: Cl_{int} unscaled = 905 µL/min/mg

Extracted ion chromatogram trace for t = 5 min sample



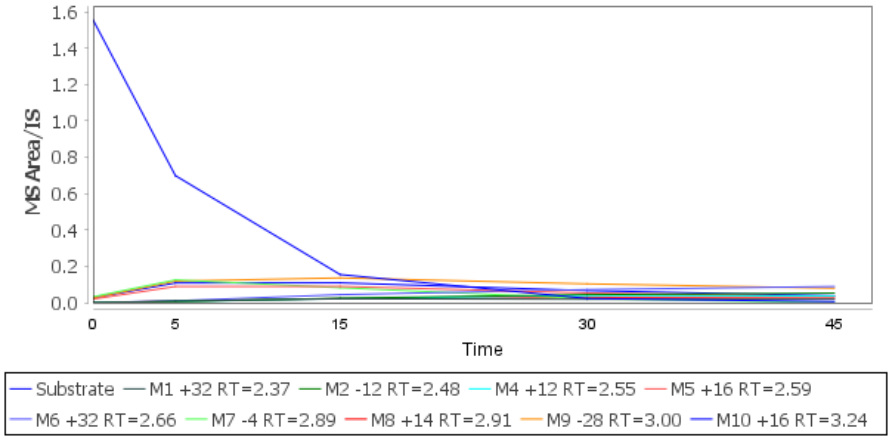
Peak Name	Mass Shift	RT (min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (65)	-	3.07	44.8	193.6237	0.3
65-M1	+32	2.37	1.0	418.2302	-2.0
65-M2	+16	2.44	8.0	402.2341	2.4
65-M3	-12	2.54	0.8	374.2035	1.1
65-M4	+32	2.61	0.5	418.2294	2.1
65-M5	+16	2.63	8.2	402.2344	1.8
65-M6	-12	2.73	0.6	374.2035	1.1
65-M7	-4	2.77	9.7	382.2286	0.8
65-M8	+32	2.78	0.4	418.2295	1.8
65-M9	+16	2.82	7.7	402.2343	1.8
65-M10	-28	2.92	18.5	358.2084	0.7

In vitro metabolic stability measurements of Compound 66 with rat liver microsomes



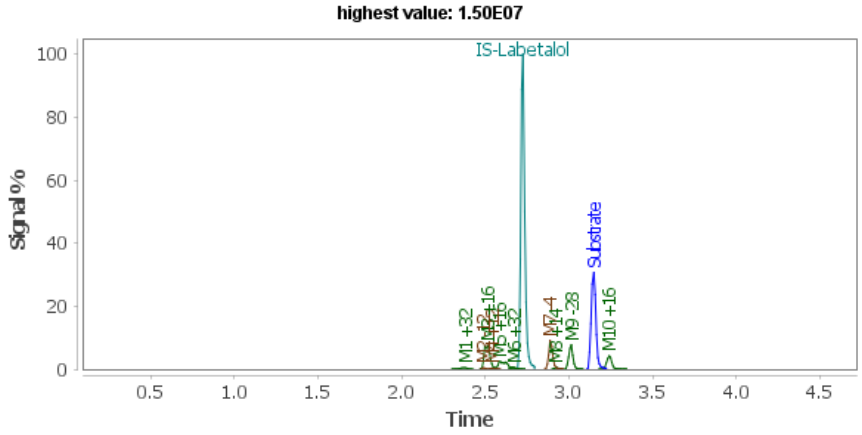
Compound **66** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



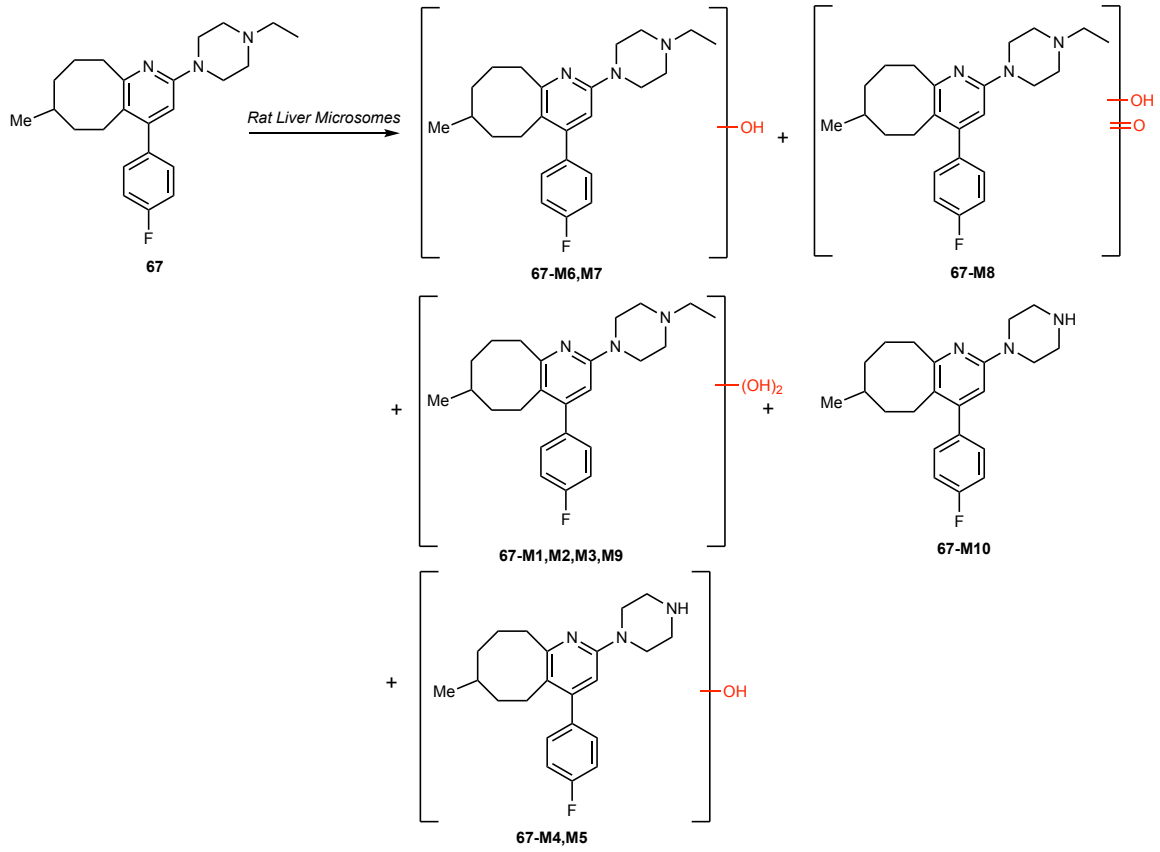
Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **66**: Cl_{int} unscaled = 555 µL/min/mg

Extracted ion chromatogram trace for t = 5 min sample



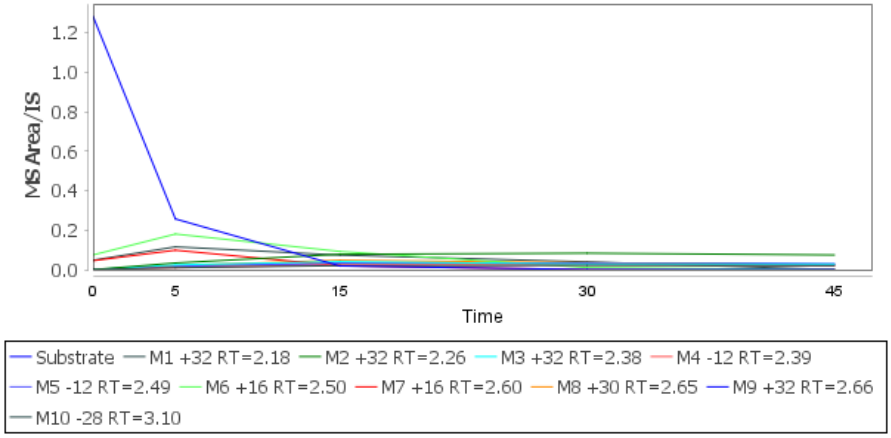
Peak Name	Mass Shift	RT (min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (66)	-	3.15	51.6	386.2396	1.7
66-M1	+32	2.37	0.7	418.2303	-1.8
66-M2	-12	2.48	0.4	374.2034	1.1
66-M3	+16	2.49	13.1	402.2343	1.6
66-M4	+12	2.55	0.5	398.2234	1.2
66-M5	+16	2.59	6.5	402.2342	2.1
66-M6	+32	2.66	0.7	418.2294	2.4
66-M7	-4	2.89	9.2	382.2285	1.1
66-M8	+14	2.91	0.6	400.2187	2.0
66-M9	-28	3.00	8.7	358.2085	1.4
66-M10	+16	3.24	8.0	321.9889	2.5

In vitro metabolic stability measurements of Compound 67 with rat liver microsomes



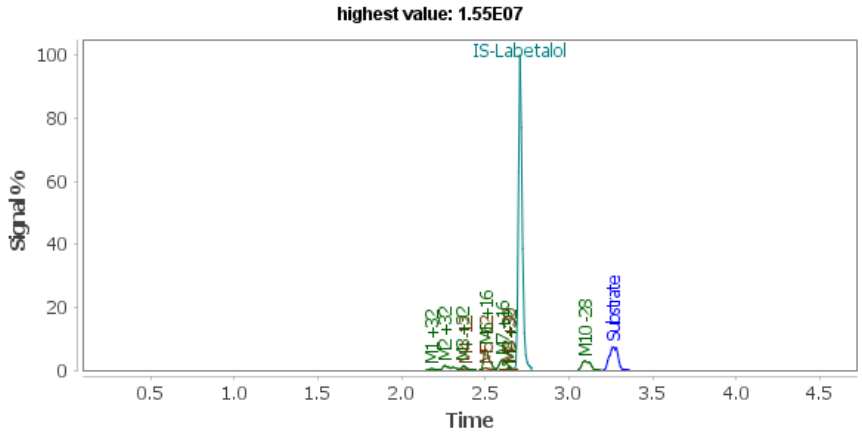
Compound **67** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



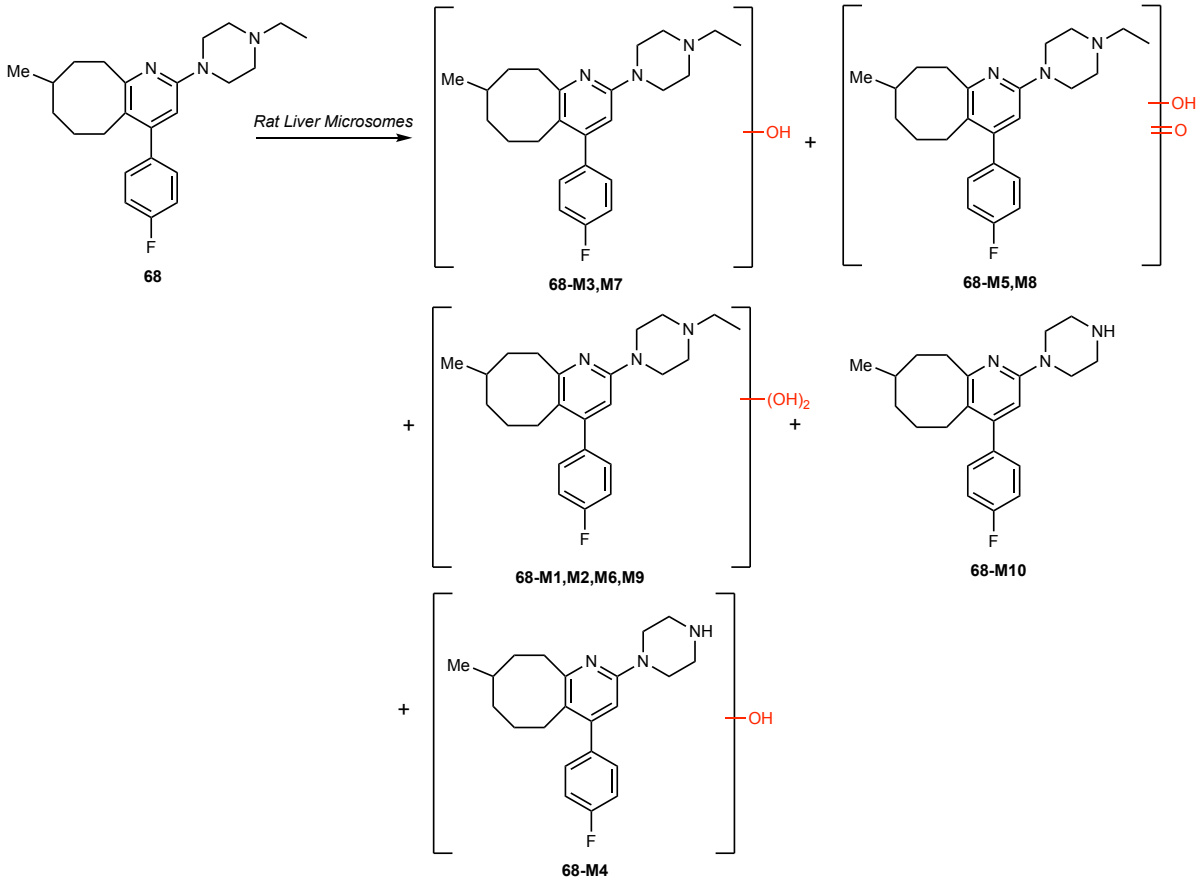
Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **67**: Cl_{int} unscaled = 1119 µL/min/mg

Extracted ion chromatogram trace for t = 5 min sample



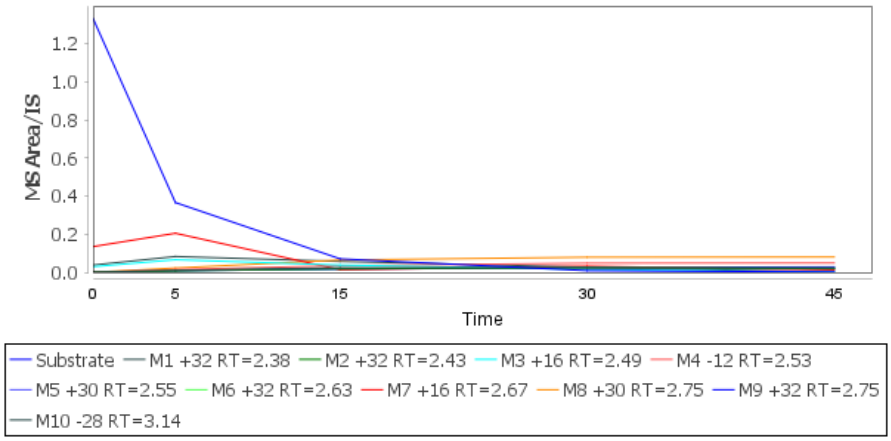
Peak Name	Mass Shift	RT (min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (67)	-	3.26	32.8	191.6362	0.9
67-M1	+32	2.18	1.2	414.2545	1.3
67-M2	+32	2.26	4.3	414.2545	1.4
67-M3	+32	2.38	3.1	414.2548	0.9
67-M4	-12	2.39	1.2	370.2295	-1.4
67-M5	-12	2.49	2.2	370.2287	0.4
67-M6	+16	2.50	23.0	249.2902	0.4
67-M7	+16	2.60	12.6	398.2600	0.6
67-M8	+30	2.65	2.7	360.8352	0.8
67-M9	+32	2.66	2.2	259.2871	0.5
67-M10	-28	3.10	14.7	177.6206	0.2

In vitro metabolic stability measurements of Compound 68 with rat liver microsomes



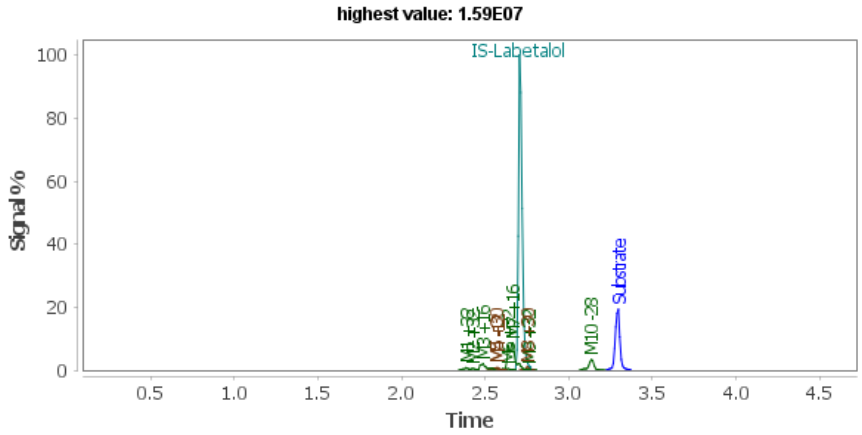
Compound **68** was treated with a preparation of rat liver microsomes as described in the general procedure. Samples were taken at predetermined time points and analyzed by LC-MS/MS as described above.

Time course of microsomal stability study



Based on the rate of disappearance of substrate, an unscaled intrinsic clearance was calculated for compound **68**: Cl_{int} unscaled = 1034 µL/min/mg

Extracted ion chromatogram trace for t = 5 min sample



Peak Name	Mass Shift	RT (min)	Area %	*m/z* (observed)	Mass error (ppm)
Substrate (68)	-	3.30	45.7	191.6363	0.2
68-M1	+32	2.38	1.2	414.2550	0.5
68-M2	+32	2.43	0.9	414.2550	0.8
68-M3	+16	2.49	8.2	199.6338	0.1
68-M4	-12	2.53	1.8	370.2289	0.5
68-M5	+30	2.55	1.2	412.2394	0.6
68-M6	+32	2.63	1.4	414.2551	0.7
68-M7	+16	2.67	25.6	358.5349	0.5
68-M8	+30	2.75	2.8	206.6235	-0.1
68-M9	+32	2.75	1.1	414.2551	0.7
68-M10	-28	3.14	10.3	177.6207	-0.3

Radioligand binding studies with Dopamine D_{2L} receptor

Measurements of binding affinity to recombinant human Dopamine D_{2L} receptor expressed in human recombinant CHO cells were carried out by Eurofins Panlabs Discovery Services, Taiwan, Ltd. 25, Wugong 6th Road, Wugu District, New Taipei City, Taiwan 24891.

Samples were incubated for 2 h at 25 °C in an incubation buffer consisting of 50 mM Tris-HCl, pH 7.4, 1.4 mM Ascorbic Acid, 0.001% BSA, 150 mM NaCl.

Bmax: 0.48 pmol/mg Protein

Ligand: 0.16 nM [^{3}H] Spiperone (K_D = 0.08 nM)

Non-Specific Ligand: 10.0 µM Holoperidol

Vehicle: 1.0% DMSO

IC_{50} values were determined by a non-linear, least squares regression analysis using MathIQ™ (ID Business Solutions Ltd., UK). Where inhibition constants (Ki) are presented, the Ki values were calculated using the equation of Cheng and Prusoff[49] using the observed IC_{50} of the tested compound,

the concentration of radioligand employed in the assay, and the historical values for the K_D of the ligand Where presented, the Hill coefficient (n_H), defining the slope of the competitive binding curve, was calculated using MathIQ™.

Compound	IC_{50} (nM)	K_i (nM)	n_H
Blonanserin	0.42	0.14	0.79
63	5.02	1.67	0.70
64	4.78	1.59	1.05
65	1.66	0.55	0.94
66	0.70	0.23	0.99
67	1.74	0.58	0.90
68	1.37	0.46	0.78

XII. References

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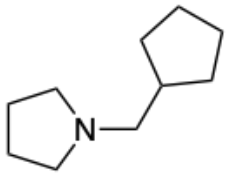

	Parameter	Value
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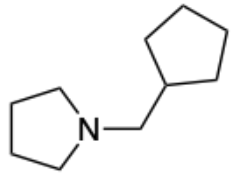
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
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8	Number of Scans	128
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
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12	Spectrometer Frequency	500.35
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15	Nucleus	1H
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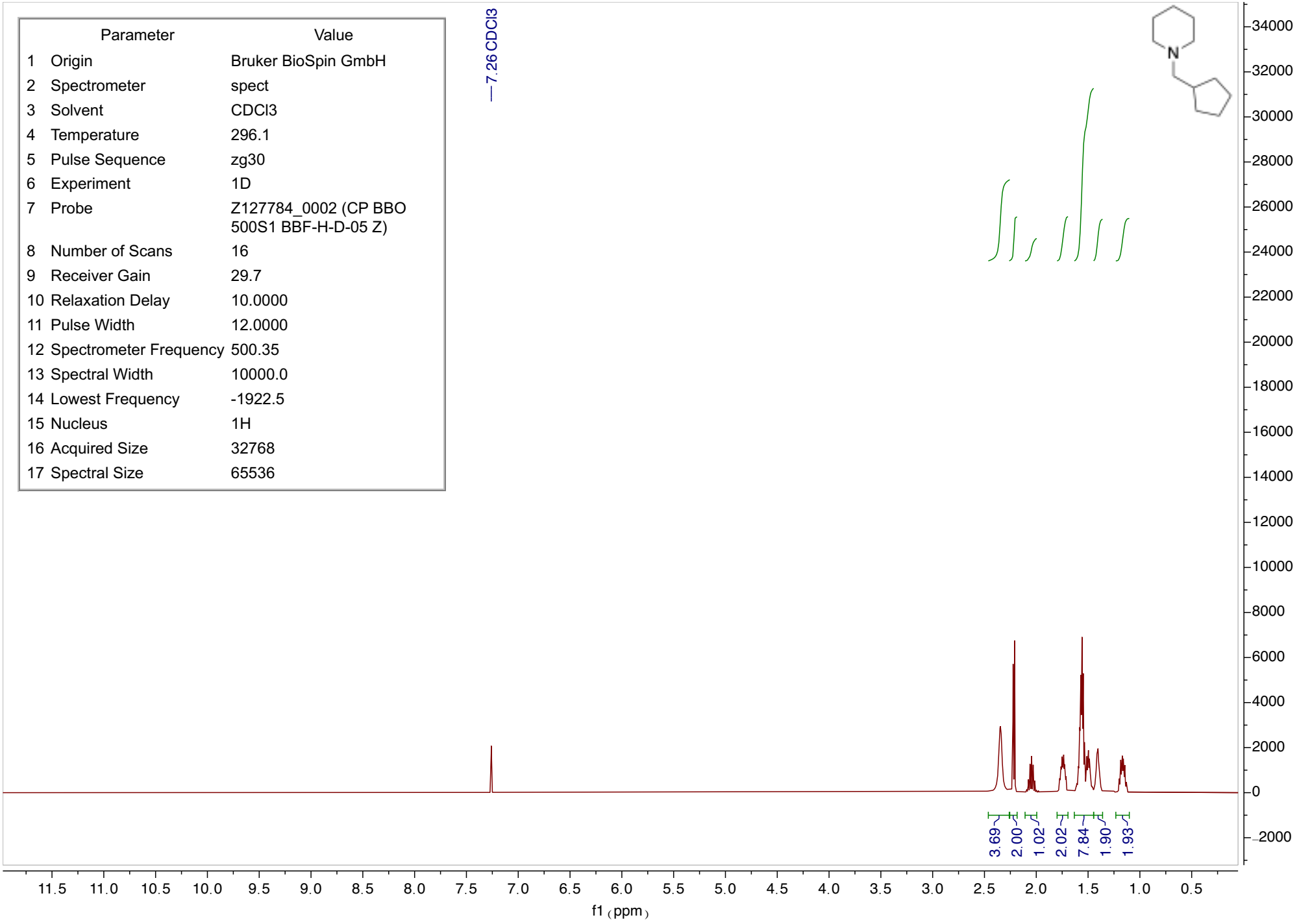

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2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
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8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
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16	Acquired Size	32768
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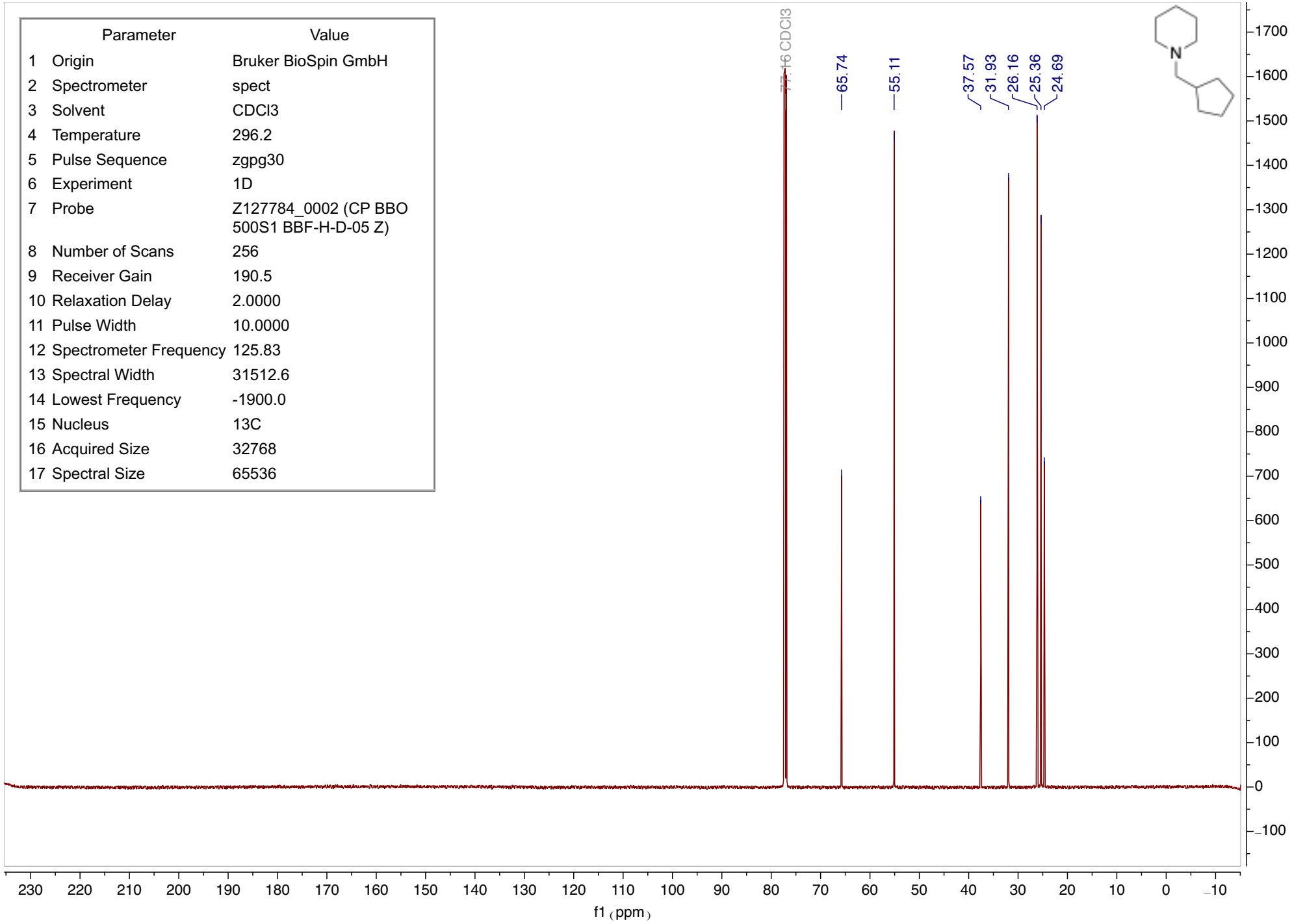

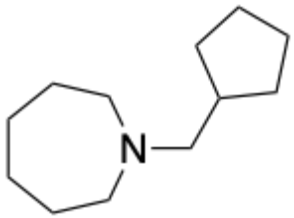

	Parameter	Value
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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
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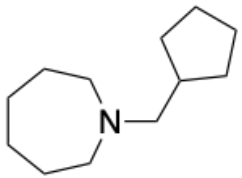
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
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15	Nucleus	13C
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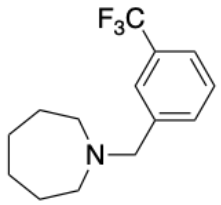

	Parameter	Value
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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
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9	Receiver Gain	107.0
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11	Pulse Width	12.0000
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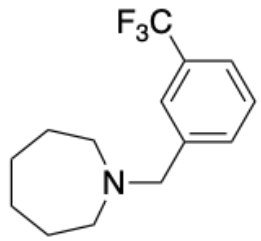
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
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8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
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15	Nucleus	13C
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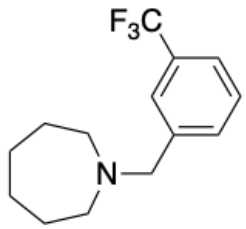

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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
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14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
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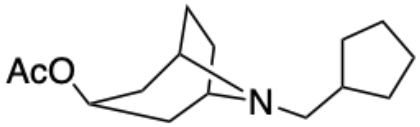

	Parameter	Value
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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
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8	Number of Scans	16
9	Receiver Gain	69.2
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11	Pulse Width	12.0000
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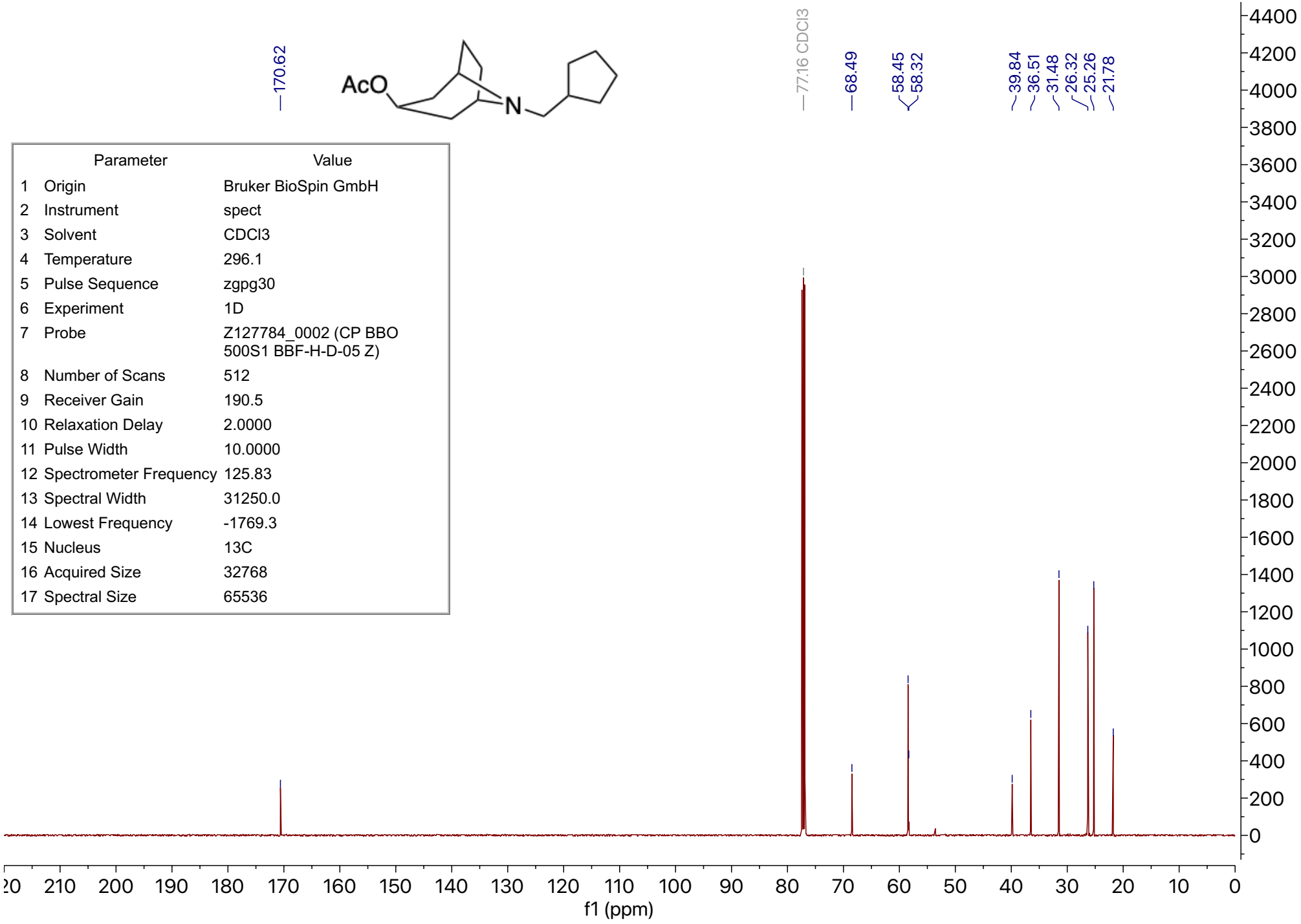

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2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
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8	Number of Scans	512
9	Receiver Gain	190.5
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14	Lowest Frequency	-1769.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
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2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
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11	Pulse Width	12.0000
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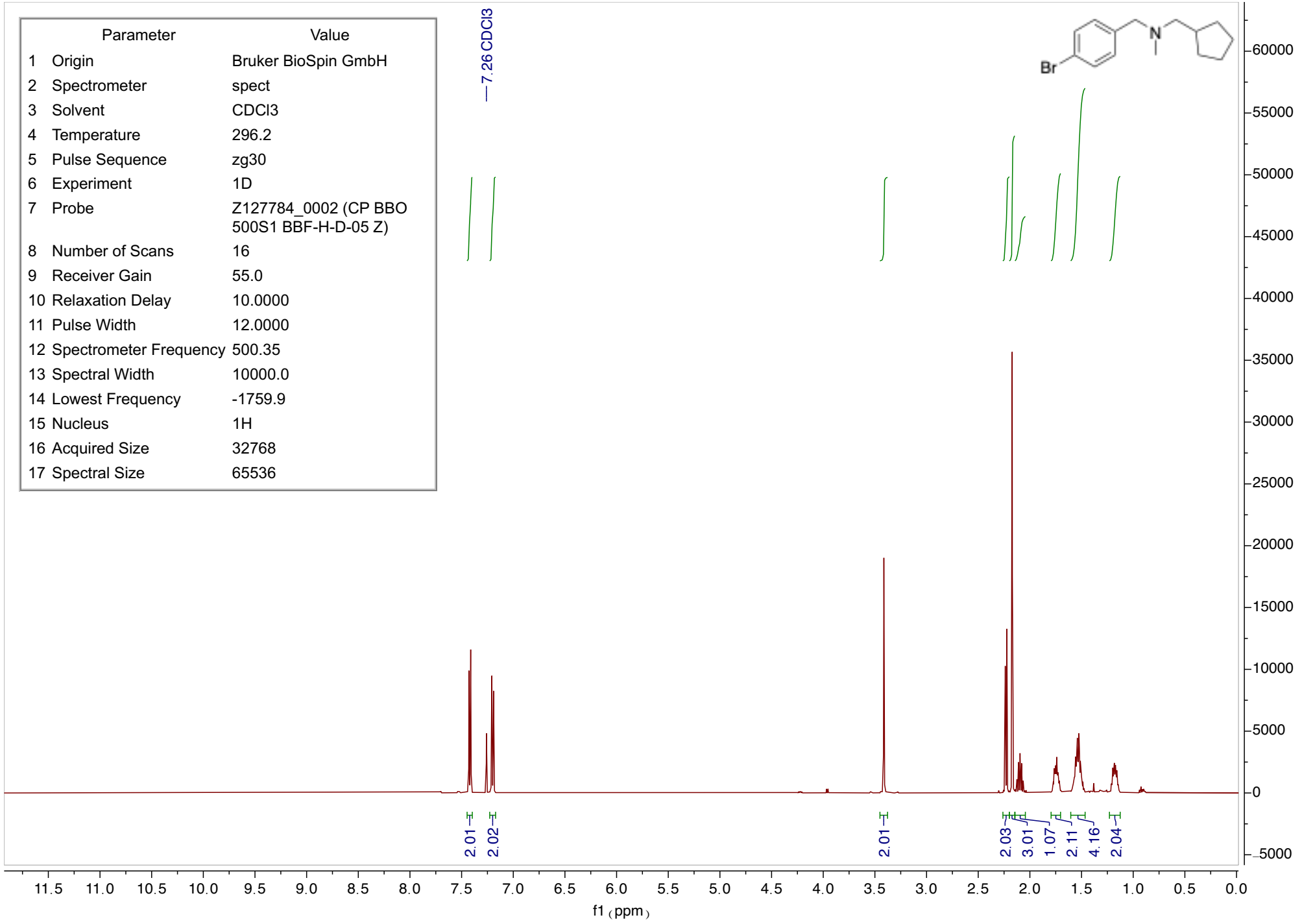

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4	Temperature	296.1
5	Pulse Sequence	zgpg30
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8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
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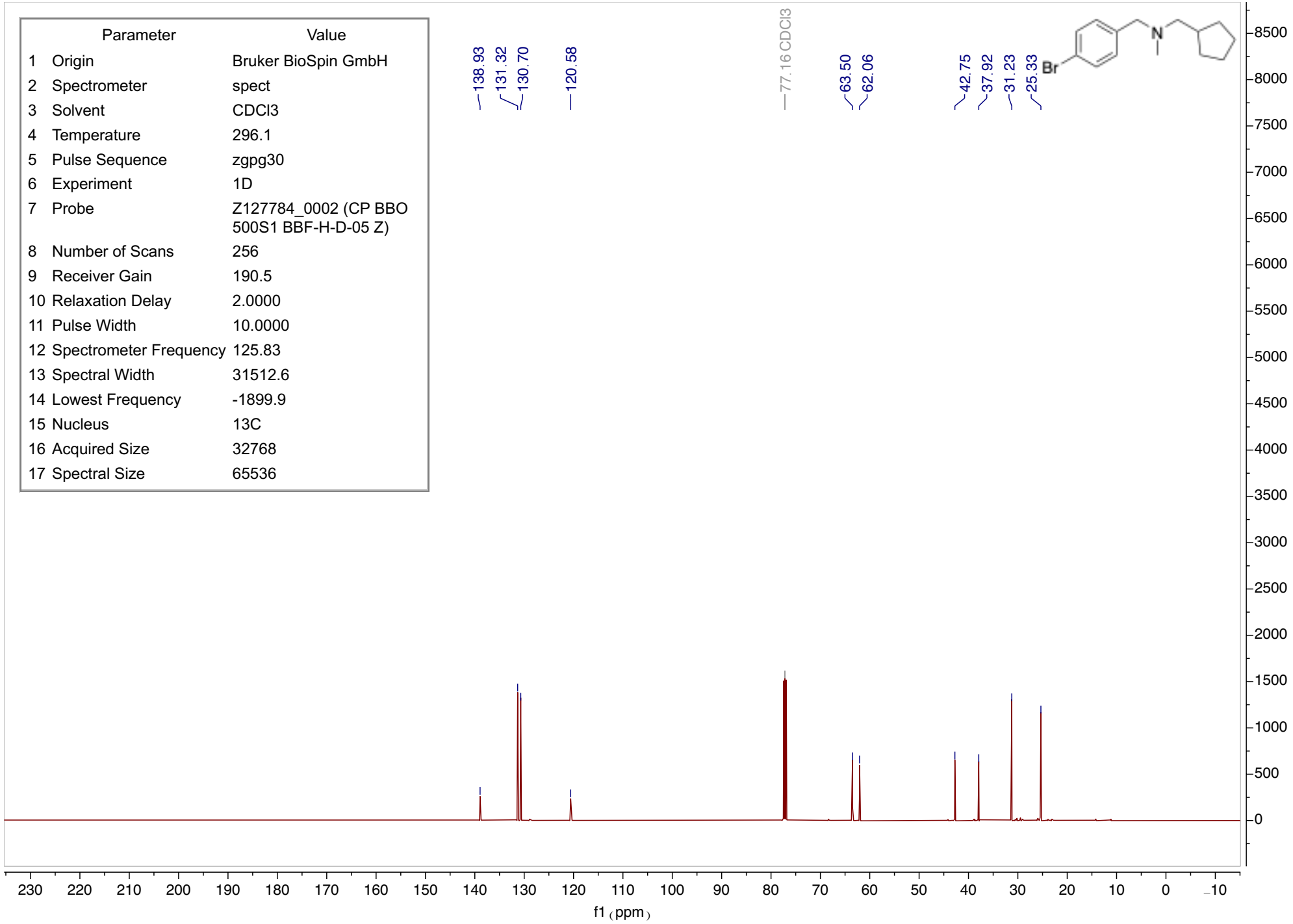

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4	Temperature	298.2
5	Pulse Sequence	zg30
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15	Nucleus	1H
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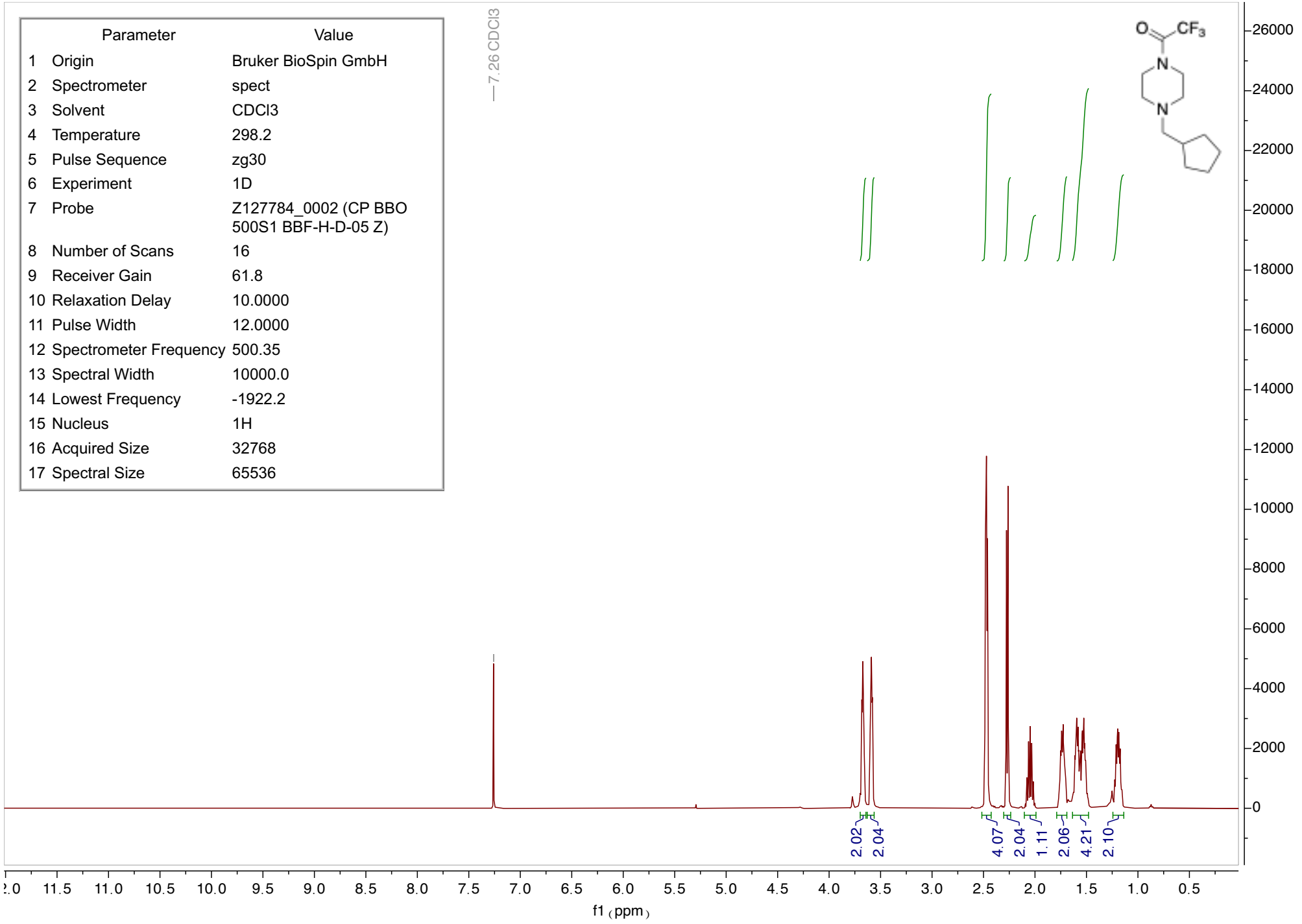

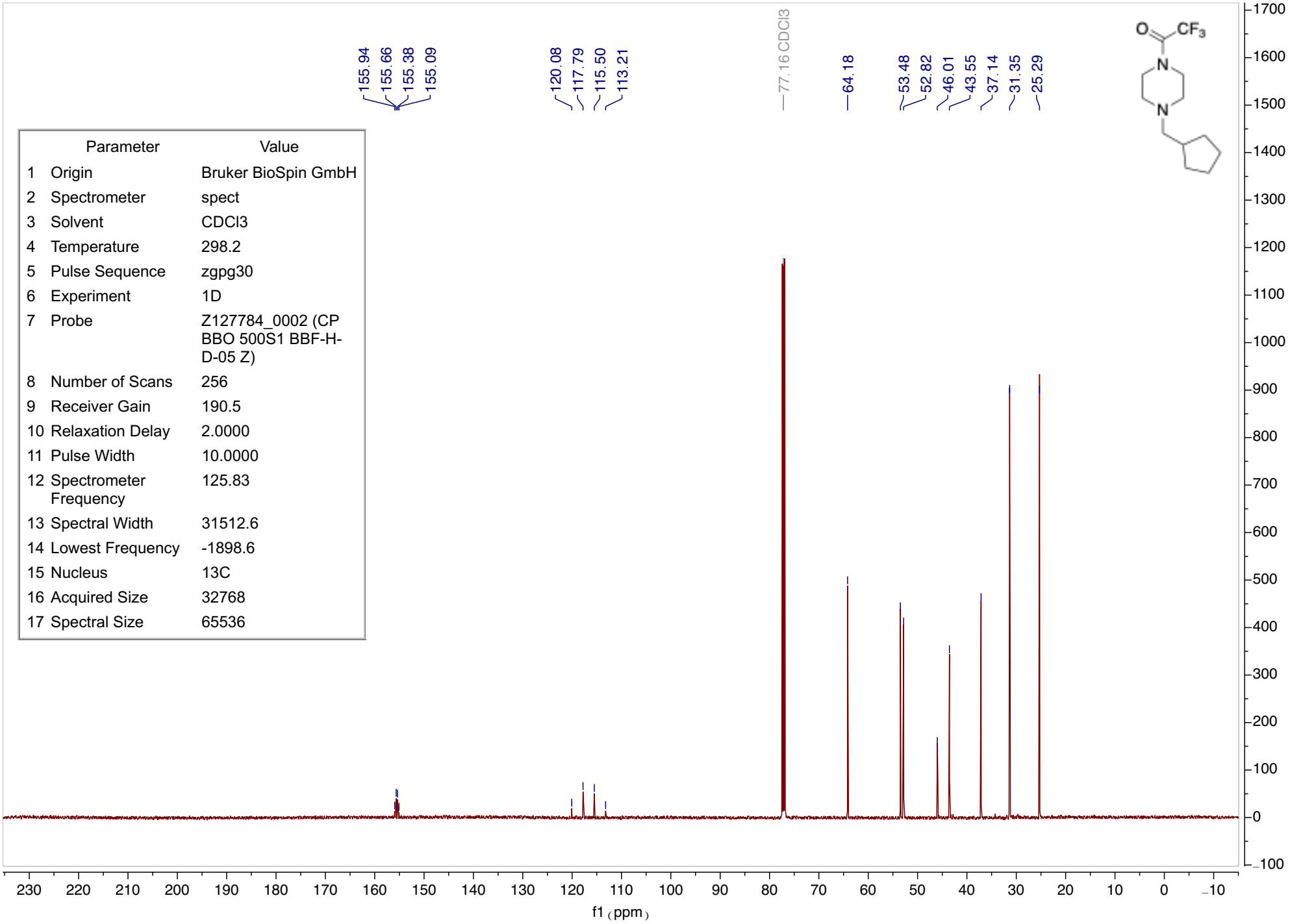

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9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
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8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
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15	Nucleus	19F
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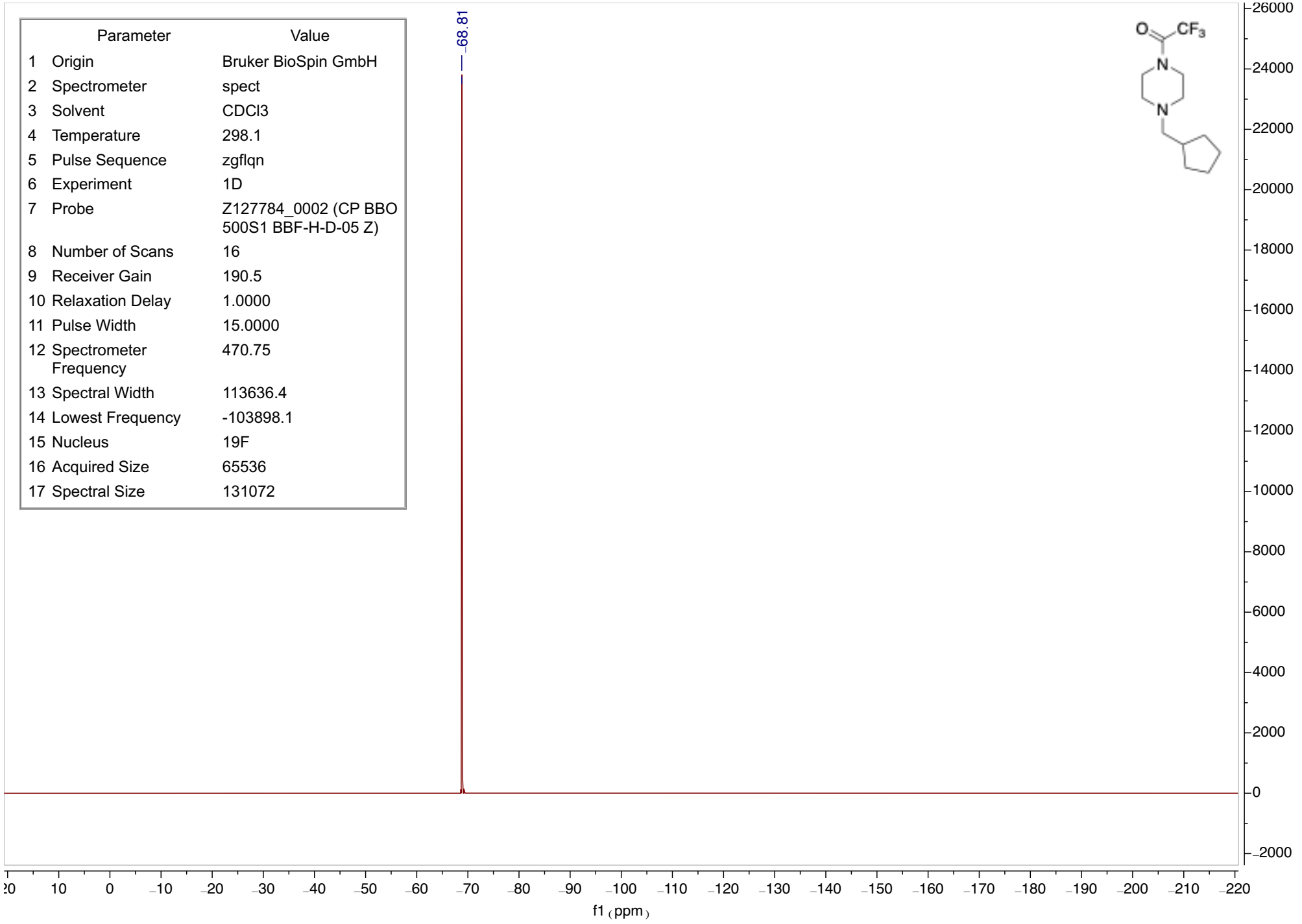

	Parameter	Value
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2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
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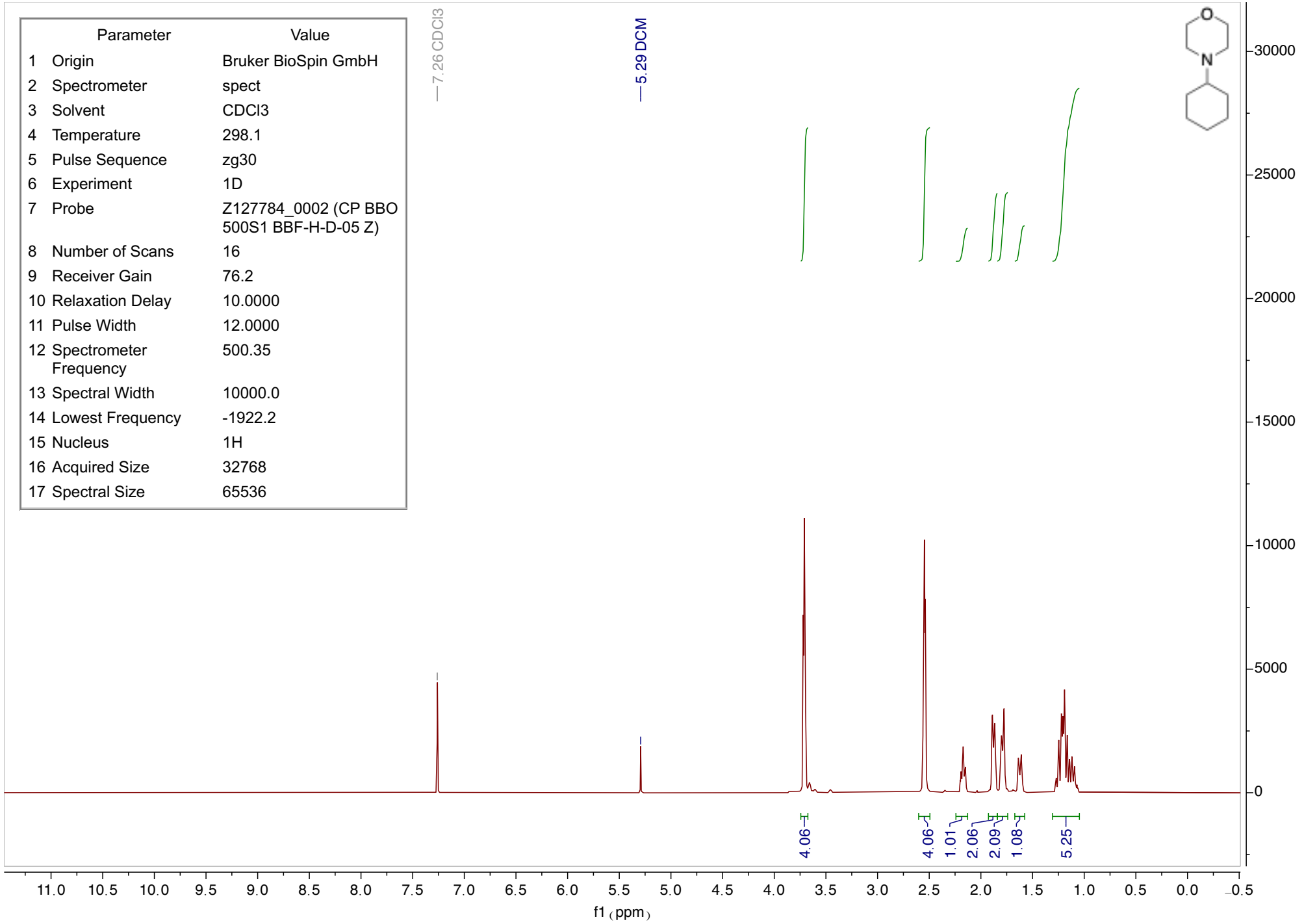

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8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
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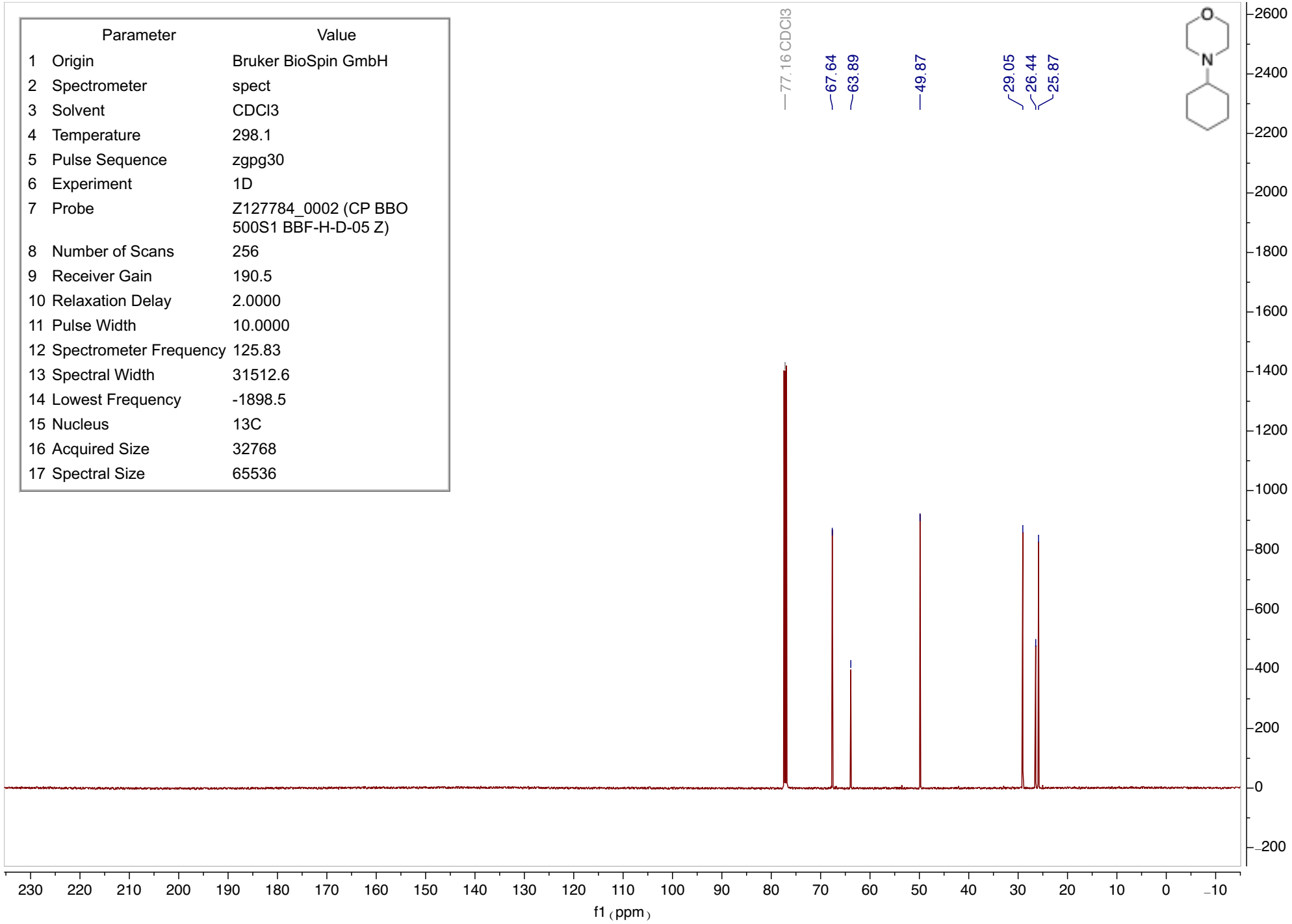

	Parameter	Value
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3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
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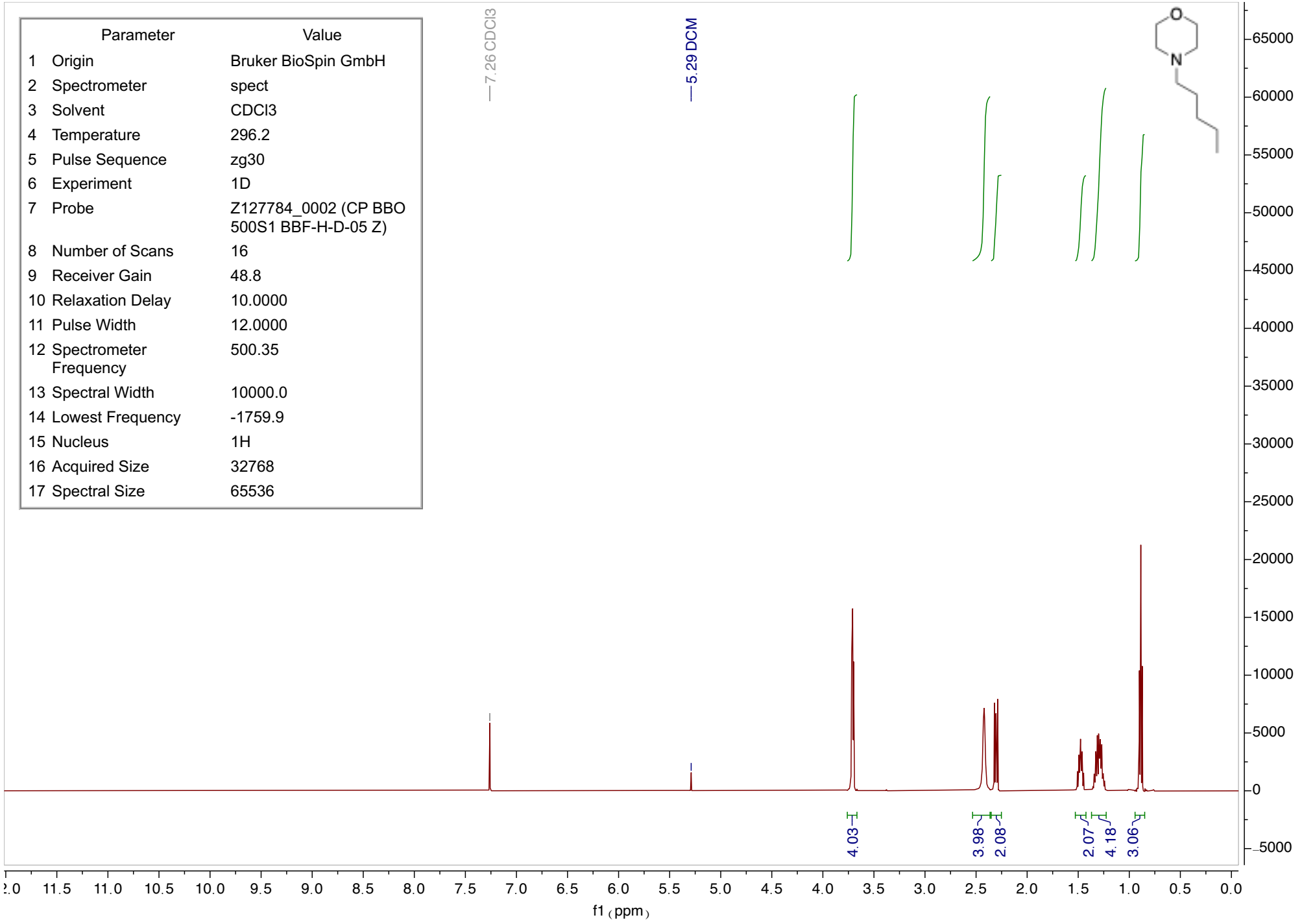
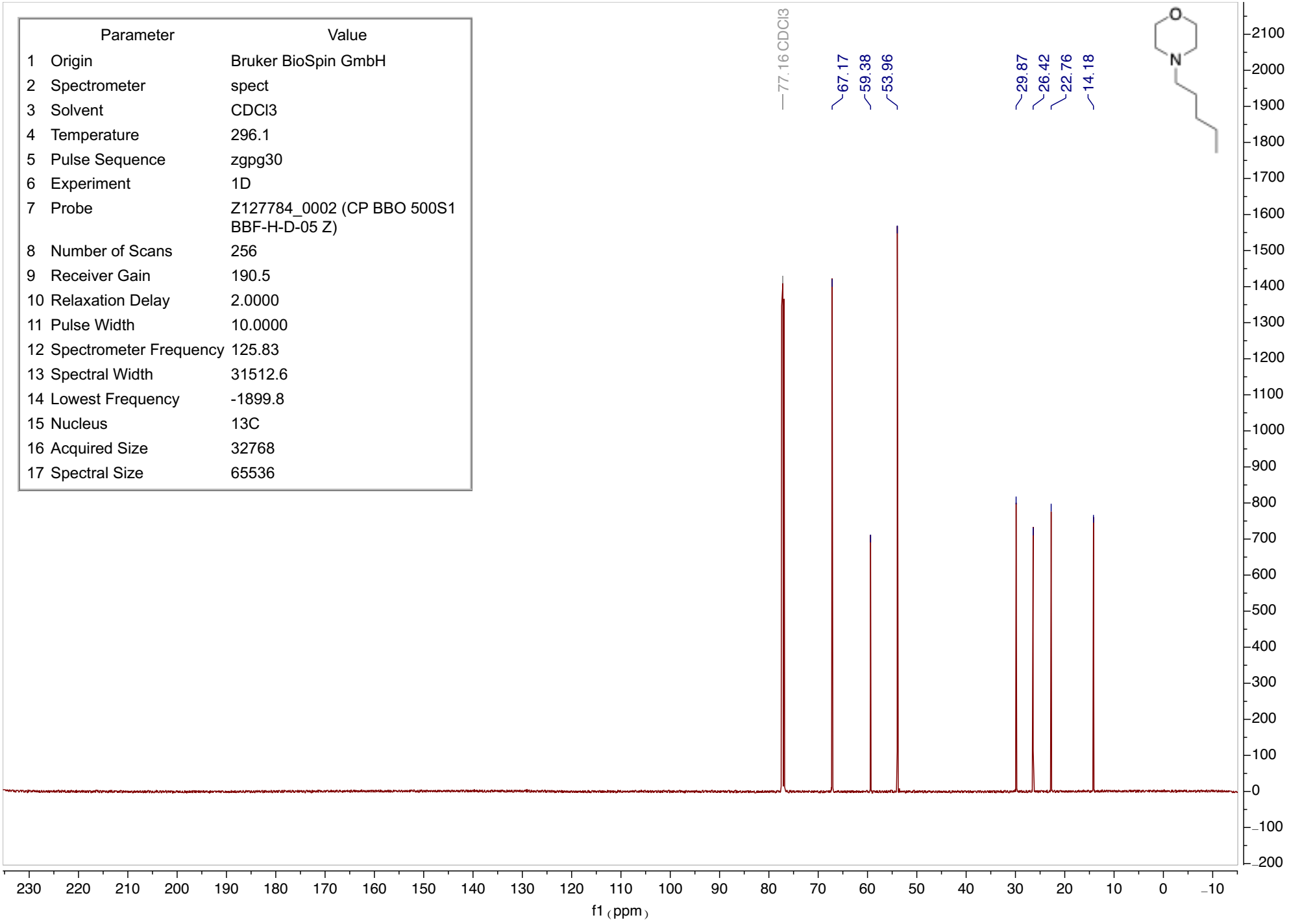
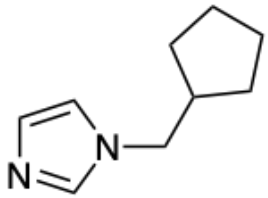
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

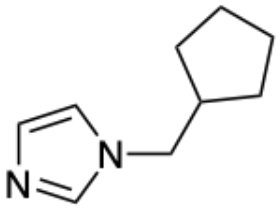


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



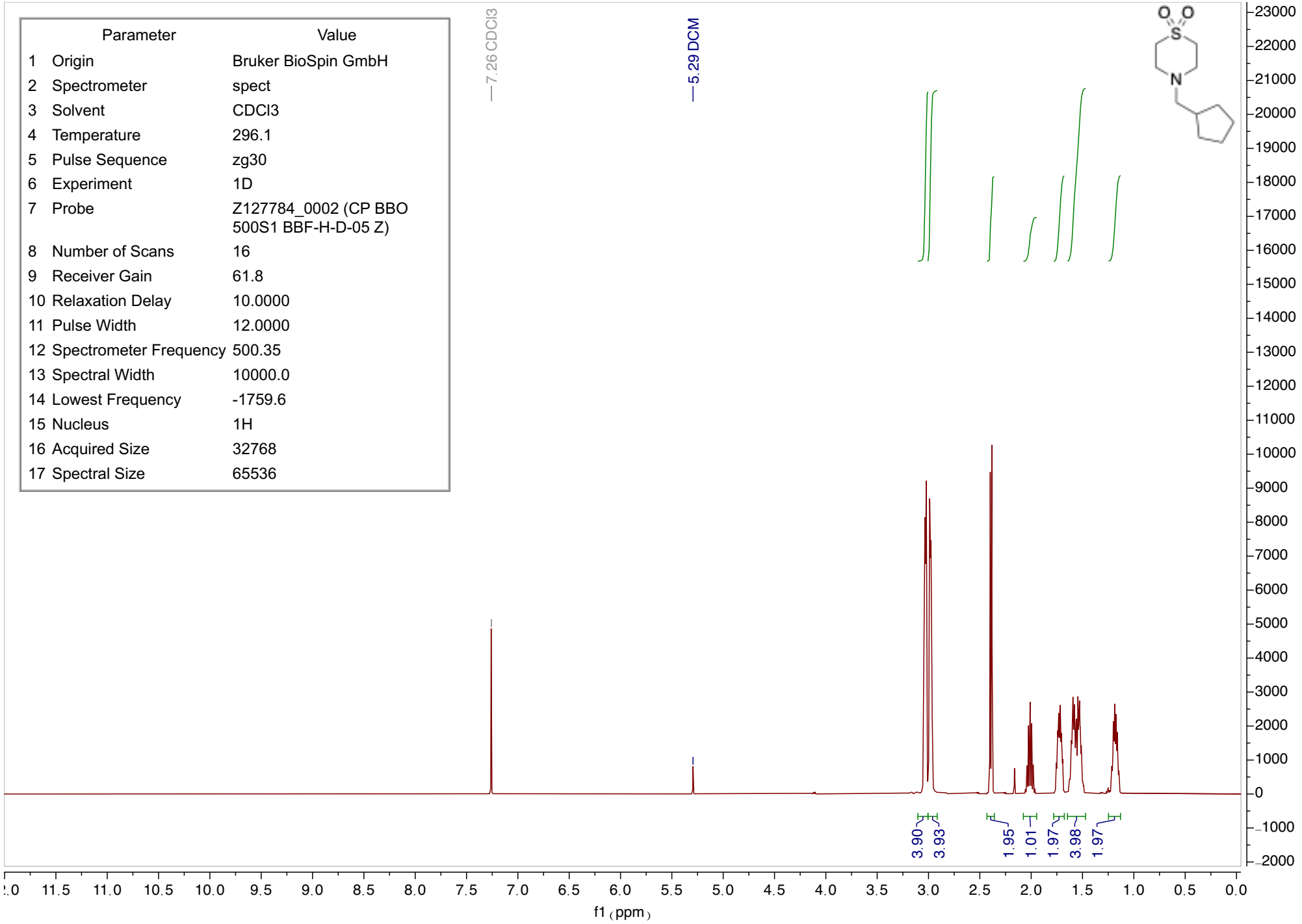


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

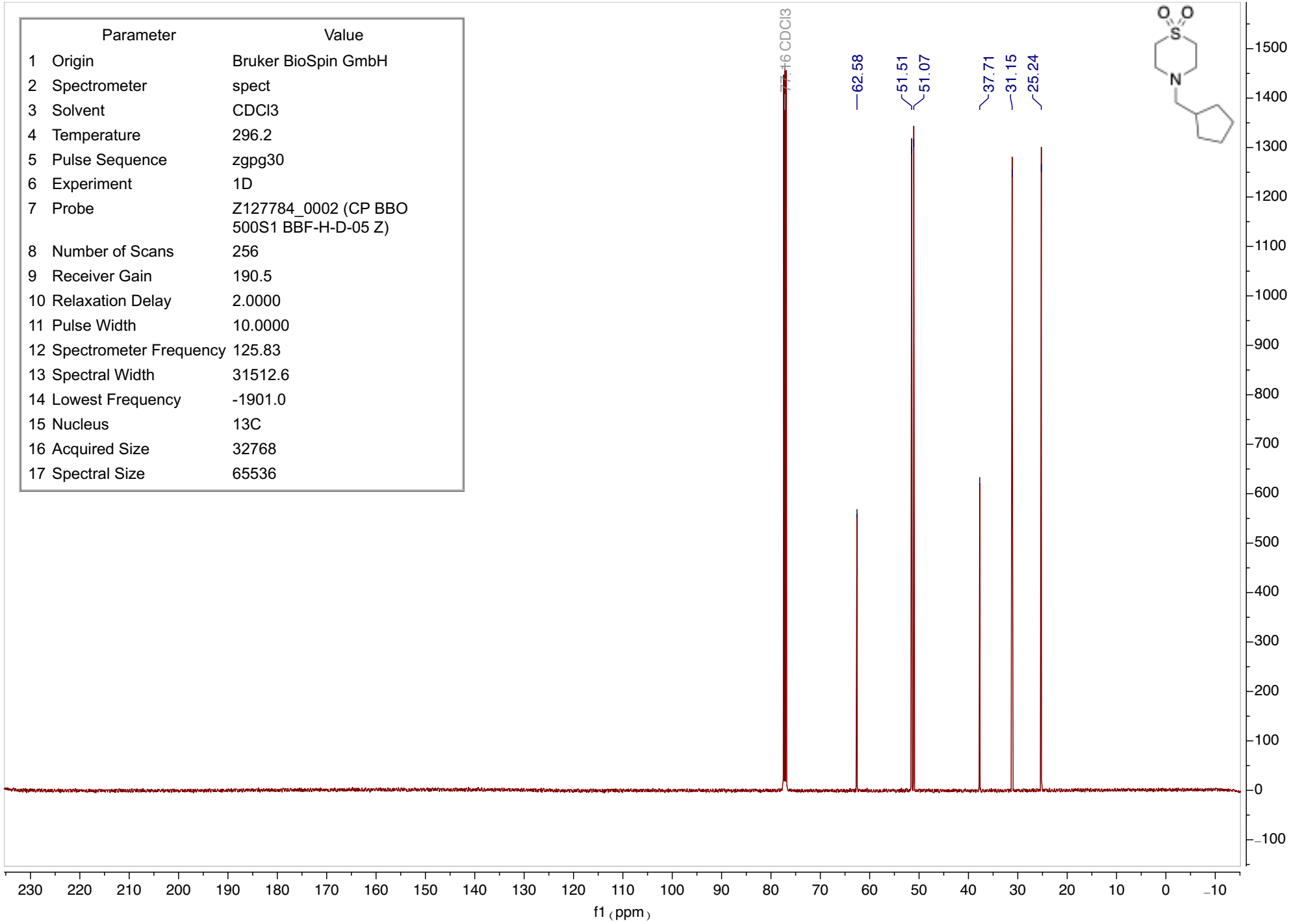


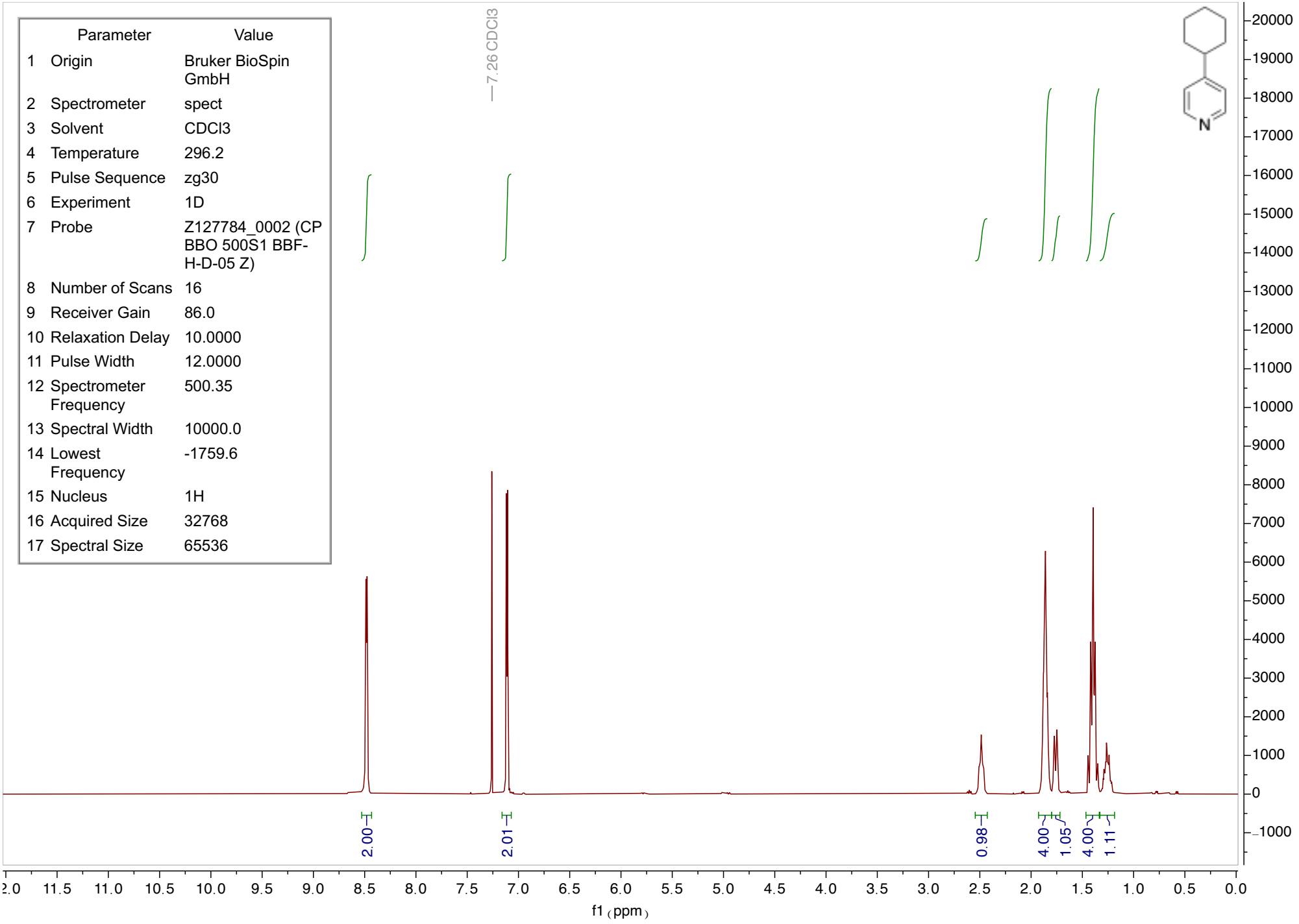
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	128
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1905.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



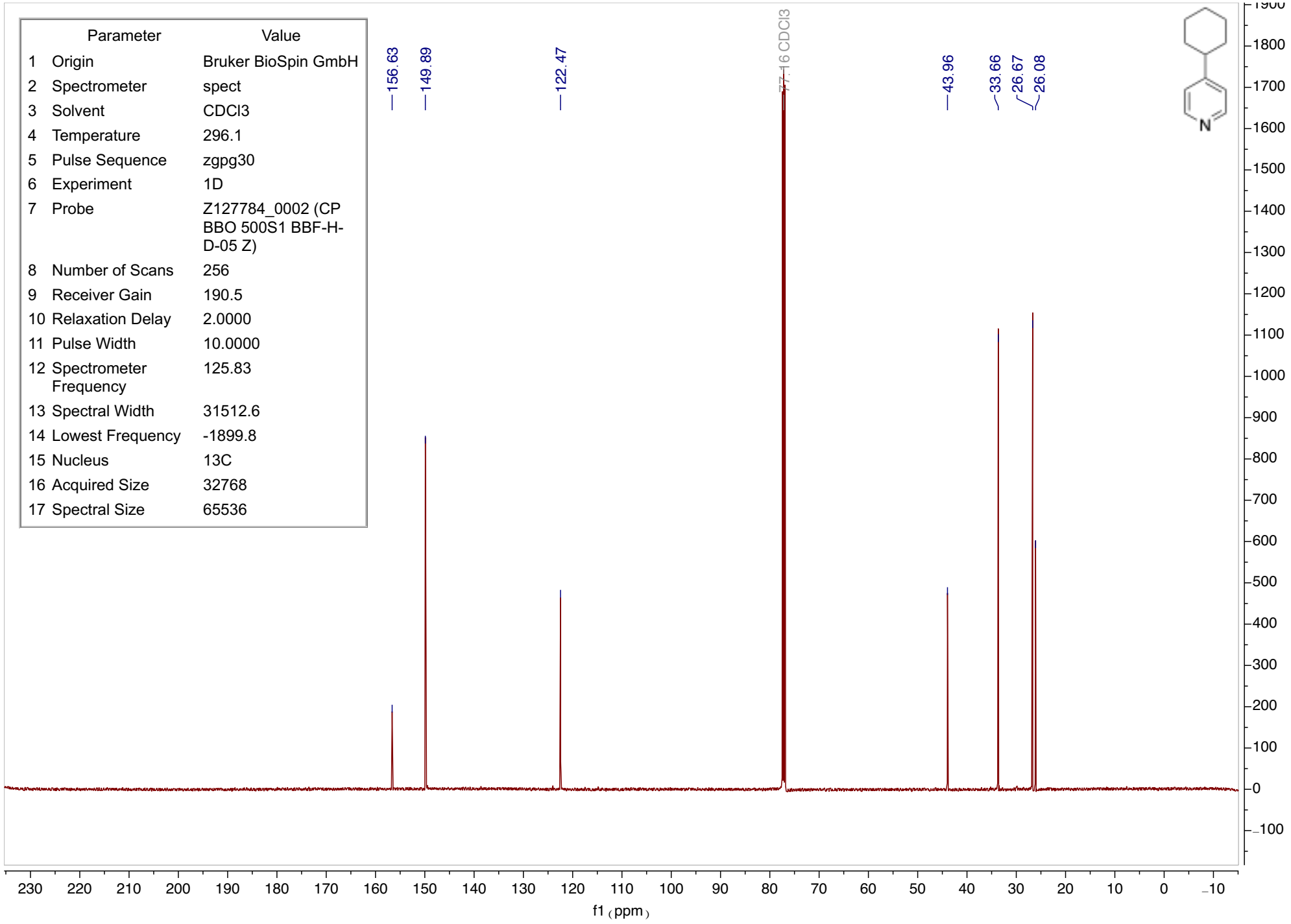
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

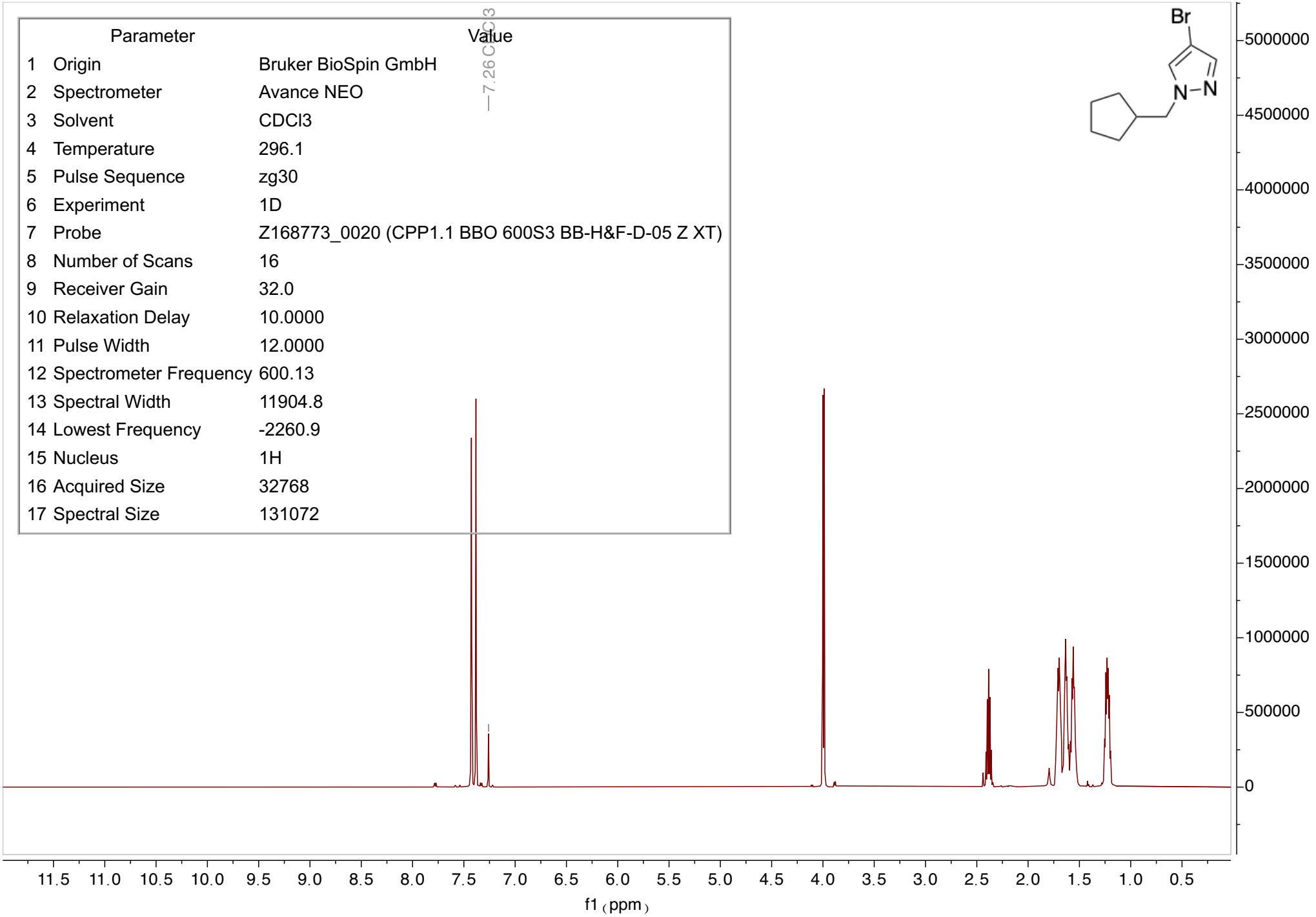




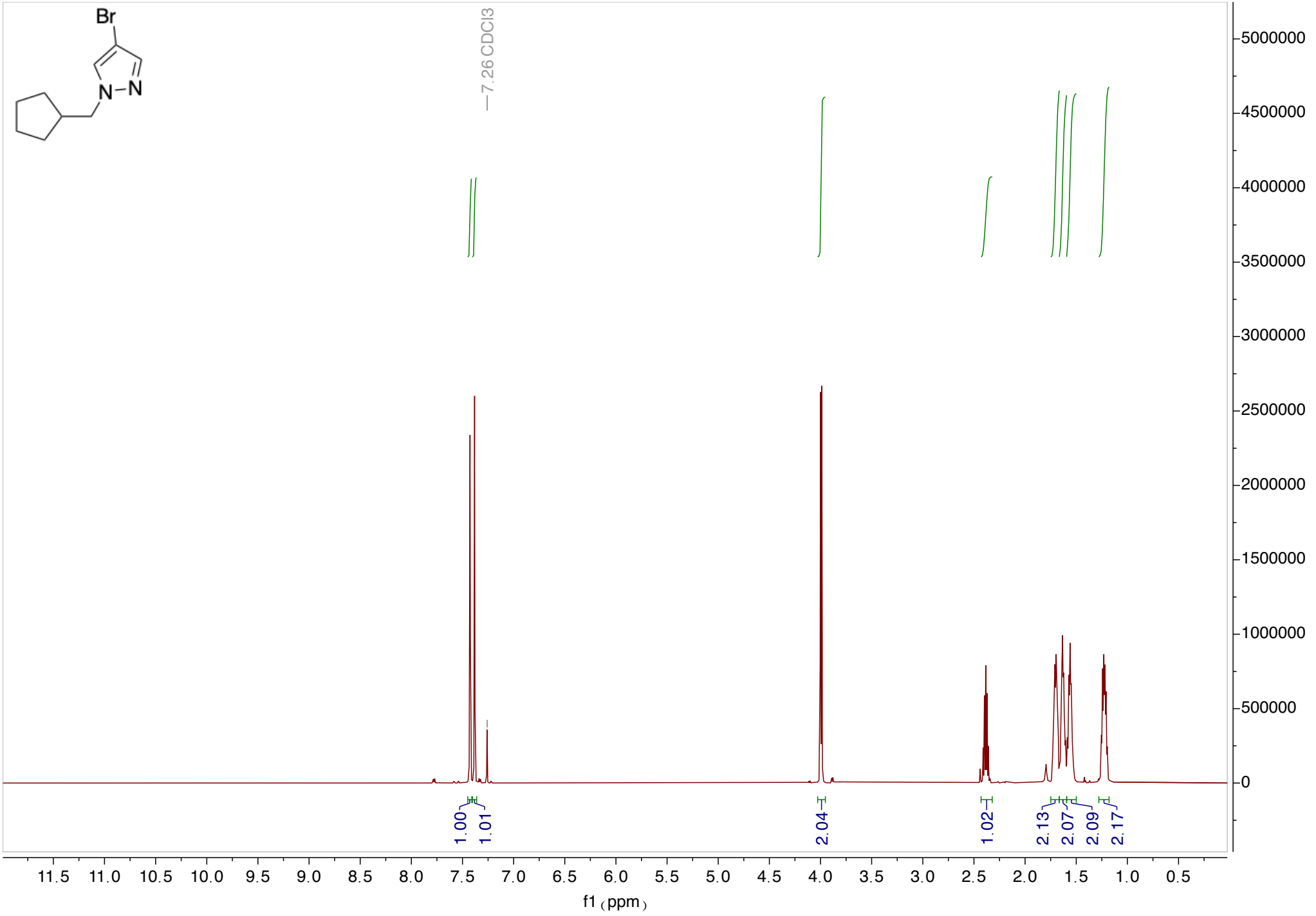
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

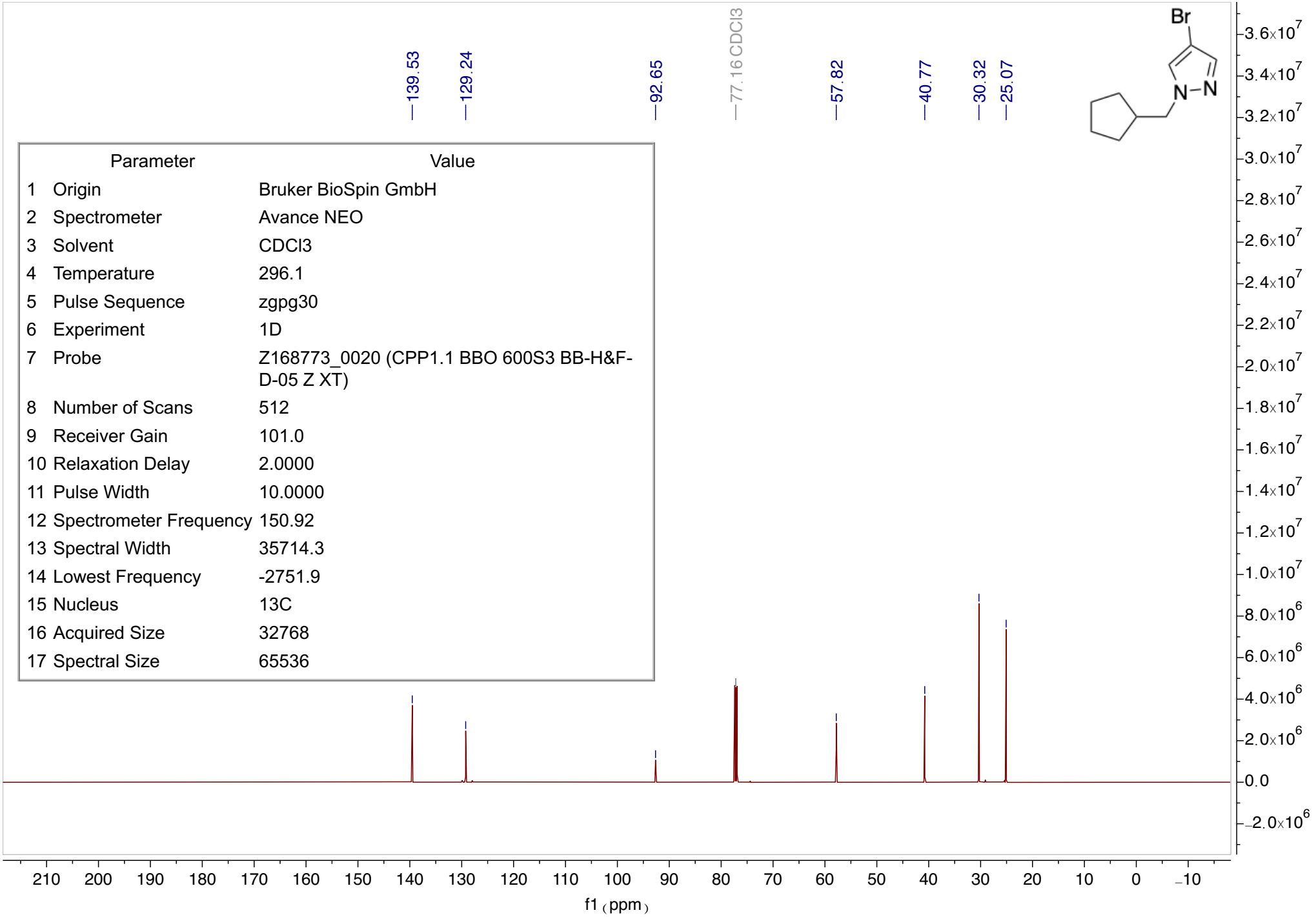
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536





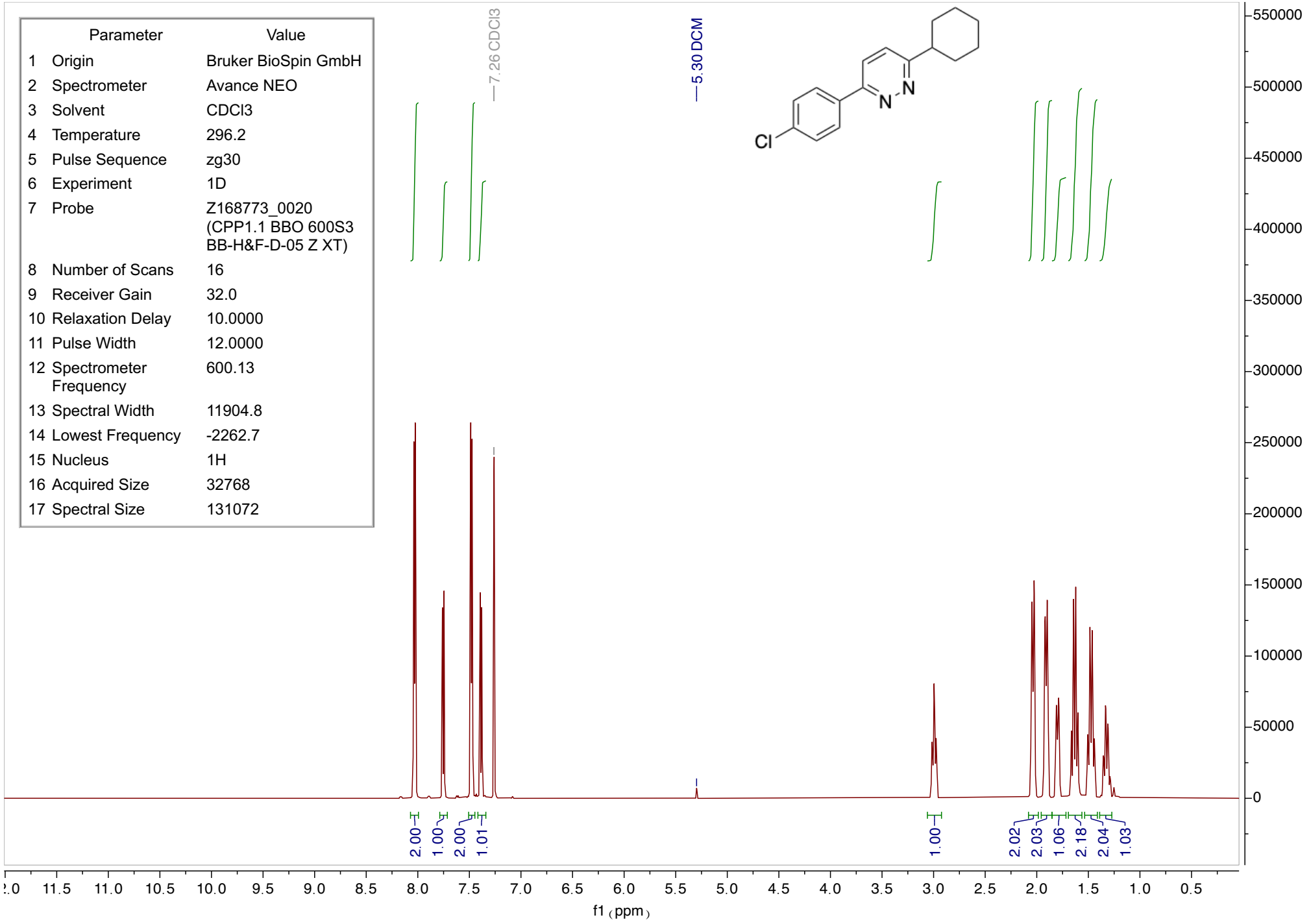
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2260.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

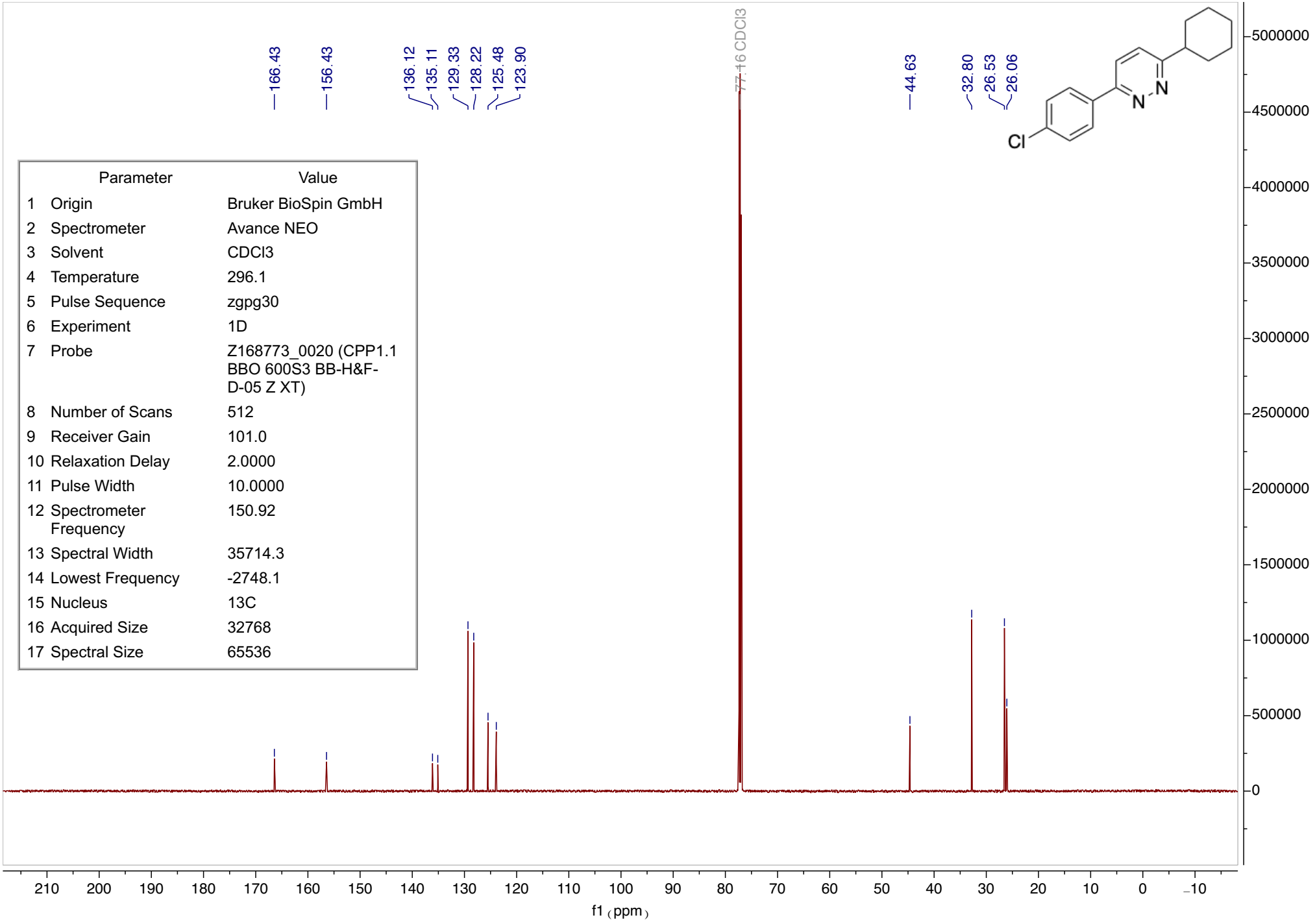

Br
N–N
7.26 CDCl3
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
1.00
1.01
2.04
1.02
2.13
2.07
2.09
2.17
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



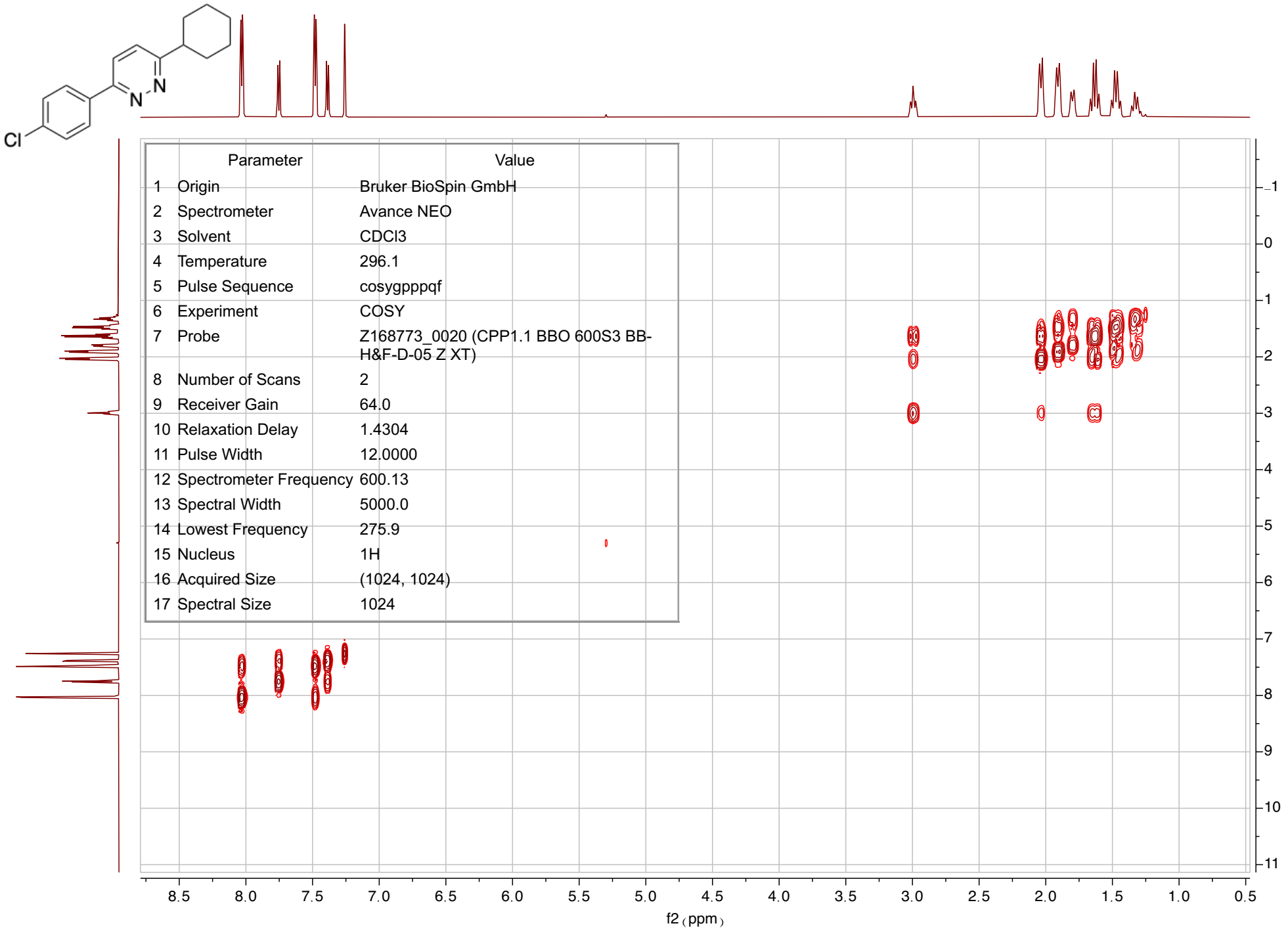
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	512
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2751.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

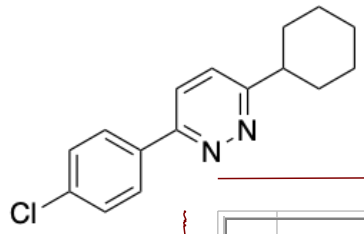
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2262.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



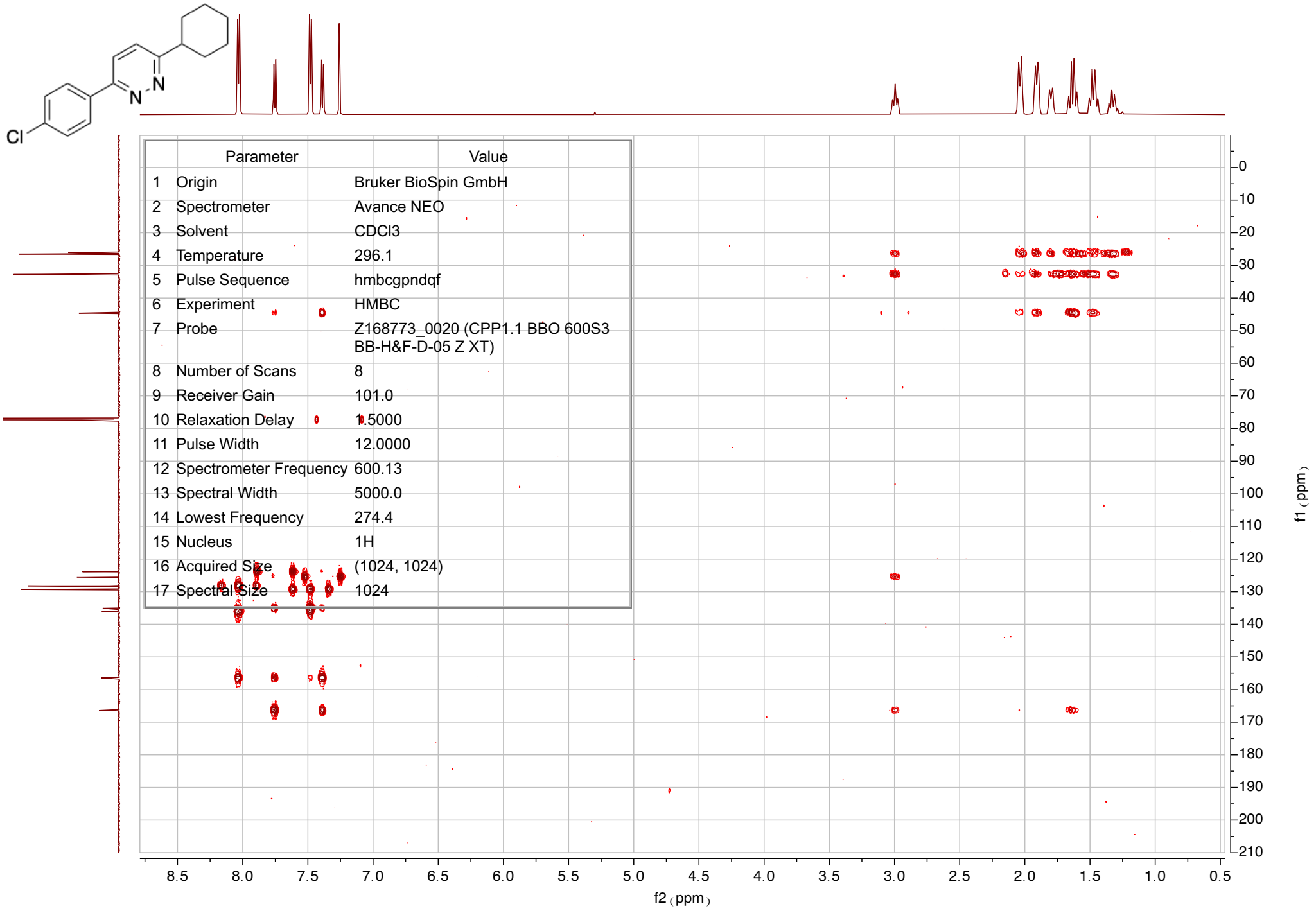


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	512
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2748.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

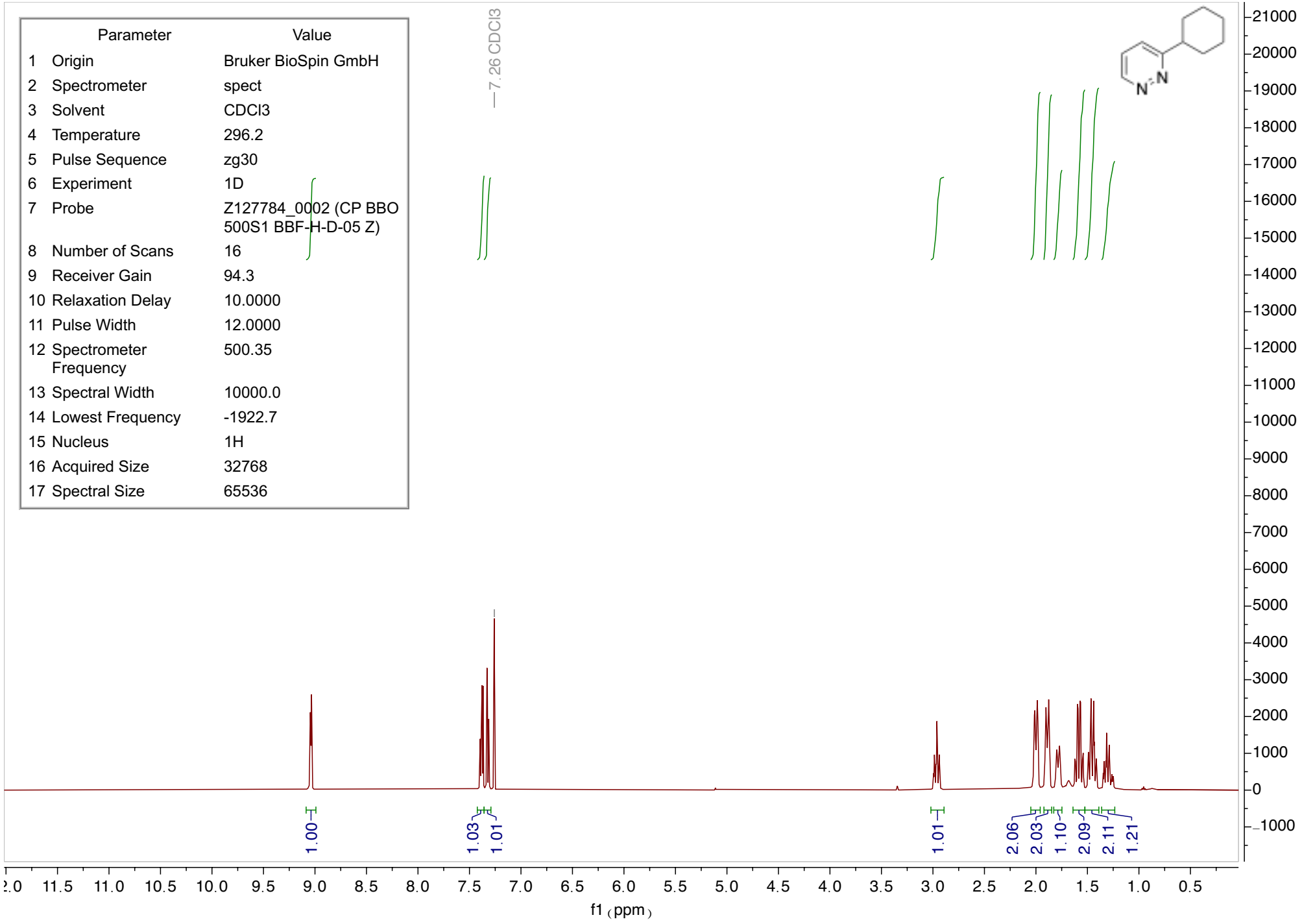

Cl
N
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 2
9 Receiver Gain 64.0
10 Relaxation Delay 1.4304
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5000.0
14 Lowest Frequency 275.9
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
-1 0 1 2 3 4 5 6 7 8 9 10 11
f1 (ppm)



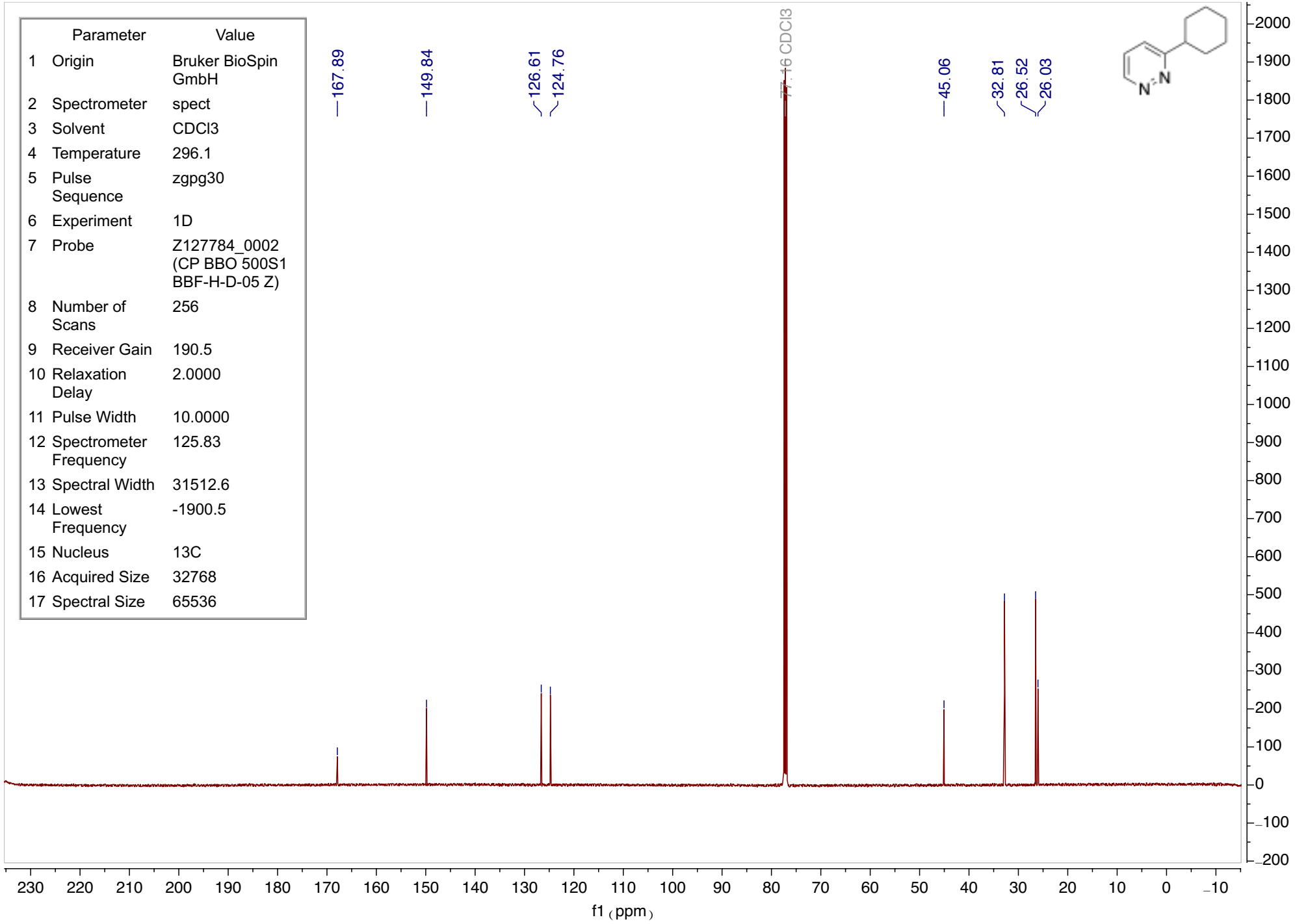
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5000.0
14	Lowest Frequency	276.0
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

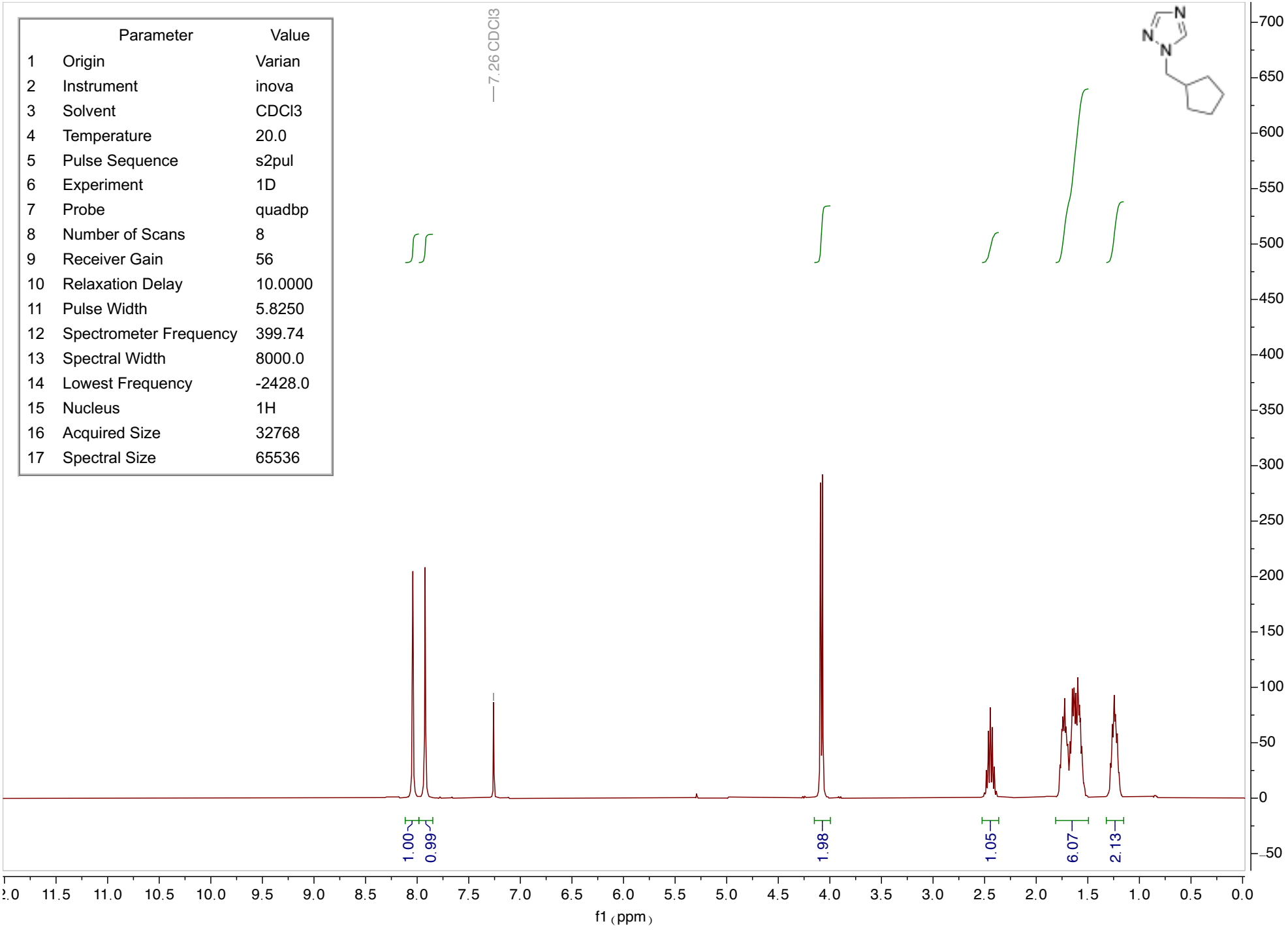

Cl
N
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence hmbcgpndqf
6 Experiment HMBC
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 8
9 Receiver Gain 101.0
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5000.0
14 Lowest Frequency 274.4
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	94.3
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



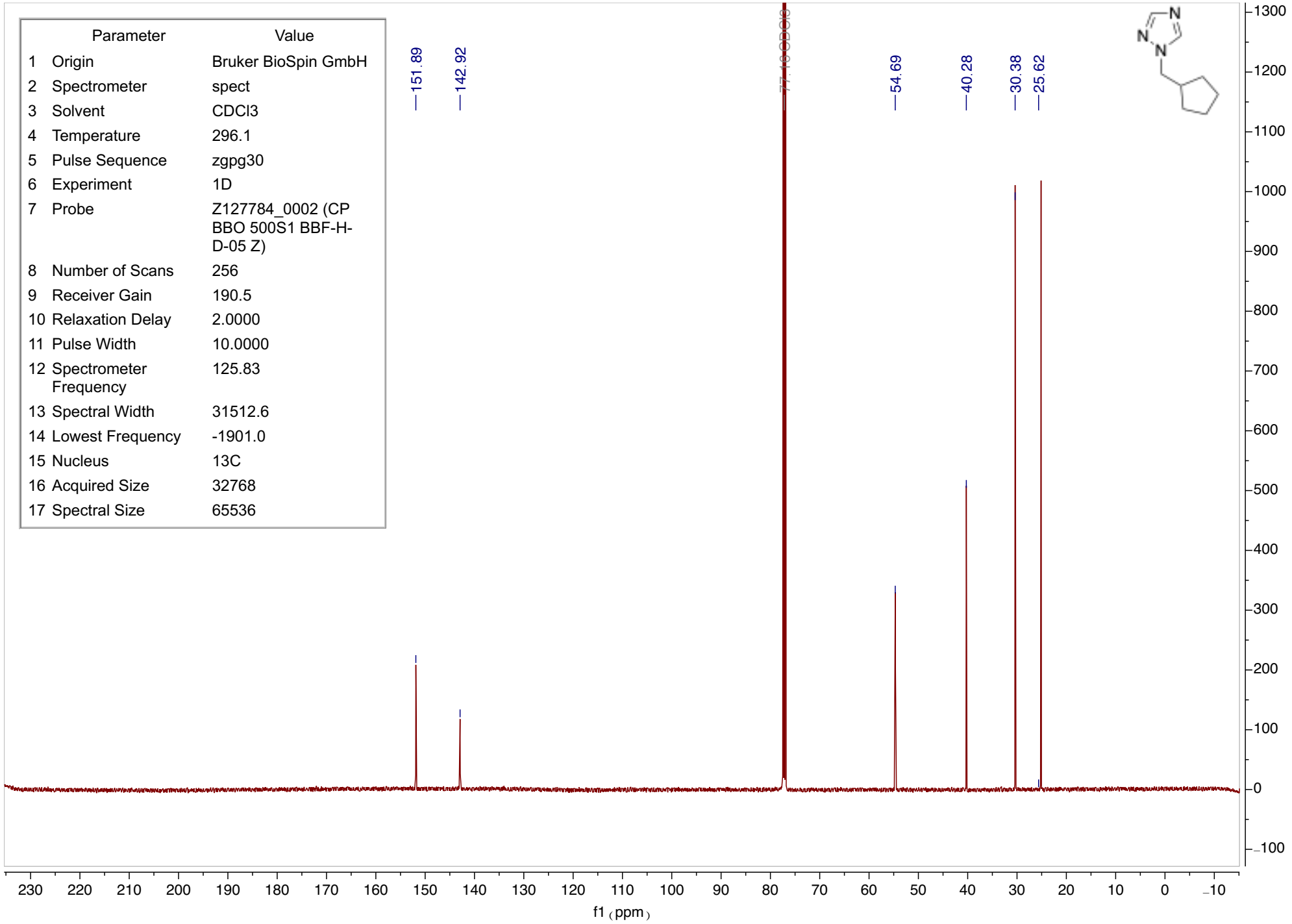
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

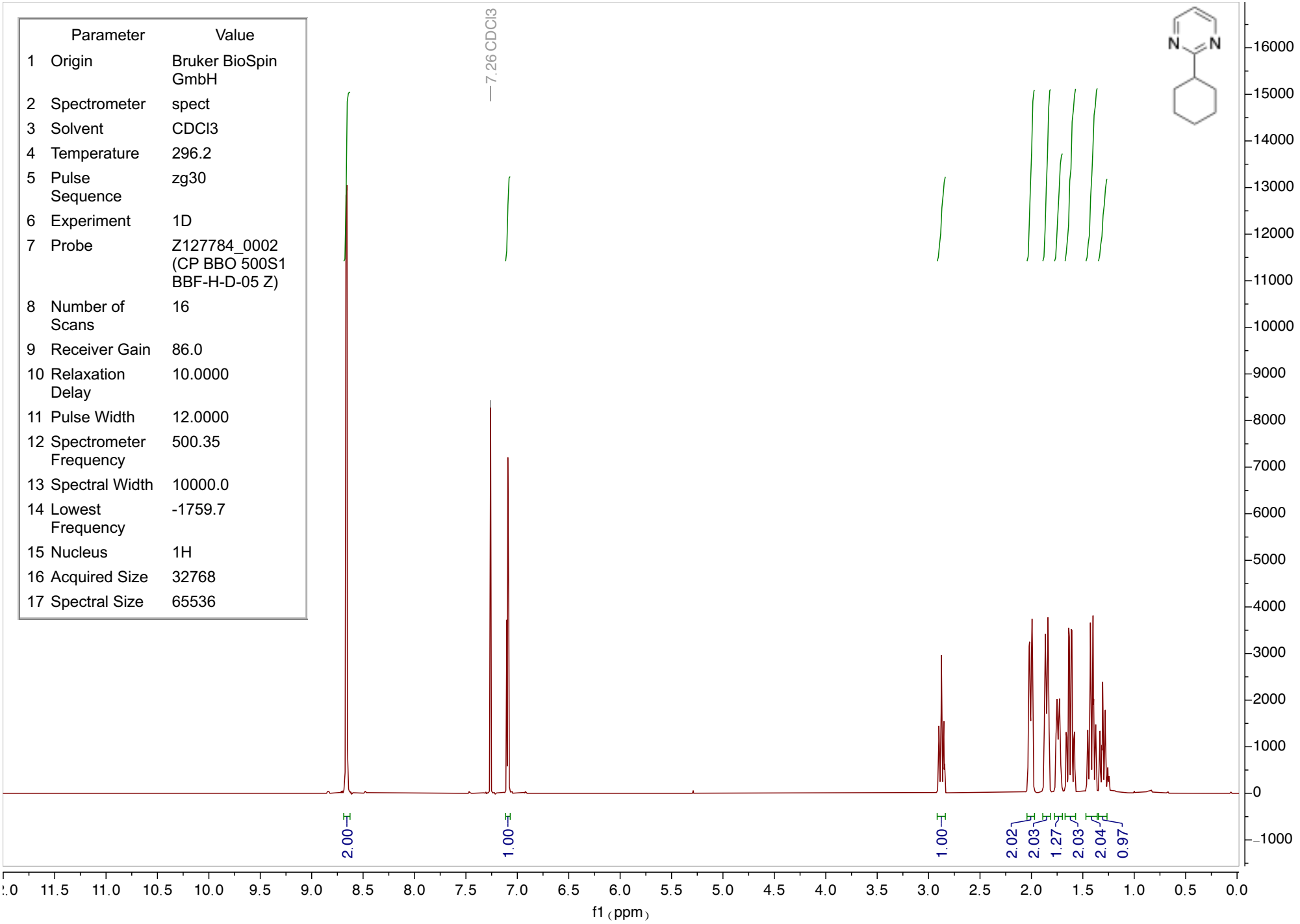




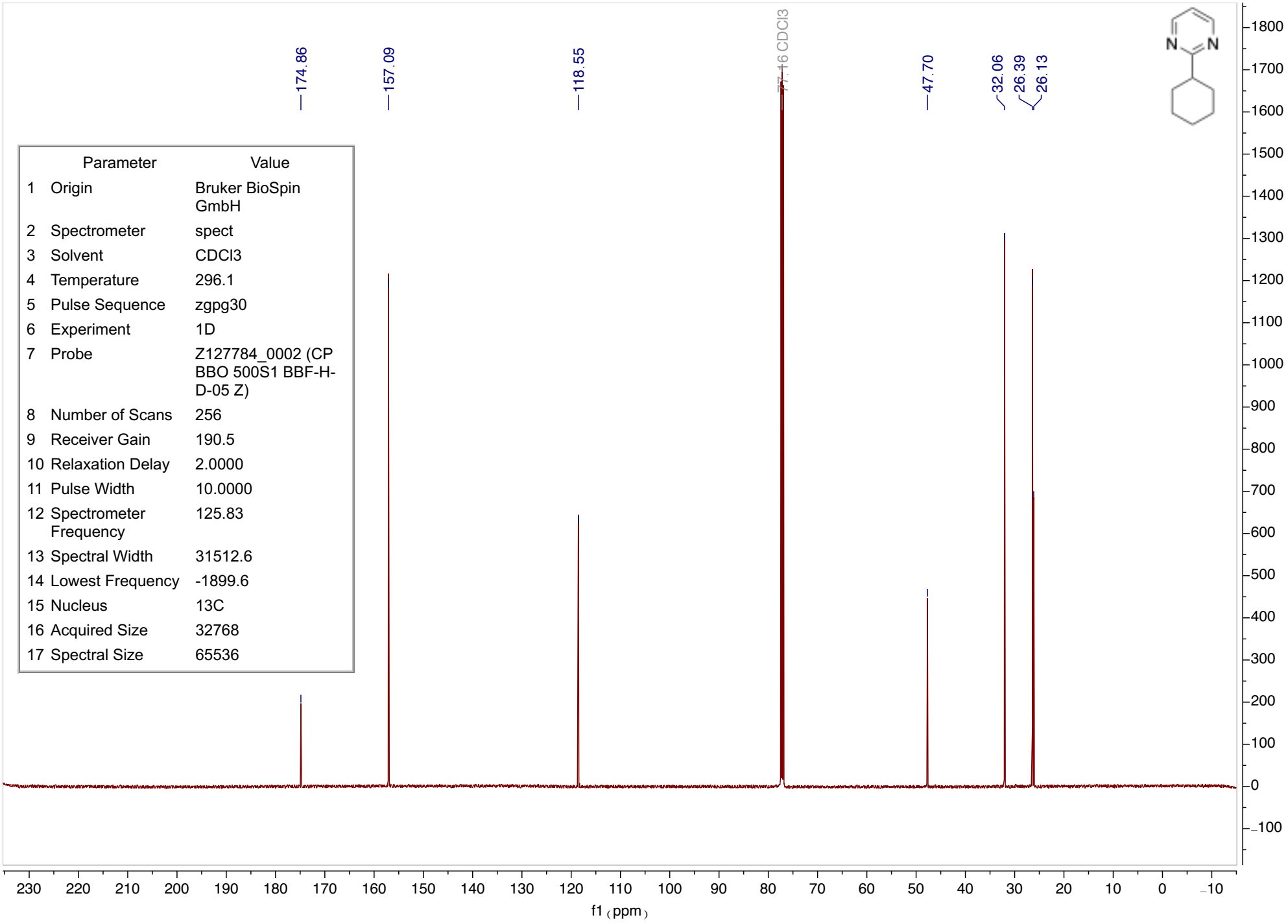
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	quadbp
8	Number of Scans	8
9	Receiver Gain	56
10	Relaxation Delay	10.0000
11	Pulse Width	5.8250
12	Spectrometer Frequency	399.74
13	Spectral Width	8000.0
14	Lowest Frequency	-2428.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



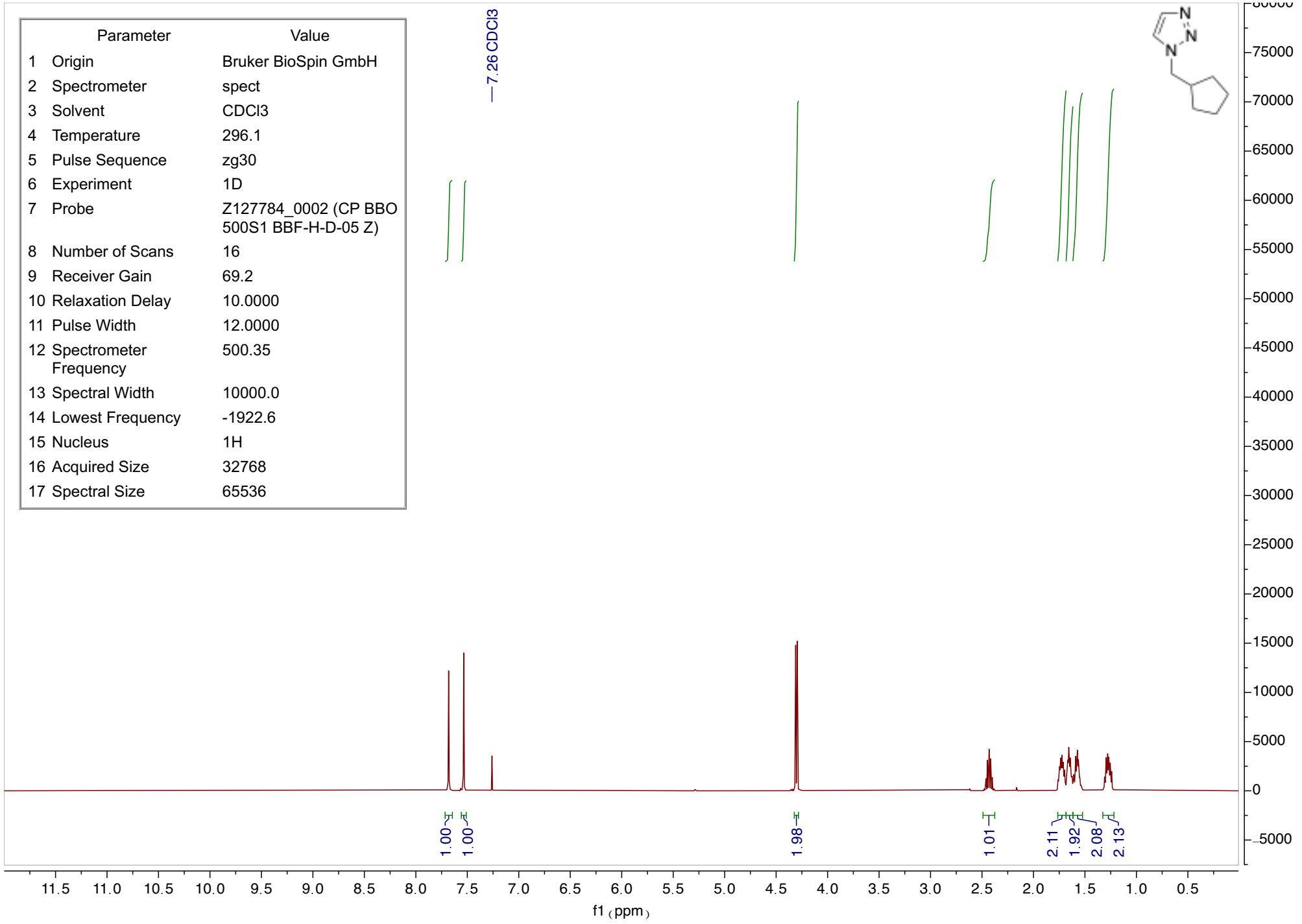


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

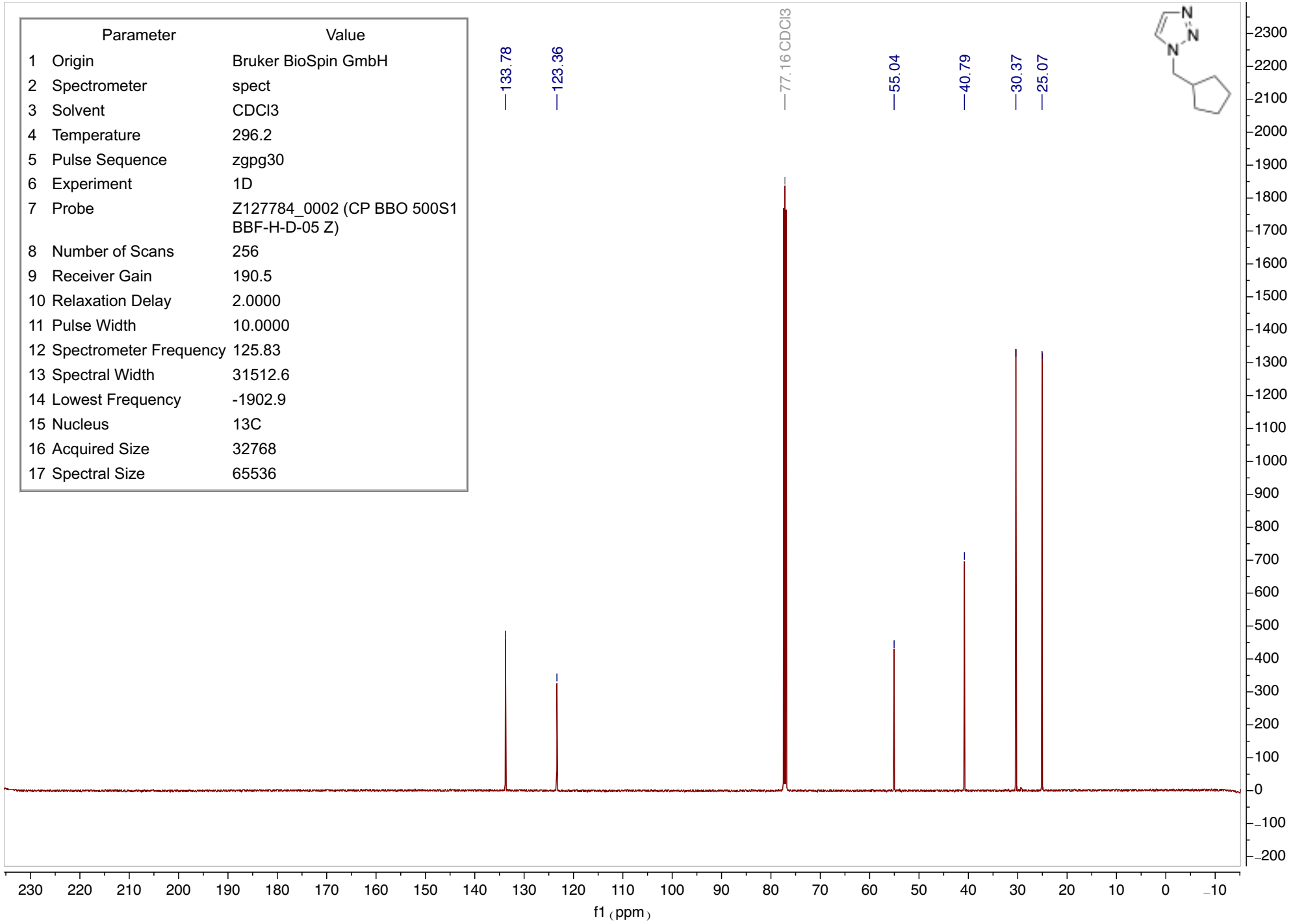


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

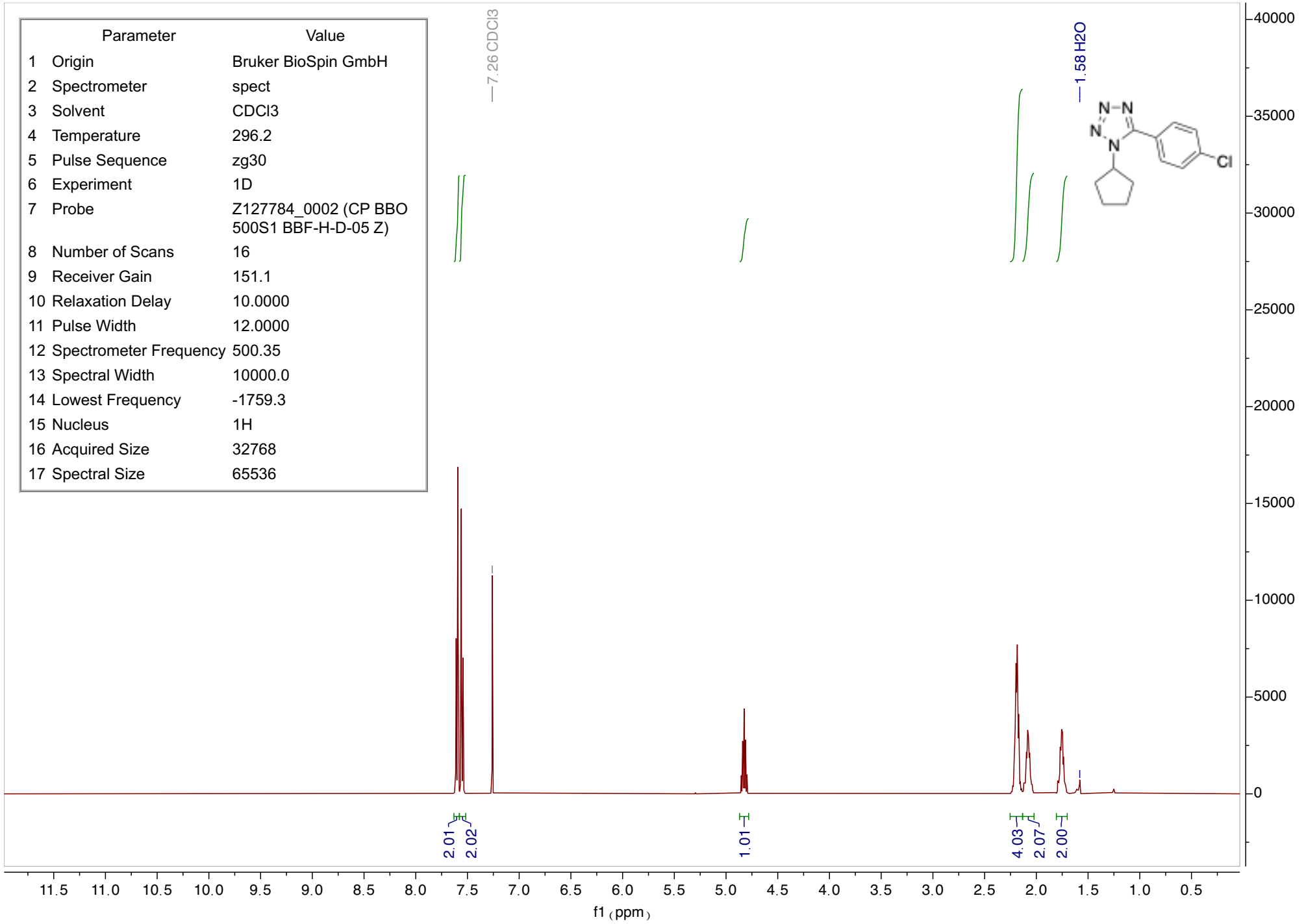
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	69.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

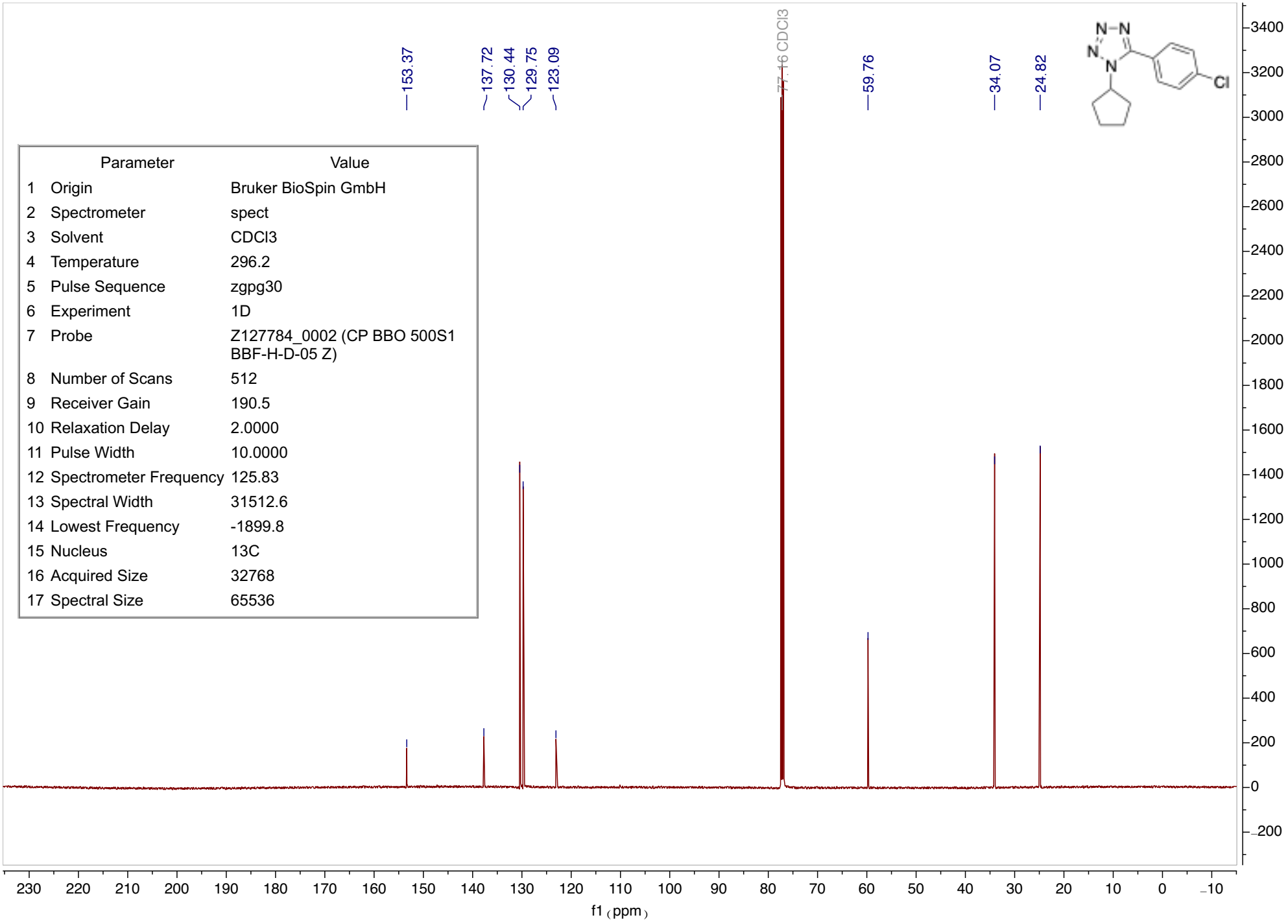


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

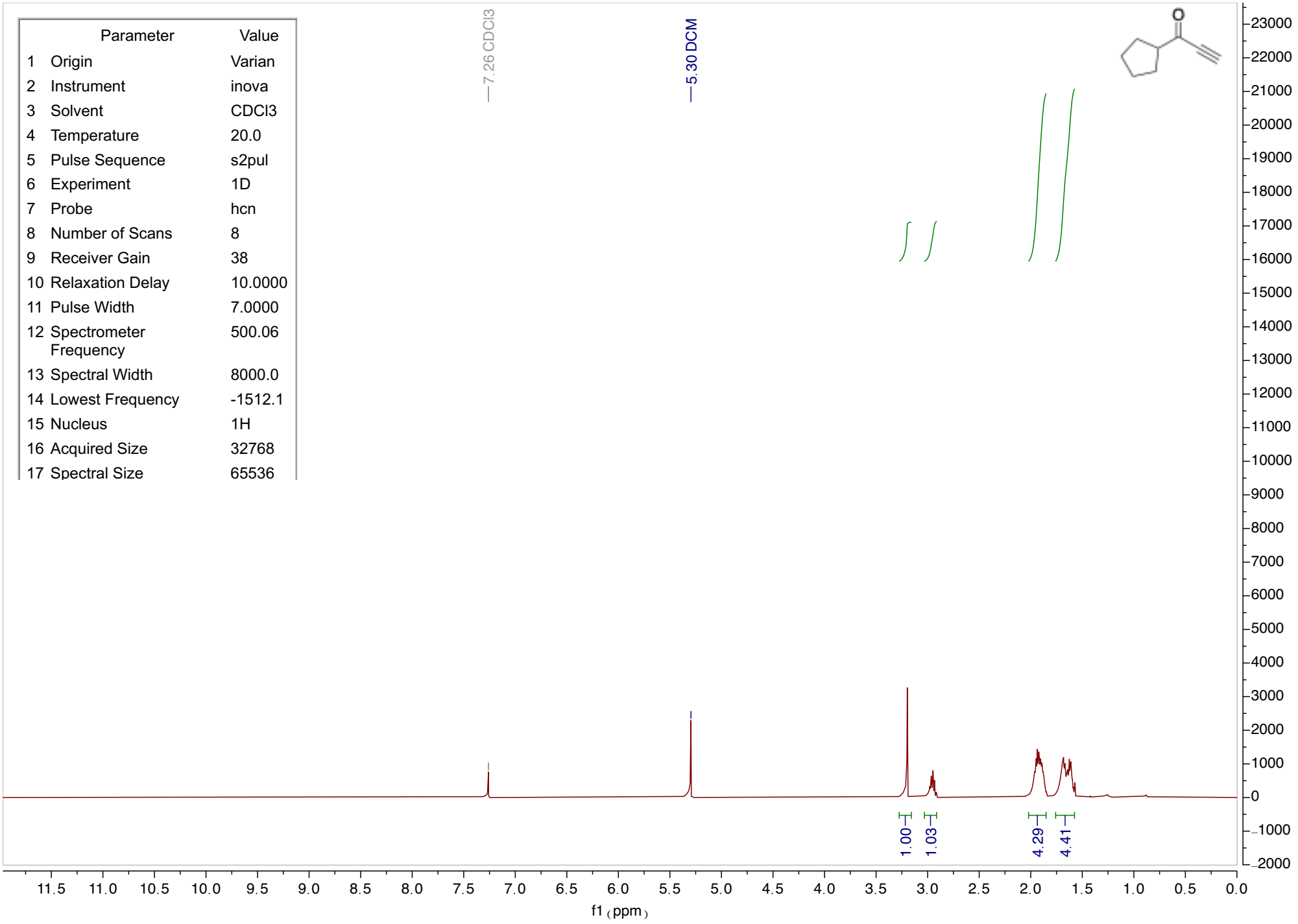


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	151.1
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

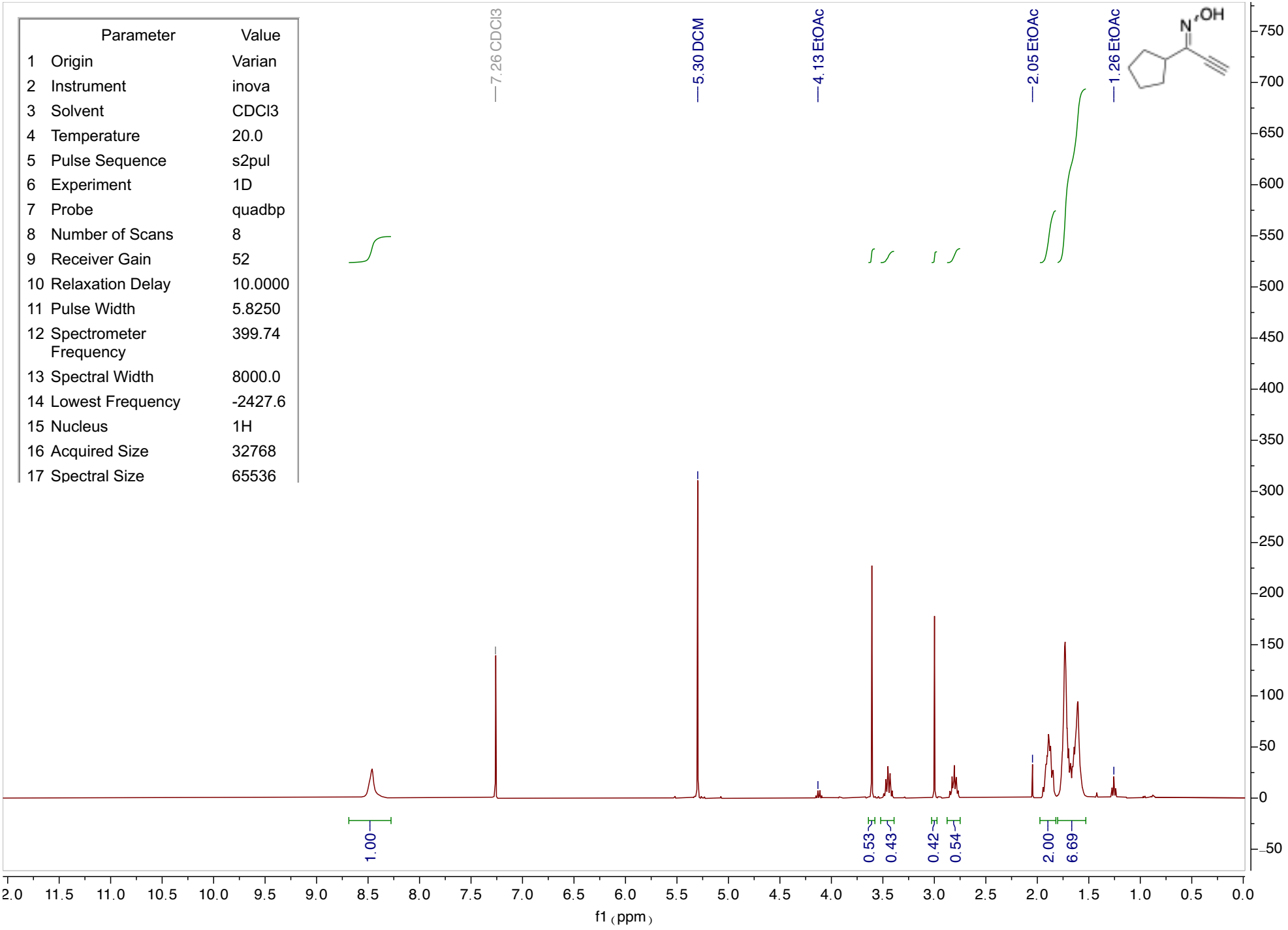




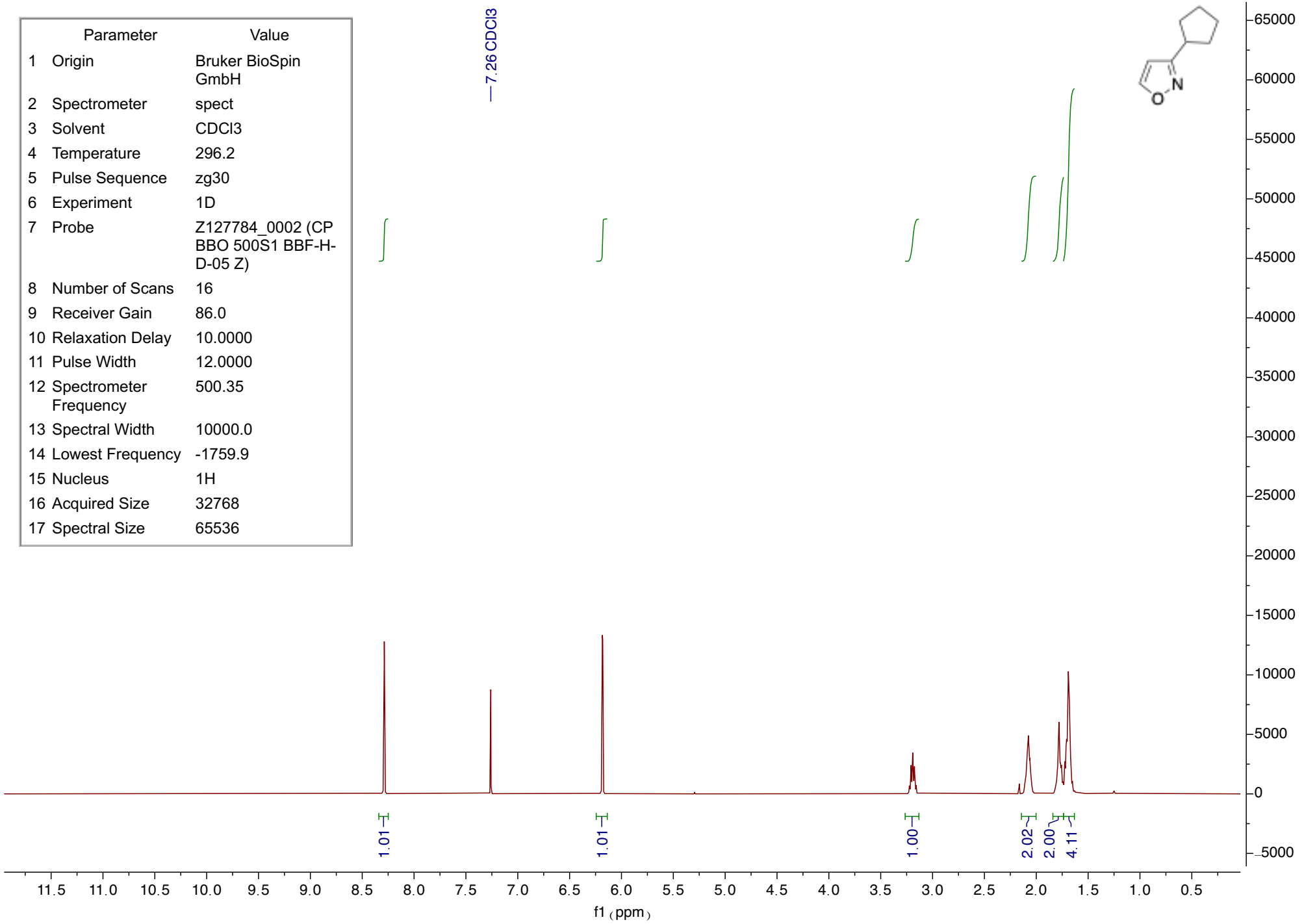
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

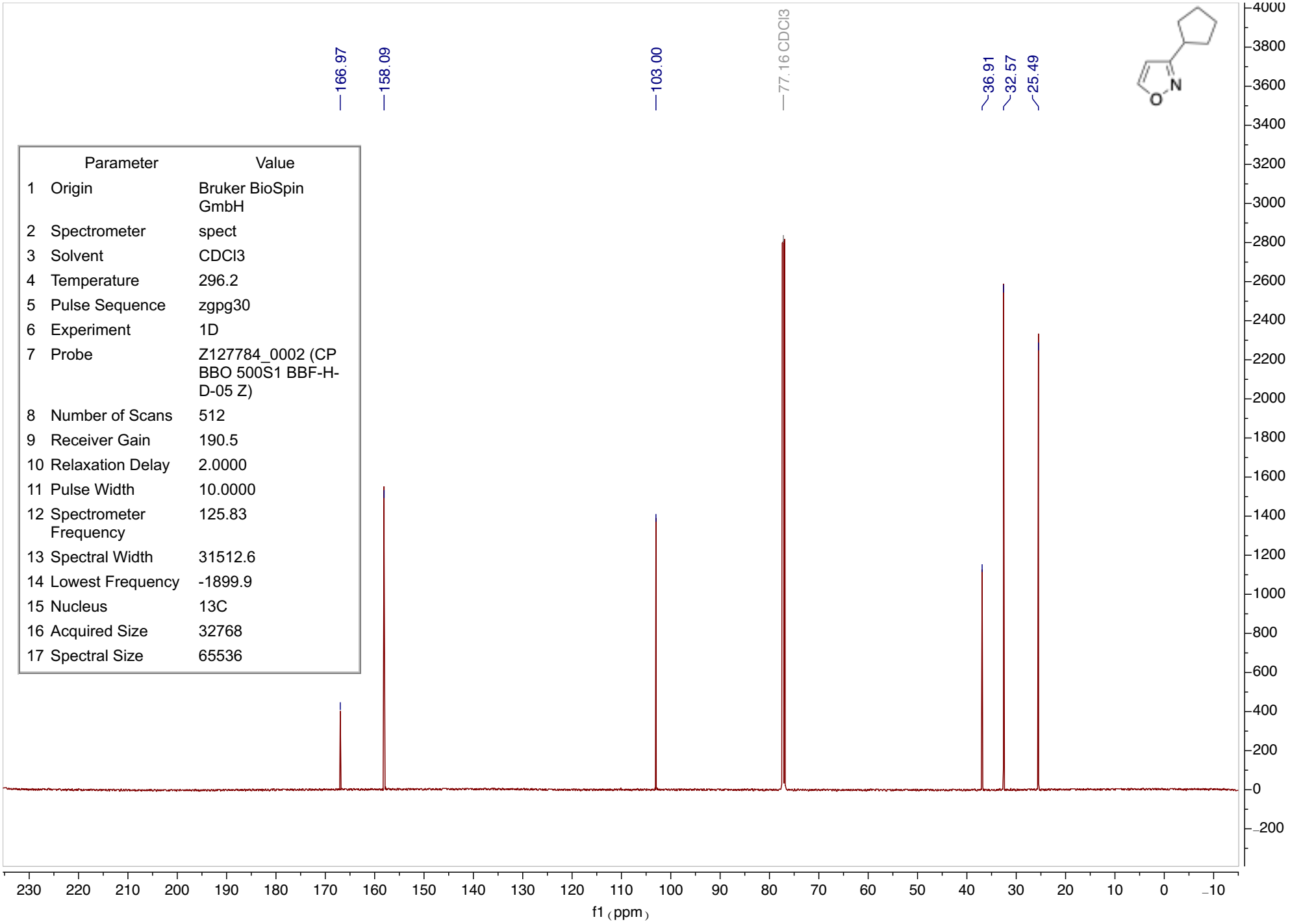


	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	hcn
8	Number of Scans	8
9	Receiver Gain	38
10	Relaxation Delay	10.0000
11	Pulse Width	7.0000
12	Spectrometer Frequency	500.06
13	Spectral Width	8000.0
14	Lowest Frequency	-1512.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536


Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe quadbp
8 Number of Scans 8
9 Receiver Gain 52
10 Relaxation Delay 10.0000
11 Pulse Width 5.8250
12 Spectrometer Frequency 399.74
13 Spectral Width 8000.0
14 Lowest Frequency -2427.6
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
5.30 DCM
4.13 EtOAc
2.05 EtOAc
1.26 EtOAc
OH
N
1.00
0.53
0.43
0.42
0.54
2.00
6.69
f1 (ppm)

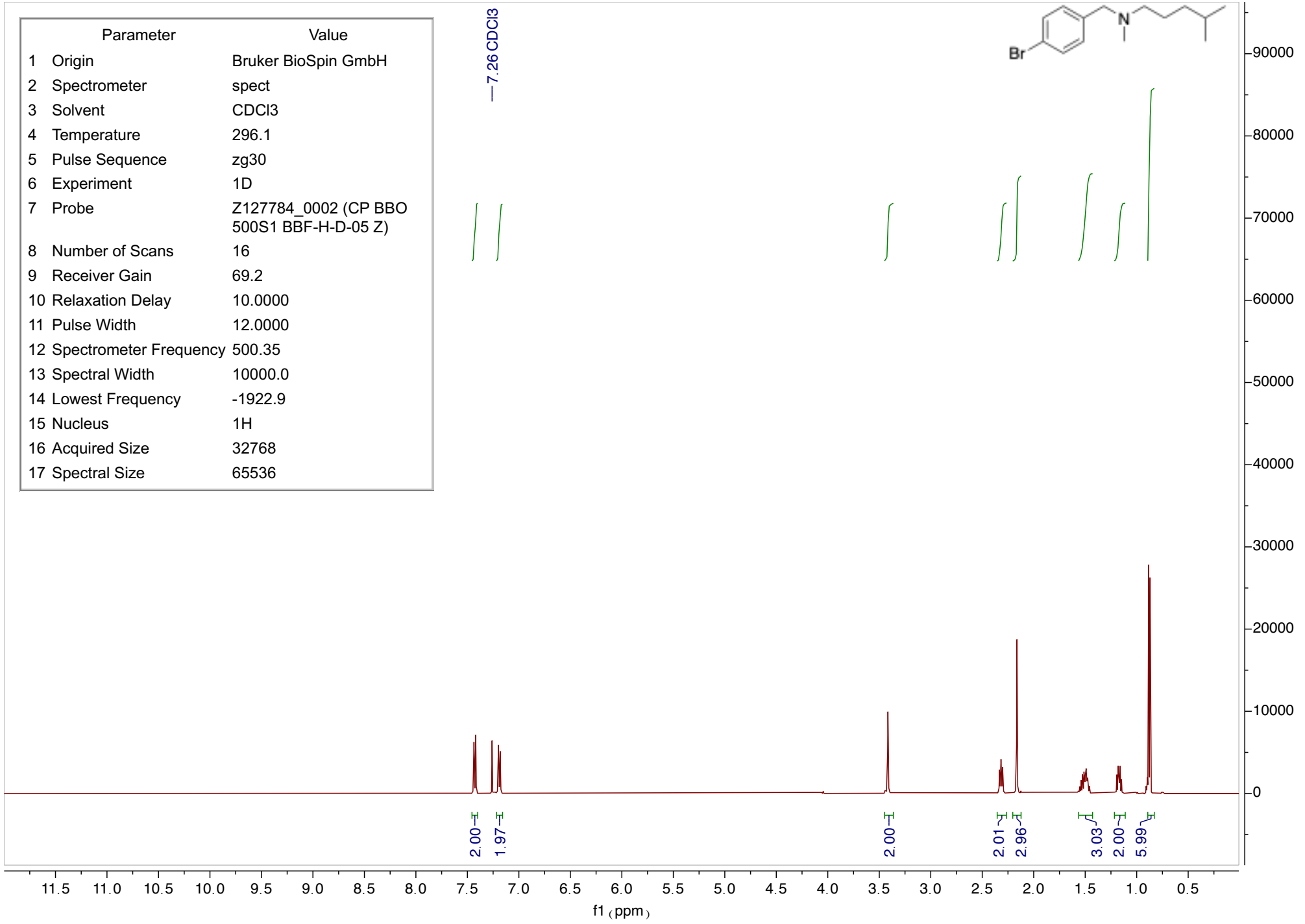
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



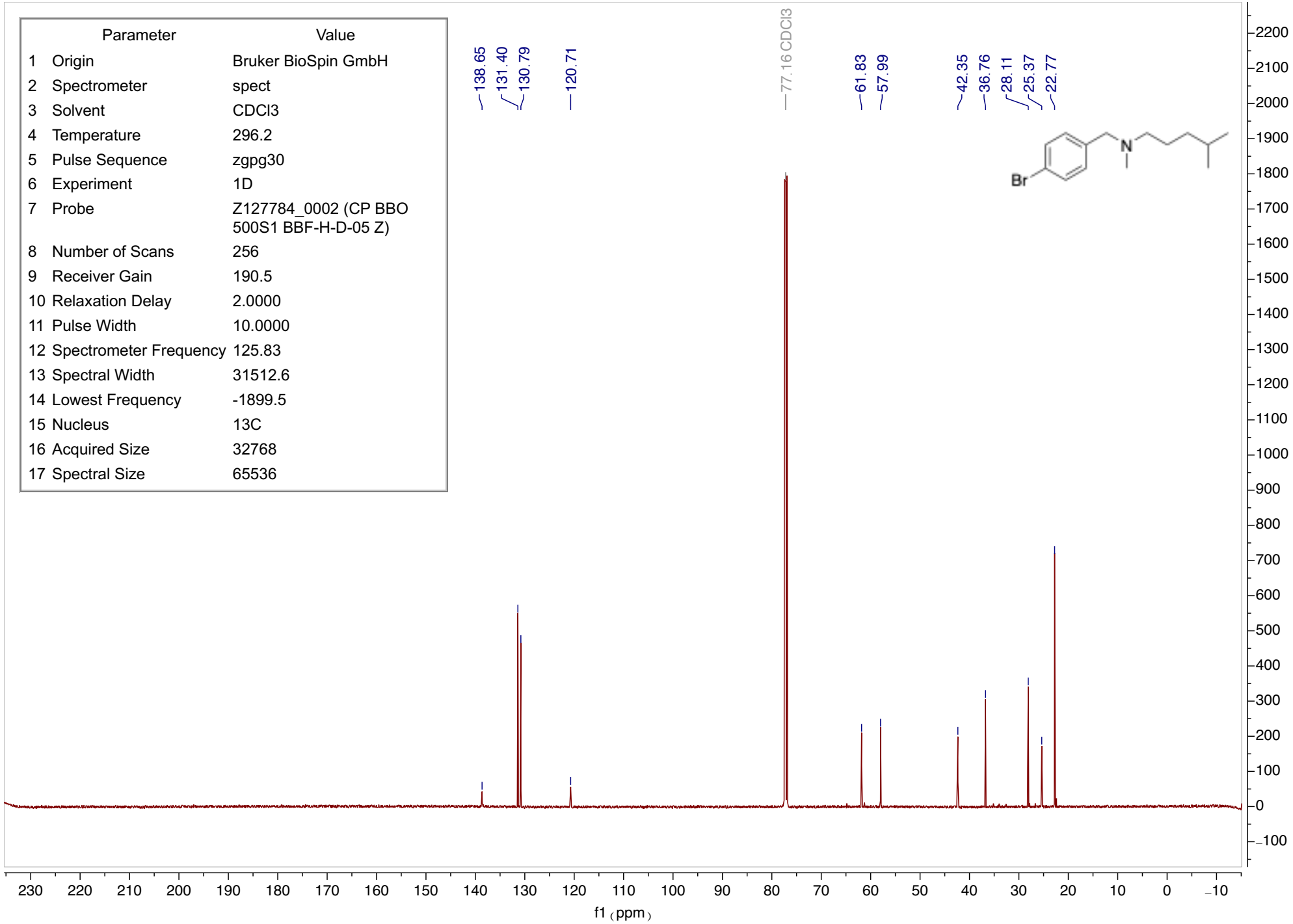


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

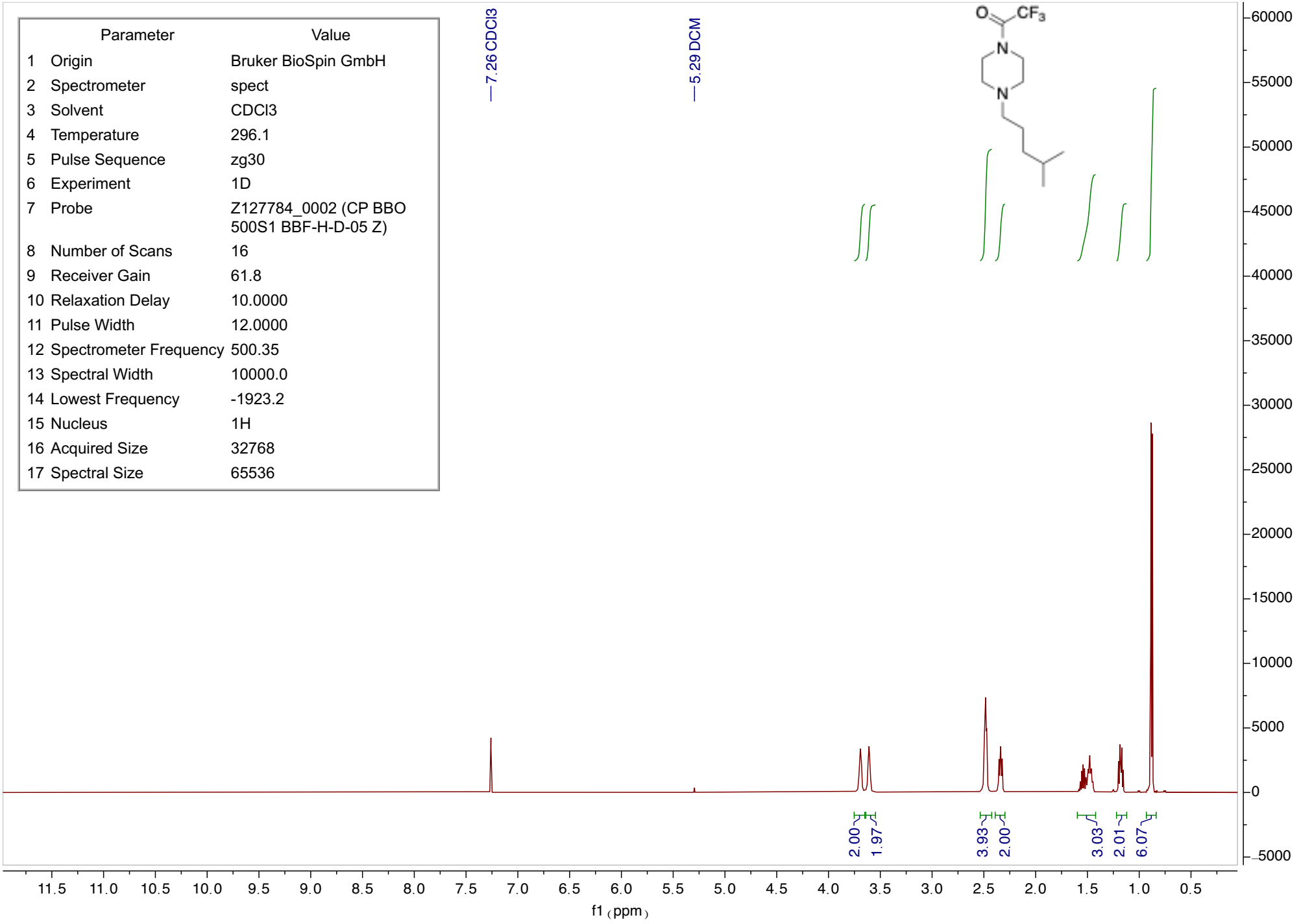
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	69.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

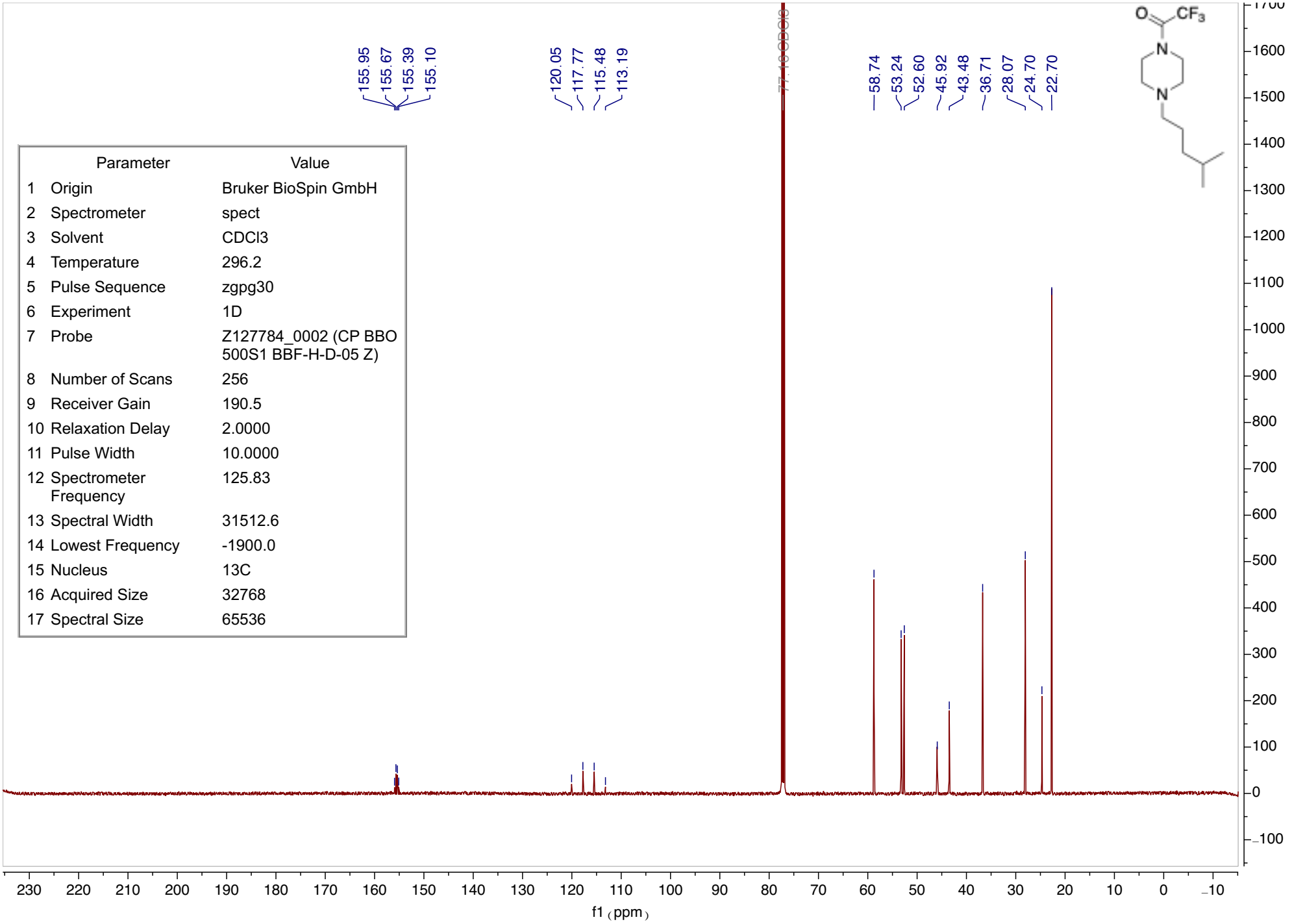


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



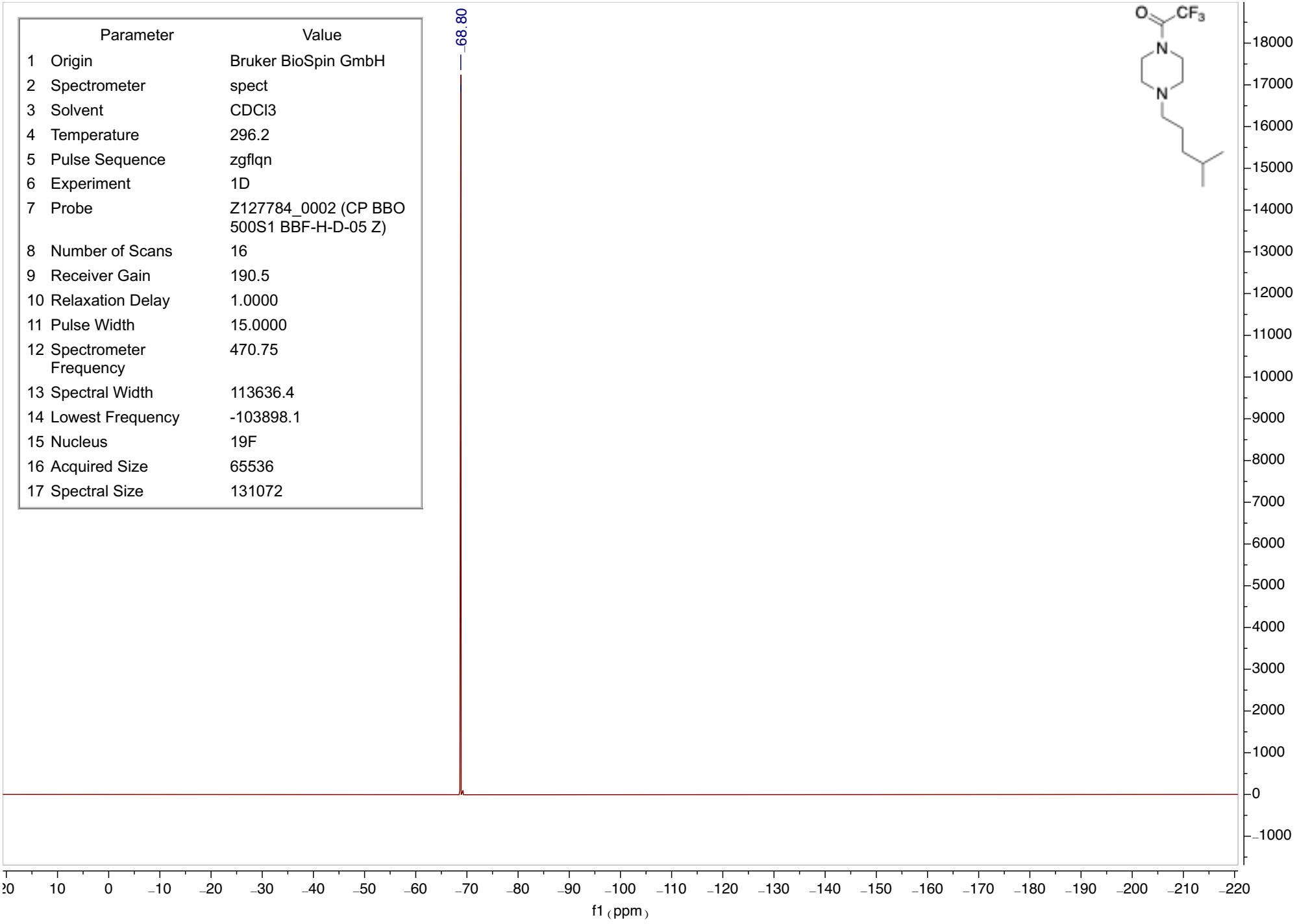
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



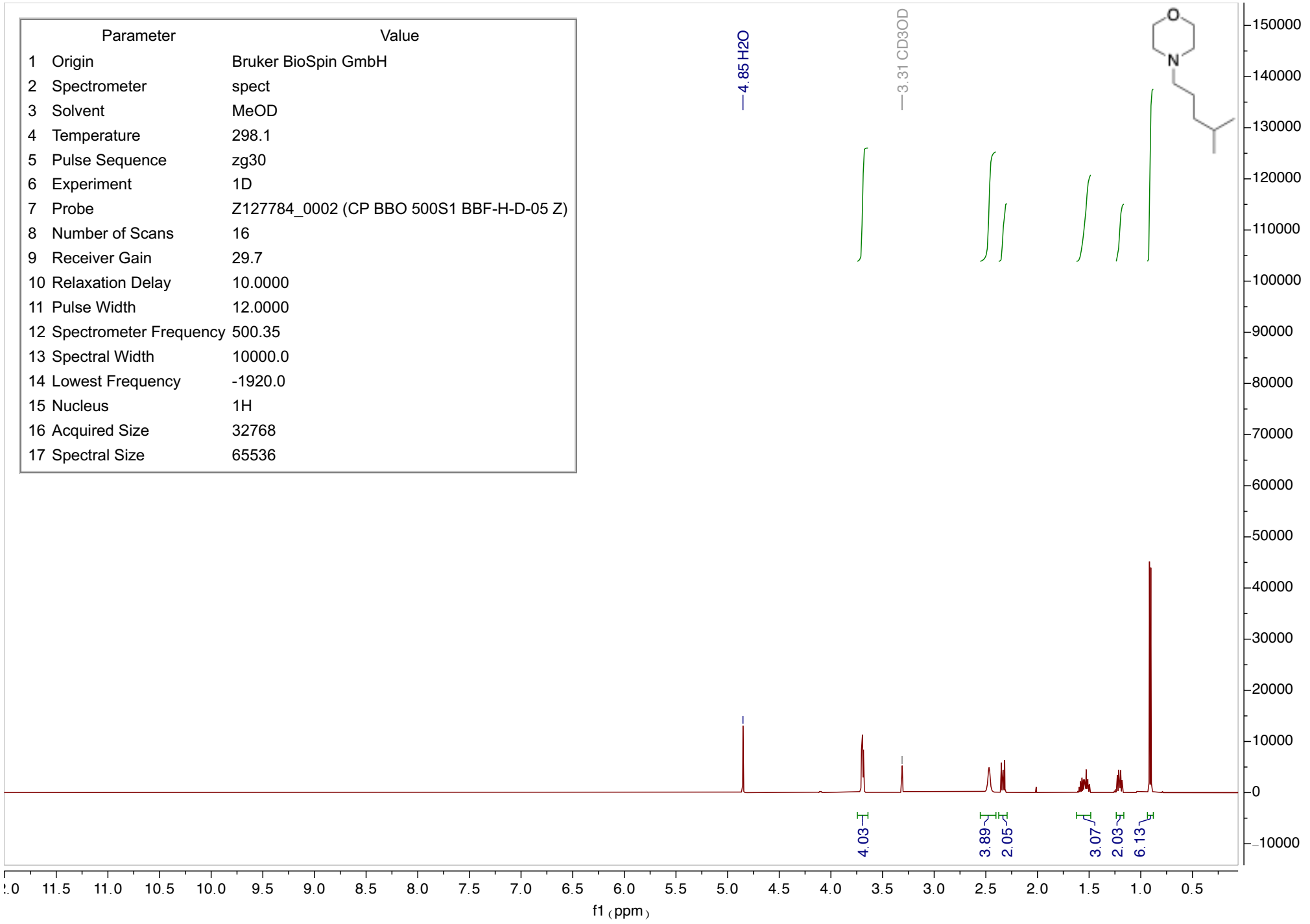


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

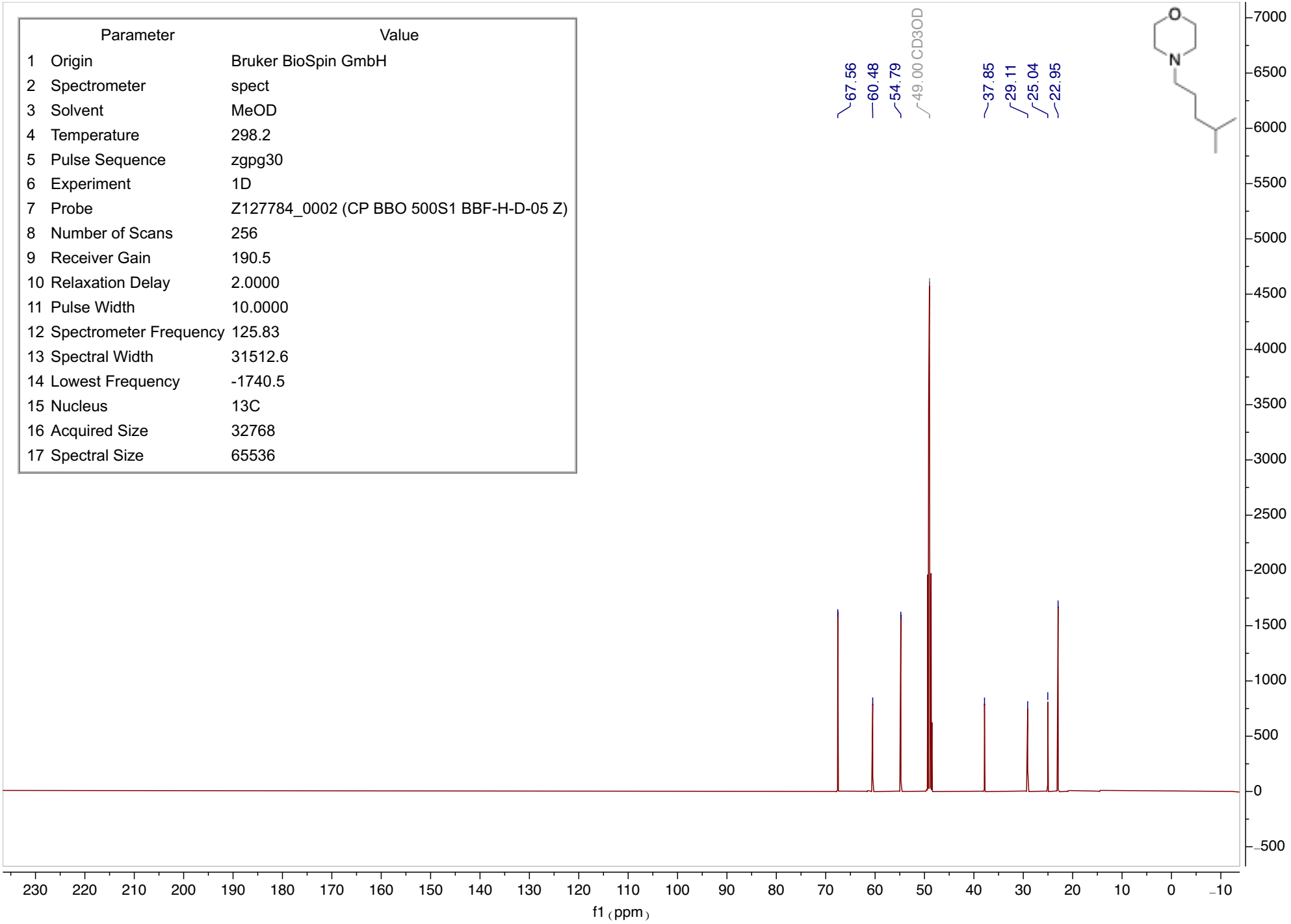
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



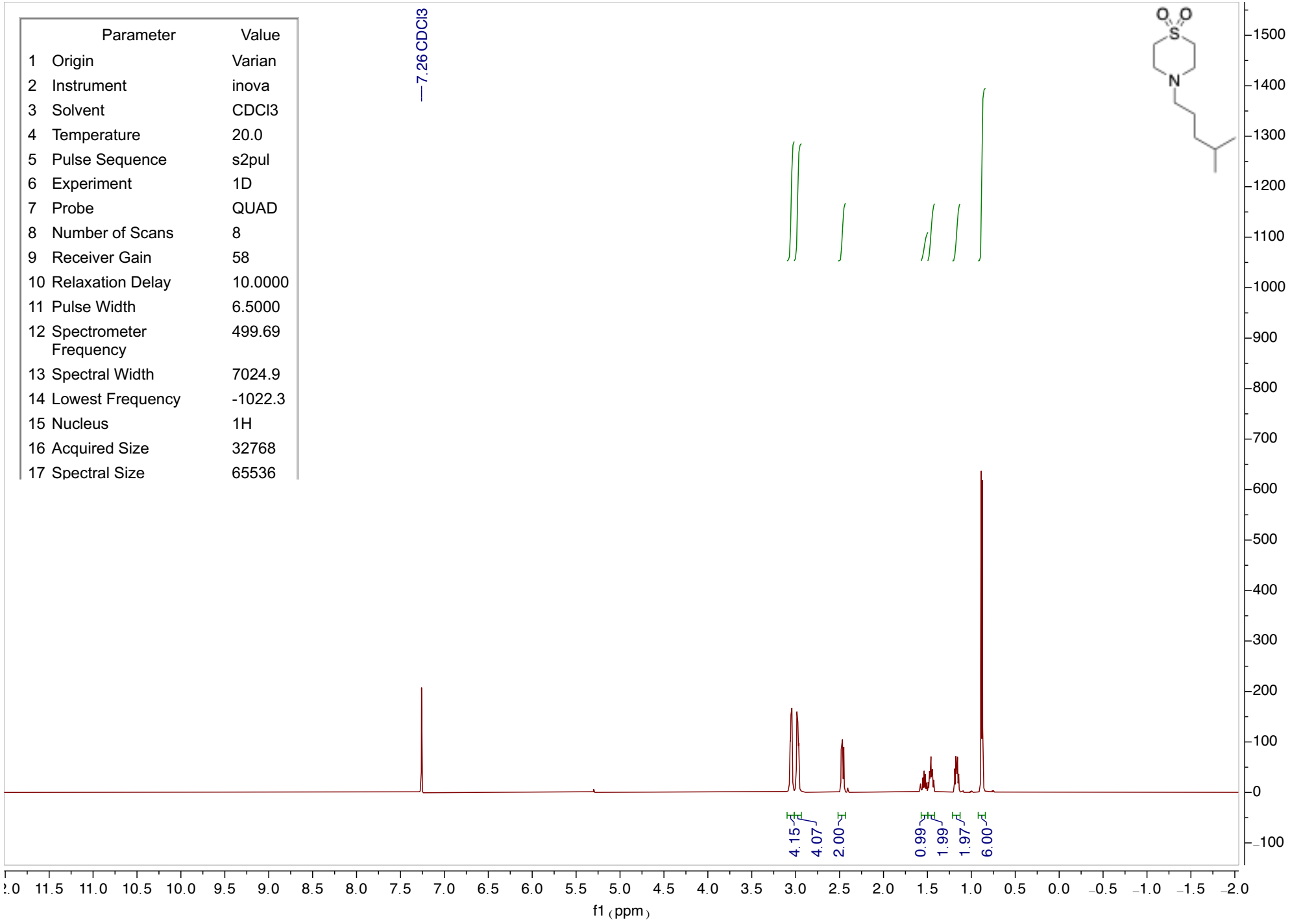
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1920.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



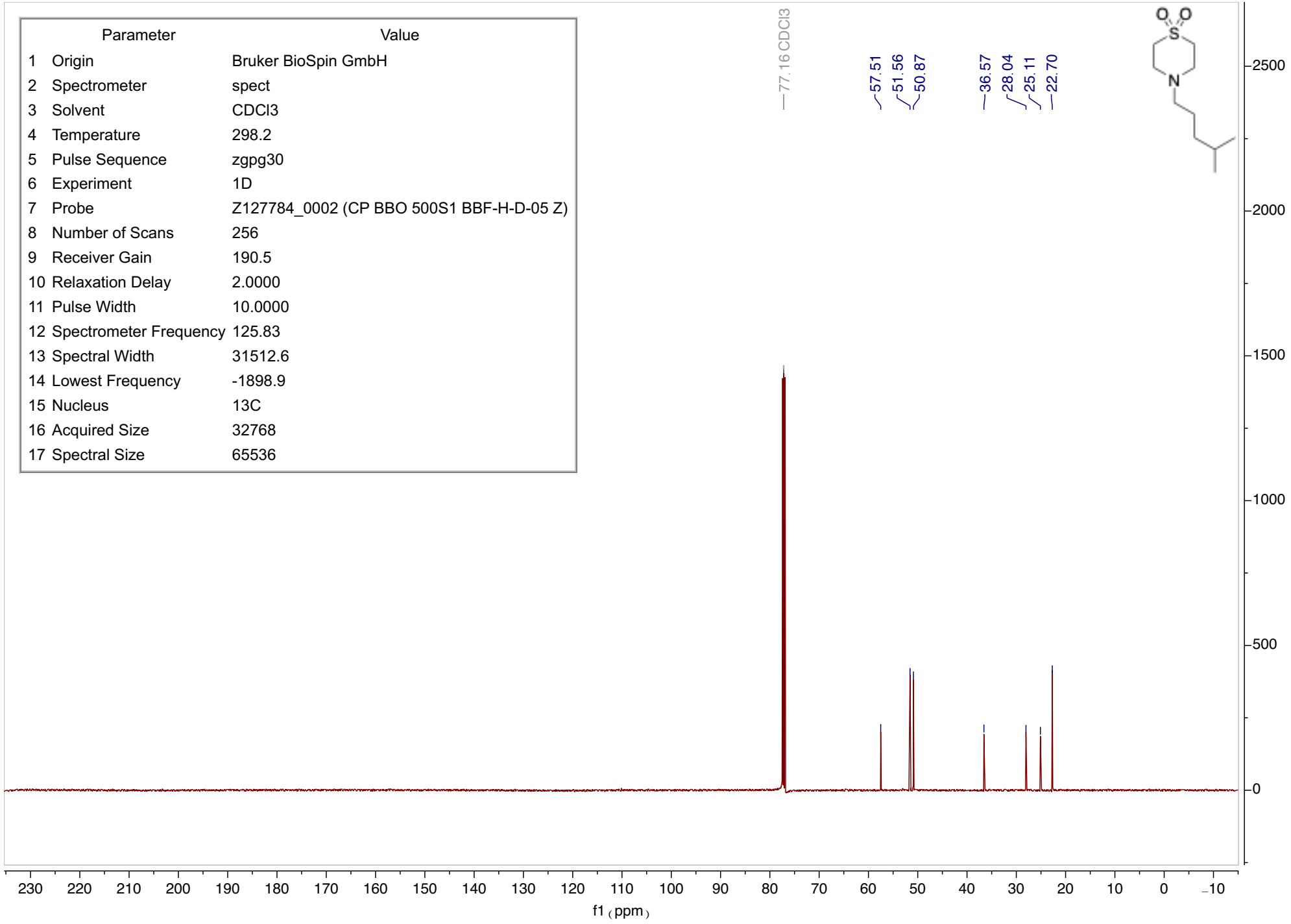
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1740.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



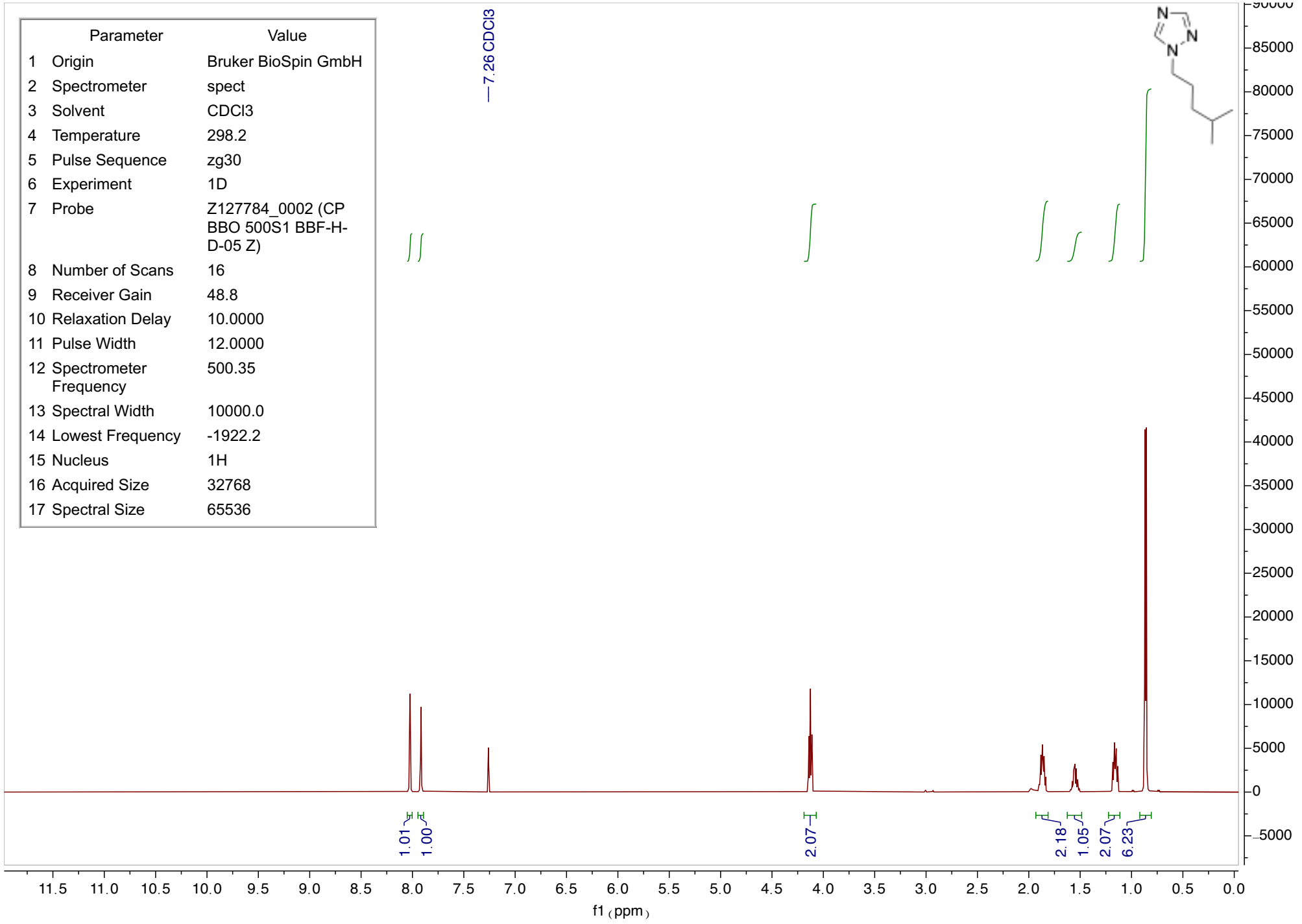
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	QUAD
8	Number of Scans	8
9	Receiver Gain	58
10	Relaxation Delay	10.0000
11	Pulse Width	6.5000
12	Spectrometer Frequency	499.69
13	Spectral Width	7024.9
14	Lowest Frequency	-1022.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



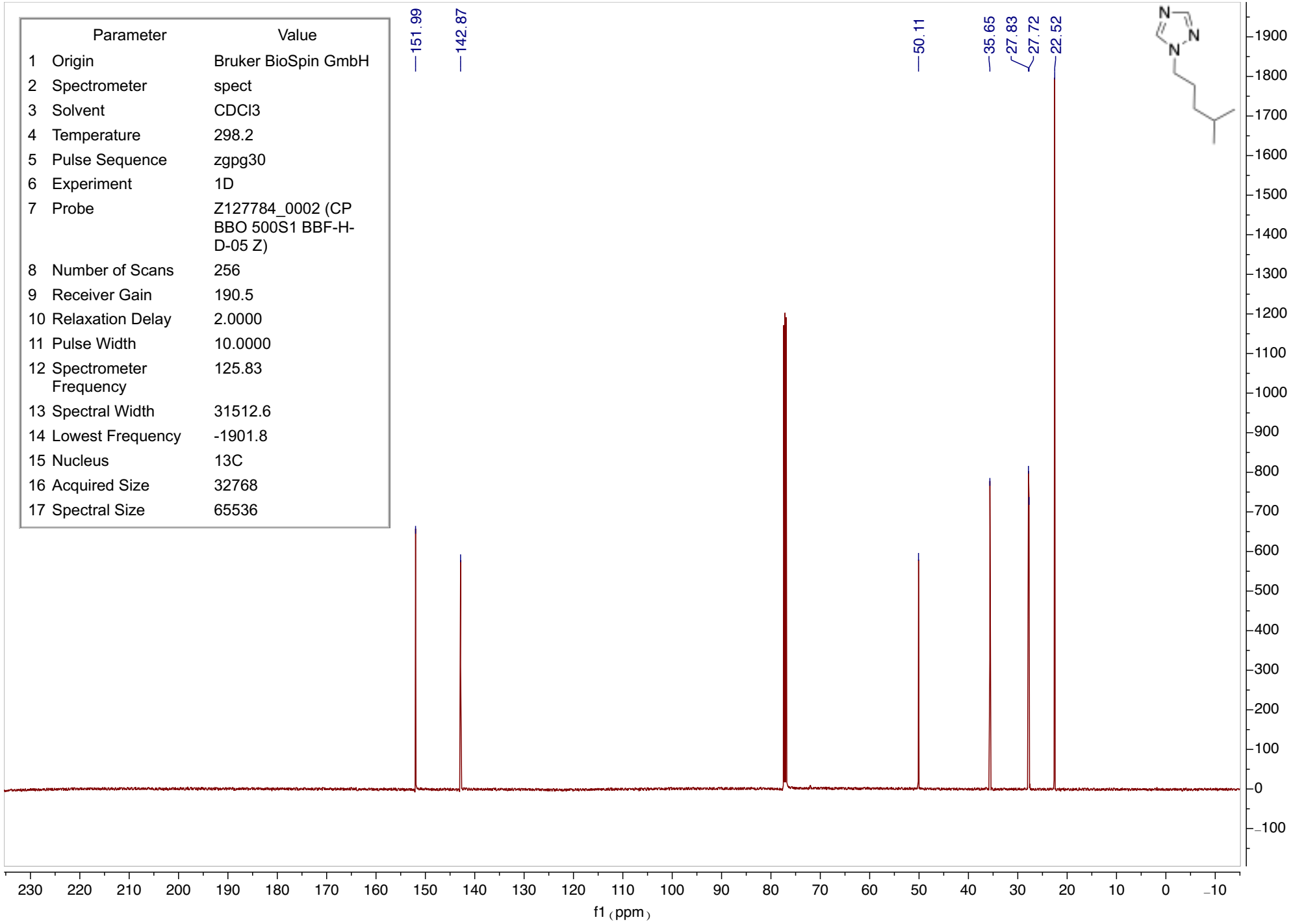
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

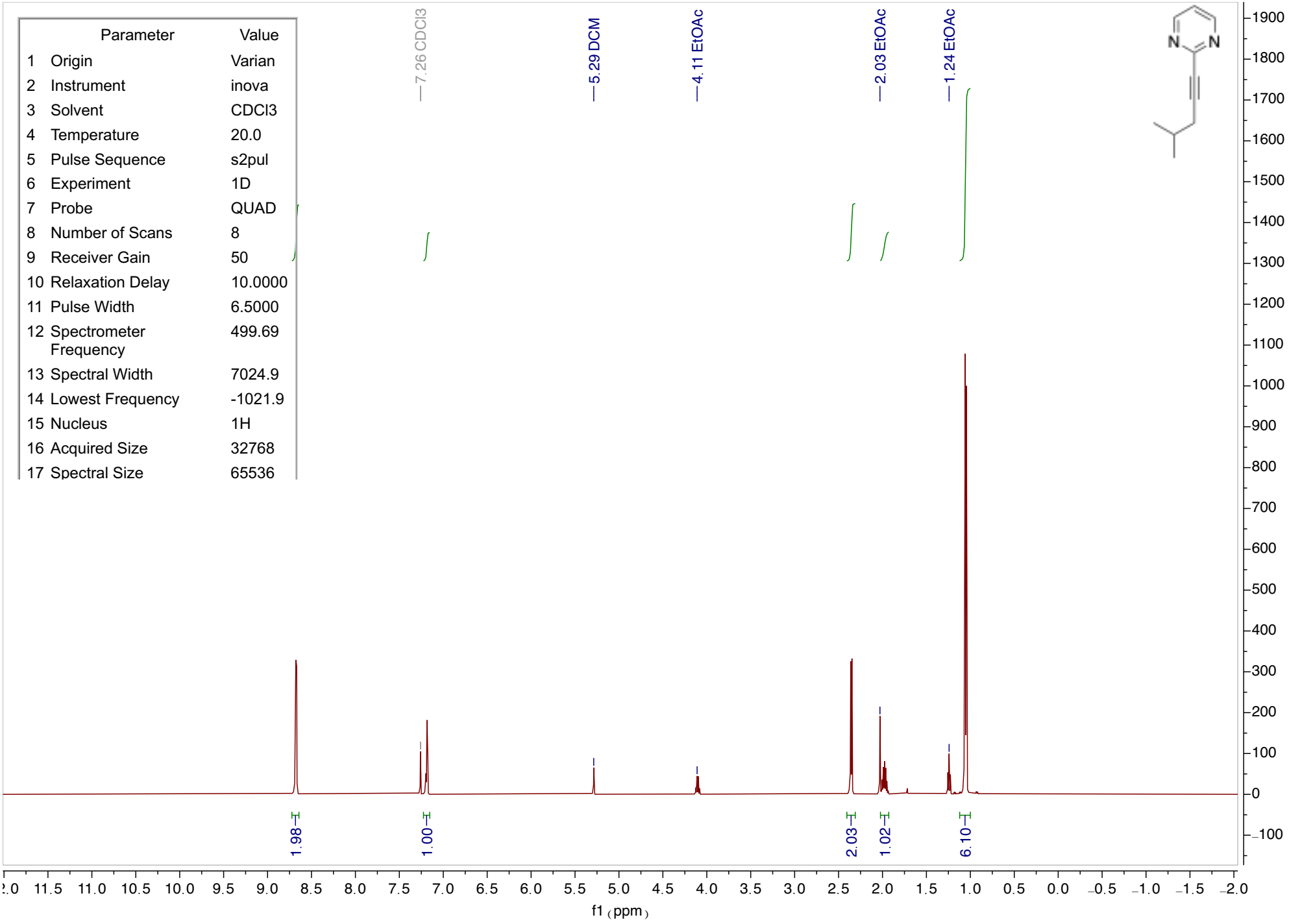


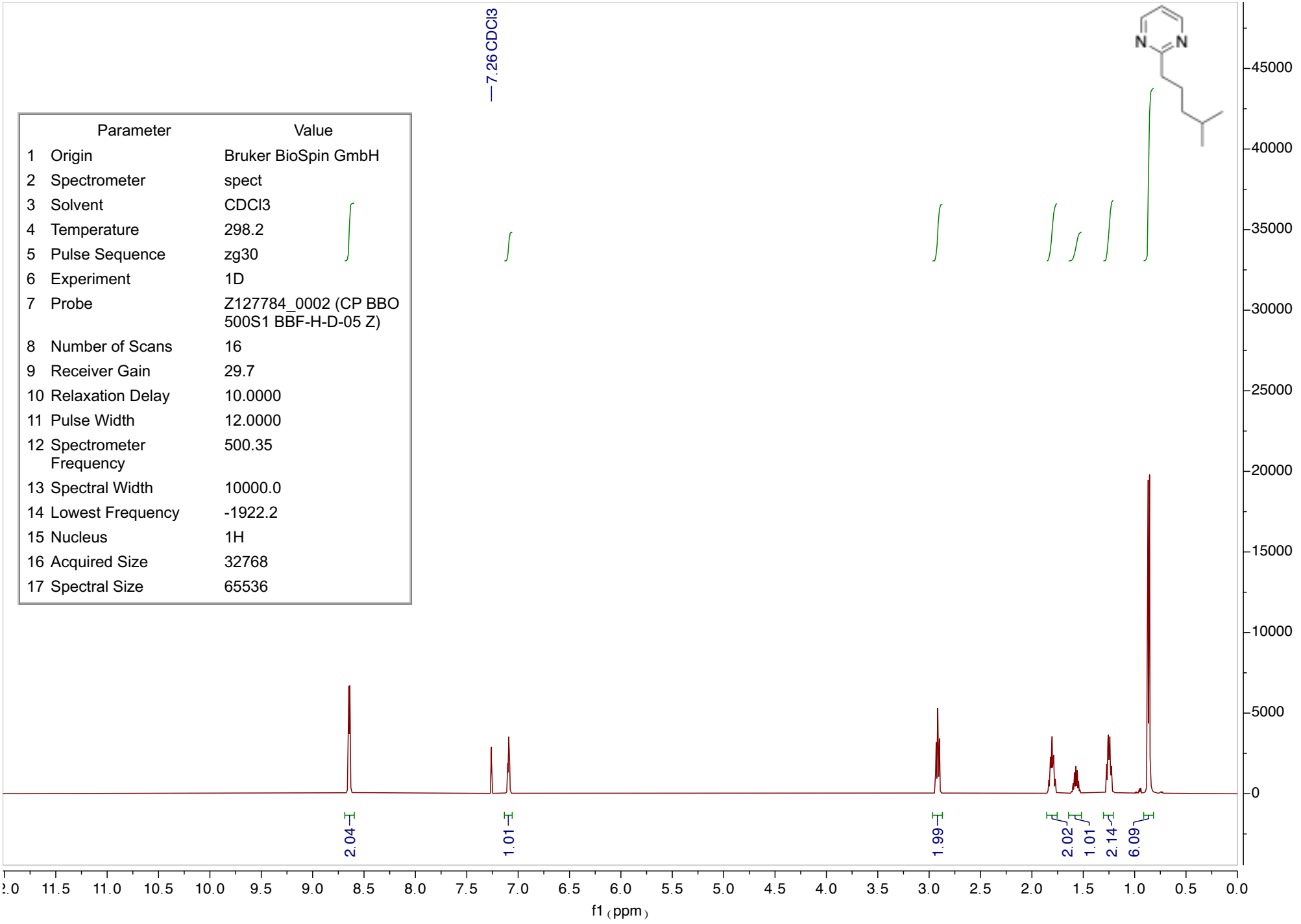
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	48.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



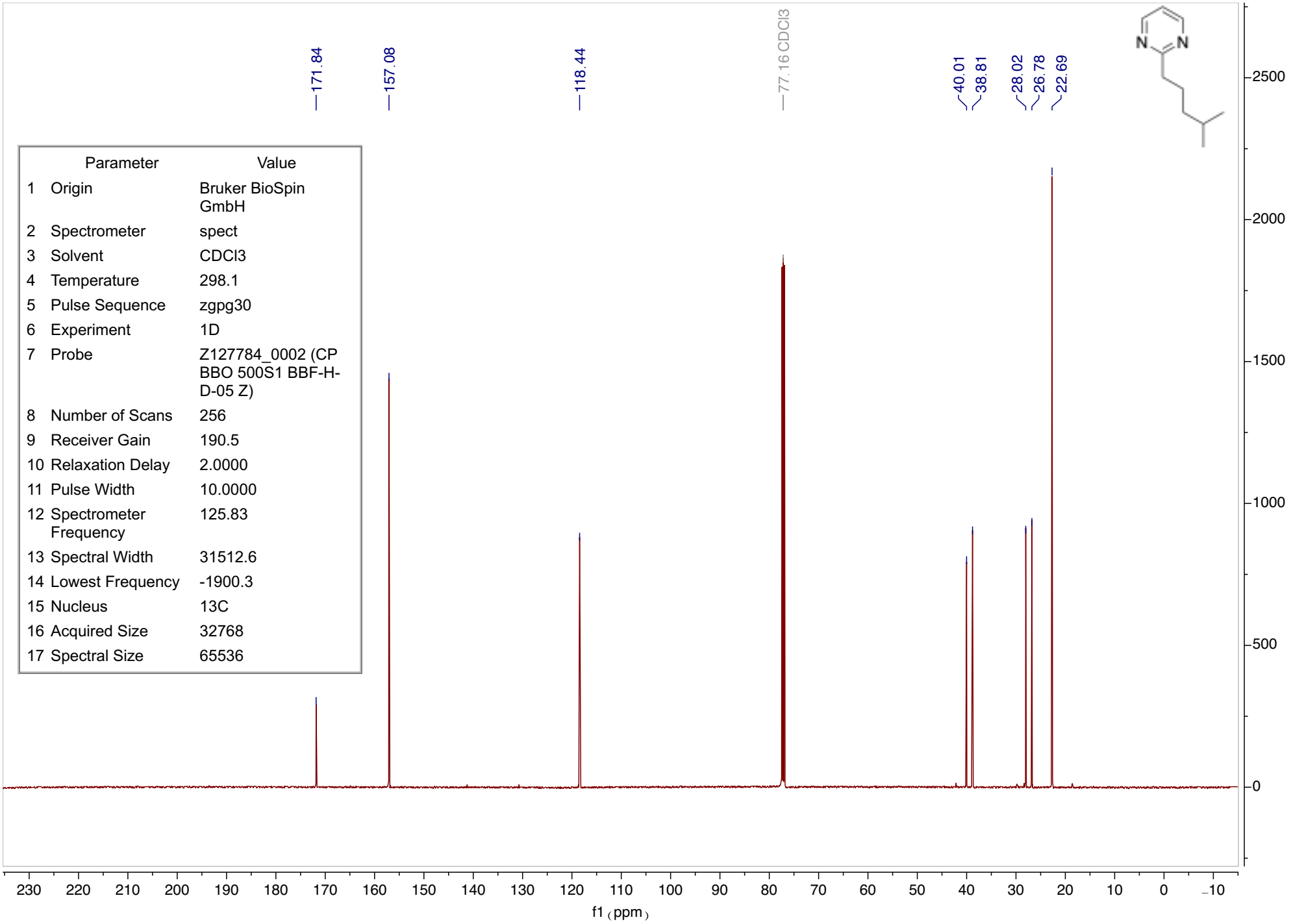
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



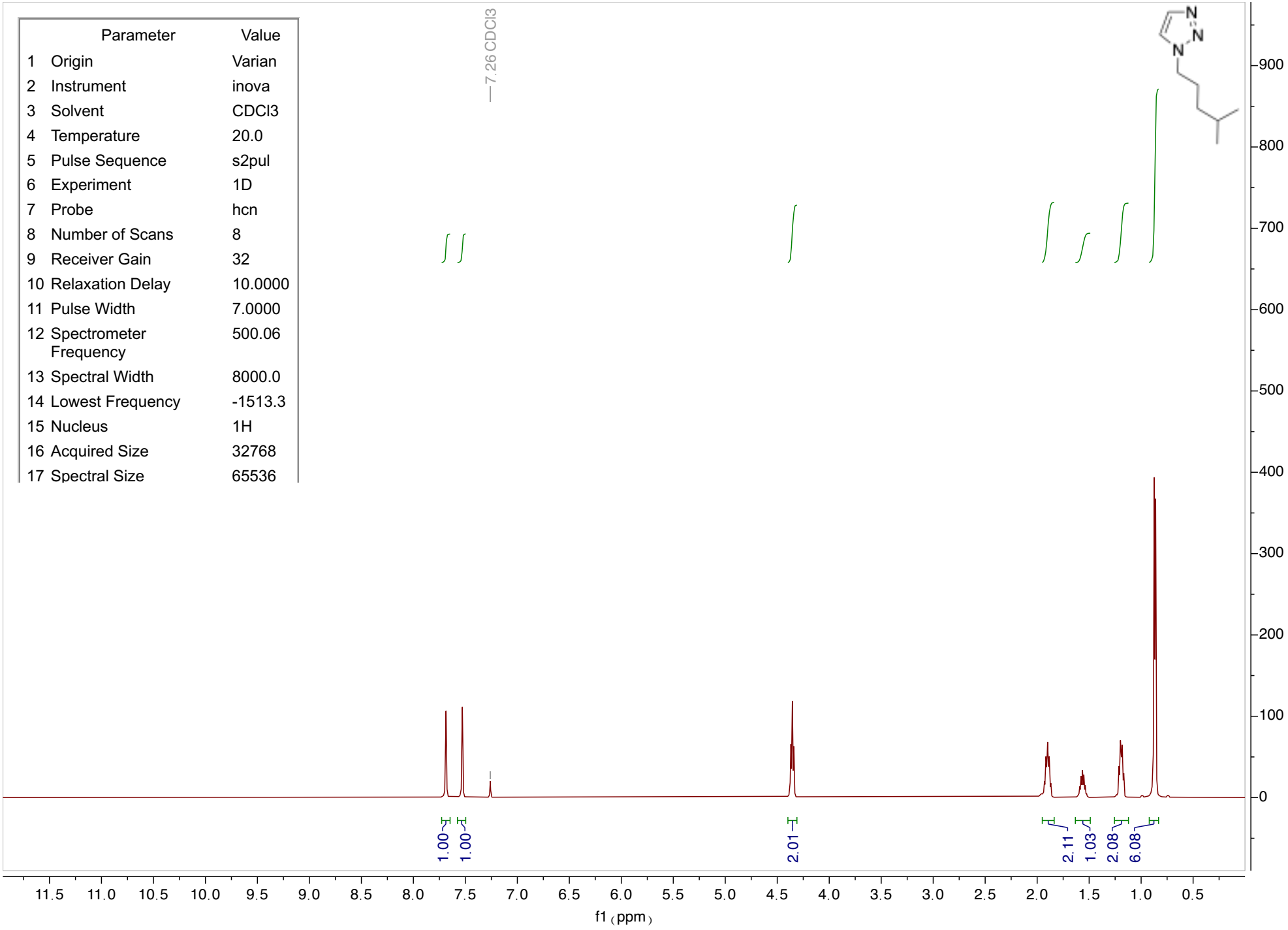

Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe QUAD
8 Number of Scans 8
9 Receiver Gain 50
10 Relaxation Delay 10.0000
11 Pulse Width 6.5000
12 Spectrometer Frequency 499.69
13 Spectral Width 7024.9
14 Lowest Frequency -1021.9
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
5.29 DCM
4.11 EtOAc
2.03 EtOAc
1.24 EtOAc
1.98
1.00
2.03
1.02
6.10
f1 (ppm)

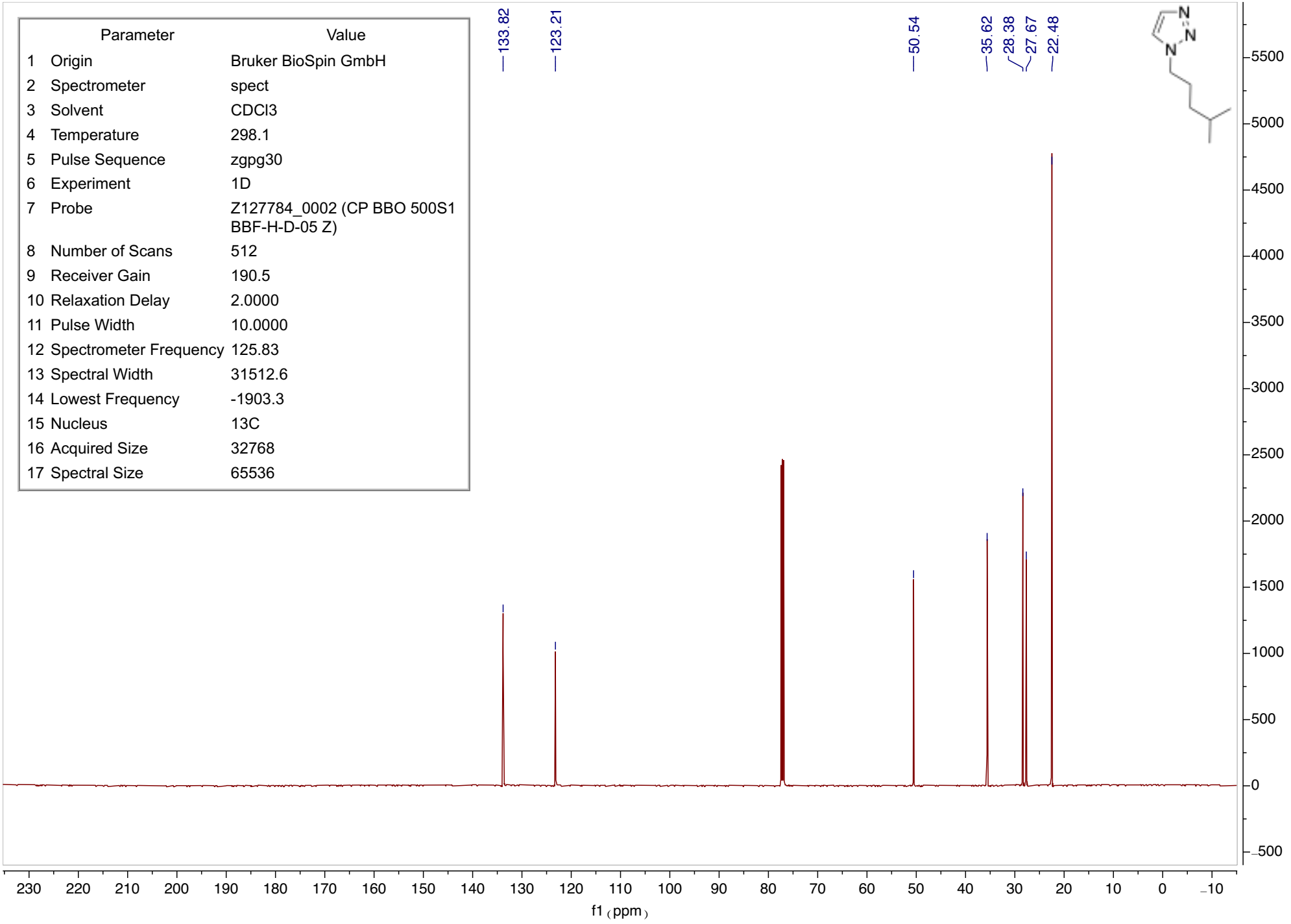


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



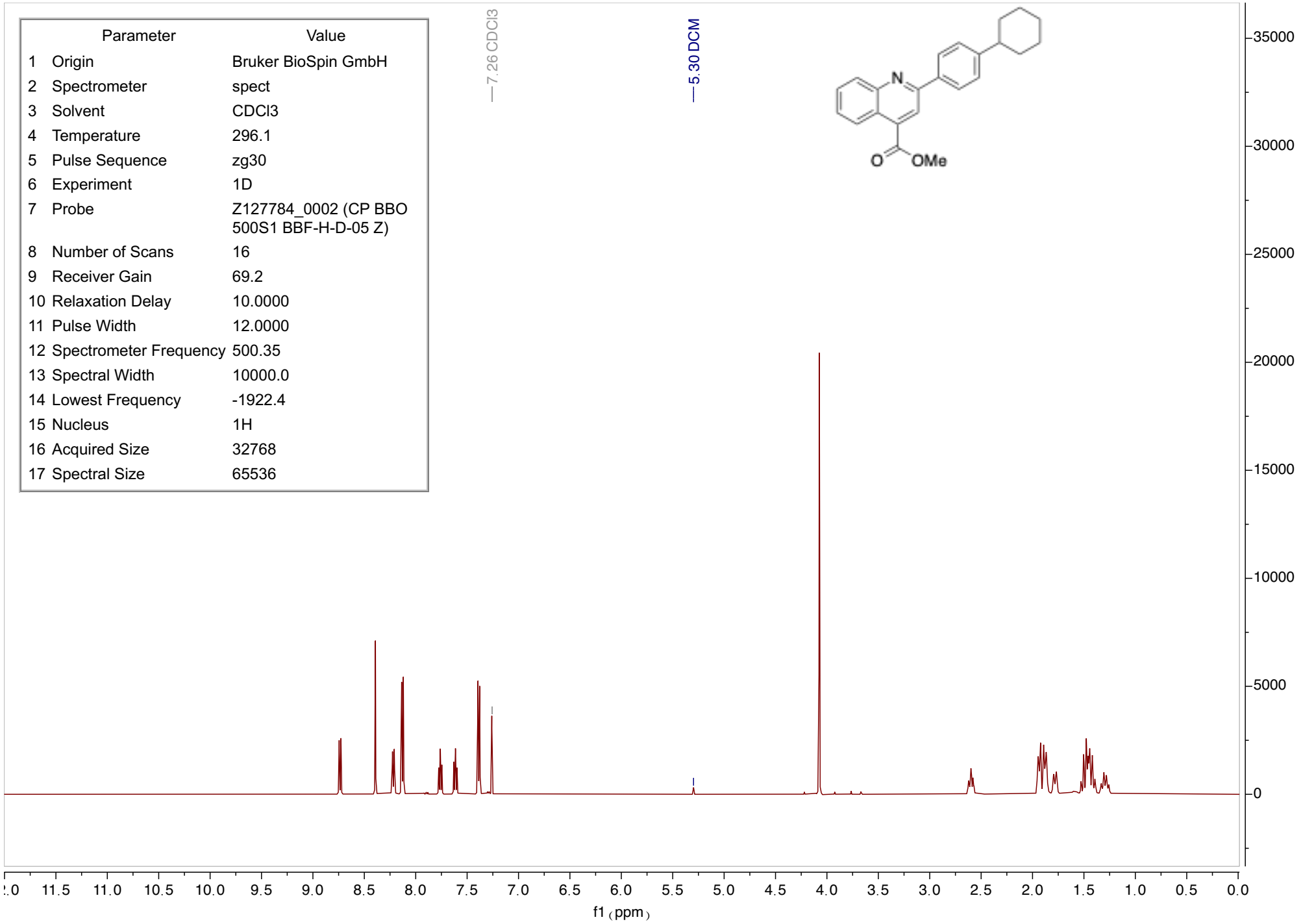
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

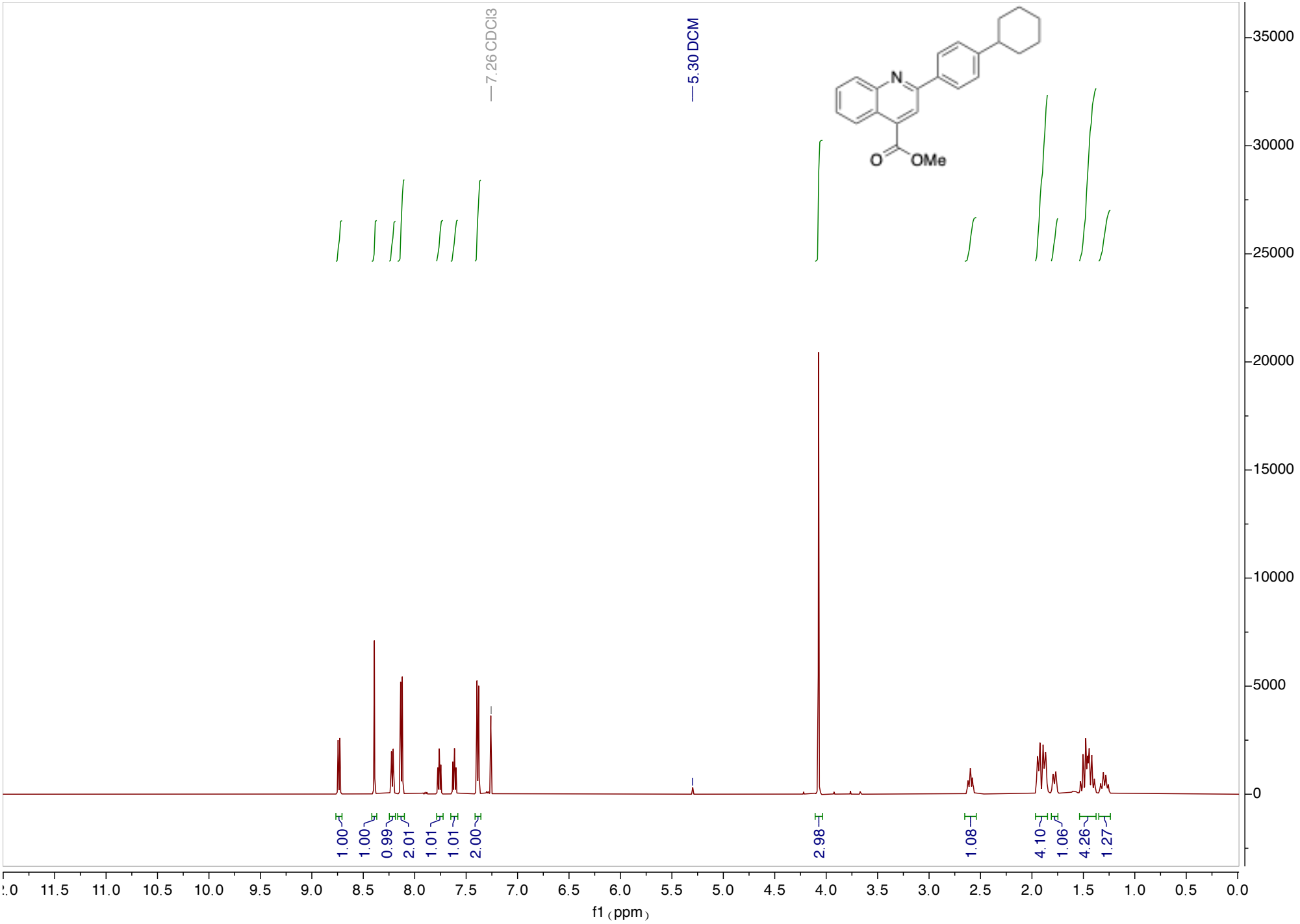

Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 32
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1513.3
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
1.00
1.00
2.01
2.11
1.03
2.08
6.08
f1 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	69.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536




7.26 CDCl3
5.30 DCM
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O
OMe
35000
30000
25000
20000
15000
10000
5000
0
1.00
1.00
0.99
2.01
1.01
1.01
2.00
2.98
1.08
4.10
1.06
4.26
1.27
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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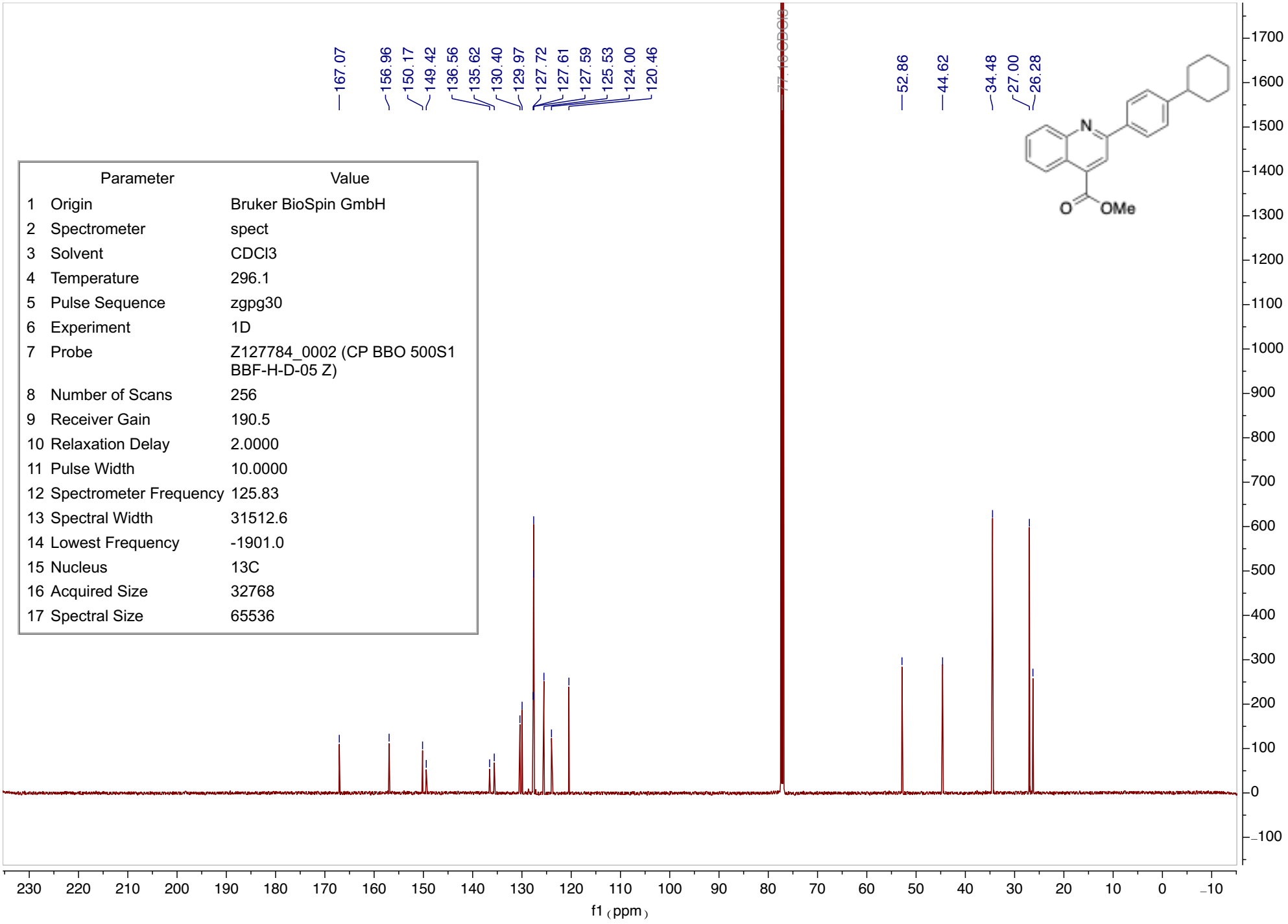
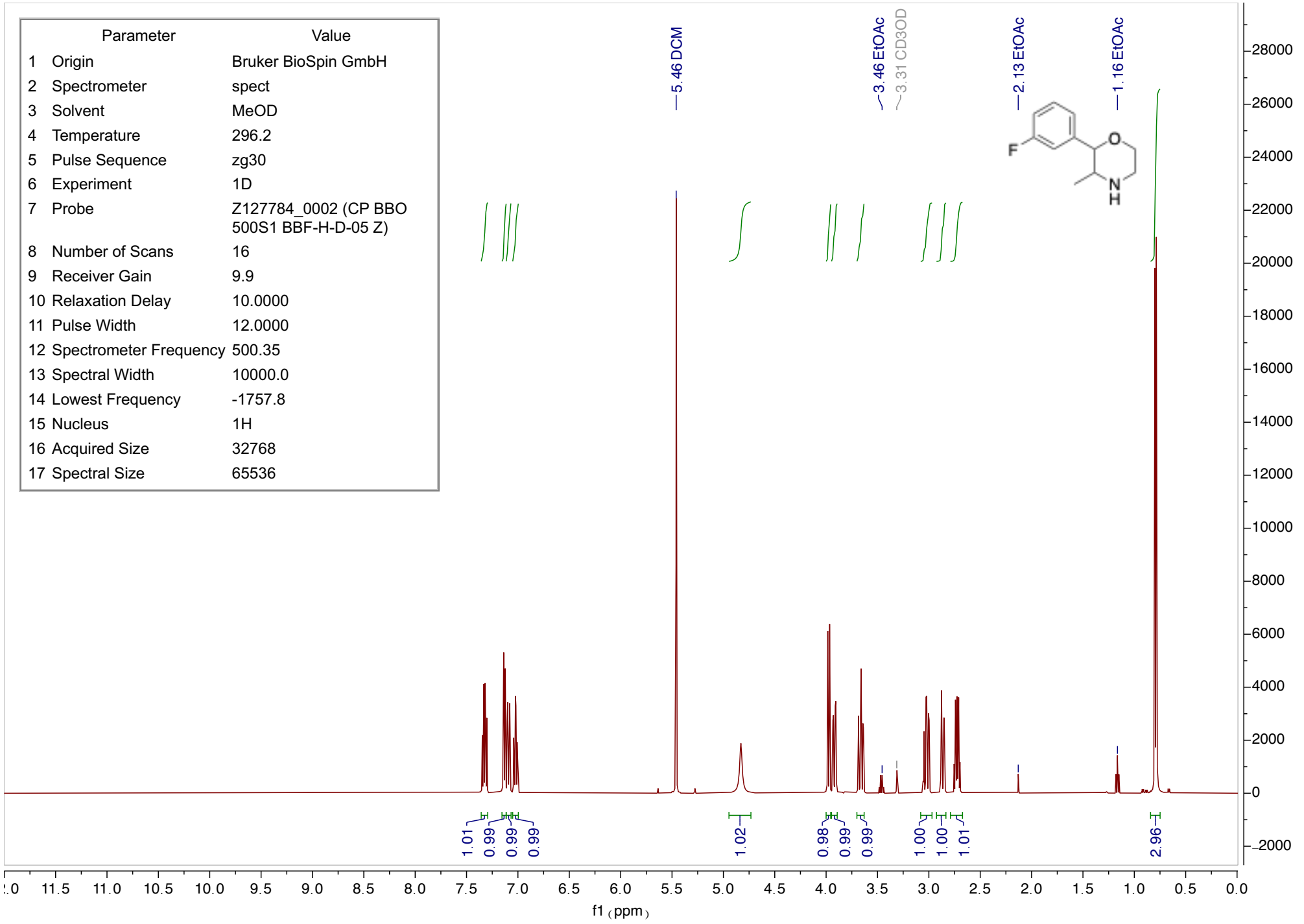
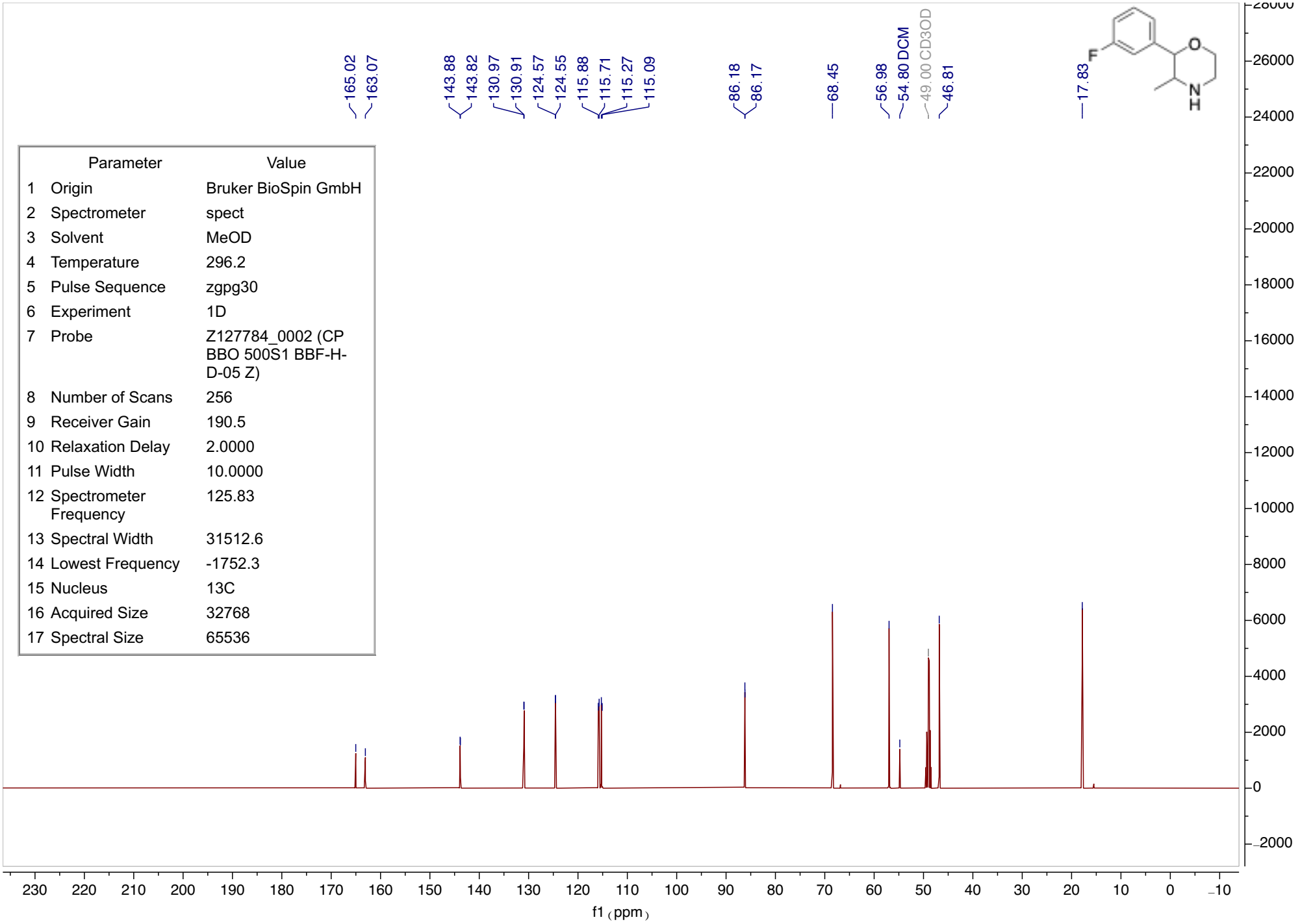
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

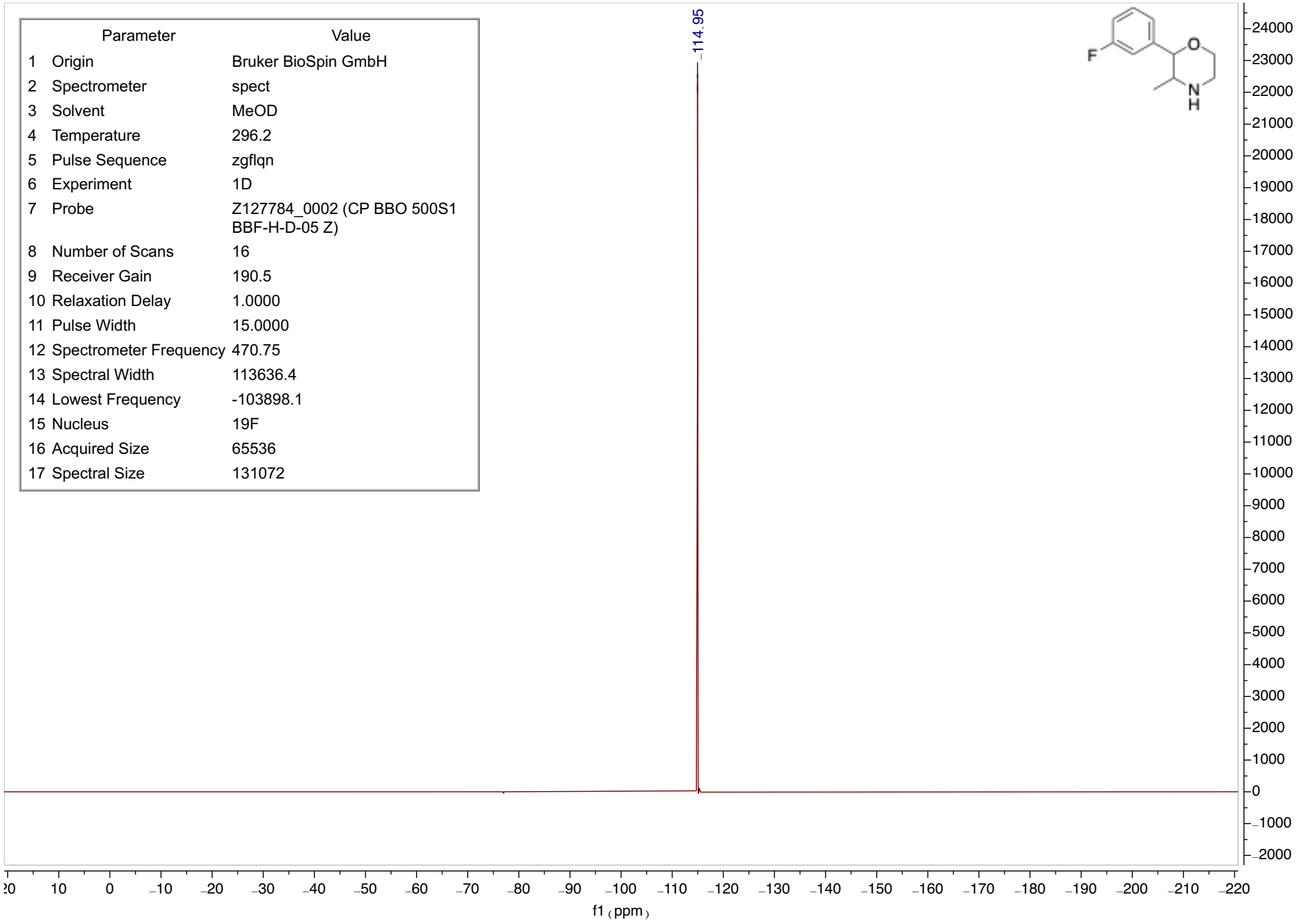
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	9.9
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1757.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



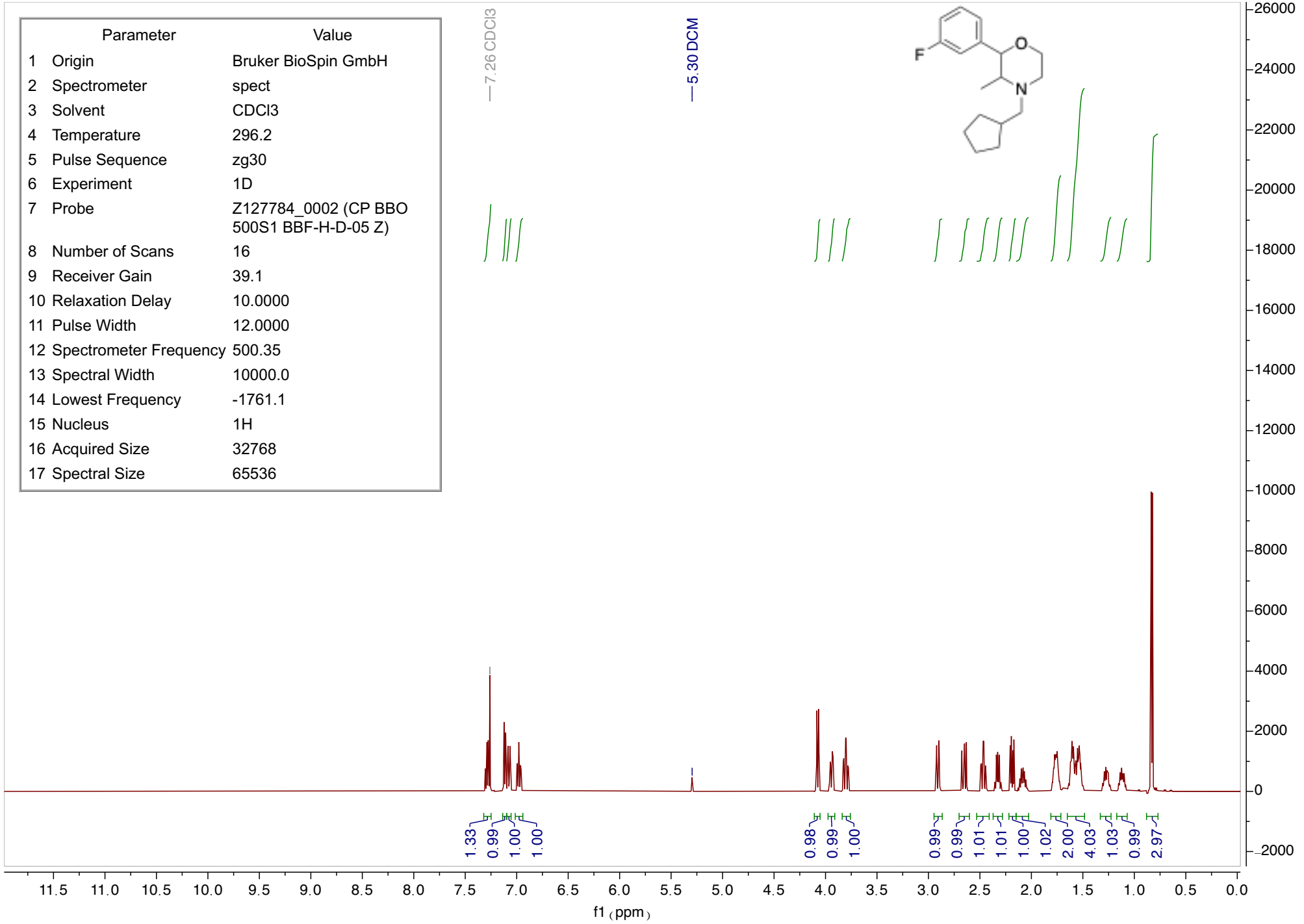


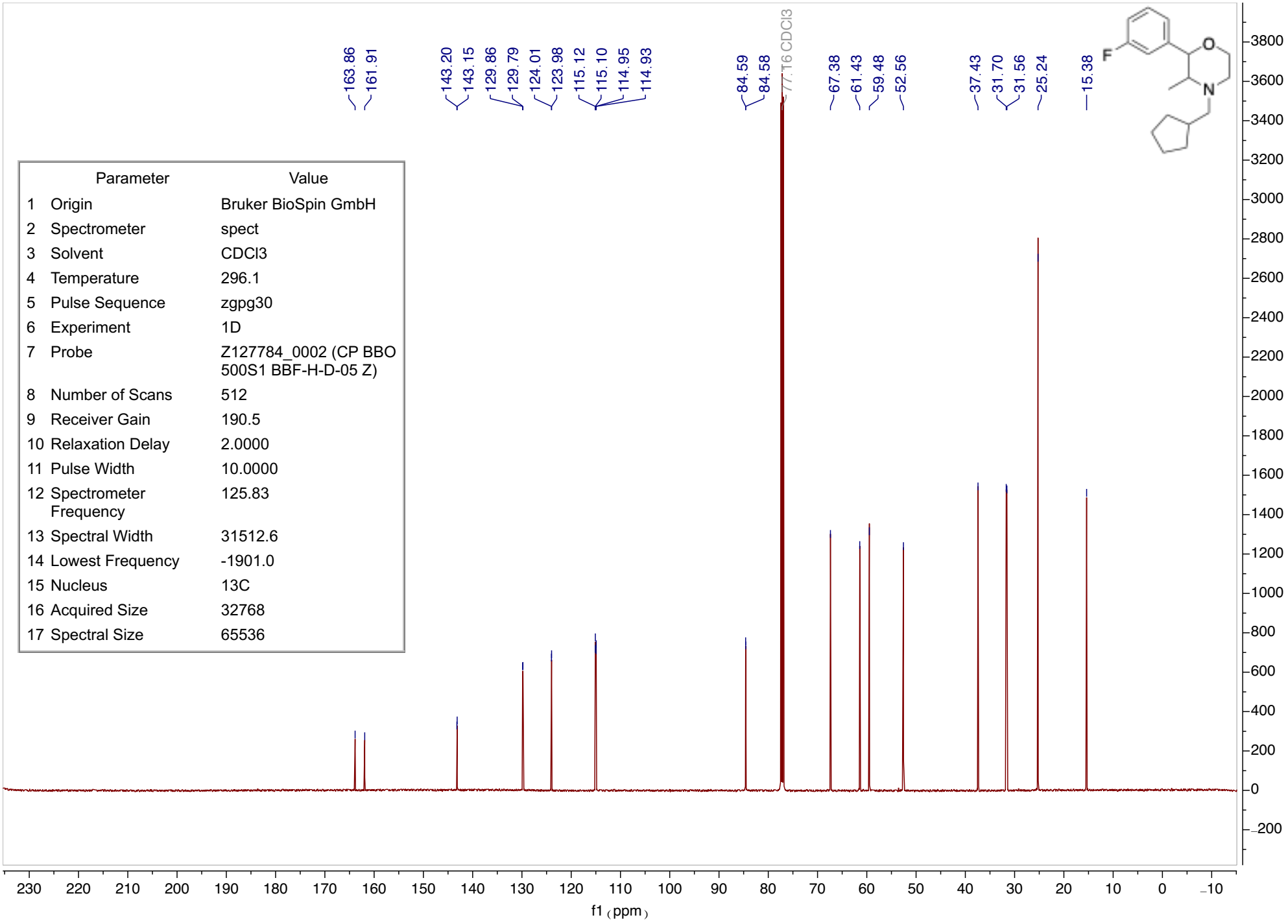
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1752.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



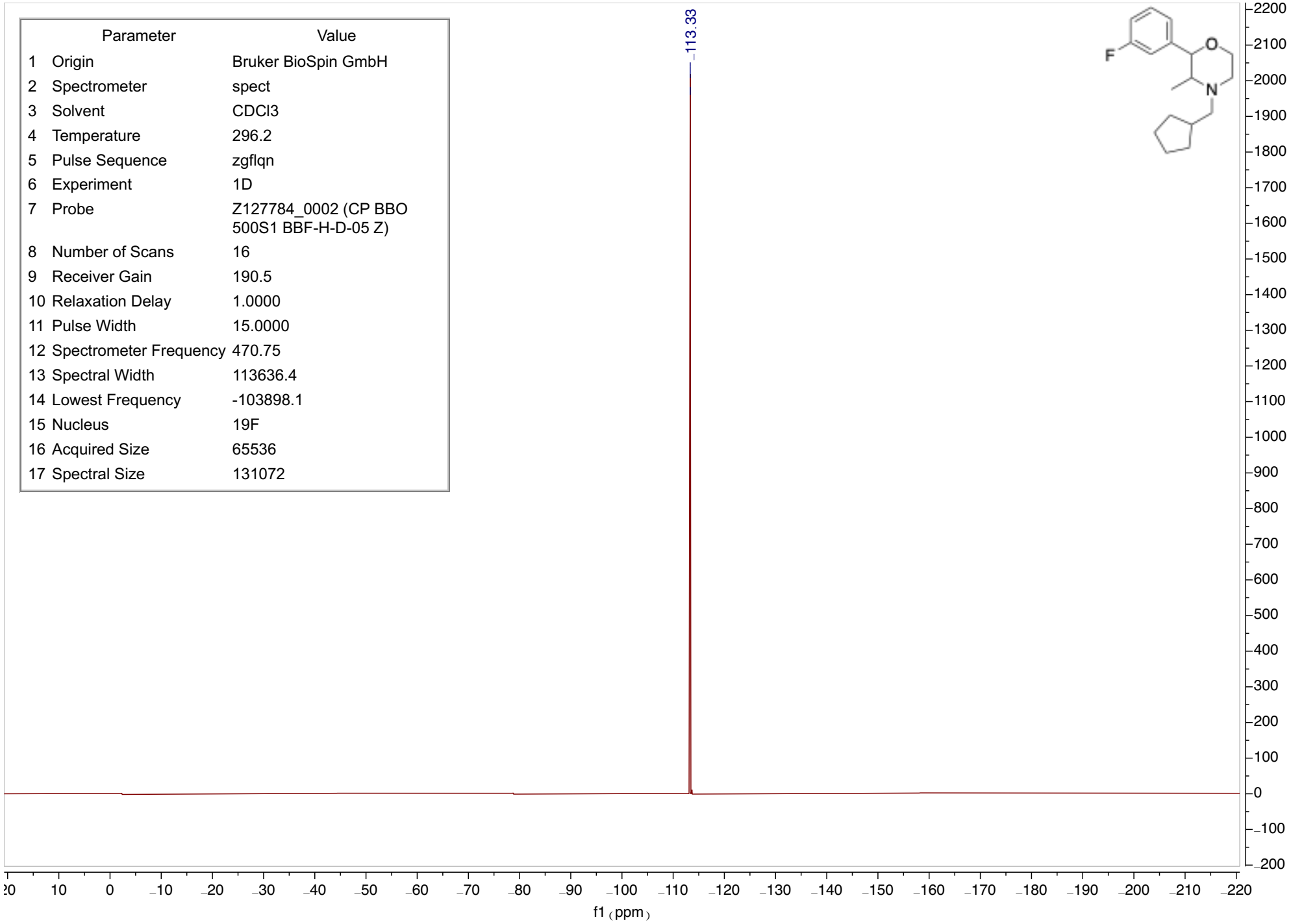
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	39.1
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1761.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

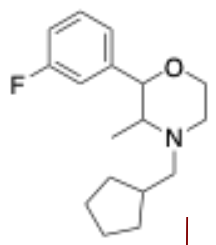




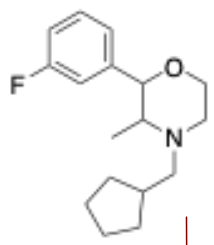
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

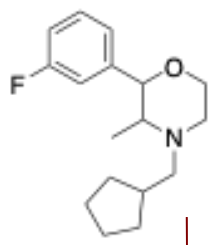




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	21.9
10	Relaxation Delay	1.9074
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-22.4
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

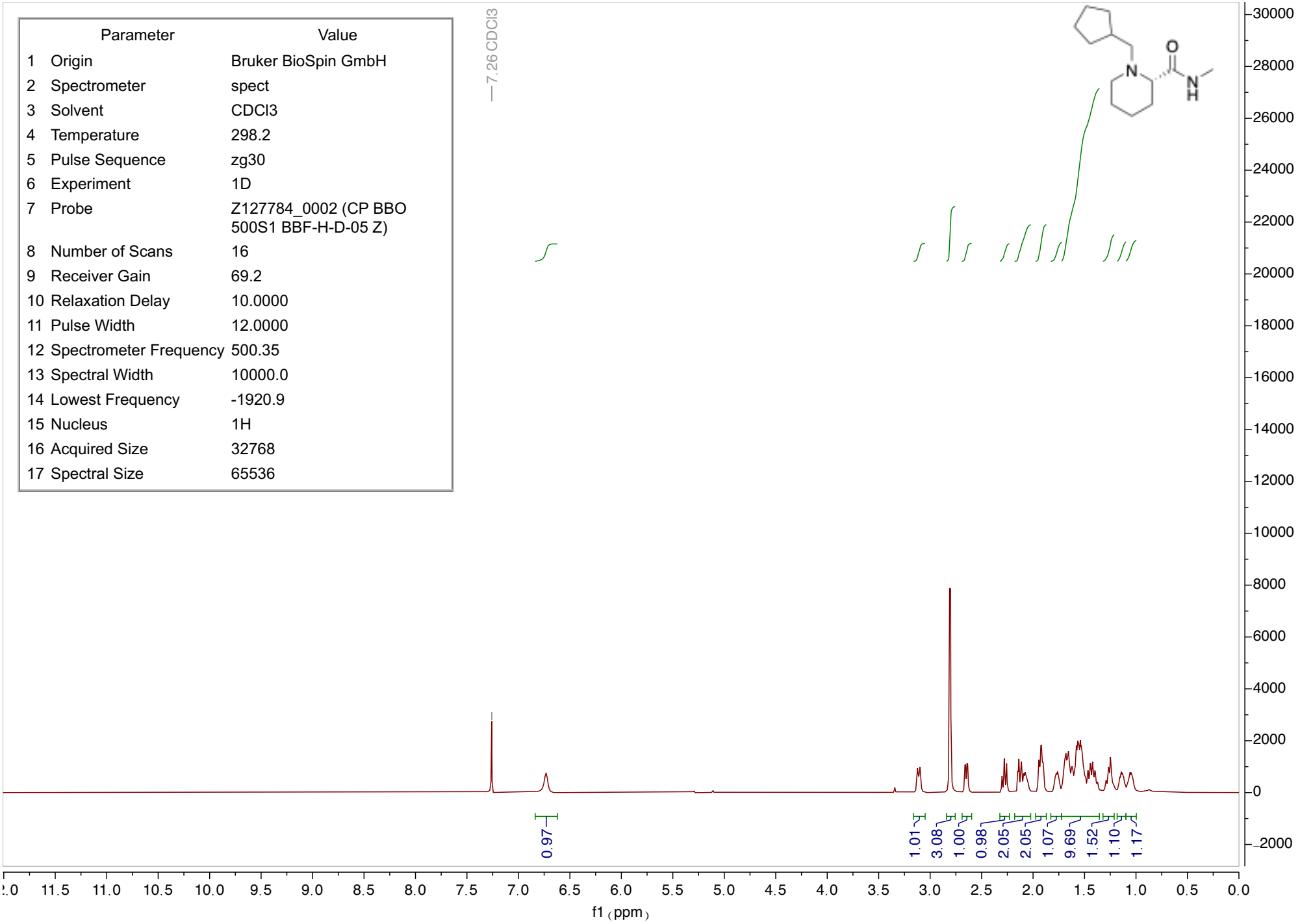


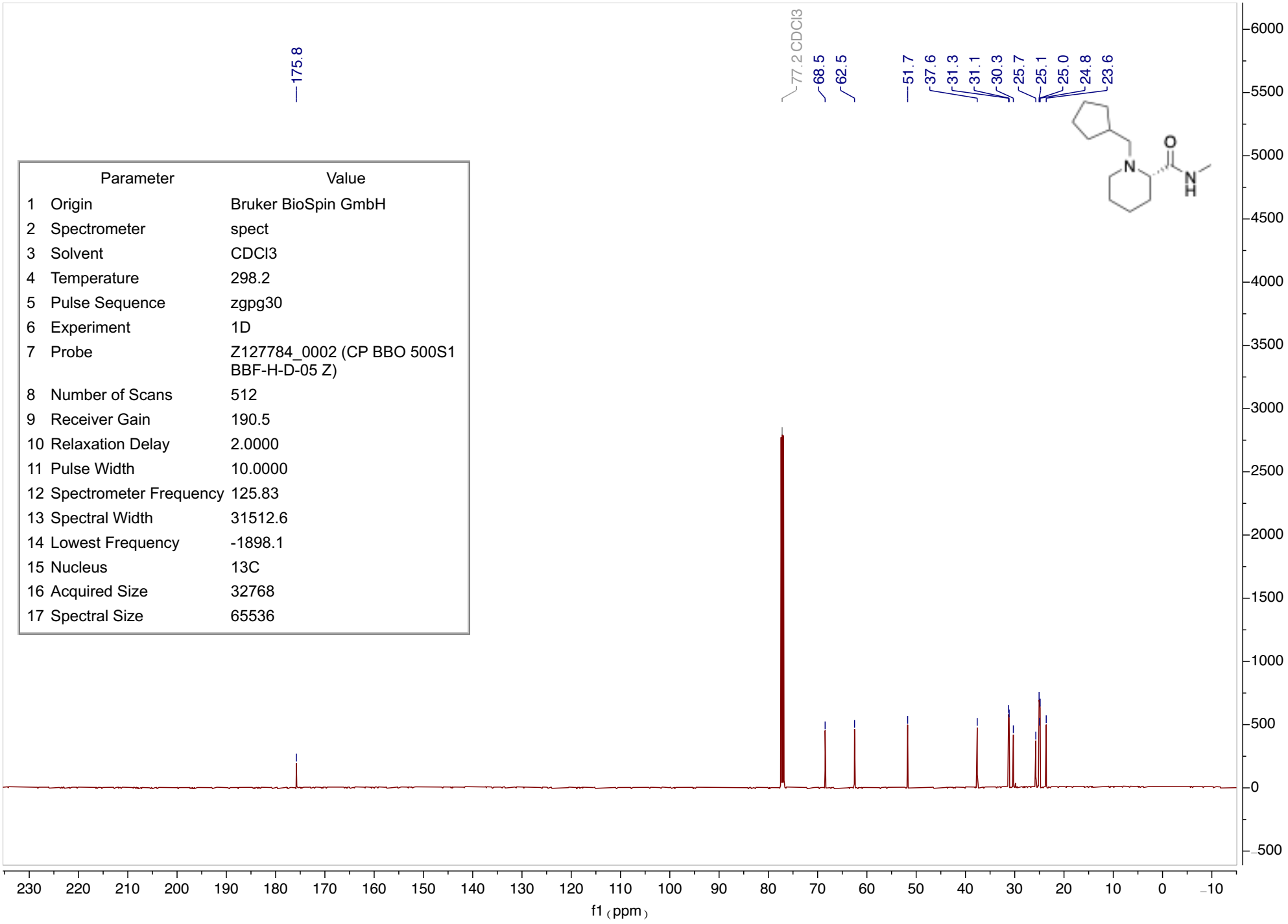
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-22.3
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512



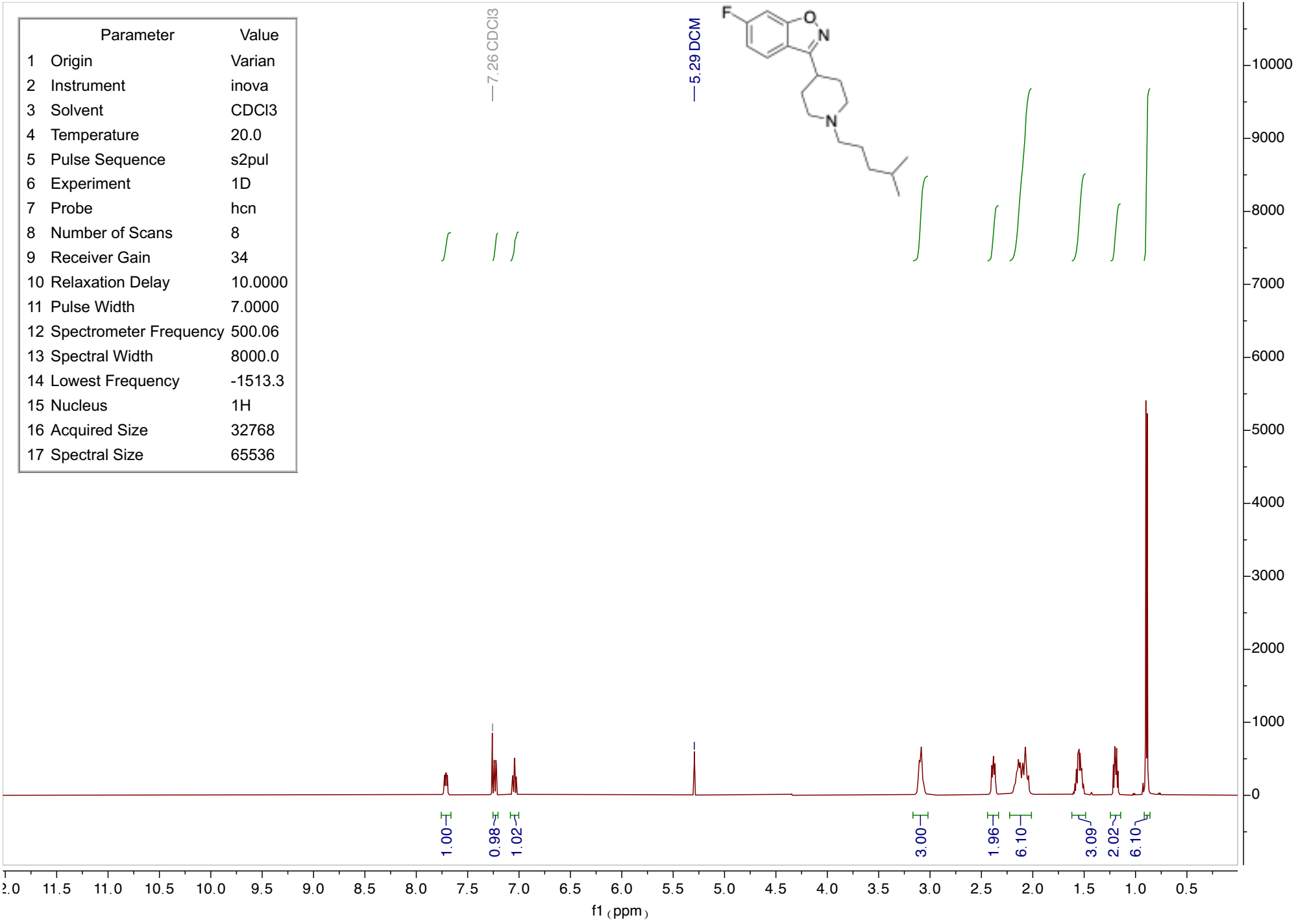
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-91.2
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

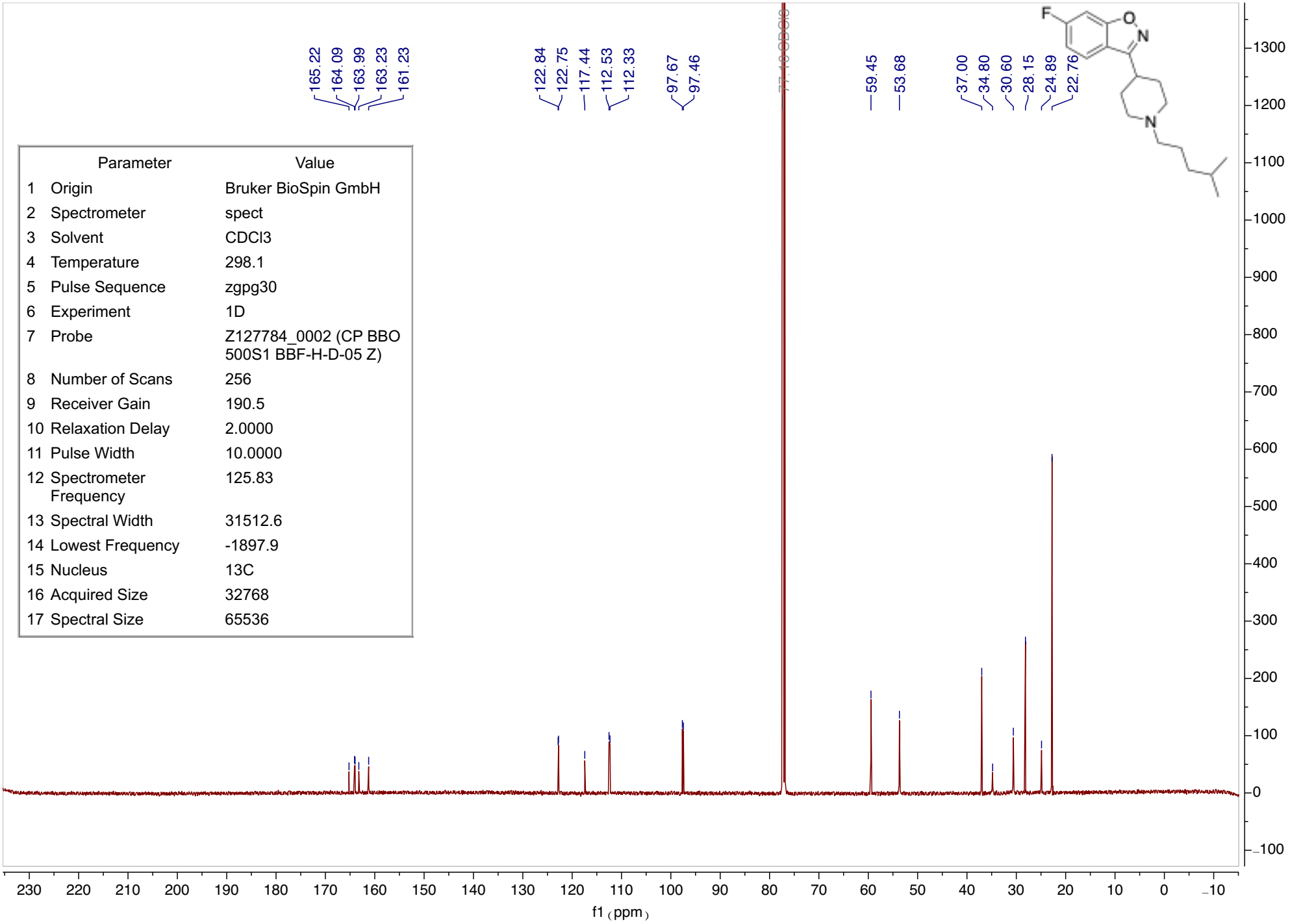
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	69.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1920.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536





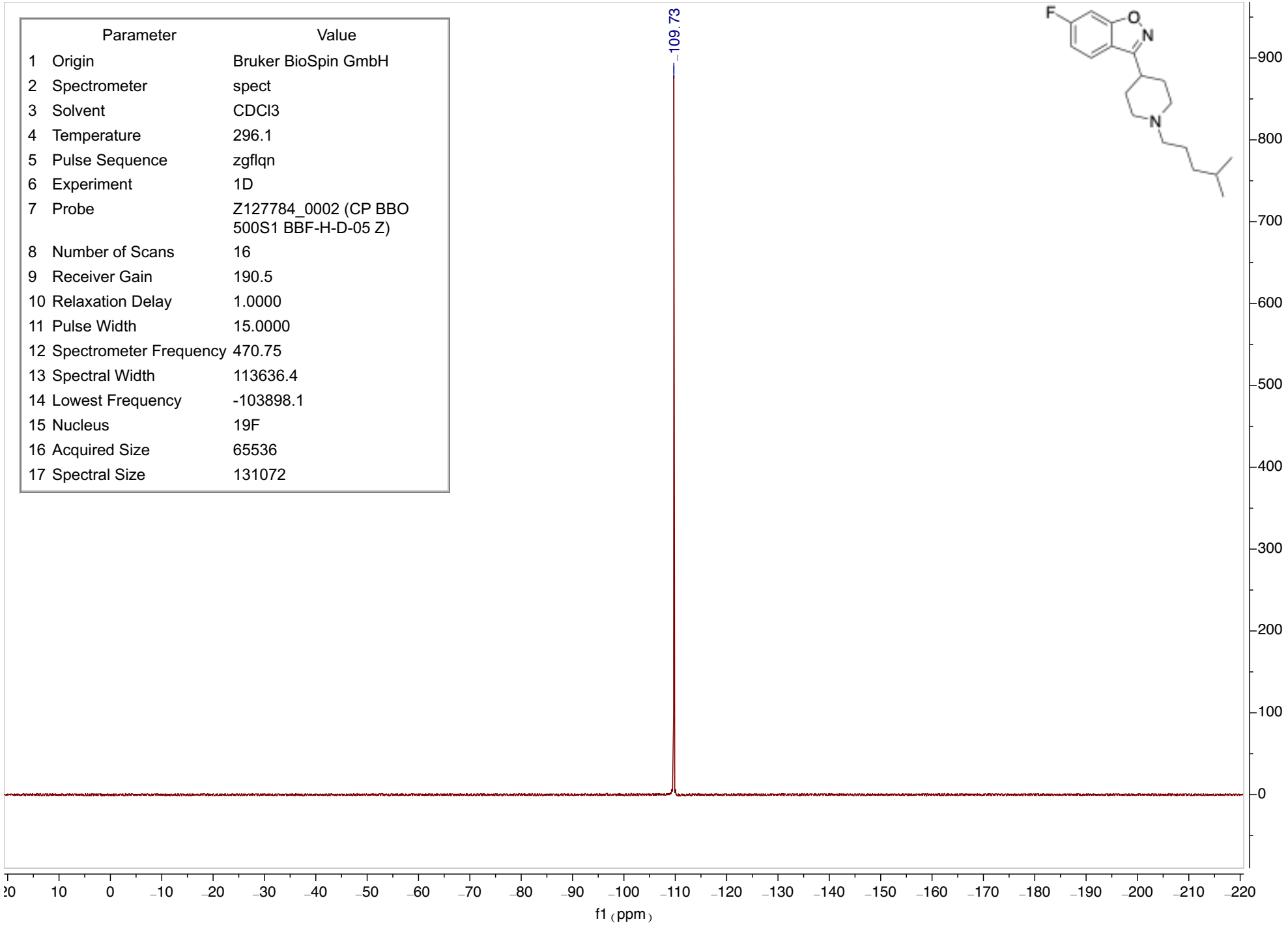
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


7.26 CDCl3
5.29 DCM
F
O
N
N
Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 34
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1513.3
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
1.00
0.98
1.02
3.00
1.96
6.10
3.09
2.02
6.10
12.0 11.5 11.0 10.5 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
f1 (ppm)

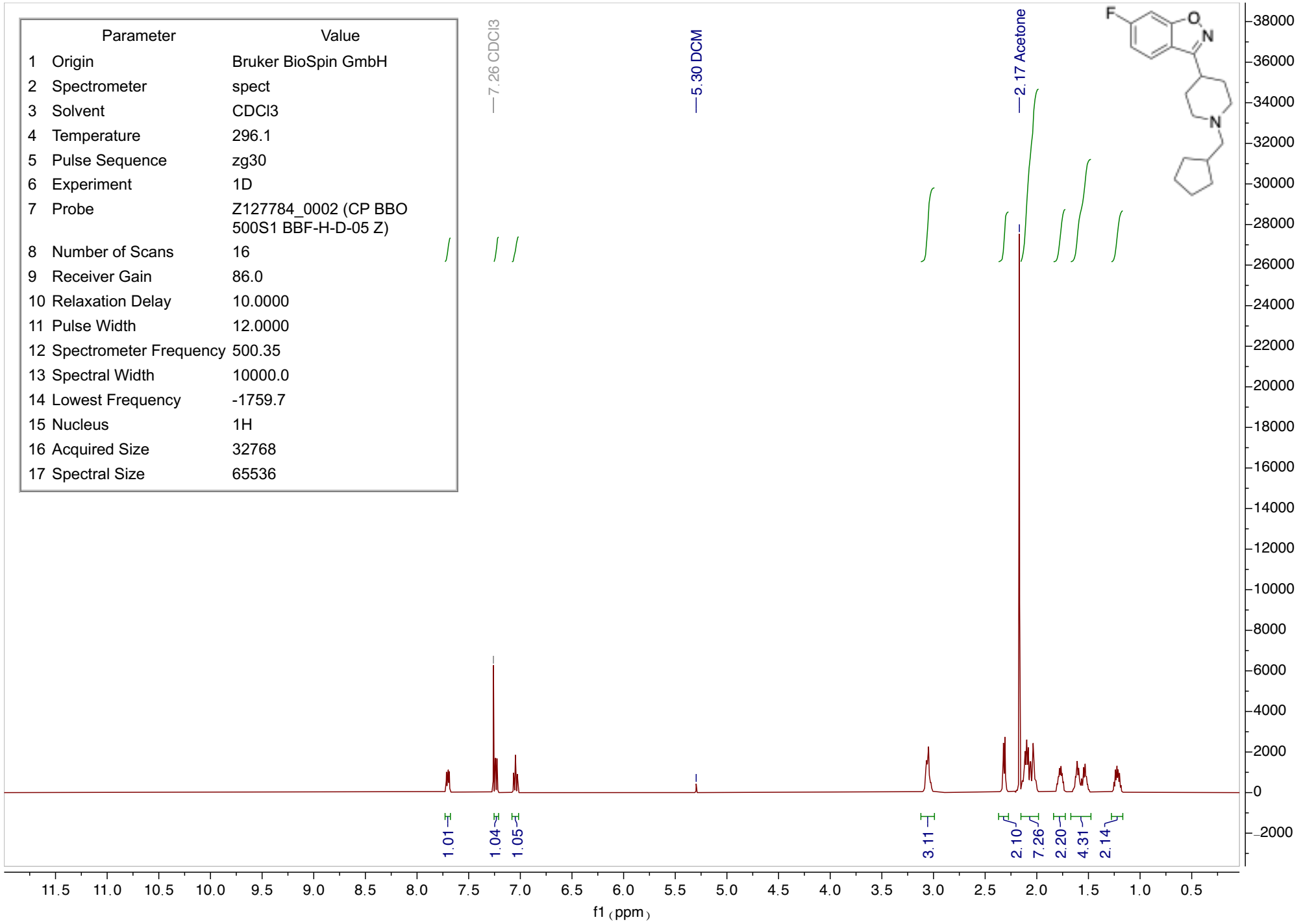


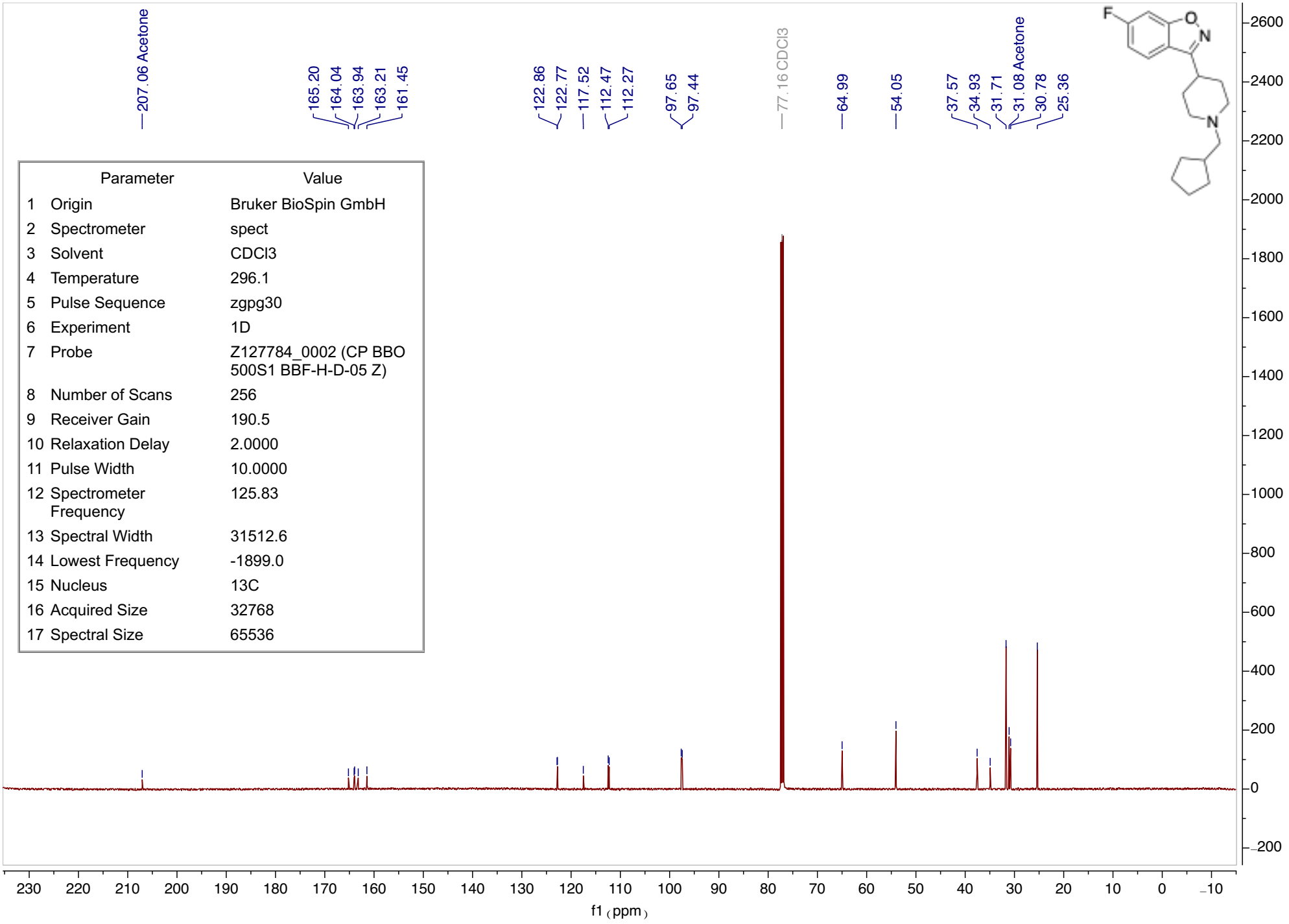
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1897.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



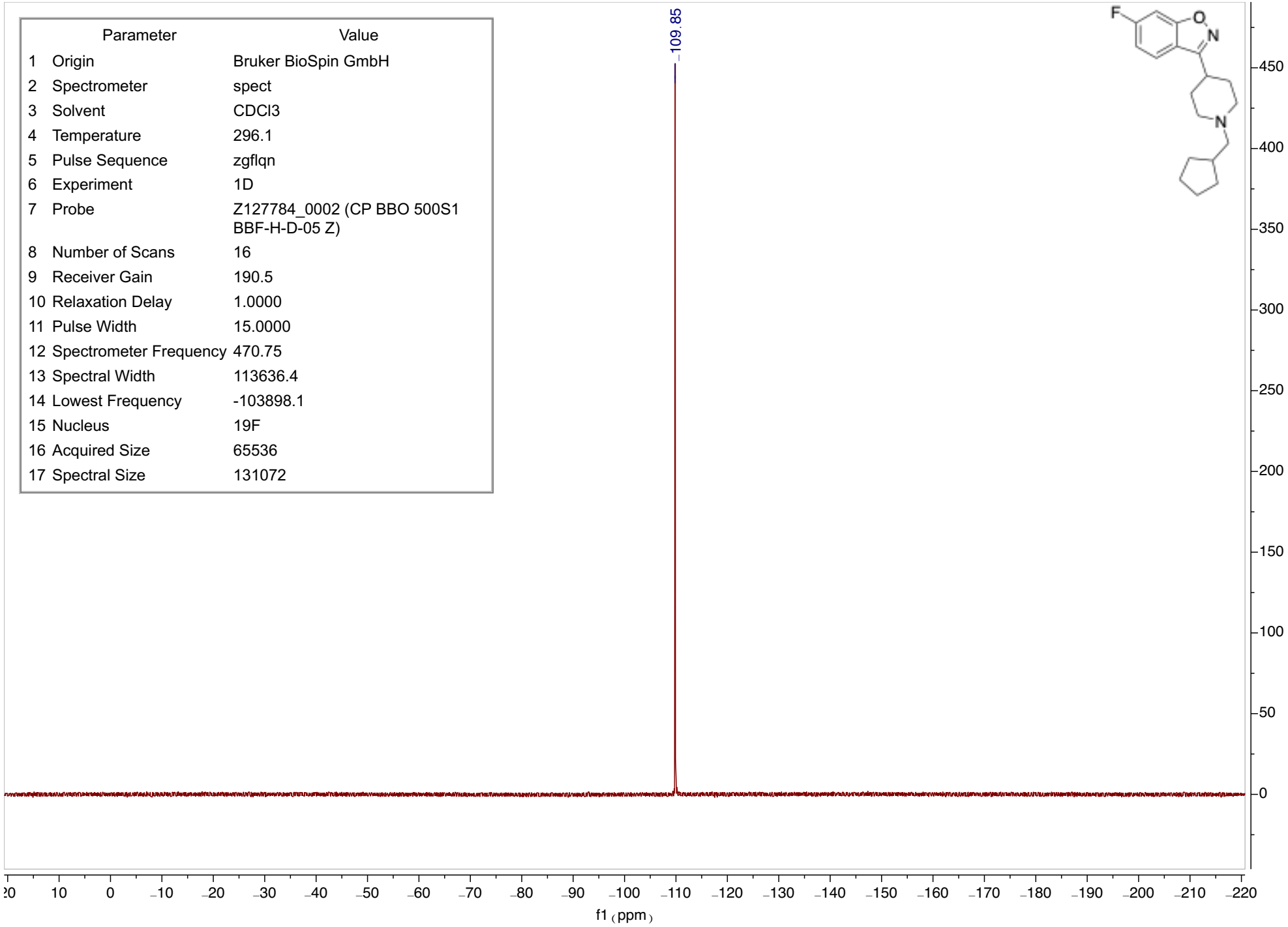
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



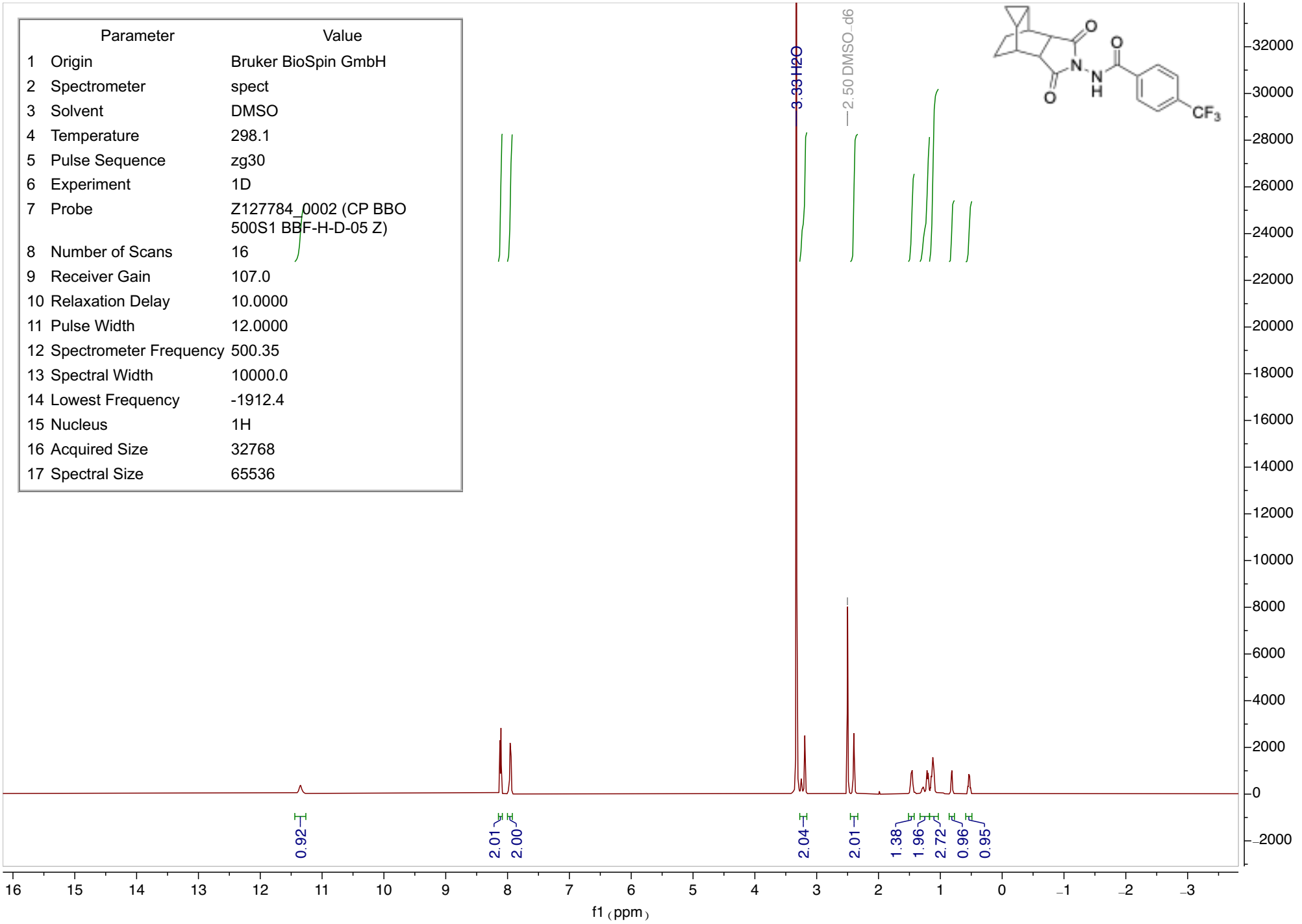


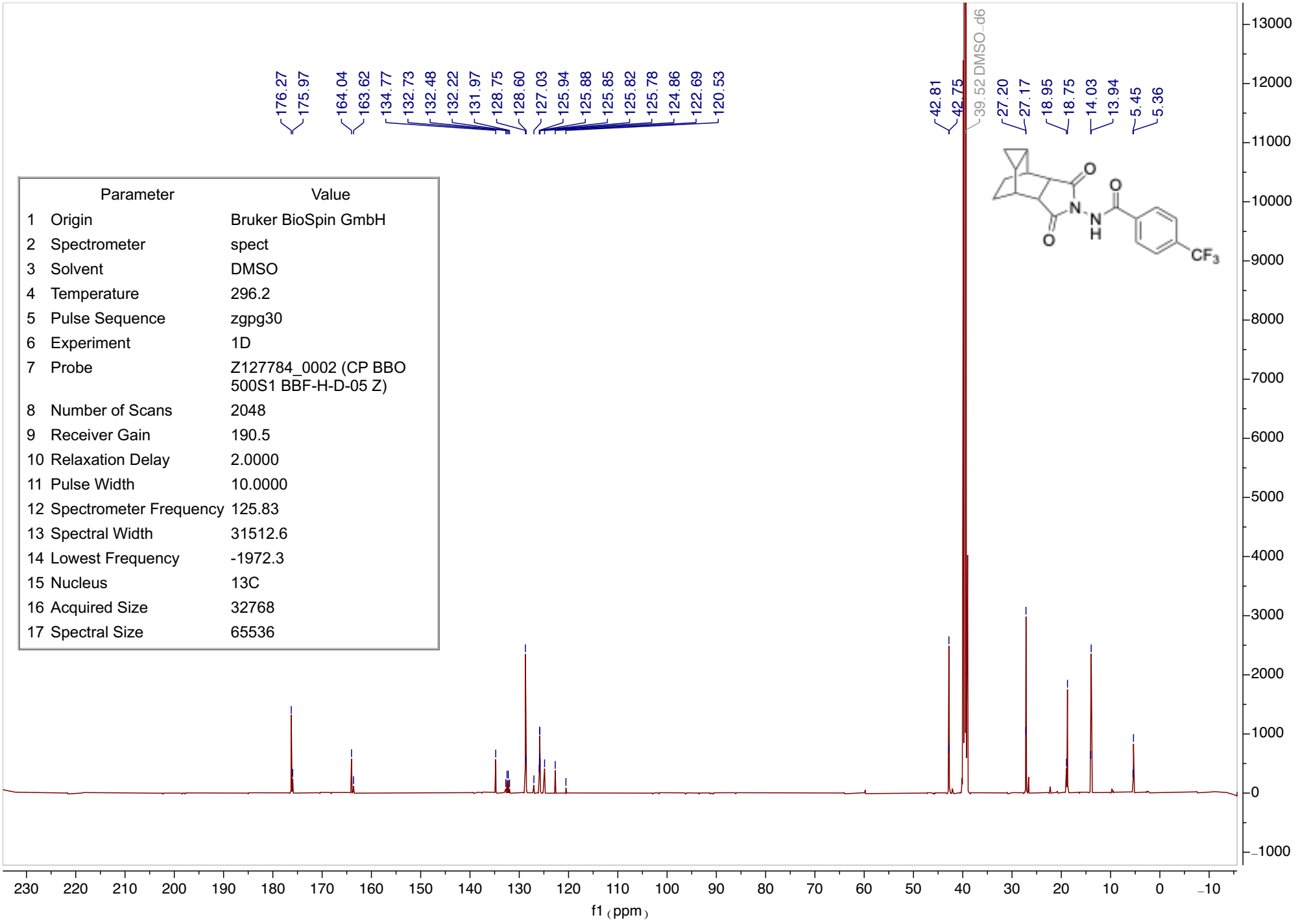
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



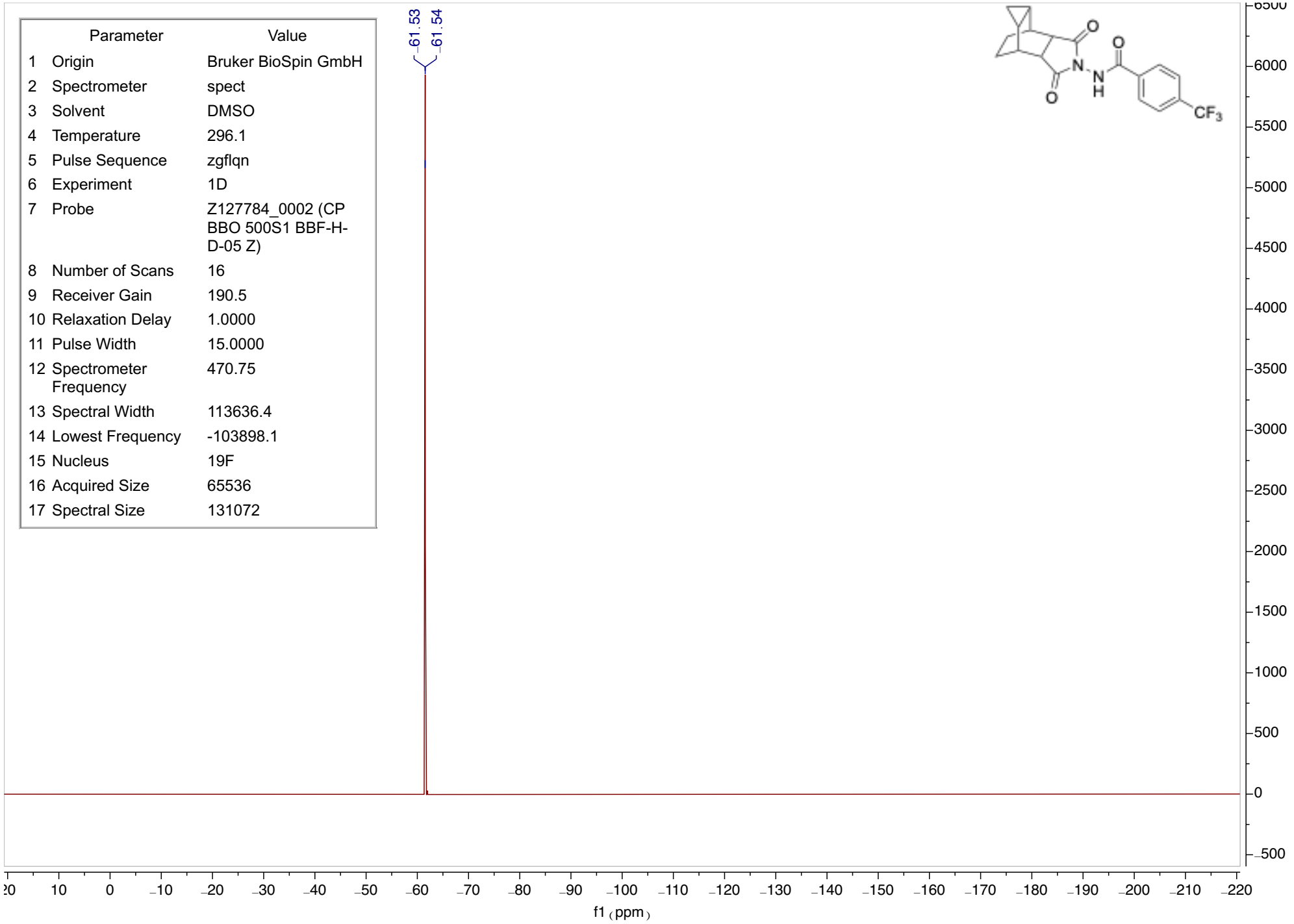
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	107.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1912.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

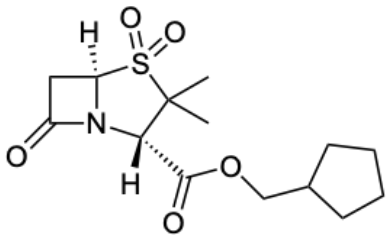




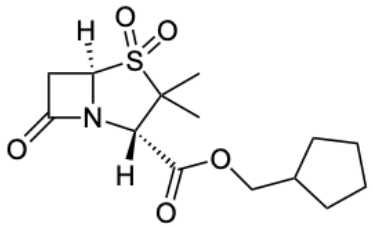
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2048
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1972.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

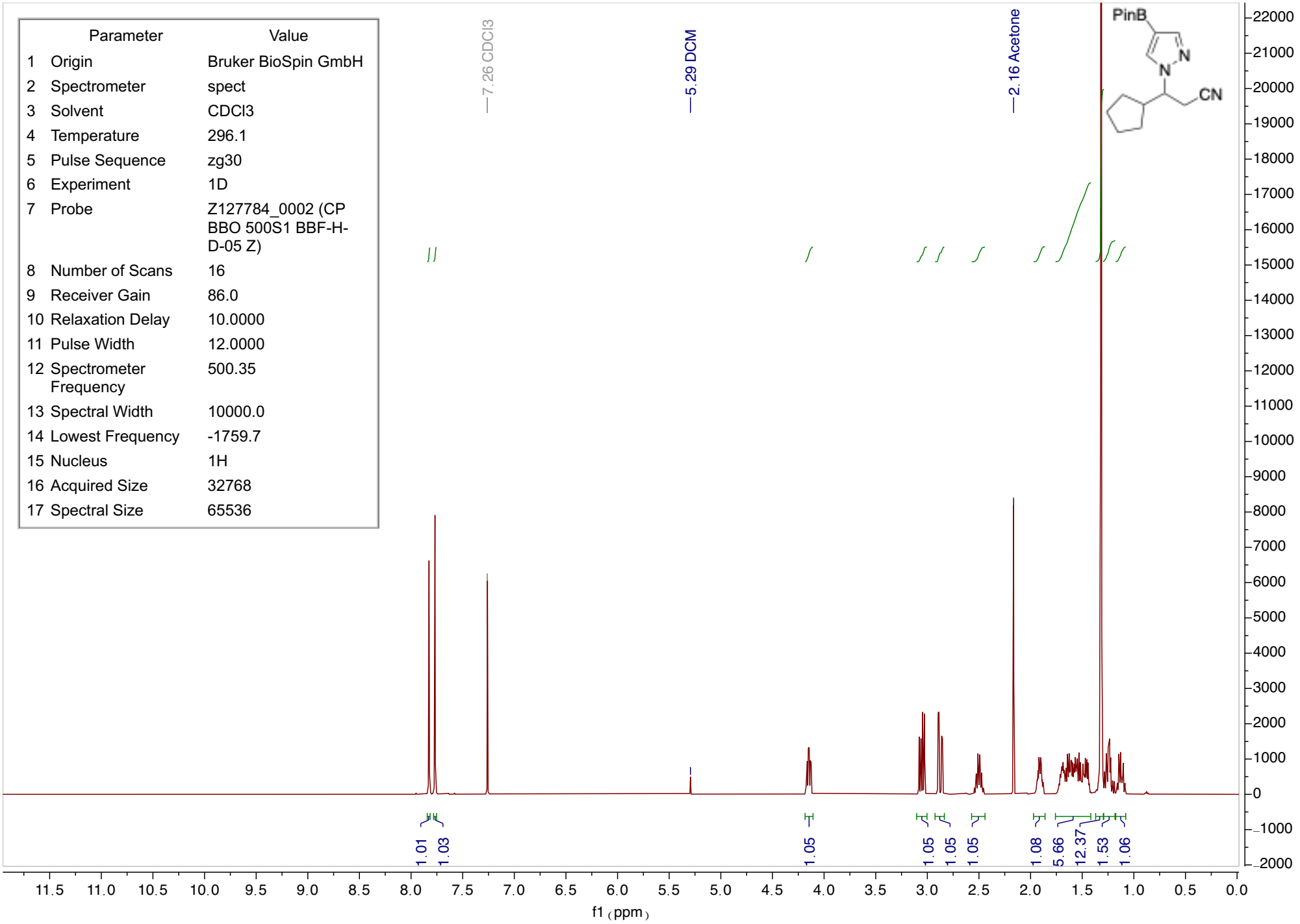




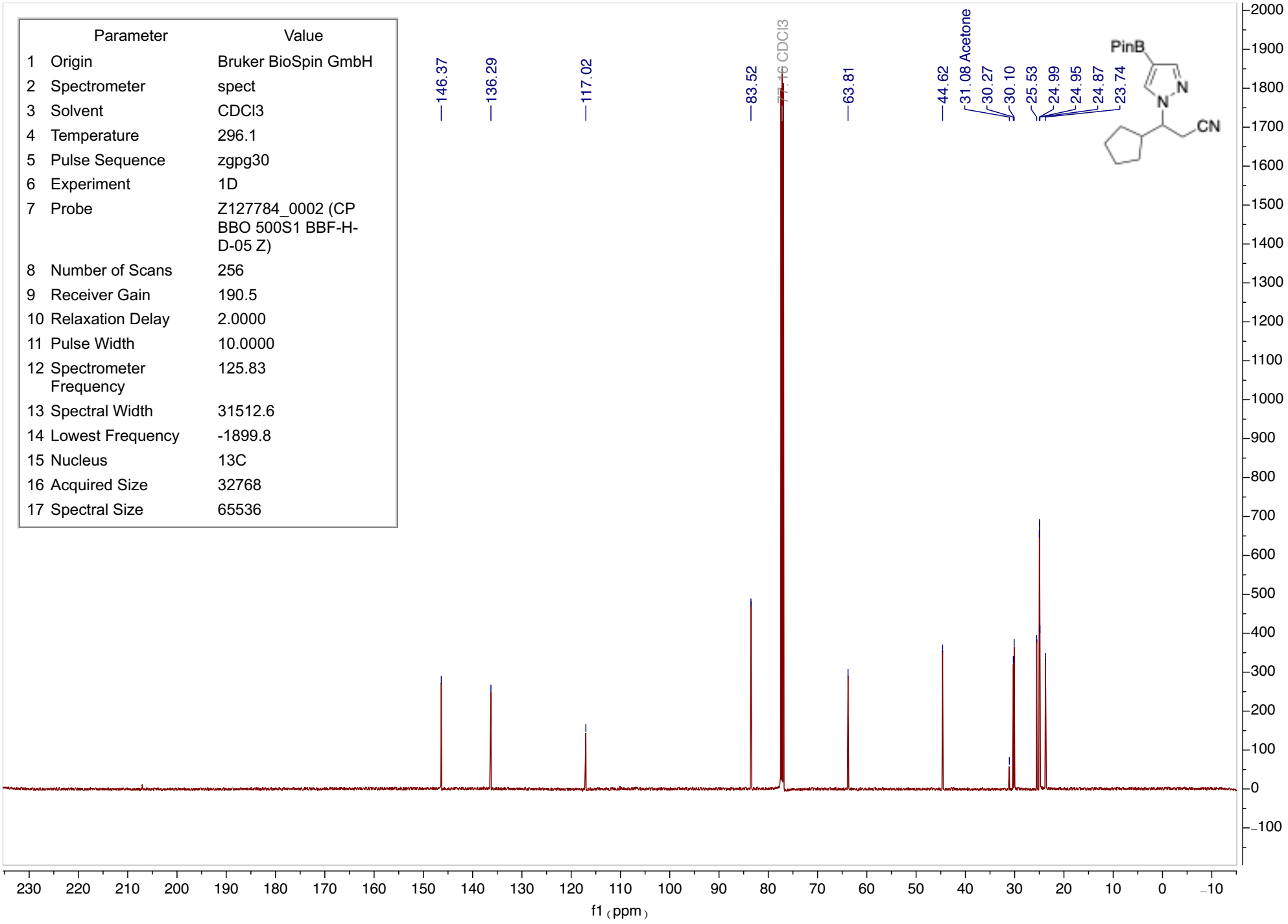
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	94.3
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

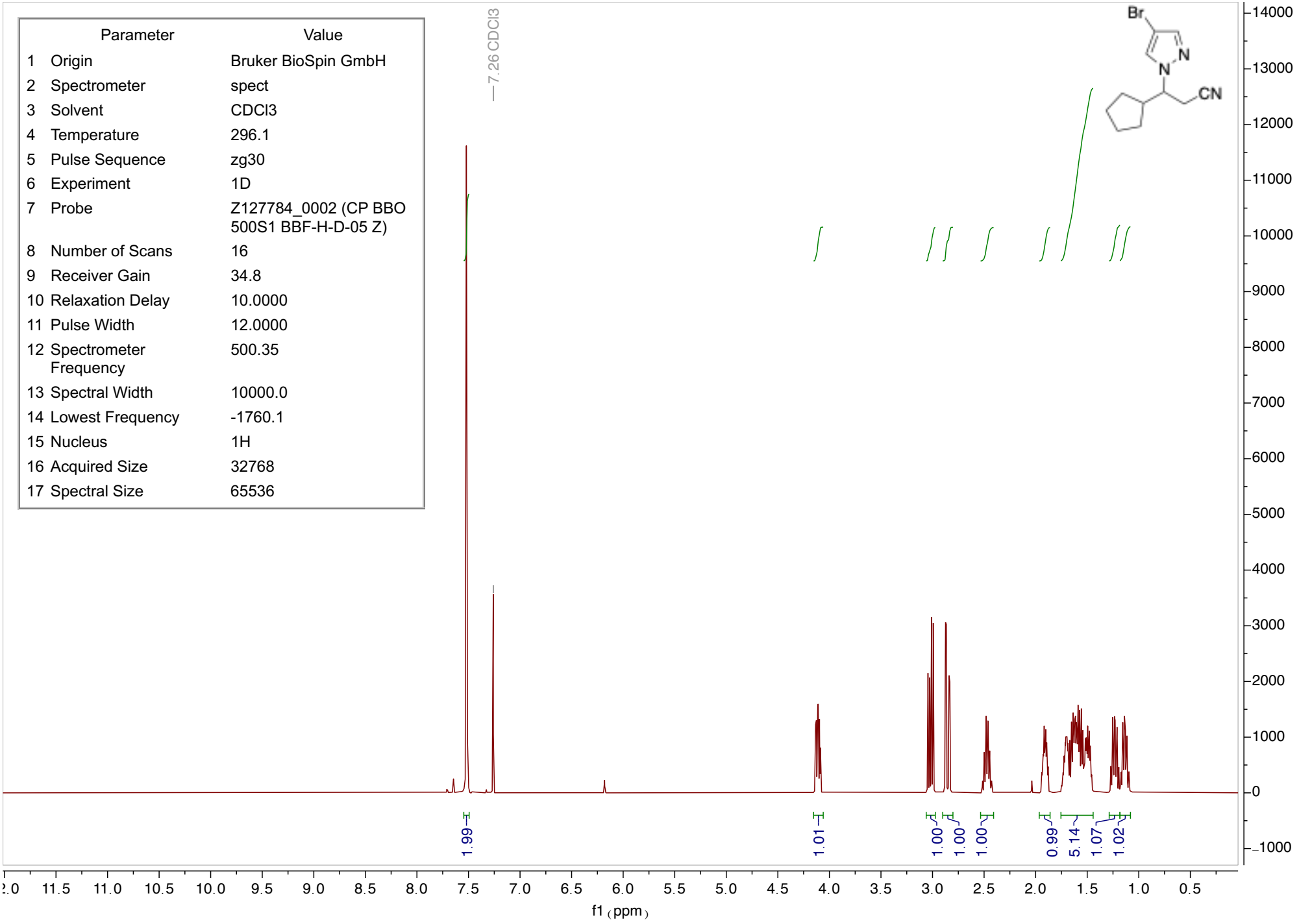


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

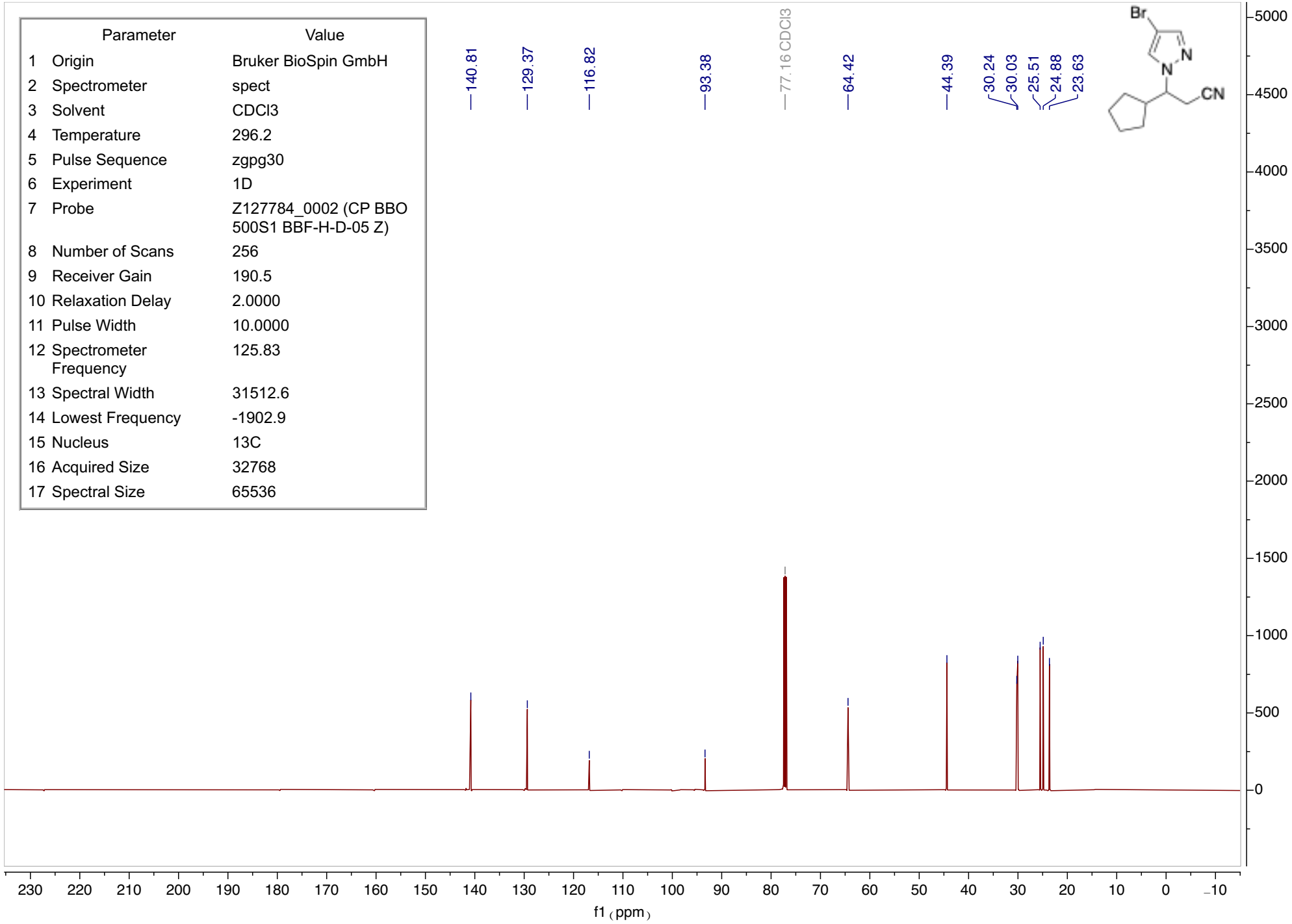


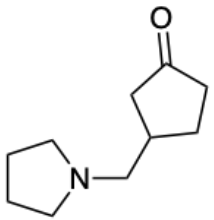
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536


Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zgpg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 256
9 Receiver Gain 190.5
10 Relaxation Delay 2.0000
11 Pulse Width 10.0000
12 Spectrometer Frequency 125.83
13 Spectral Width 31512.6
14 Lowest Frequency -1899.8
15 Nucleus 13C
16 Acquired Size 32768
17 Spectral Size 65536
146.37
136.29
117.02
83.52
77.16 CDCl3
63.81
44.62
31.08 Acetone
30.27
30.10
25.53
24.99
24.95
24.87
23.74
PinB
N
N
CN
f1 (ppm)

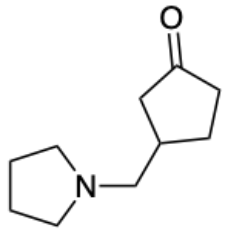

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 16
9 Receiver Gain 34.8
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 10000.0
14 Lowest Frequency -1760.1
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
Br
N
N
CN
1.99
1.01
1.00
1.00
1.00
0.99
5.14
1.07
1.02
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

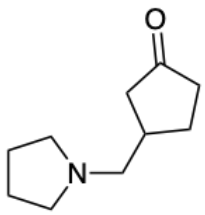




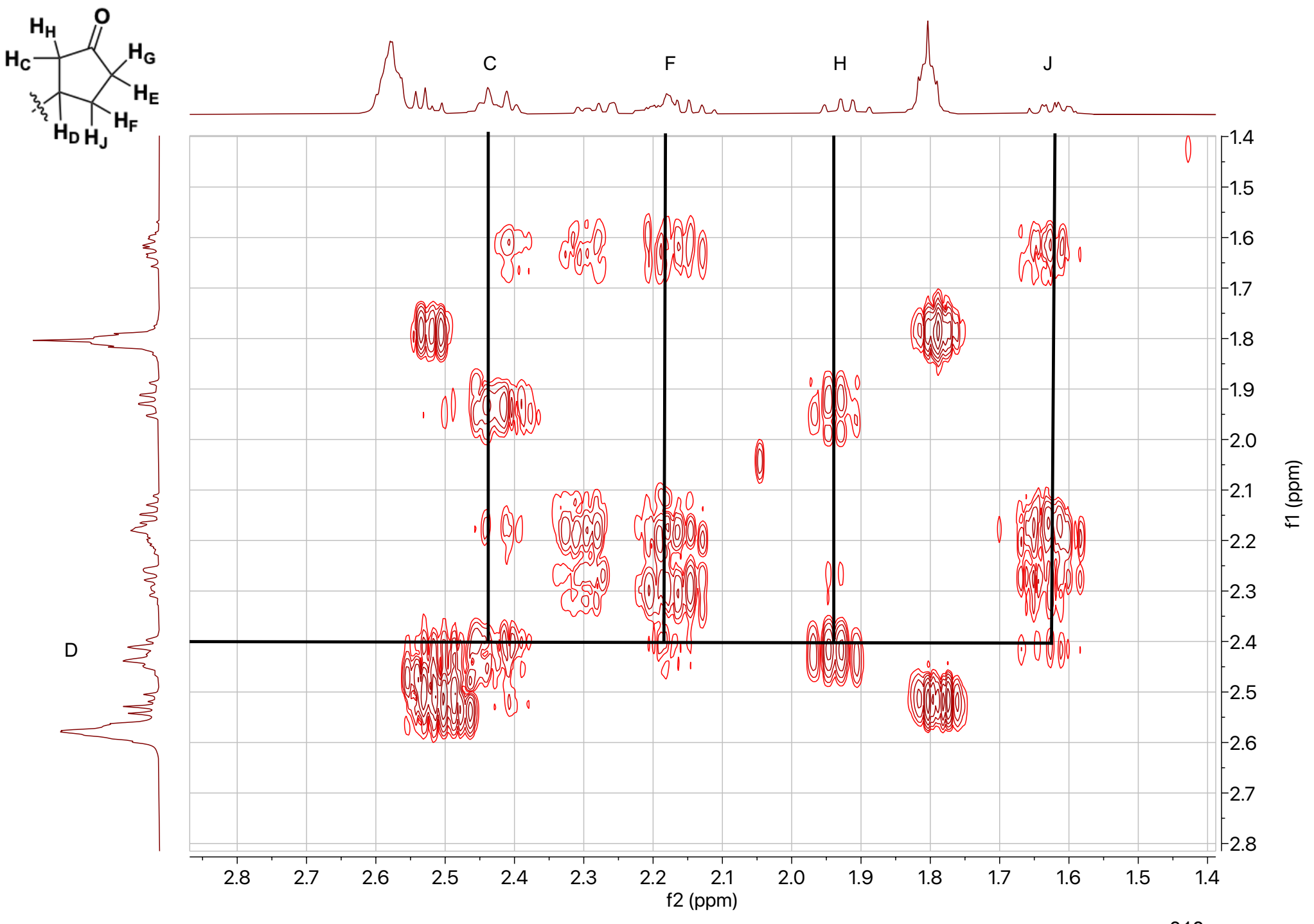
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

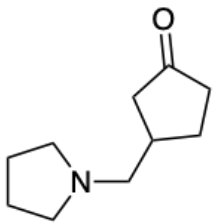


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1904.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

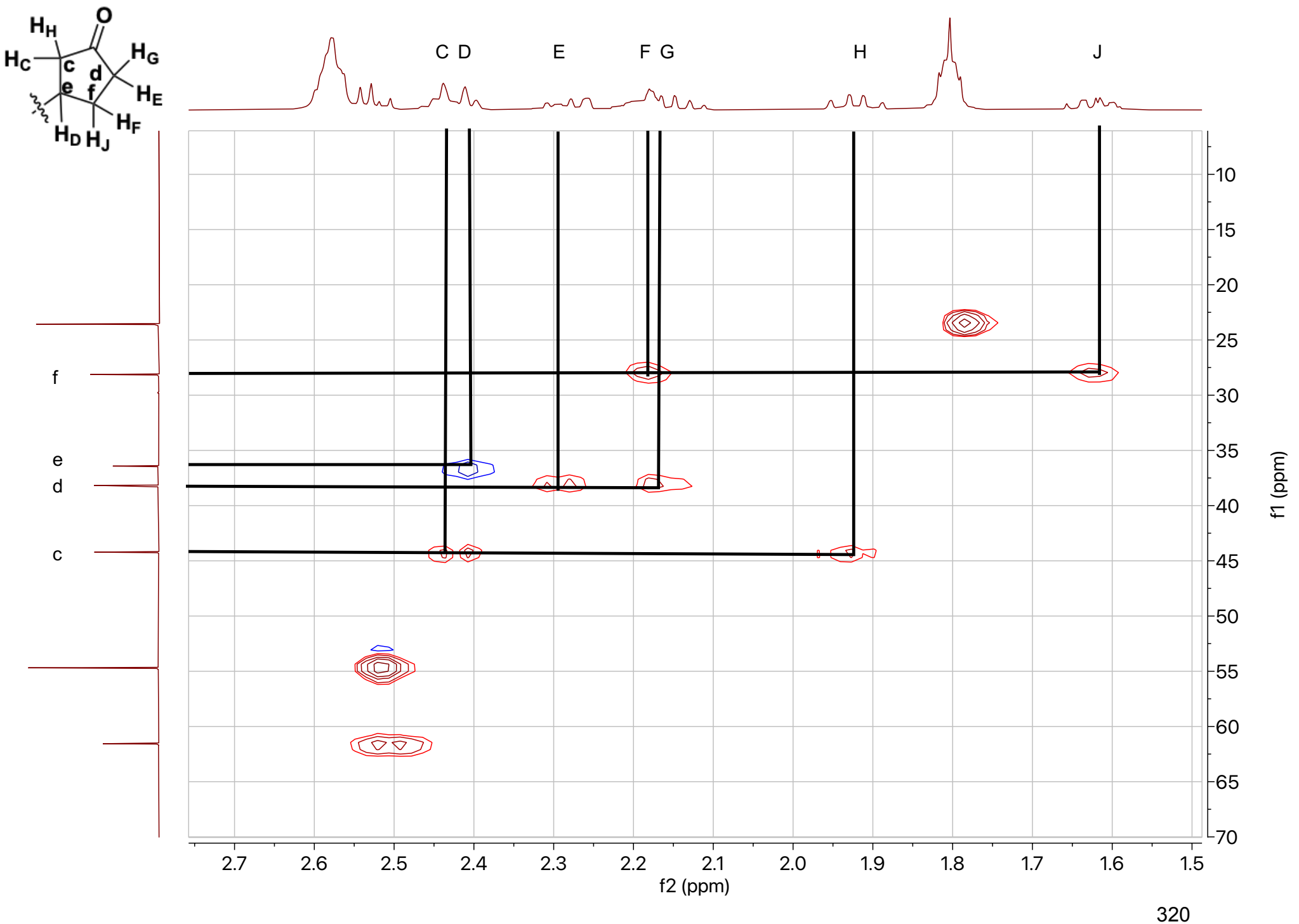


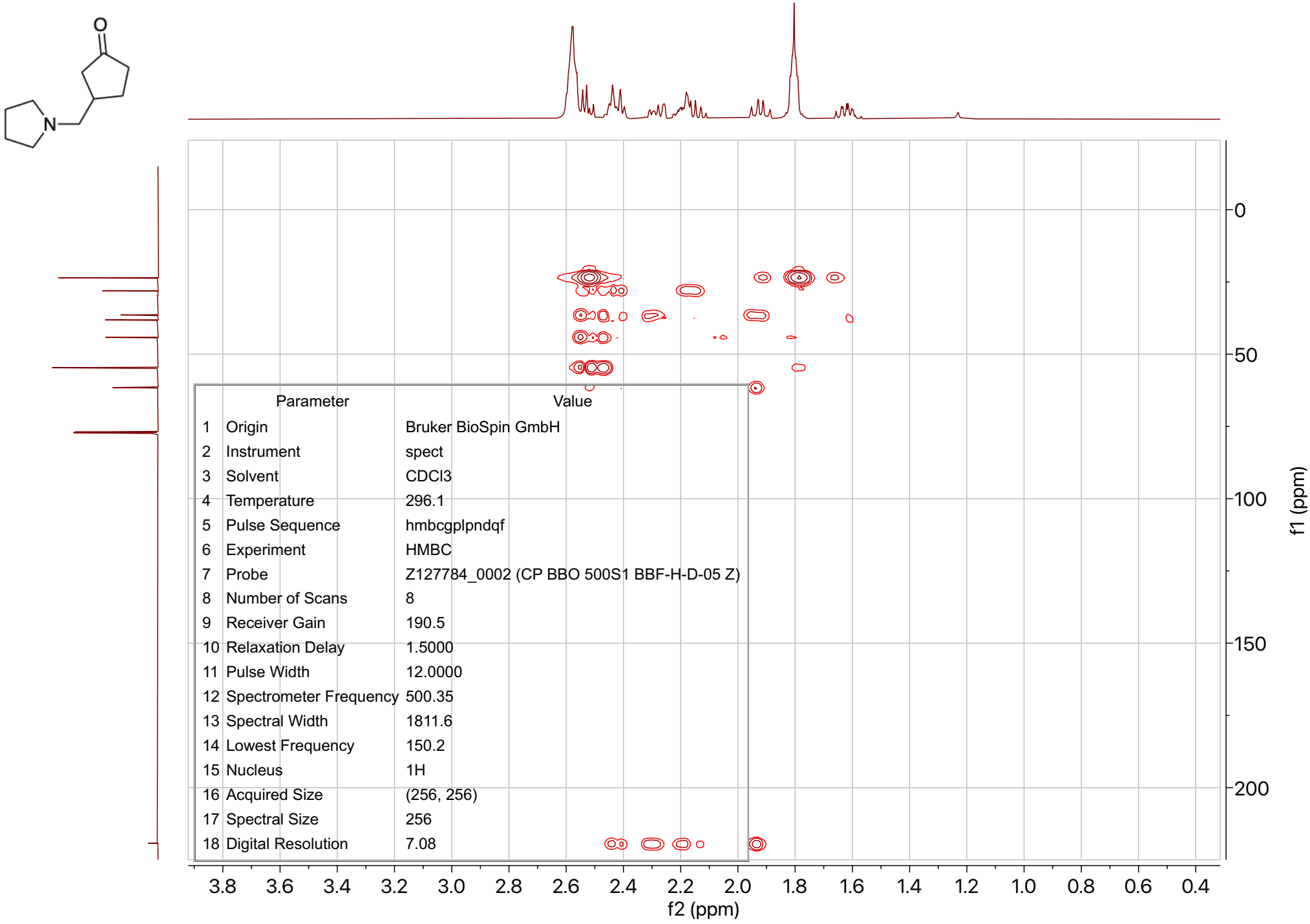
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.5920
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	1811.6
14	Lowest Frequency	150.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024
18	Digital Resolution	1.77


O
H_H
H_C
H_G
H_E
H_F
H_D H_J
C
F
H
J
D
f2 (ppm)
f1 (ppm)
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4

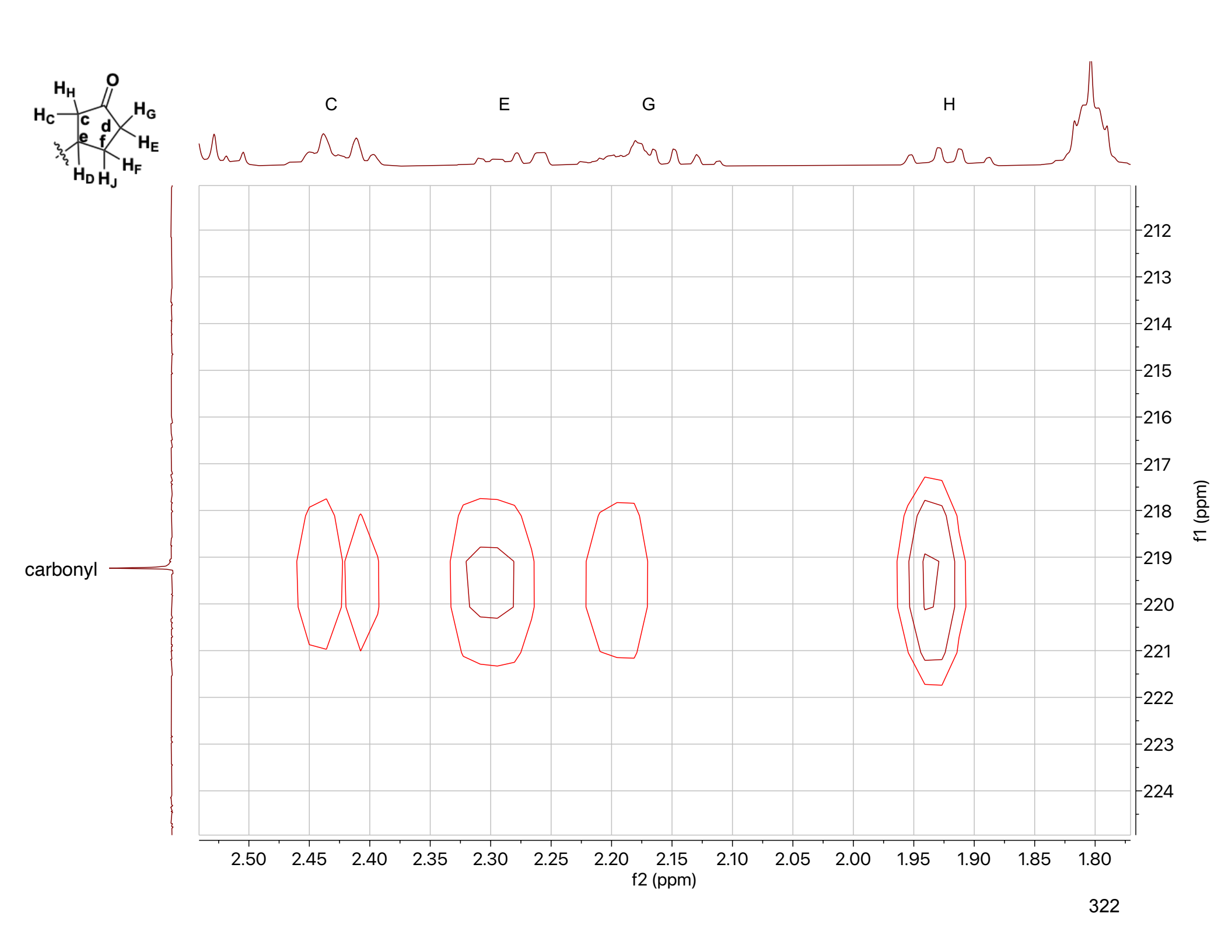


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	1811.6
14	Lowest Frequency	150.2
15	Nucleus	1H
16	Acquired Size	(256, 256)
17	Spectral Size	256
18	Digital Resolution	7.08

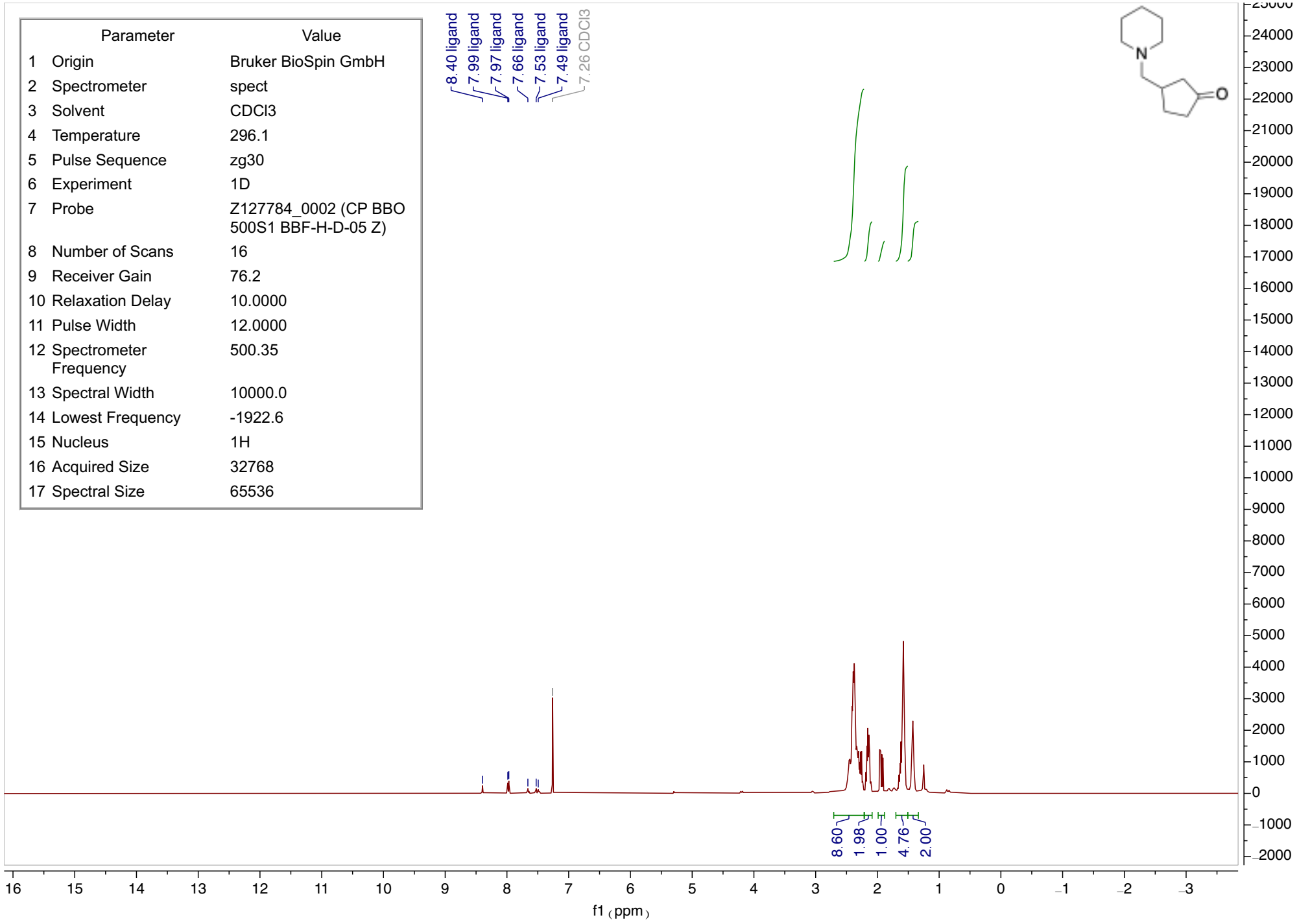

O
H_H
H_C
H_G
H_E
H_F
H_D
H_J
c
d
e
f
C D
E
F G
H
J
f
e
d
c
10
15
20
25
30
35
40
45
50
55
60
65
70
f1 (ppm)
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
f2 (ppm)

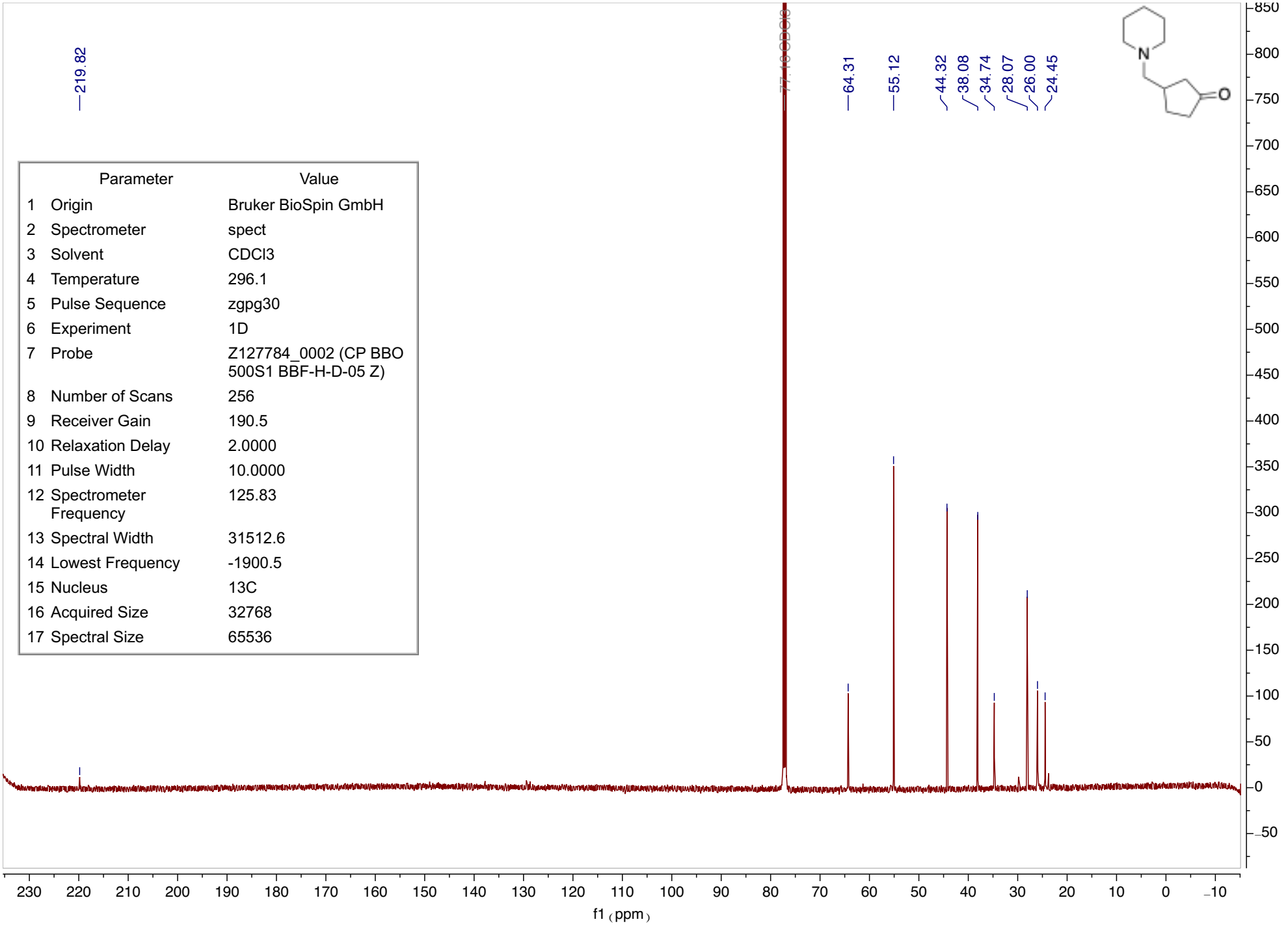


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	8
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	1811.6
14	Lowest Frequency	150.2
15	Nucleus	1H
16	Acquired Size	(256, 256)
17	Spectral Size	256
18	Digital Resolution	7.08

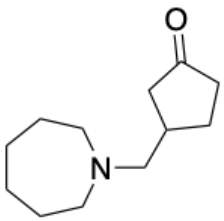

O
H_H
H_C
H_G
c
d
e
f
H_E
H_F
H_D H_J
C
E
G
H
carbonyl
212
213
214
215
216
217
218
219
220
221
222
223
224
f1 (ppm)
2.50
2.45
2.40
2.35
2.30
2.25
2.20
2.15
2.10
2.05
2.00
1.95
1.90
1.85
1.80
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	76.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

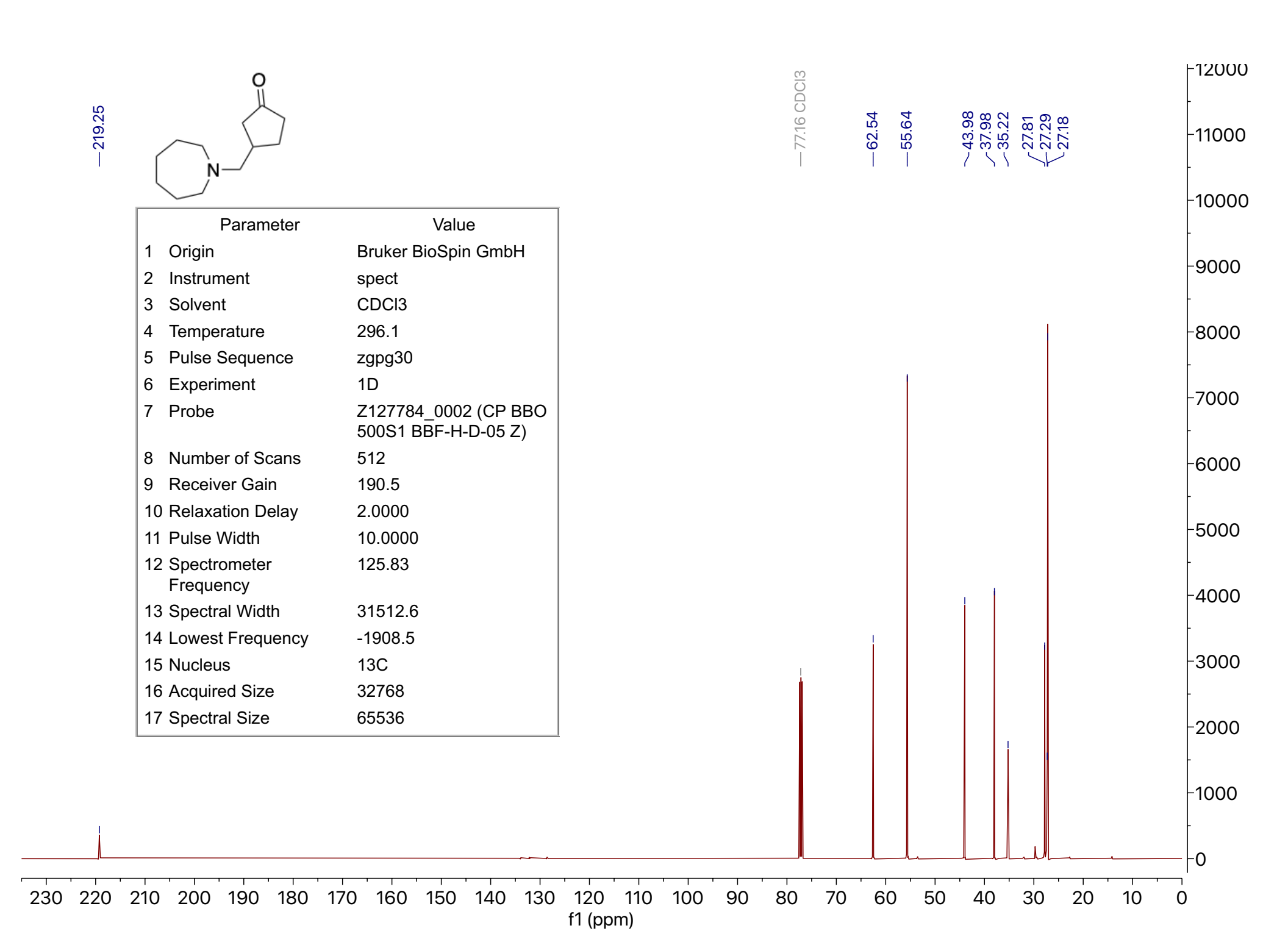




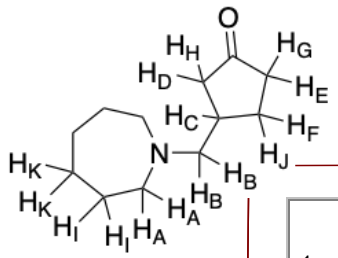
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



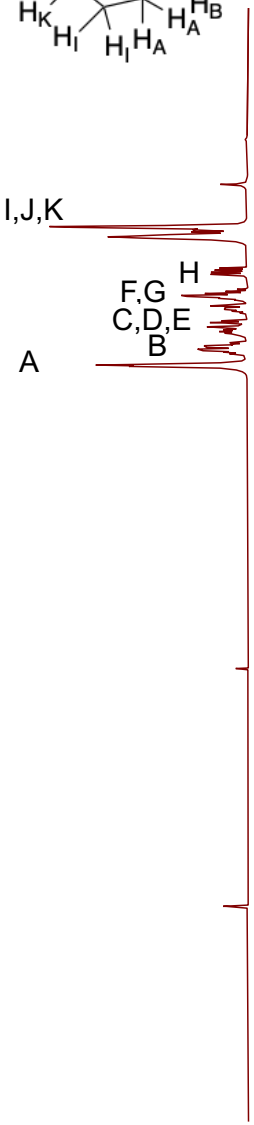
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	17.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

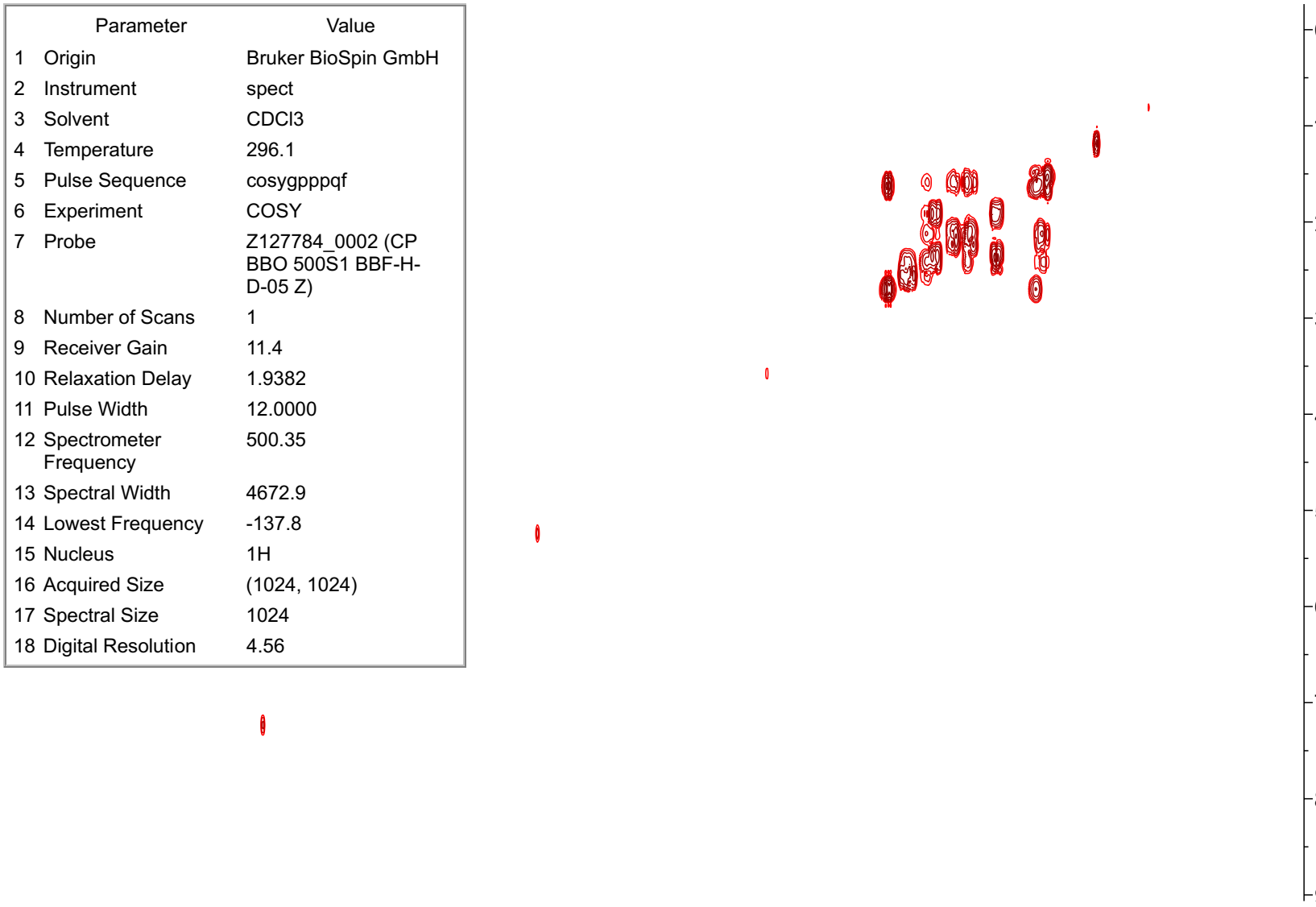


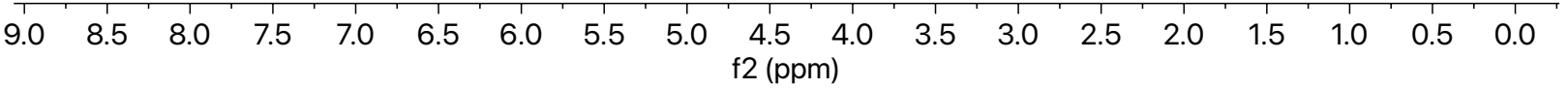
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1908.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

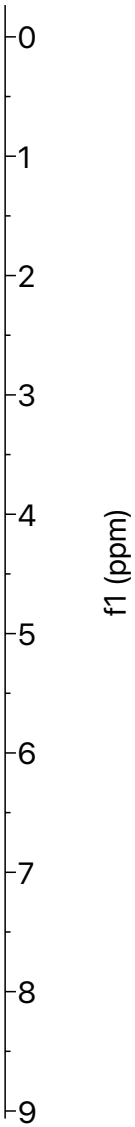


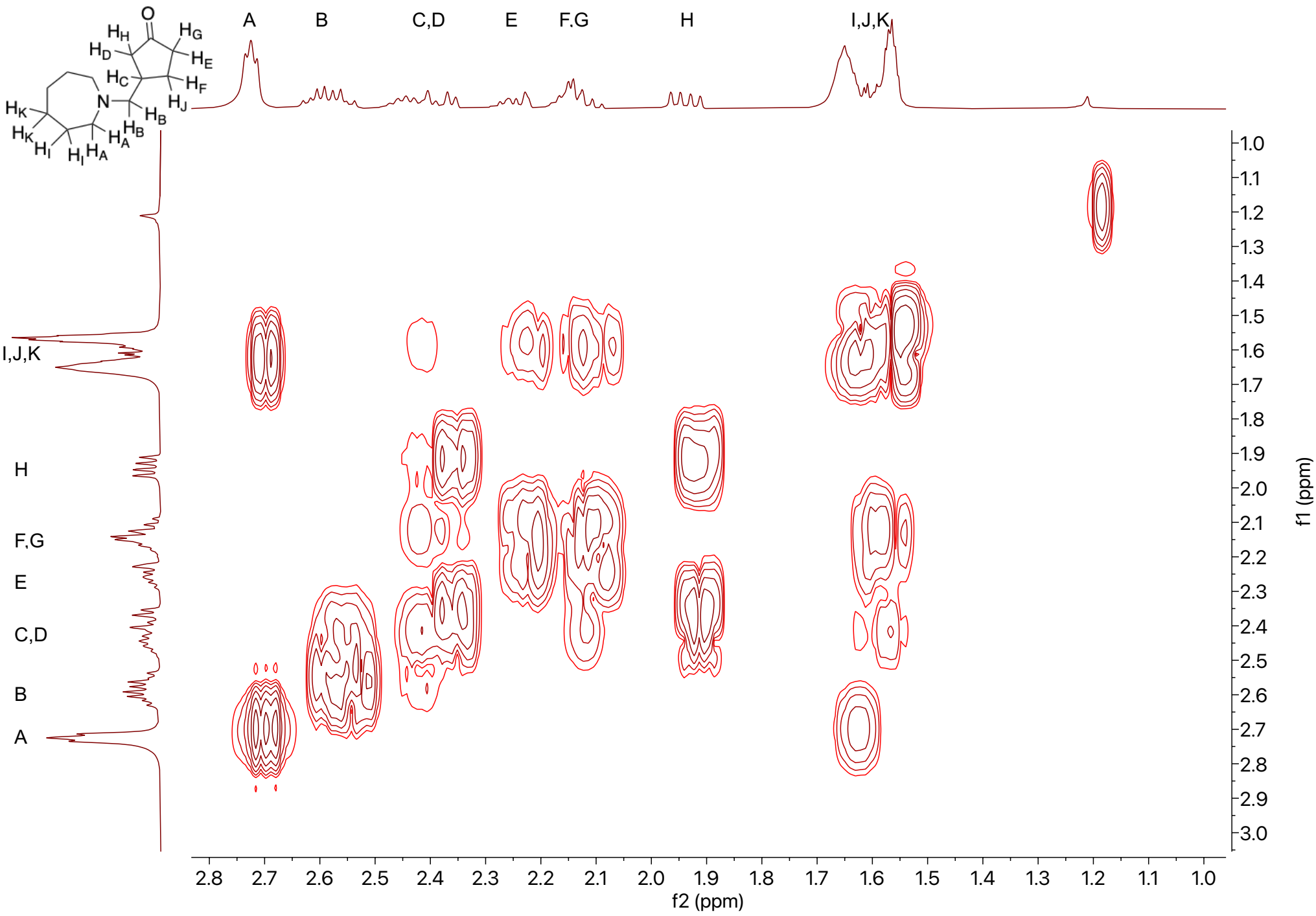
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	11.4
10	Relaxation Delay	1.9382
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4672.9
14	Lowest Frequency	-137.8
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024
18	Digital Resolution	4.56

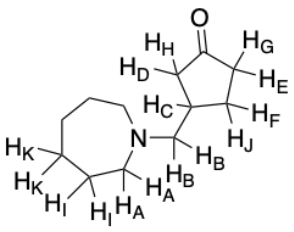




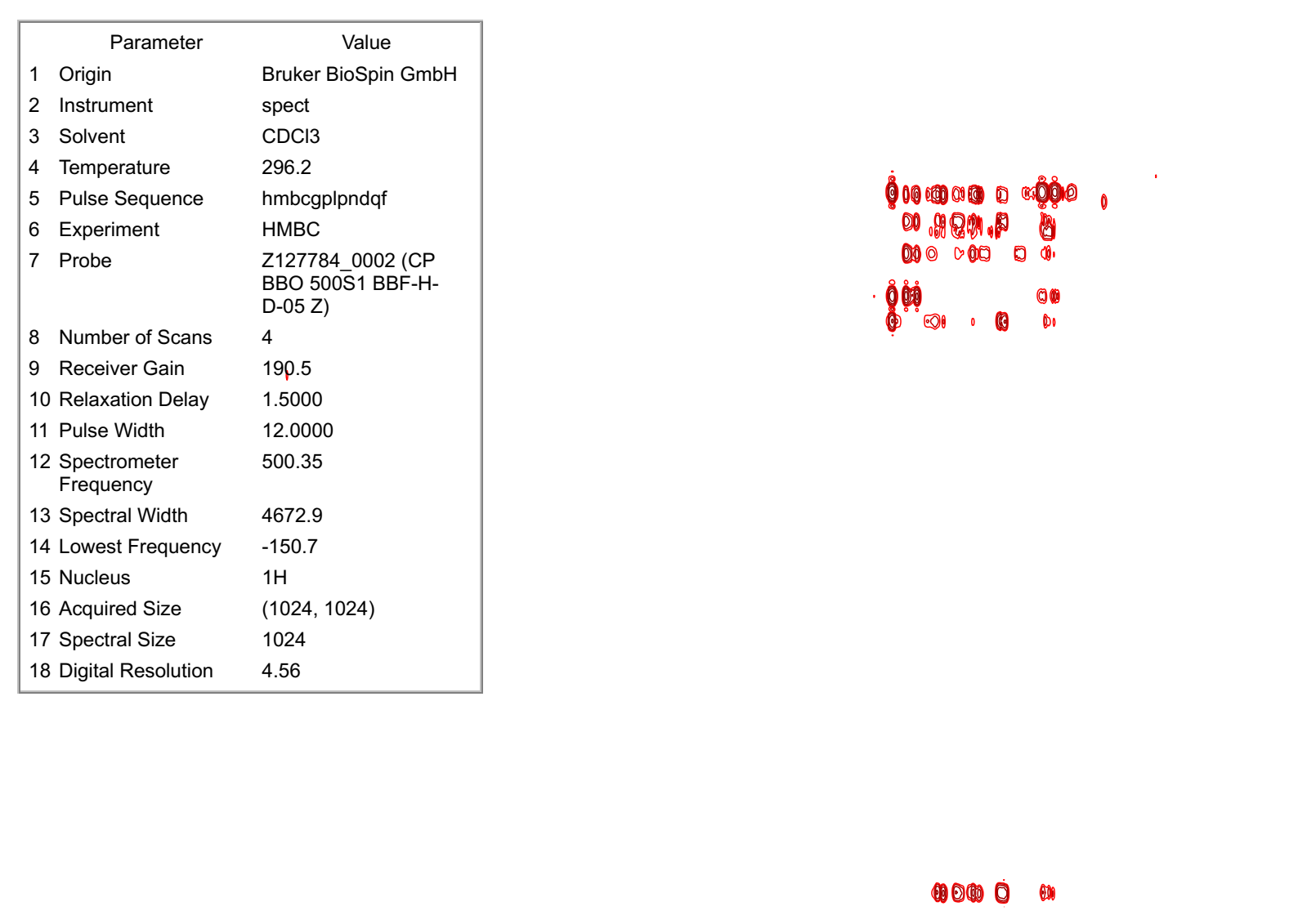


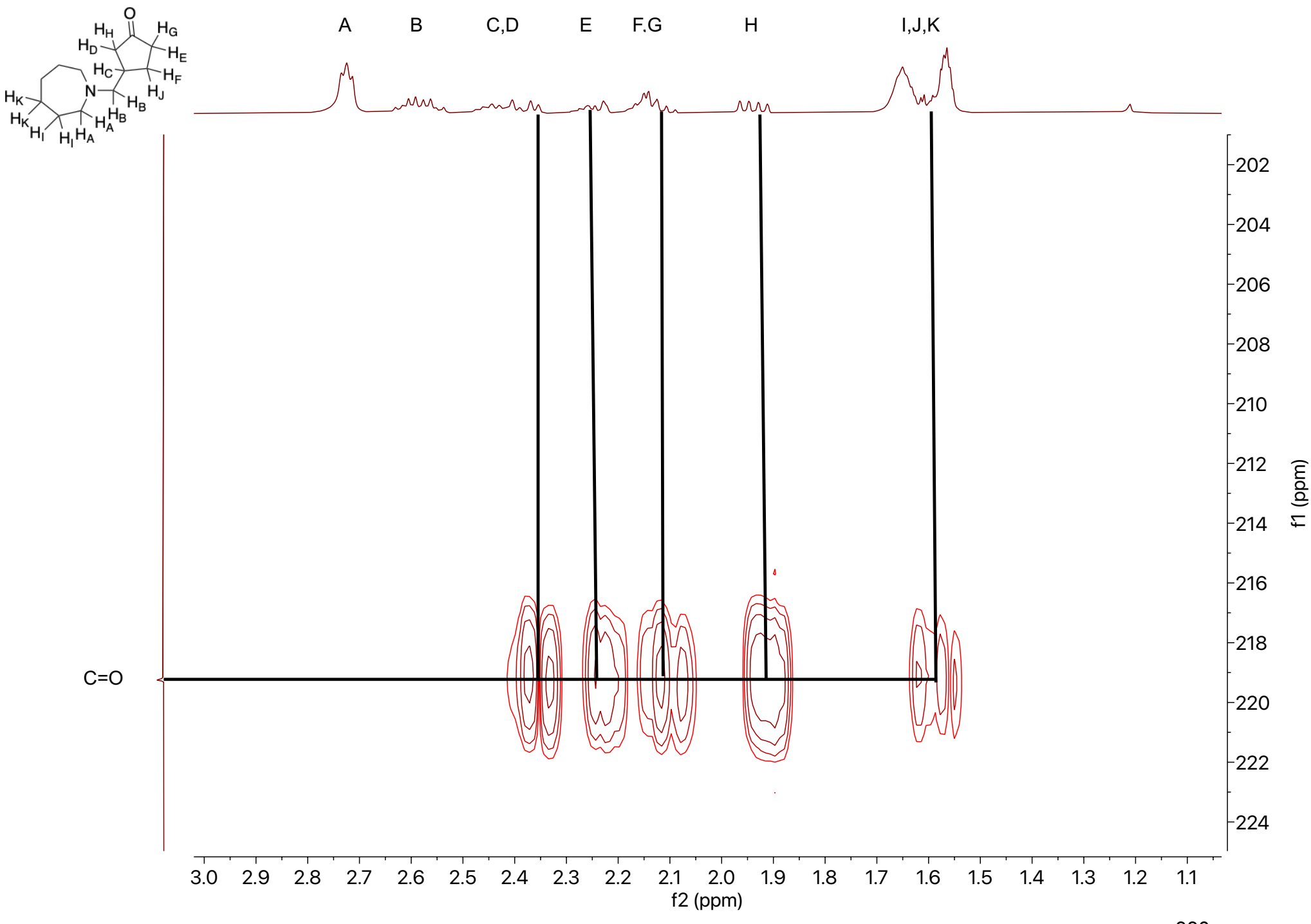



A
B
C,D
E
F,G
H
I,J,K
f2 (ppm)
f1 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4672.9
14	Lowest Frequency	-150.7
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024
18	Digital Resolution	4.56




A
B
C,D
E
F,G
H
I,J,K
C=O
f2 (ppm)
f1 (ppm)
3.0
2.9
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2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
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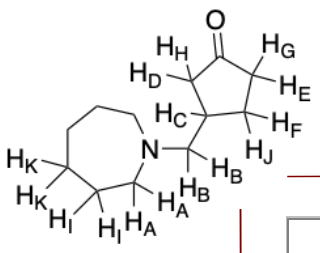
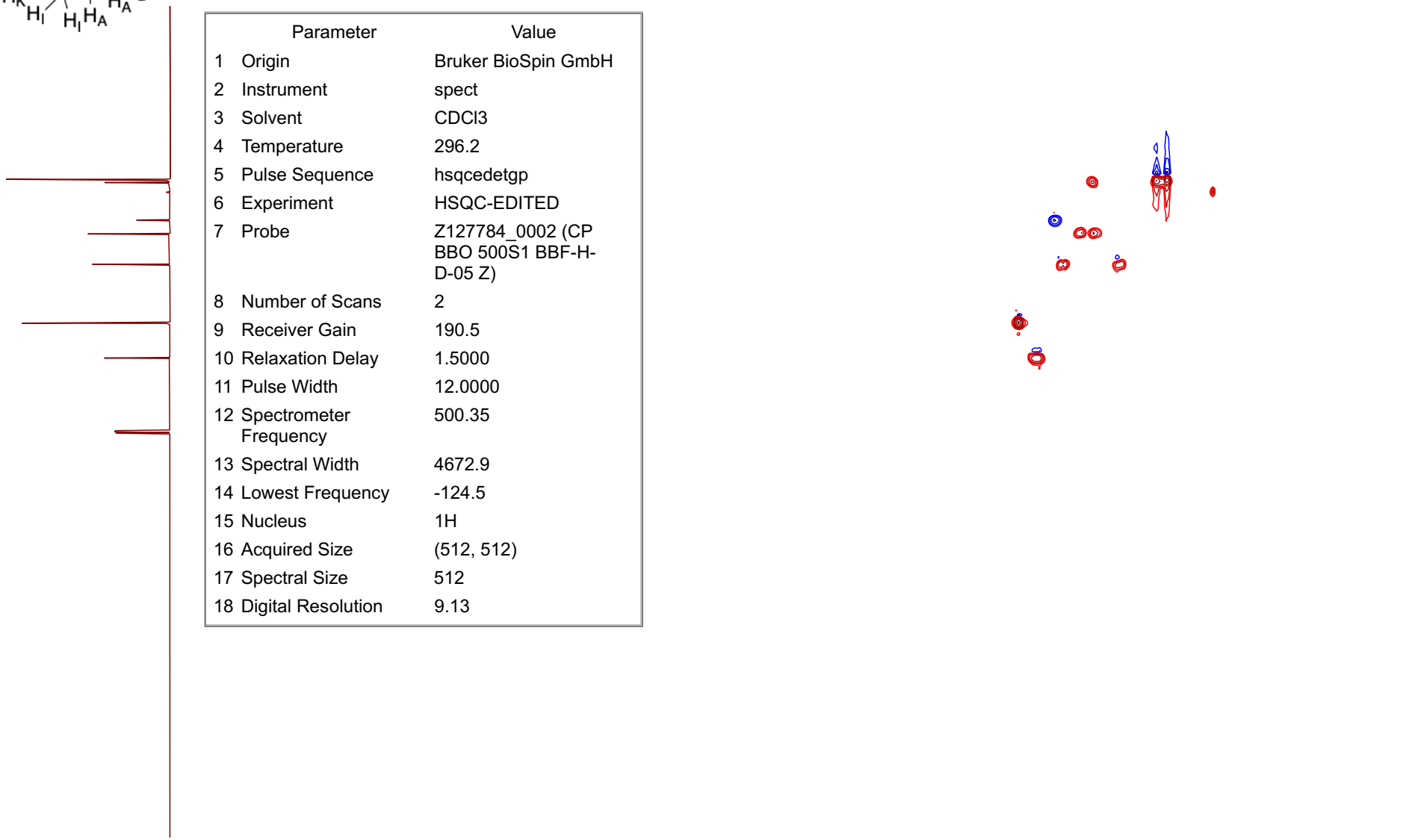
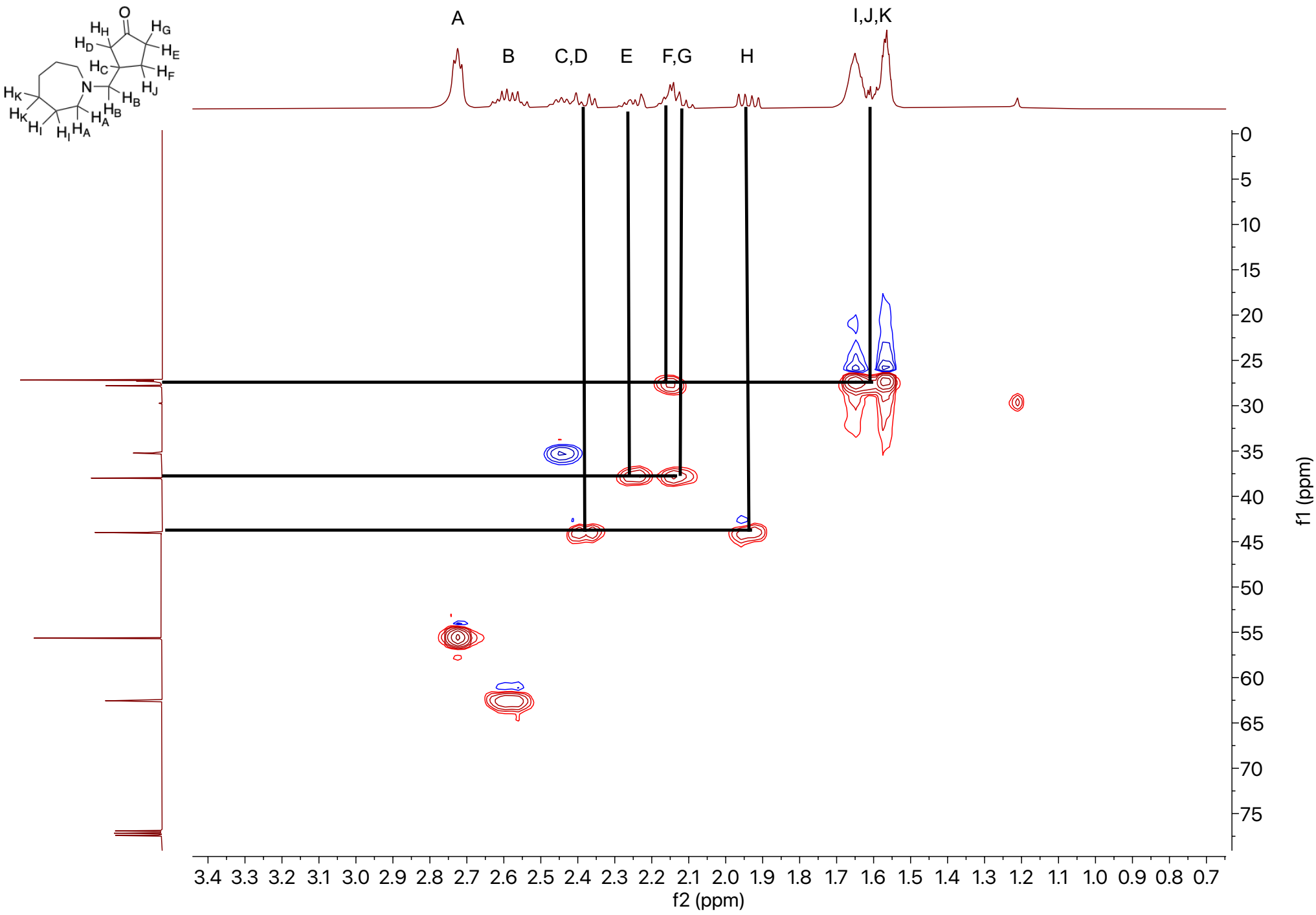
224

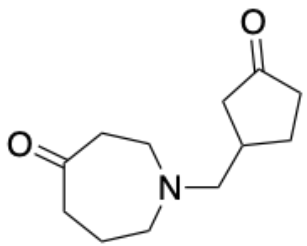
330



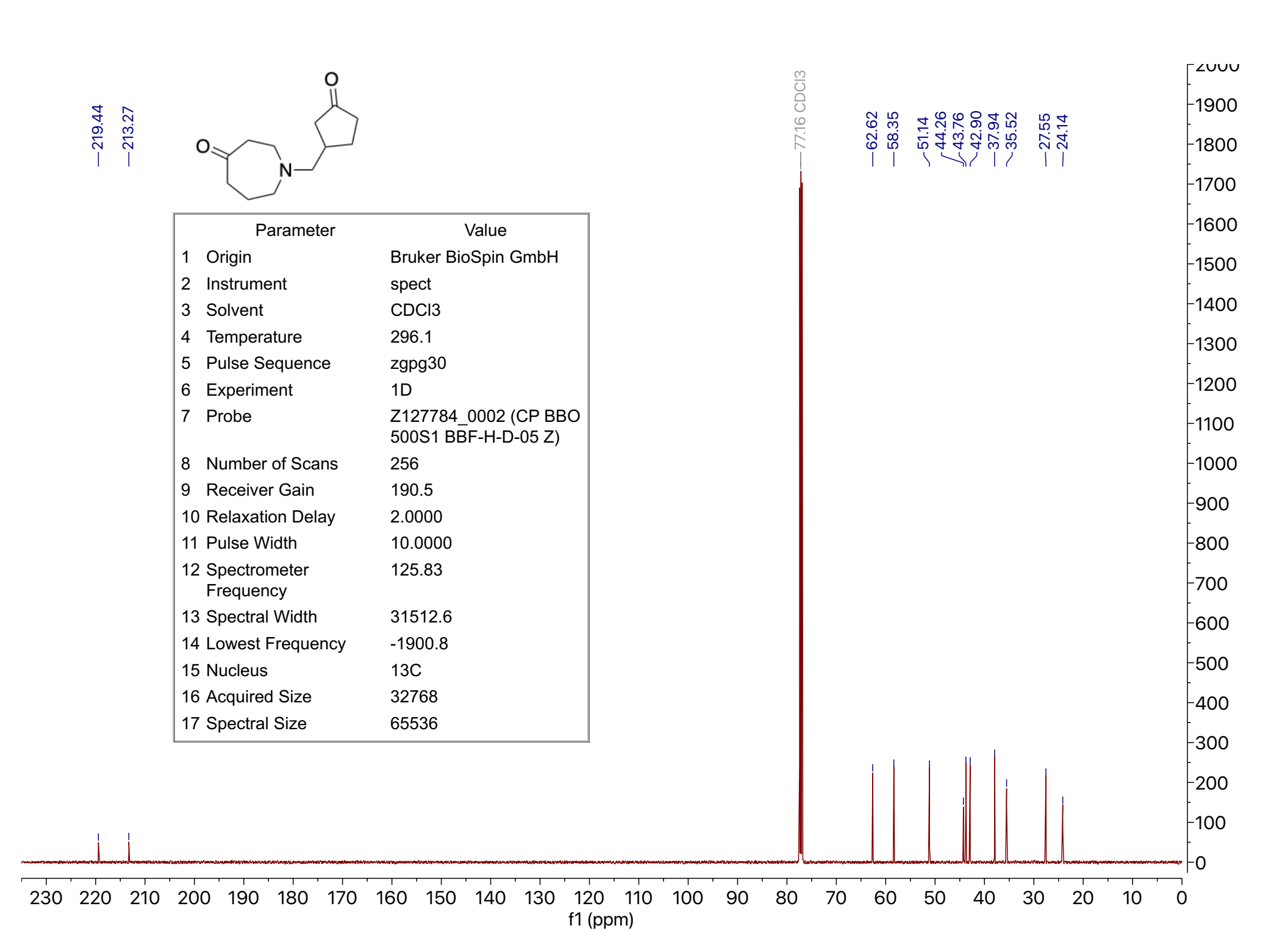
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4672.9
14	Lowest Frequency	-124.5
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	9.13



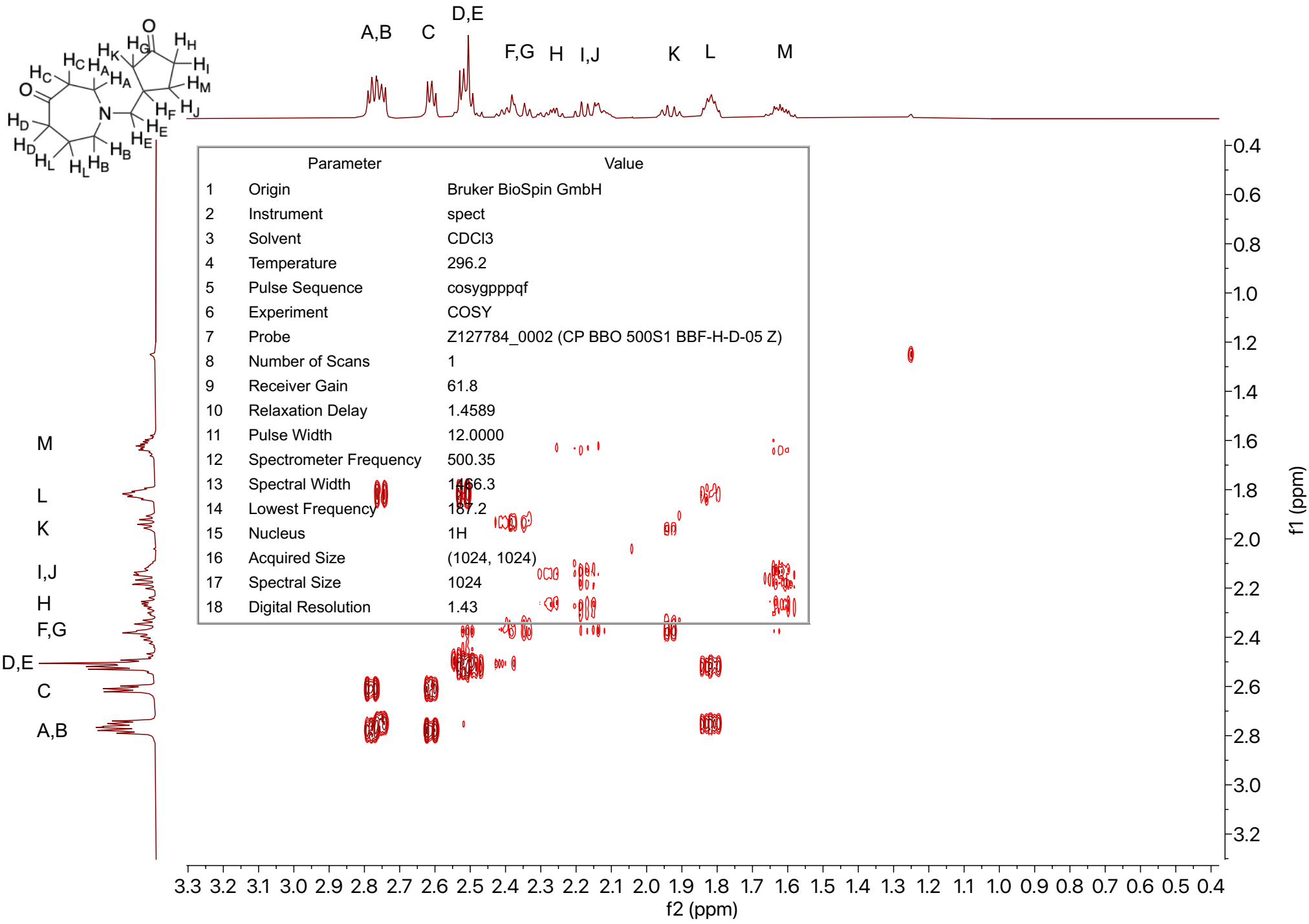

A
B
C,D
E
F,G
H
I,J,K
f2 (ppm)
f1 (ppm)



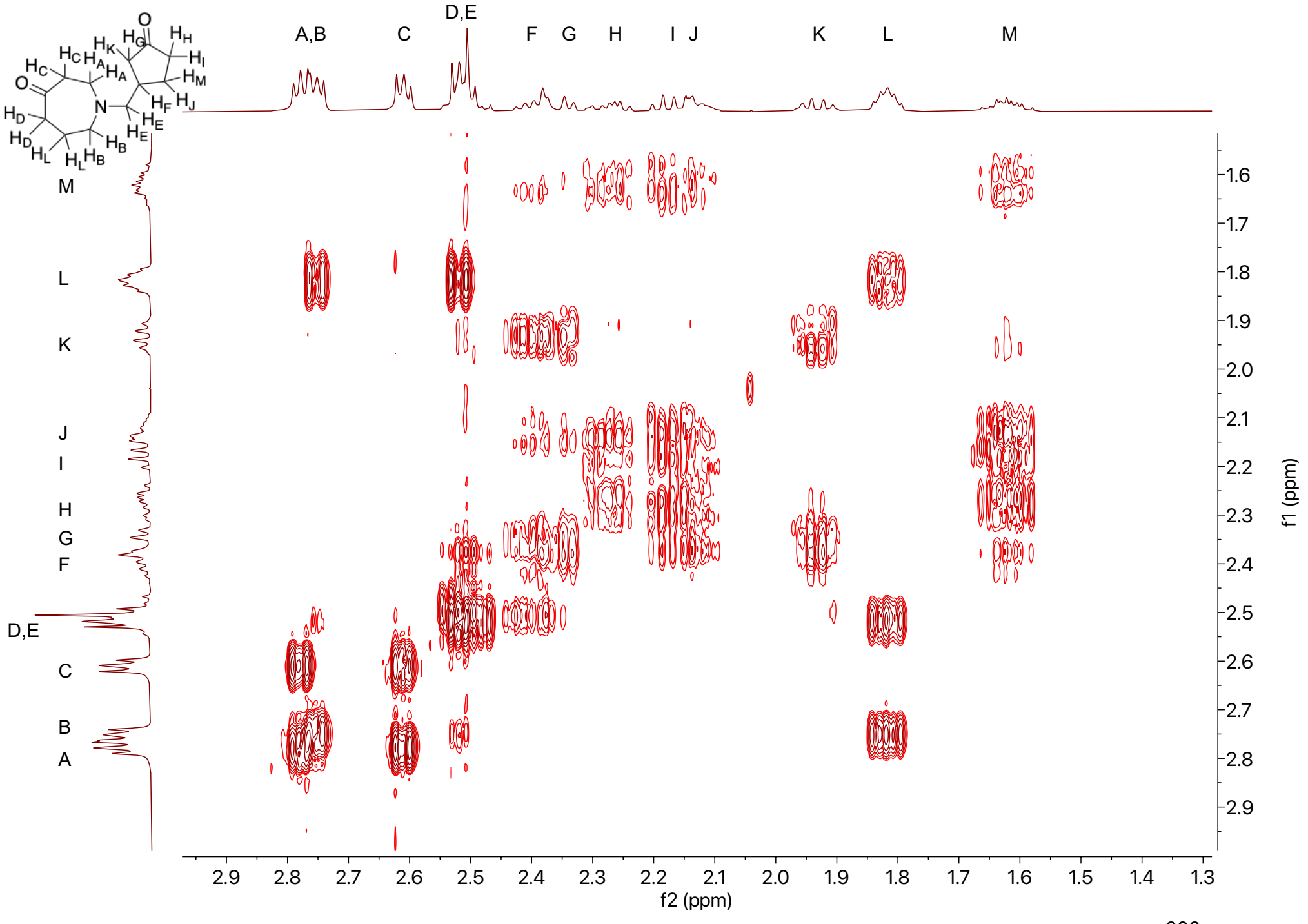
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	107.0
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.4589
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	1466.3
14	Lowest Frequency	187.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024
18	Digital Resolution	1.43


A,B
C
D,E
F
G
H
I
J
K
L
M
f2 (ppm)
f1 (ppm)
2.9
2.8
2.7
2.6
2.5
2.4
2.3
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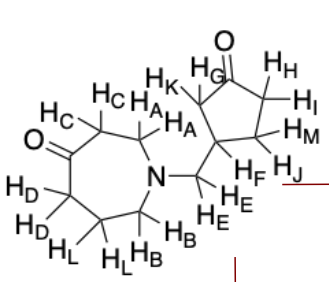
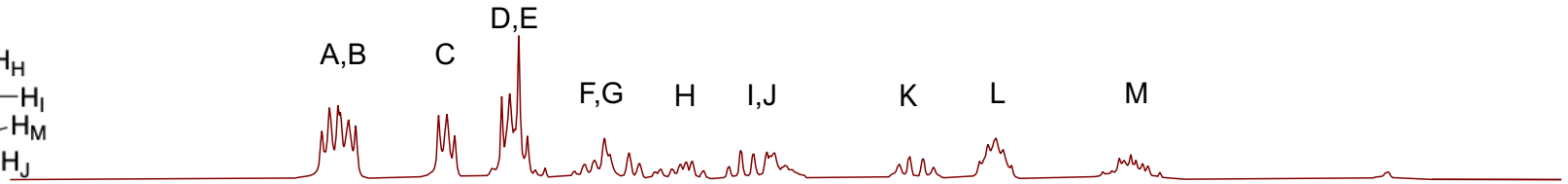
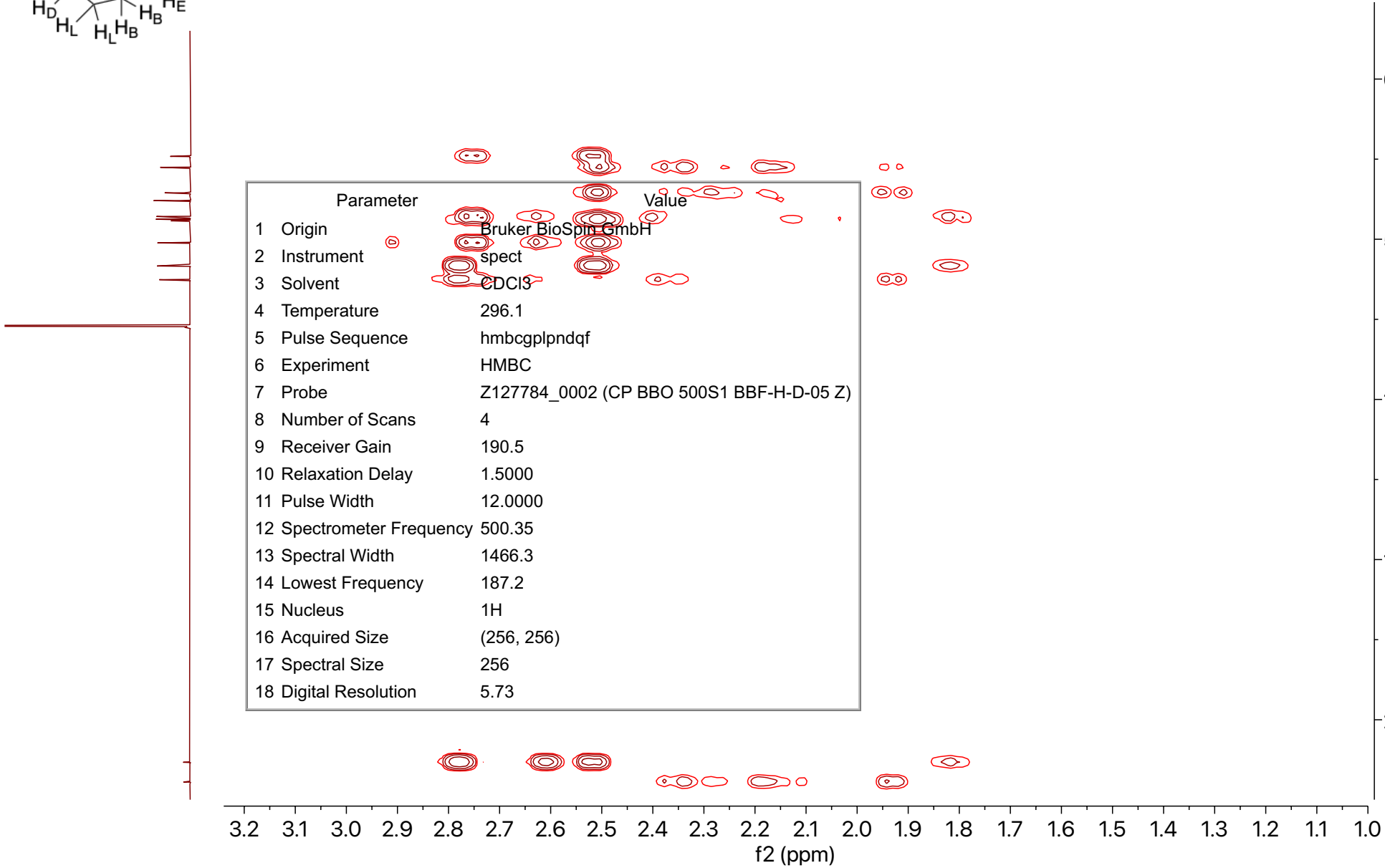
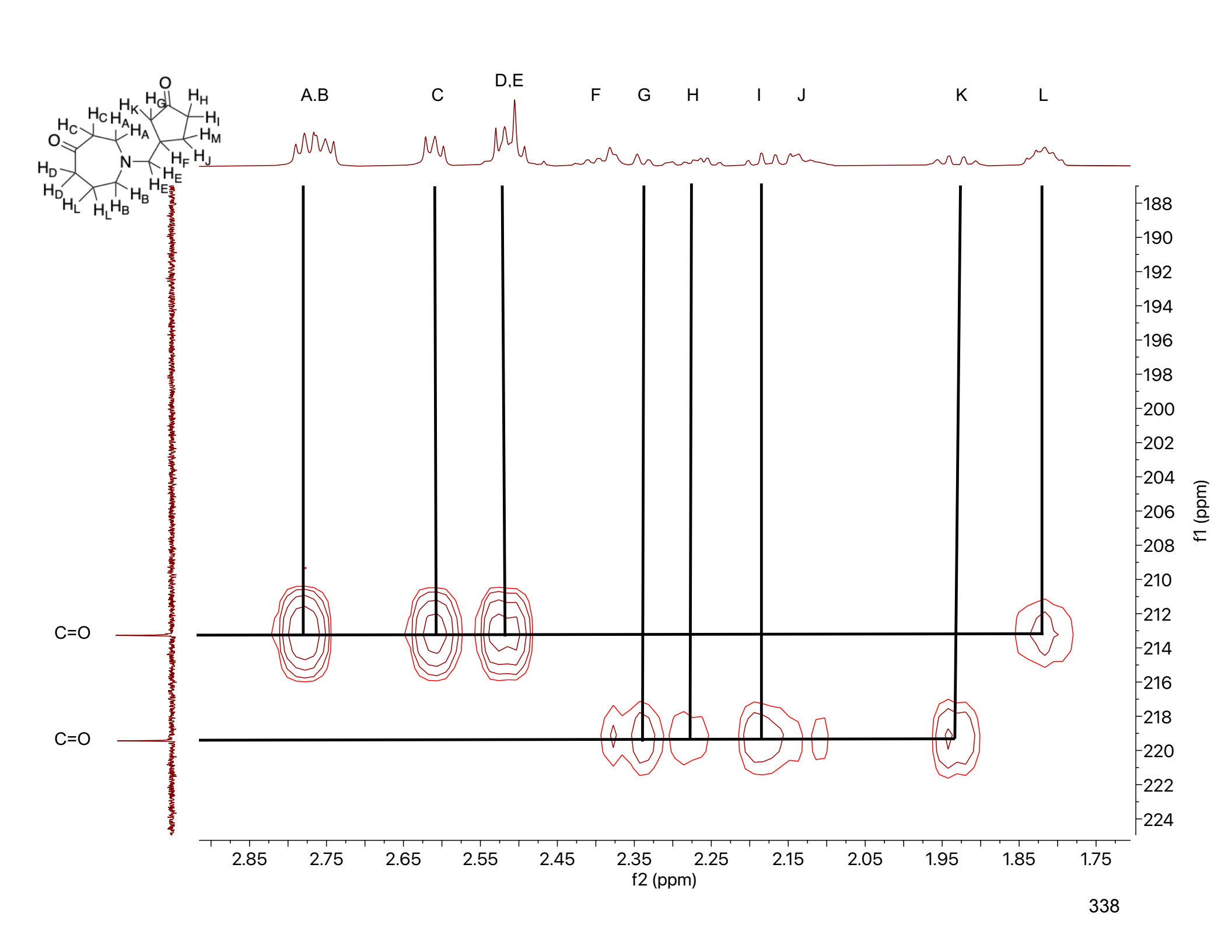
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3





	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	1466.3
14	Lowest Frequency	187.2
15	Nucleus	1H
16	Acquired Size	(256, 256)
17	Spectral Size	256
18	Digital Resolution	5.73




A.B
C
D,E
F
G
H
I
J
K
L
C=O
C=O
f2 (ppm)
f1 (ppm)
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1.95
1.85
1.75
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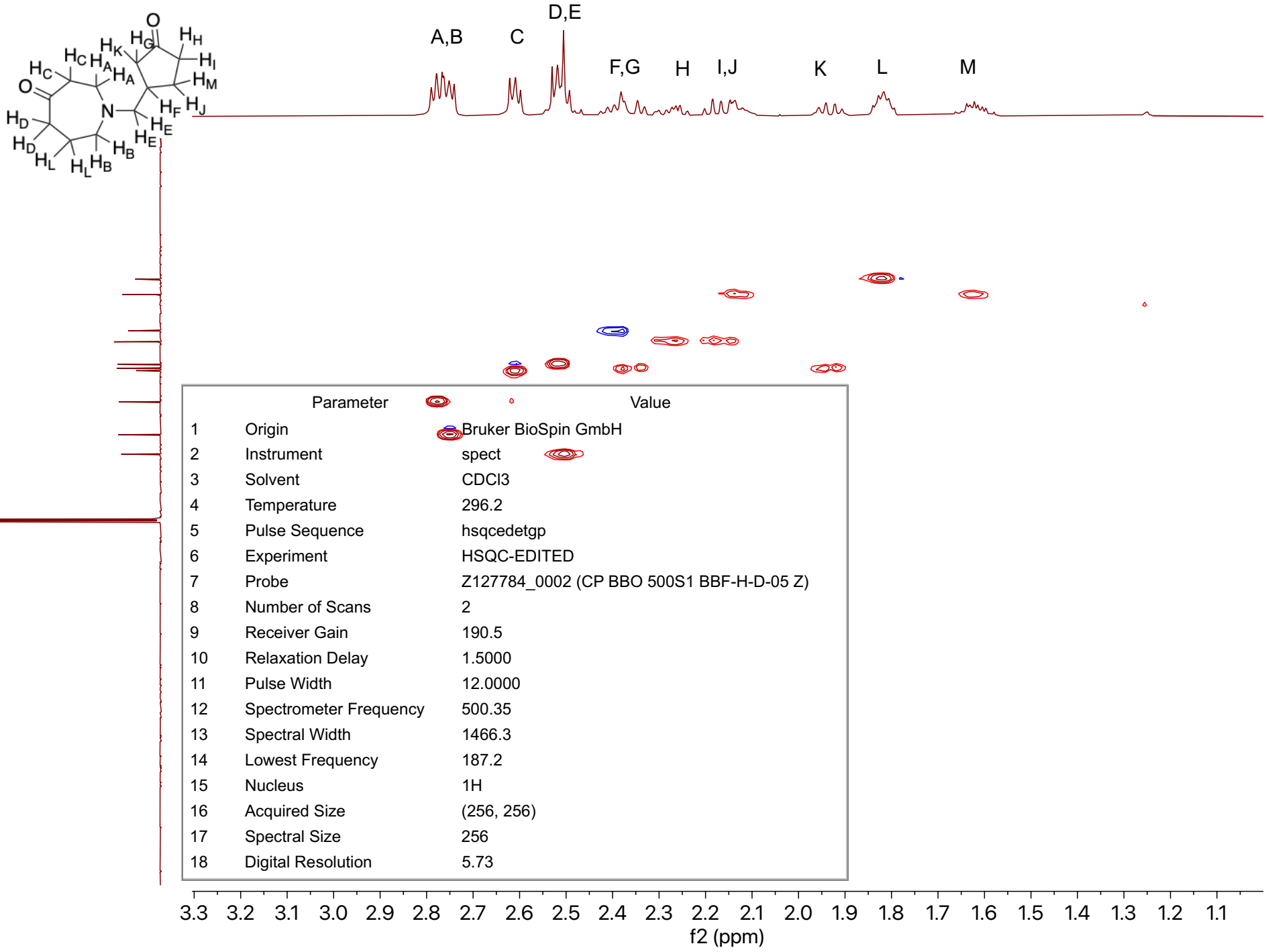
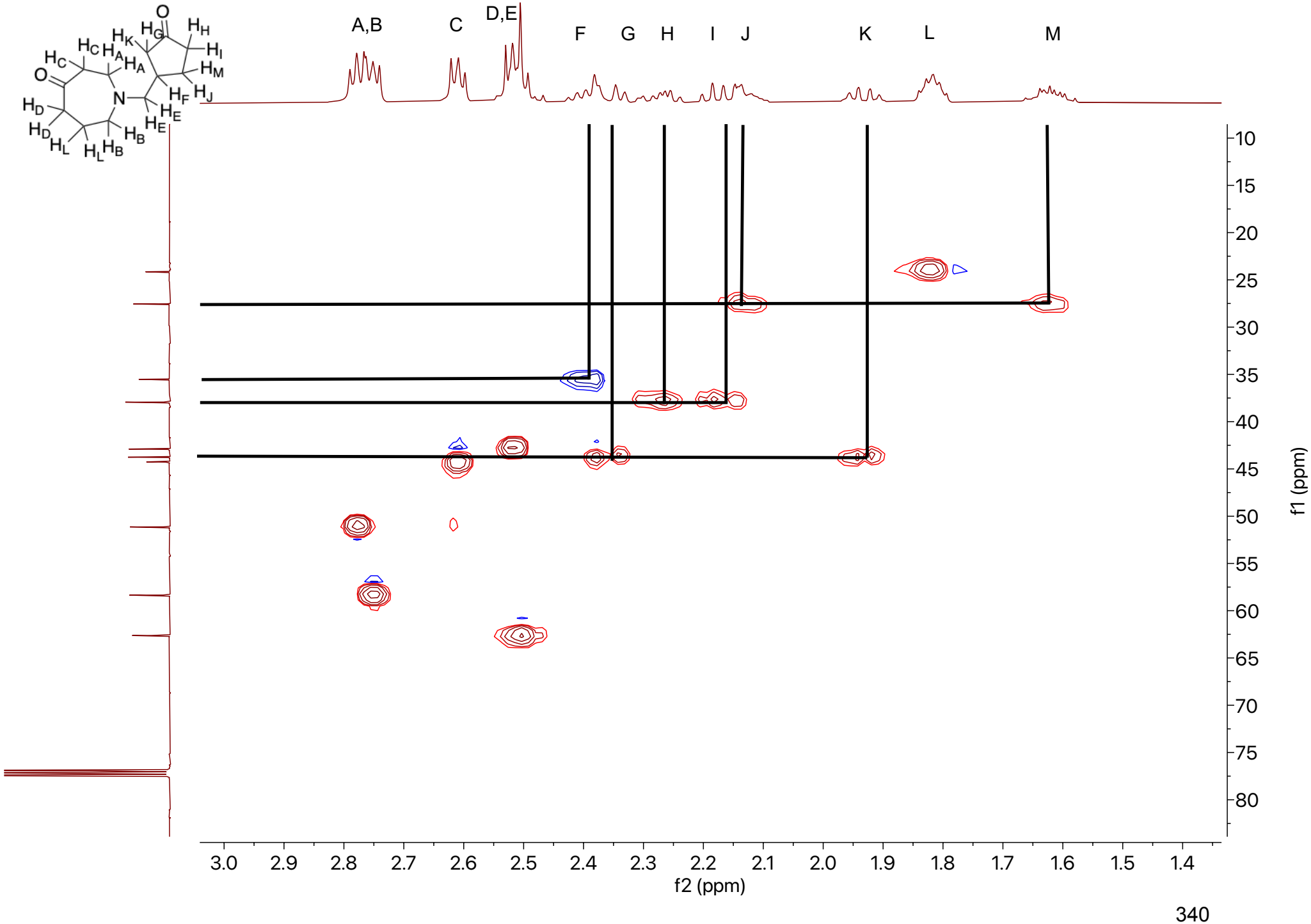
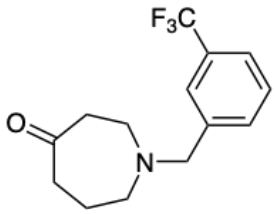
224

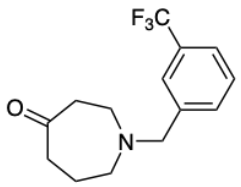


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	1466.3
14	Lowest Frequency	187.2
15	Nucleus	1H
16	Acquired Size	(256, 256)
17	Spectral Size	256
18	Digital Resolution	5.73


A,B
C
D,E
F
G
H
I
J
K
L
M
f2 (ppm)
f1 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	17.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



213.28

140.21
131.99
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130.90
130.64
130.39
128.92
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125.38
125.32
125.30
125.27
125.24
124.13
124.10
124.07
124.04
123.21
121.05
77.16 CDCl3

58.08
50.70
44.32
42.94

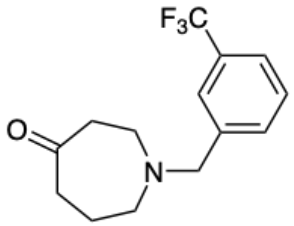
24.21

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1905.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

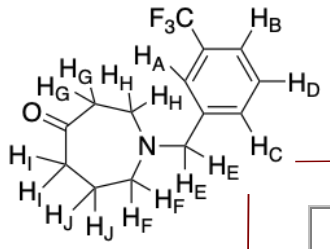
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

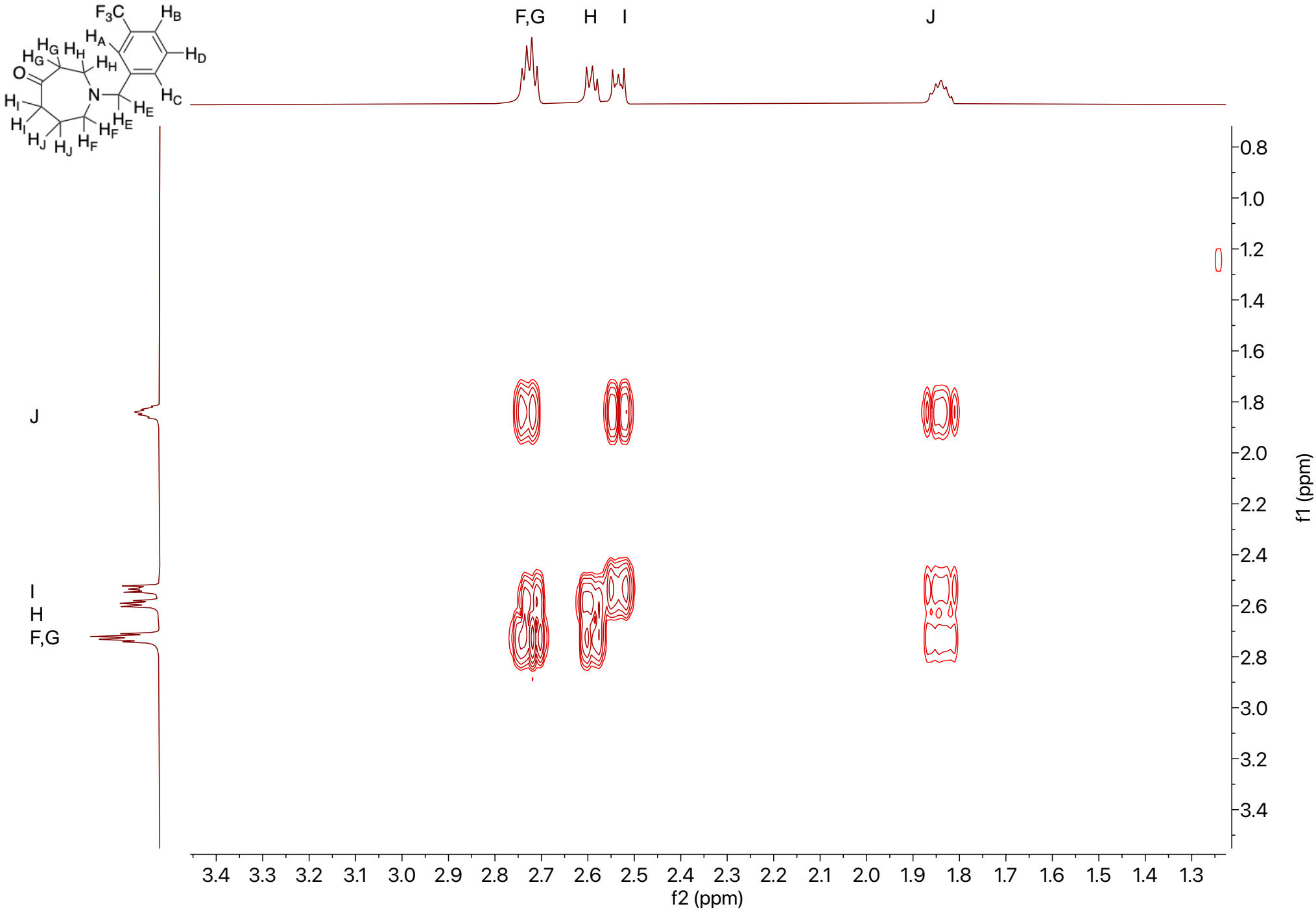
f1 (ppm)

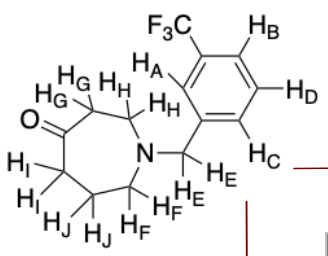


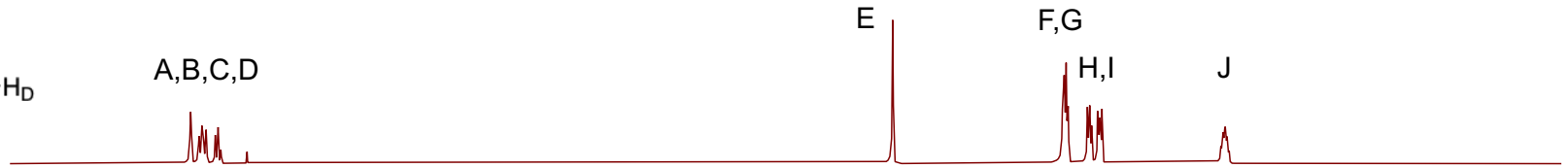
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



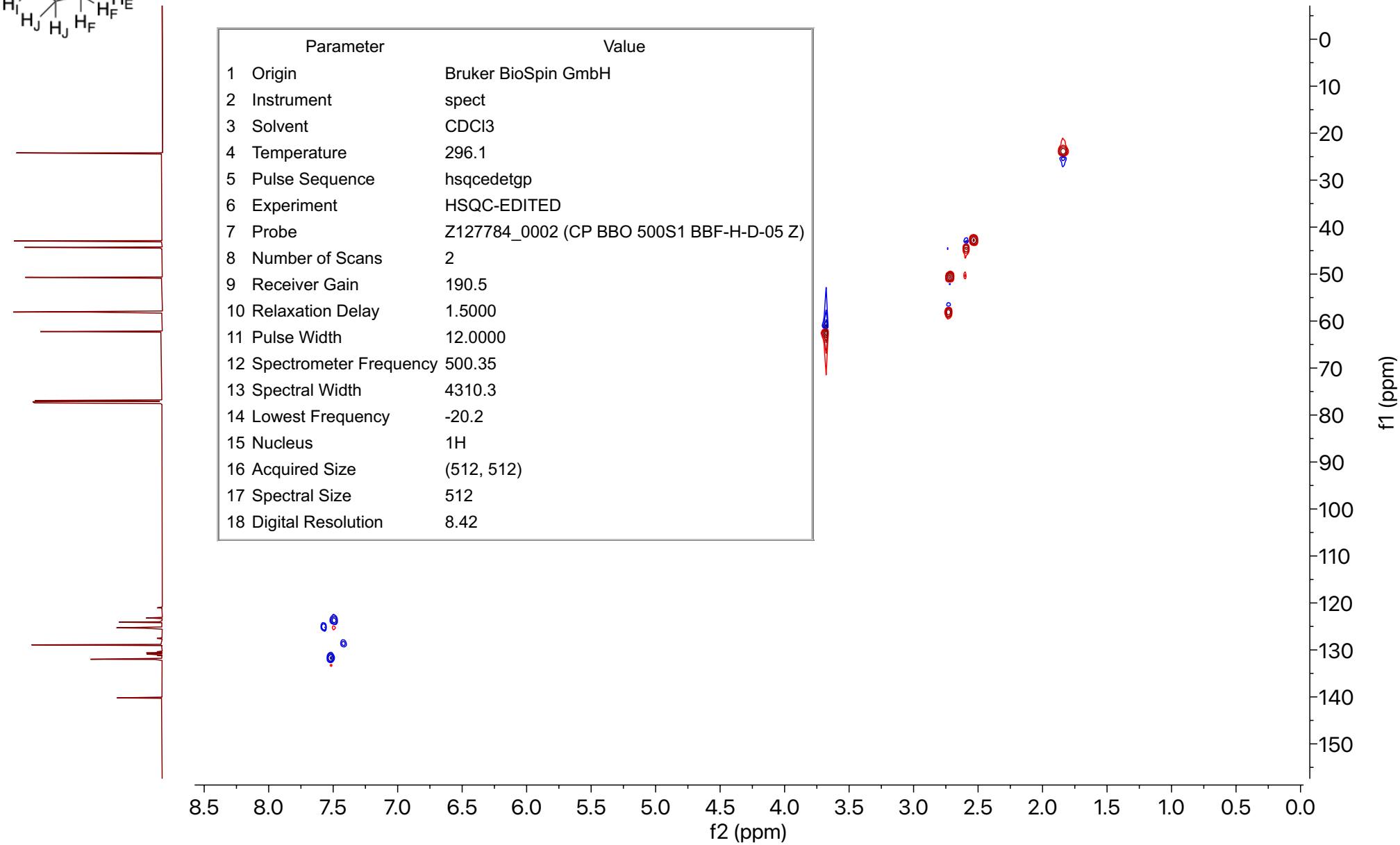
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	12.8
10	Relaxation Delay	1.9197
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4310.3
14	Lowest Frequency	-20.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024
18	Digital Resolution	4.21

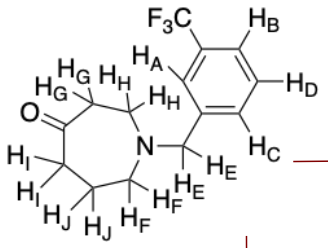

F,G
H
I
J
J
I
H
F,G
f1 (ppm)
f2 (ppm)
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3
0.8 1.0 1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4



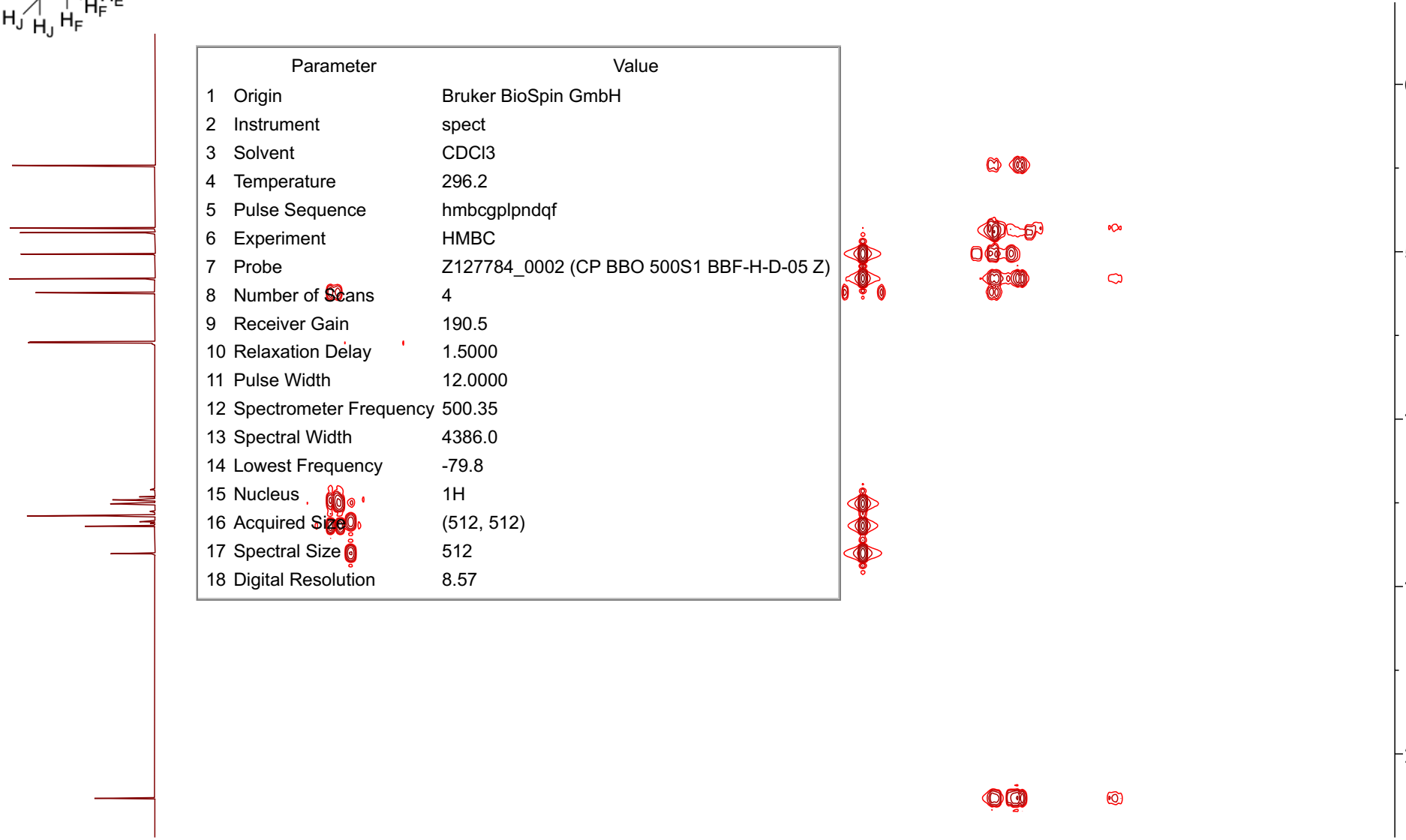


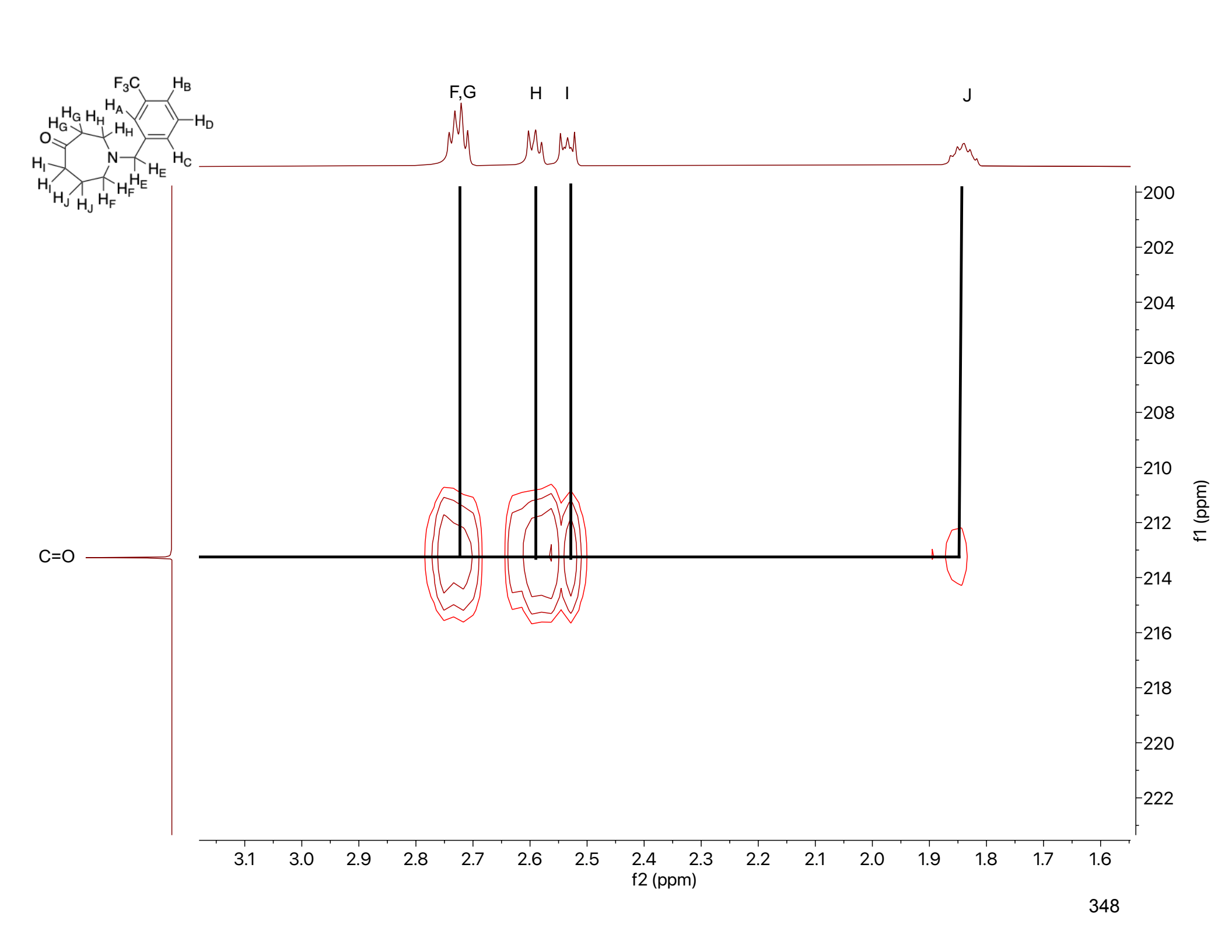
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4310.3
14	Lowest Frequency	-20.2
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	8.42

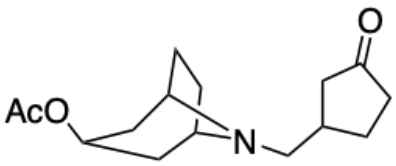




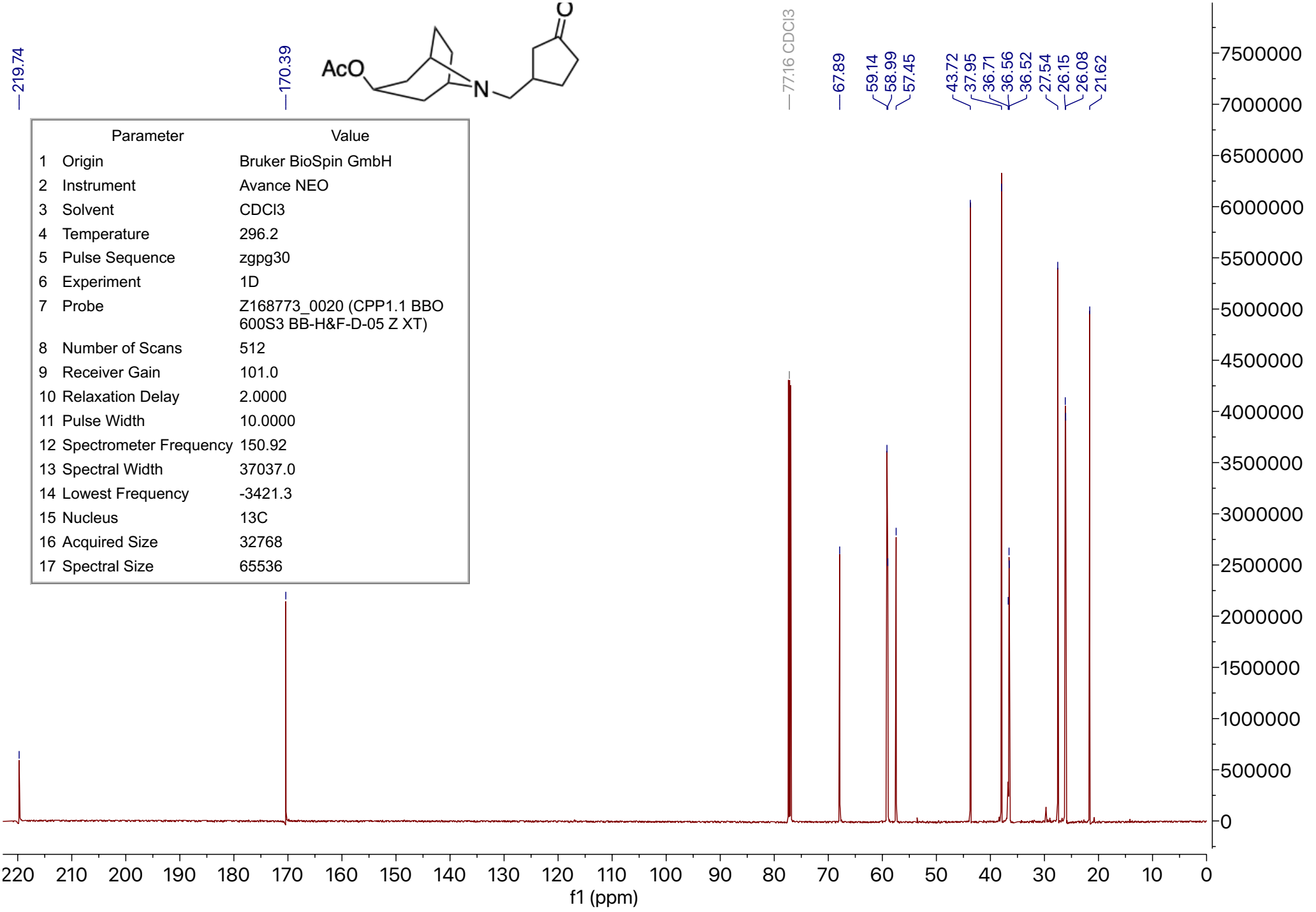
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4386.0
14	Lowest Frequency	-79.8
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	8.57



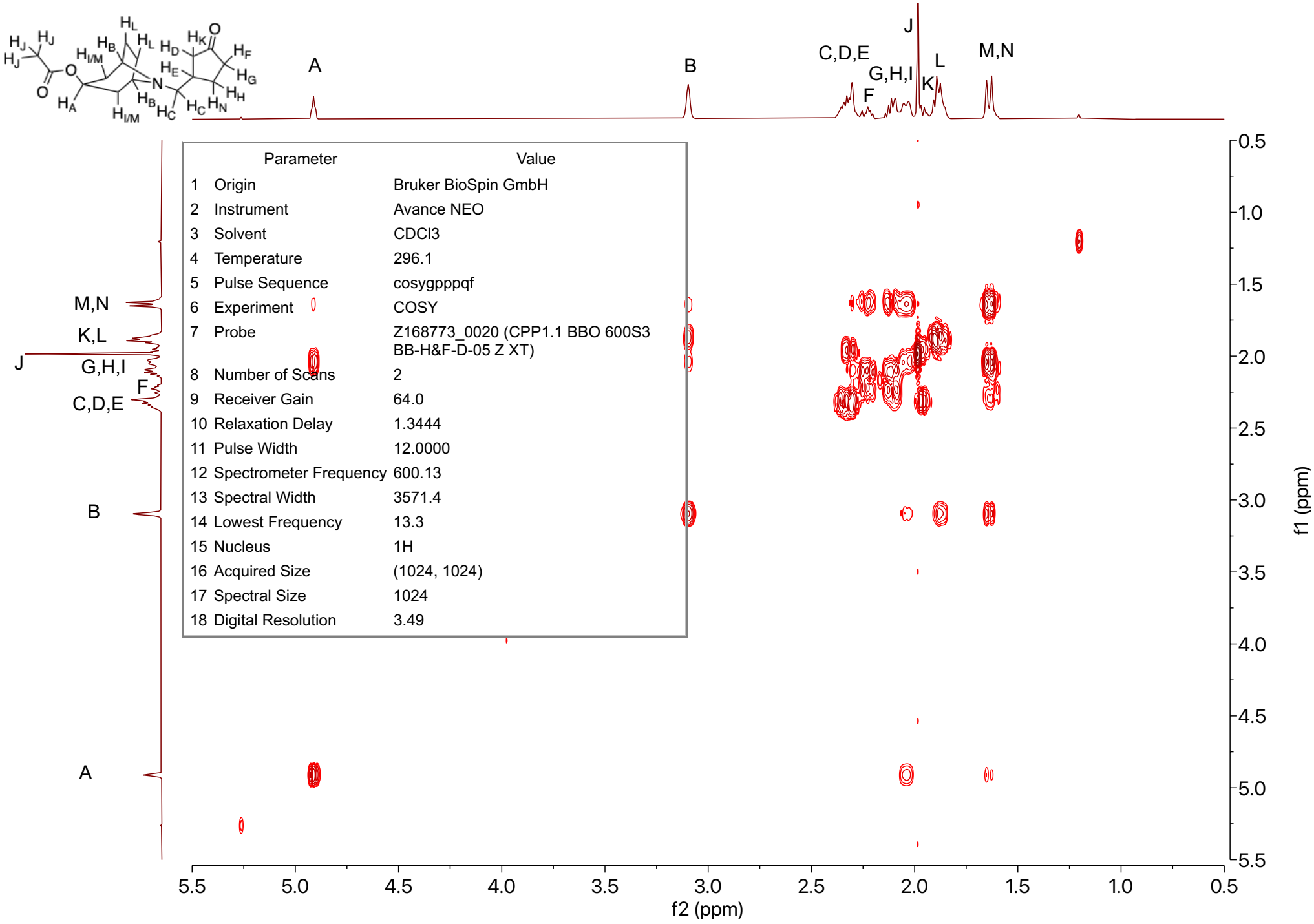

F,G
H
I
J
C=O
f2 (ppm)
f1 (ppm)
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
200
202
204
206
208
210
212
214
216
218
220
222

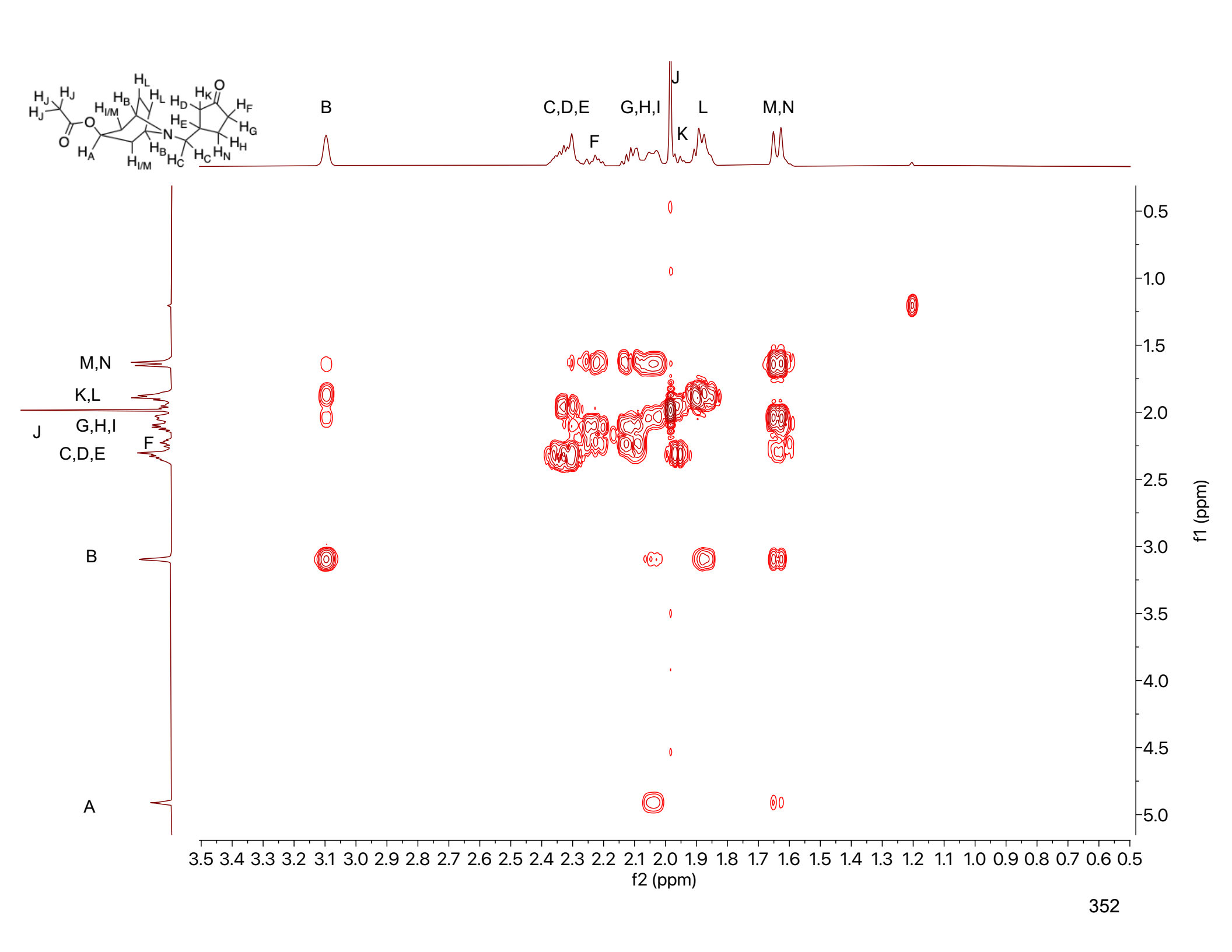


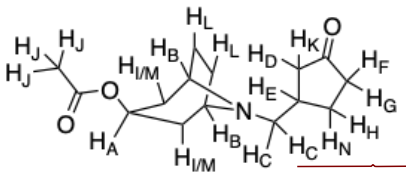
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2261.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

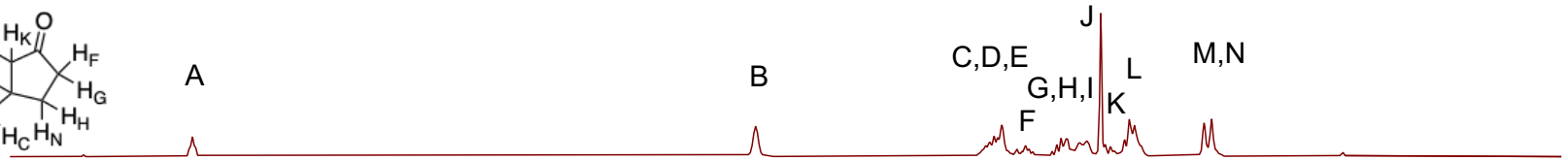


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	512
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	37037.0
14	Lowest Frequency	-3421.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

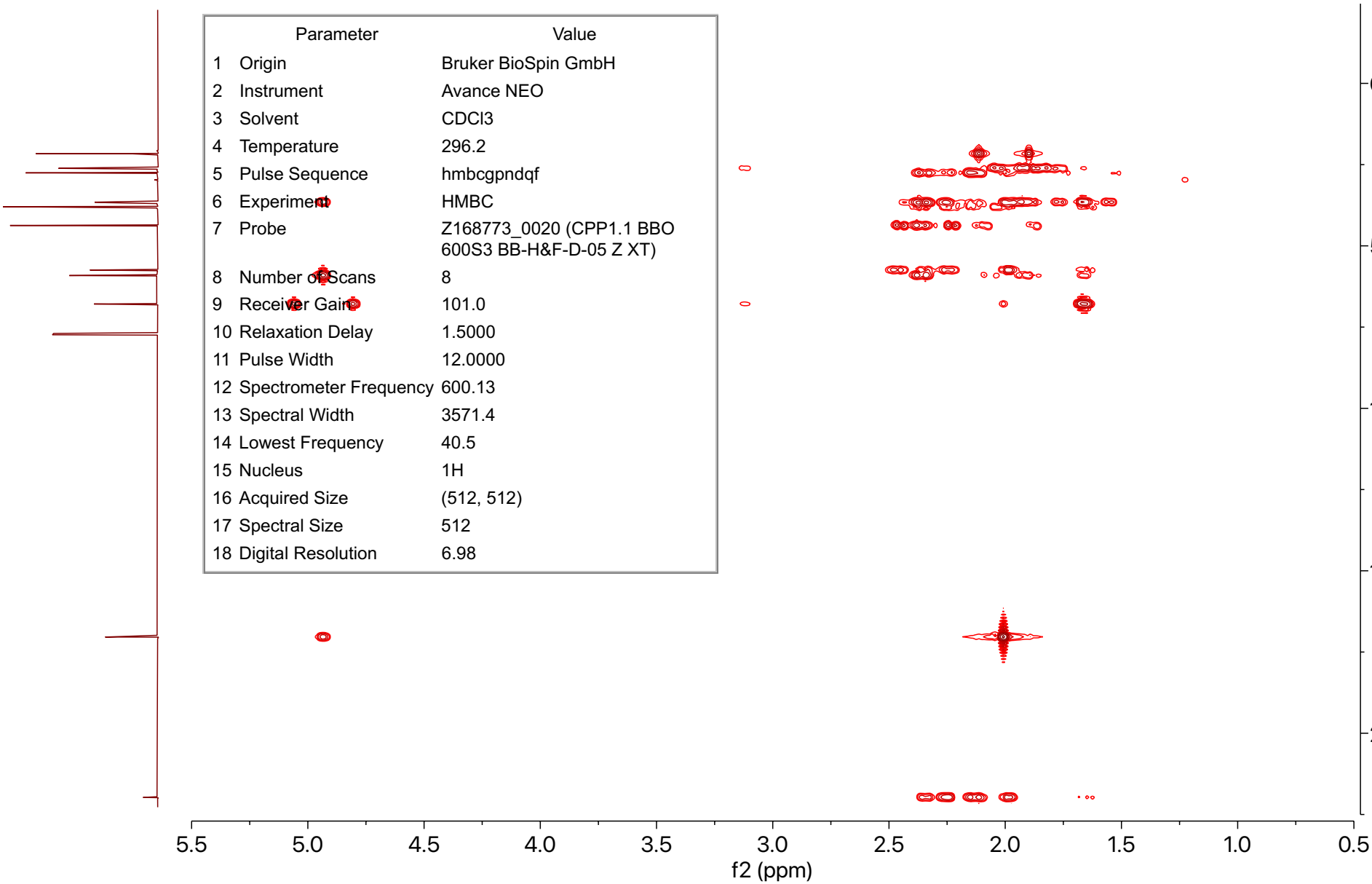

A
B
C,D,E
F
G,H,I
J
K
L
M,N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 2
9 Receiver Gain 64.0
10 Relaxation Delay 1.3444
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 3571.4
14 Lowest Frequency 13.3
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
18 Digital Resolution 3.49
5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f2 (ppm)
f1 (ppm)

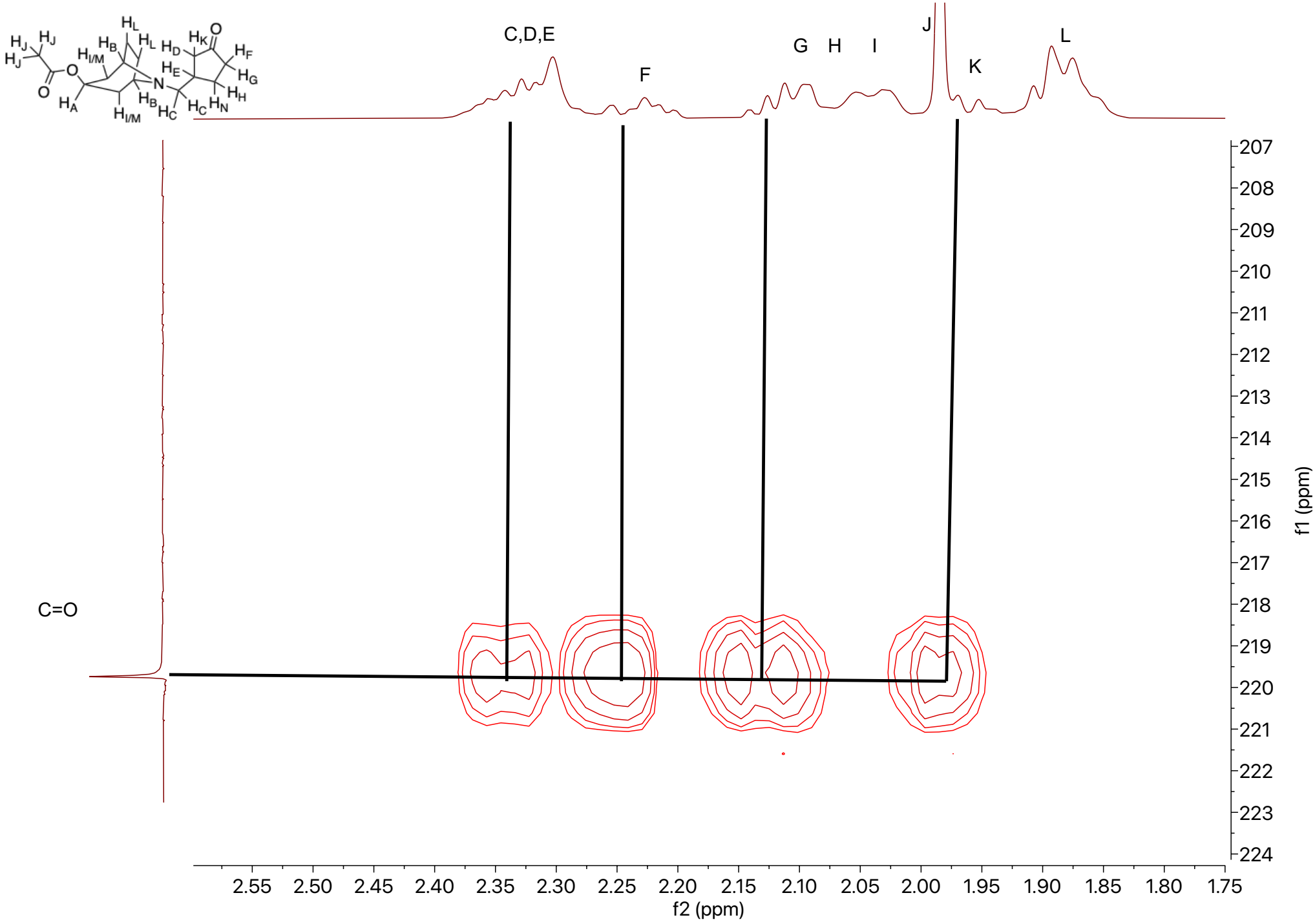

B
C,D,E
F
G,H,I
J
K
L
M,N
M,N
K,L
J
G,H,I
F
C,D,E
B
A
3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5
f2 (ppm)
0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0
f1 (ppm)





	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgpndqf
6	Experiment	HMBC
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	8
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	3571.4
14	Lowest Frequency	40.5
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	6.98




C,D,E
F
G
H
I
J
K
L
C=O
f1 (ppm)
f2 (ppm)
207
208
209
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211
212
213
214
215
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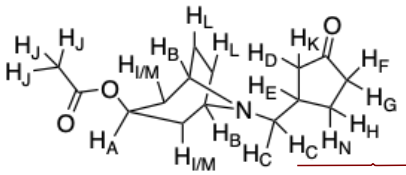
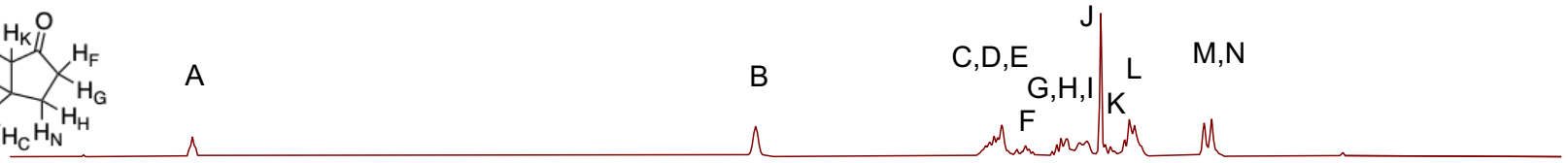
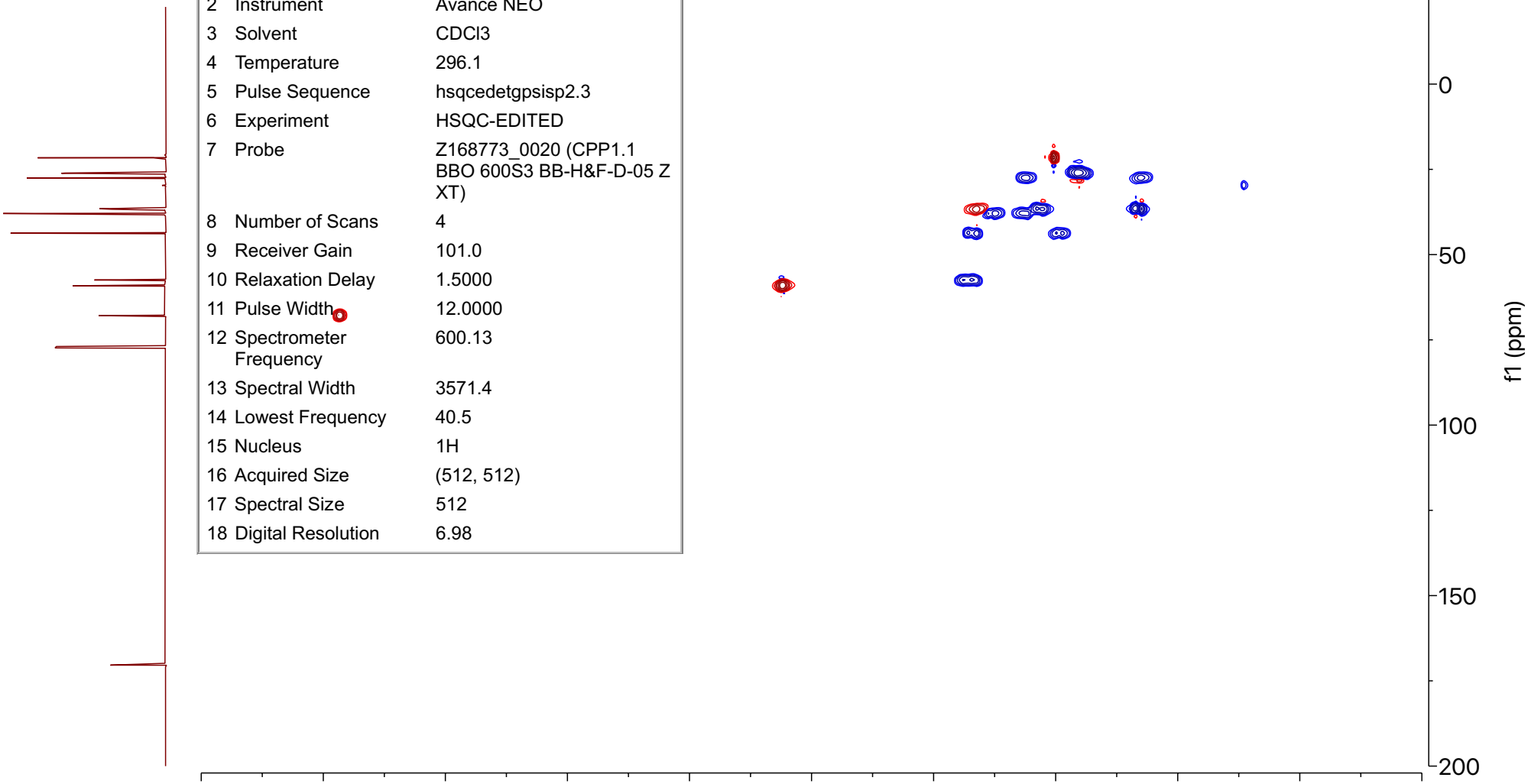
217
218
219
220
221
222
223
224
2.55
2.50
2.45
2.40
2.35
2.30
2.25
2.20
2.15
2.10
2.05
2.00
1.95
1.90
1.85
1.80
1.75

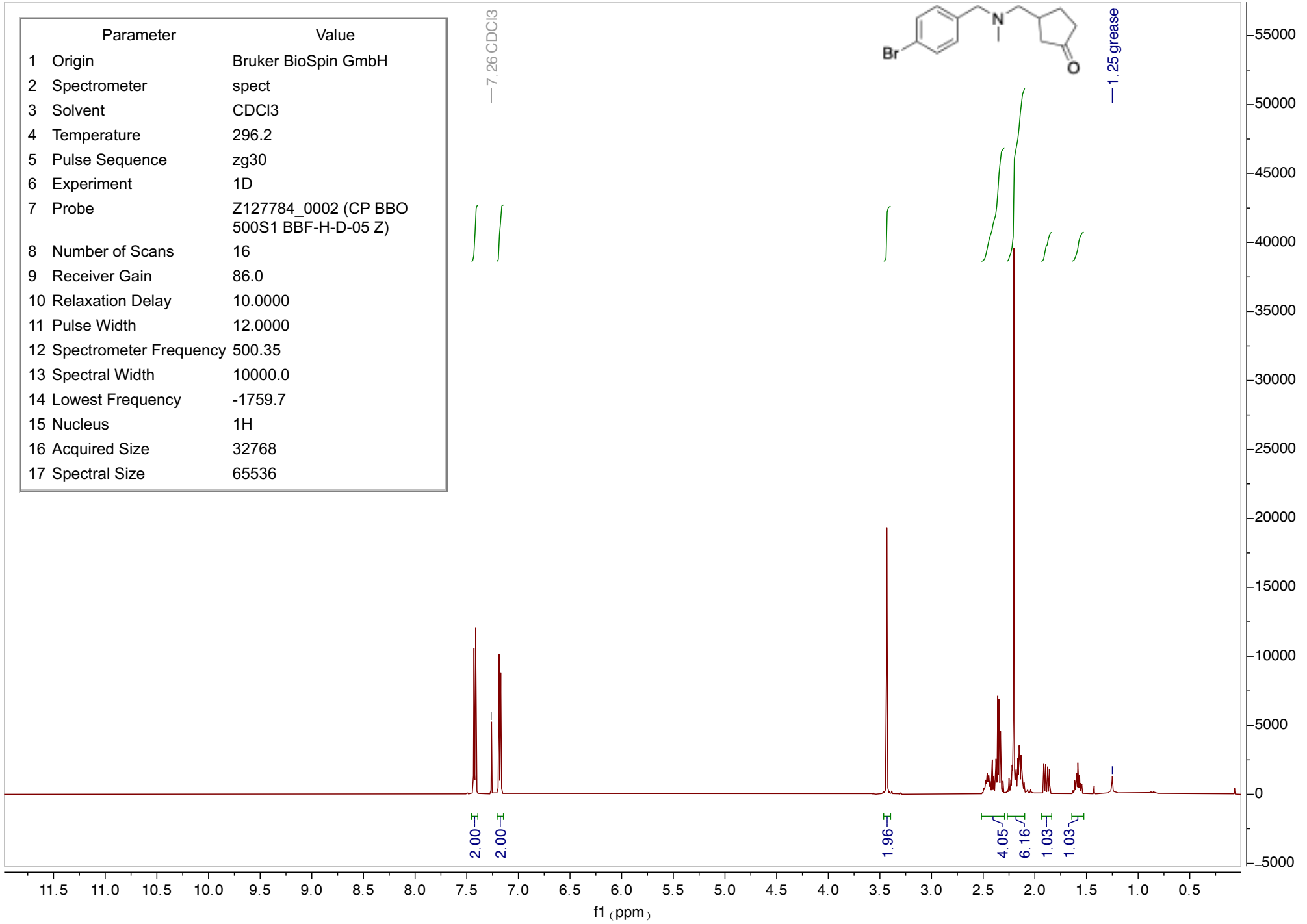


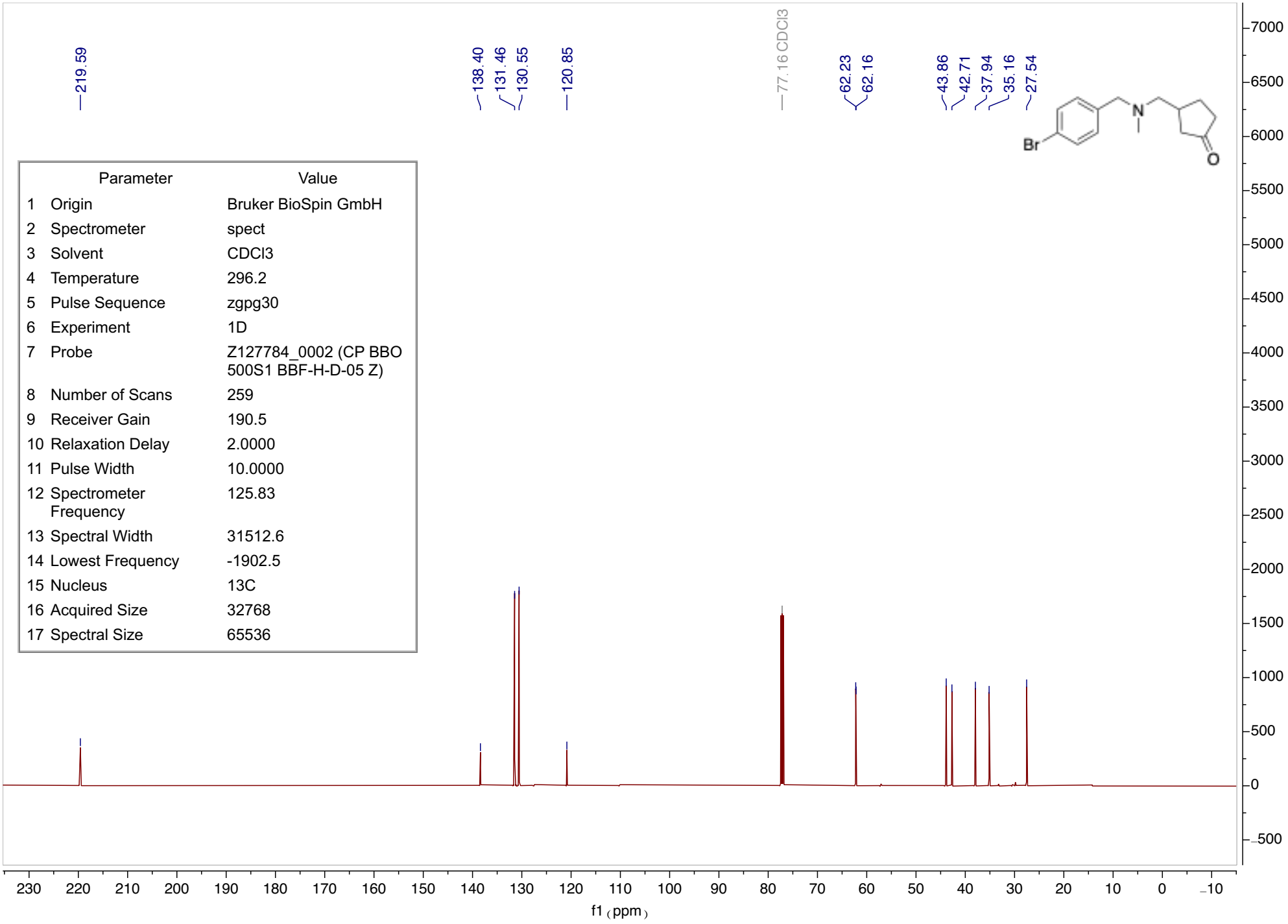


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	3571.4
14	Lowest Frequency	40.5
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	6.98



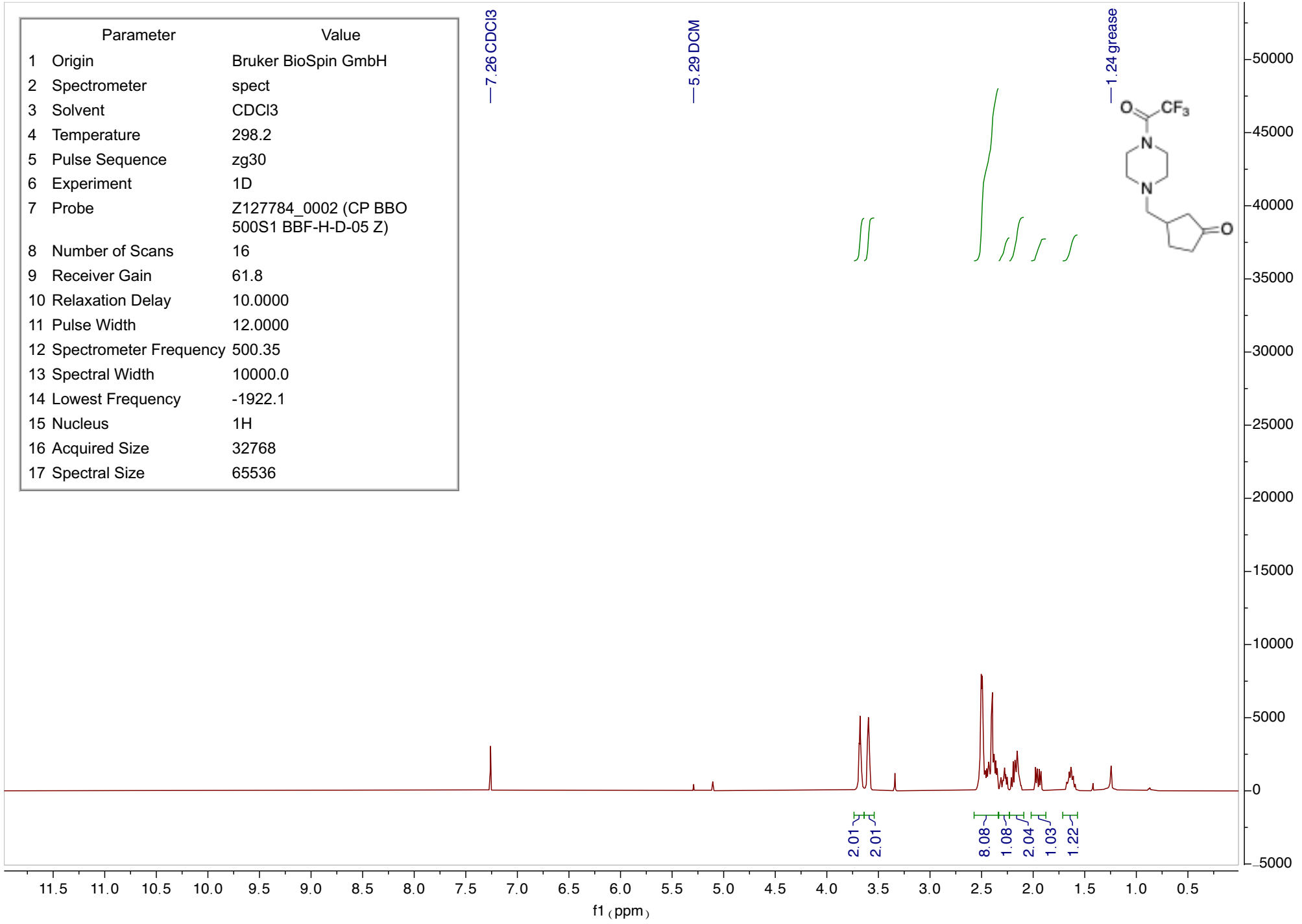
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

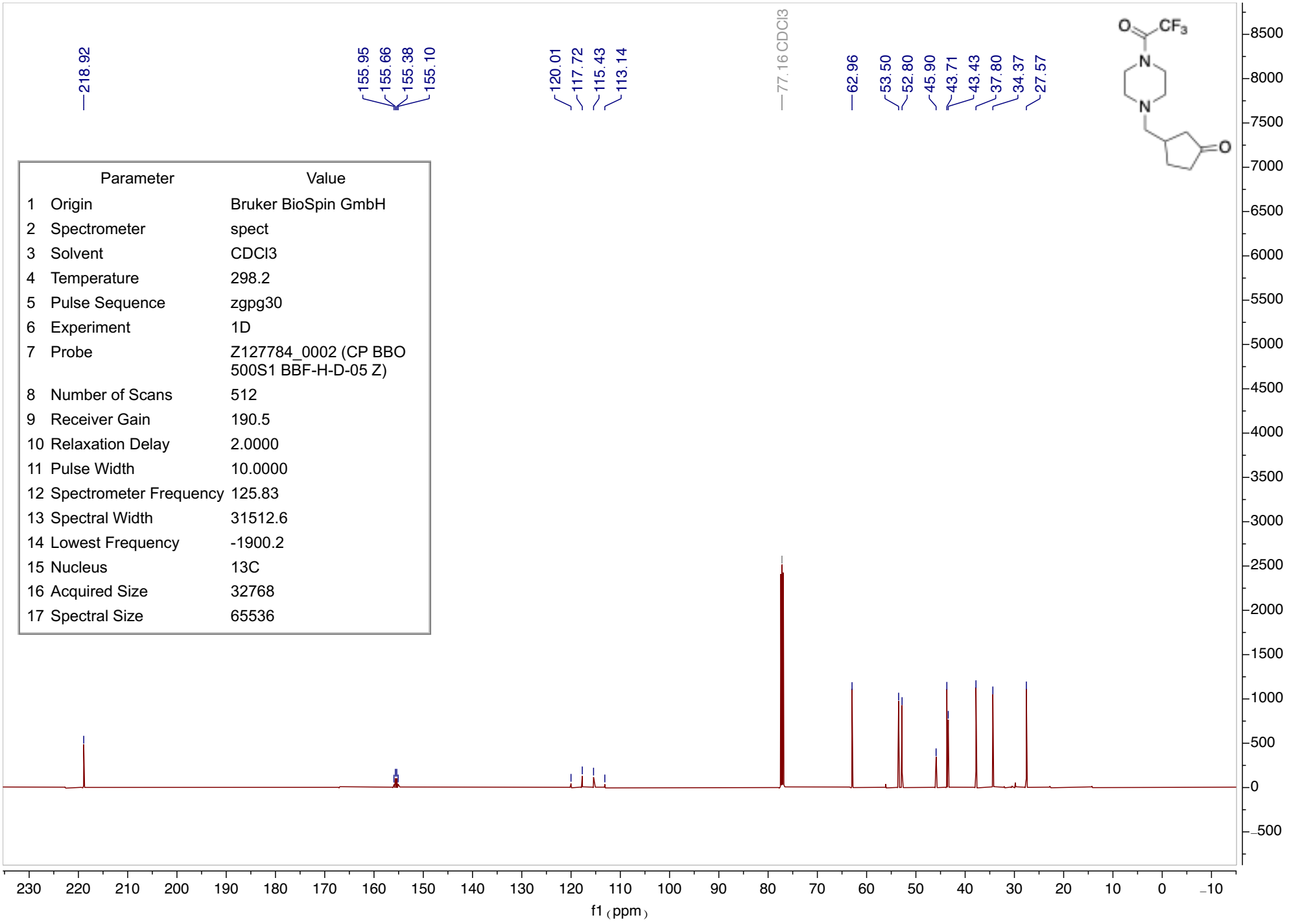




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	259
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

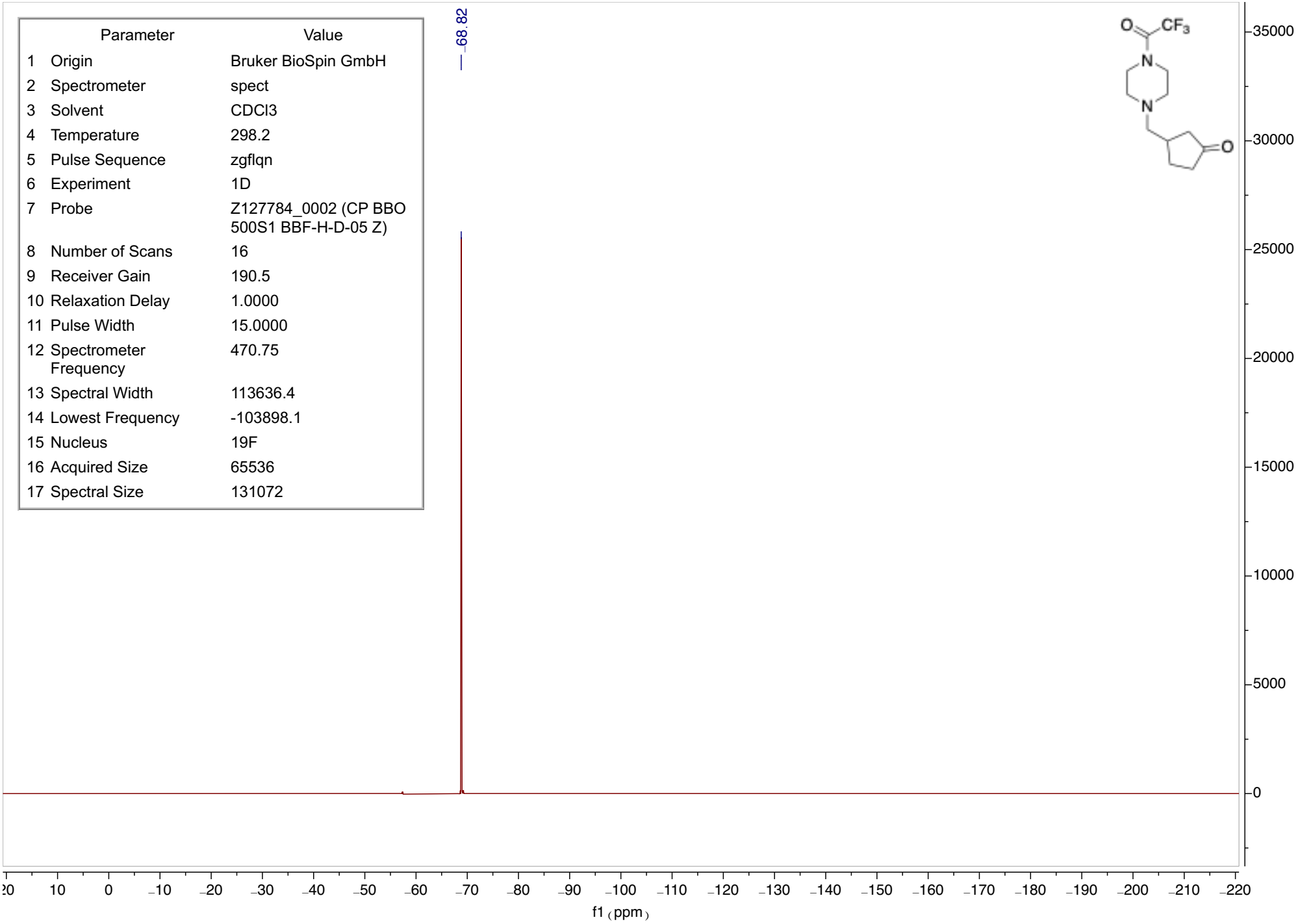
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



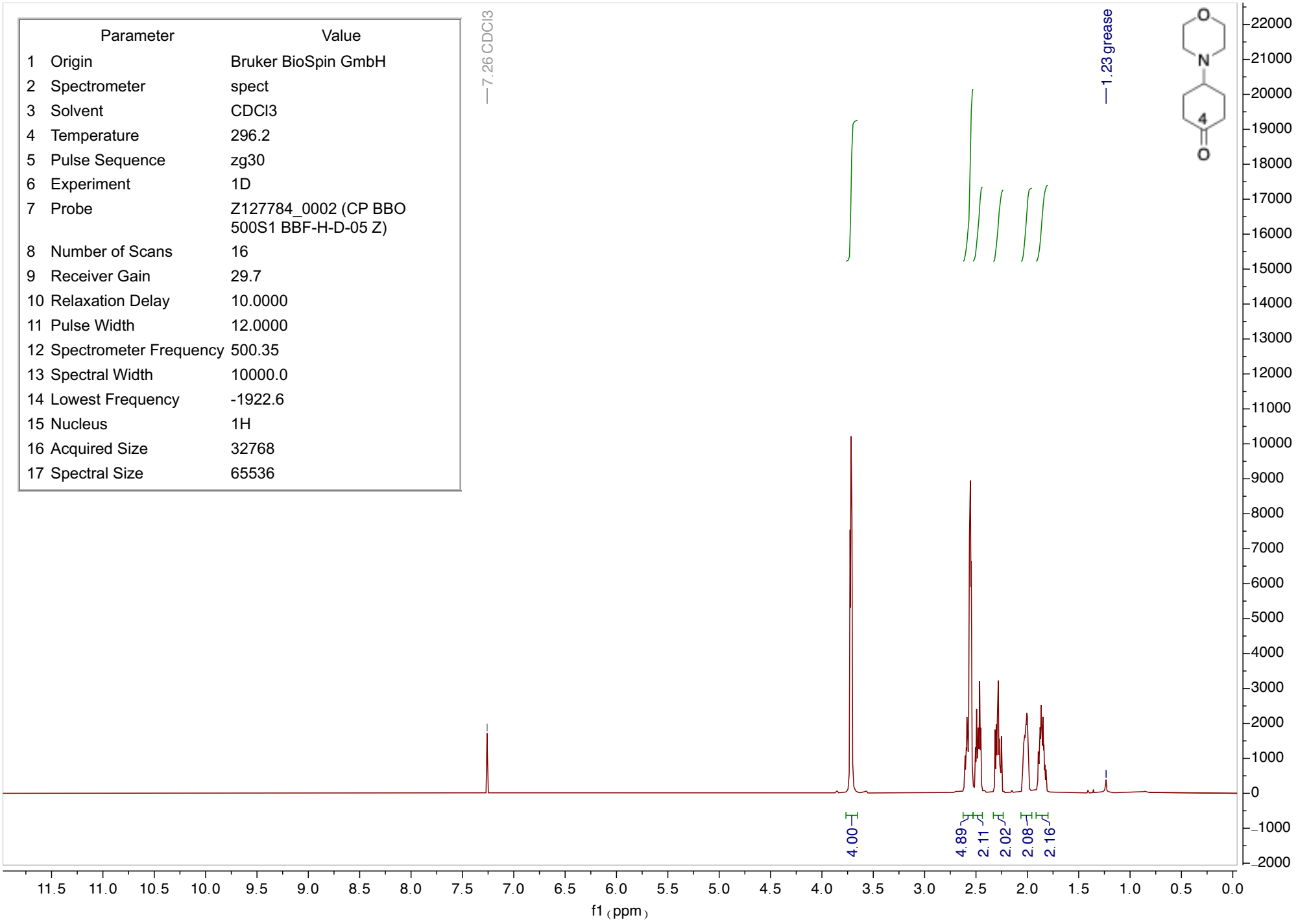


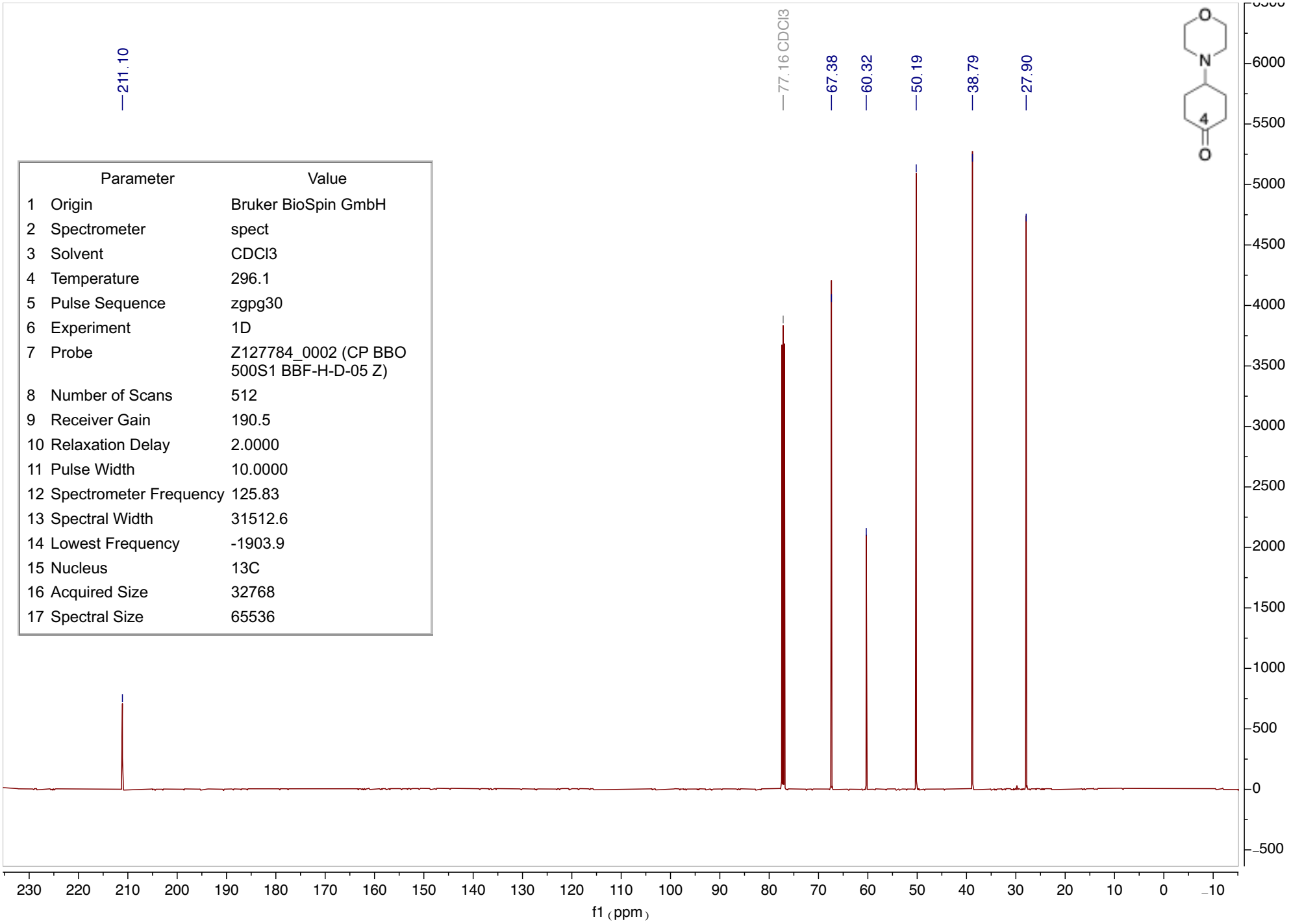
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



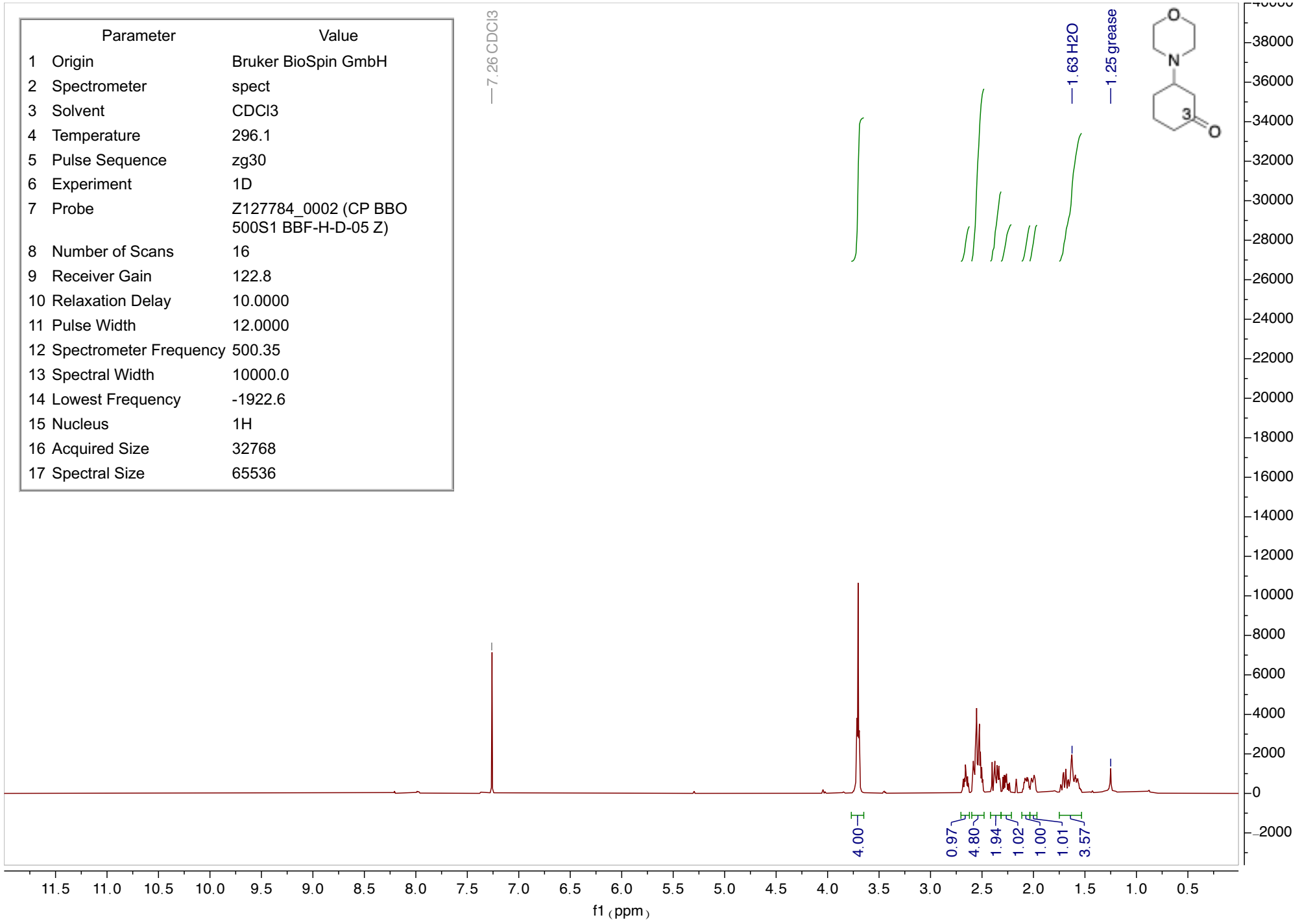
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

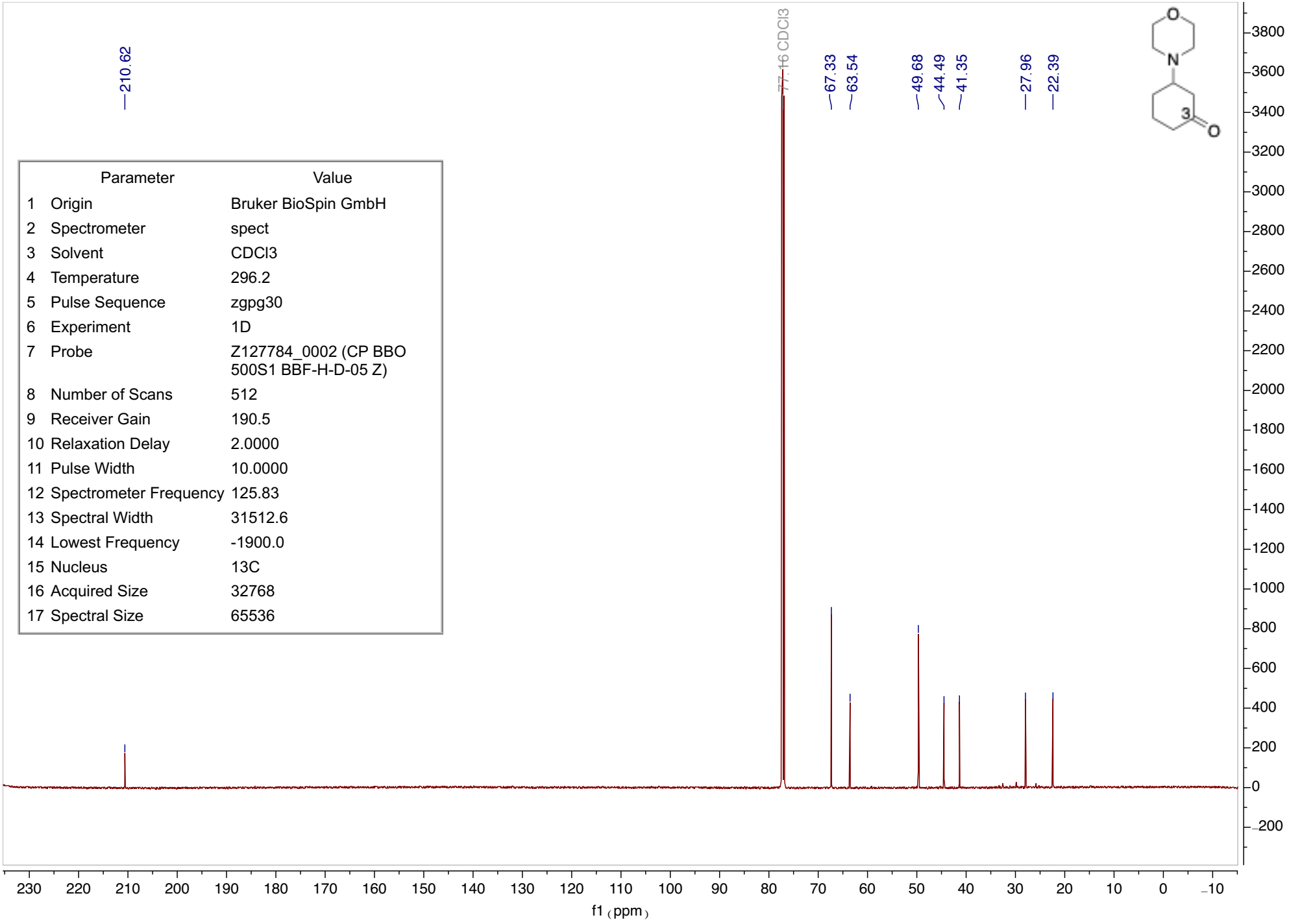




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

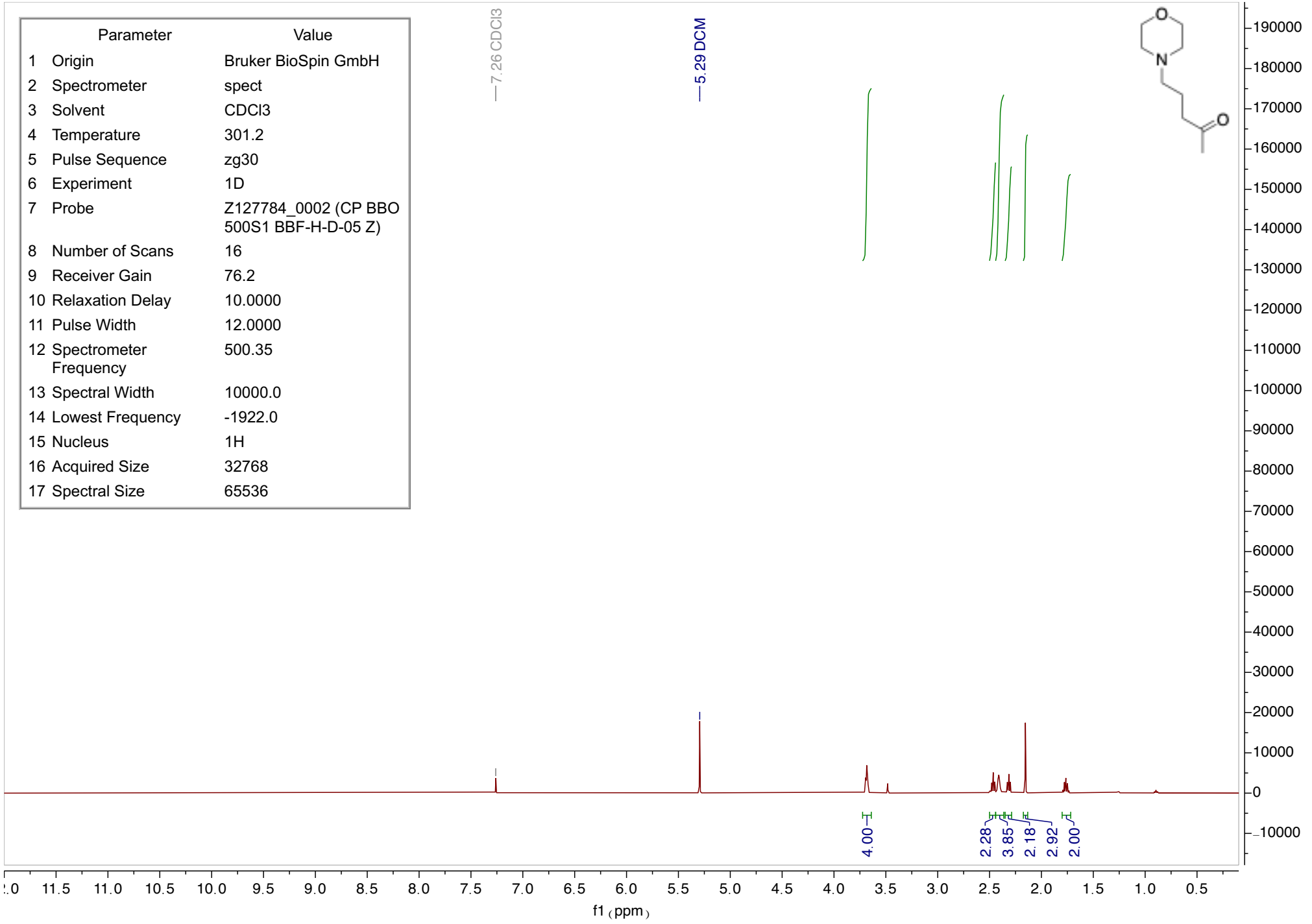
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	122.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

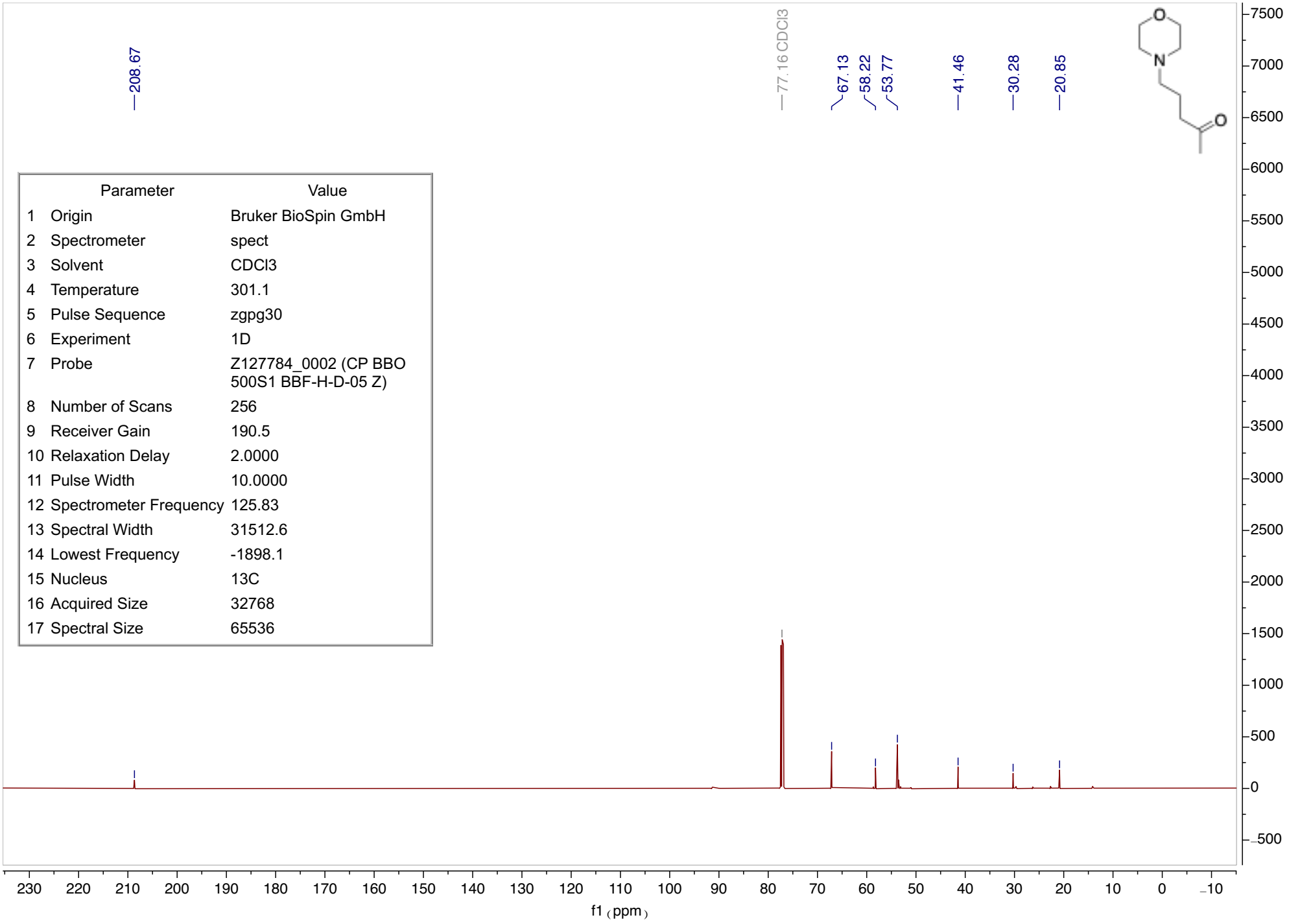




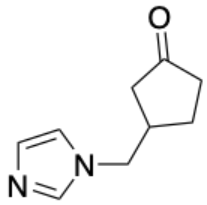
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	301.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	76.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

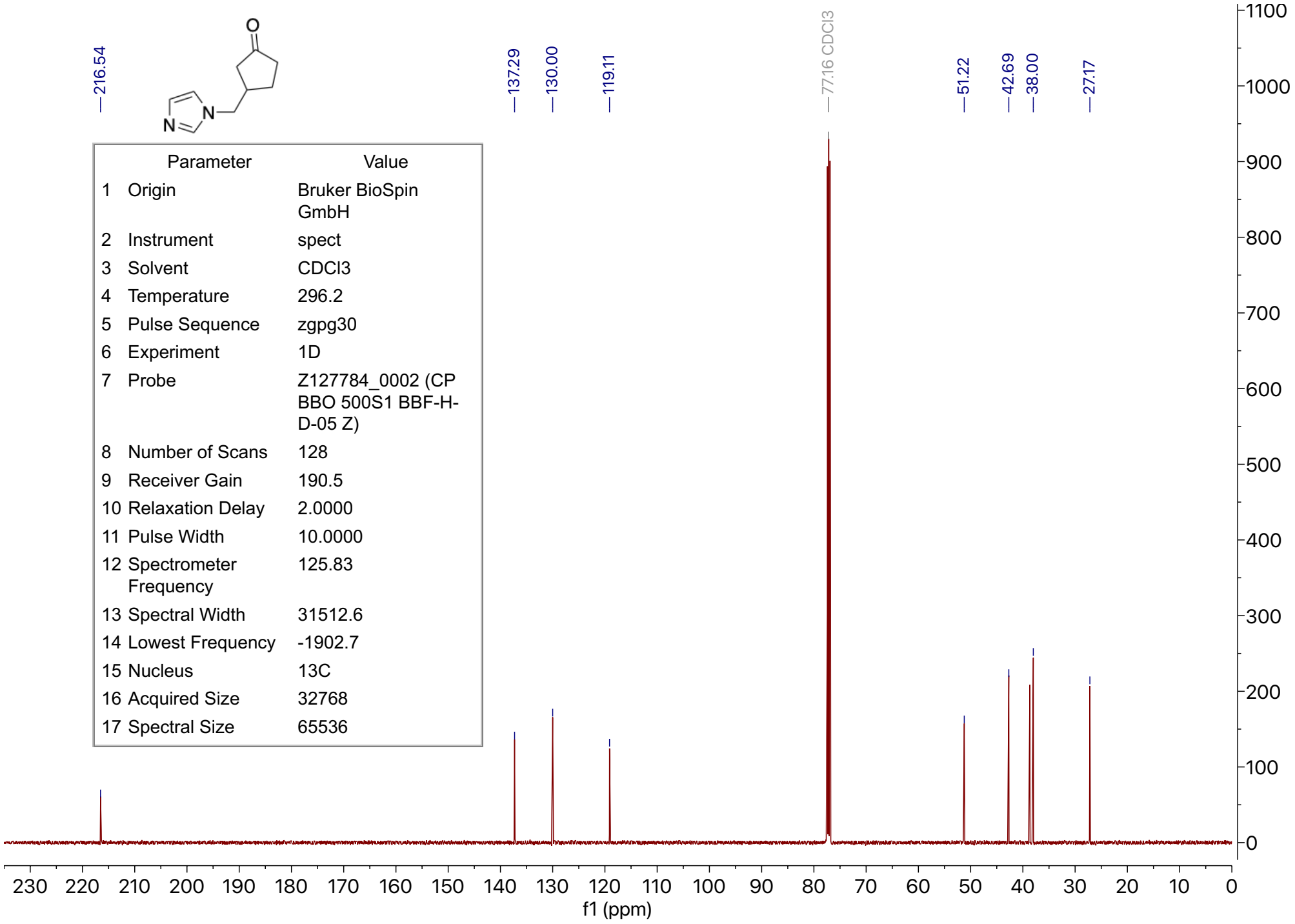


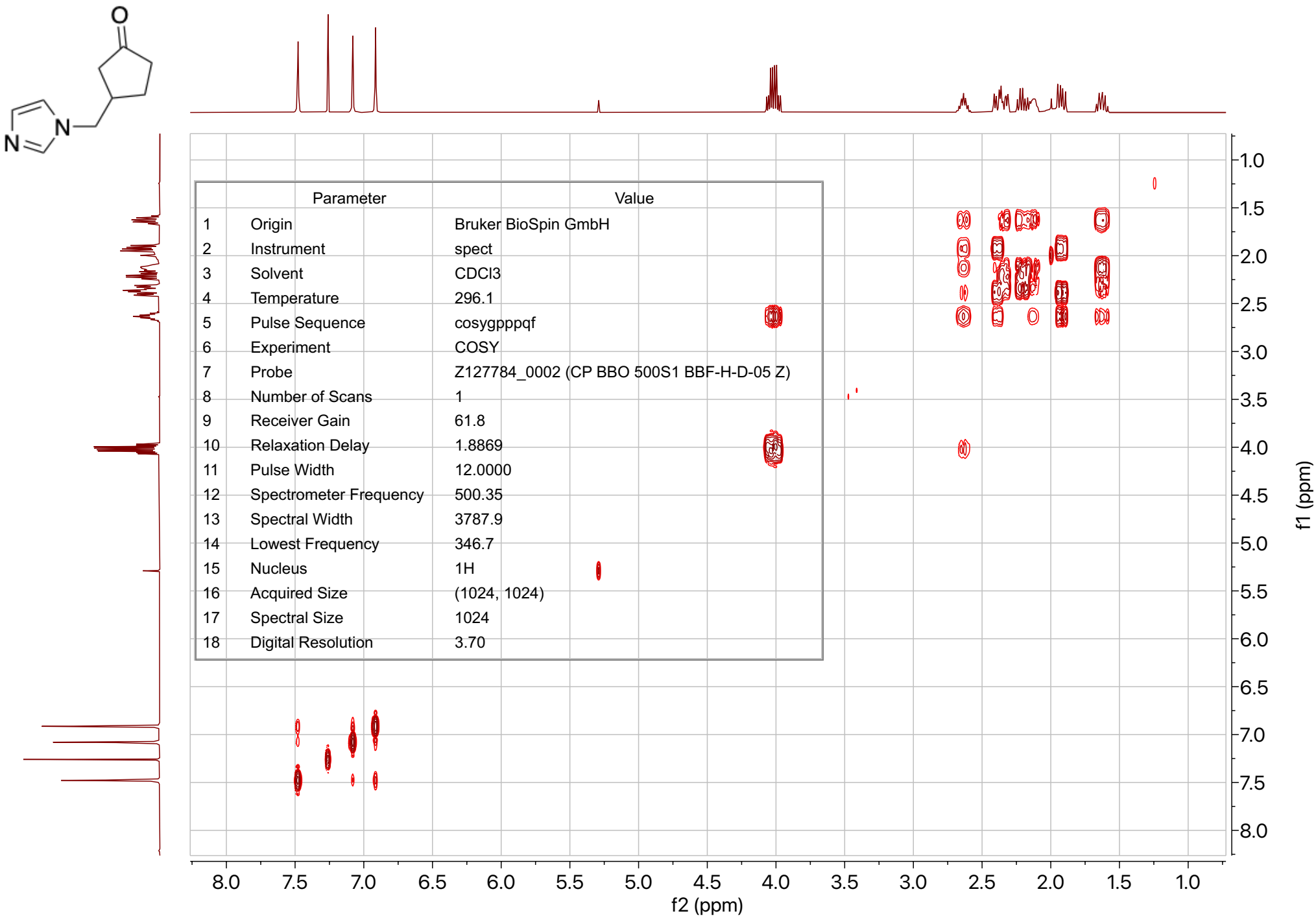


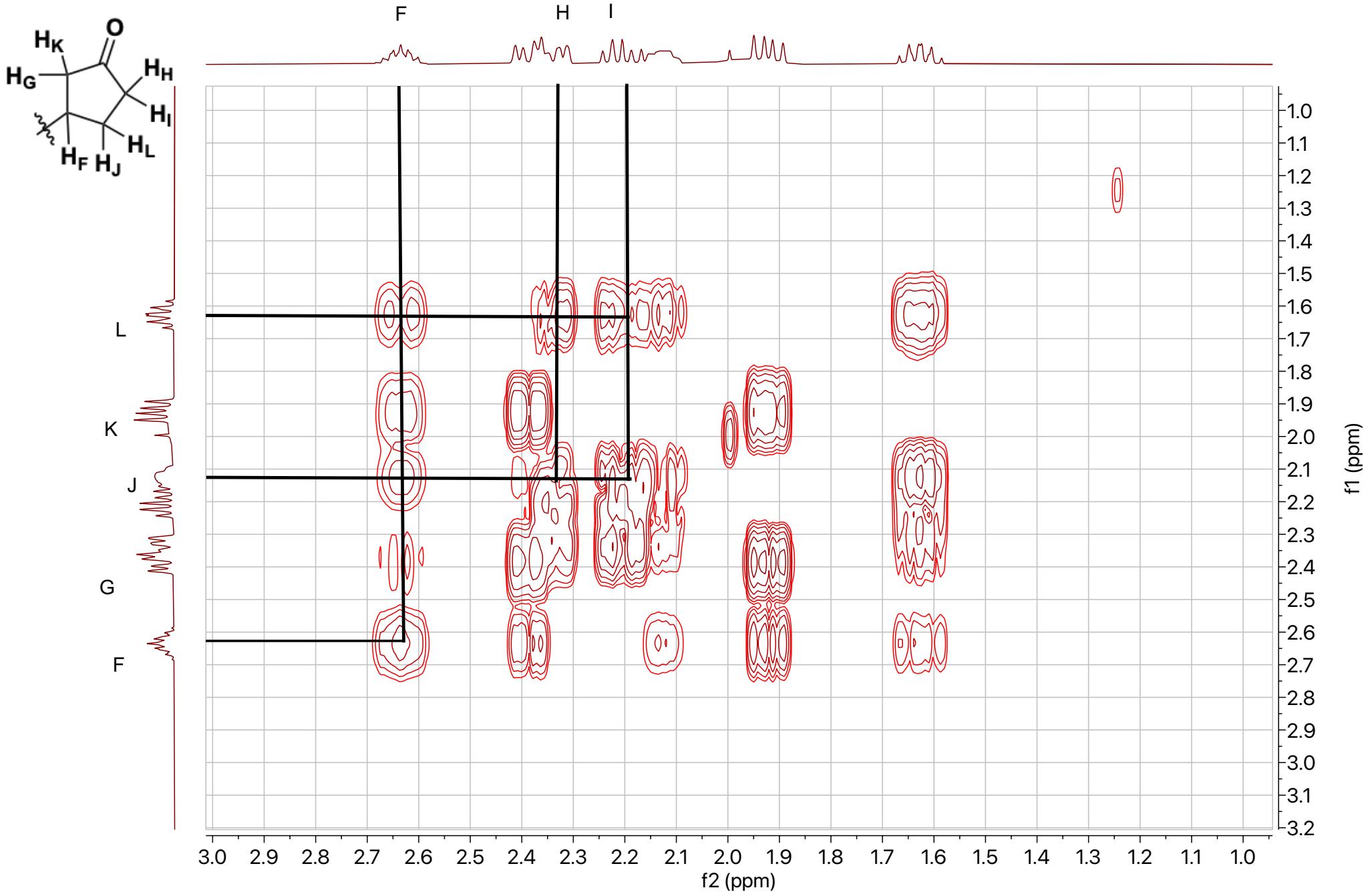
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	301.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

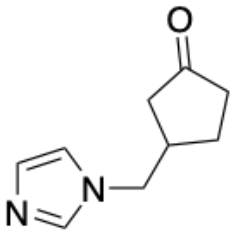


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	107.0
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

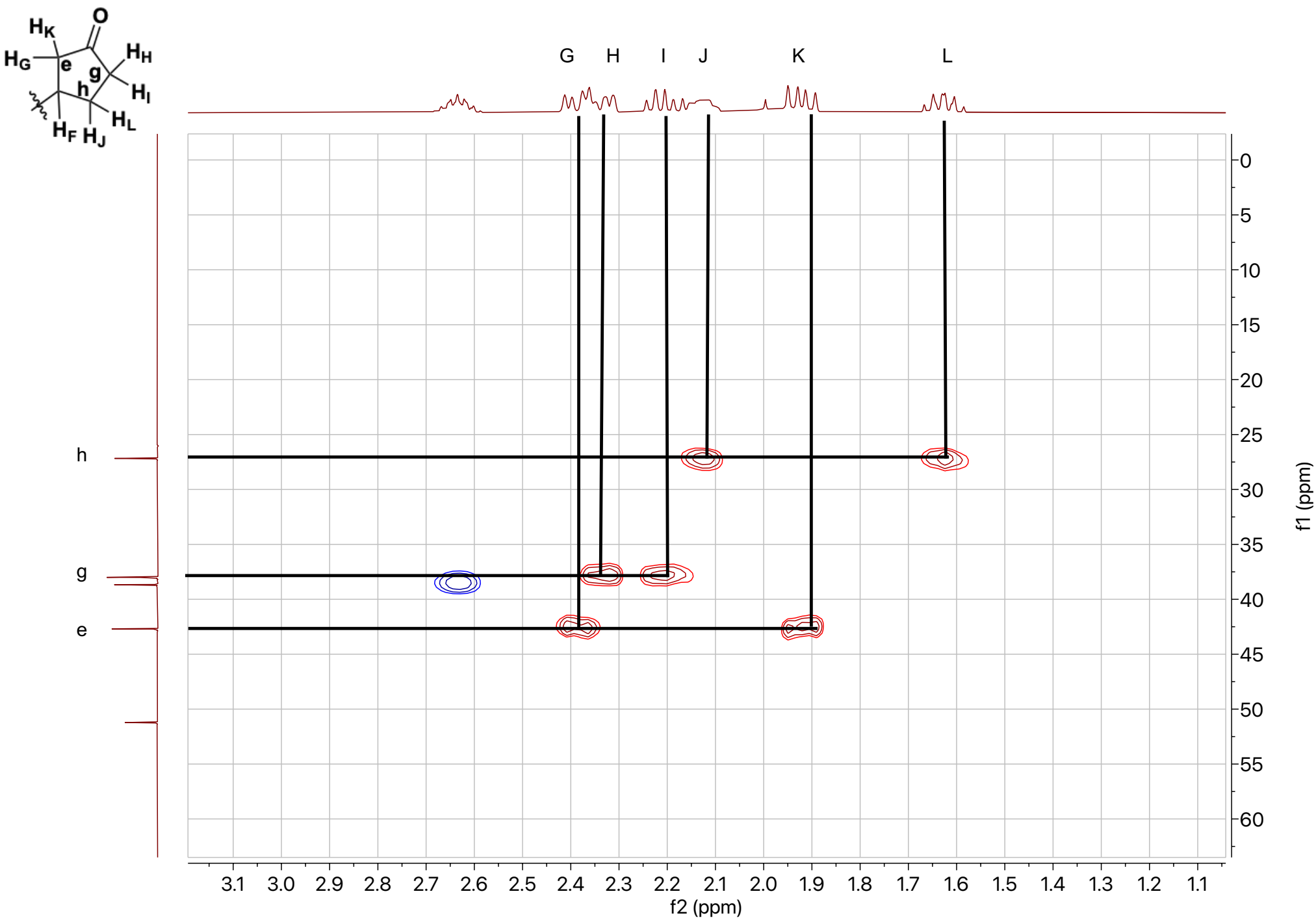

216.54
137.29
130.00
119.11
77.16 CDCl3
51.22
42.69
38.00
27.17
O
N
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence zgpg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 128
9 Receiver Gain 190.5
10 Relaxation Delay 2.0000
11 Pulse Width 10.0000
12 Spectrometer Frequency 125.83
13 Spectral Width 31512.6
14 Lowest Frequency -1902.7
15 Nucleus 13C
16 Acquired Size 32768
17 Spectral Size 65536
1100
1000
900
800
700
600
500
400
300
200
100
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

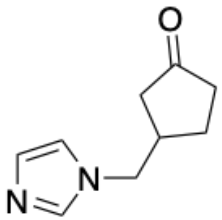

O
N
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 1
9 Receiver Gain 61.8
10 Relaxation Delay 1.8869
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 3787.9
14 Lowest Frequency 346.7
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
18 Digital Resolution 3.70
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
f2 (ppm)
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
f1 (ppm)


O
H_K
H_G
H_H
H_I
H_L
H_F H_J
F
H
I
L
K
J
G
F
3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
f2 (ppm)
1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8 2.9 3.0 3.1 3.2
f1 (ppm)

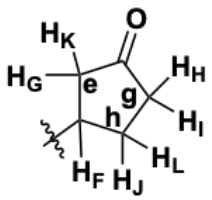


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	3787.9
14	Lowest Frequency	346.7
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	7.40


O
H_K
H_G
e
g
h
H_H
H_I
H_L
H_F H_J
G H I J K L
h
g
e
0 5 10 15 20 25 30 35 40 45 50 55 60
f1 (ppm)
3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1
f2 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	8
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	3787.9
14	Lowest Frequency	346.7
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	7.40



H I K

carbonyl

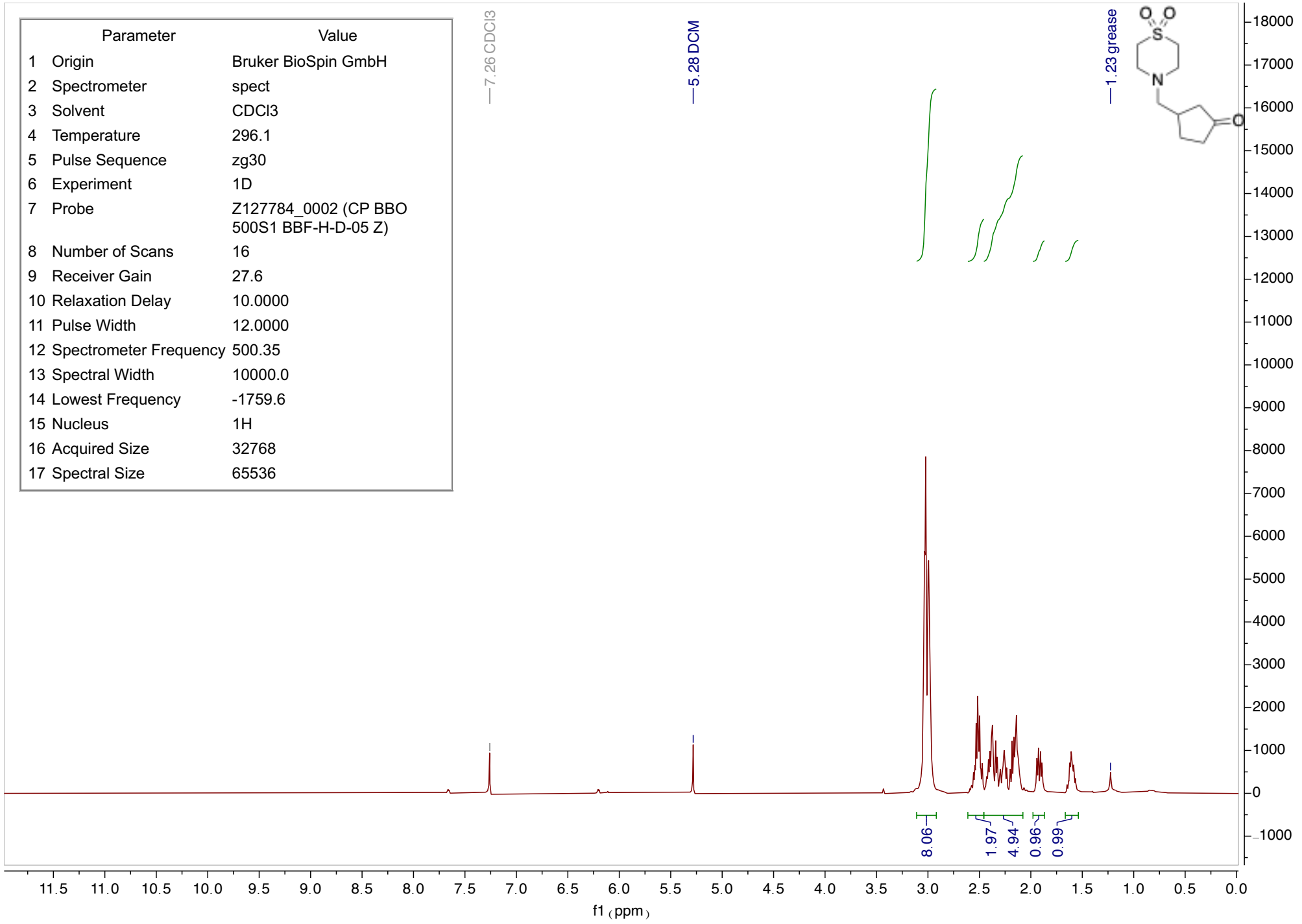
207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223

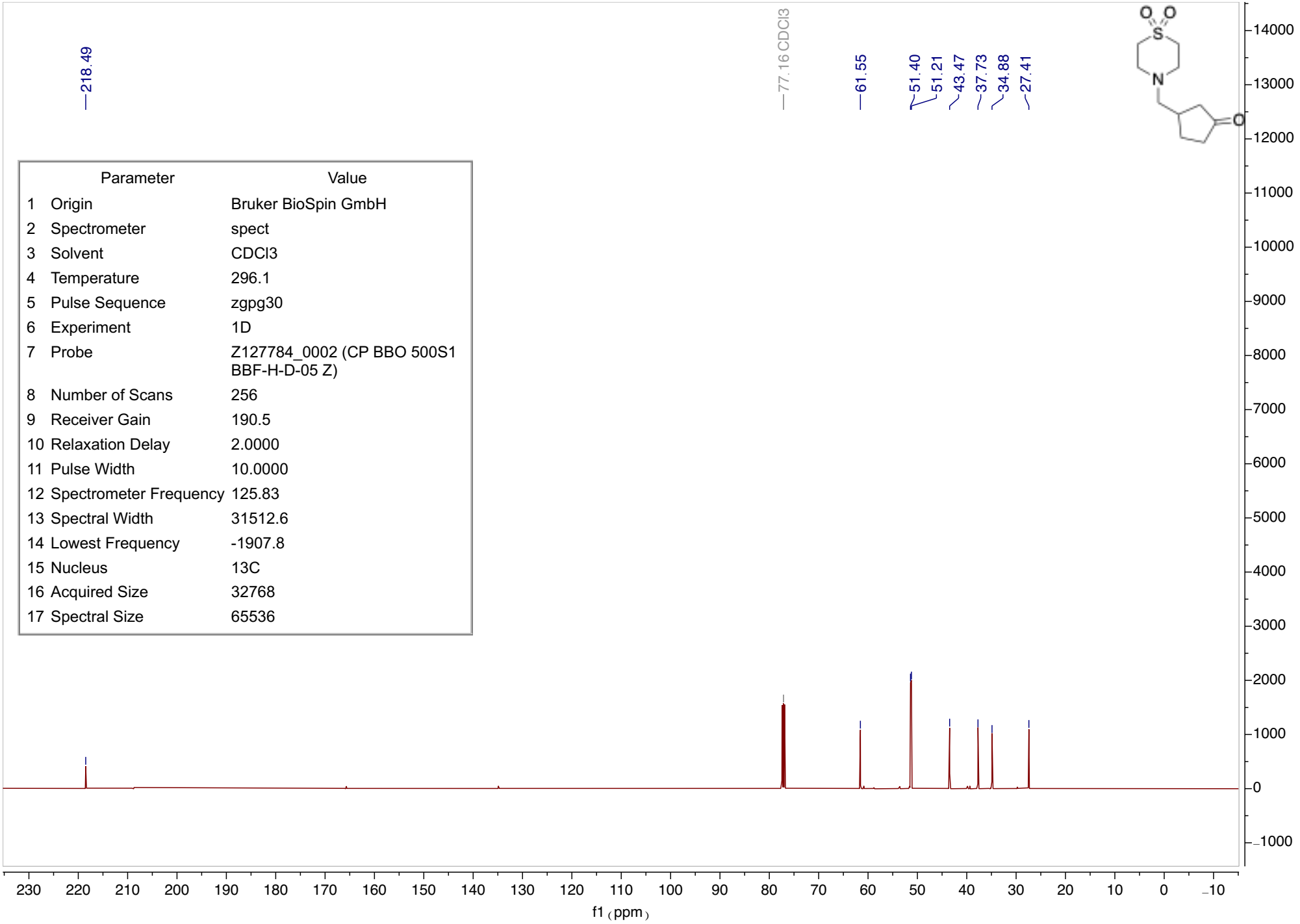
f1 (ppm)

2.65 2.60 2.55 2.50 2.45 2.40 2.35 2.30 2.25 2.20 2.15 2.10 2.05 2.00 1.95 1.90 1.85 1.80 1.75 1.70 1.65

f2 (ppm)

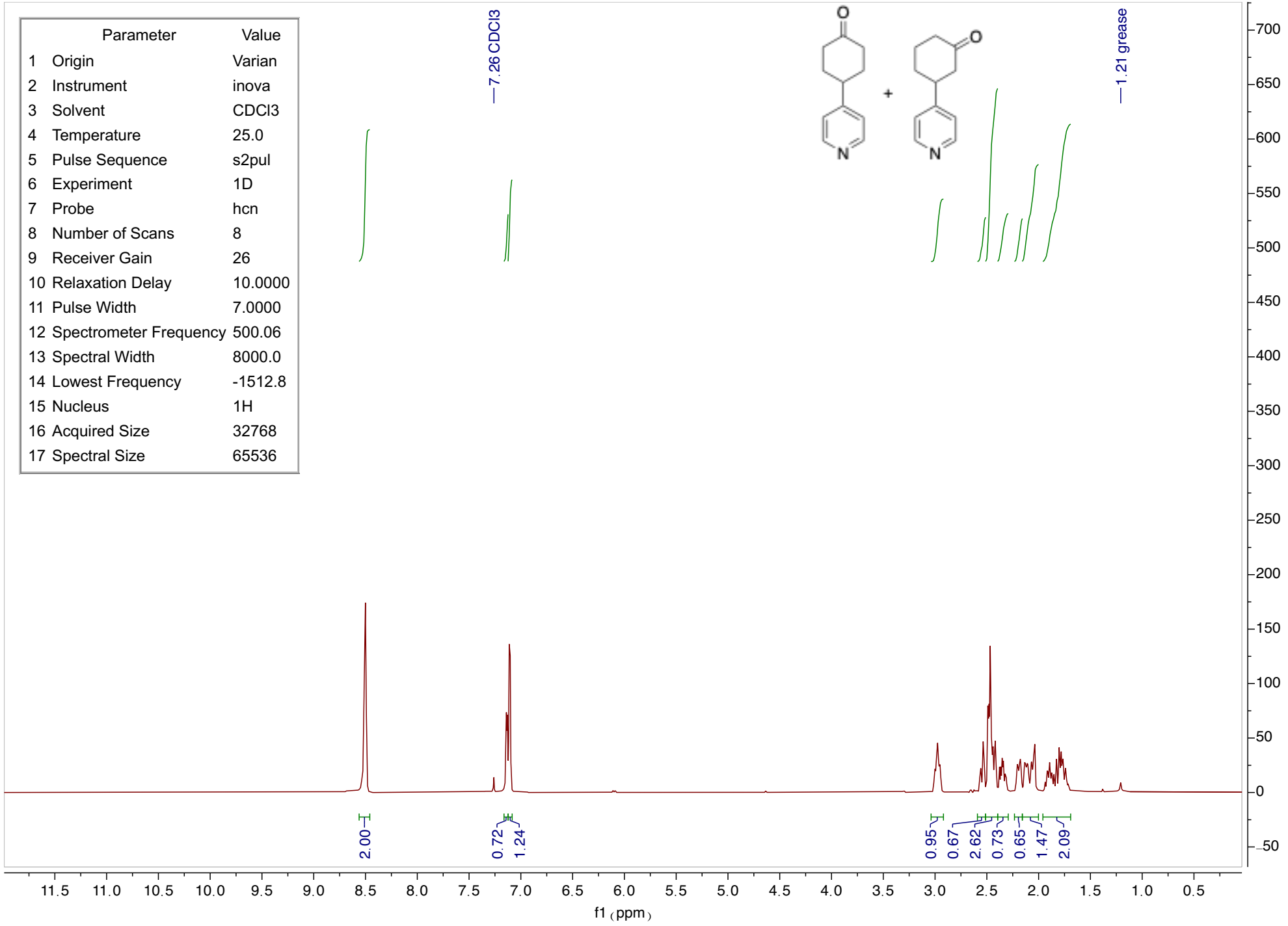
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	27.6
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

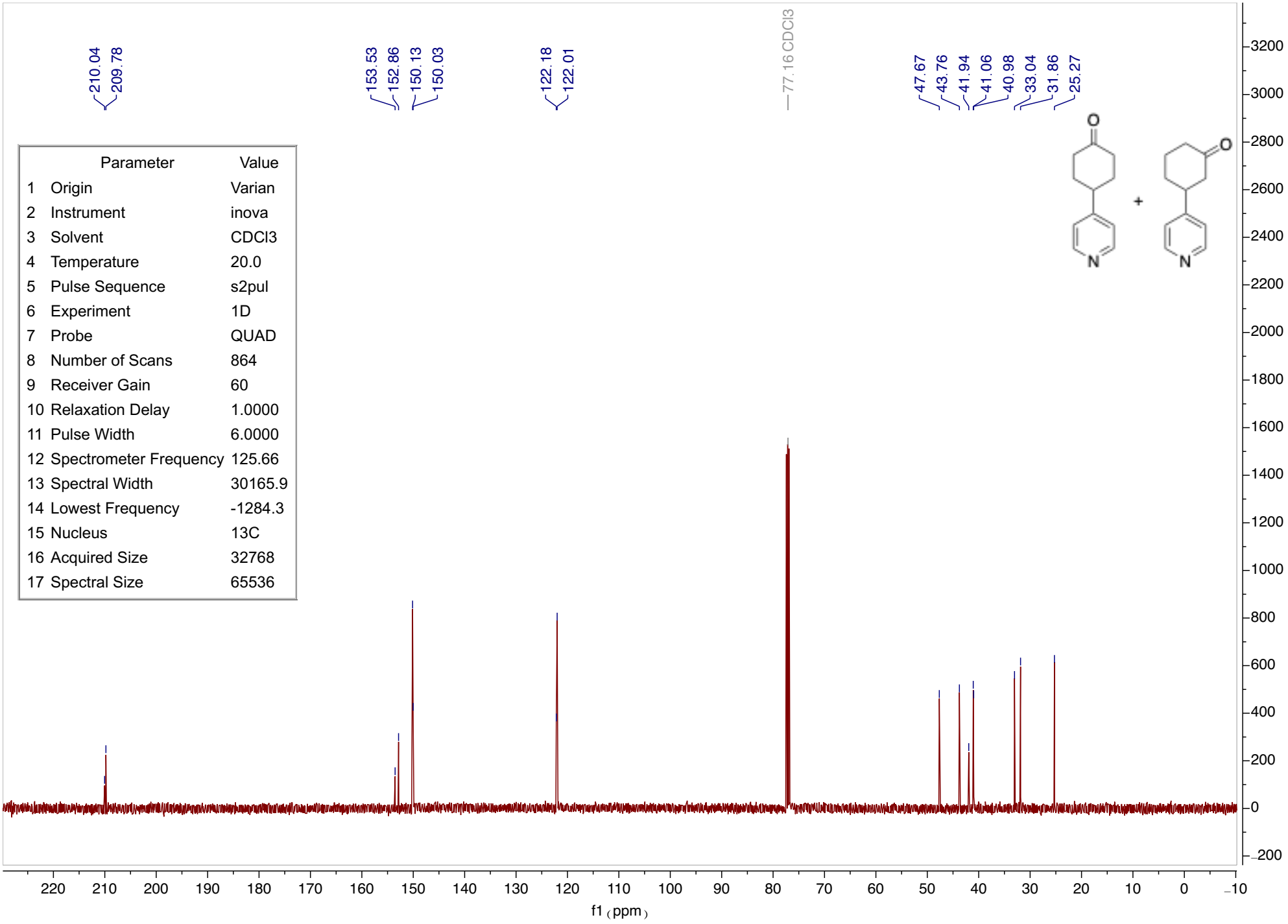




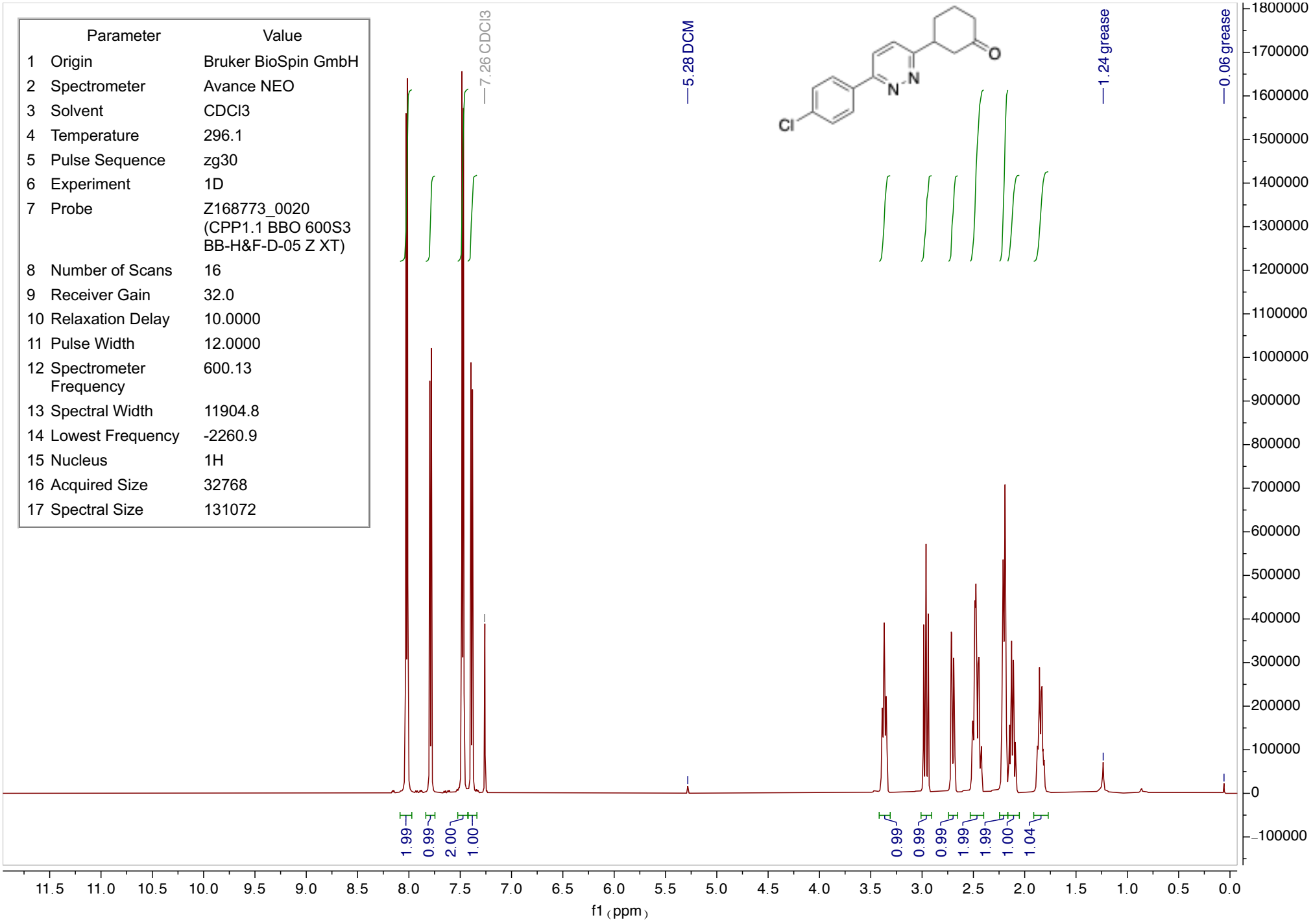
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1907.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

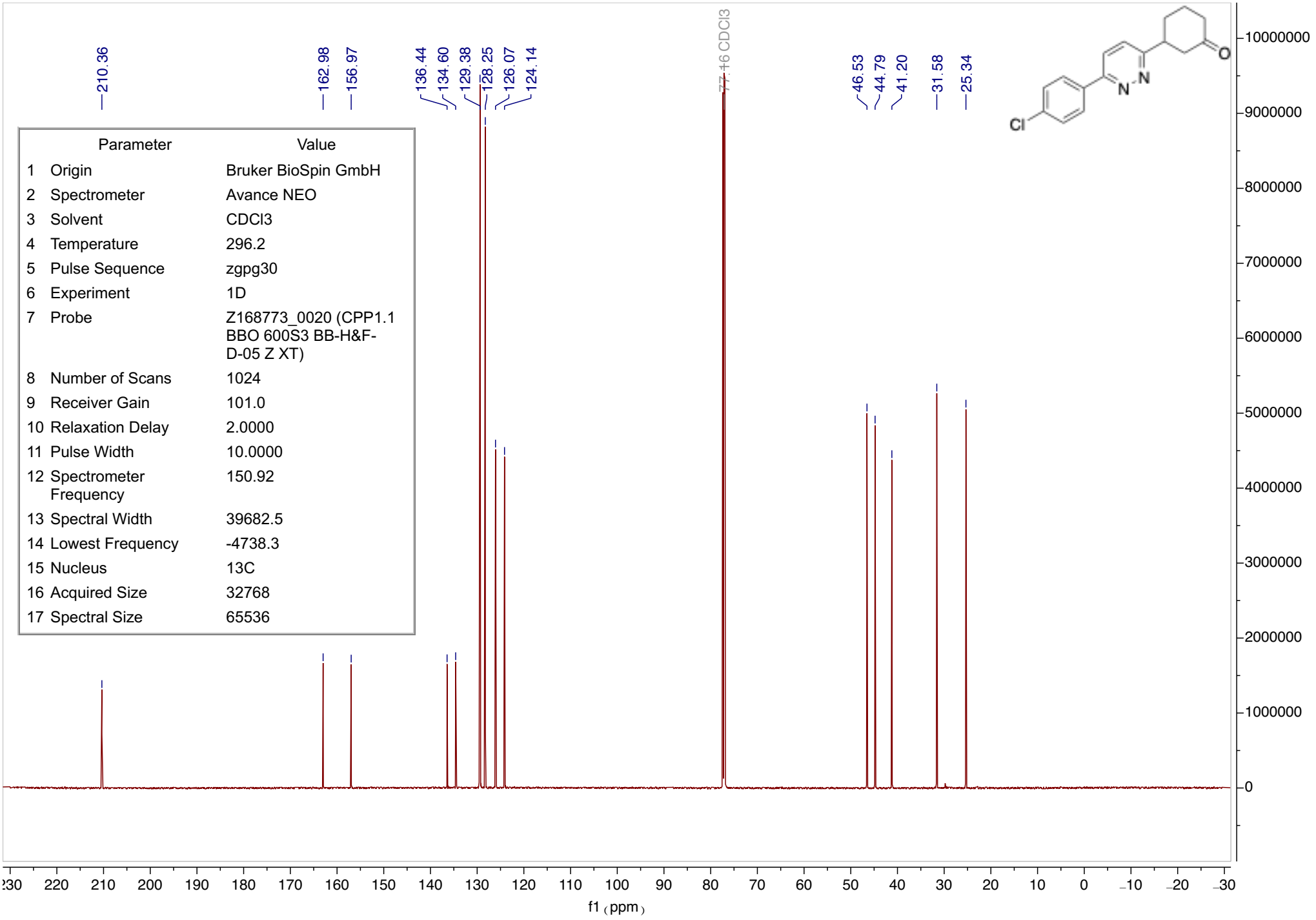
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	hcn
8	Number of Scans	8
9	Receiver Gain	26
10	Relaxation Delay	10.0000
11	Pulse Width	7.0000
12	Spectrometer Frequency	500.06
13	Spectral Width	8000.0
14	Lowest Frequency	-1512.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



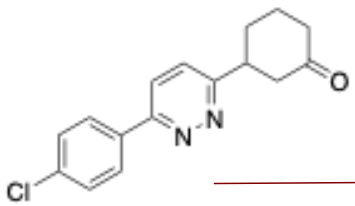


	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	QUAD
8	Number of Scans	864
9	Receiver Gain	60
10	Relaxation Delay	1.0000
11	Pulse Width	6.0000
12	Spectrometer Frequency	125.66
13	Spectral Width	30165.9
14	Lowest Frequency	-1284.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

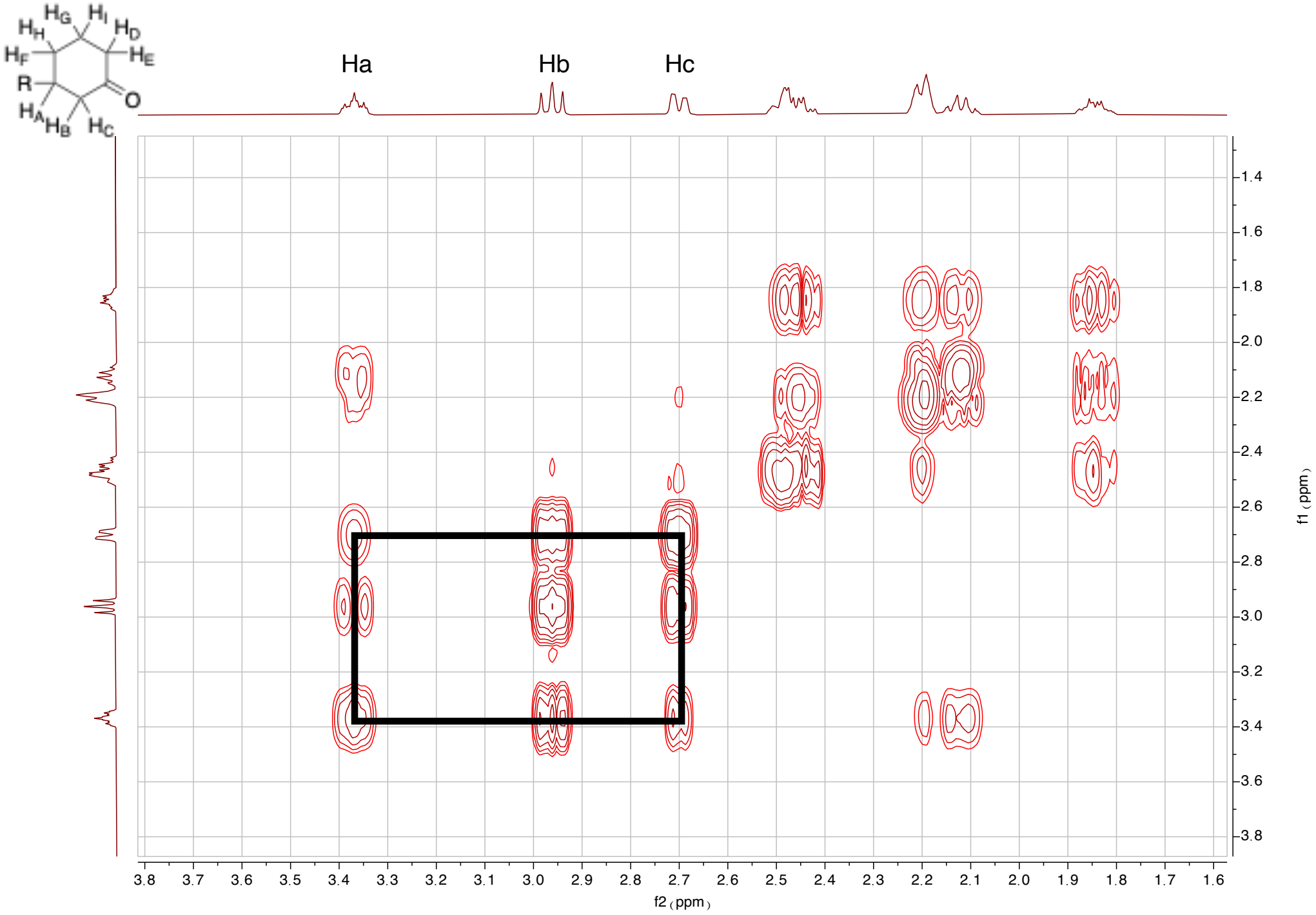

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 32.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2260.9
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.26 CDCl3
5.28 DCM
1.24 grease
0.06 grease
Cl
N
N
O
1.99
0.99
2.00
1.00
0.99
0.99
0.99
1.99
1.99
1.00
1.04
f1 (ppm)

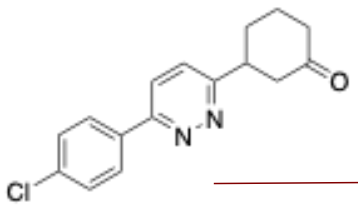


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	39682.5
14	Lowest Frequency	-4738.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

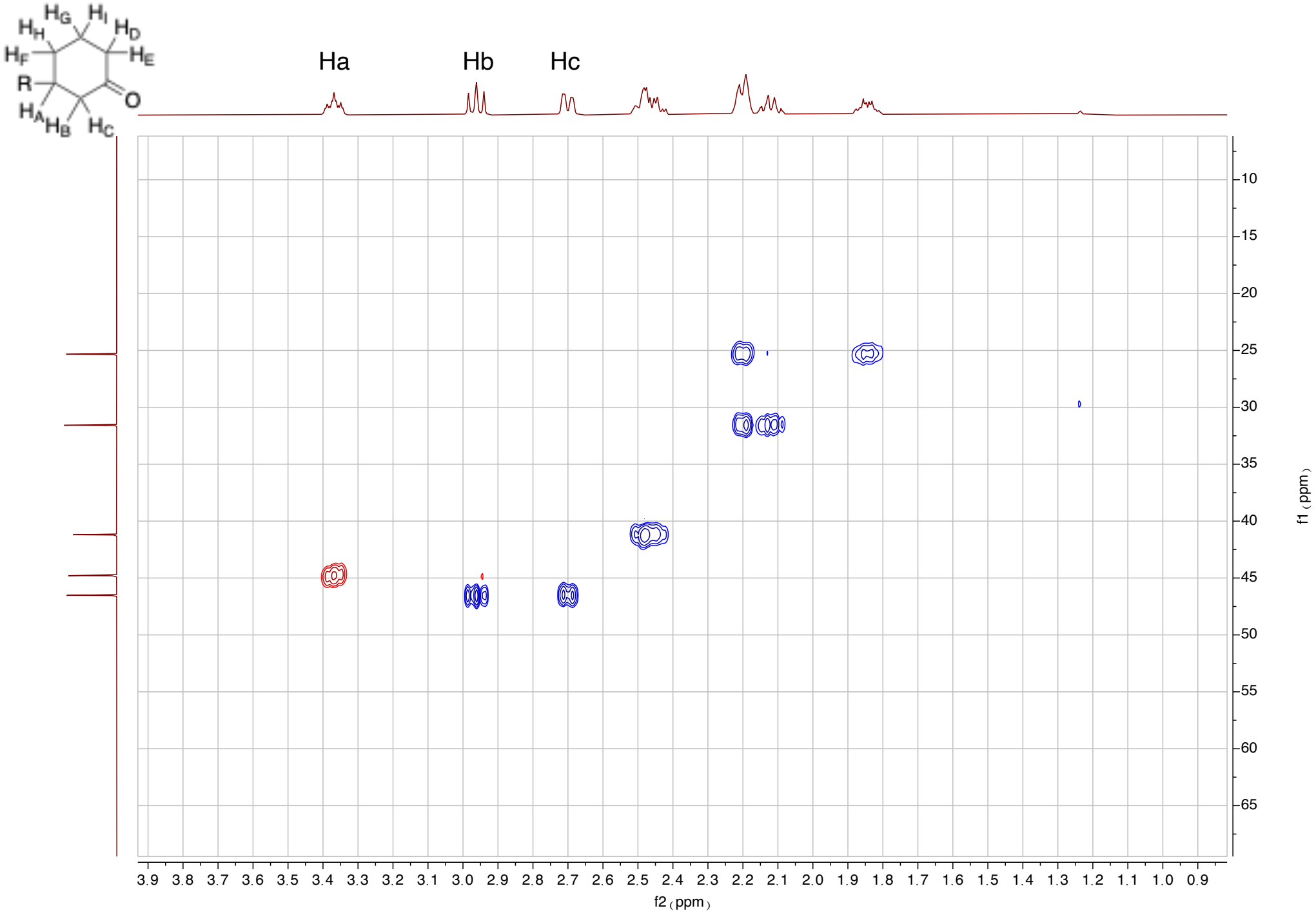


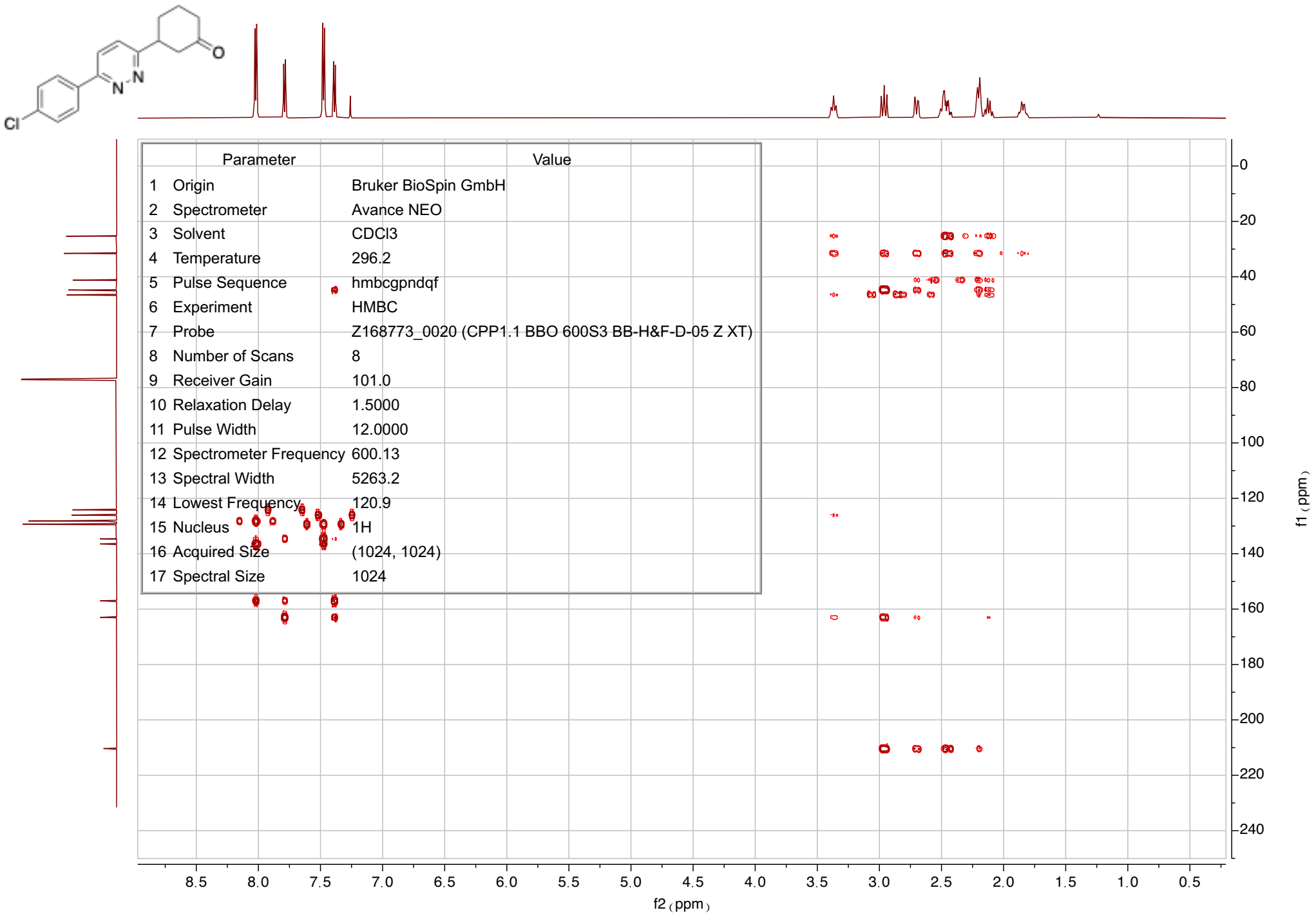
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	2
9	Receiver Gain	64.0
10	Relaxation Delay	1.4345
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5263.2
14	Lowest Frequency	122.1
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

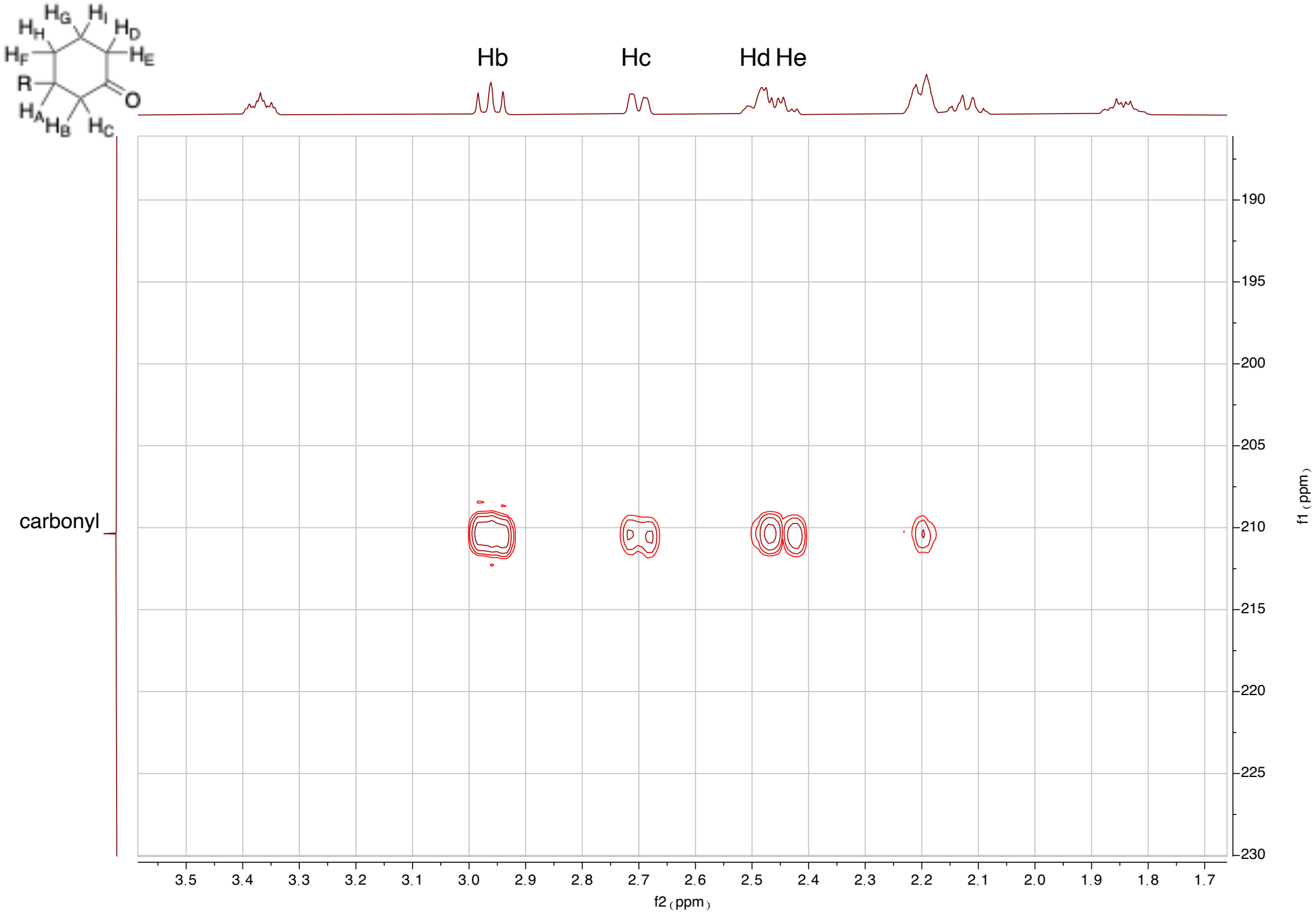

HG
HI
HD
HH
HE
HF
R
O
HA
HB
HC
Ha
Hb
Hc
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
f1 (ppm)
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
f2 (ppm)

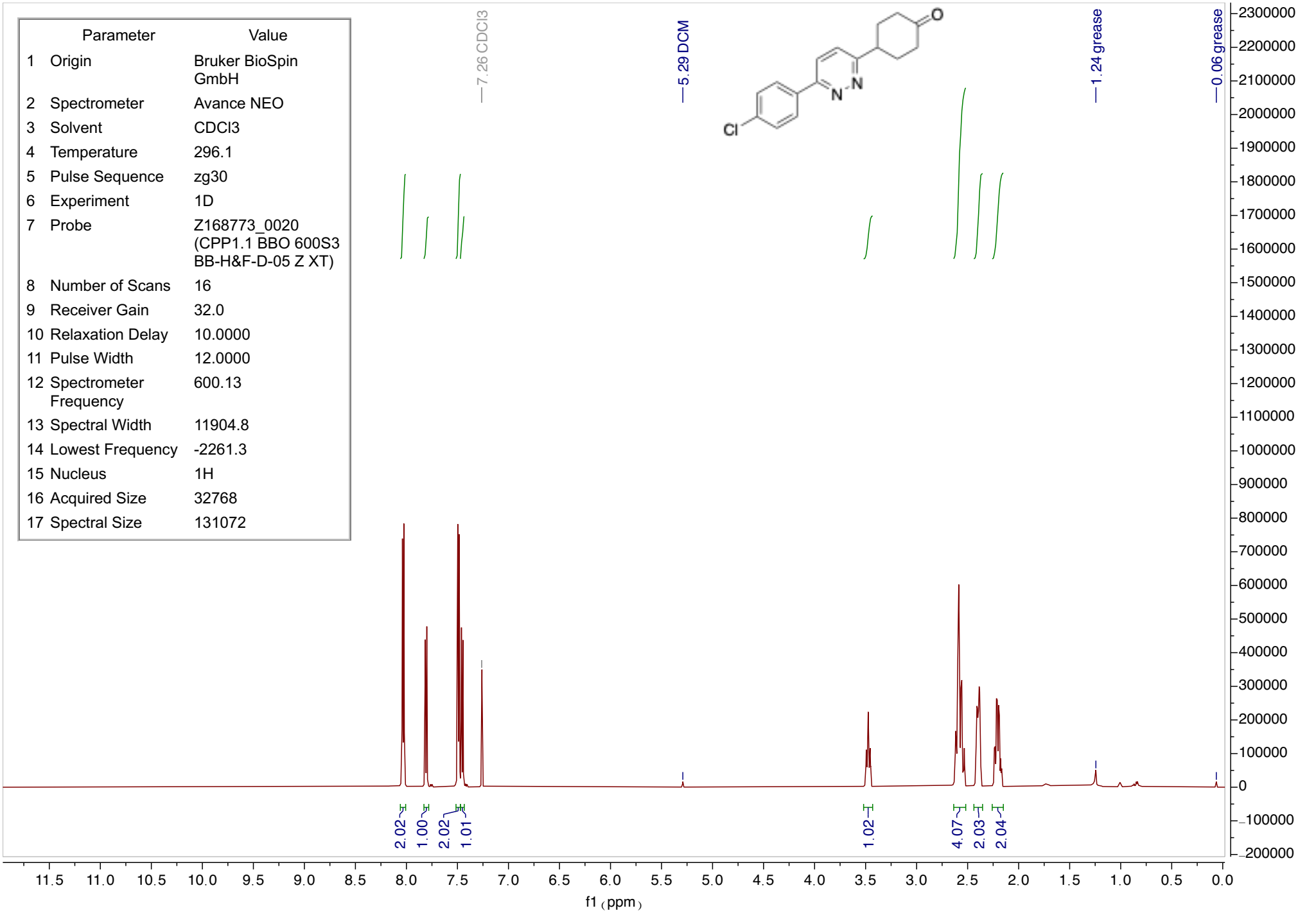


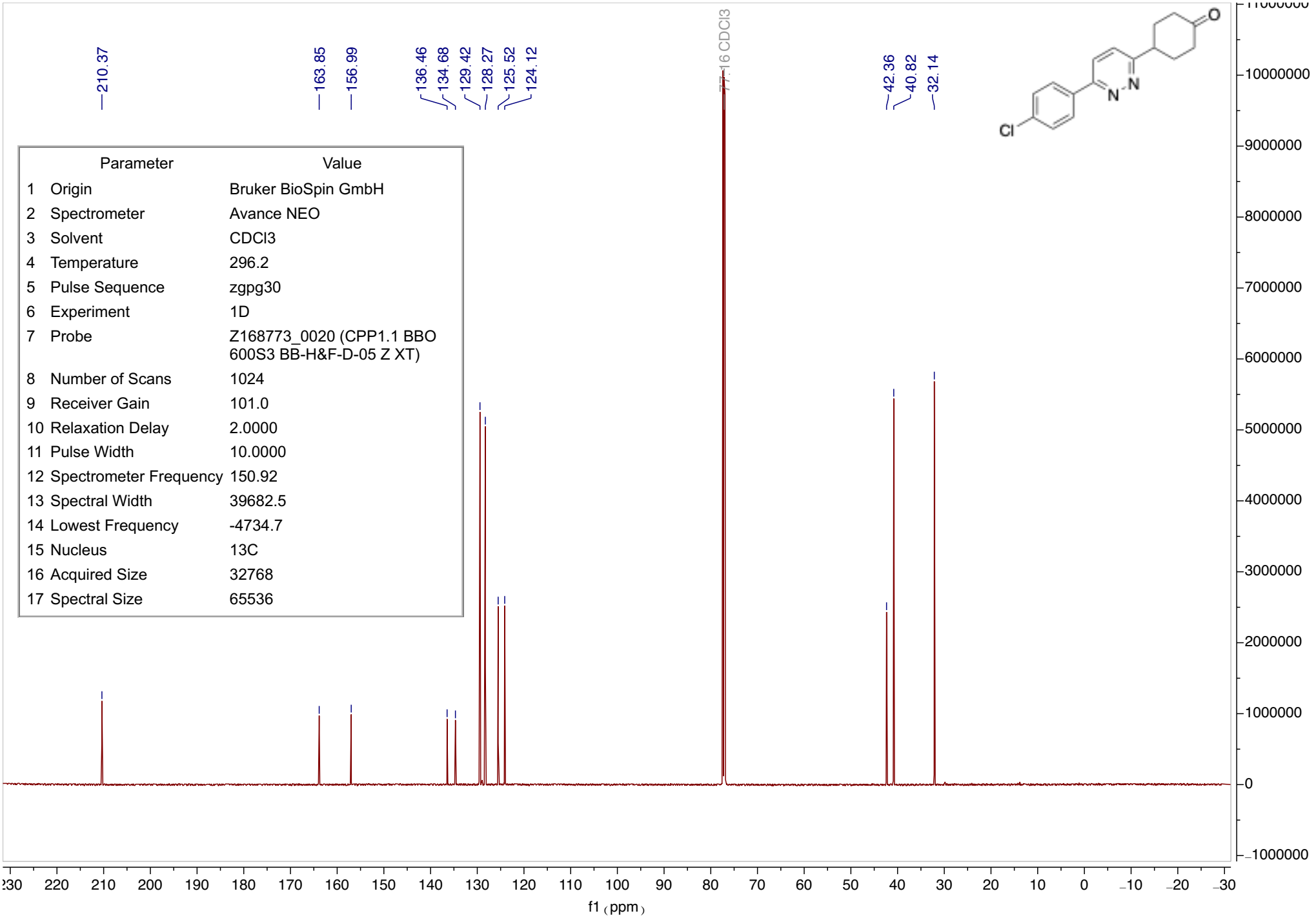
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5263.2
14	Lowest Frequency	121.9
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


Ha
Hb
Hc
f2 (ppm)
f1 (ppm)


Cl
N
N
O
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hmbcgpndqf
6 Experiment HMBC
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 8
9 Receiver Gain 101.0
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5263.2
14 Lowest Frequency 120.9
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 20 40 60 80 100 120 140 160 180 200 220 240
f1 (ppm)

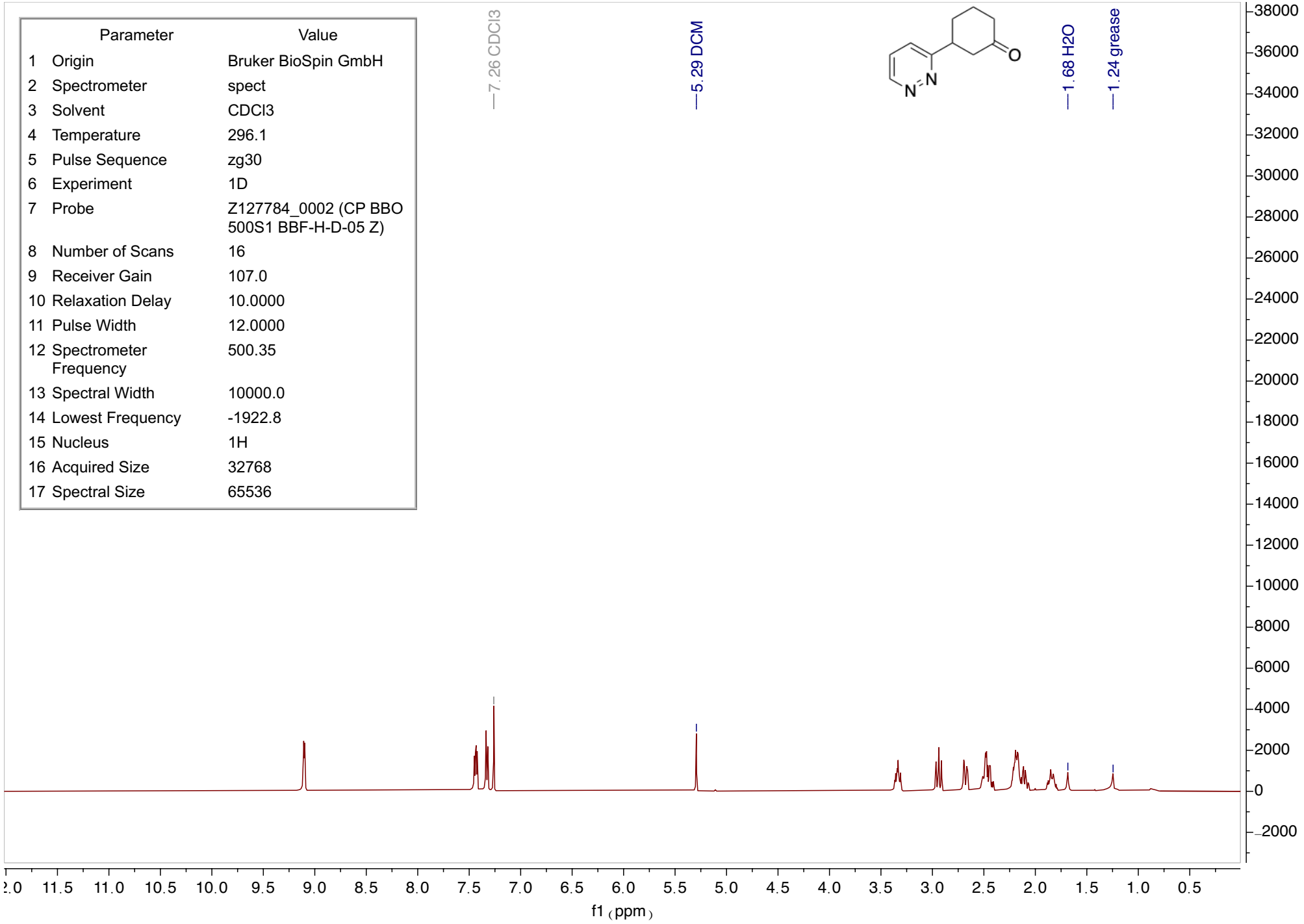

HG
HI
HH
HD
HF
HE
R
O
HA
HB
HC
Hb
Hc
Hd He
carbonyl
190
195
200
205
210
215
220
225
230
f1 (ppm)
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
f2 (ppm)

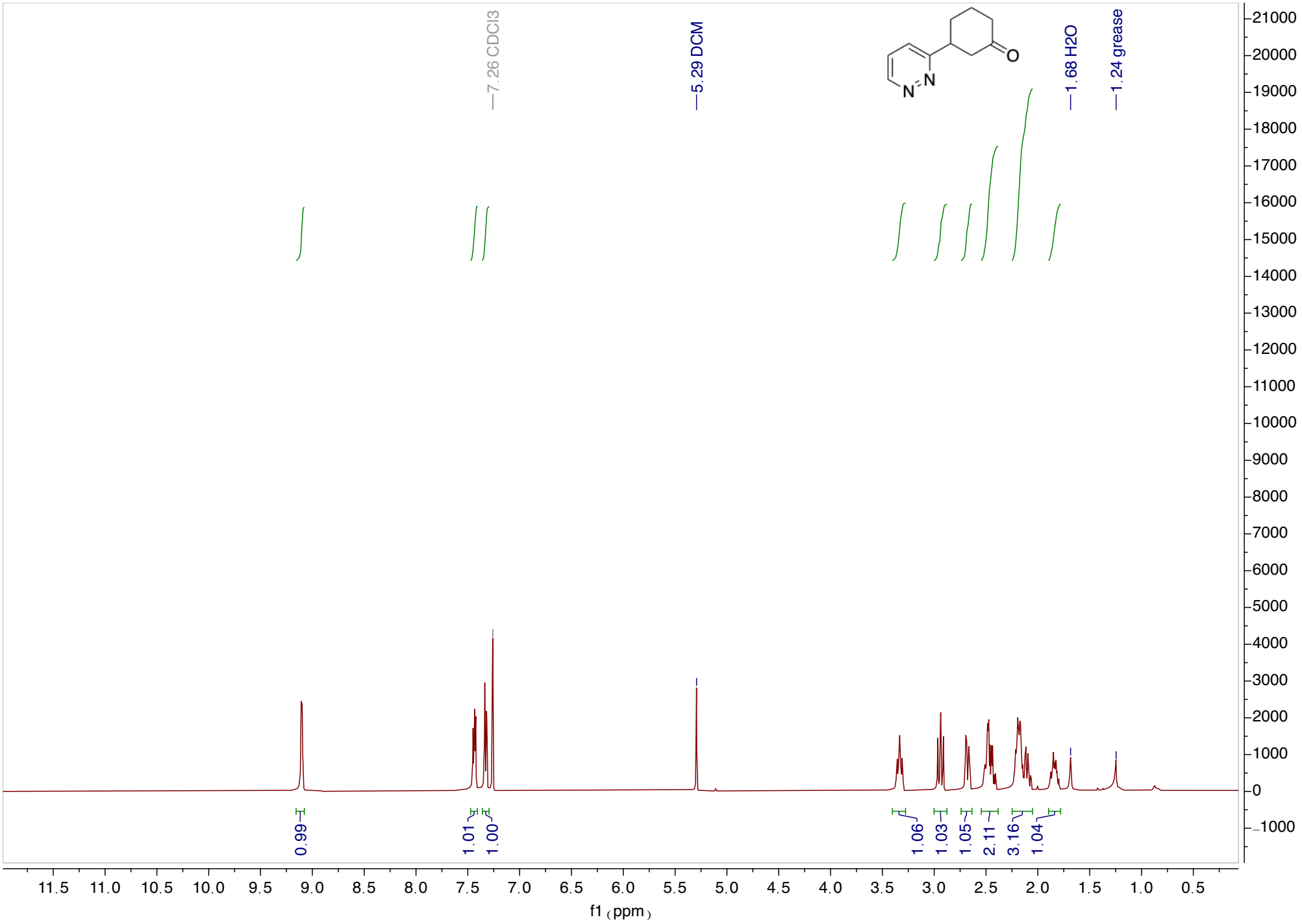

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 32.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2261.3
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.26 CDCl3
5.29 DCM
1.24 grease
0.06 grease
O
N
N
Cl
2.02
1.00
2.02
1.01
1.02
4.07
2.03
2.04
f1 (ppm)

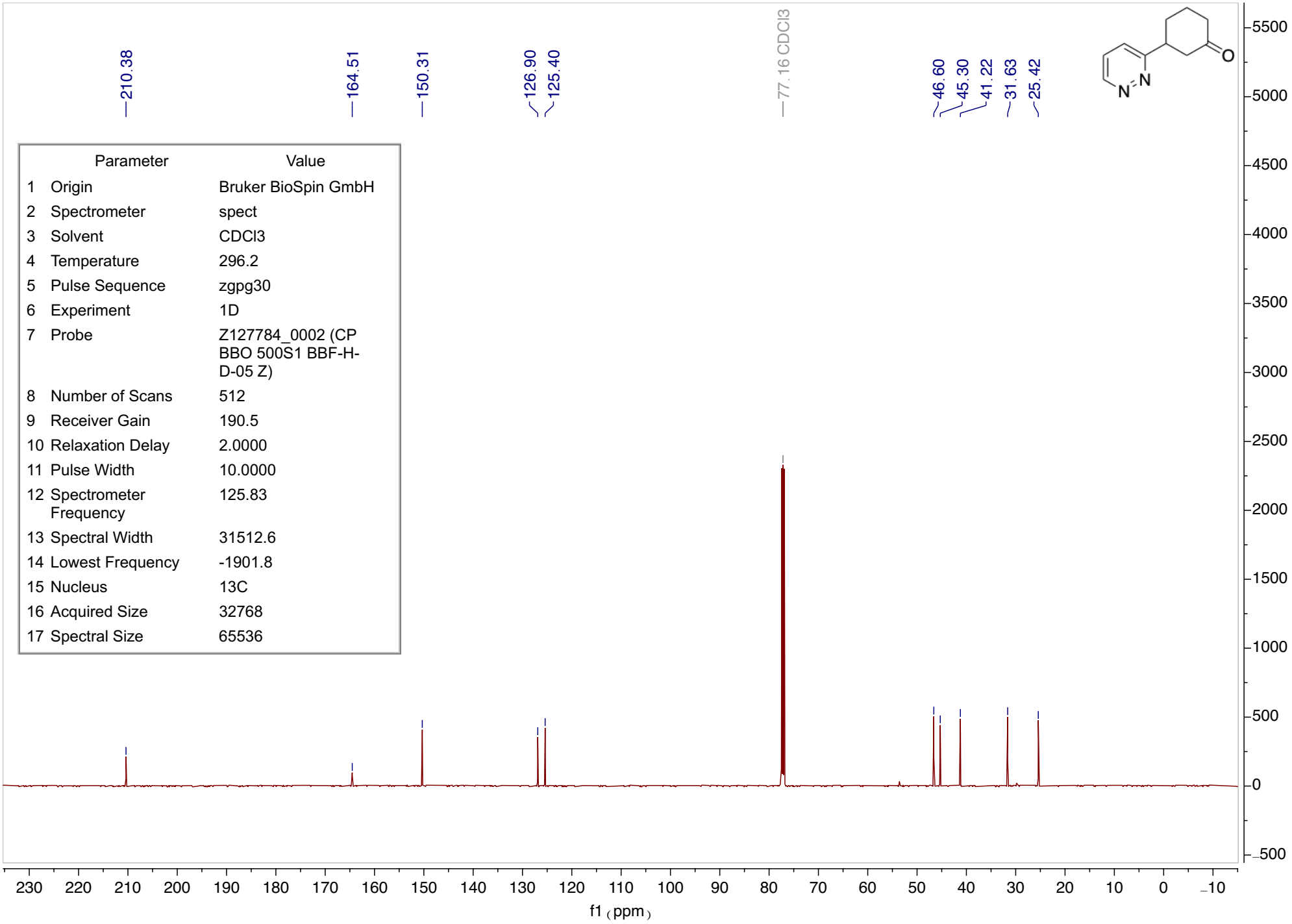


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	39682.5
14	Lowest Frequency	-4734.7
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

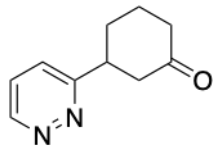
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	107.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



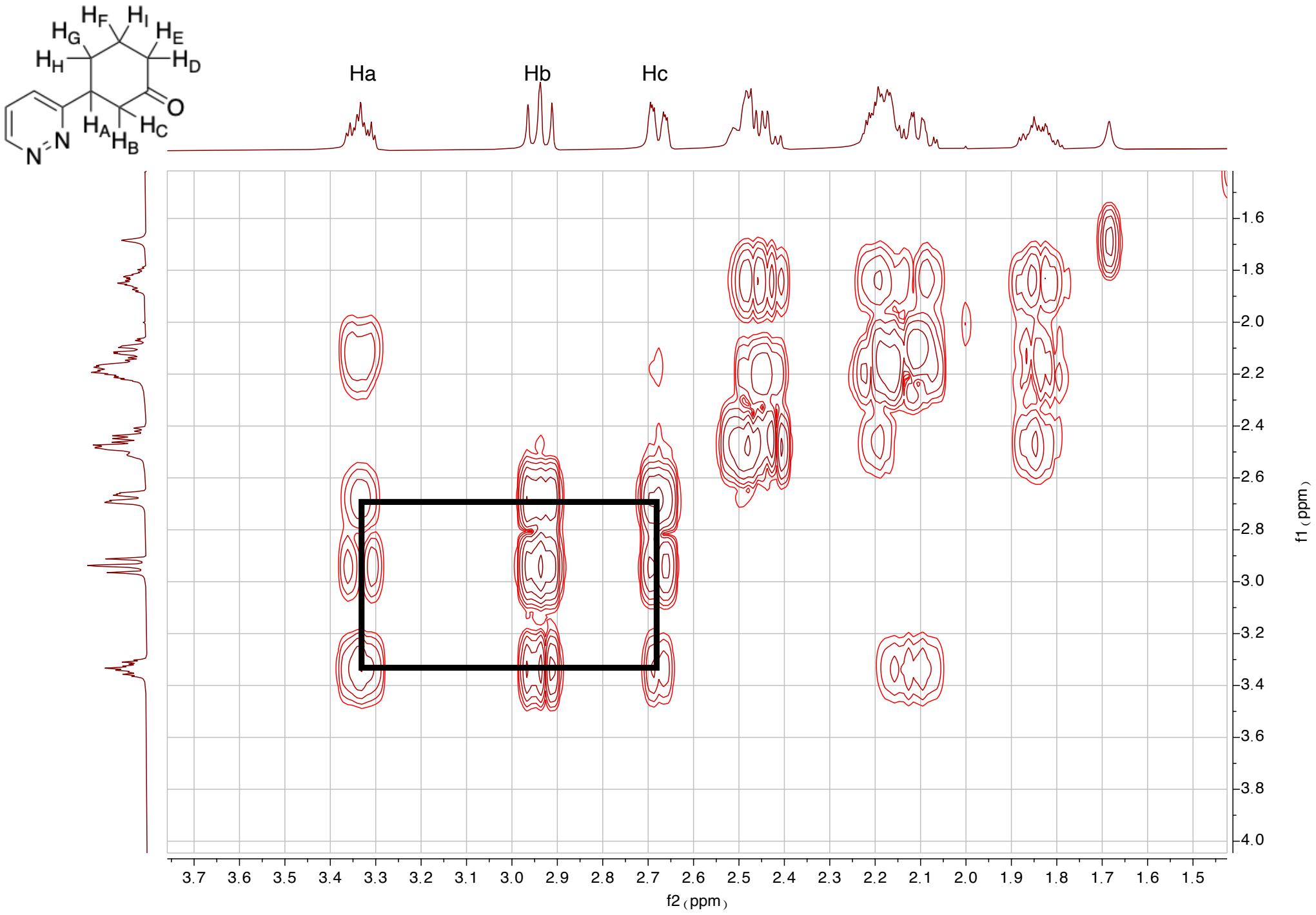

7.26 CDCl3
5.29 DCM
1.68 H2O
1.24 grease
O
N
N
0.99
1.01
1.00
1.06
1.03
1.05
2.11
3.16
1.04
f1 (ppm)

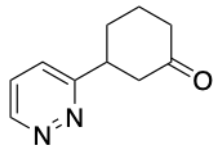


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

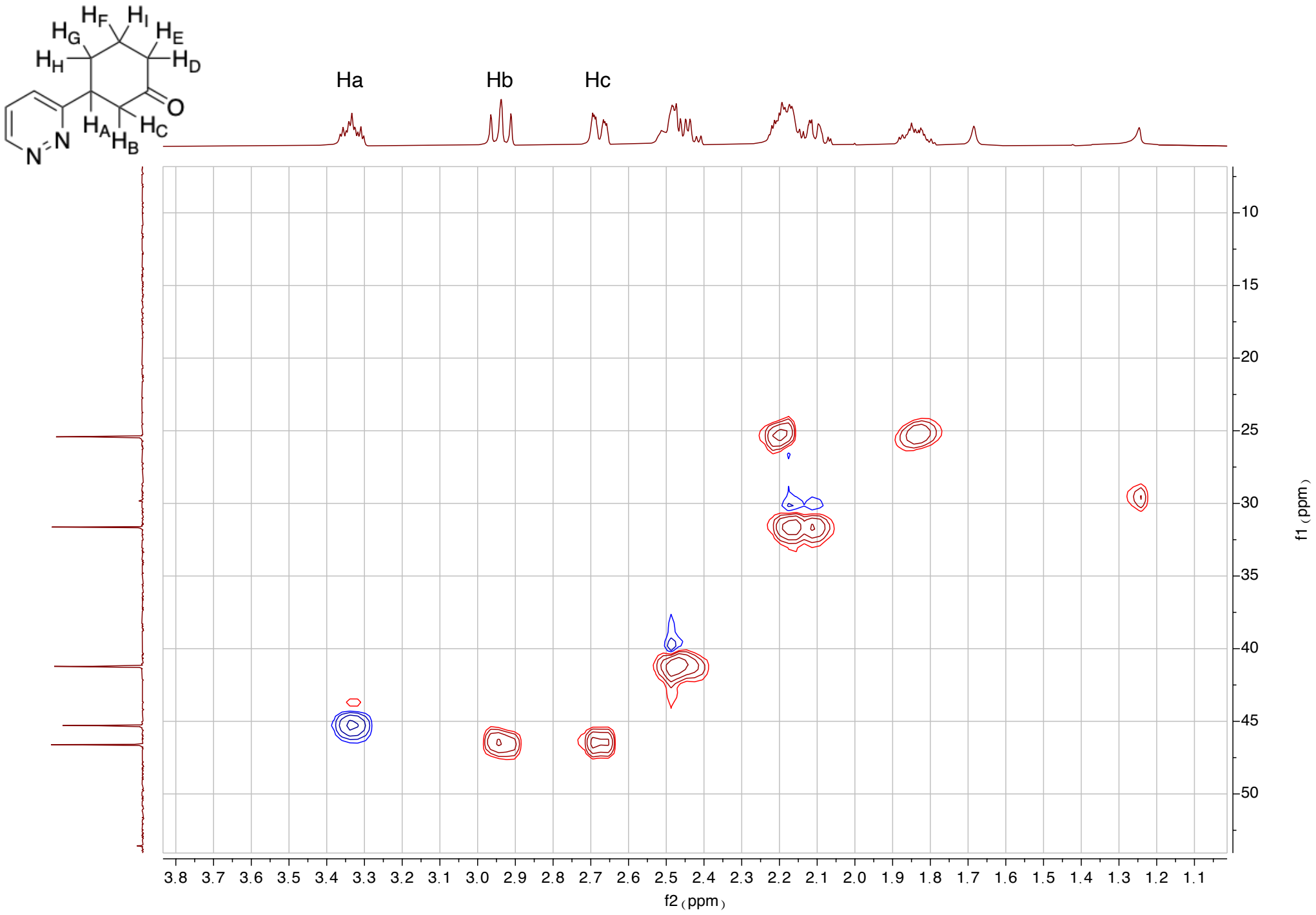


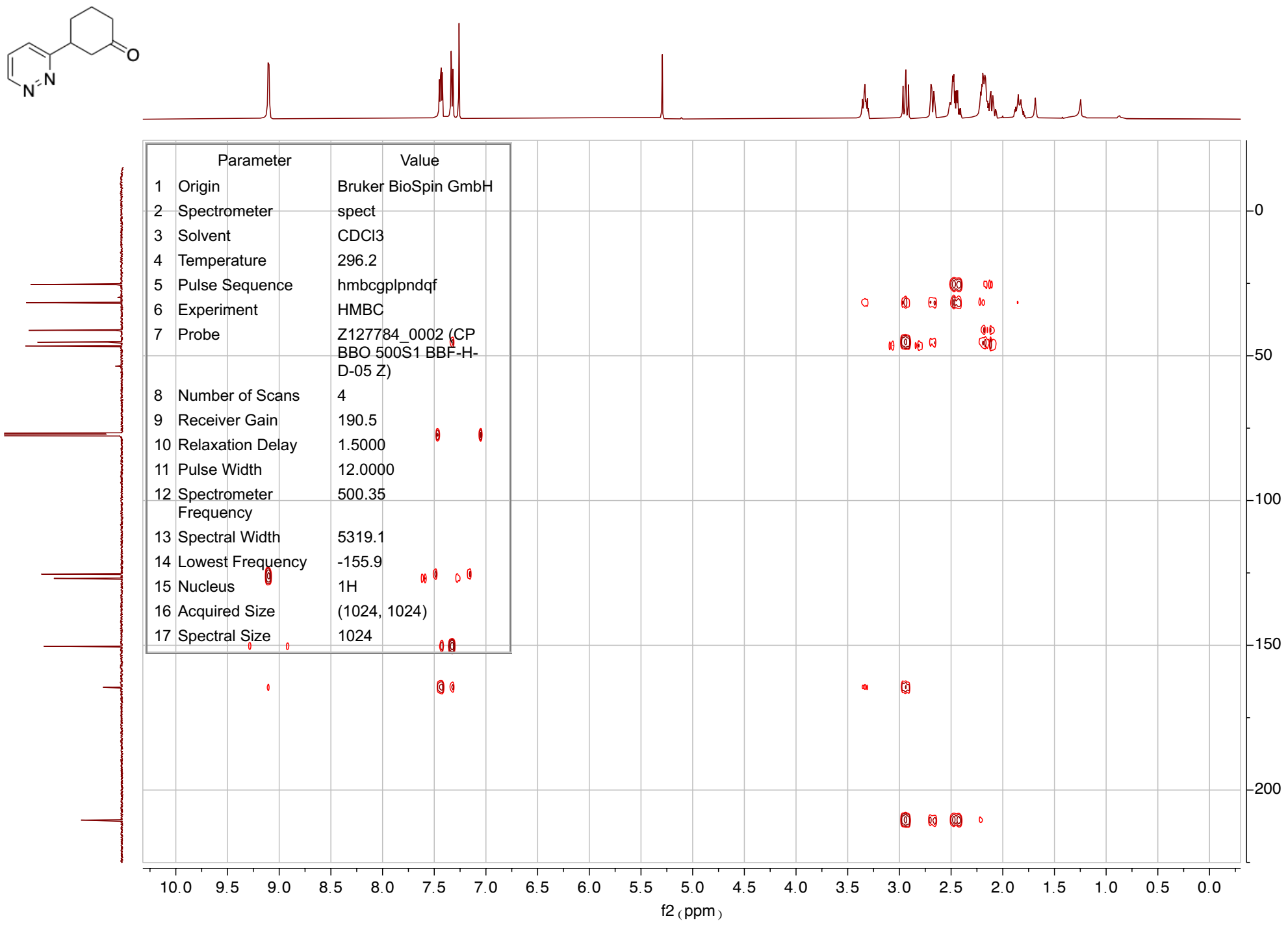
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.9648
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	5319.1
14	Lowest Frequency	-156.8
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

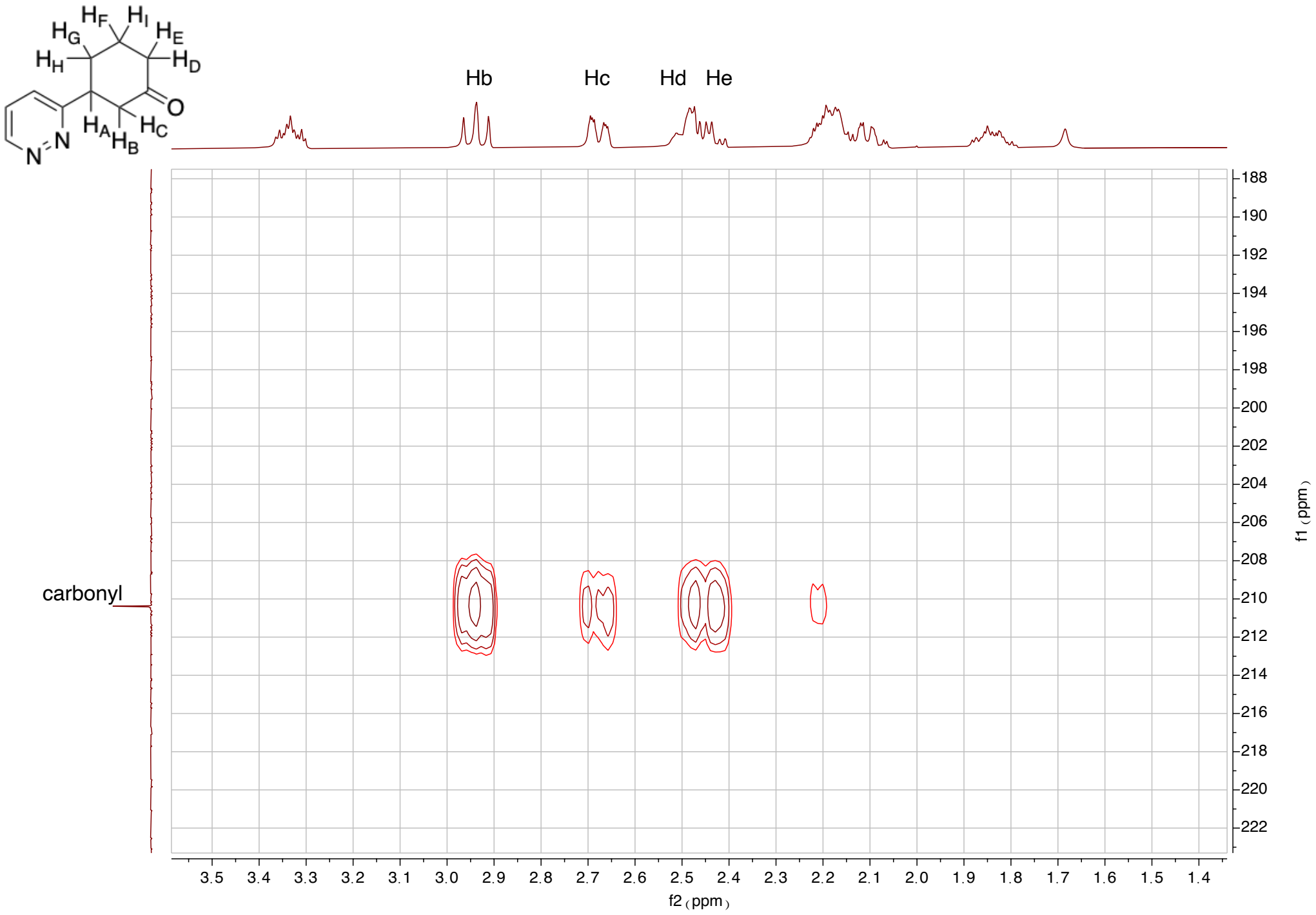

HF
HI
HG
HE
HH
HD
O
HA
HB
HC
N
N
Ha
Hb
Hc
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
f1 (ppm)
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
f2 (ppm)



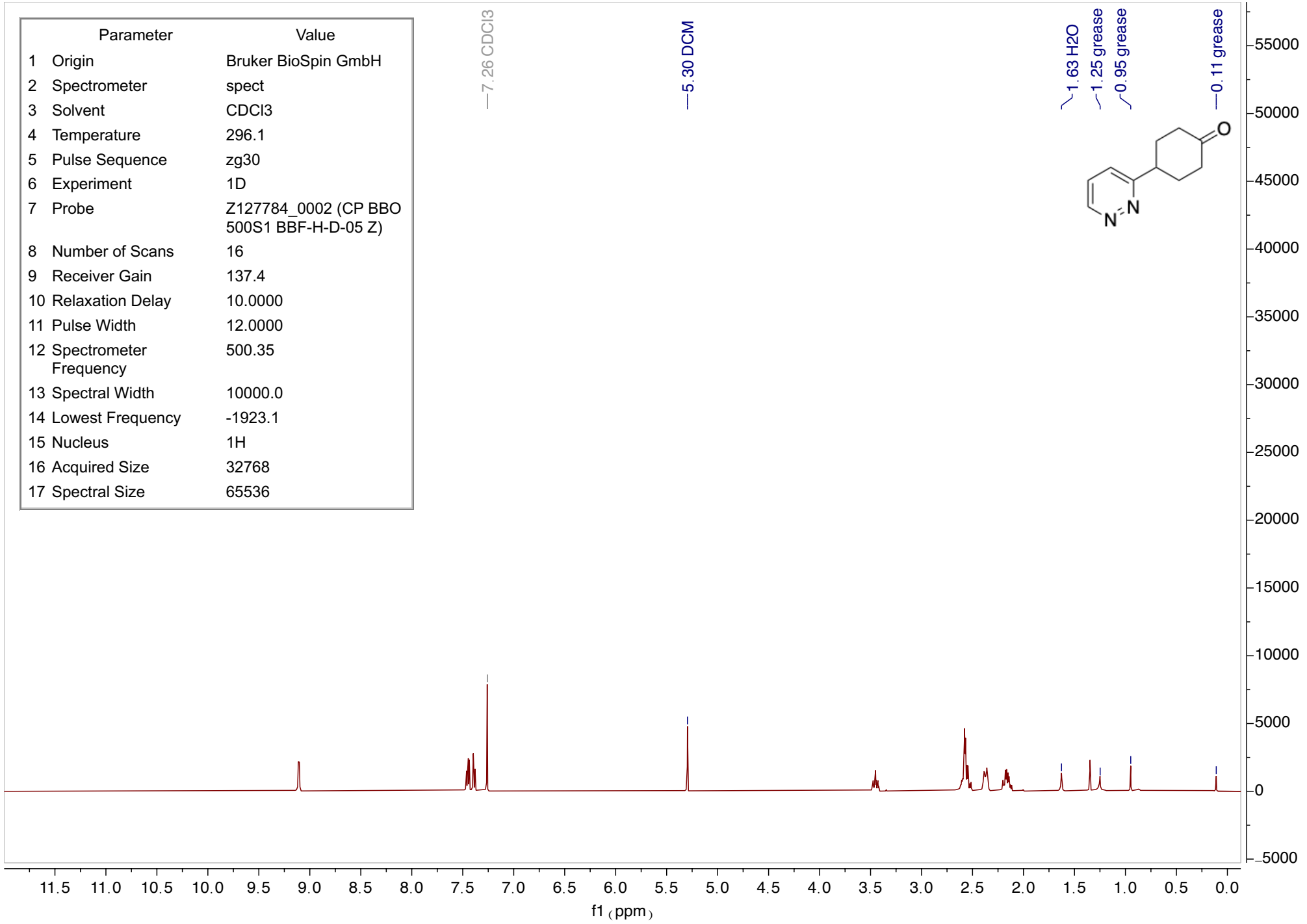
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	5319.1
14	Lowest Frequency	-157.9
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

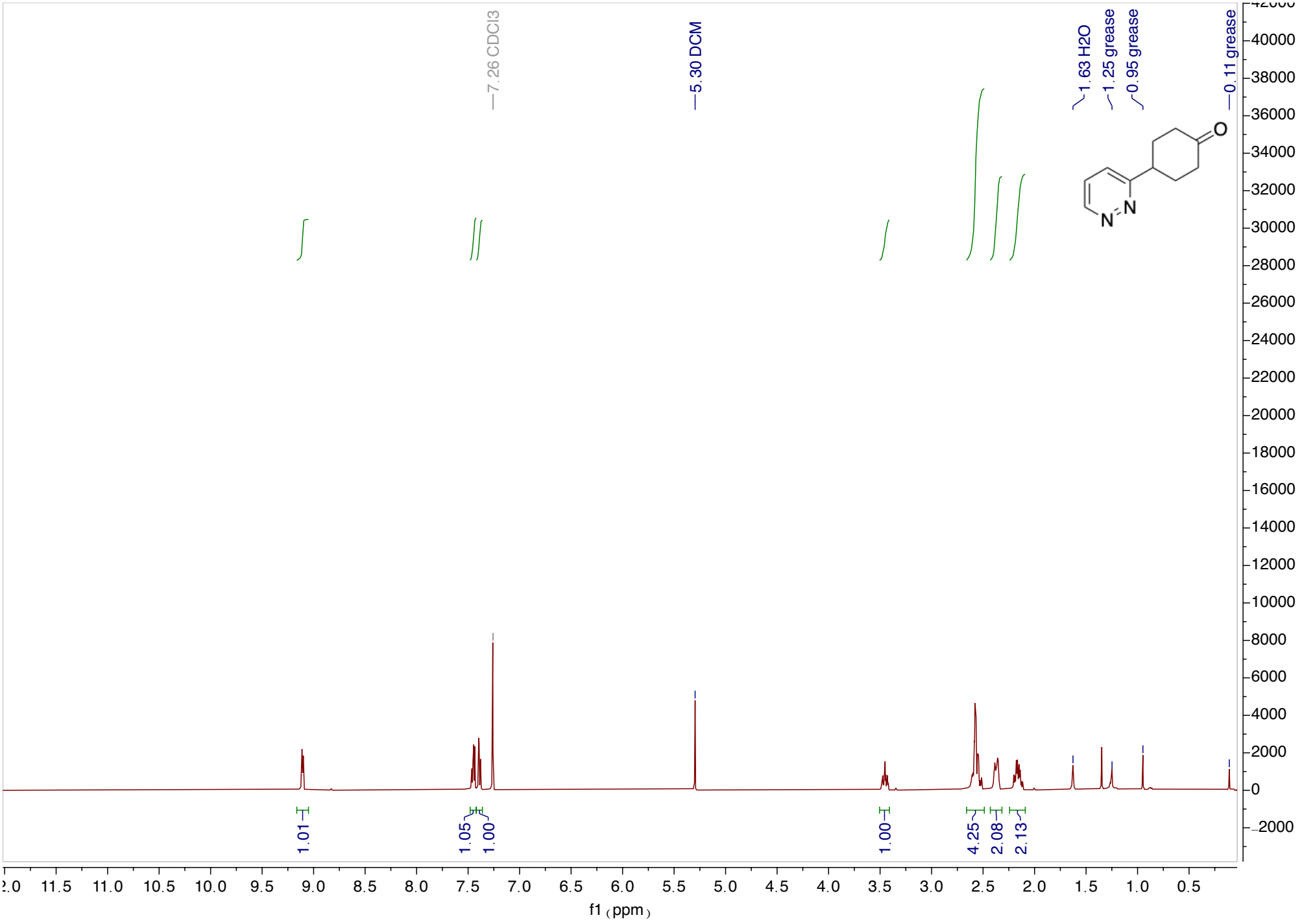

HF
HI
HG
HE
HH
HD
O
HA
HB
HC
N
N
Ha
Hb
Hc
10
15
20
25
30
35
40
45
50
f1 (ppm)
3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1
f2 (ppm)

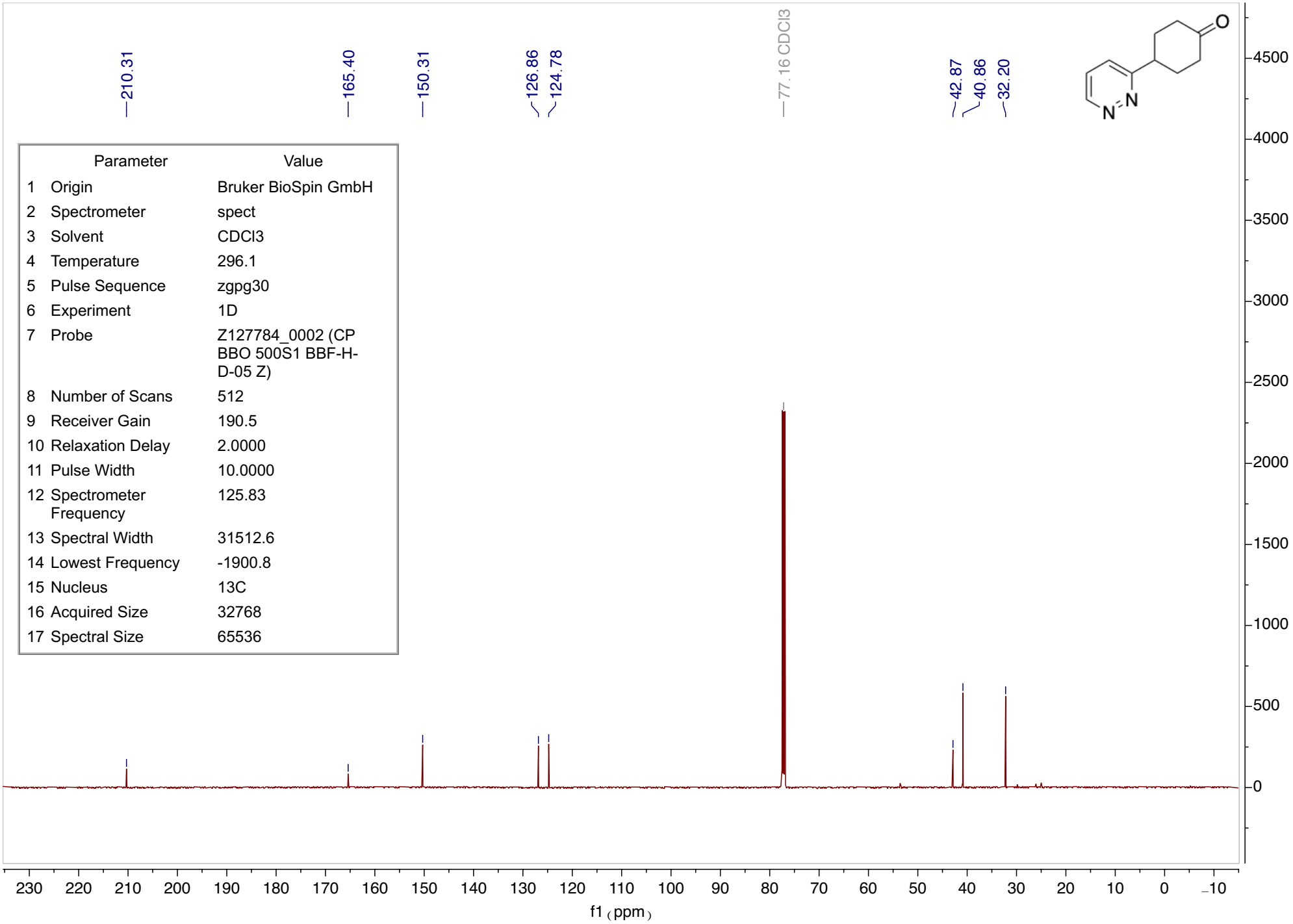

O
N
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 5319.1
14 Lowest Frequency -155.9
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 50 100 150 200
f1 (ppm)


HF
HI
HG
HE
HH
HD
O
HA
HB
HC
N
N
Hb
Hc
Hd
He
carbonyl
188
190
192
194
196
198
200
202
204
206
208
210
212
214
216
218
220
222
f1 (ppm)
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
f2 (ppm)

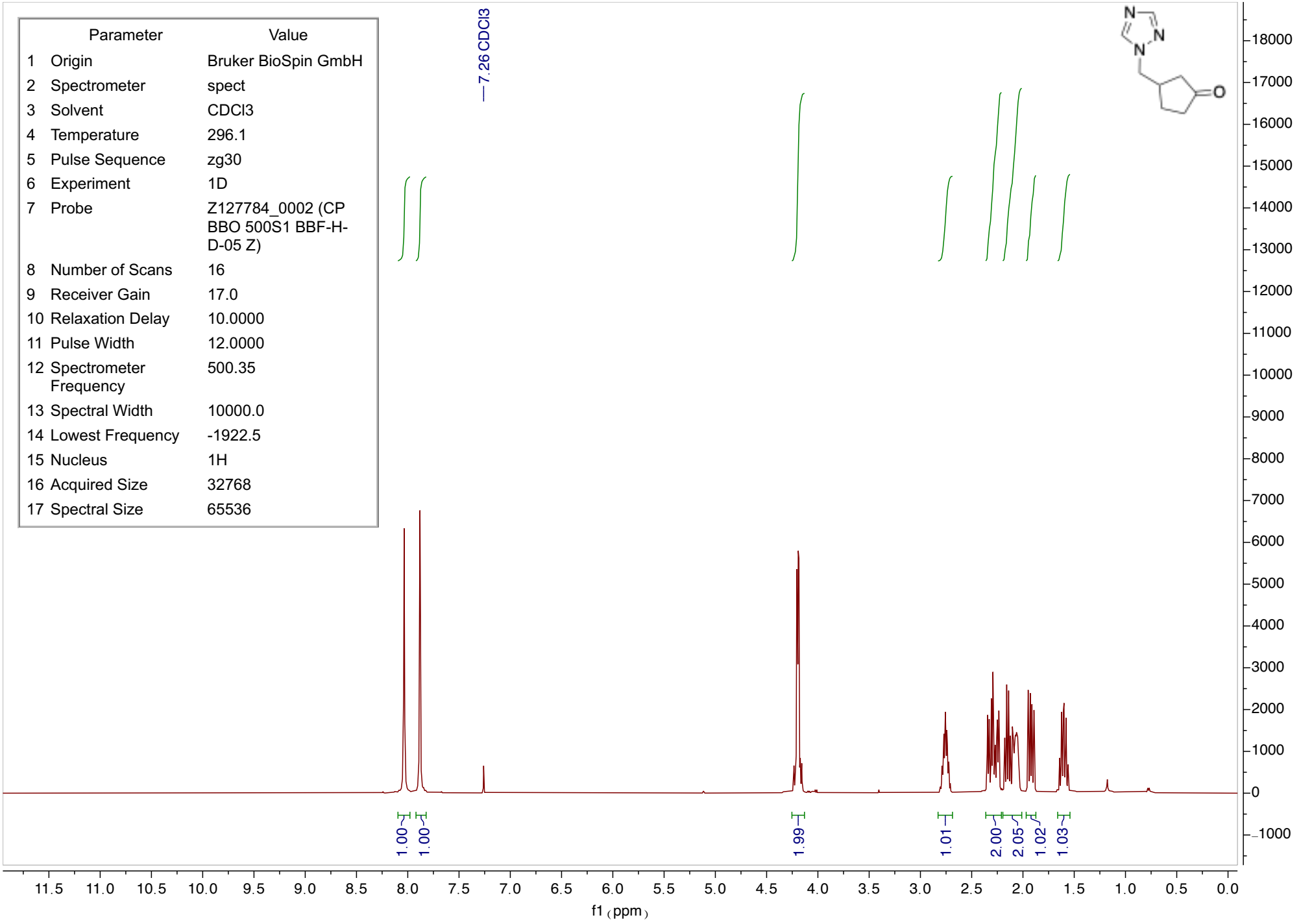
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	137.4
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



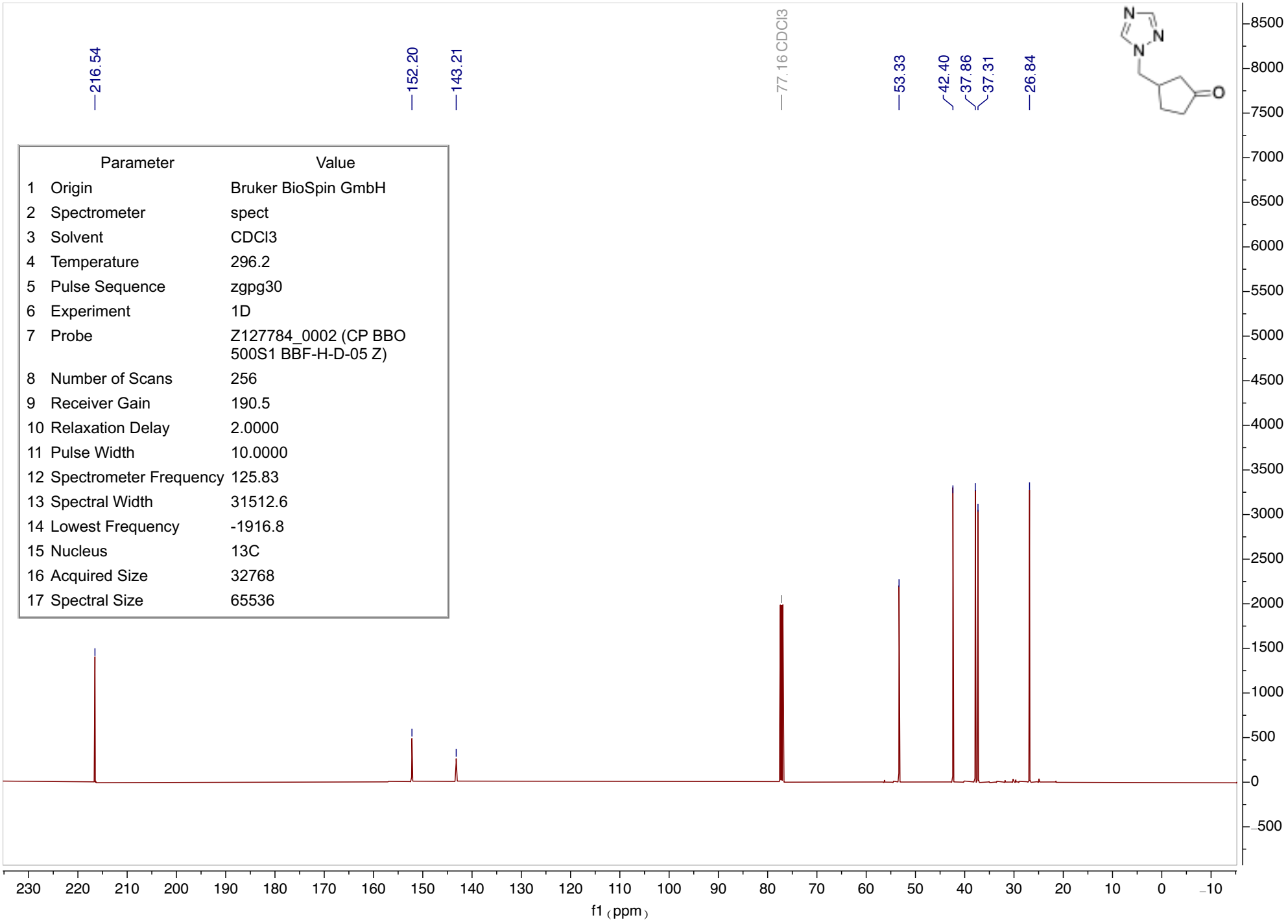

7.26 CDCl3
5.30 DCM
1.63 H2O
1.25 grease
0.95 grease
0.11 grease
O
N
N
1.01
1.05
1.00
1.00
4.25
2.08
2.13
f1 (ppm)



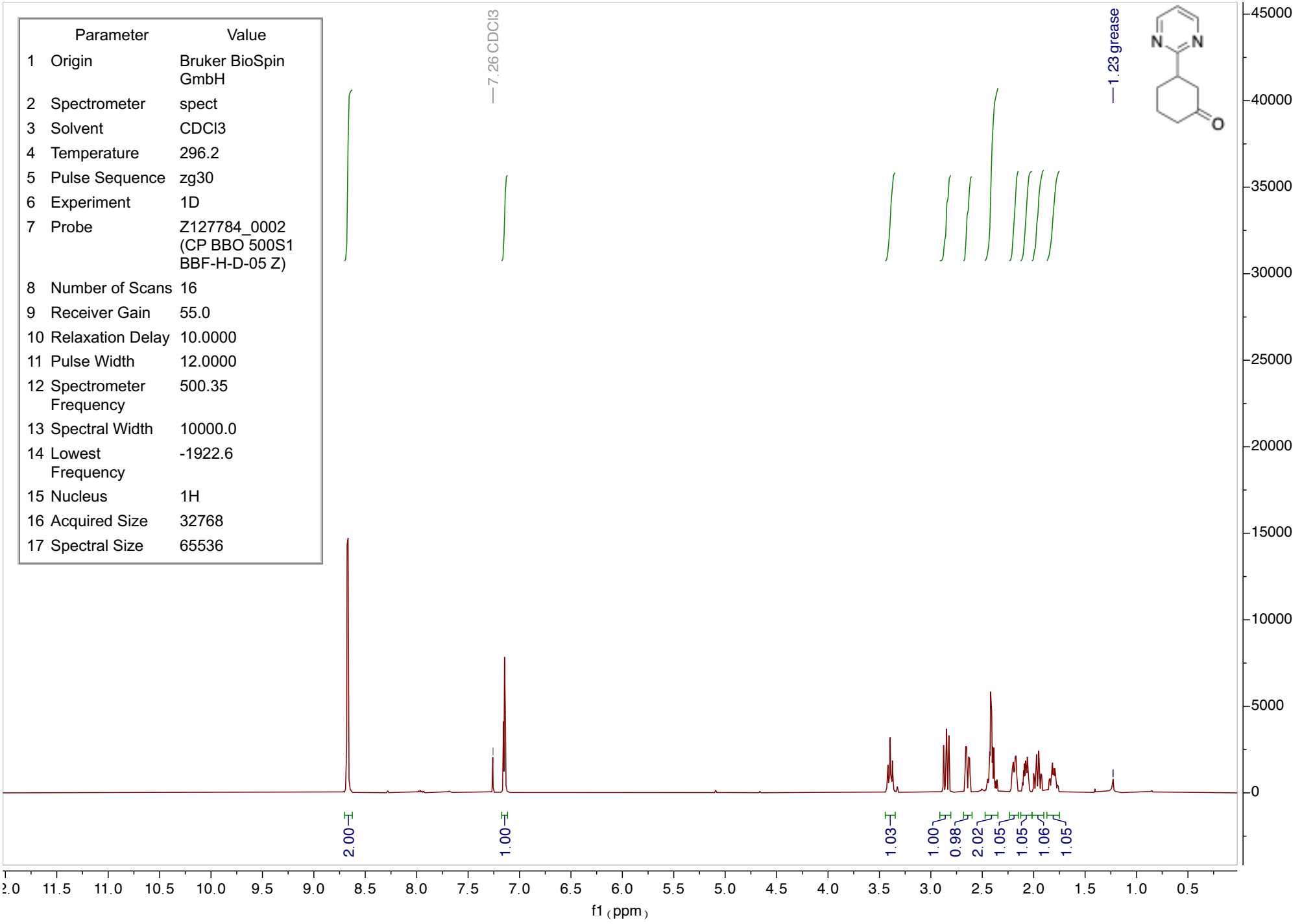
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



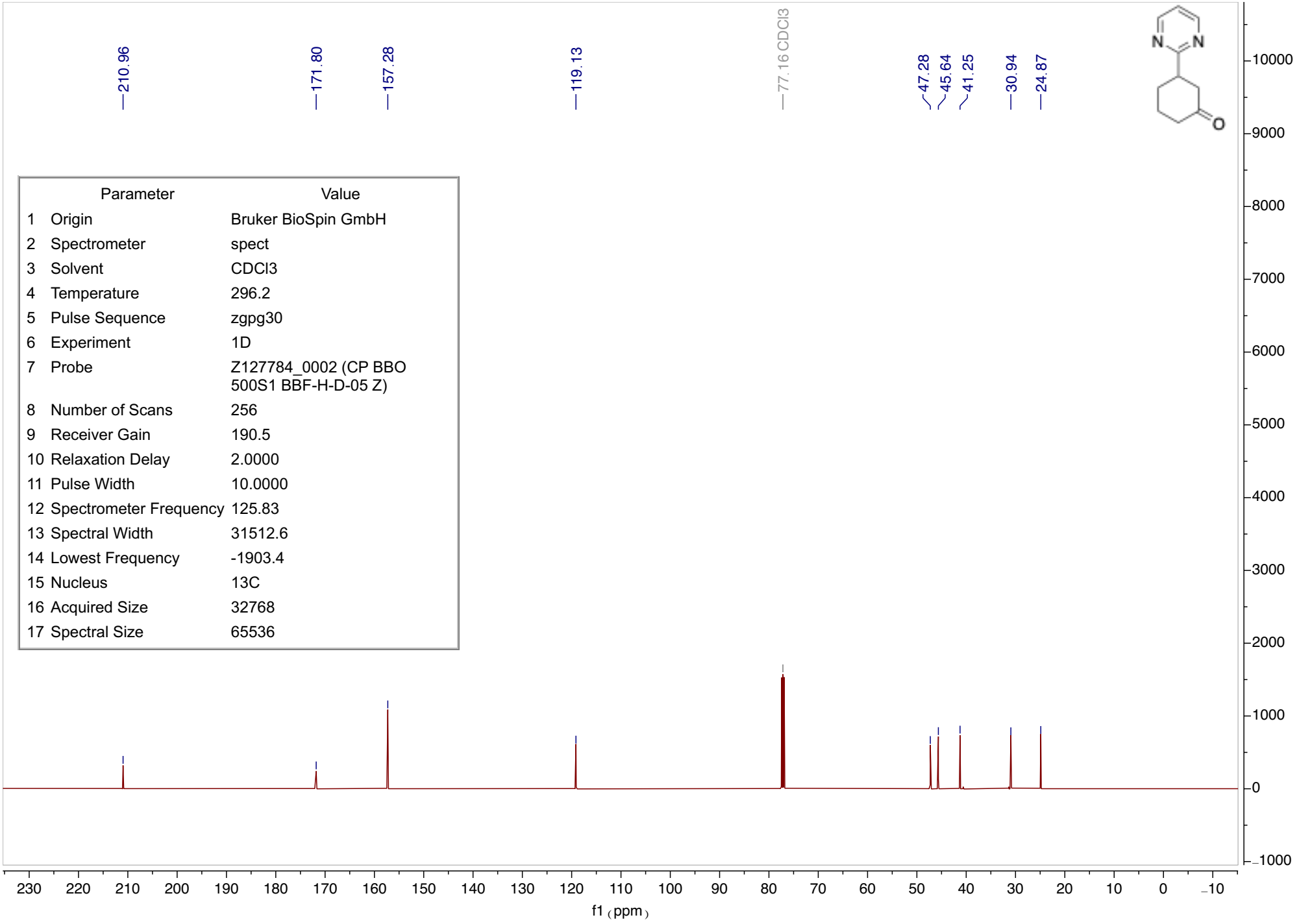
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	17.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1916.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

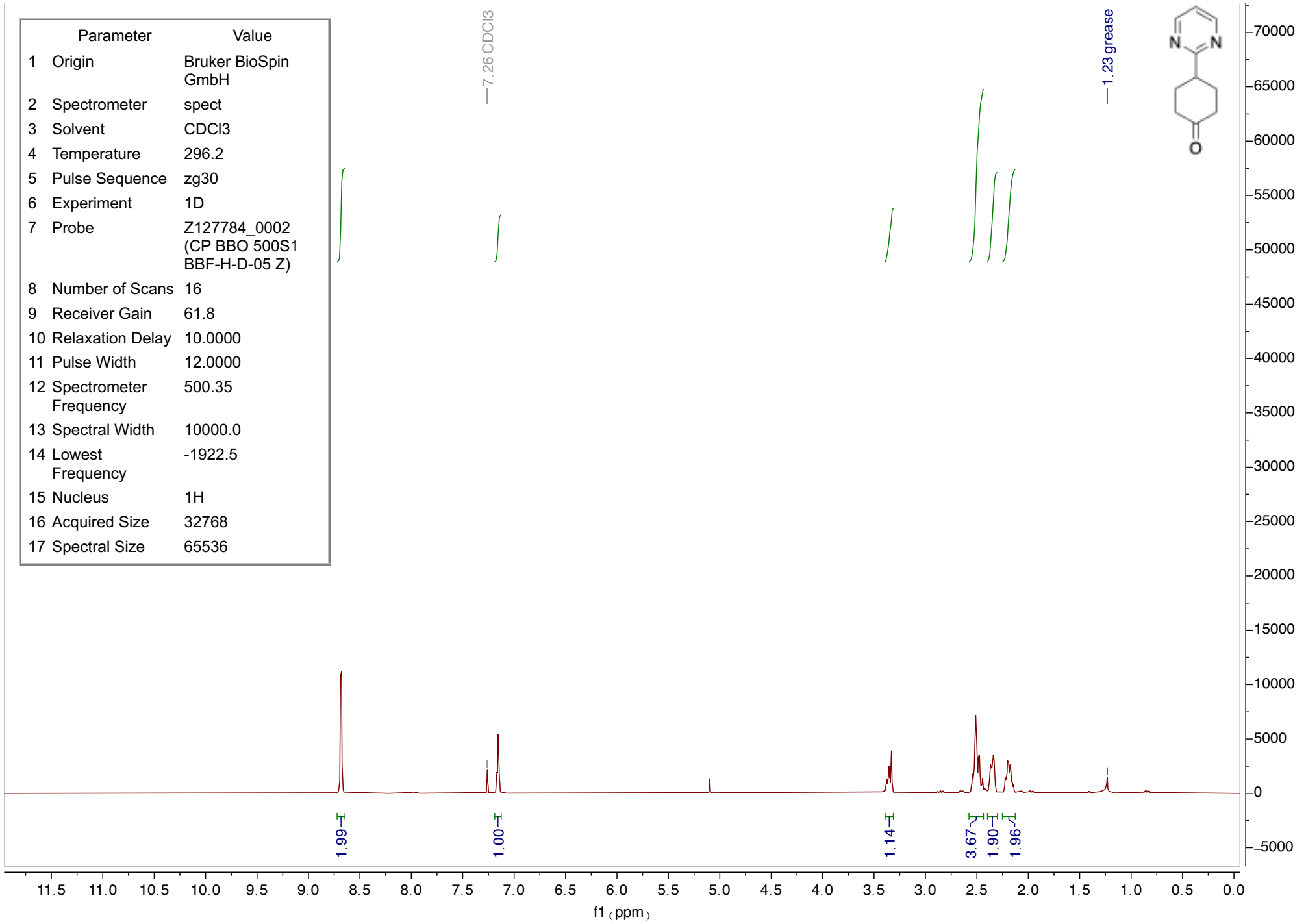


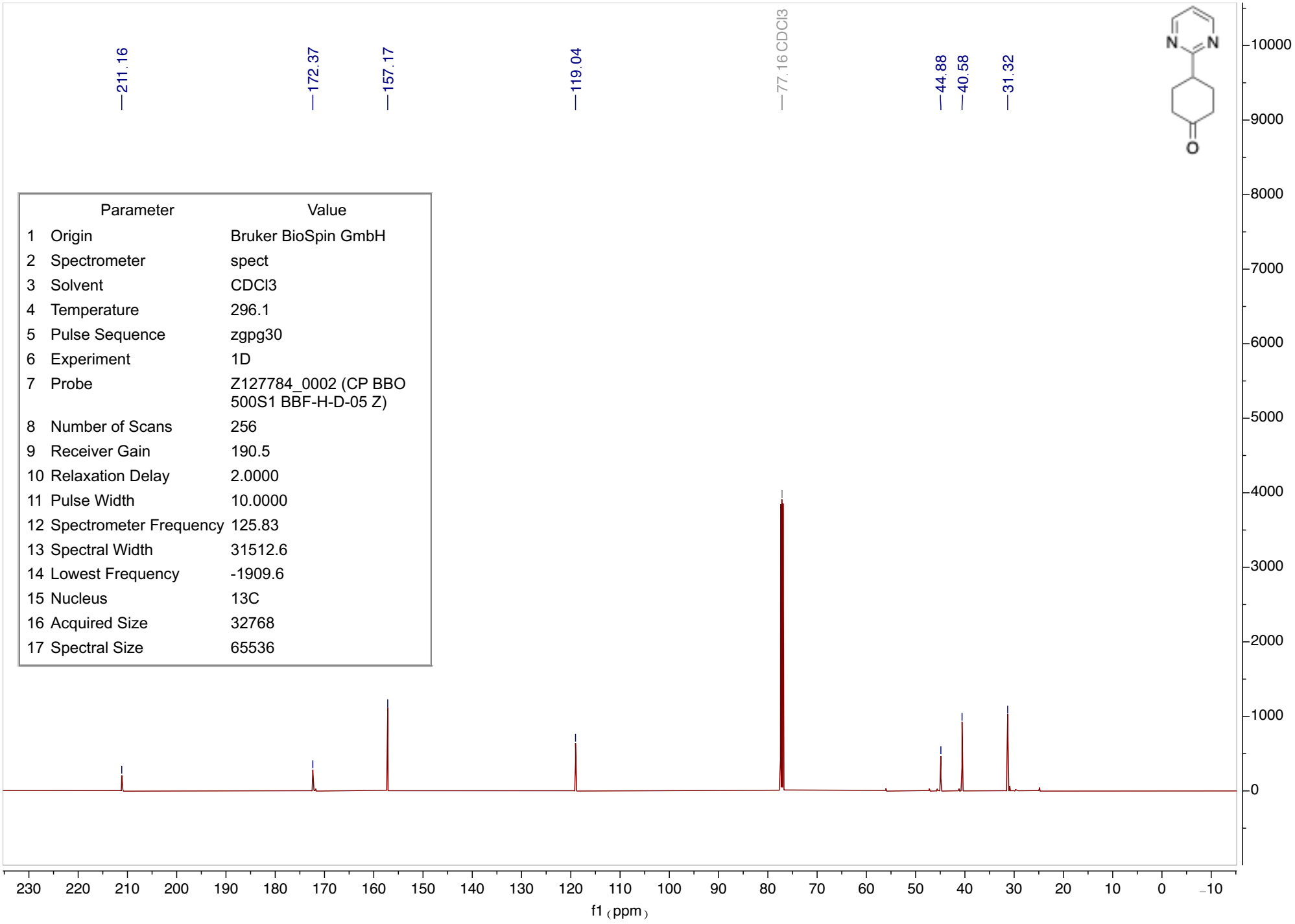
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	55.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.4
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

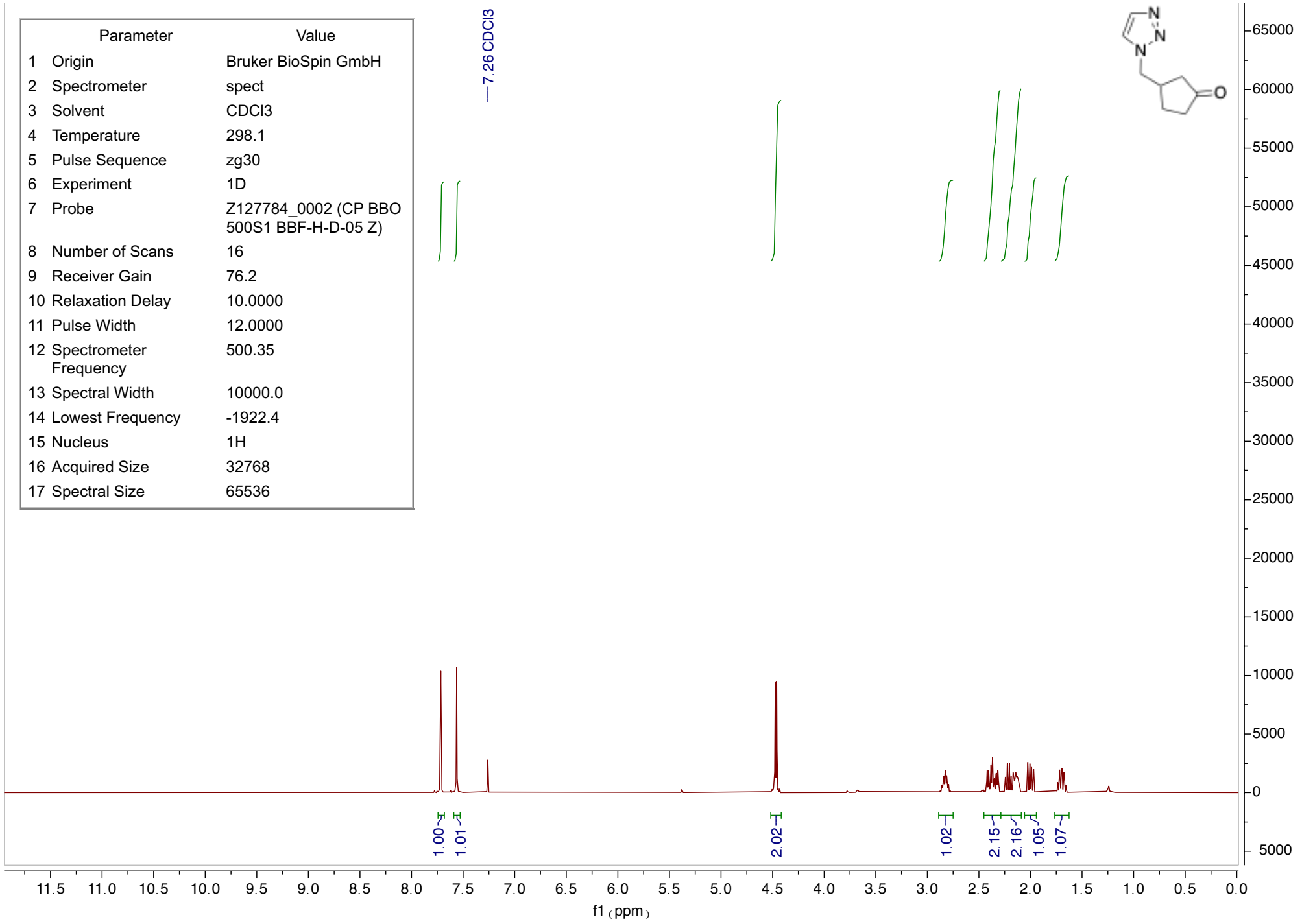
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

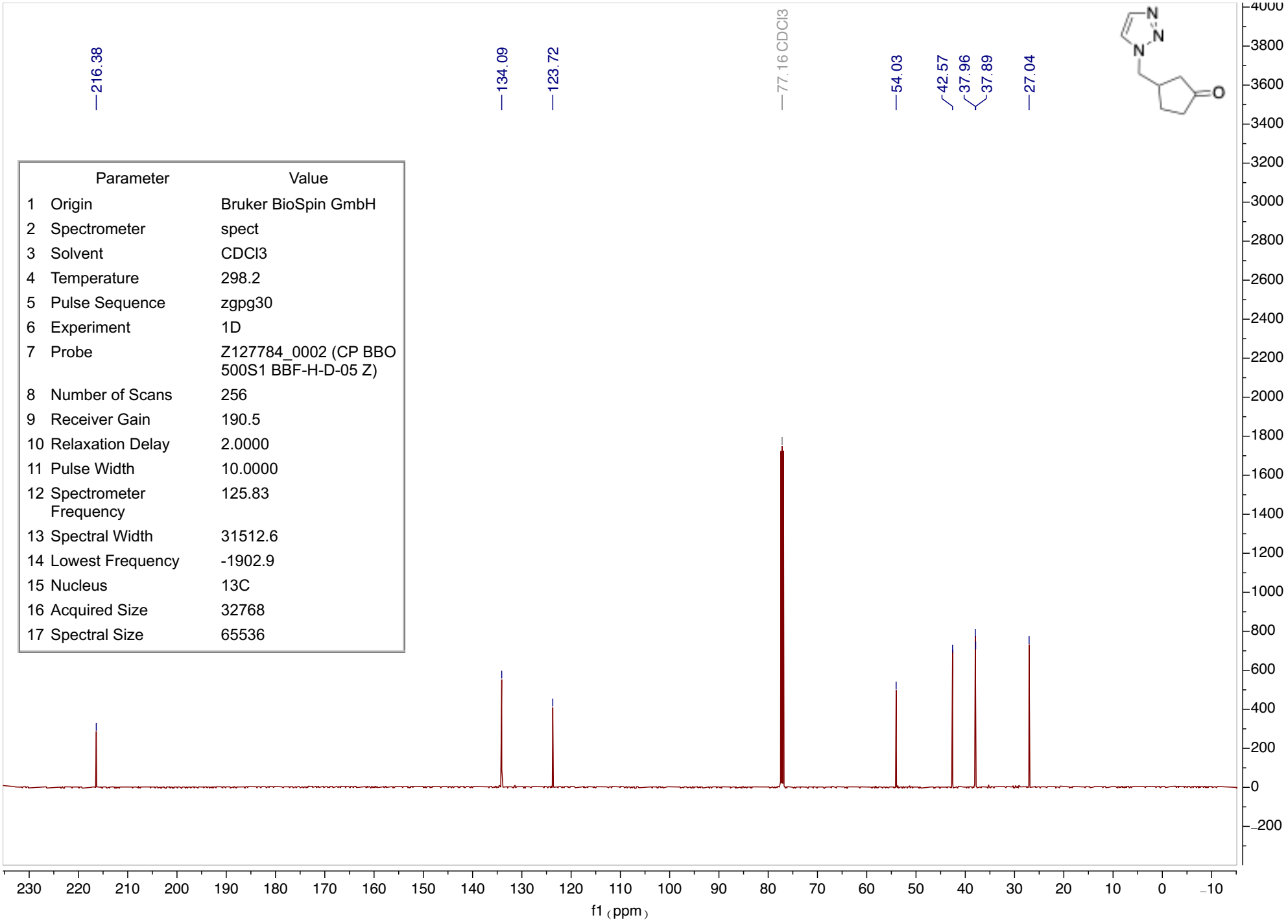




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1909.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

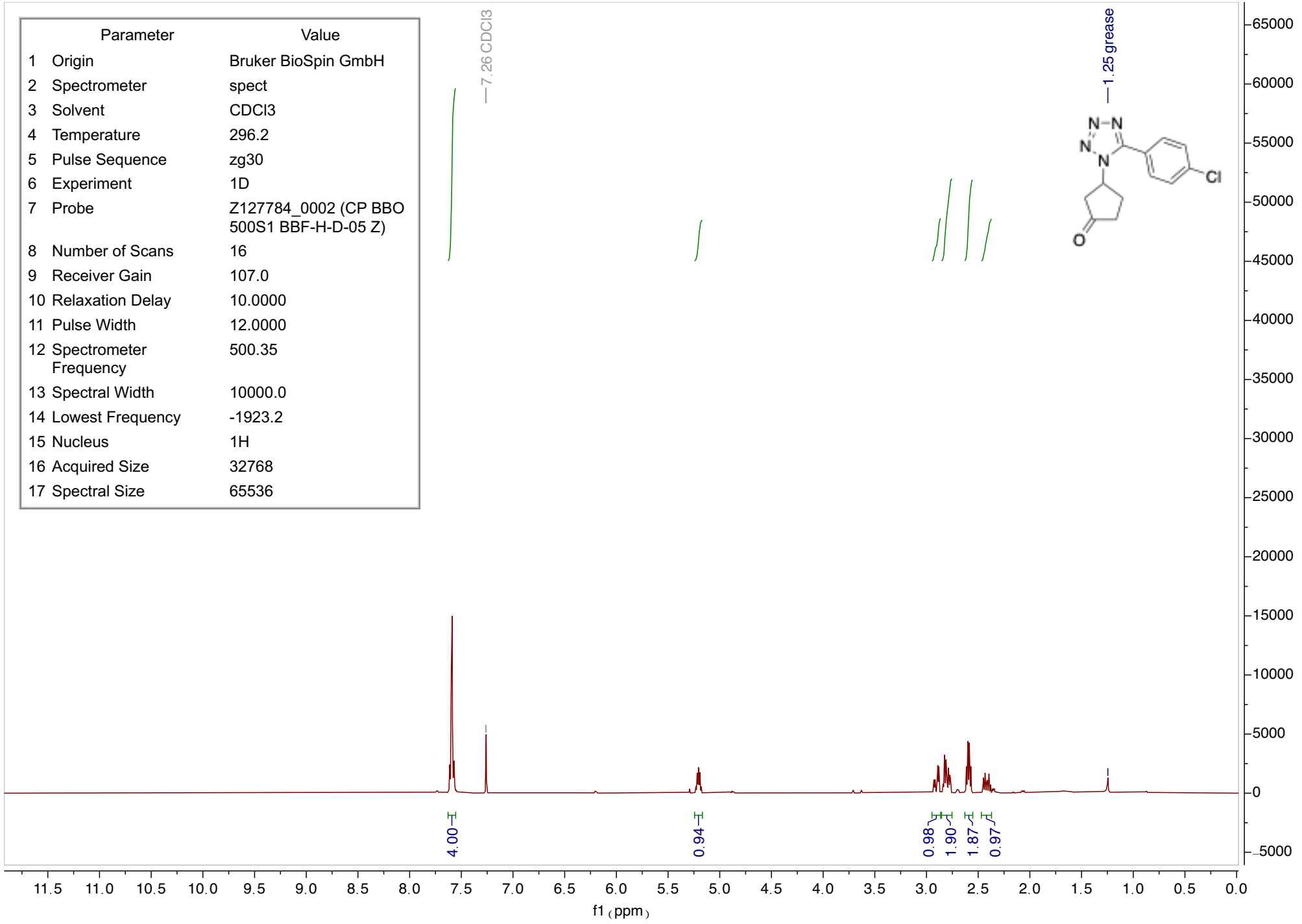
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	76.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

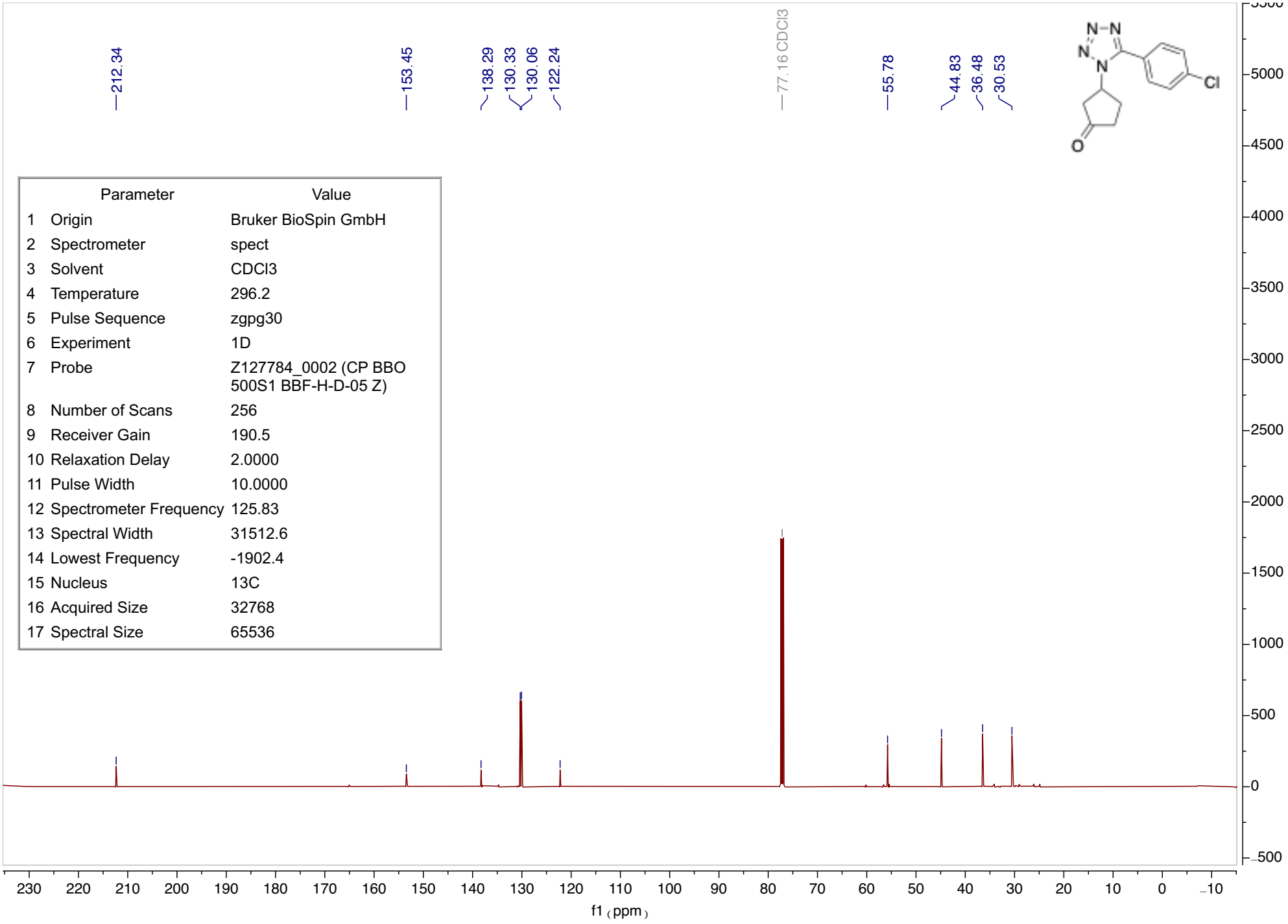




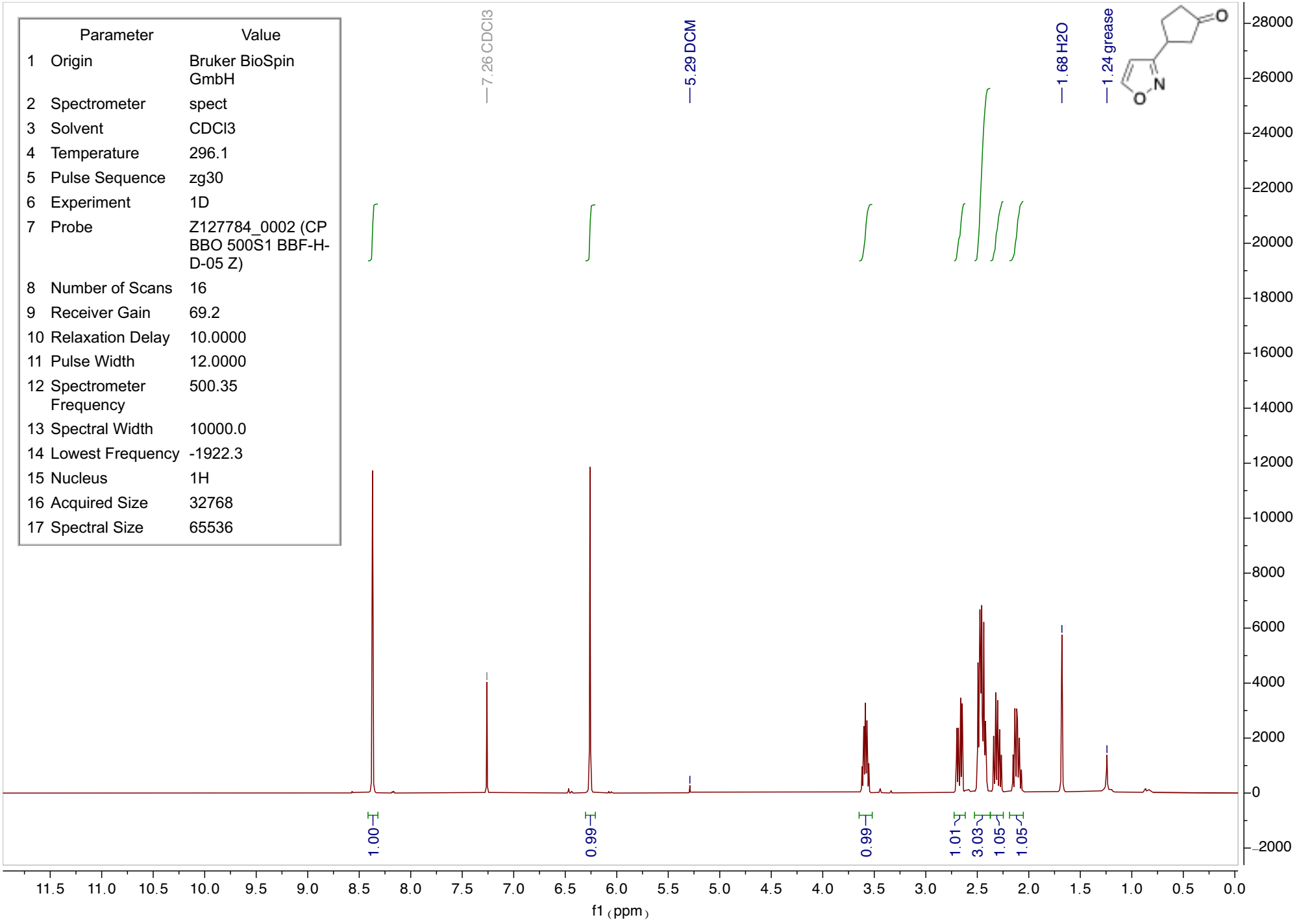
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

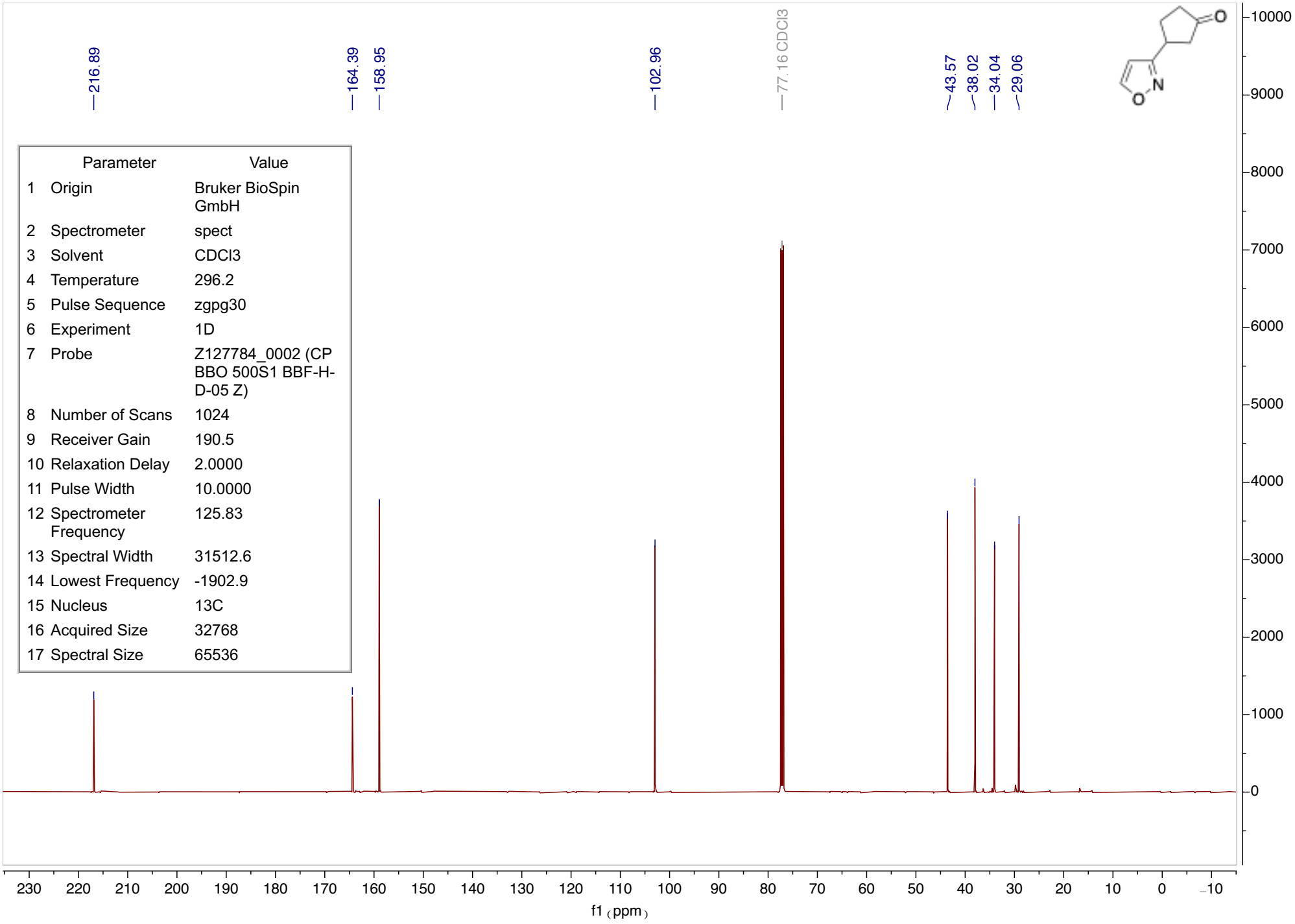
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	107.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536





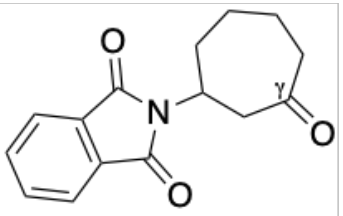
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.4
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

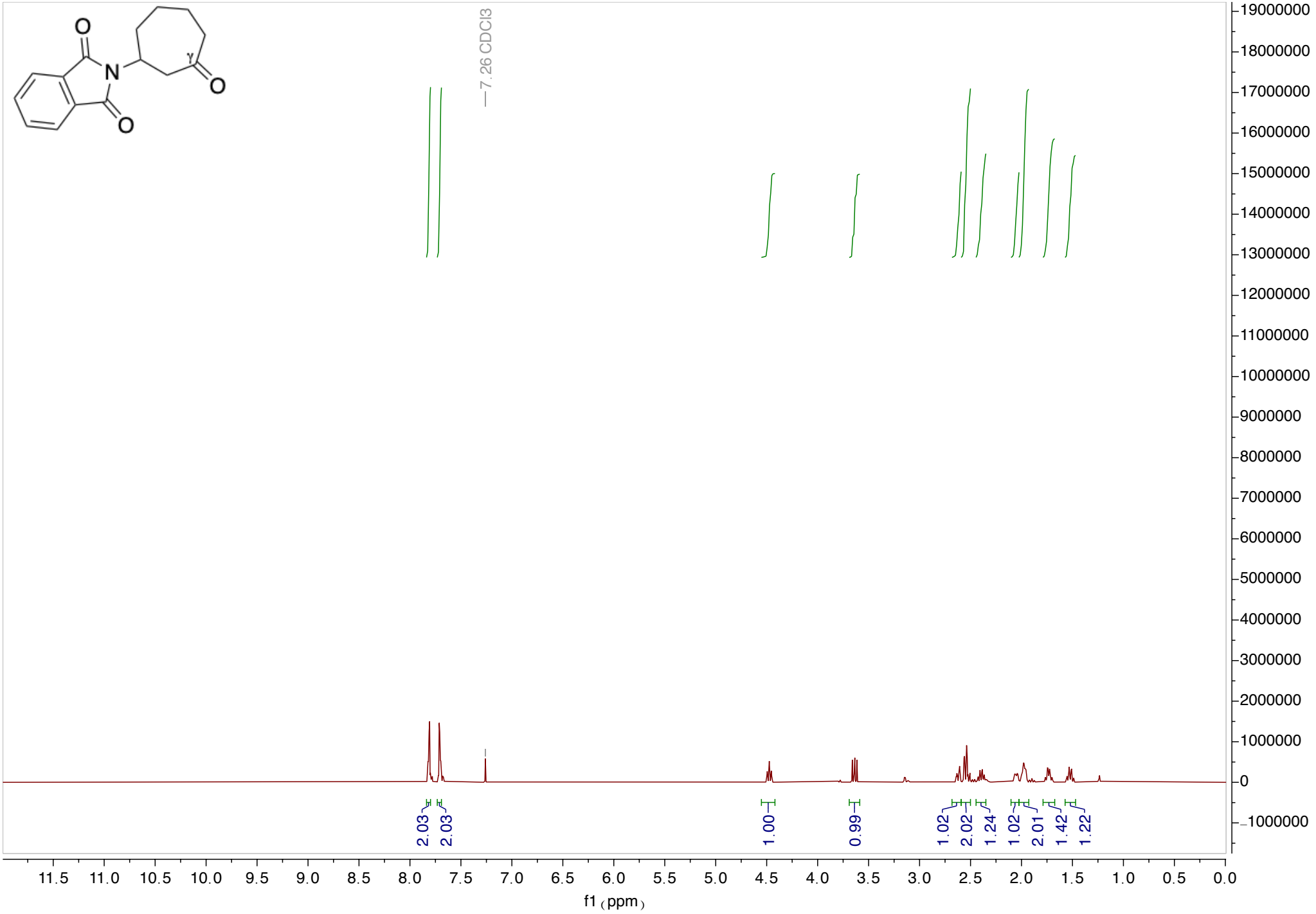

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 16
9 Receiver Gain 69.2
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 10000.0
14 Lowest Frequency -1922.3
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
5.29 DCM
1.68 H2O
1.24 grease
O
N
O
1.00
0.99
0.99
1.01
3.03
1.05
1.05
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
11.5 11.0 10.5 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)



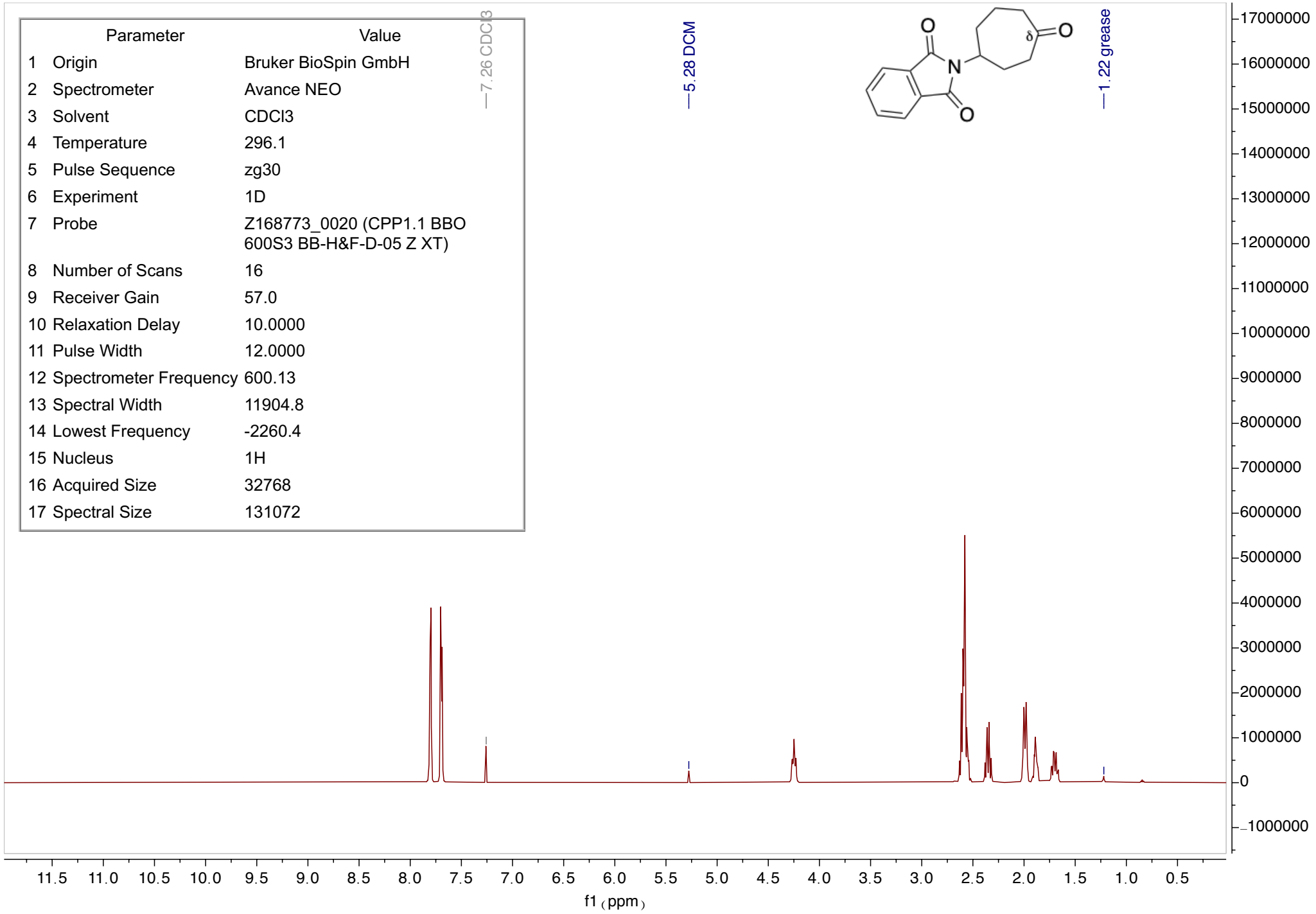
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

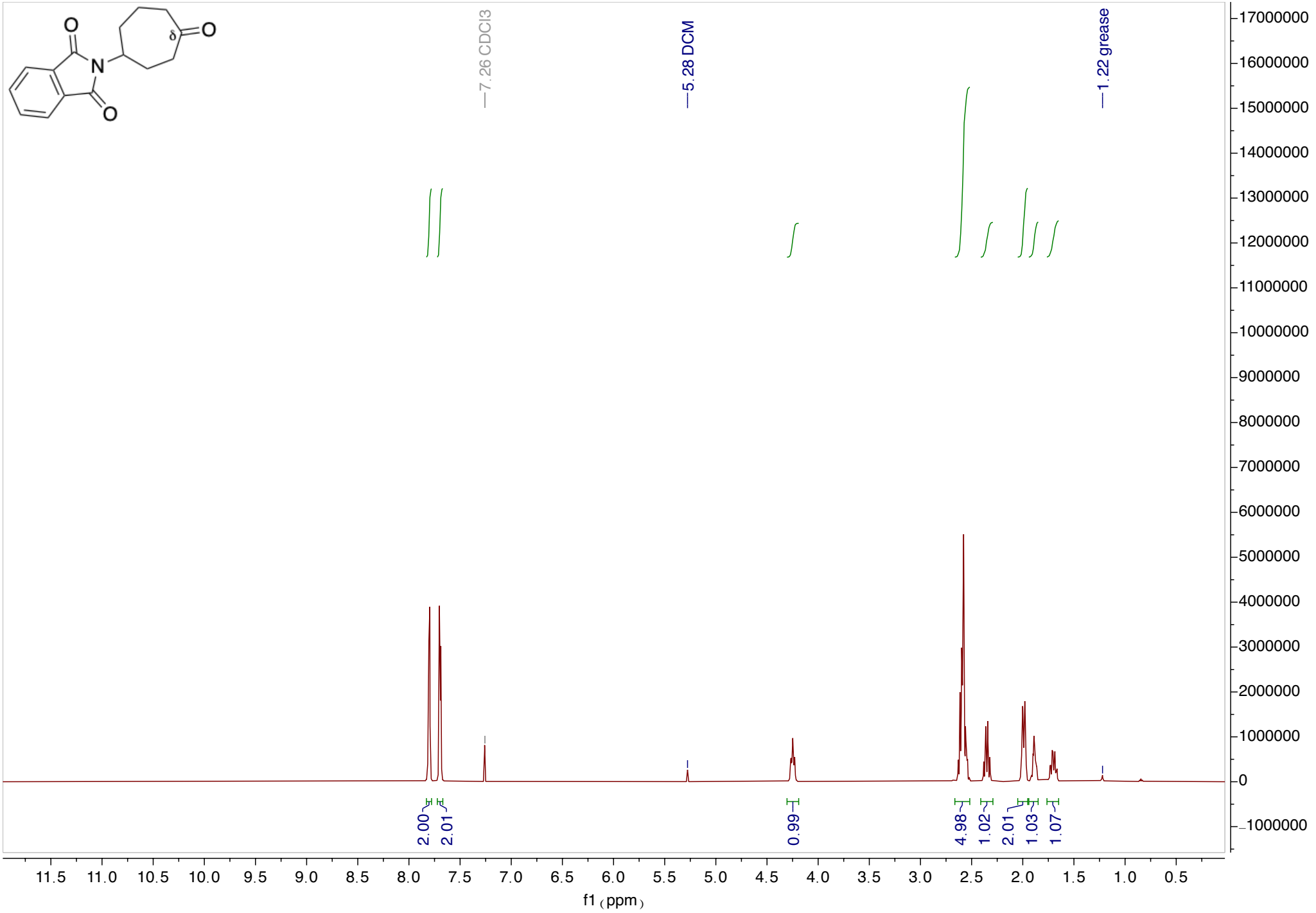
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2260.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



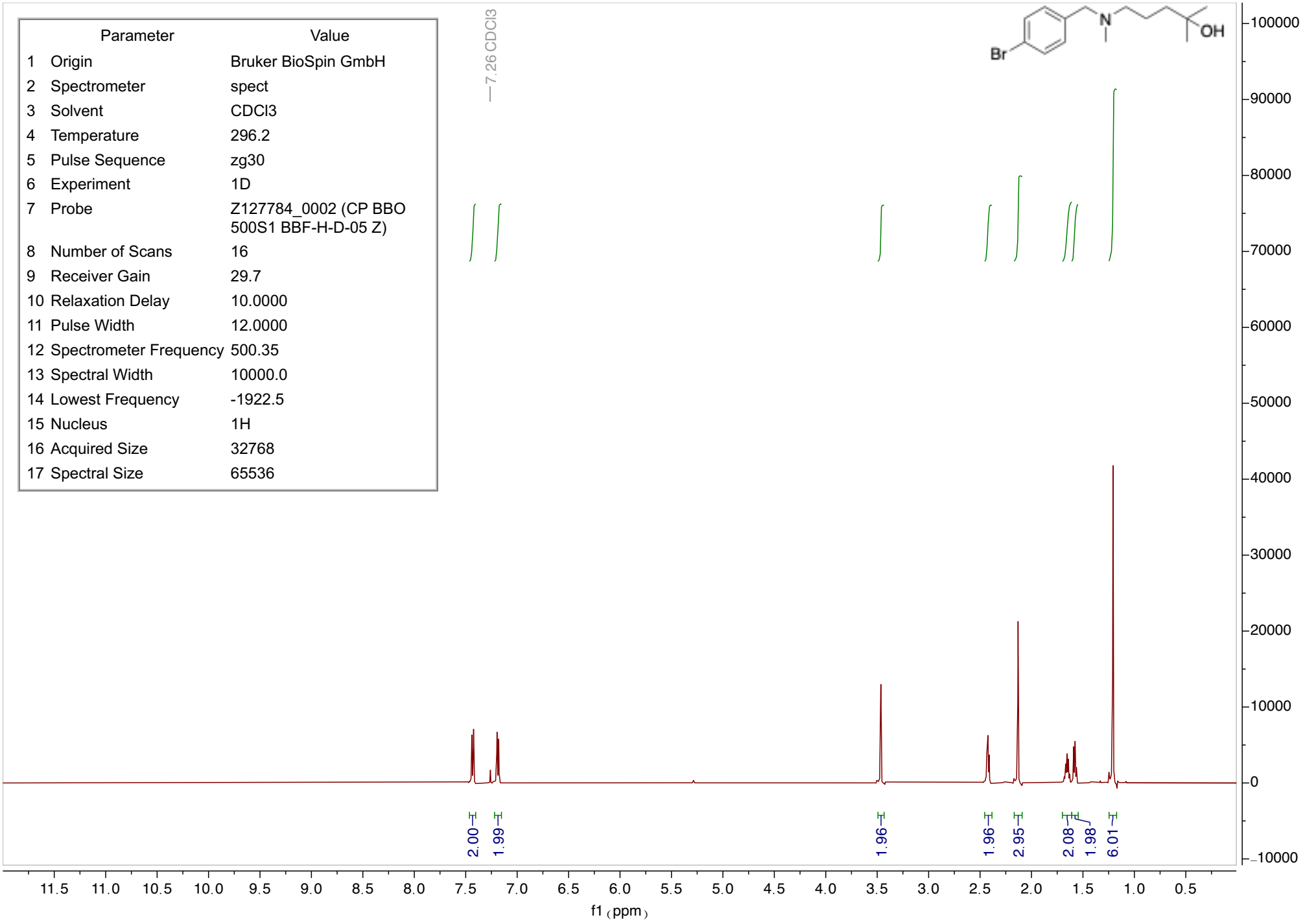

O
N
O
O
γ
7.26 CDCl3
2.03
2.03
1.00
0.99
1.02
2.02
1.24
1.02
2.01
1.42
1.22
f1 (ppm)

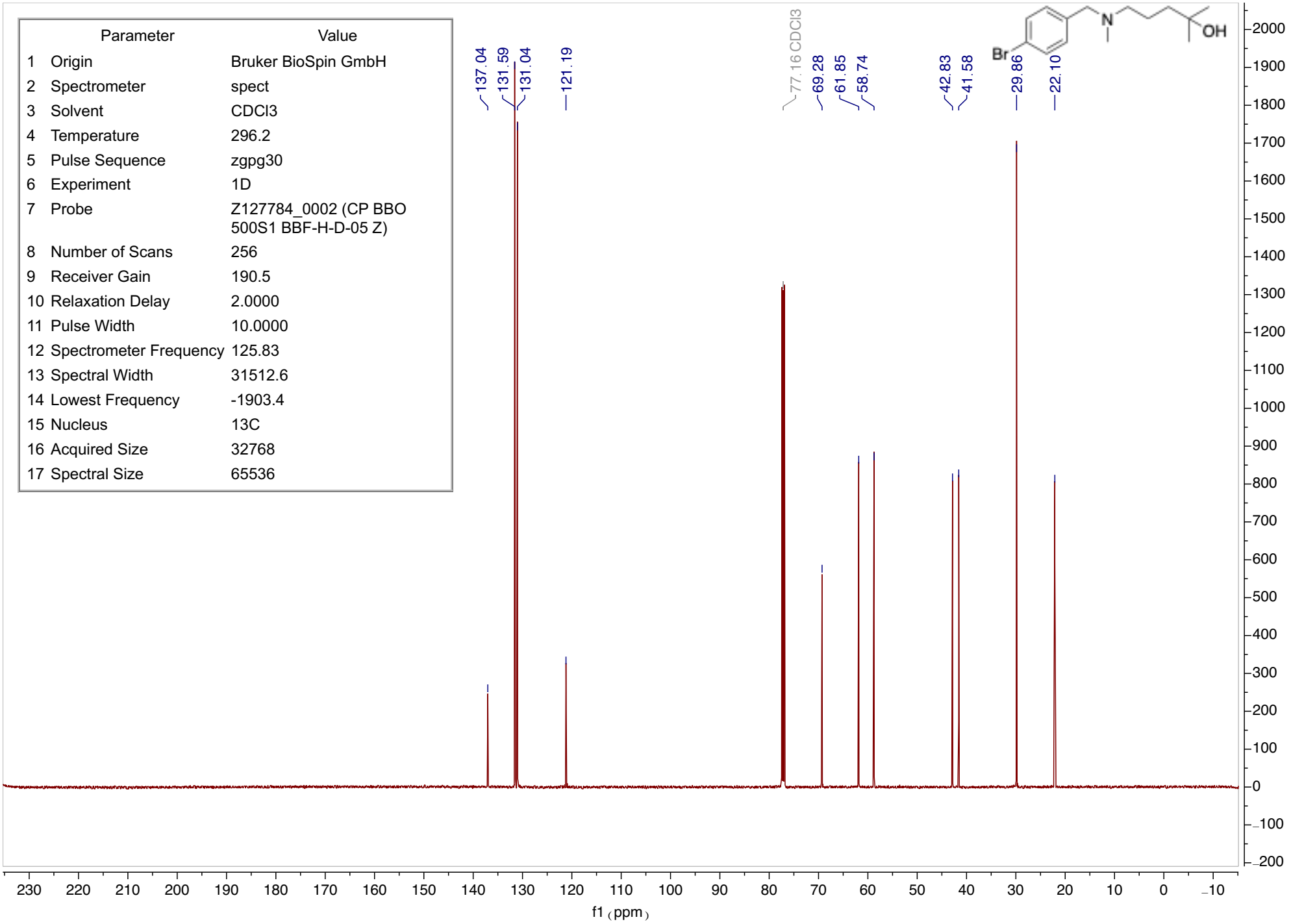
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	57.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2260.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



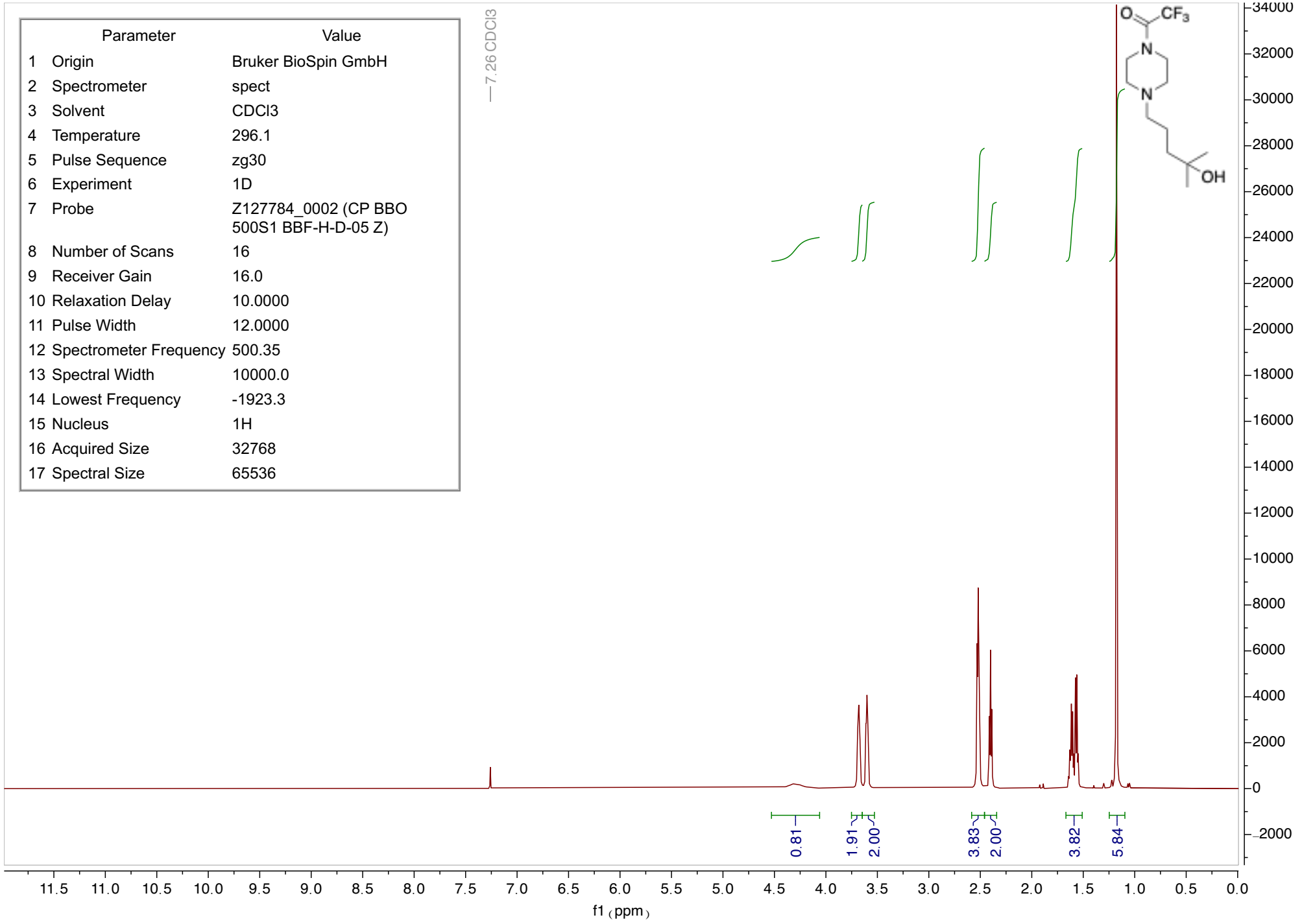

7.26 CDCl3
5.28 DCM
1.22 grease
2.00
2.01
0.99
4.98
1.02
2.01
1.03
1.07
f1 (ppm)

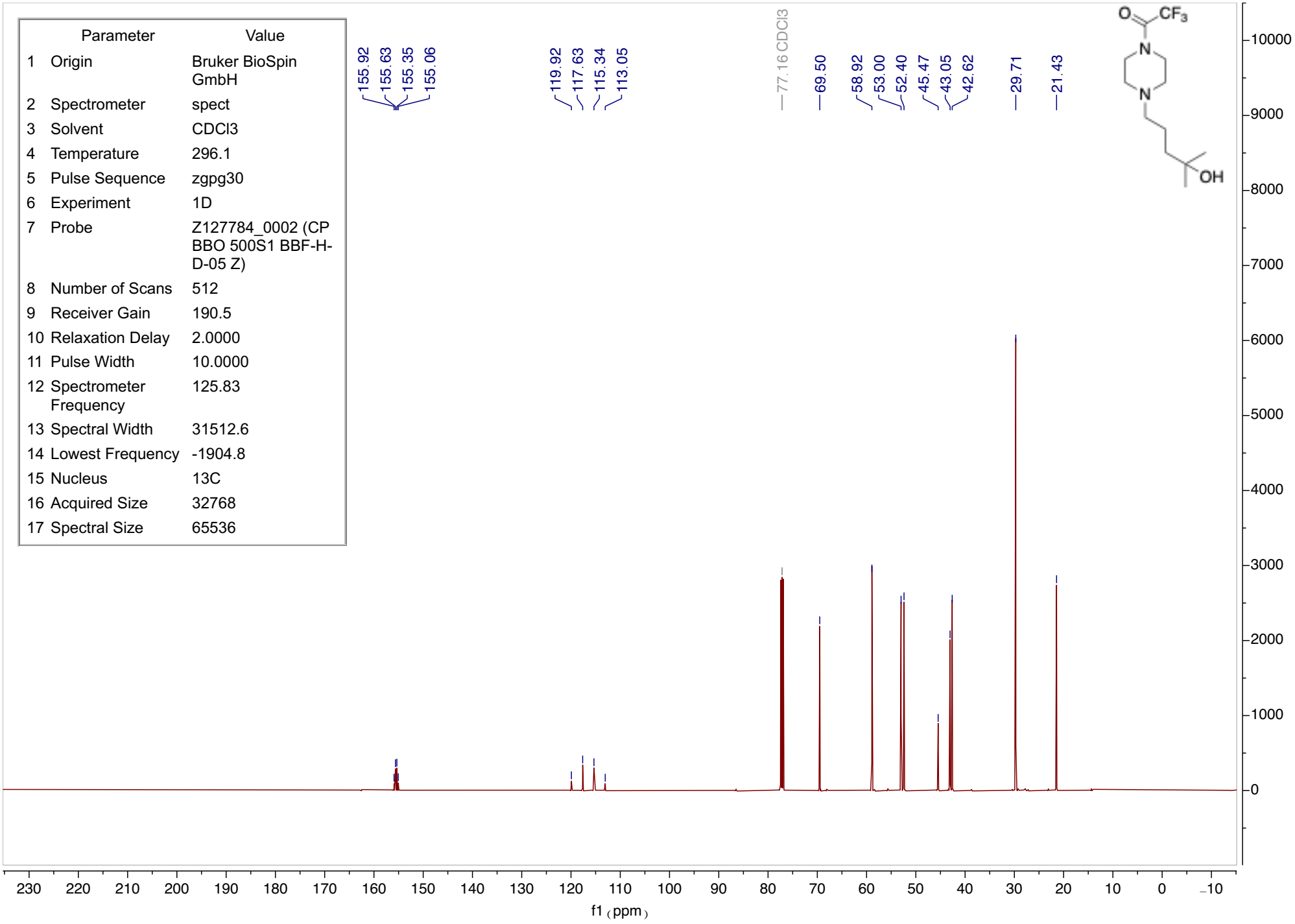
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



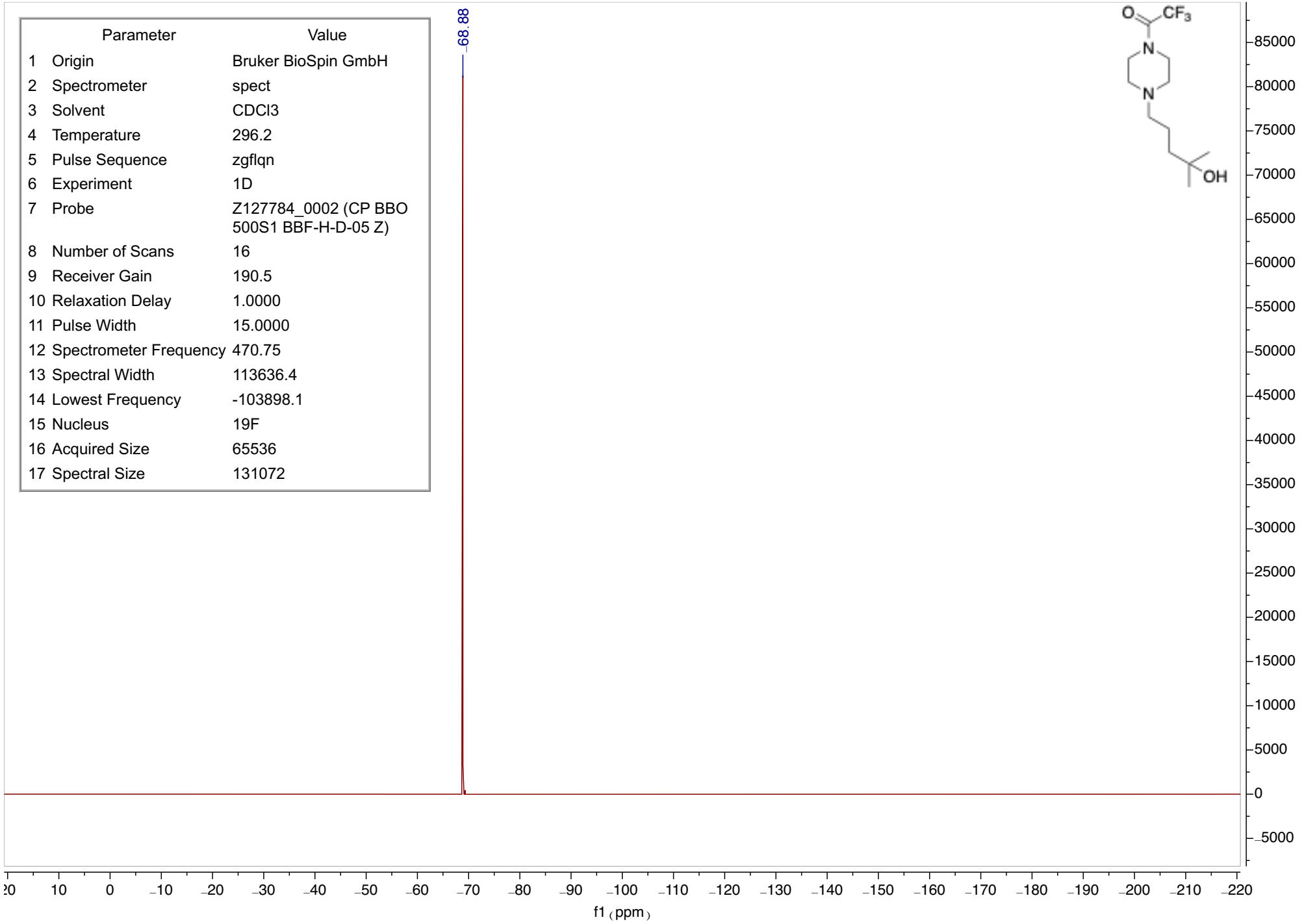

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence zgpg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 256
9 Receiver Gain 190.5
10 Relaxation Delay 2.0000
11 Pulse Width 10.0000
12 Spectrometer Frequency 125.83
13 Spectral Width 31512.6
14 Lowest Frequency -1903.4
15 Nucleus 13C
16 Acquired Size 32768
17 Spectral Size 65536
137.04
131.59
131.04
121.19
77.16 CDCl3
69.28
61.85
58.74
42.83
41.58
29.86
22.10
Br
N
OH
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	16.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

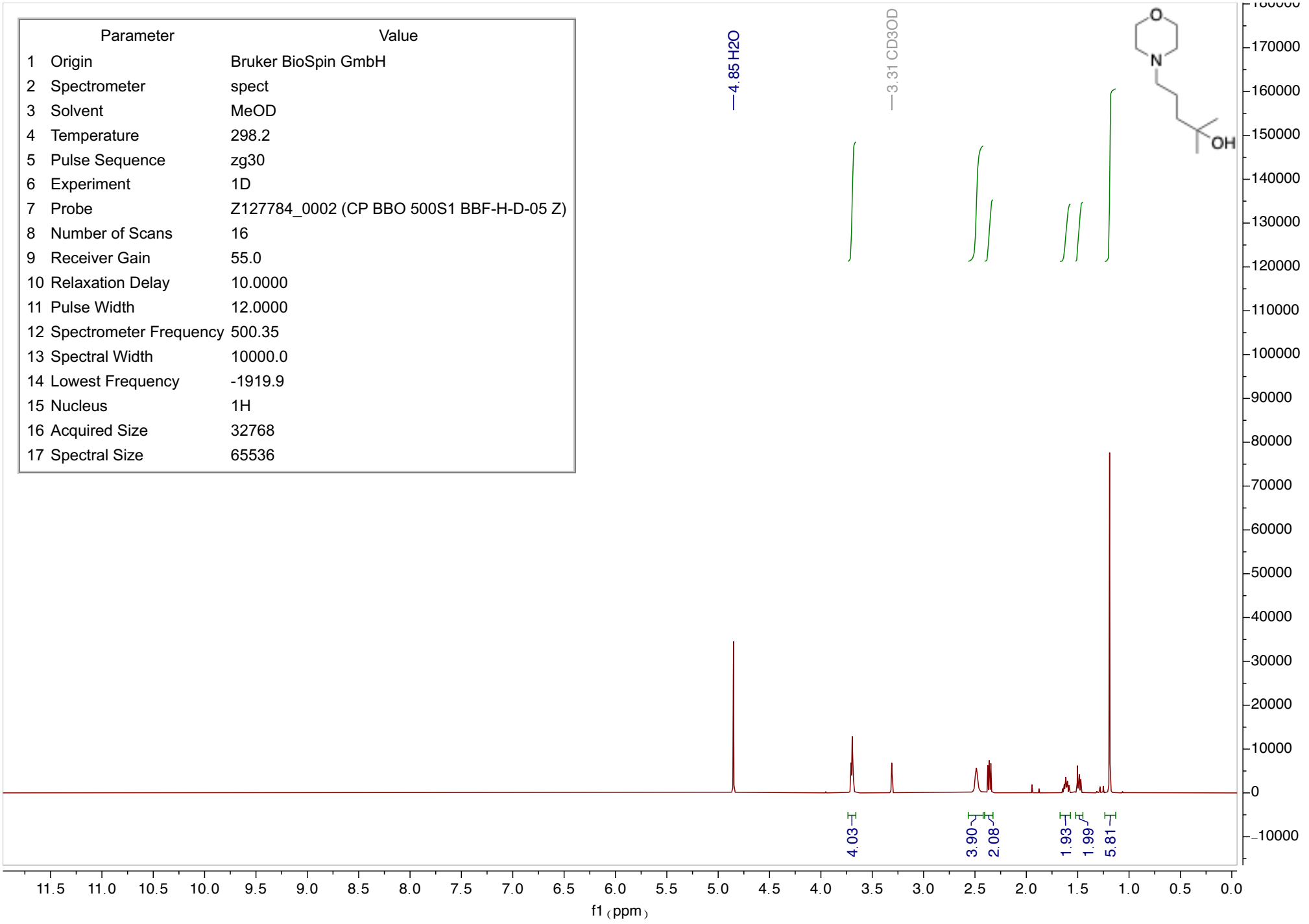



Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zgpg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 512
9 Receiver Gain 190.5
10 Relaxation Delay 2.0000
11 Pulse Width 10.0000
12 Spectrometer Frequency 125.83
13 Spectral Width 31512.6
14 Lowest Frequency -1904.8
15 Nucleus 13C
16 Acquired Size 32768
17 Spectral Size 65536
155.92
155.63
155.35
155.06
119.92
117.63
115.34
113.05
77.16 CDCl3
69.50
58.92
53.00
52.40
45.47
43.05
42.62
29.71
21.43
O
CF3
N
N
OH
f1 (ppm)

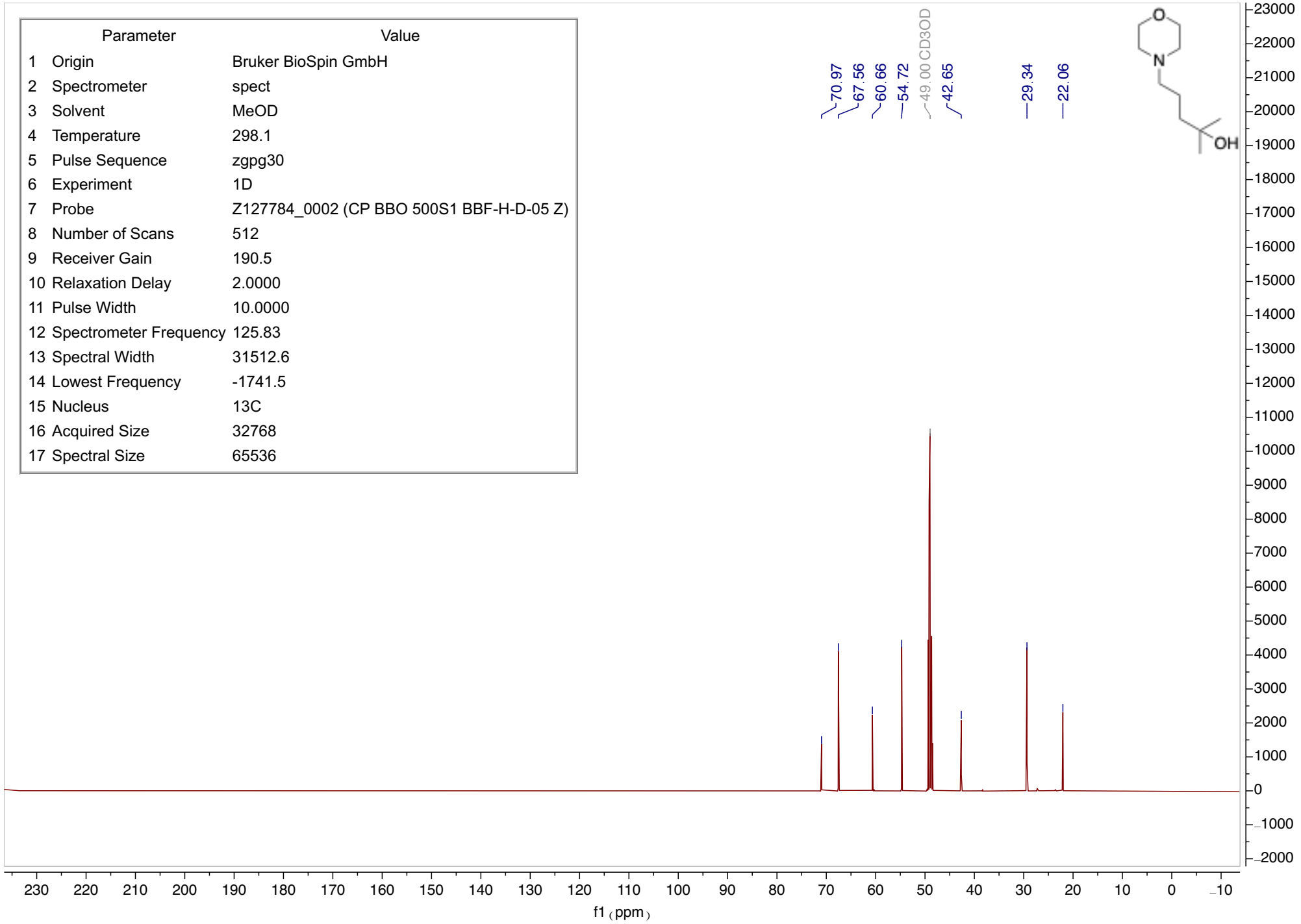
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



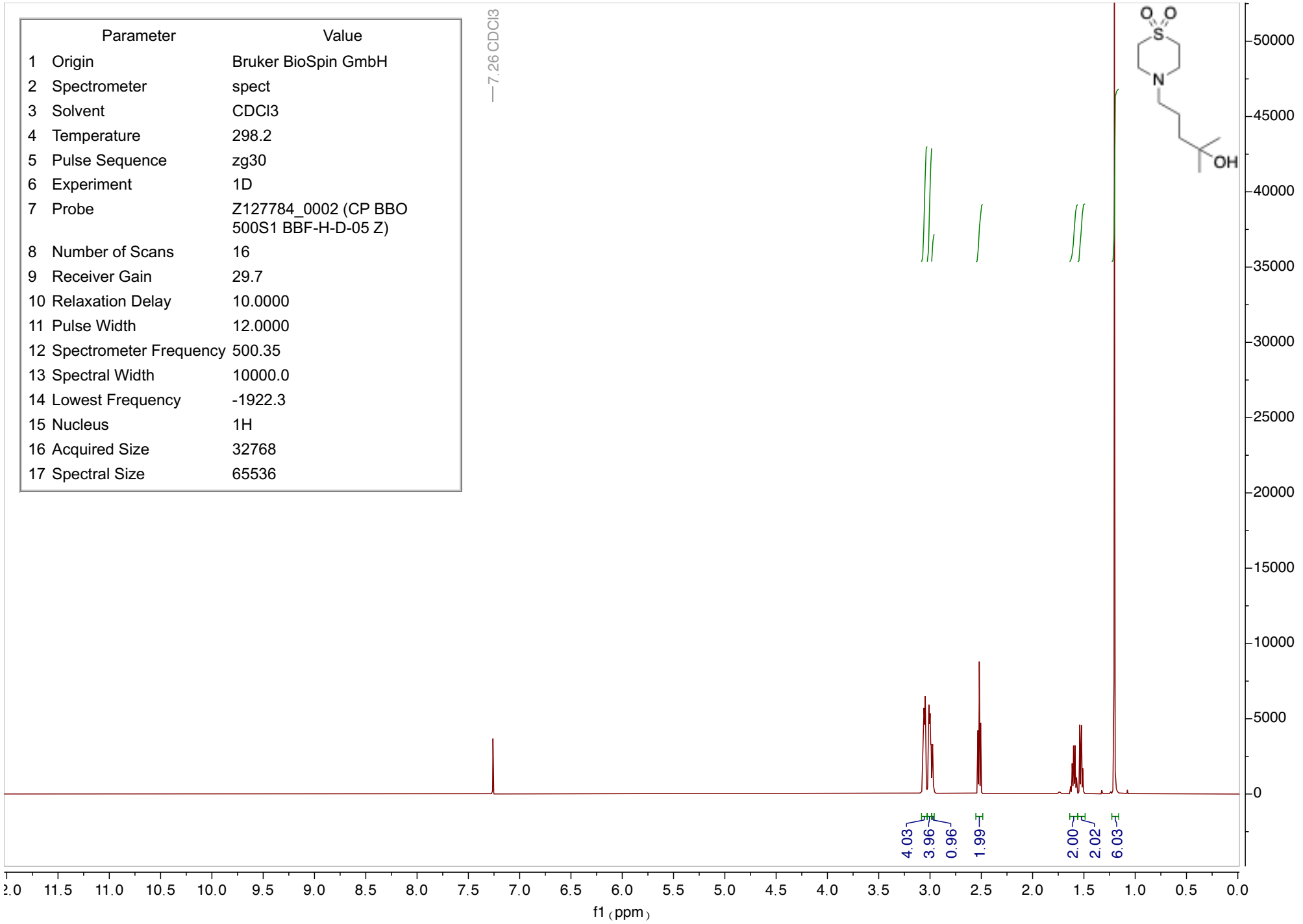
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	55.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1919.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



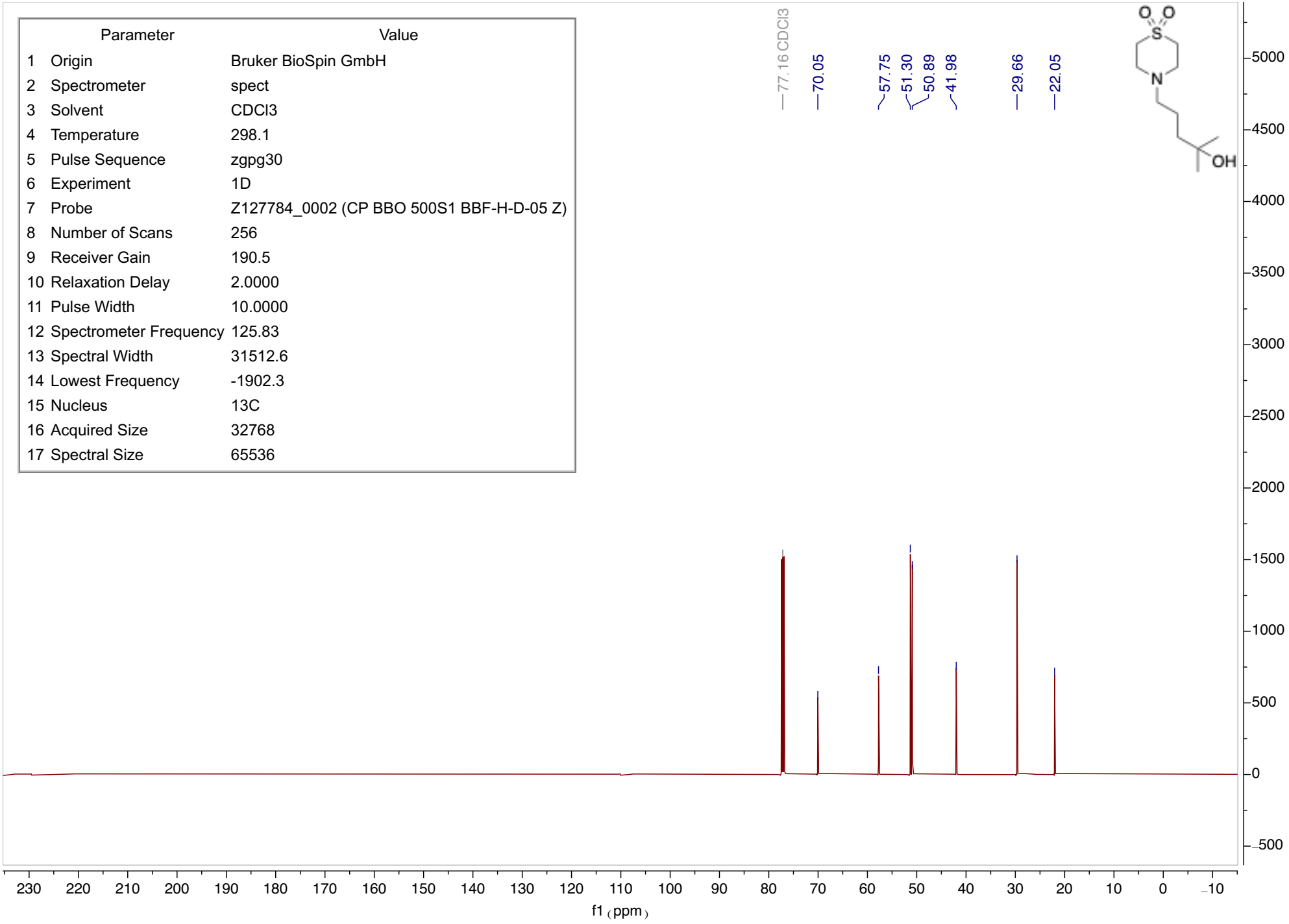
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1741.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



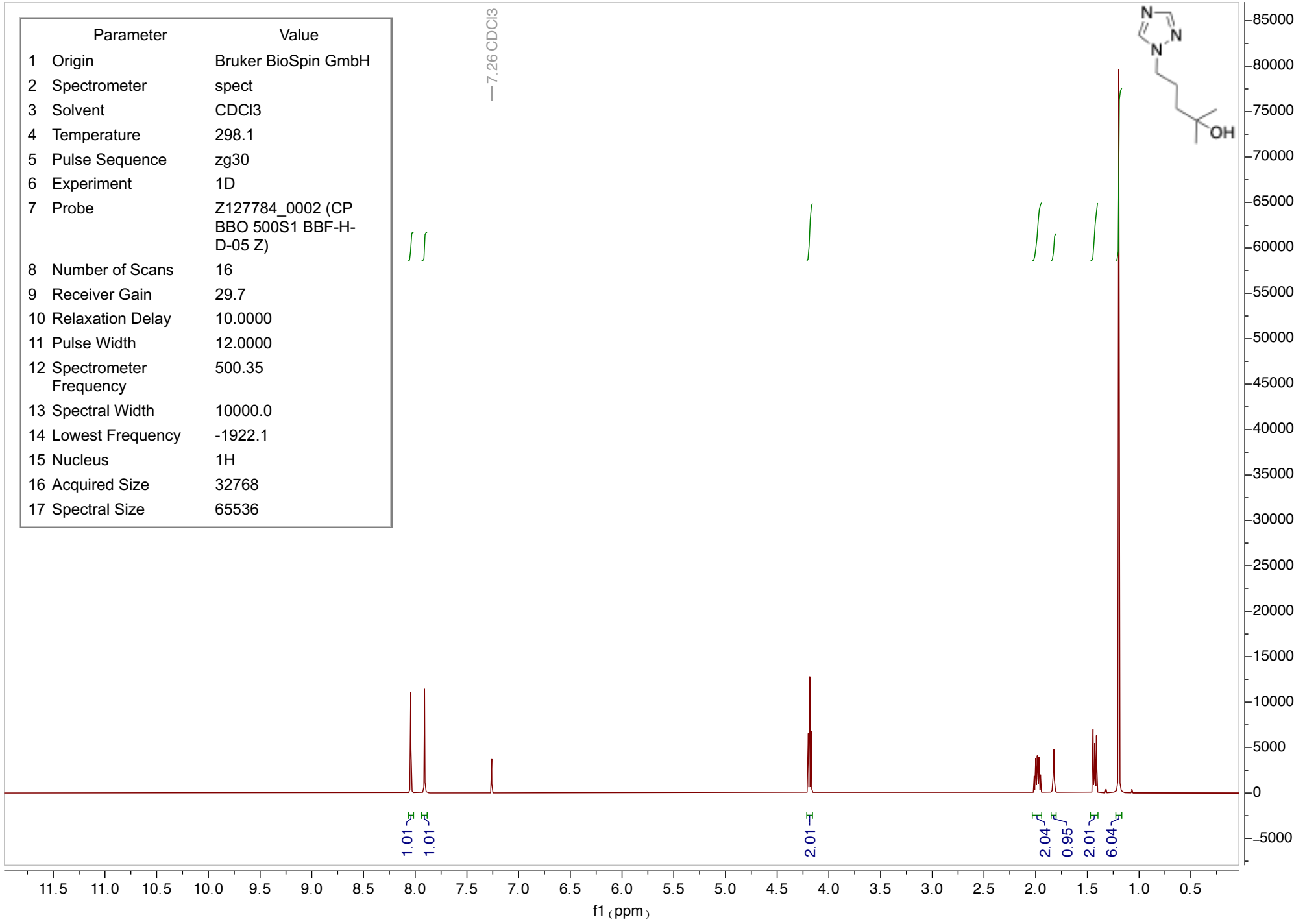
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



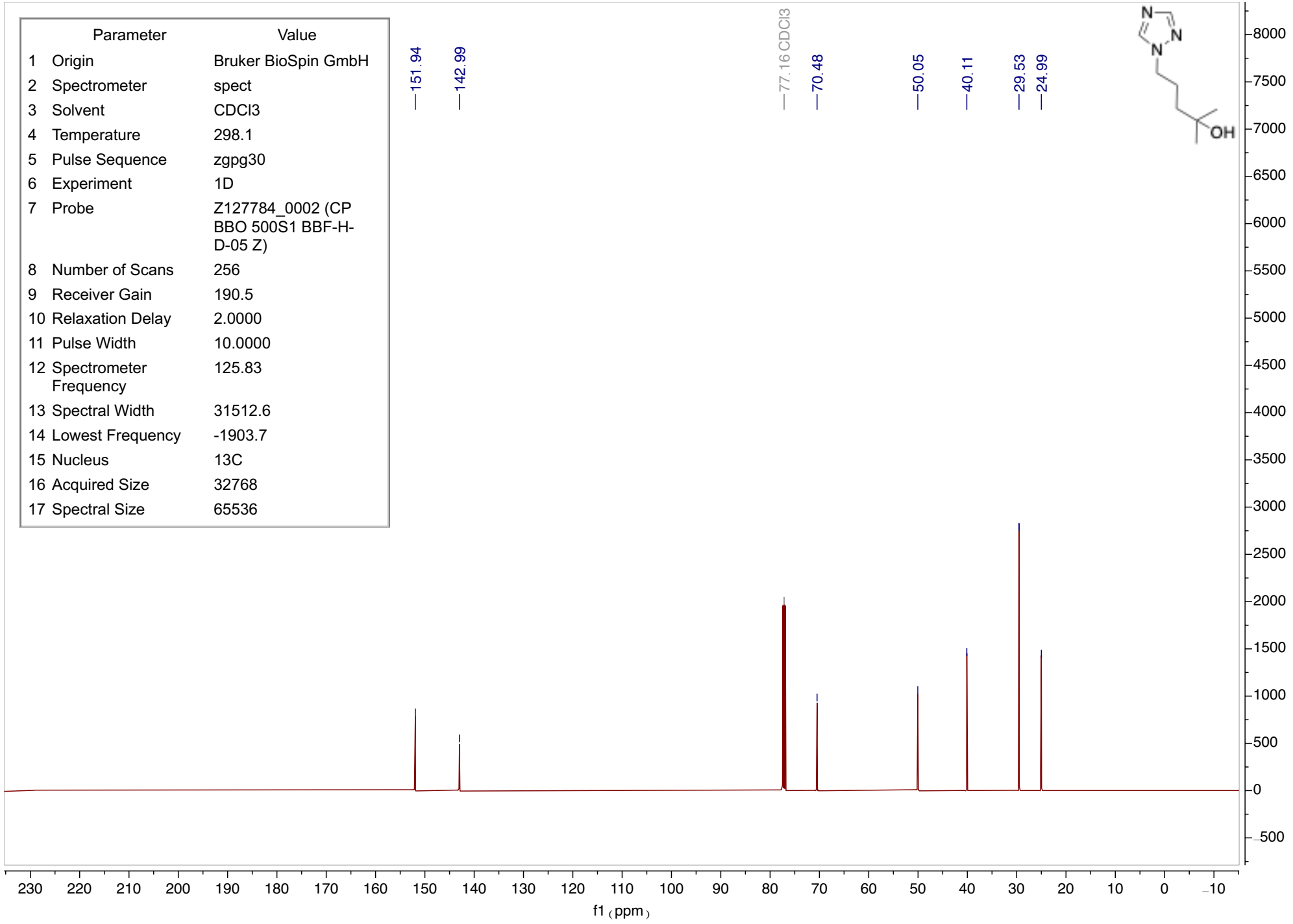
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

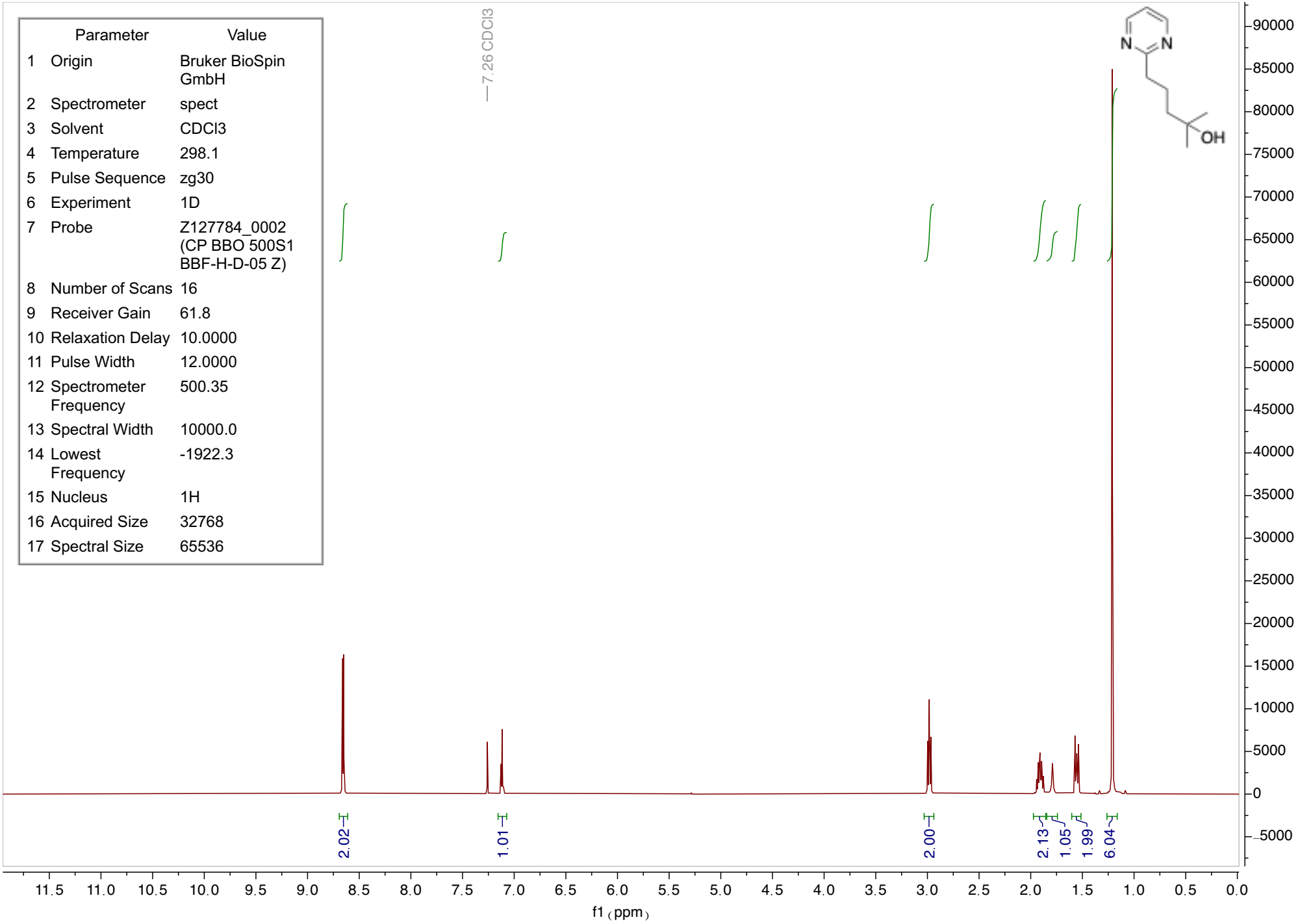


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

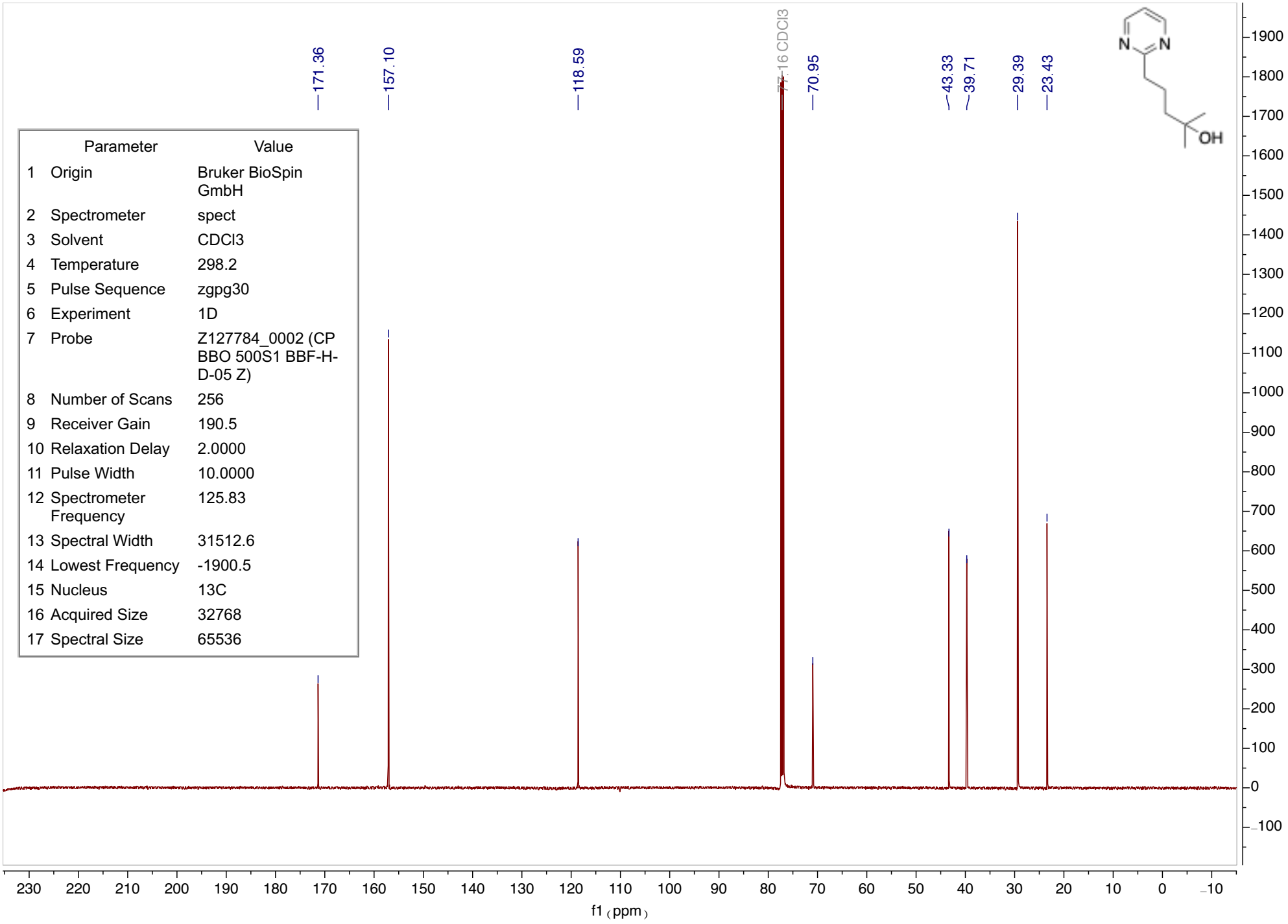


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.7
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



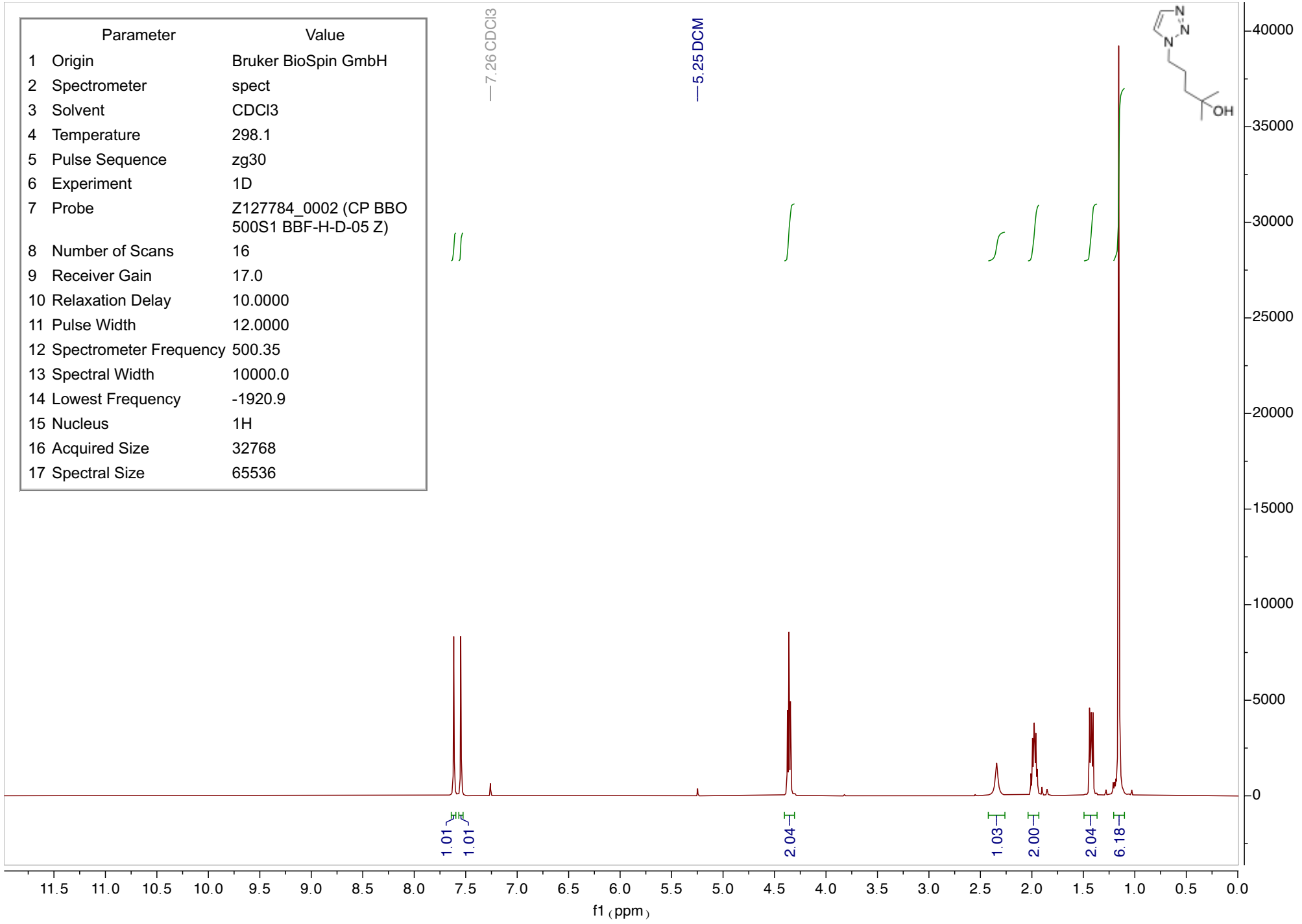


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

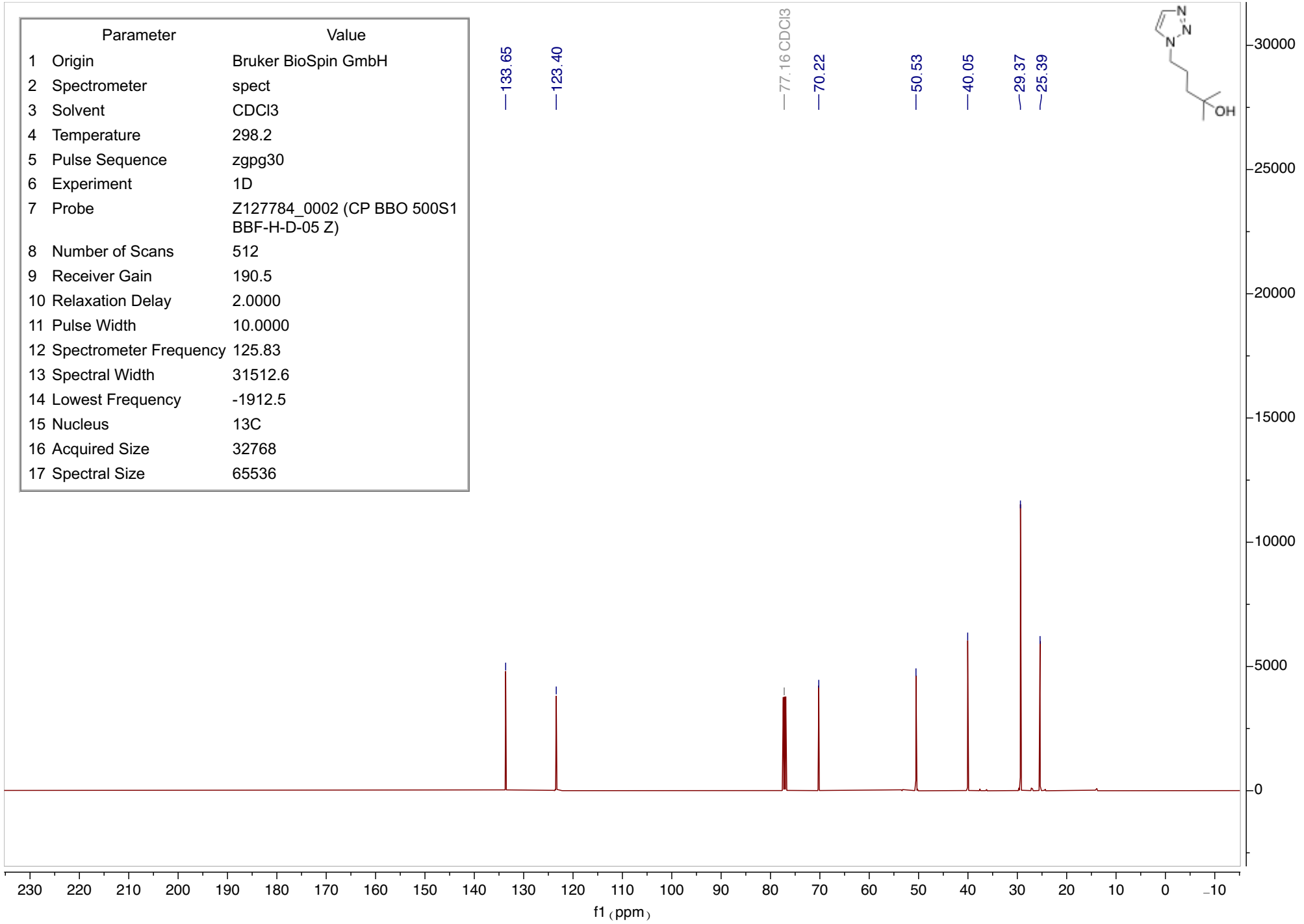


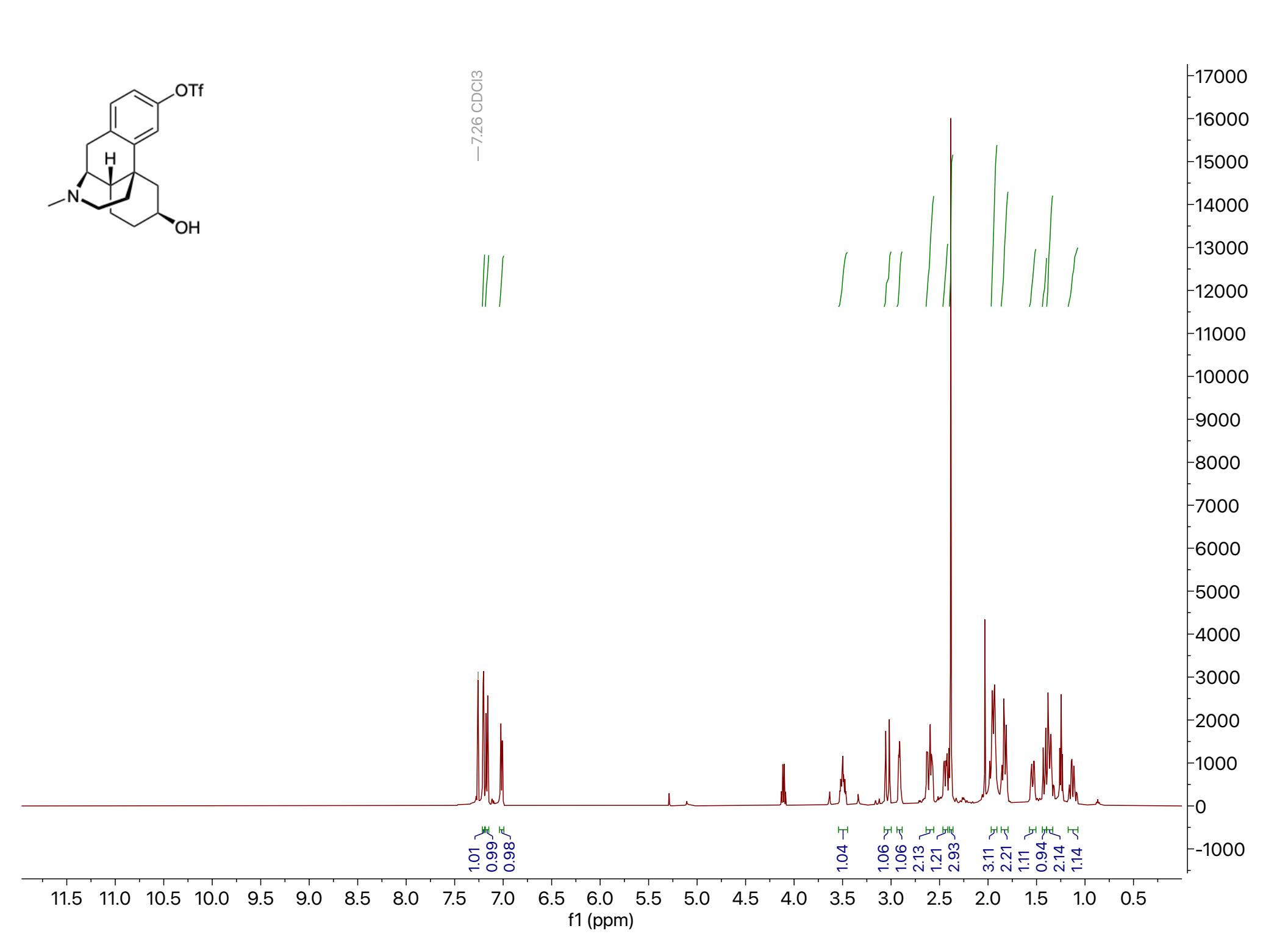
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	17.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1920.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1912.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536




OTf
H
N
OH
7.26 CDCl3
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.01
0.99
0.98
1.04
1.06
1.06
2.13
1.21
2.93
3.11
2.21
1.11
0.94
2.14
1.14
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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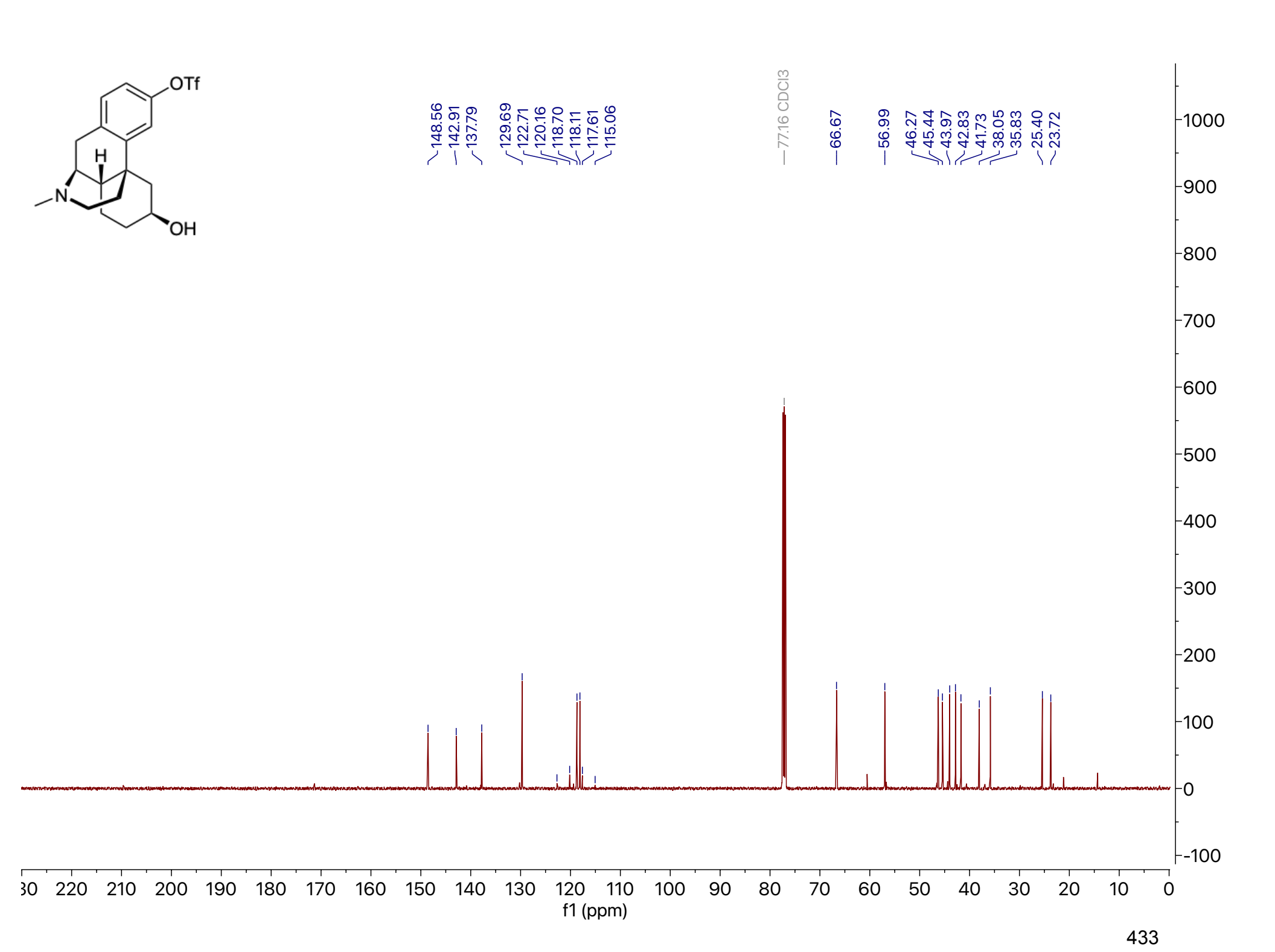
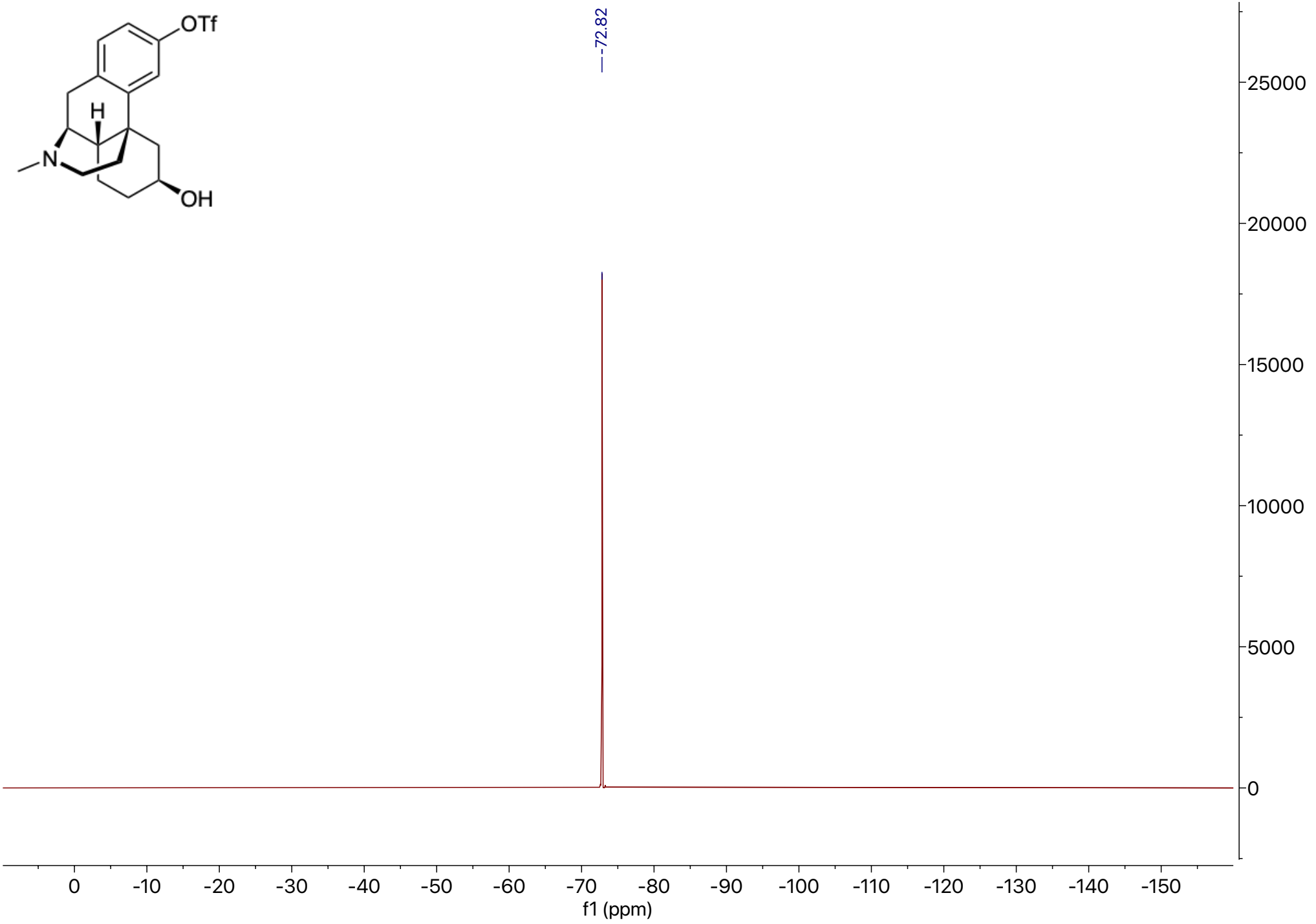
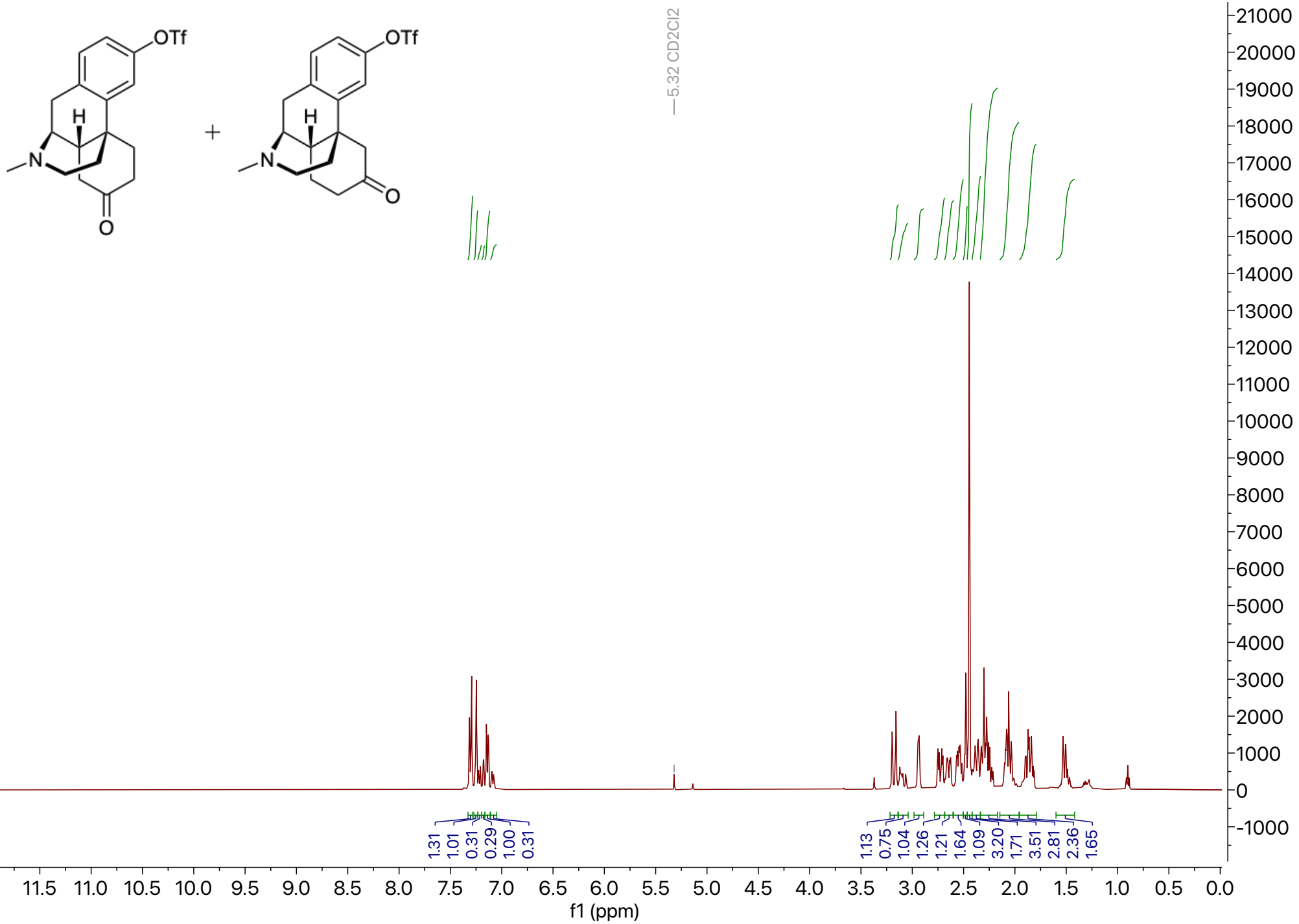
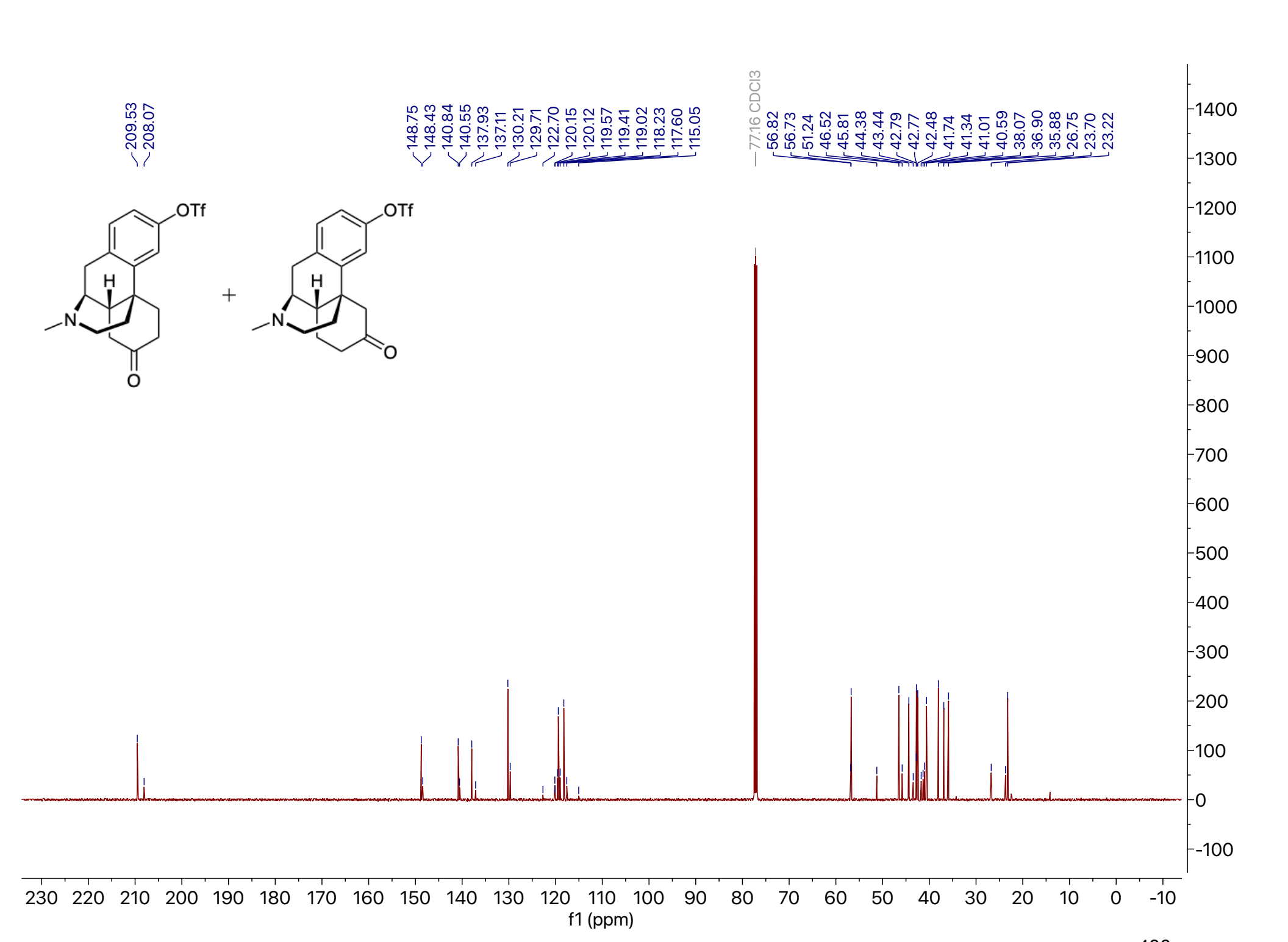
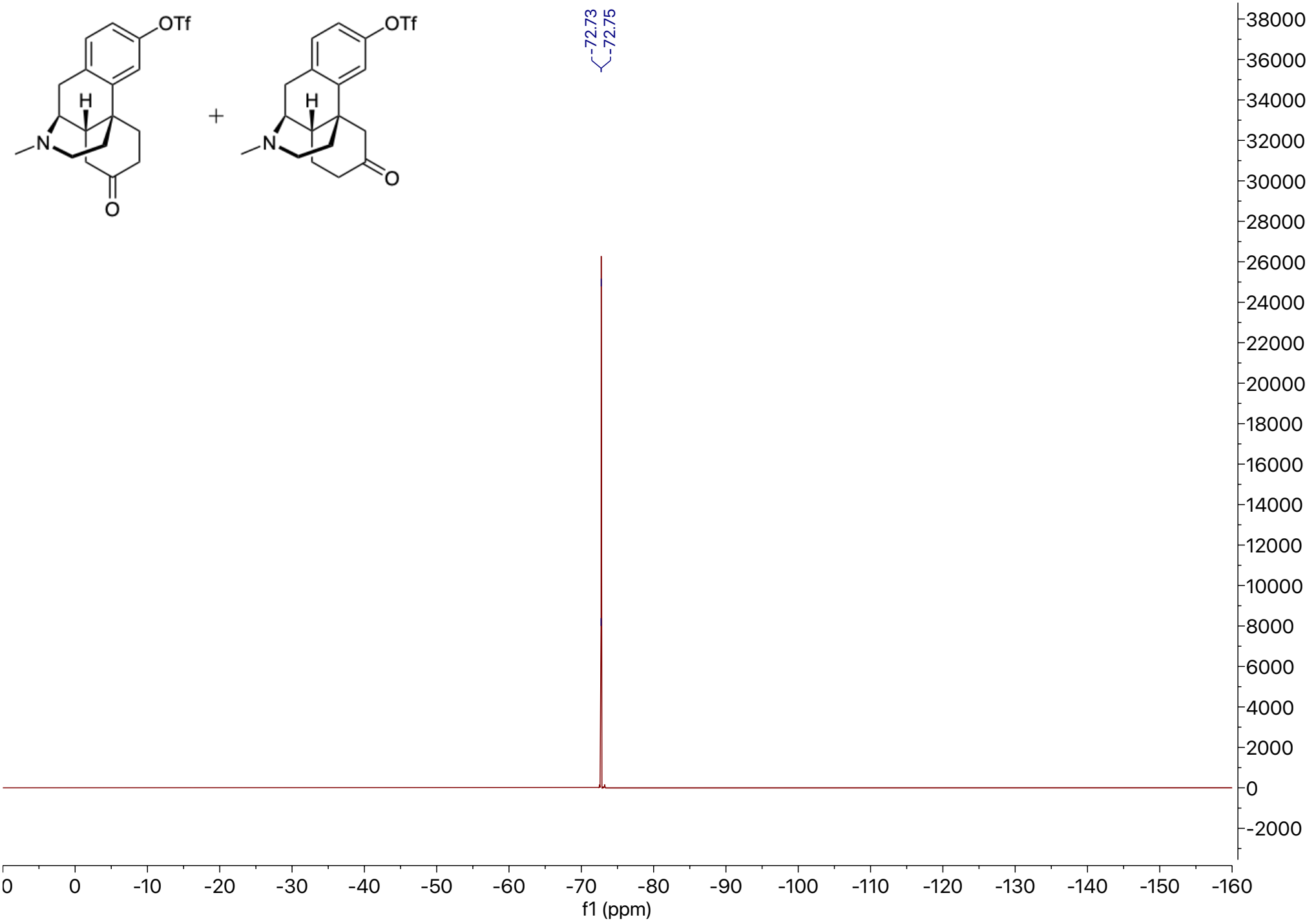
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


OTf
H
N
OH
148.56
142.91
137.79
129.69
122.71
120.16
118.70
118.11
117.61
115.06
77.16 CDCl3
66.67
56.99
46.27
45.44
43.97
42.83
41.73
38.05
35.83
25.40
23.72
1000
900
800
700
600
500
400
300
200
100
0
-100
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

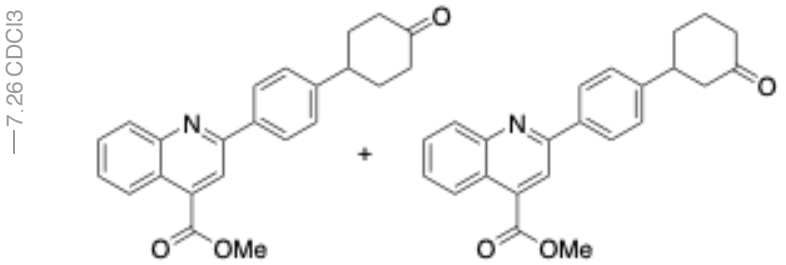

OTf
H
N
OH
-72.82
25000
20000
15000
10000
5000
0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

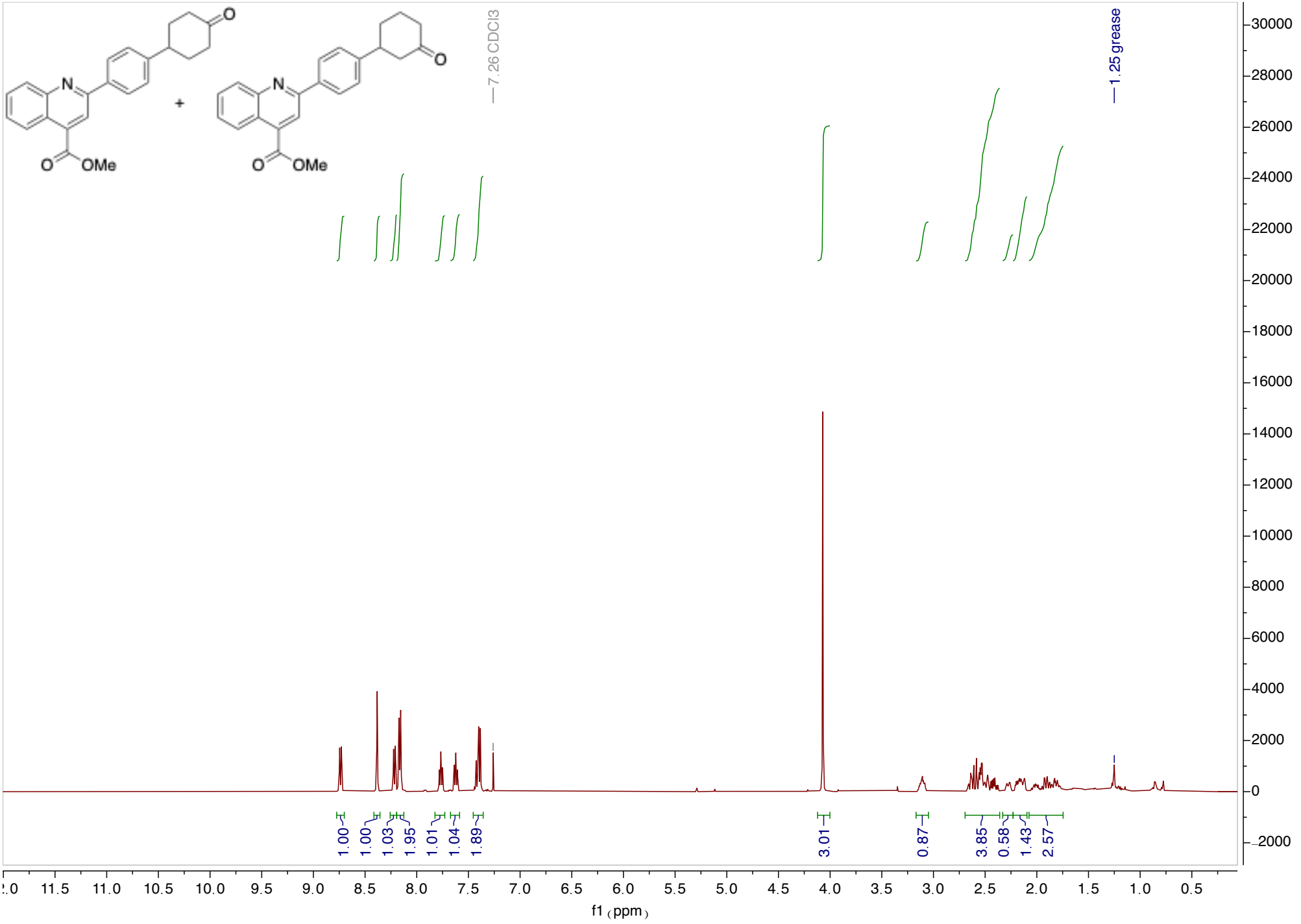

OTf
H
N
O
+
OTf
H
N
O
5.32 CD2Cl2
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.31
1.01
0.31
0.29
1.00
0.31
1.13
0.75
1.04
1.26
1.21
1.64
1.09
3.20
1.71
3.51
2.81
2.36
1.65
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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)

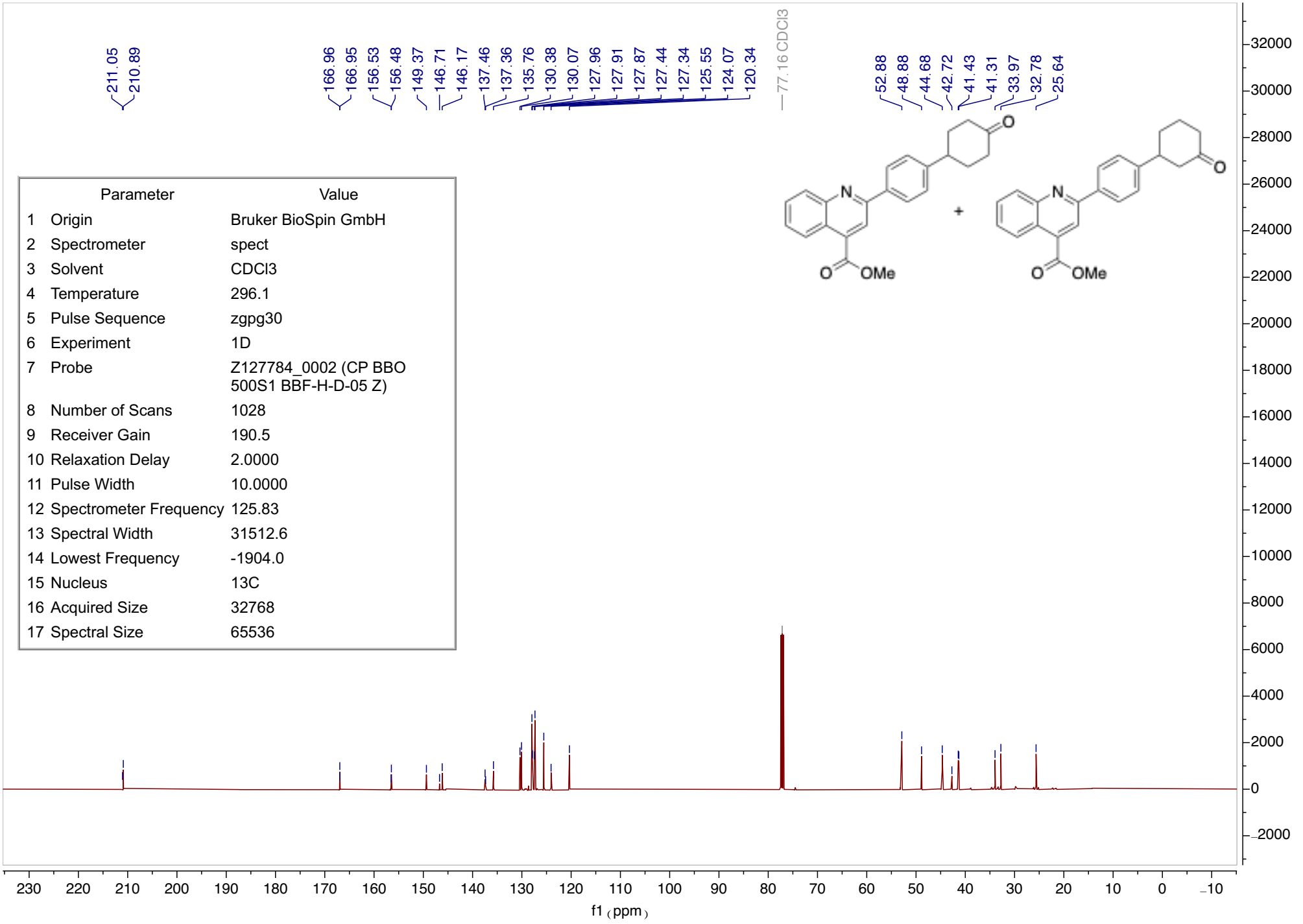

209.53
208.07
148.75
148.43
140.84
140.55
137.93
137.11
130.21
129.71
122.70
120.15
120.12
119.57
119.41
119.02
118.23
117.60
115.05
77.16 CDCl3
56.82
56.73
51.24
46.52
45.81
44.38
43.44
42.79
42.77
42.48
41.74
41.34
41.01
40.59
38.07
36.90
35.88
26.75
23.70
23.22
OTf
H
N
O
+
OTf
H
N
O
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OTf
H
N
O
+
OTf
H
N
O
-72.73
-72.75
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

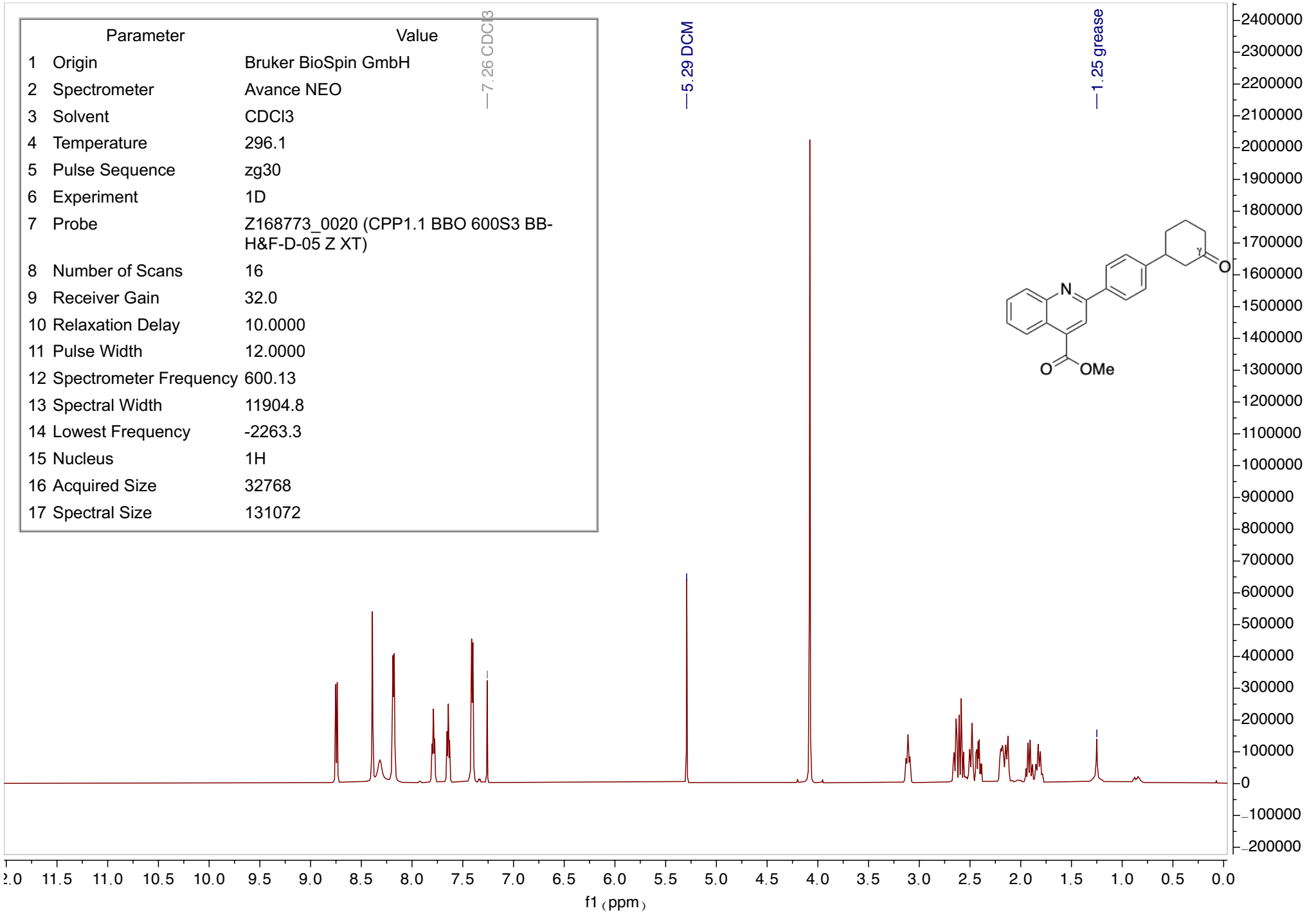


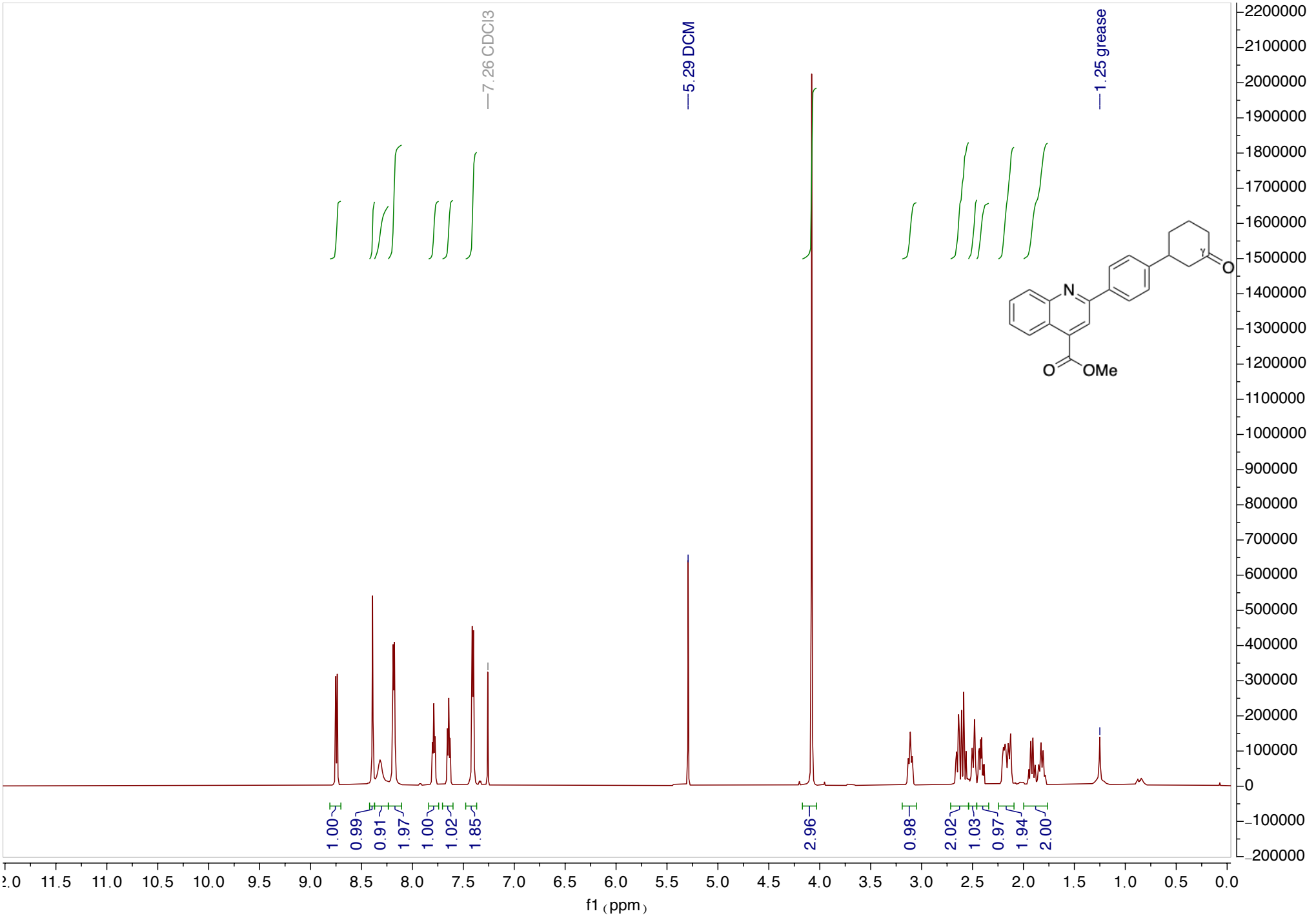

7.26 CDCl3
1.25 grease
1.00
1.00
1.03
1.95
1.01
1.04
1.89
3.01
0.87
3.85
0.58
1.43
2.57
f1 (ppm)

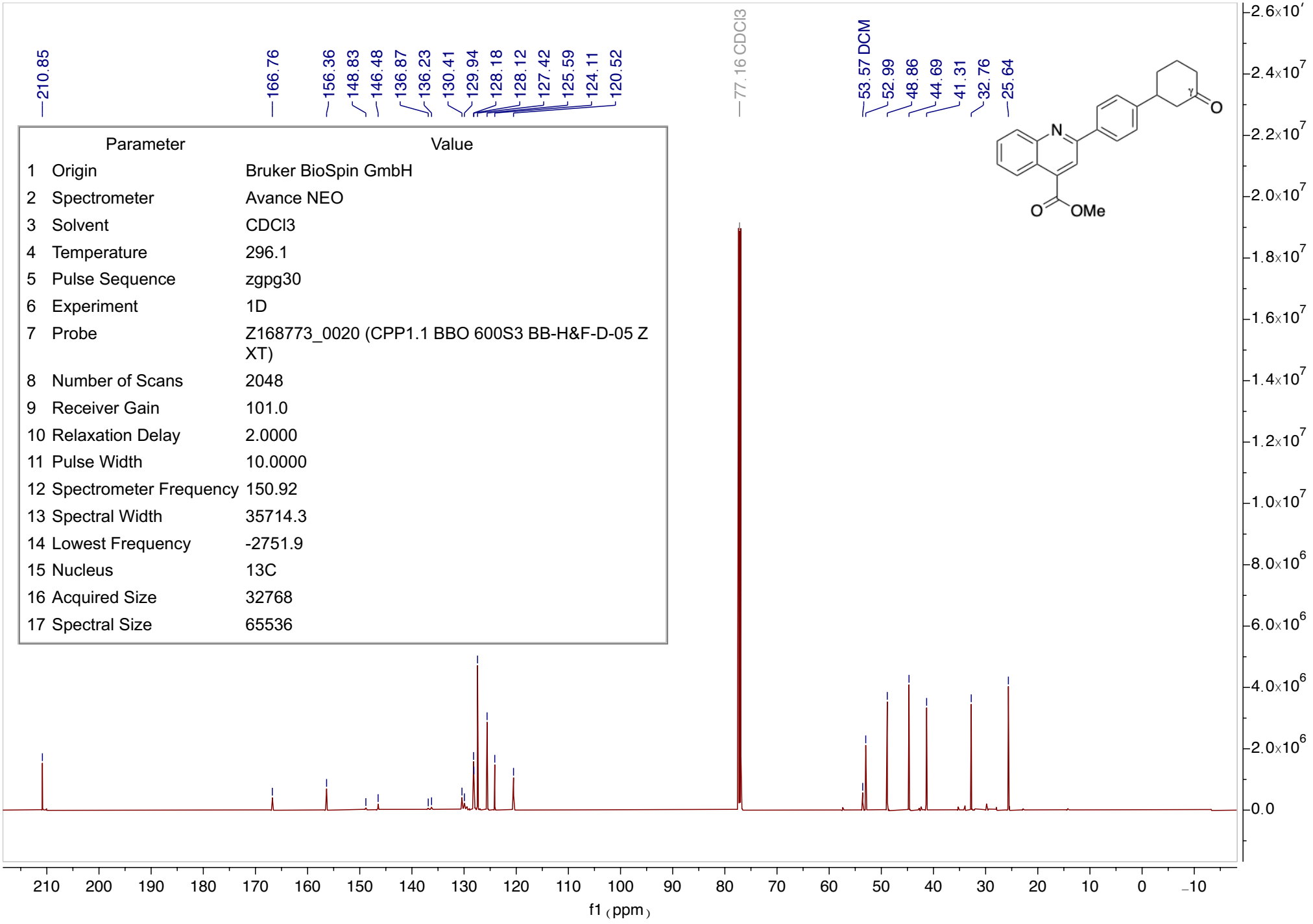


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1028
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1904.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

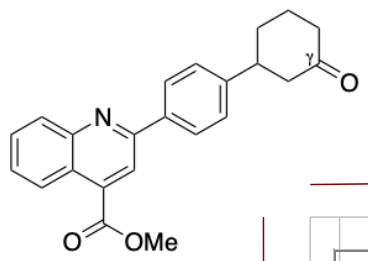
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2263.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



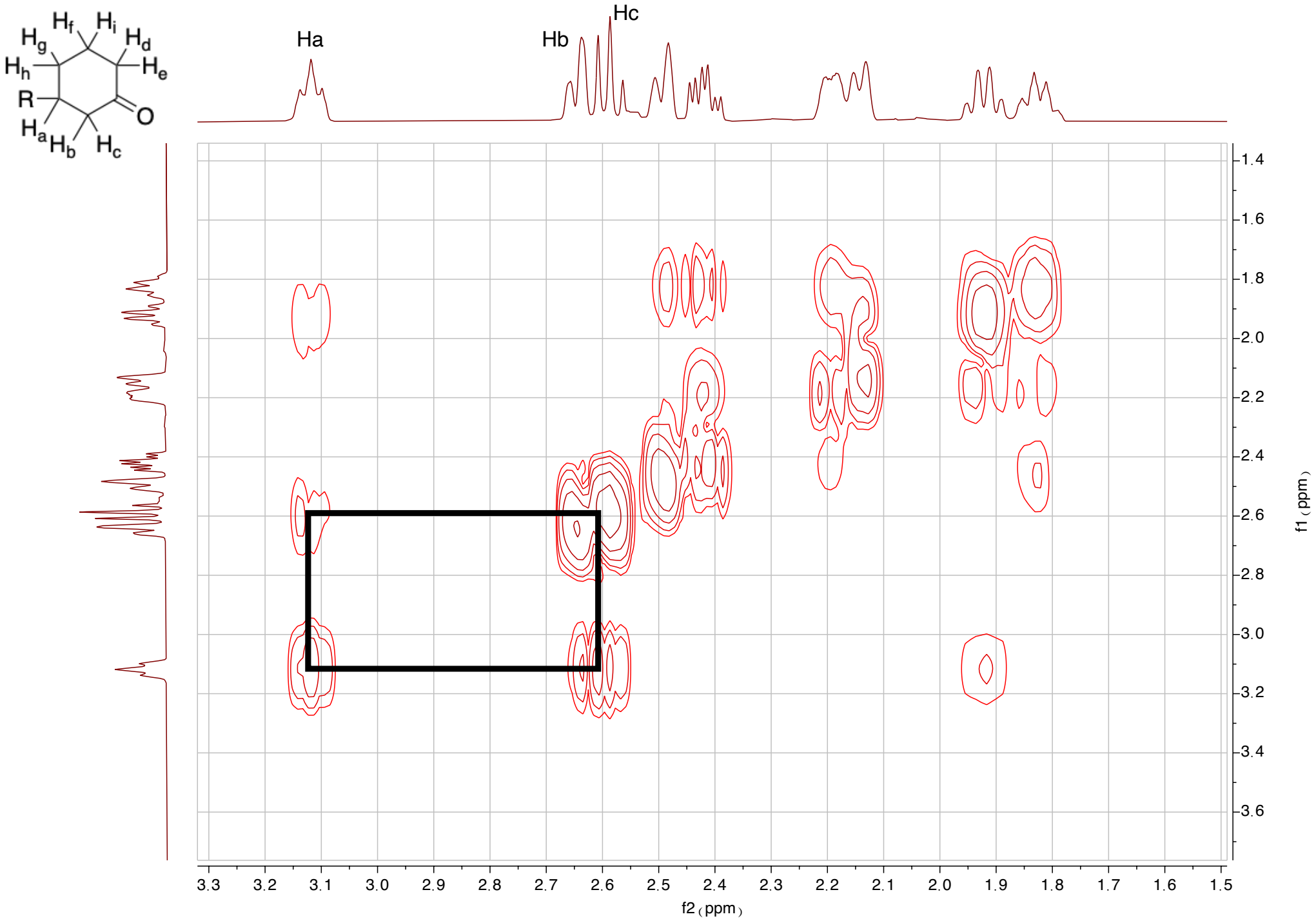

7.26 CDCl3
5.29 DCM
1.25 grease
N
O
O
OMe
1.00
0.99
0.91
1.97
1.00
1.02
1.85
2.96
0.98
2.02
1.03
0.97
1.94
2.00
f1 (ppm)

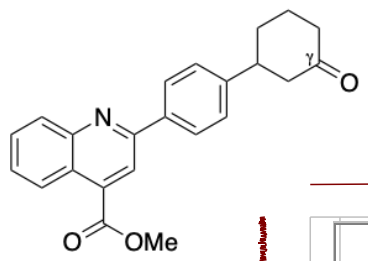


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	2048
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2751.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

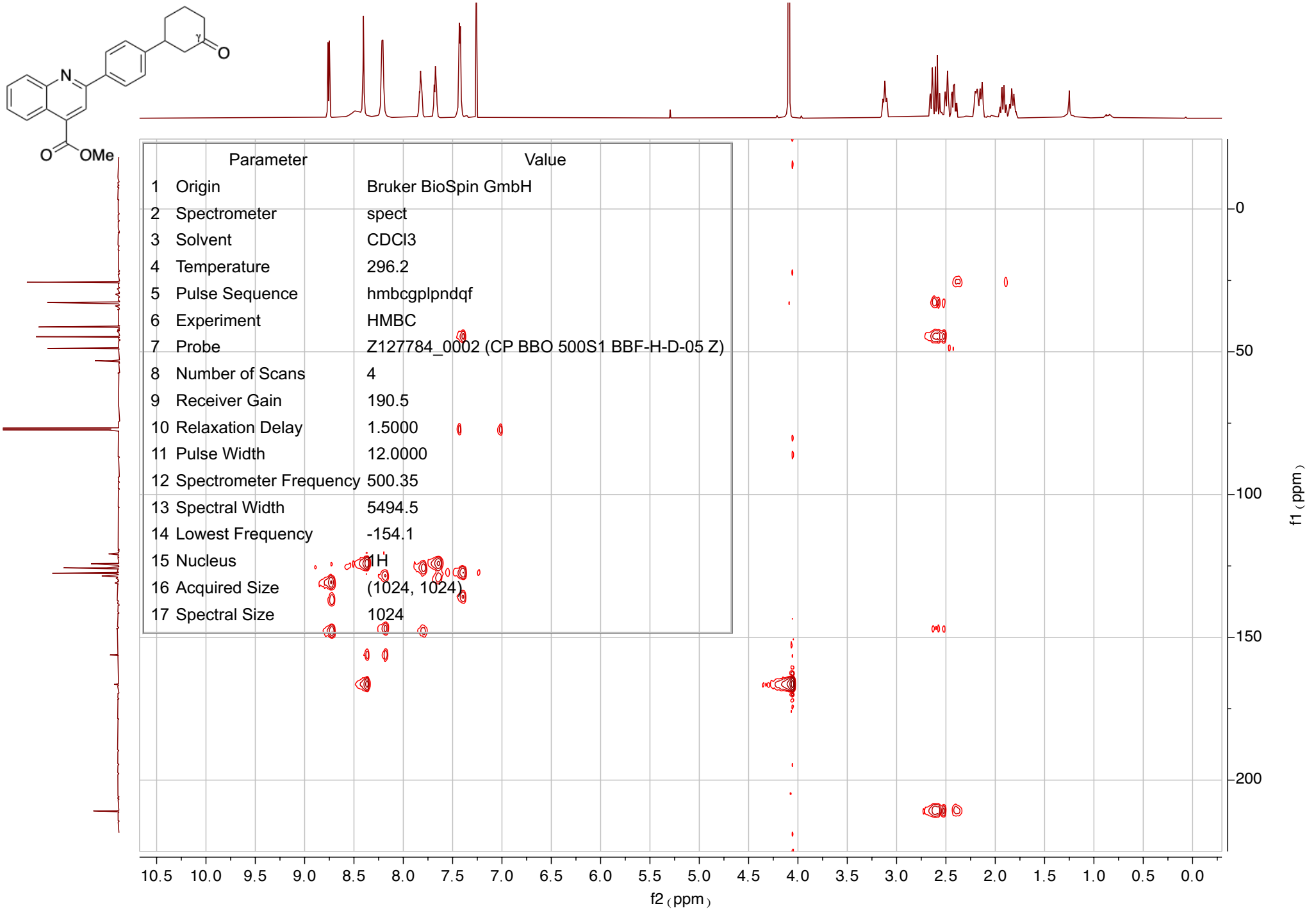


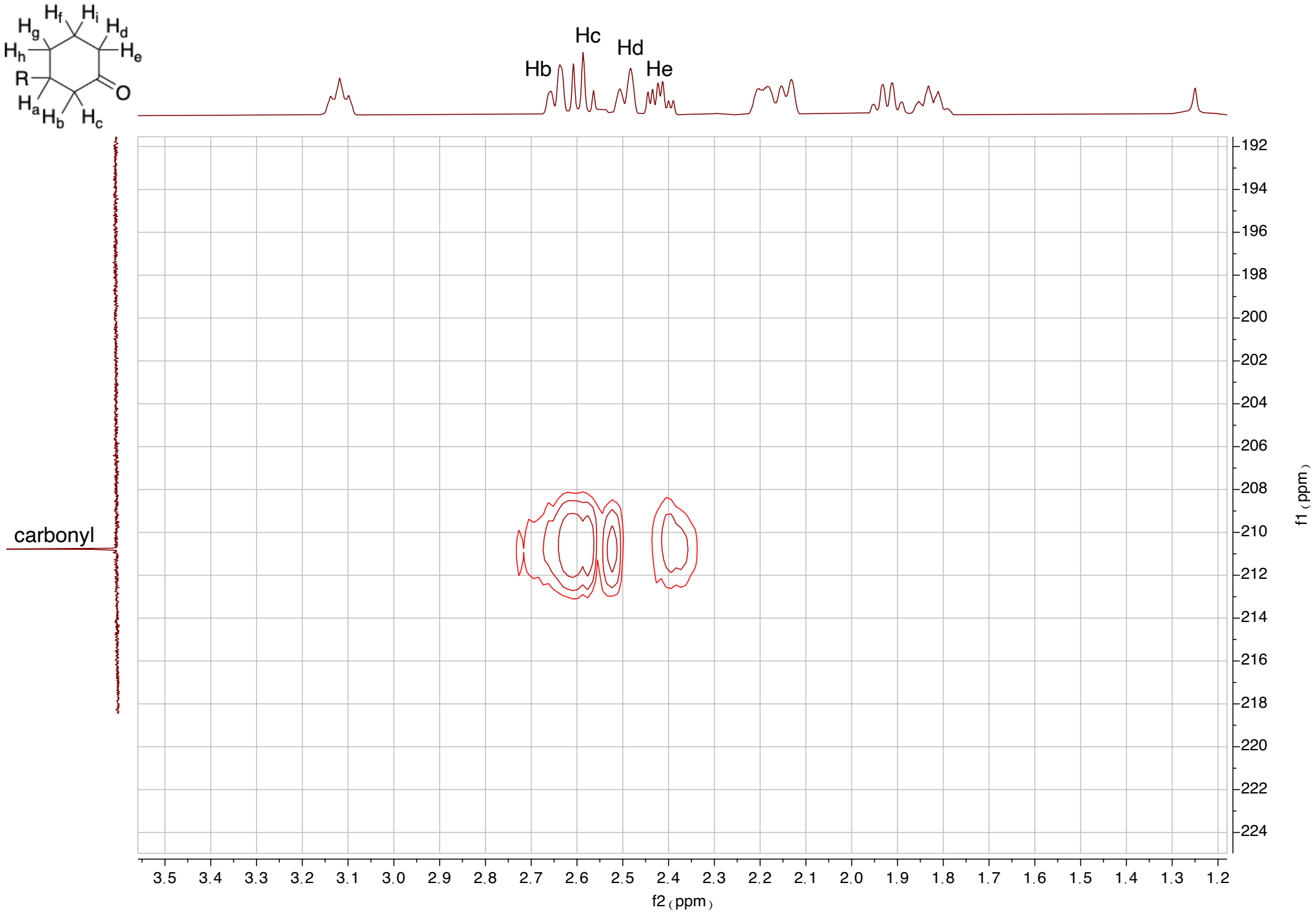
Parameter		Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	2
9	Receiver Gain	64.0
10	Relaxation Delay	1.4590
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-73.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


Hf
Hi
Hg
Hd
Hh
He
R
O
Ha
Hb
Hc
Ha
Hb
Hc
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
f1 (ppm)
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
f2 (ppm)

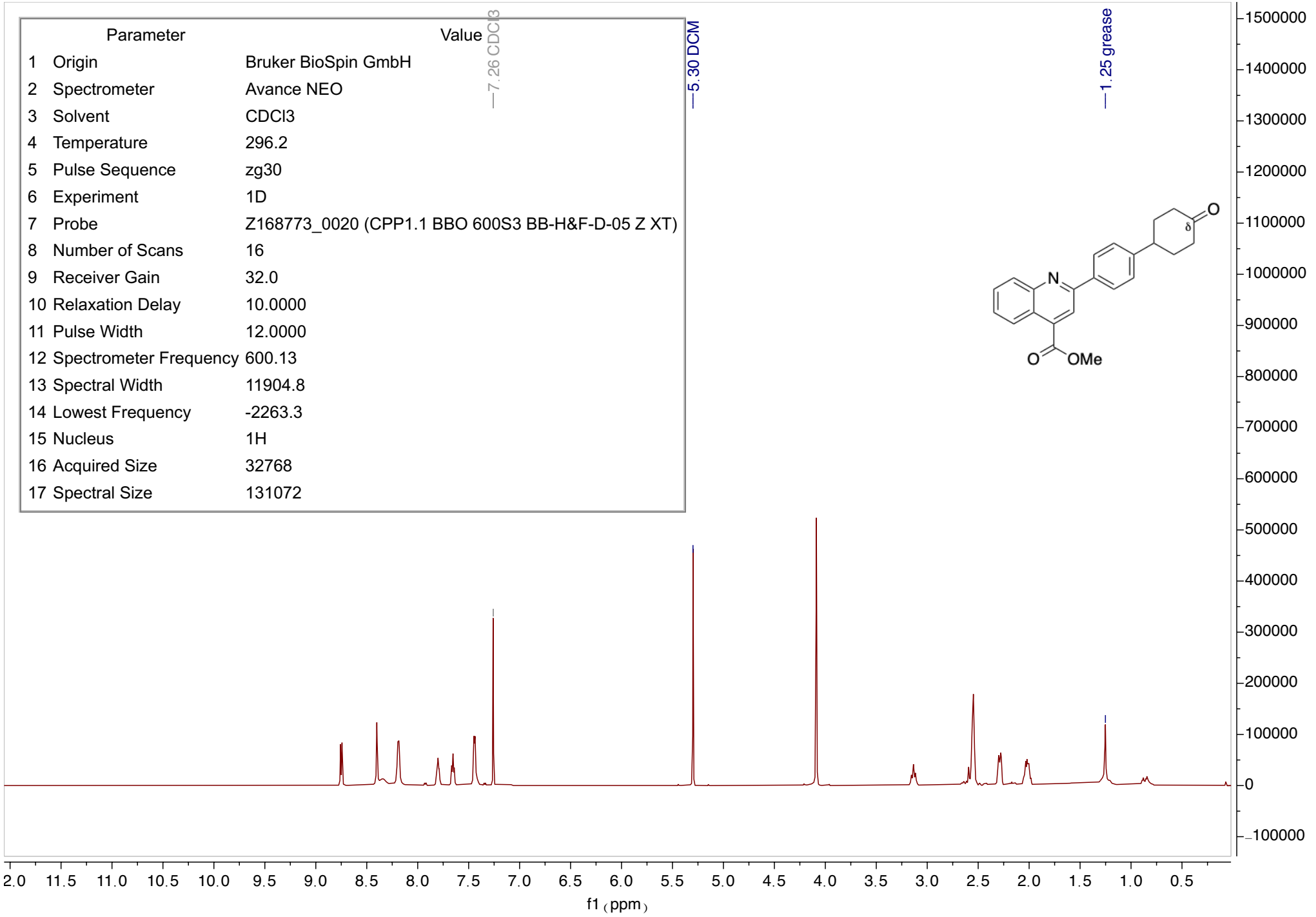


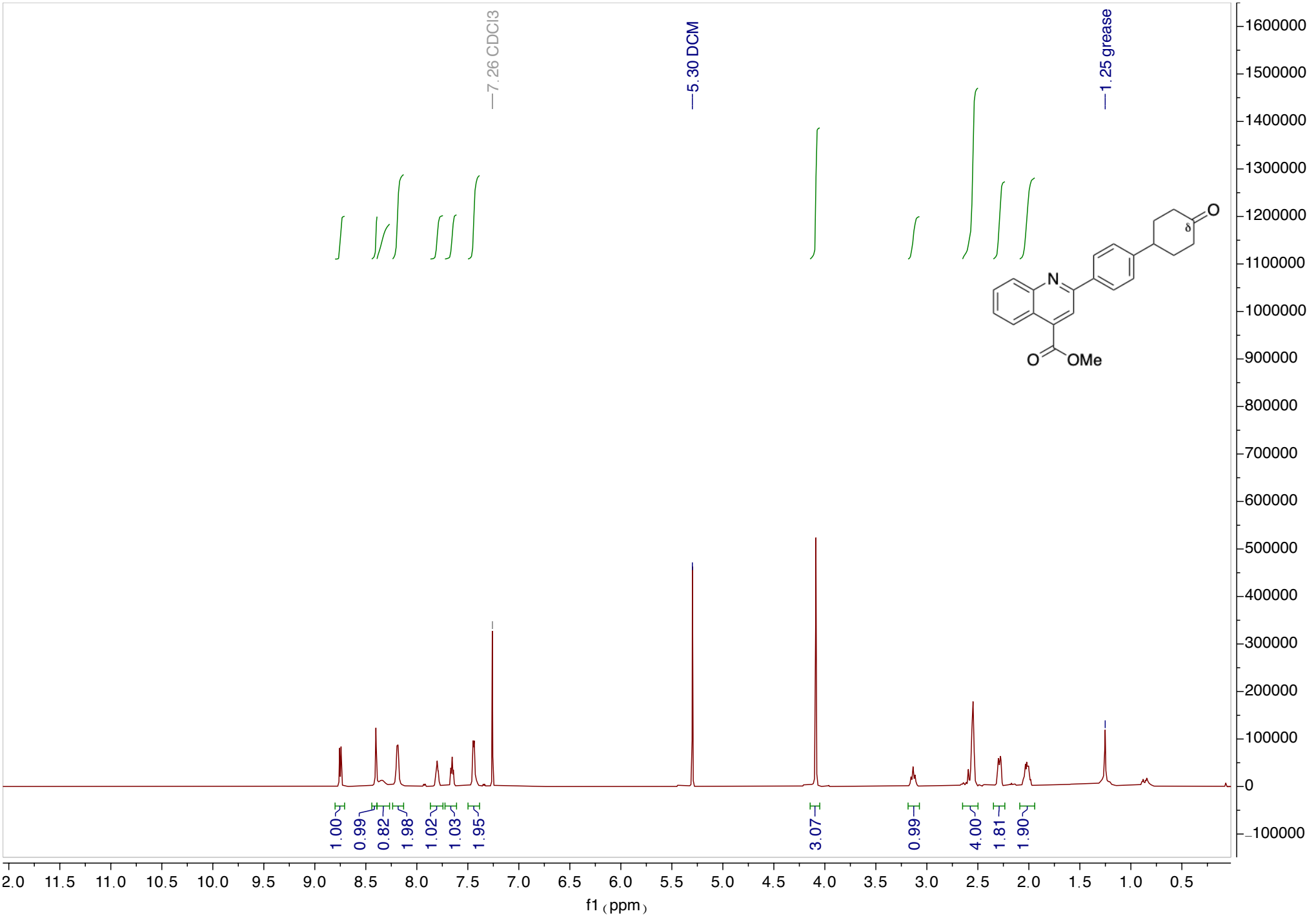
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-71.8
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

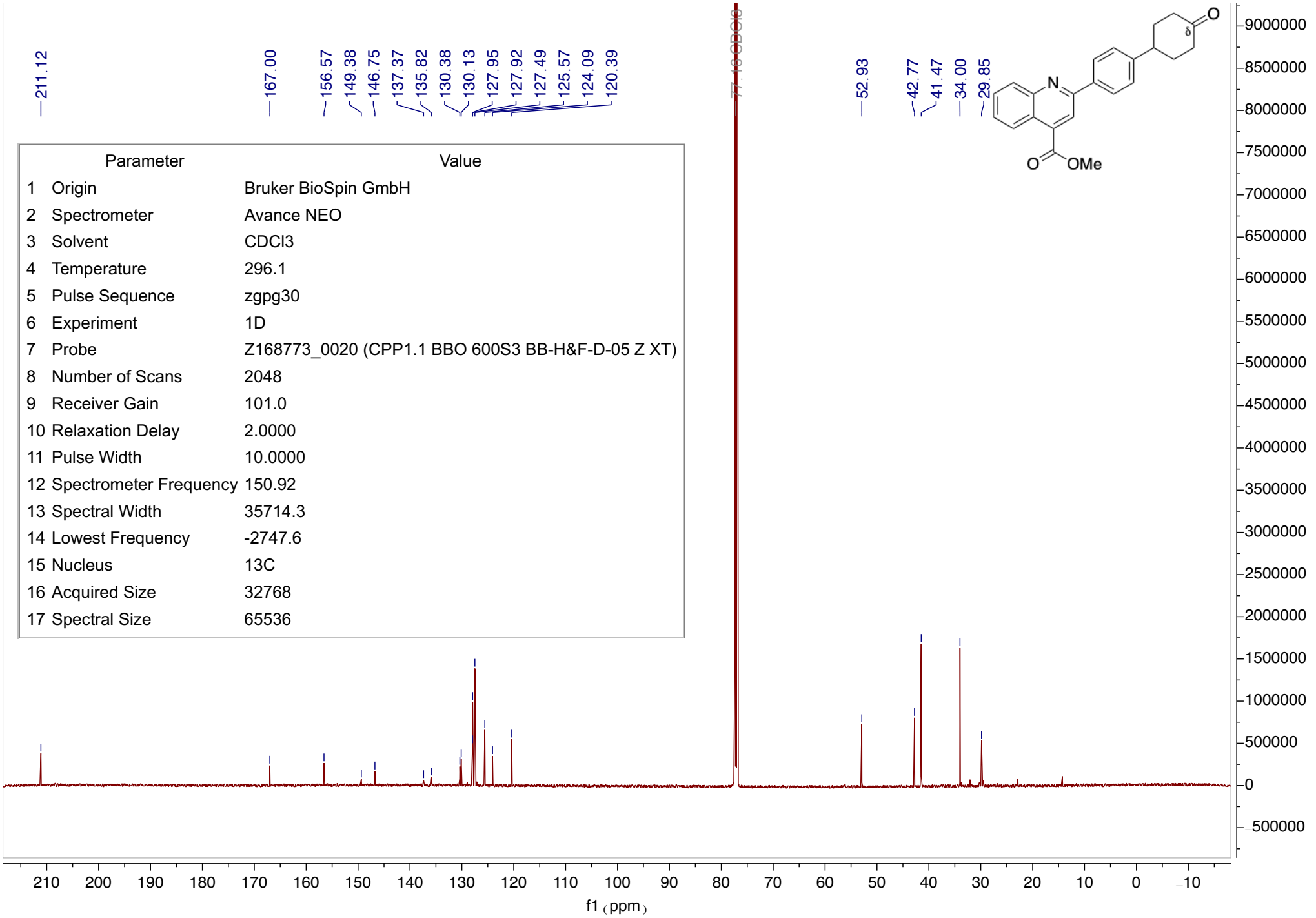

N
O
O
OMe
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 5494.5
14 Lowest Frequency -154.1
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
10.5 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
f2 (ppm)
0 50 100 150 200
f1 (ppm)


Hf
Hi
Hg
Hd
Hh
He
R
O
Ha
Hb
Hc
Hb
Hc
Hd
He
carbonyl
192
194
196
198
200
202
204
206
208
210
212
214
216
218
220
222
224
f1 (ppm)
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2263.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

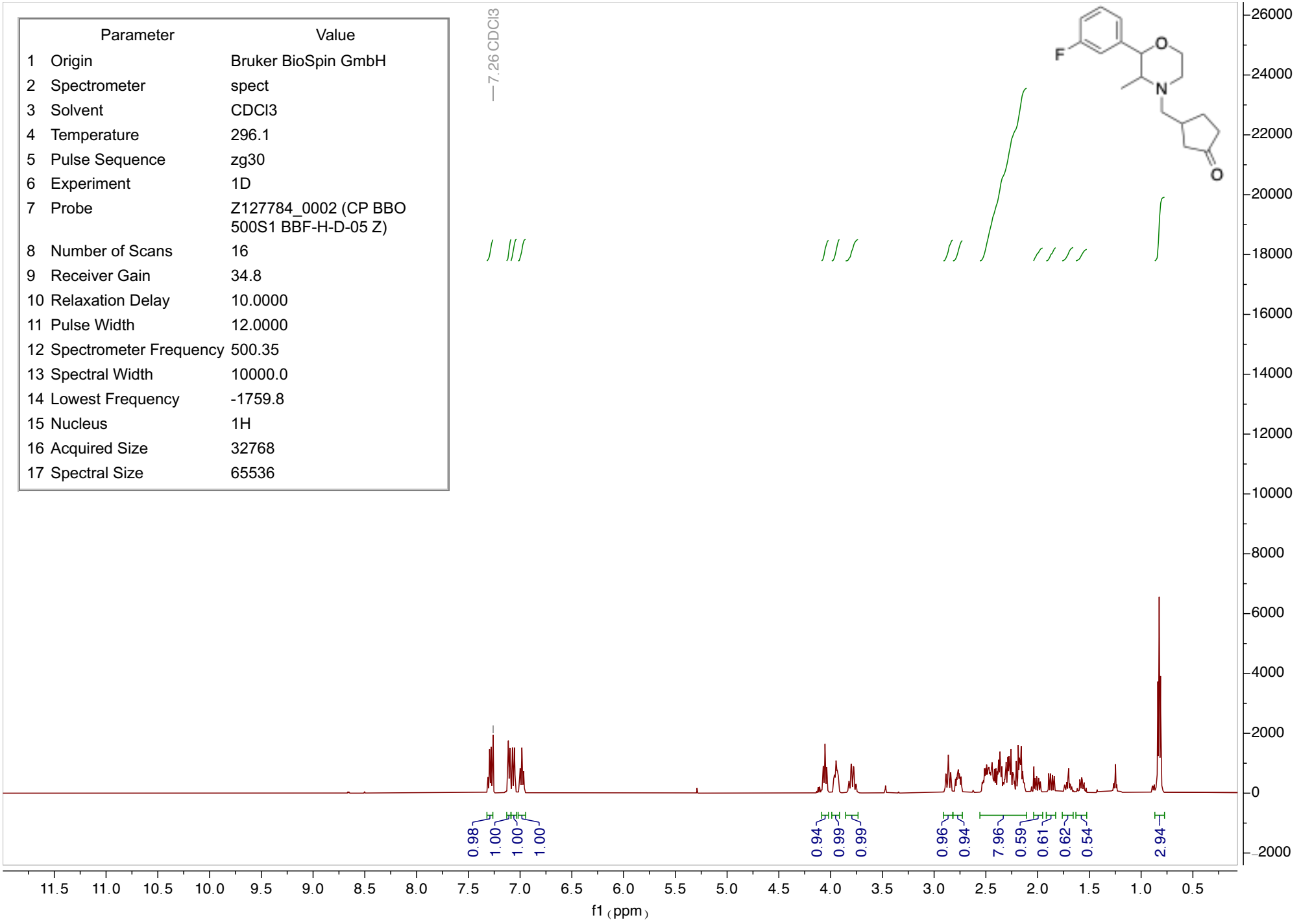


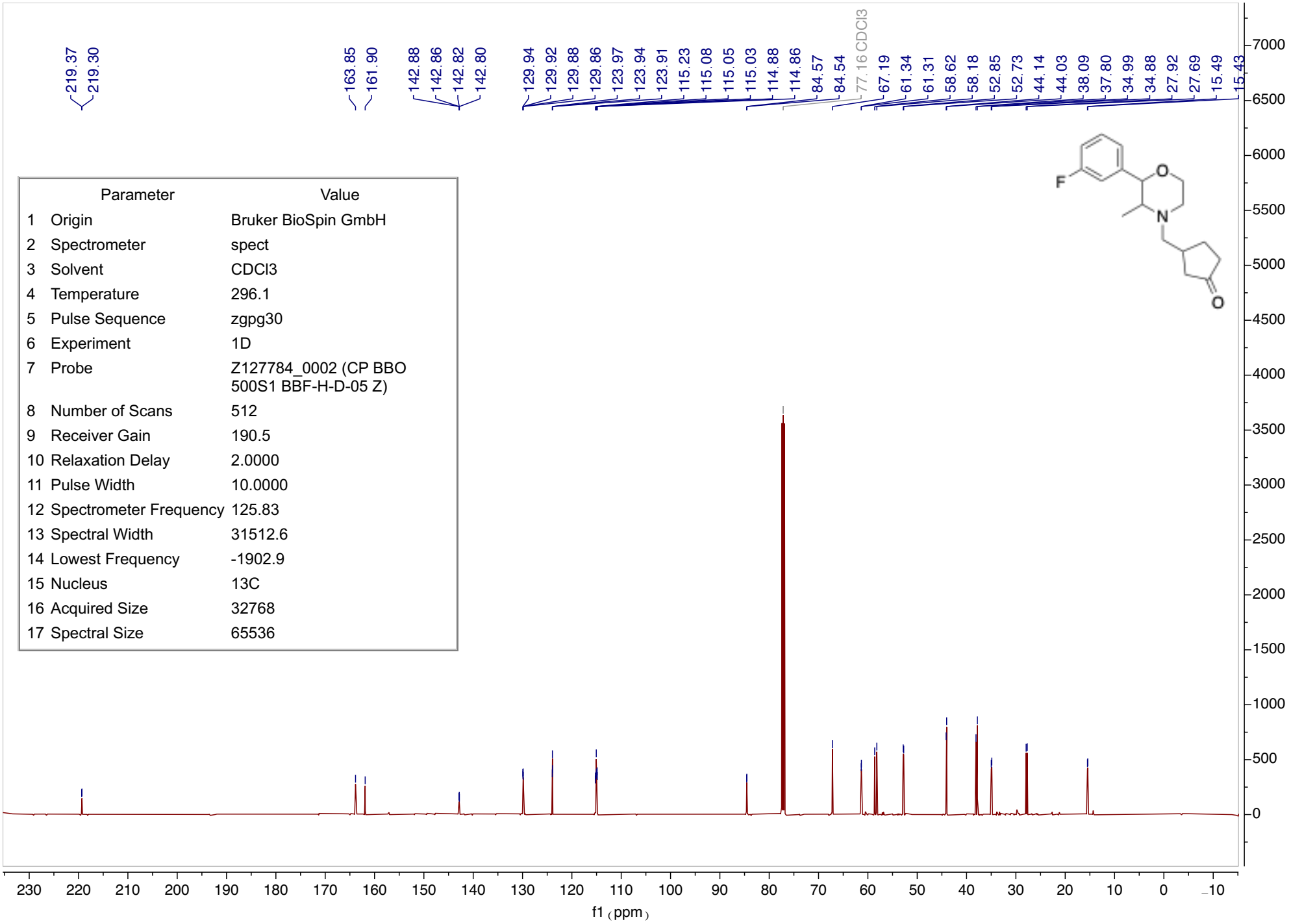

7.26 CDCl3
5.30 DCM
1.25 grease
1.00
0.99
0.82
1.98
1.02
1.03
1.95
3.07
0.99
4.00
1.81
1.90
f1 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	2048
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2747.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

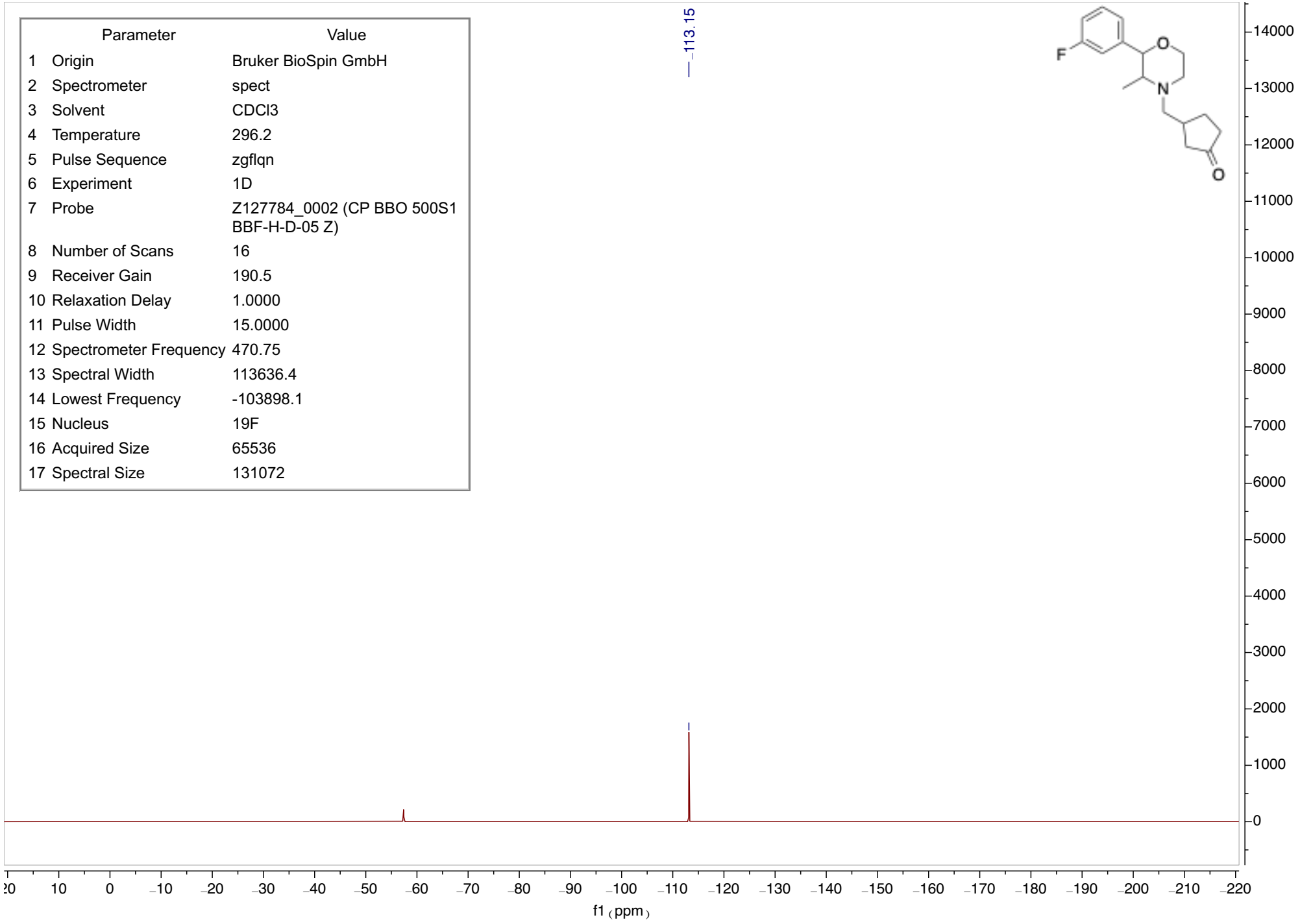
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	34.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



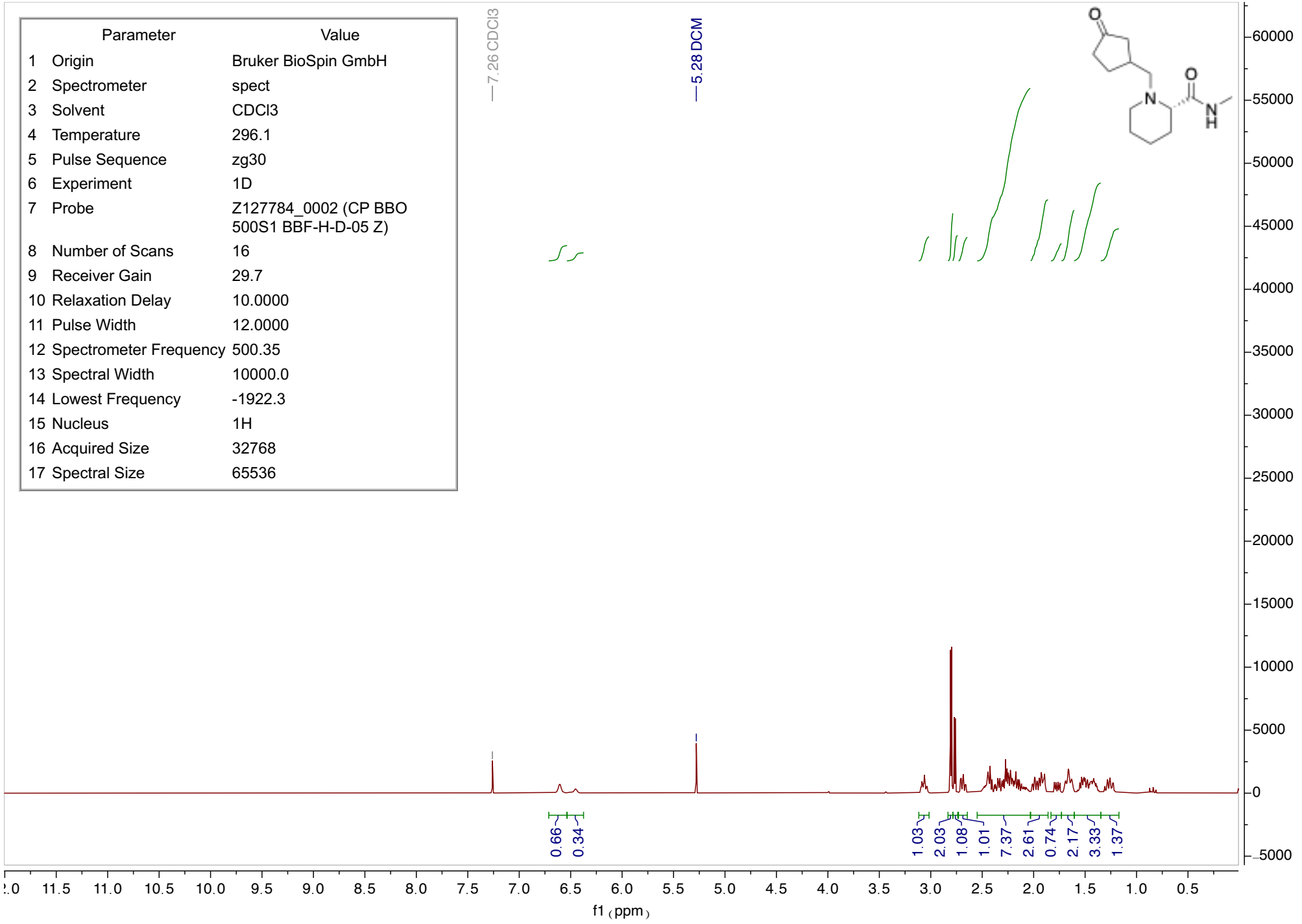


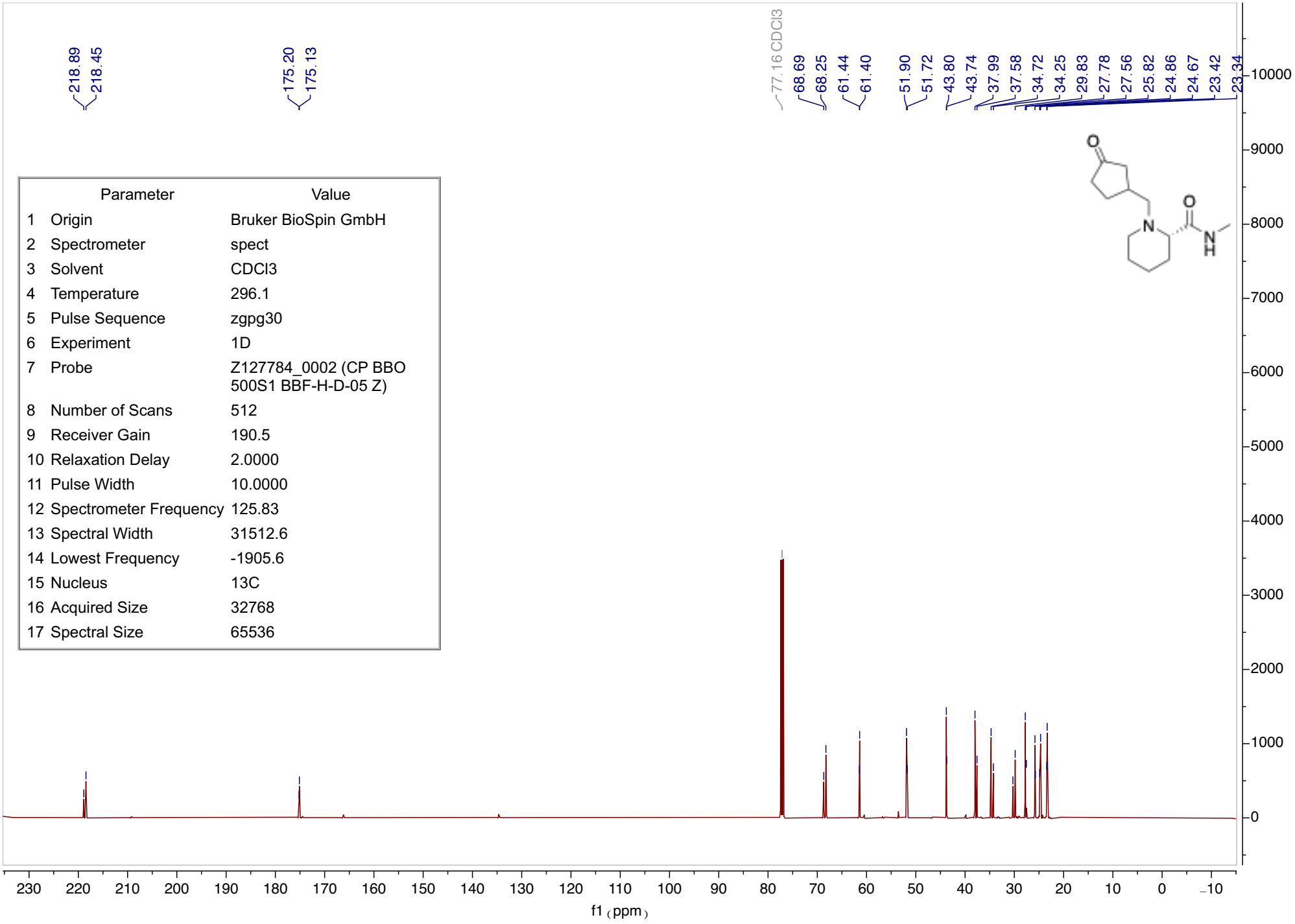
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

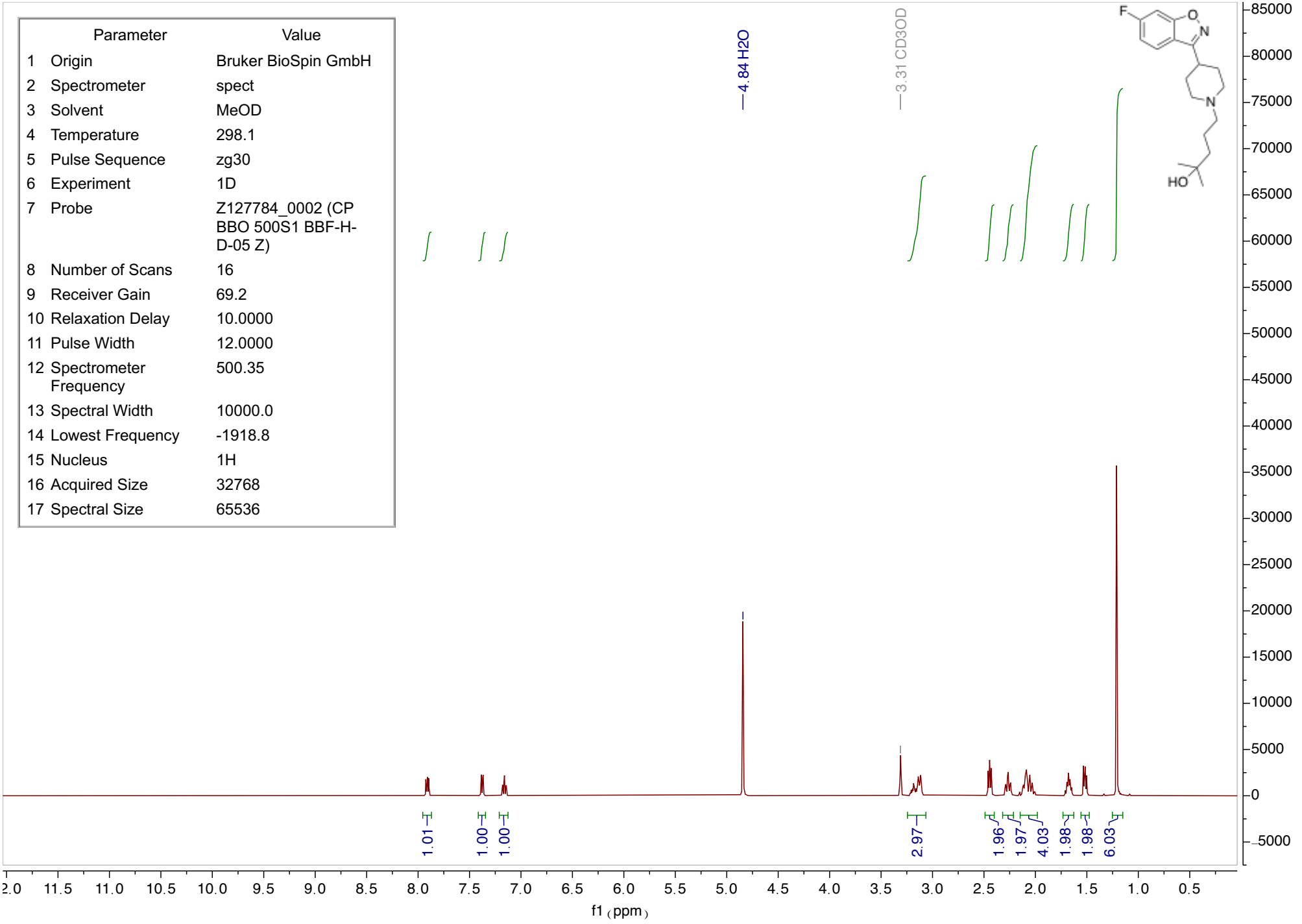


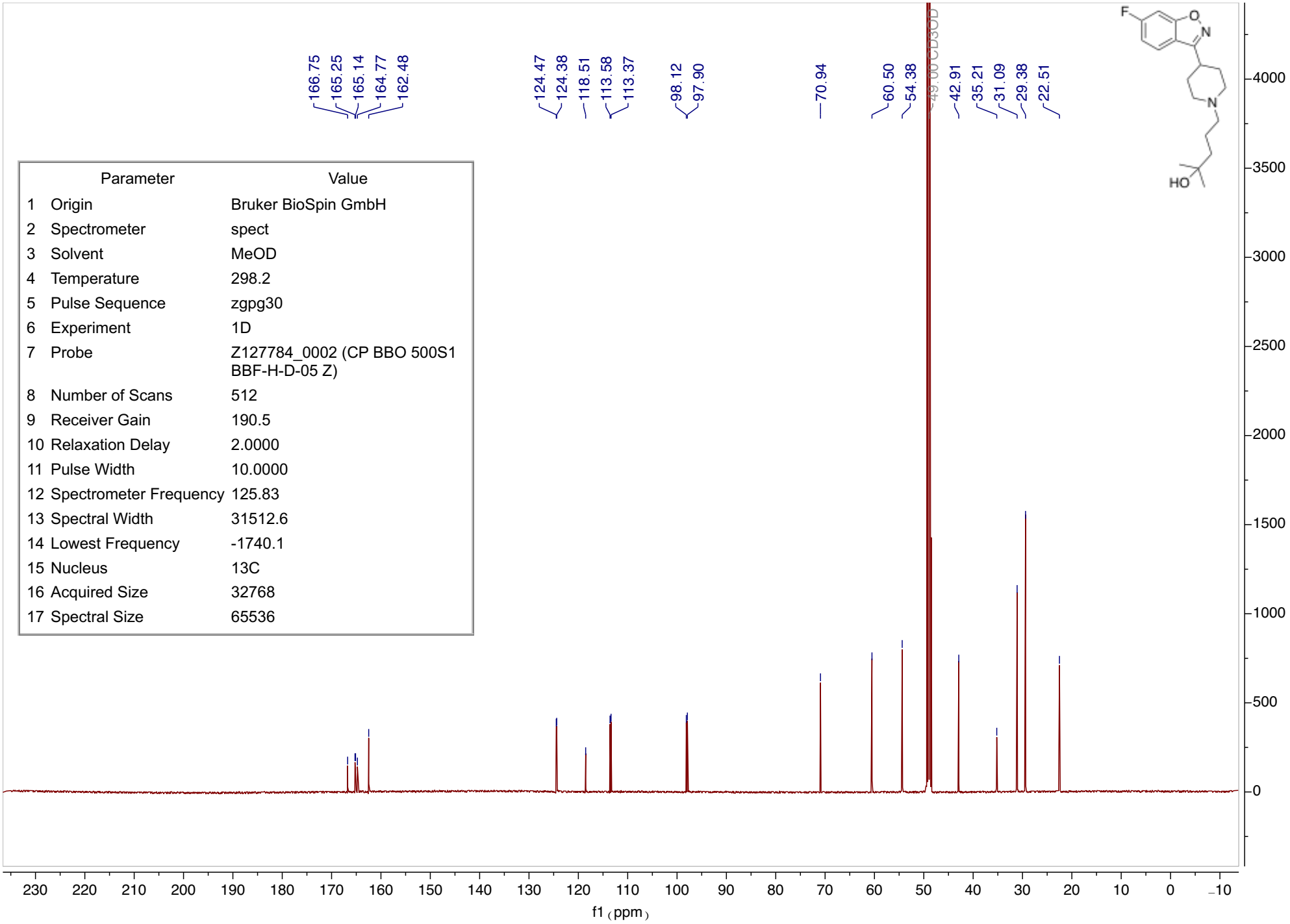
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536





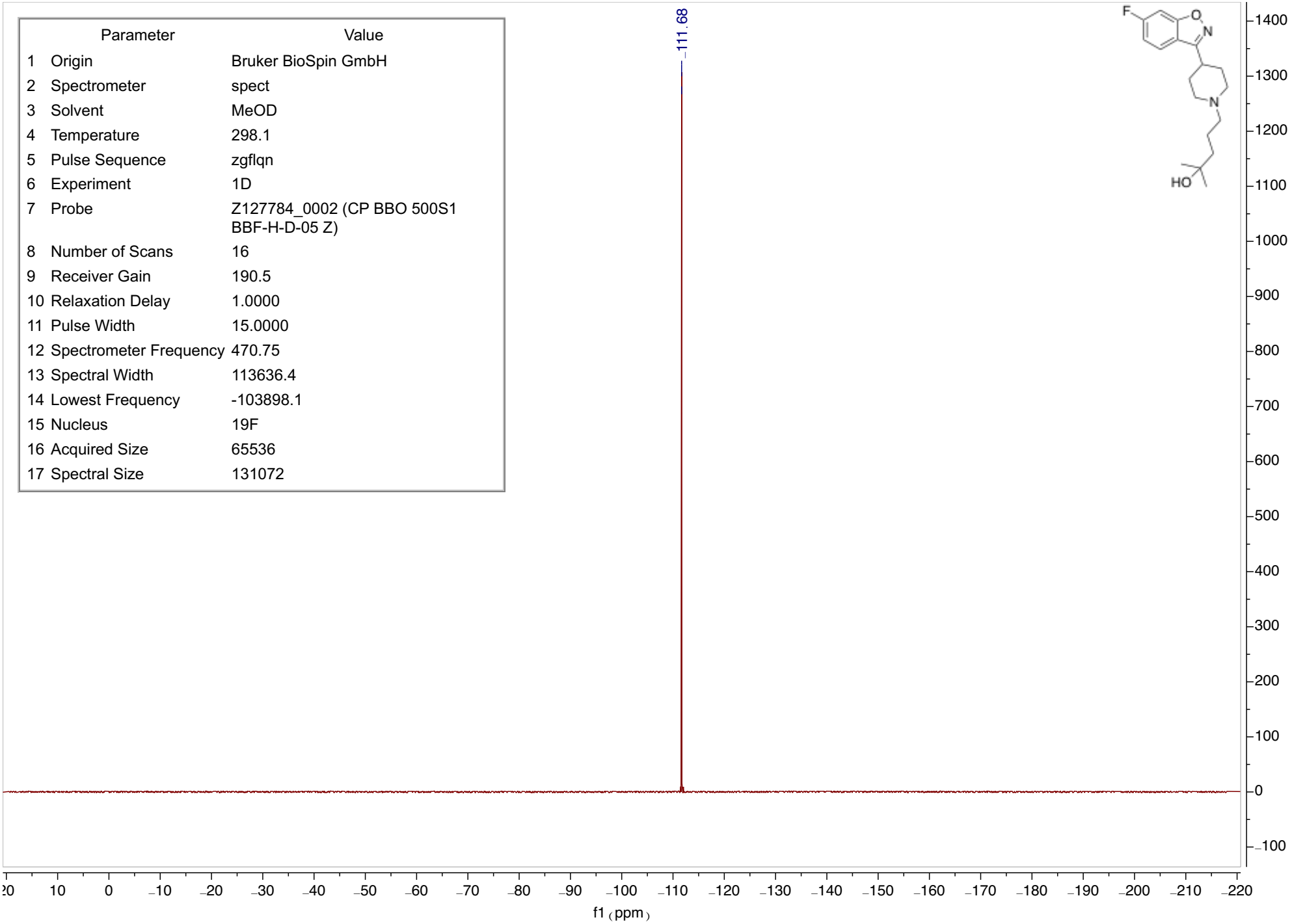
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1905.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent MeOD
4 Temperature 298.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 16
9 Receiver Gain 69.2
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 10000.0
14 Lowest Frequency -1918.8
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
4.84 H2O
3.31 CD3OD
F
O
N
N
HO
1.01
1.00
1.00
2.97
1.96
1.97
4.03
1.98
1.98
6.03
f1 (ppm)

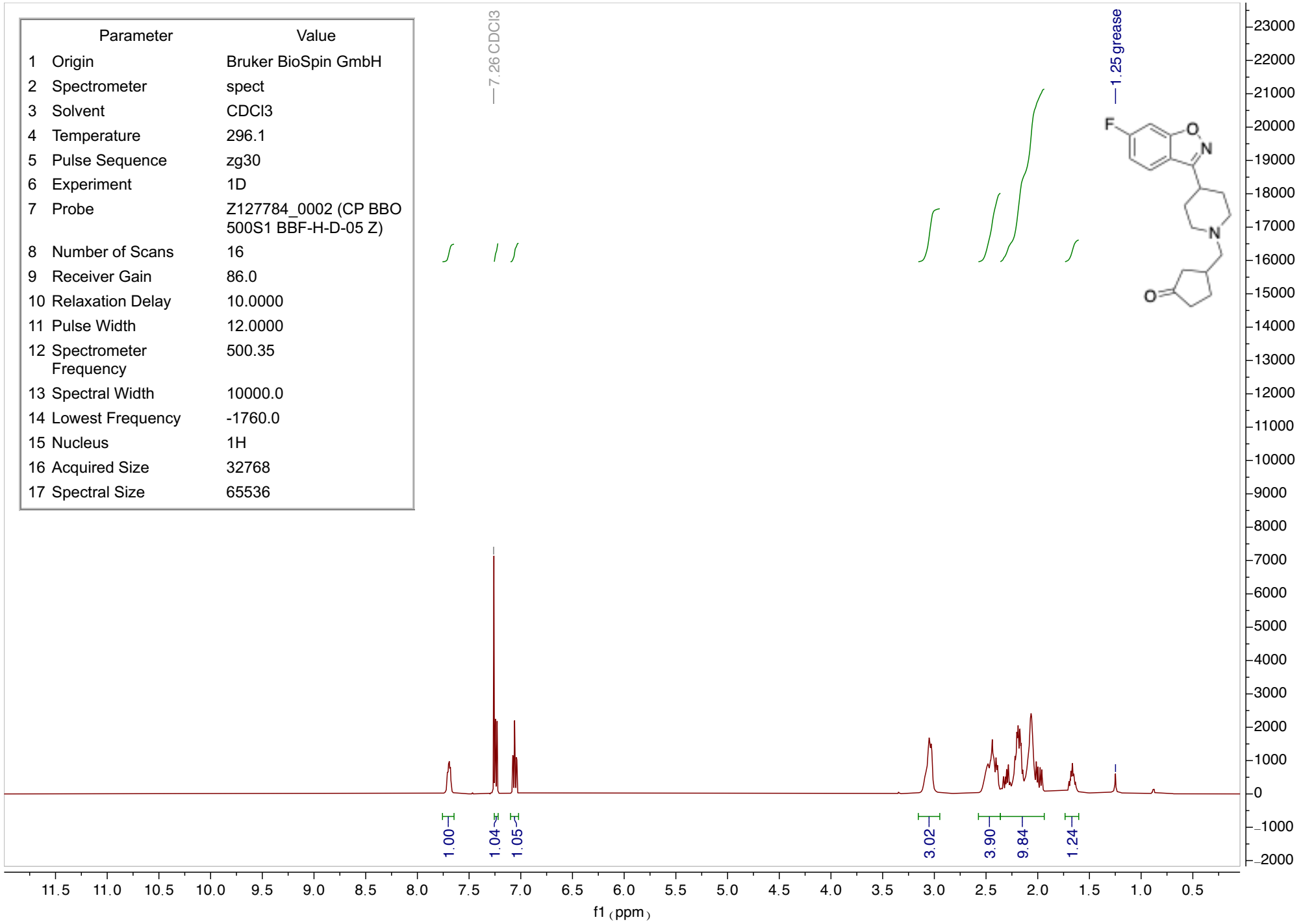


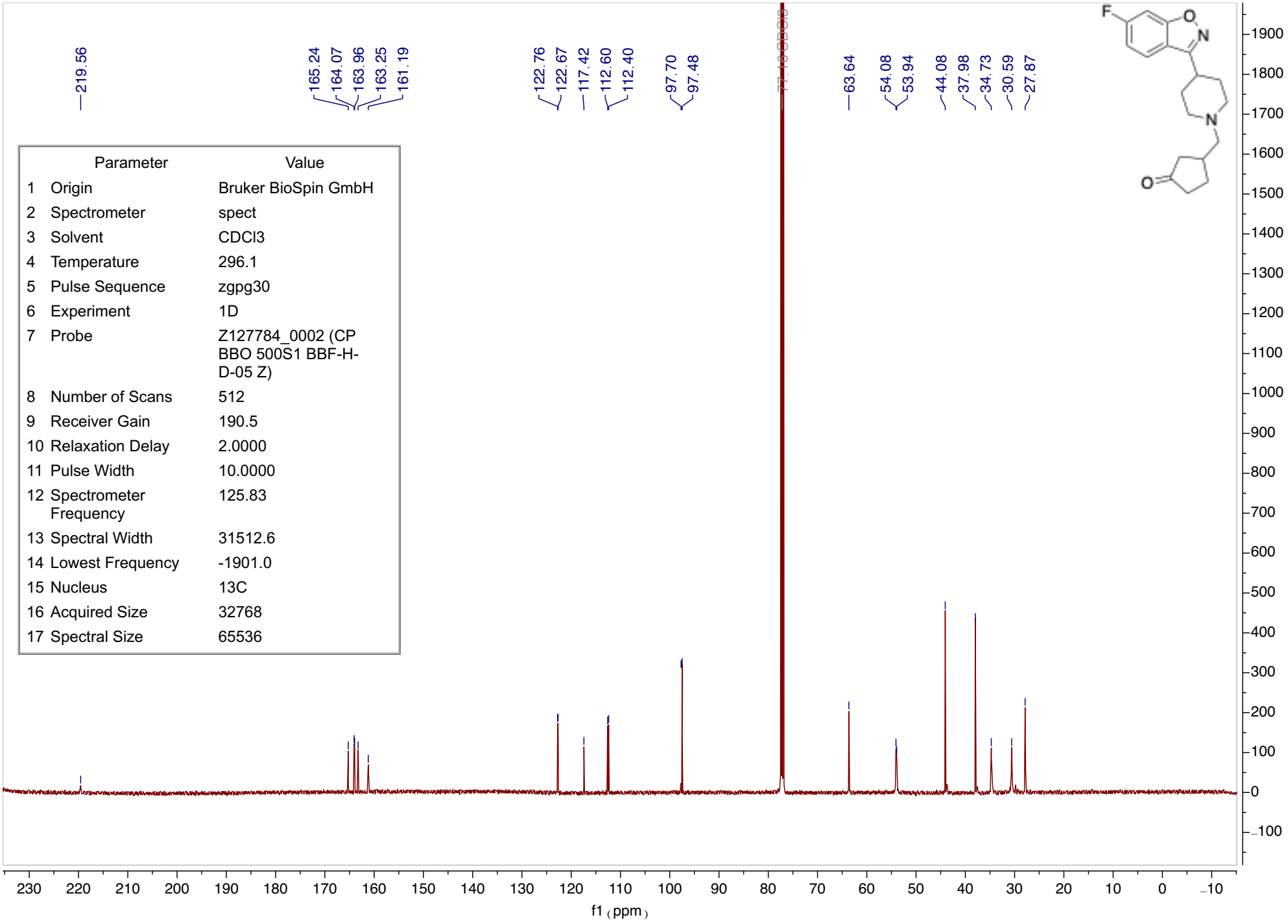
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1740.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



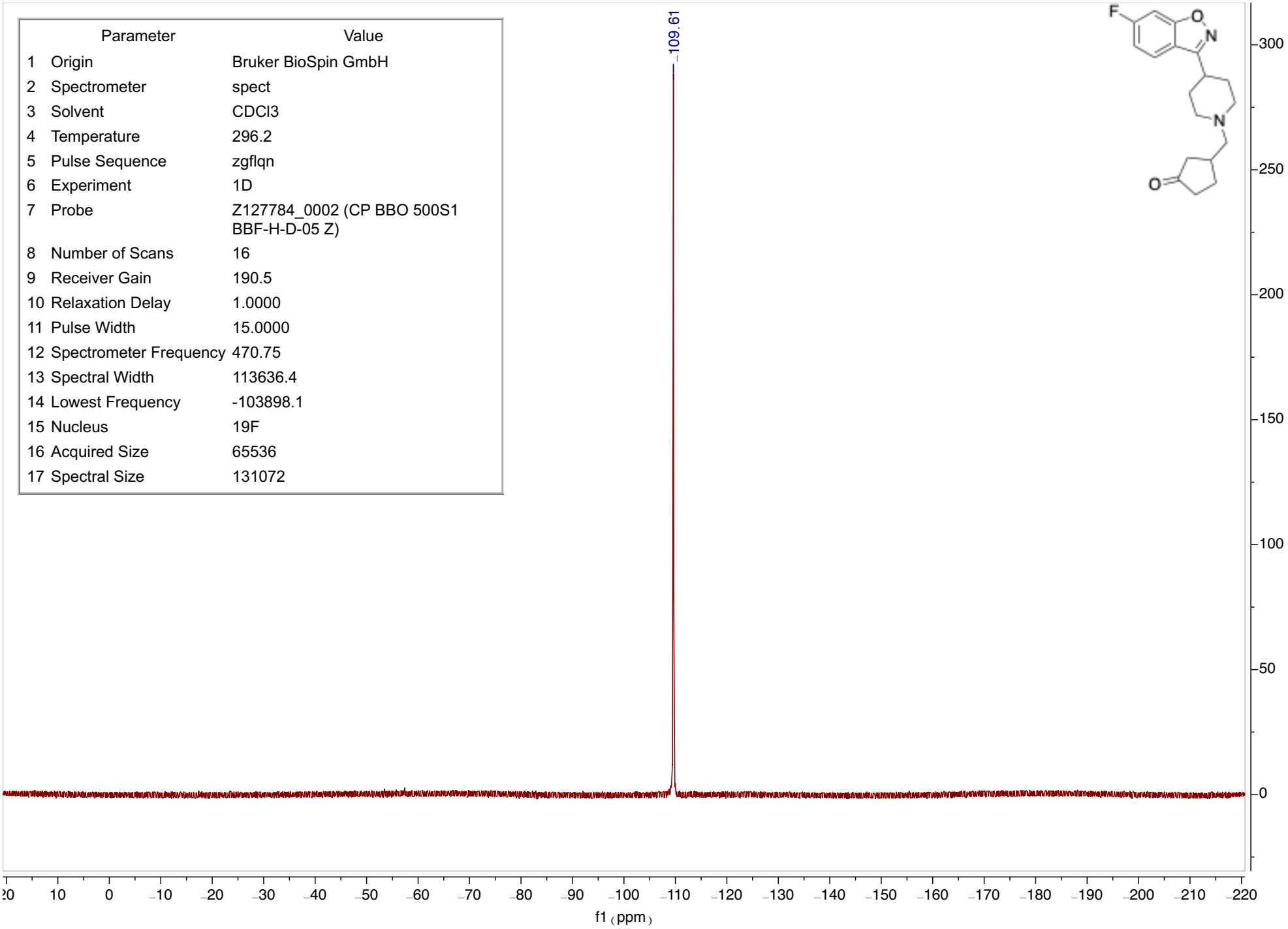
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

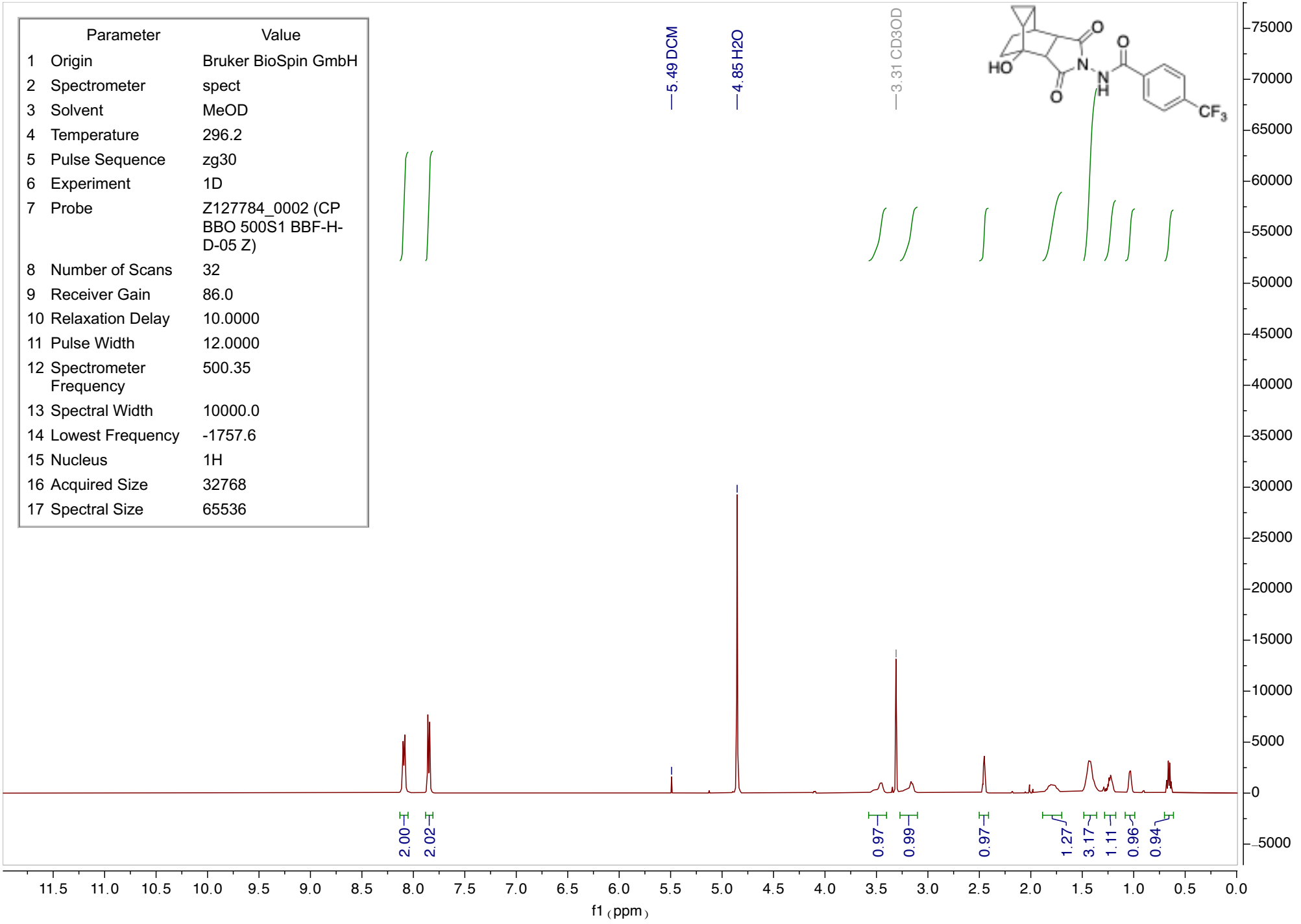


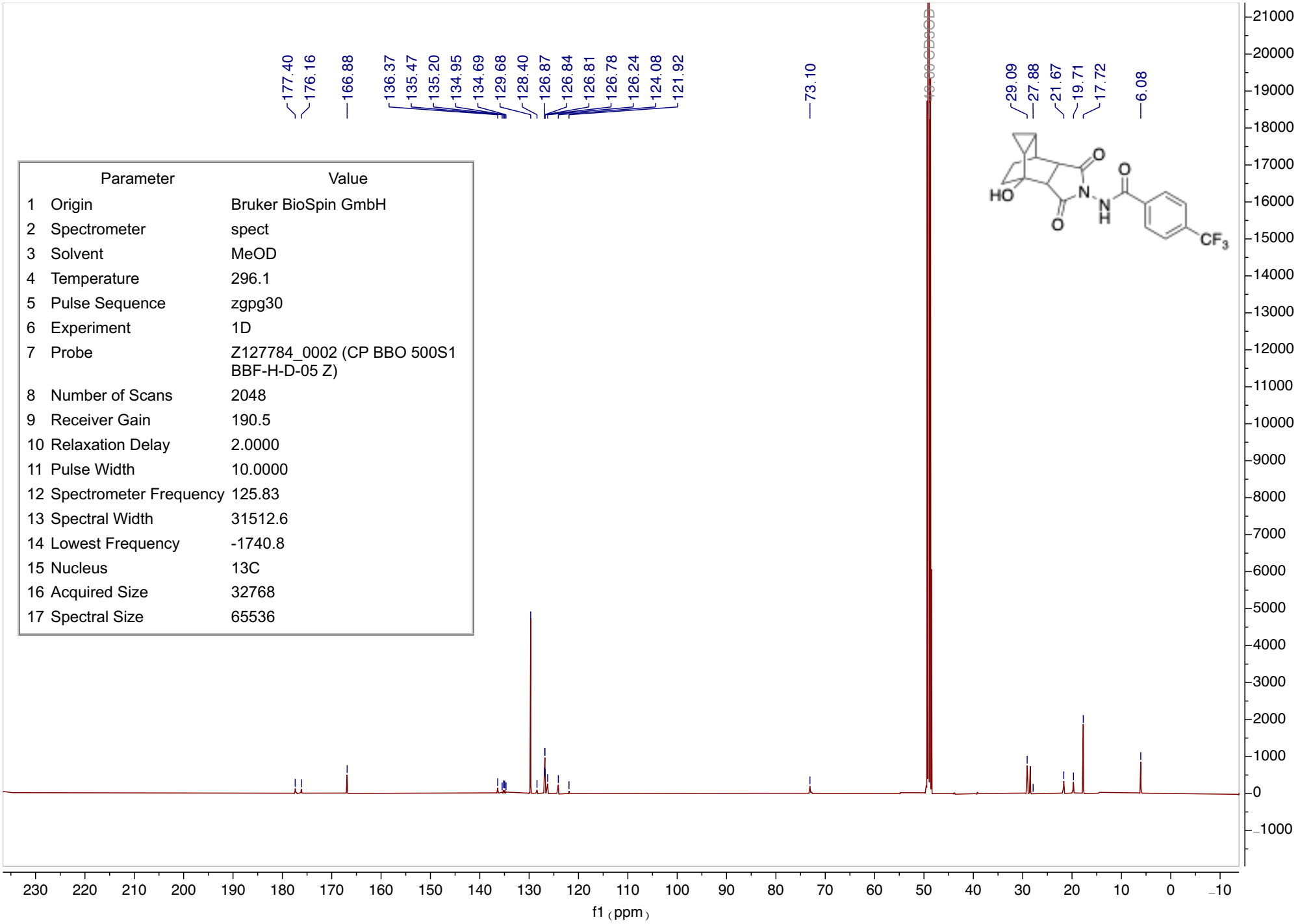


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

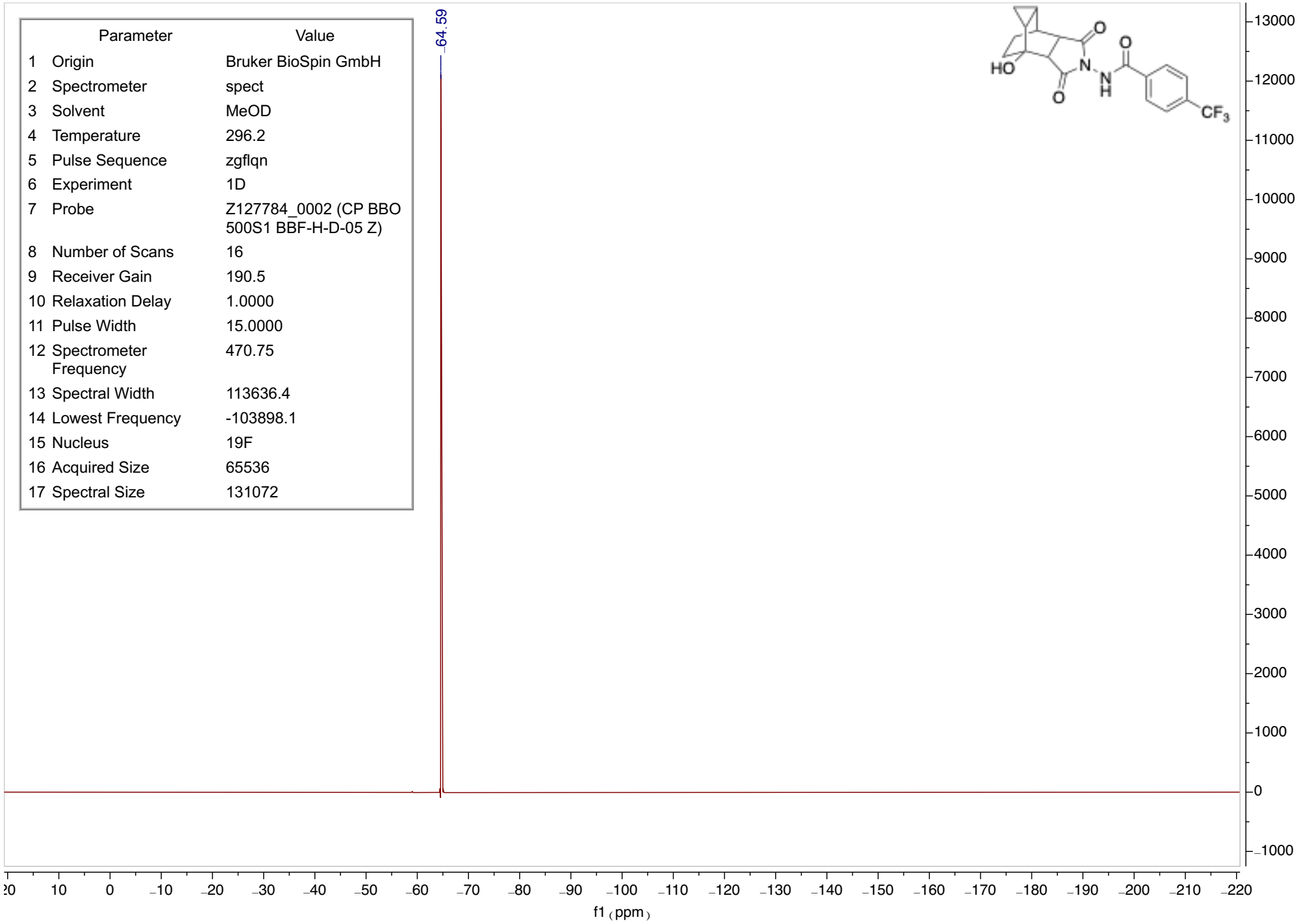


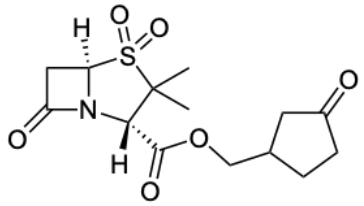

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent MeOD
4 Temperature 296.2
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 32
9 Receiver Gain 86.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 10000.0
14 Lowest Frequency -1757.6
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
5.49 DCM
4.85 H2O
3.31 CD3OD
HO
O
N
N
H
O
O
CF3
2.00
2.02
0.97
0.99
0.97
1.27
3.17
1.11
0.96
0.94
f1 (ppm)



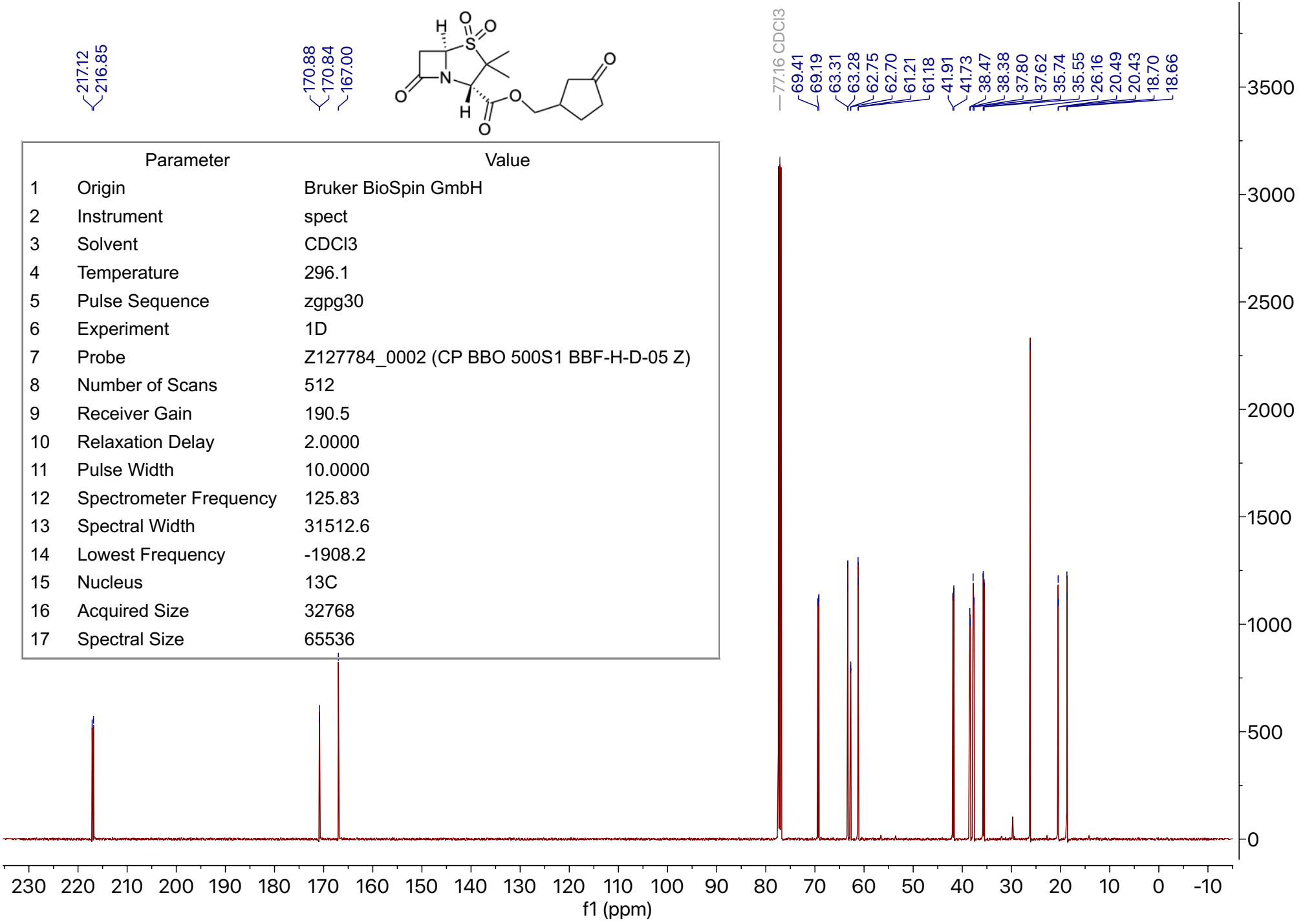
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2048
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1740.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

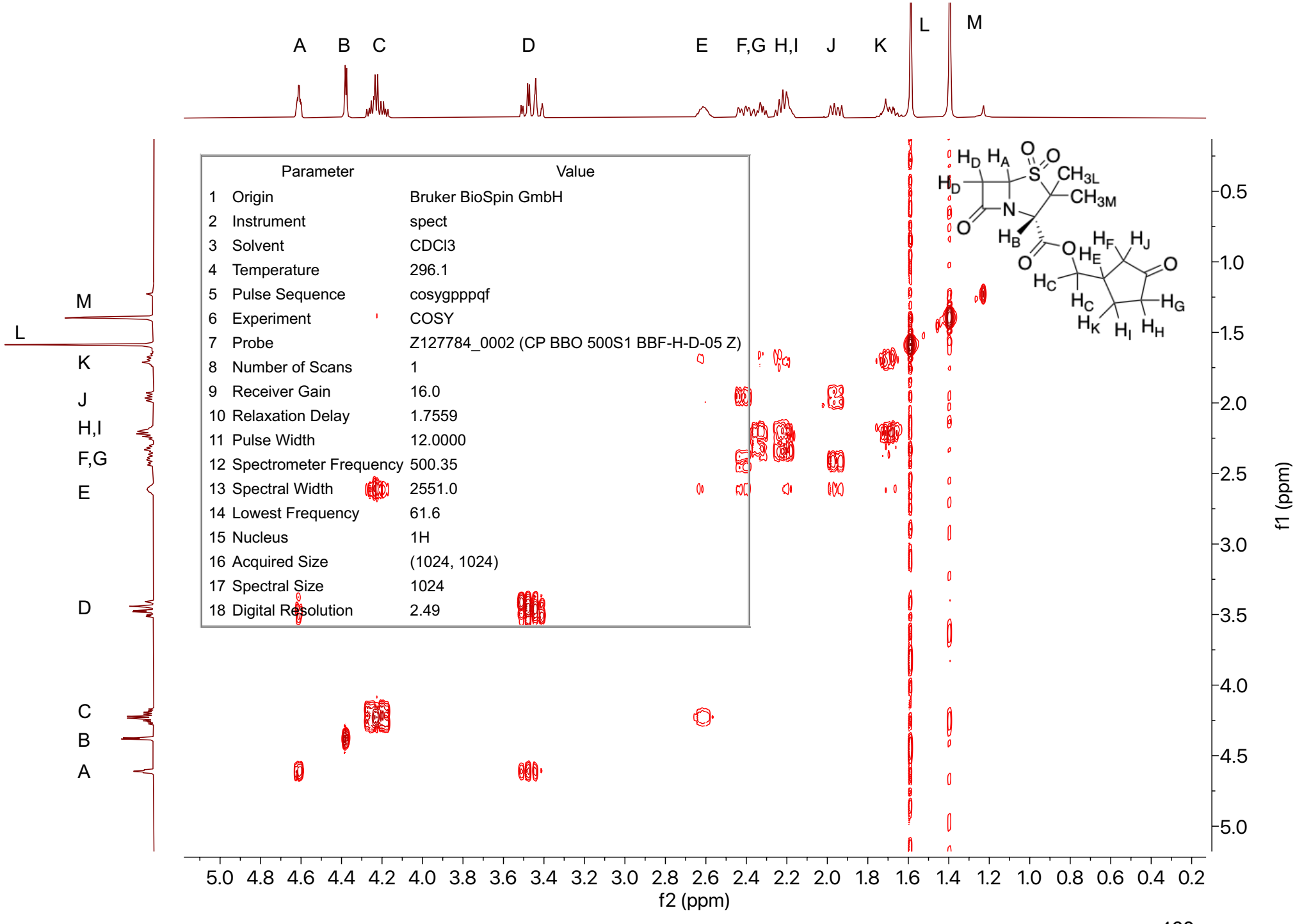




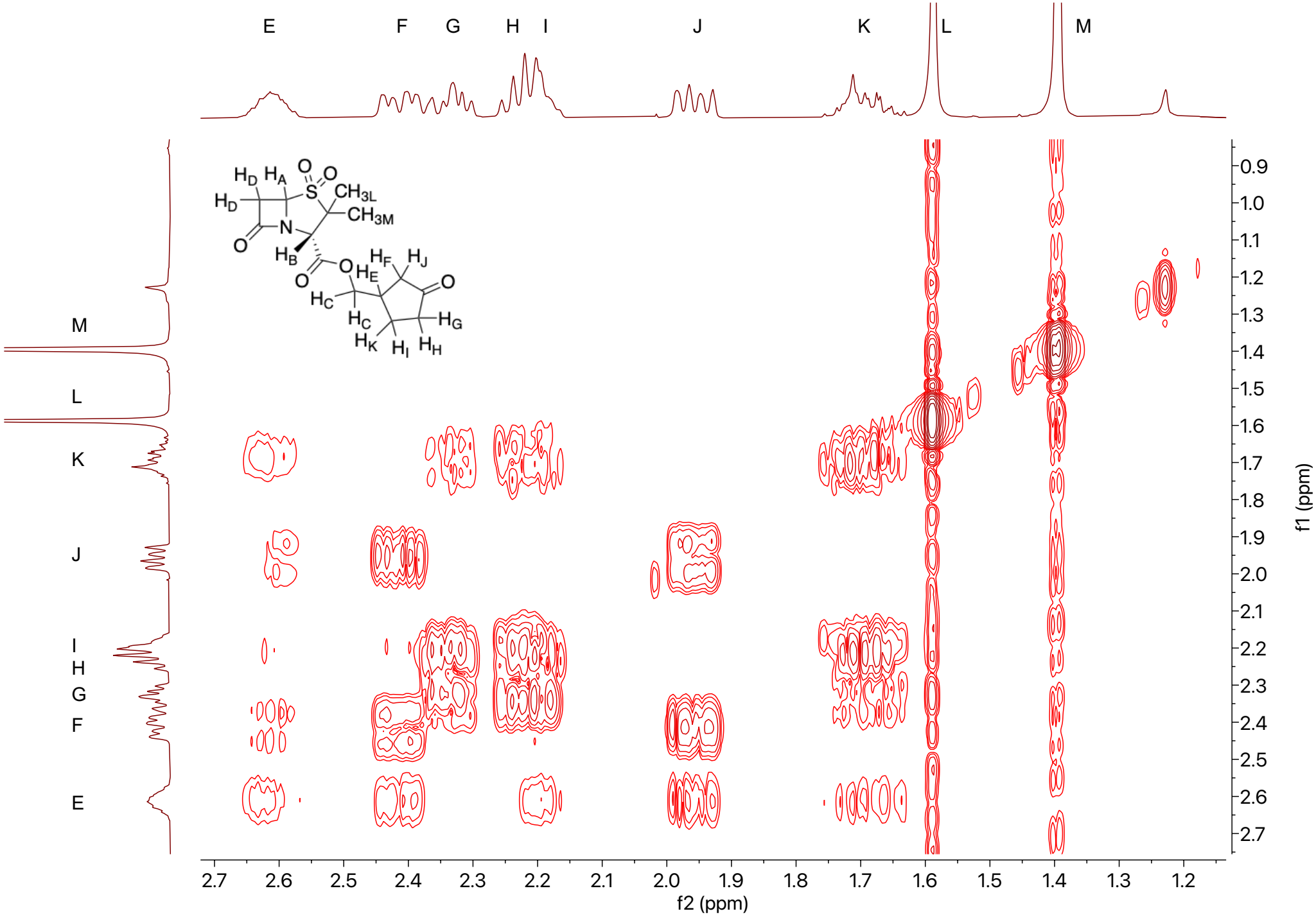
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

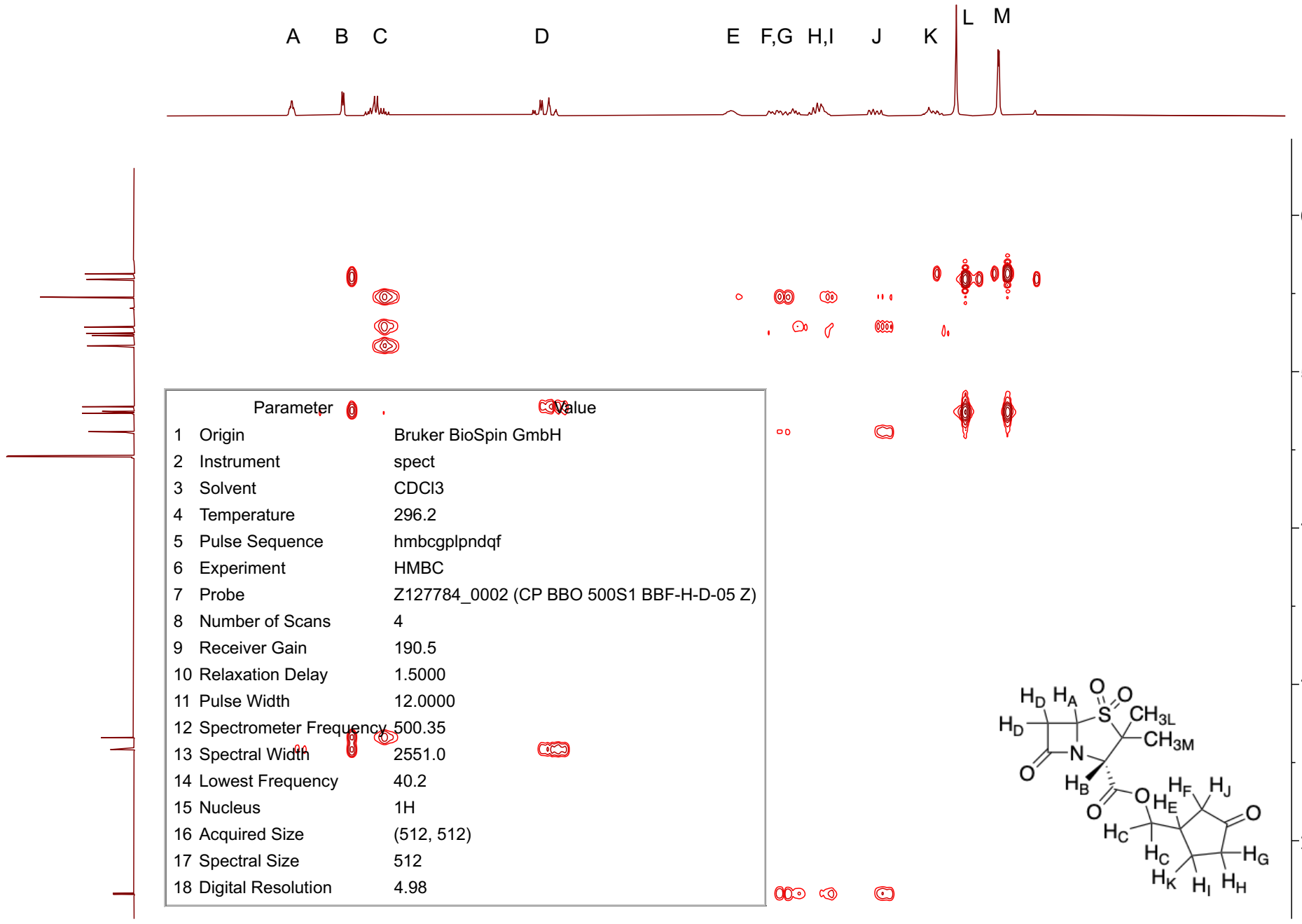


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1908.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

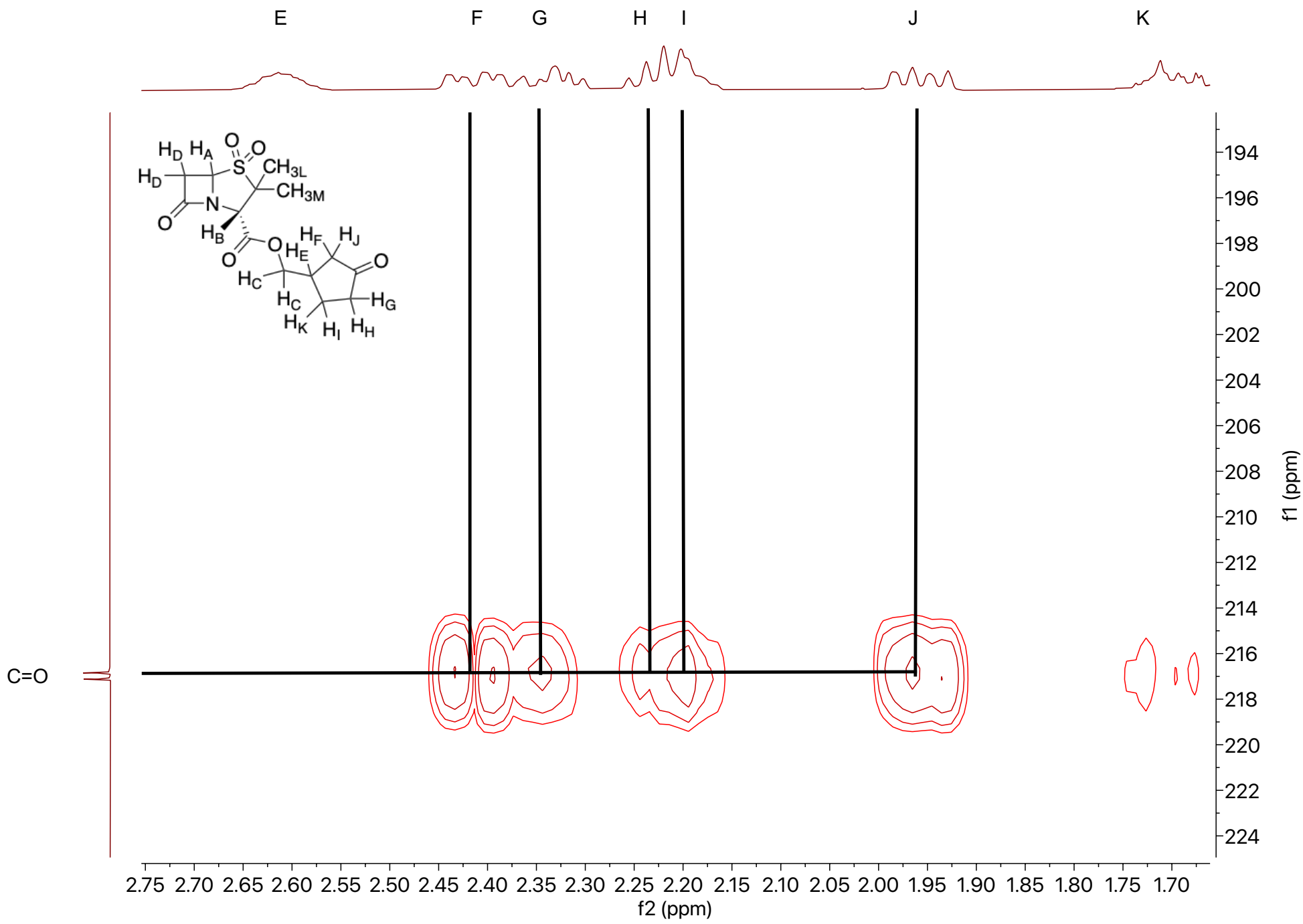


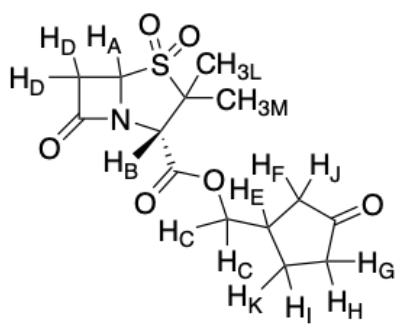
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	16.0
10	Relaxation Delay	1.7559
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	2551.0
14	Lowest Frequency	61.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024
18	Digital Resolution	2.49


E
F
G
H
I
J
K
L
M
M
L
K
J
I
H
G
F
E
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
f2 (ppm)
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2.0
2.1
2.2
2.3
2.4
2.5
2.6
2.7
f1 (ppm)

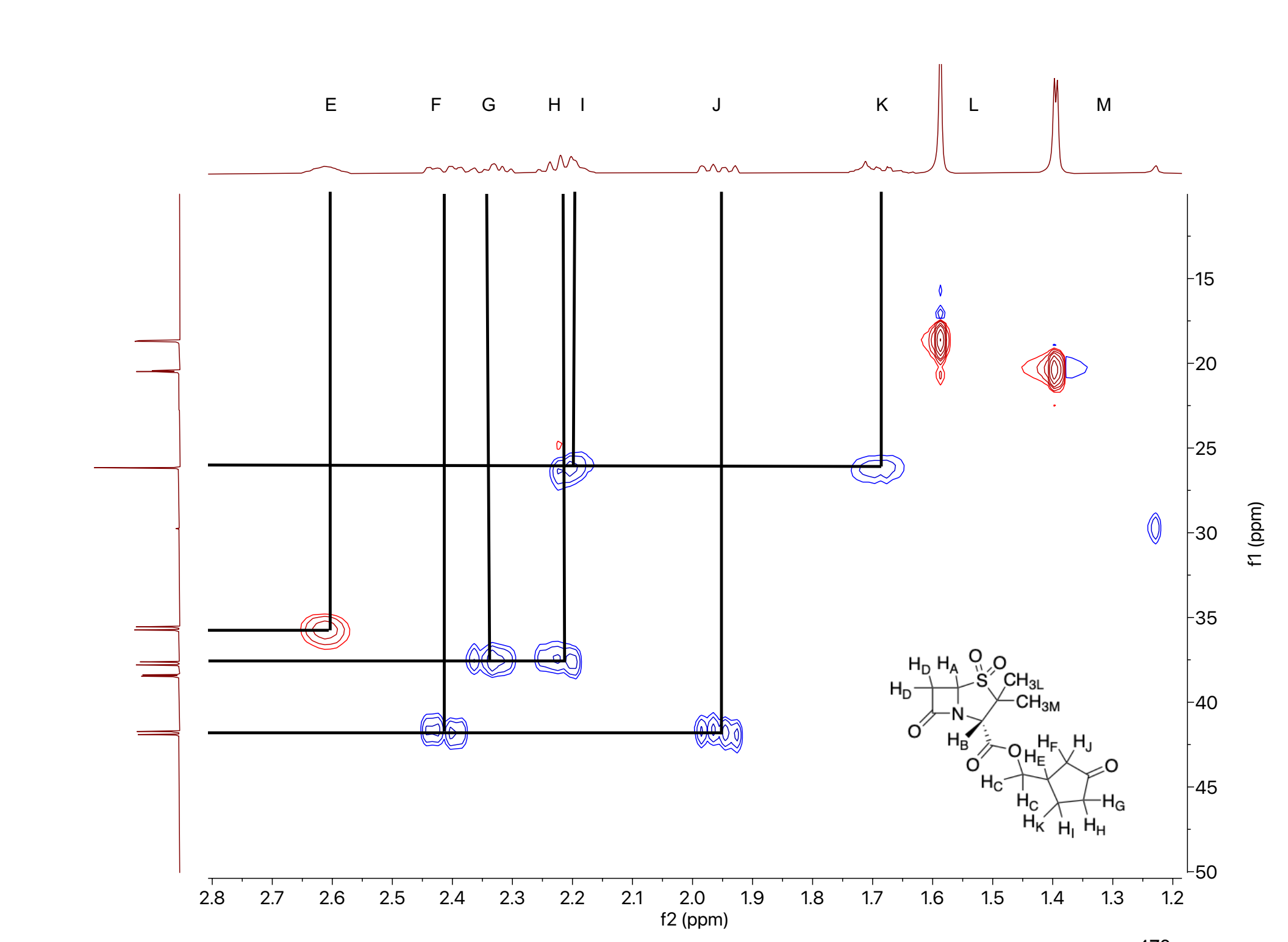


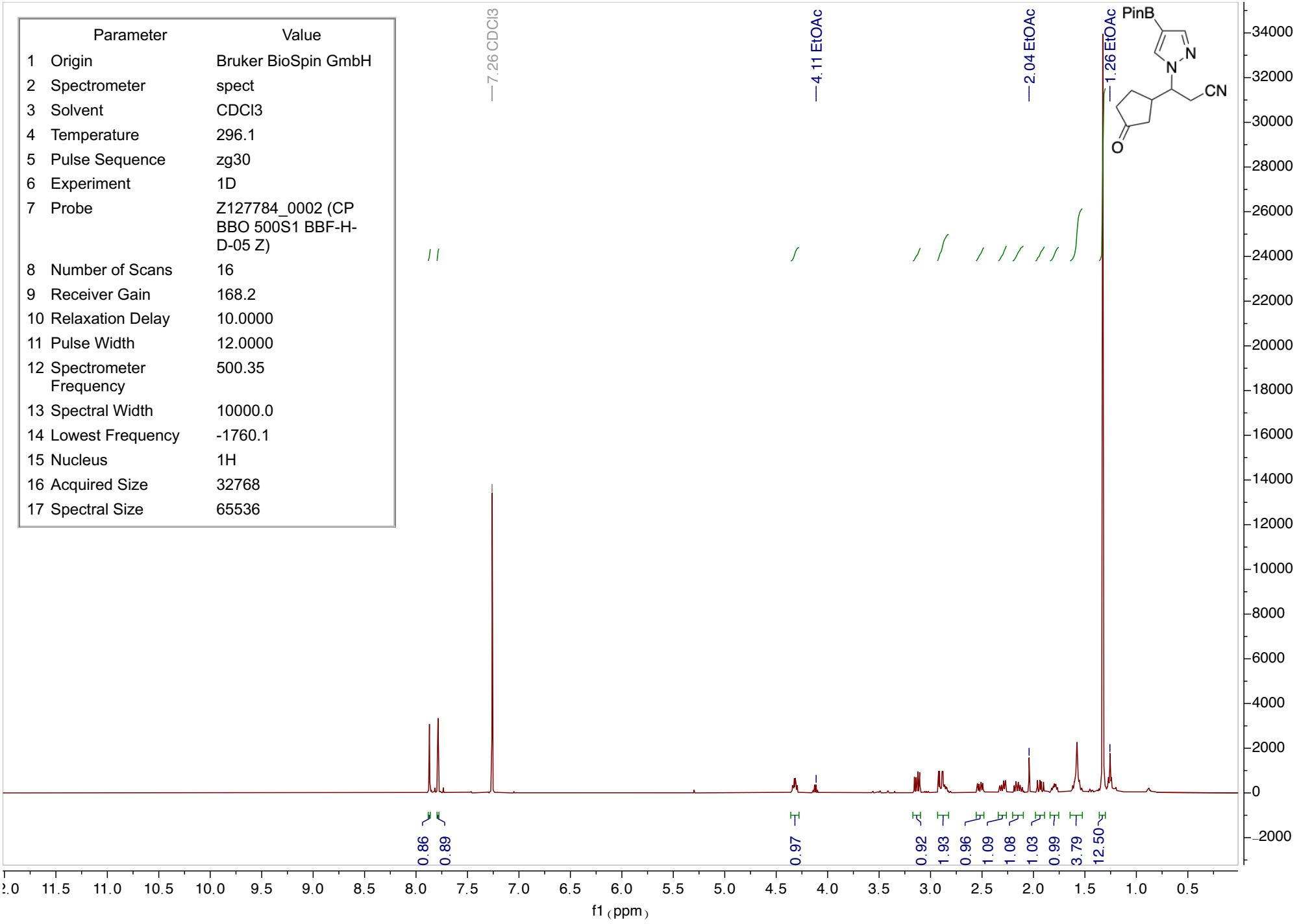
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	2551.0
14	Lowest Frequency	40.2
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	4.98


E
F
G
H
I
J
K
C=O
f1 (ppm)
f2 (ppm)
194
196
198
200
202
204
206
208
210
212
214
216
218
220
222
224
2.75 2.70 2.65 2.60 2.55 2.50 2.45 2.40 2.35 2.30 2.25 2.20 2.15 2.10 2.05 2.00 1.95 1.90 1.85 1.80 1.75 1.70
H_D H_A
H_D
CH_{3L}
CH_{3M}
H_B
H_F H_J
H_E
H_C
H_C
H_G
H_K H_I H_H

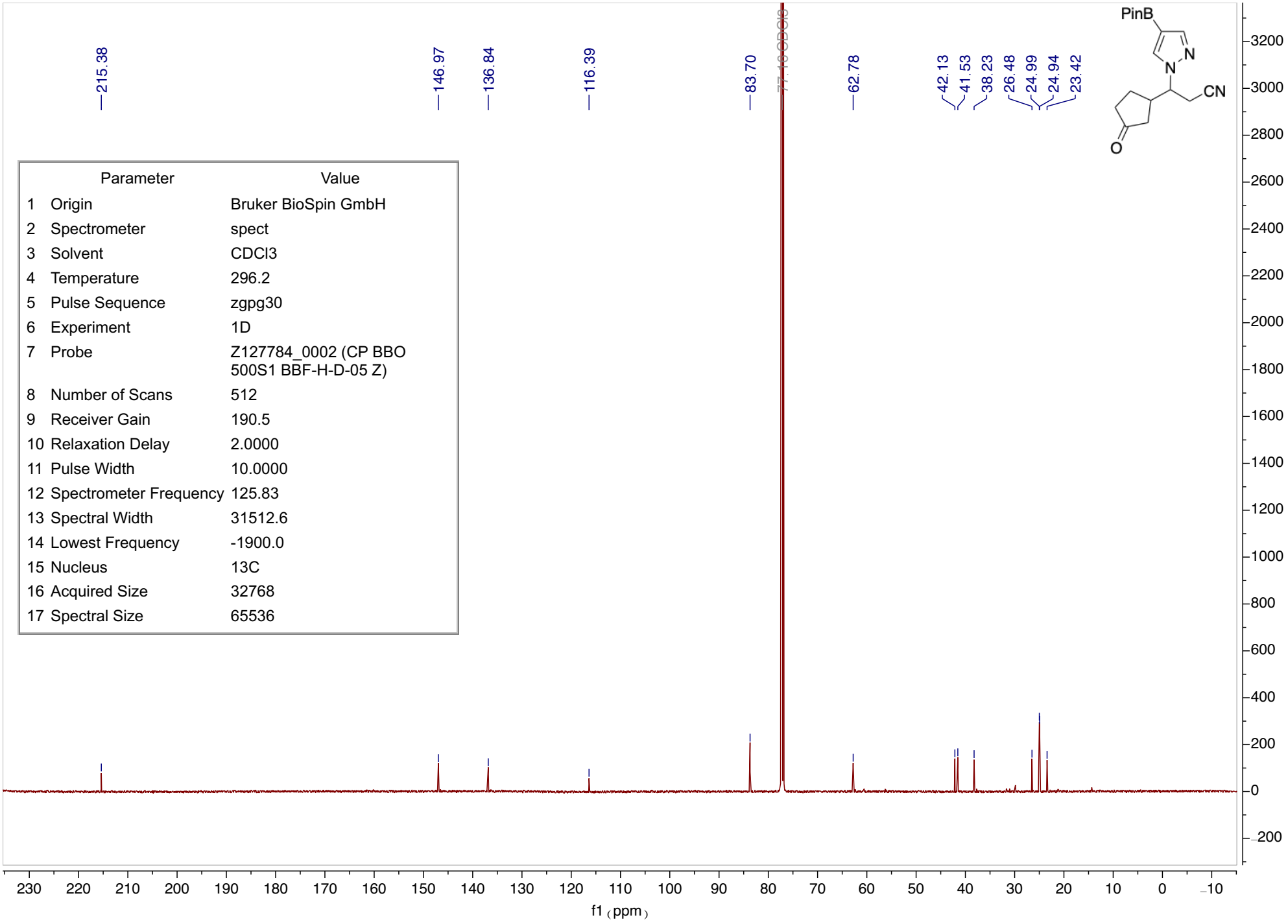


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	2551.0
14	Lowest Frequency	61.6
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512
18	Digital Resolution	4.98

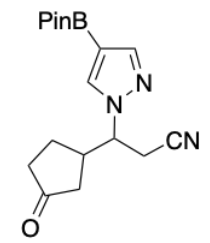

E
F
G
H
I
J
K
L
M
15
20
25
30
35
40
45
50
f1 (ppm)
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
f2 (ppm)
H_D H_A
H_D
O
O
S
CH_{3L}
CH_{3M}
N
O
H_B
O
O
H_E
H_F
H_J
H_C
H_C
O
H_G
H_K
H_I
H_H



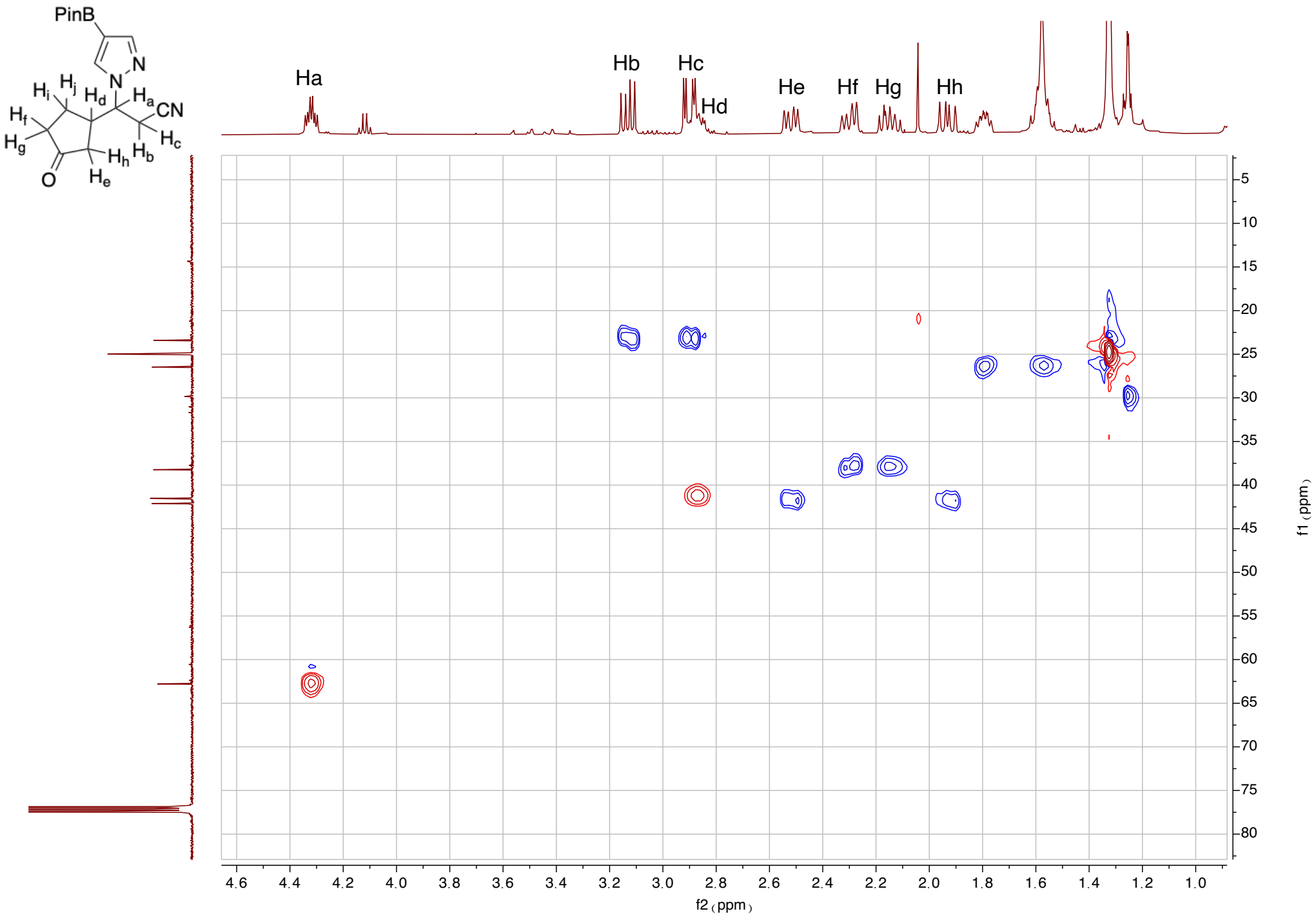
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	168.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

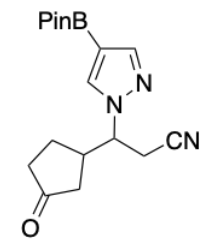


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

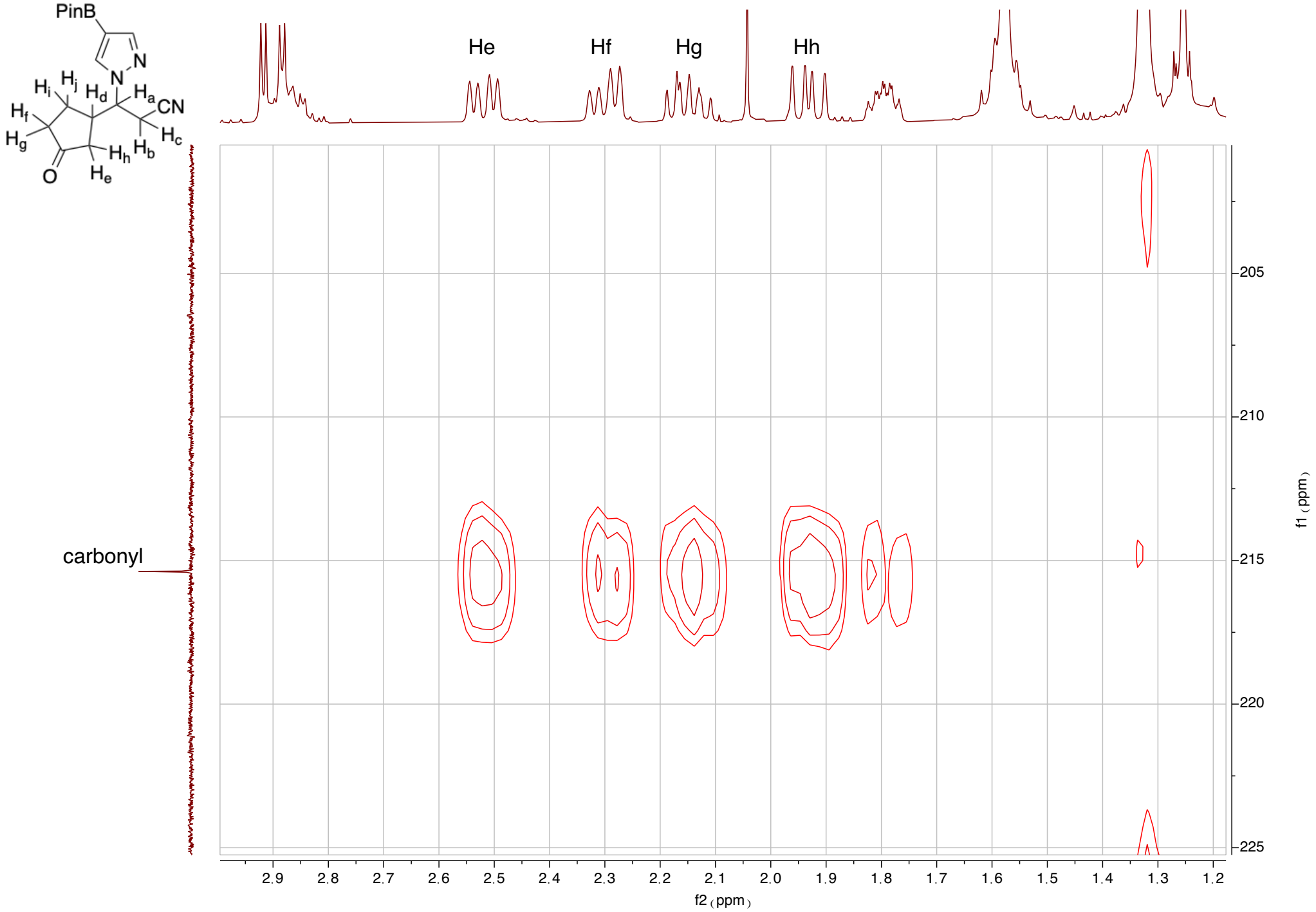


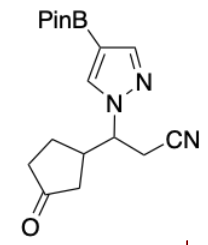
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-86.6
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


PinB
N
N
Hi
Hj
Hd
Ha
CN
Hf
Hg
Hc
Hh
Hb
O
He
Ha
Hb
Hc
Hd
He
Hf
Hg
Hh
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
f1 (ppm)
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
f2 (ppm)

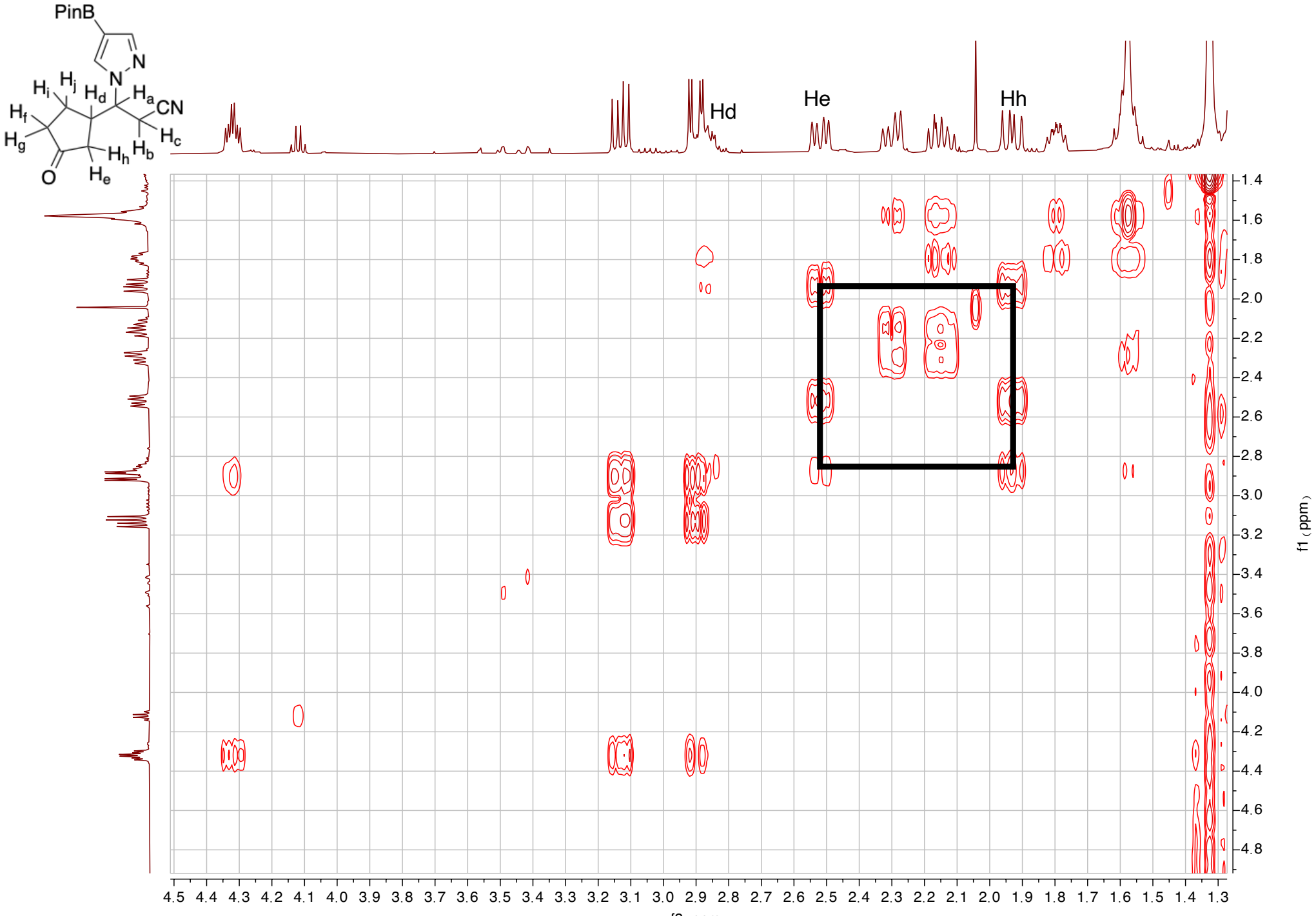


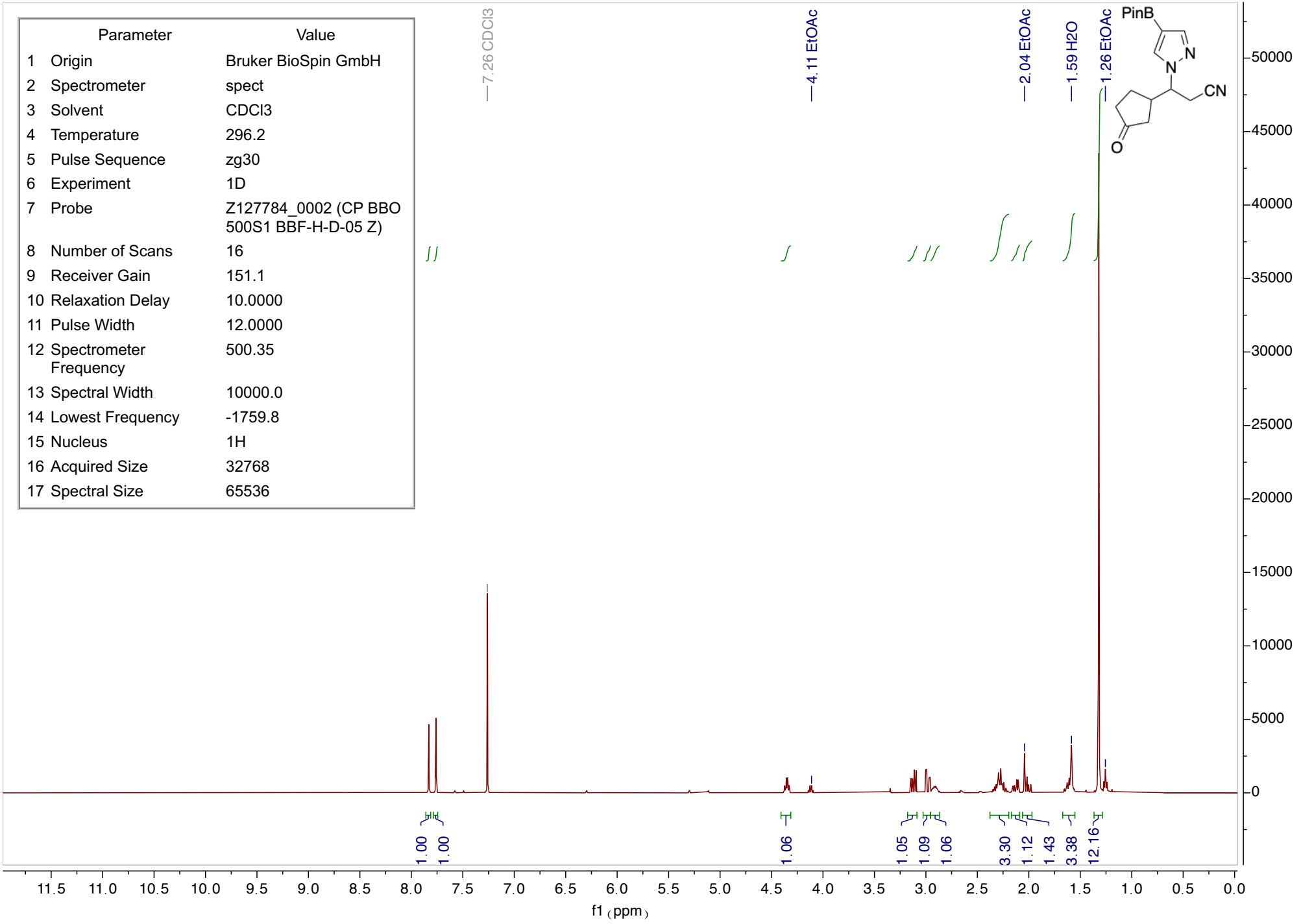
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-89.7
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


PinB
N
N
Hi
Hj
Hd
Ha
CN
Hf
Hg
Hc
Hh
Hb
O
He
He
Hf
Hg
Hh
carbonyl
205
210
215
220
225
f1 (ppm)
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
f2 (ppm)

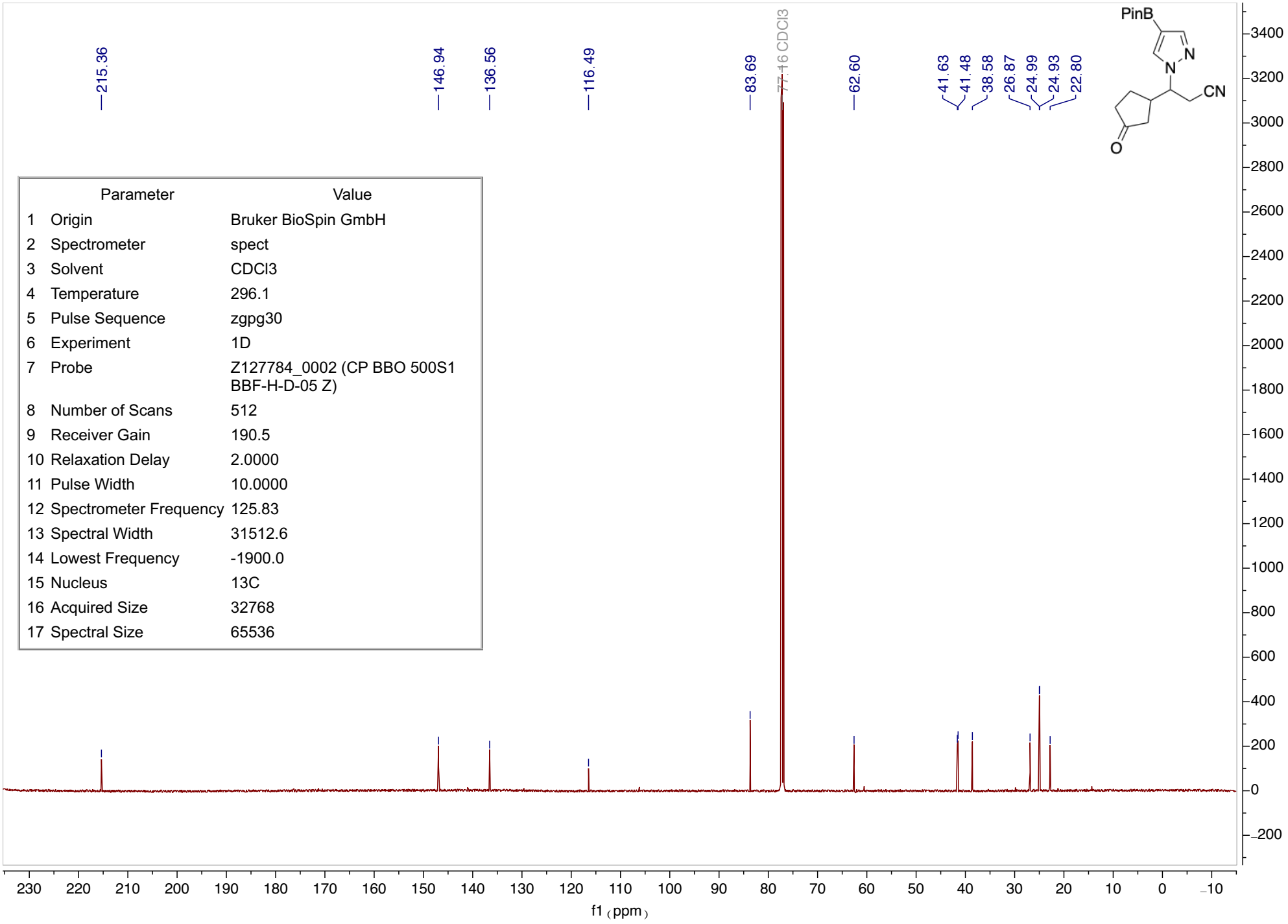


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	94.3
10	Relaxation Delay	1.9279
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-86.7
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

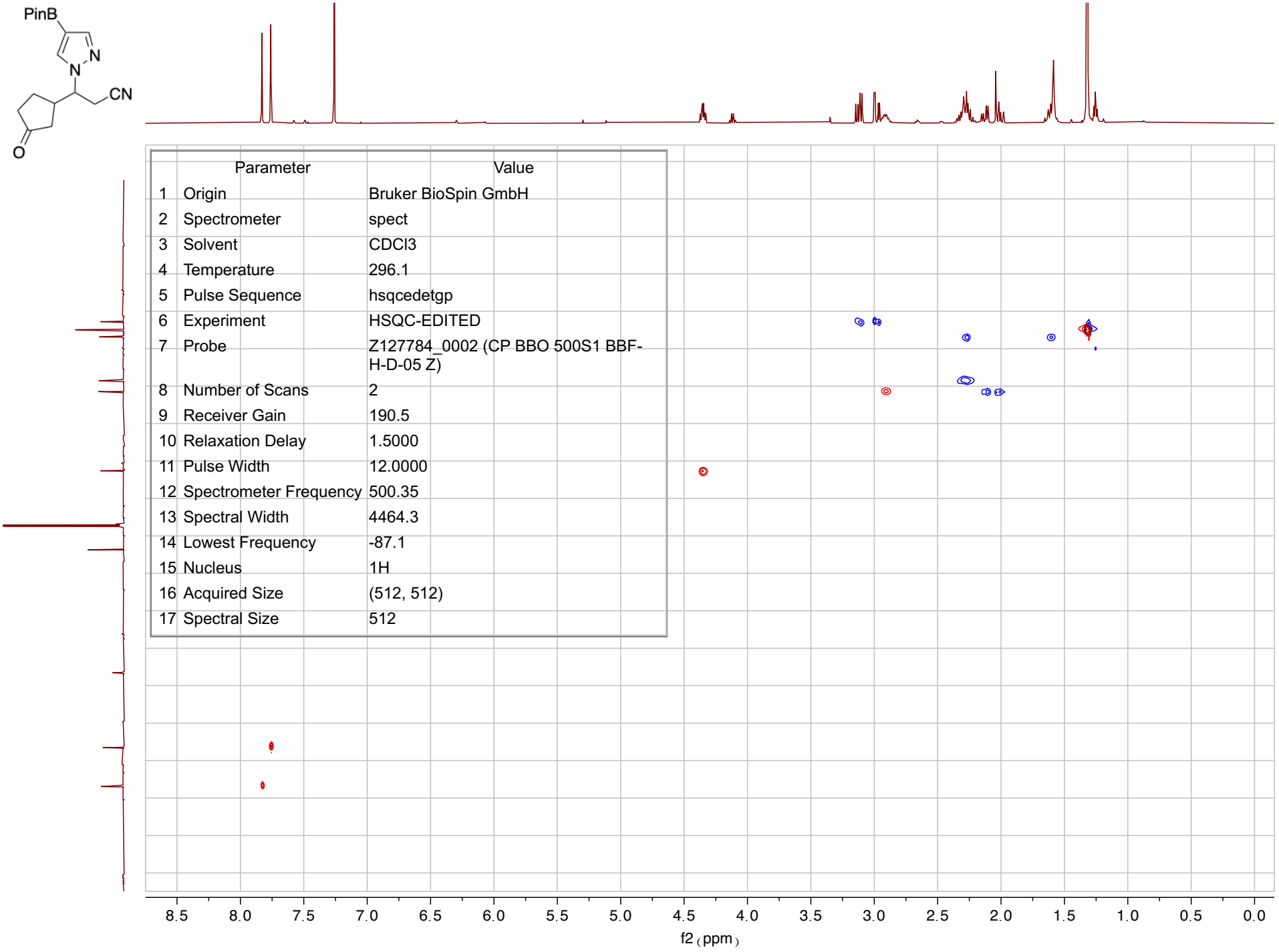

PinB
N
N
Hi
Hj
Hd
Ha
CN
Hf
Hg
Hc
Hh
Hb
O
He
Hd
He
Hh
f1 (ppm)
4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3
1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8 4.0 4.2 4.4 4.6 4.8



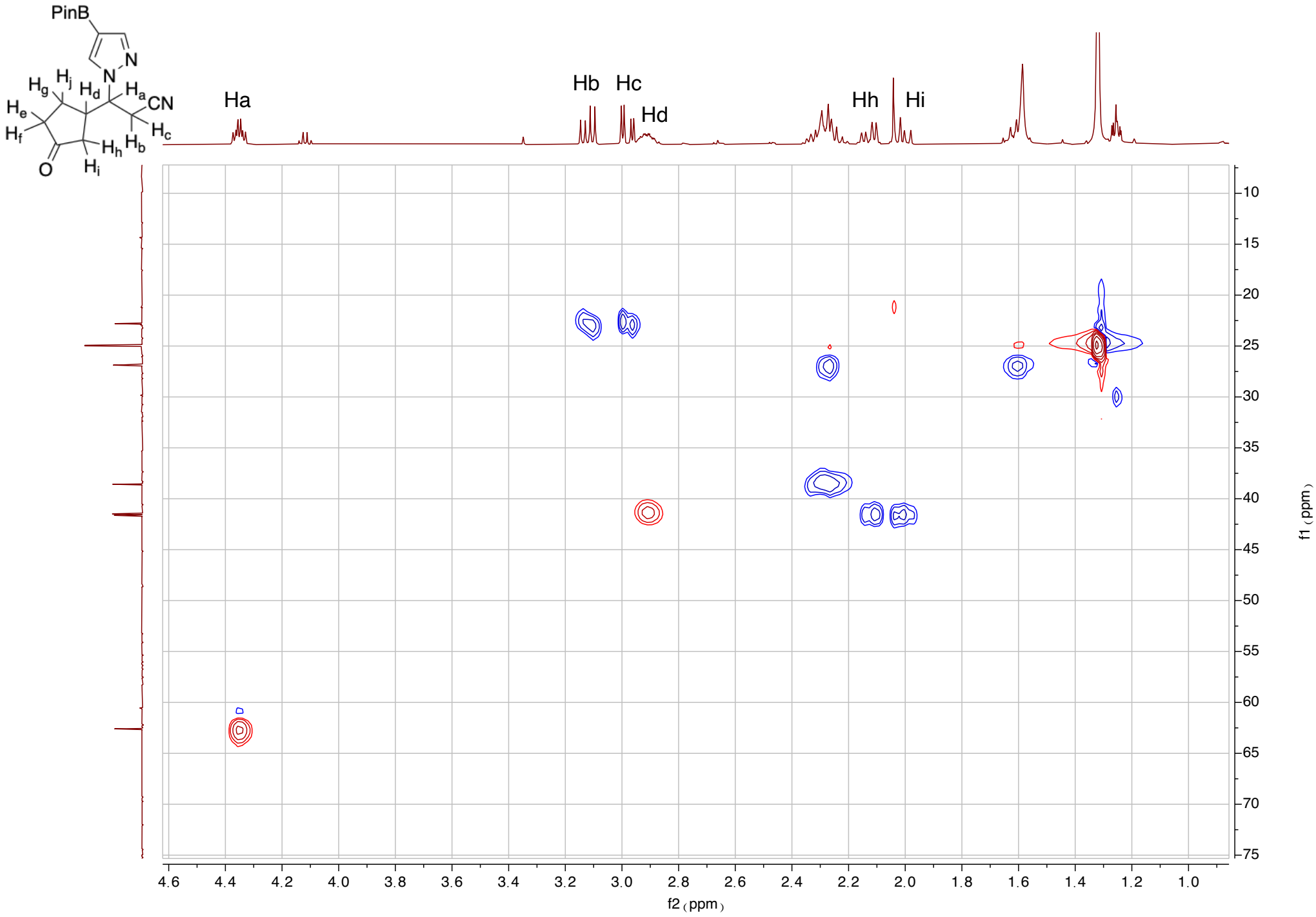
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	151.1
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

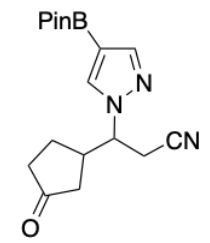


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

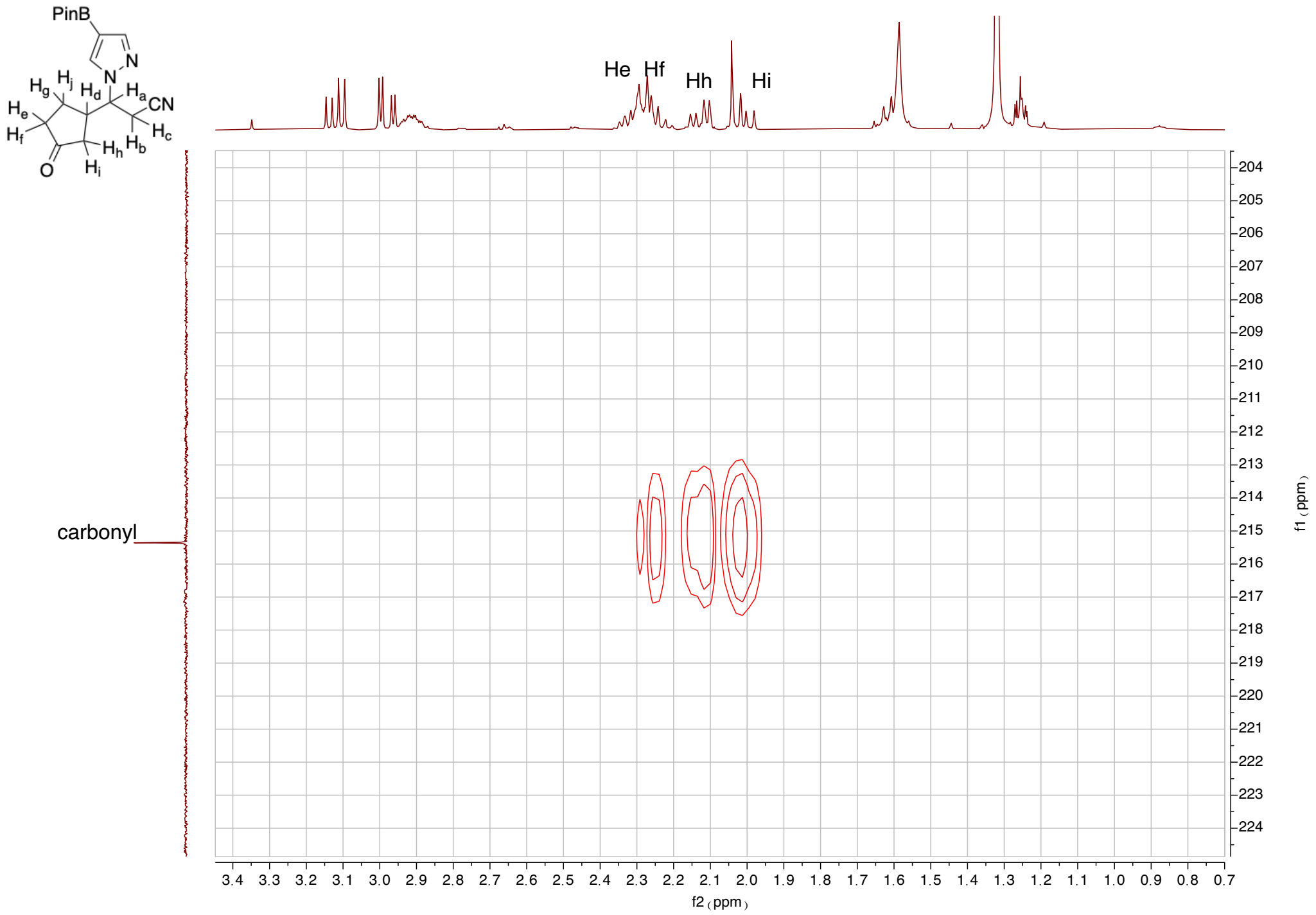


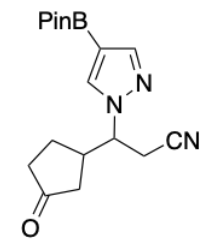
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-87.1
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


PinB
N
N
Hg
Hj
Hd
Ha
CN
He
Hf
Hc
Hh
Hb
O
Hi
Ha
Hb
Hc
Hd
Hh
Hi
f2 (ppm)
f1 (ppm)
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
10
15
20
25
30
35
40
45
50
55
60
65
70
75

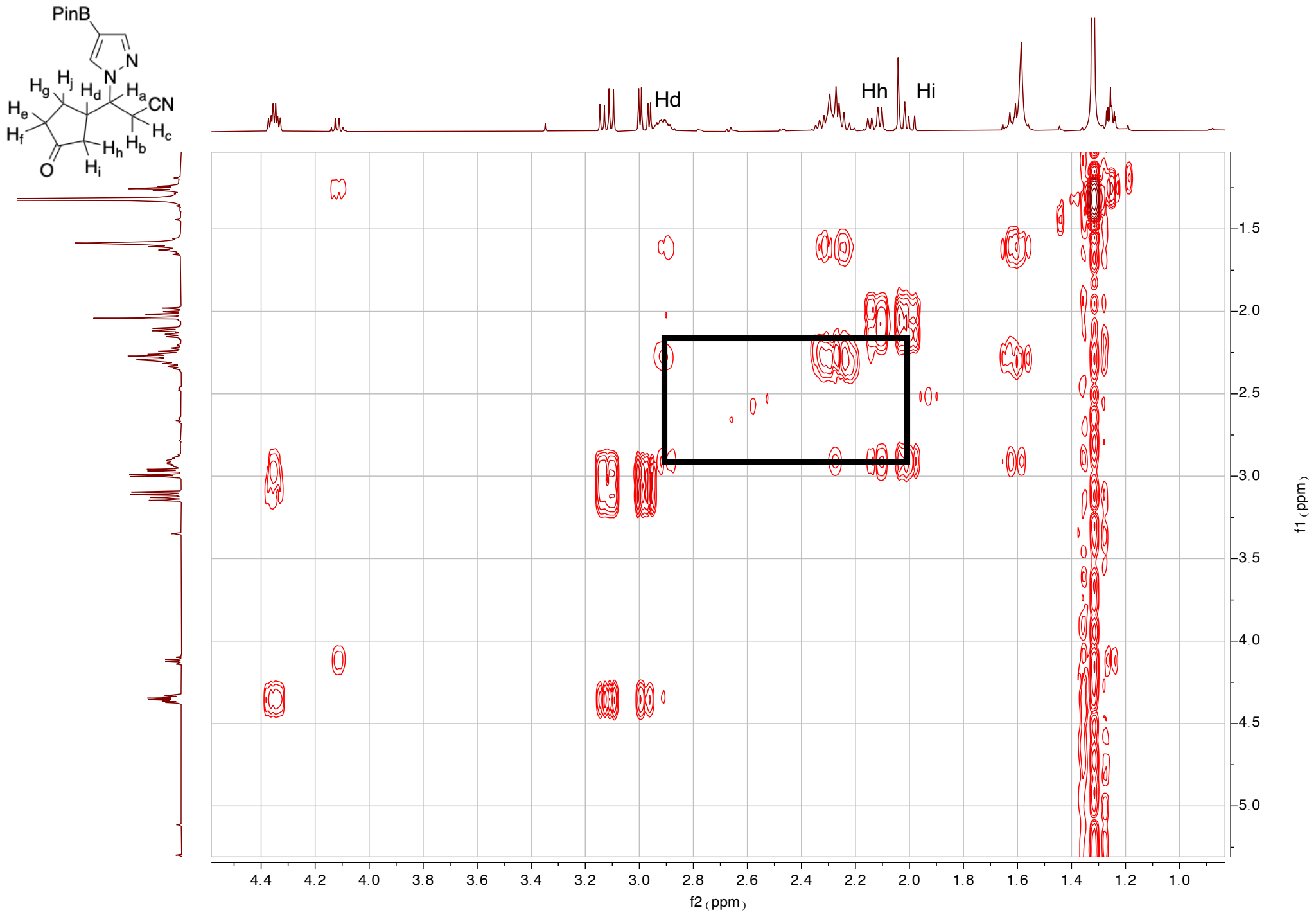


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-82.8
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

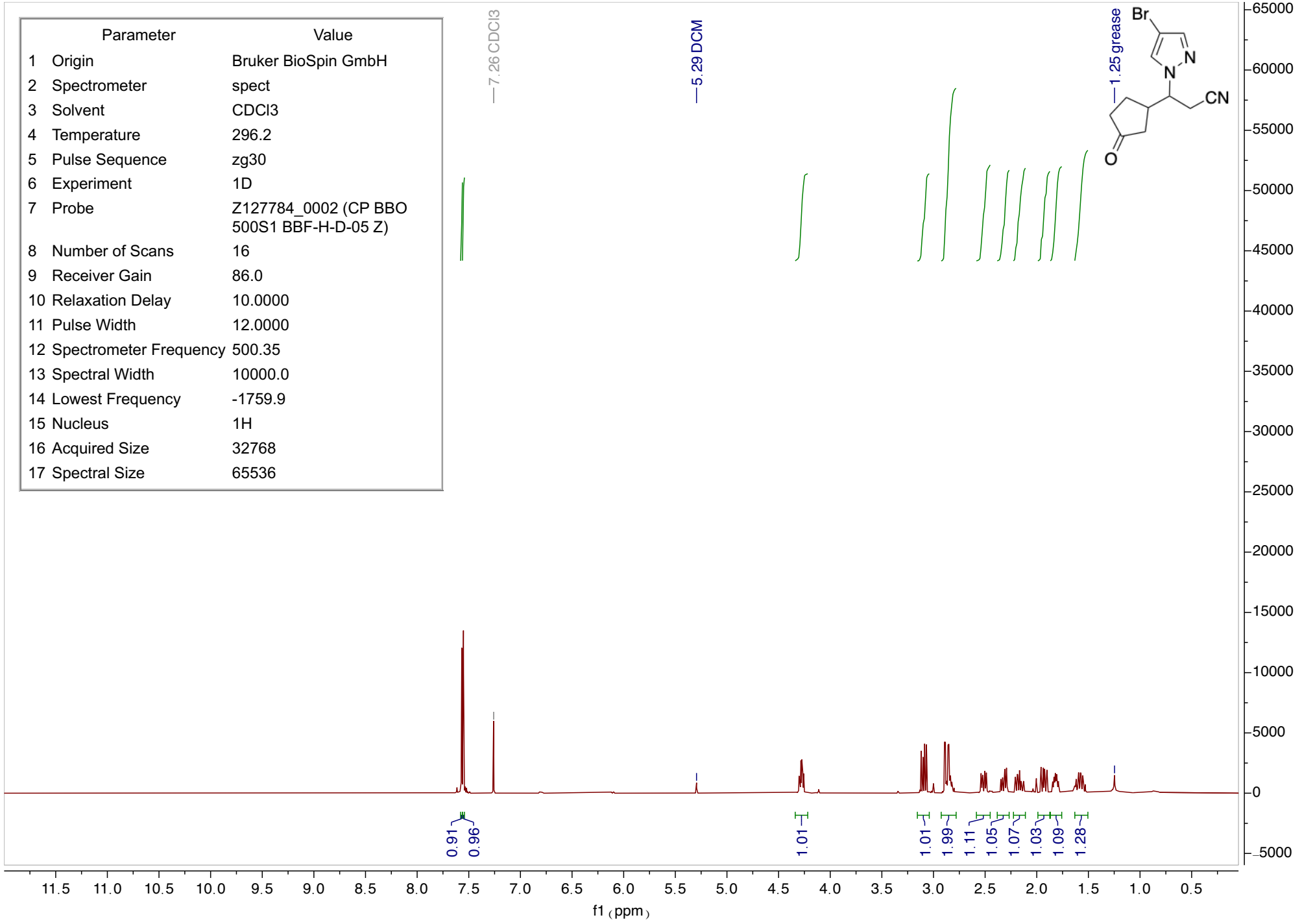

PinB
N
N
Hg
Hj
Hd
Ha
CN
He
Hf
Hc
Hh
Hb
O
Hi
He
Hf
Hh
Hi
carbonyl
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
f1 (ppm)
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
f2 (ppm)

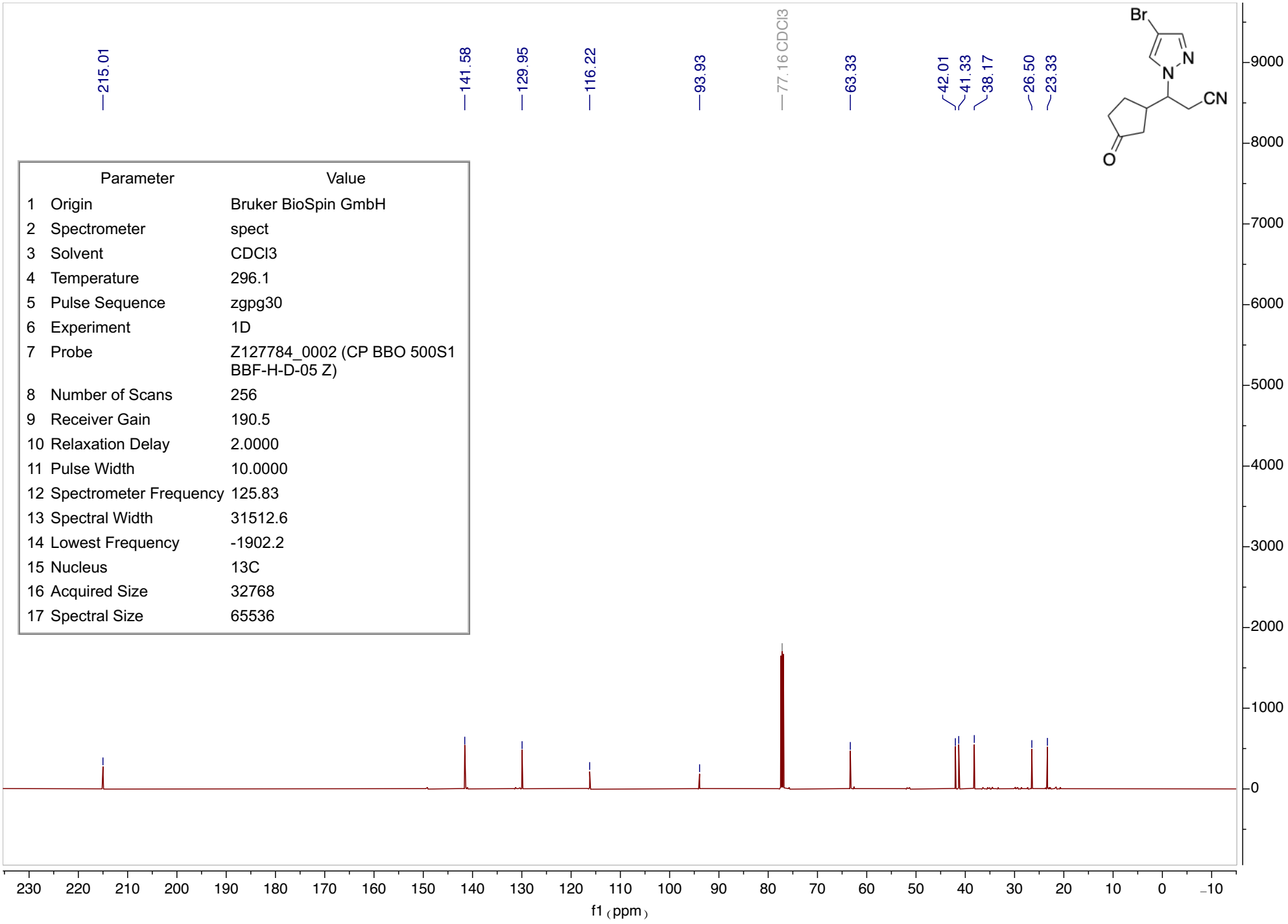


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	55.0
10	Relaxation Delay	1.9279
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-87.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

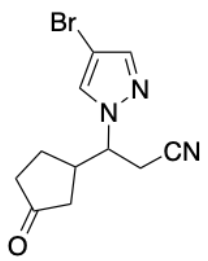

PinB
N
N
Hg
Hj
Hd
Ha
CN
He
Hf
Hc
Hh
Hb
O
Hi
Hd
Hh
Hi
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
f1 (ppm)
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

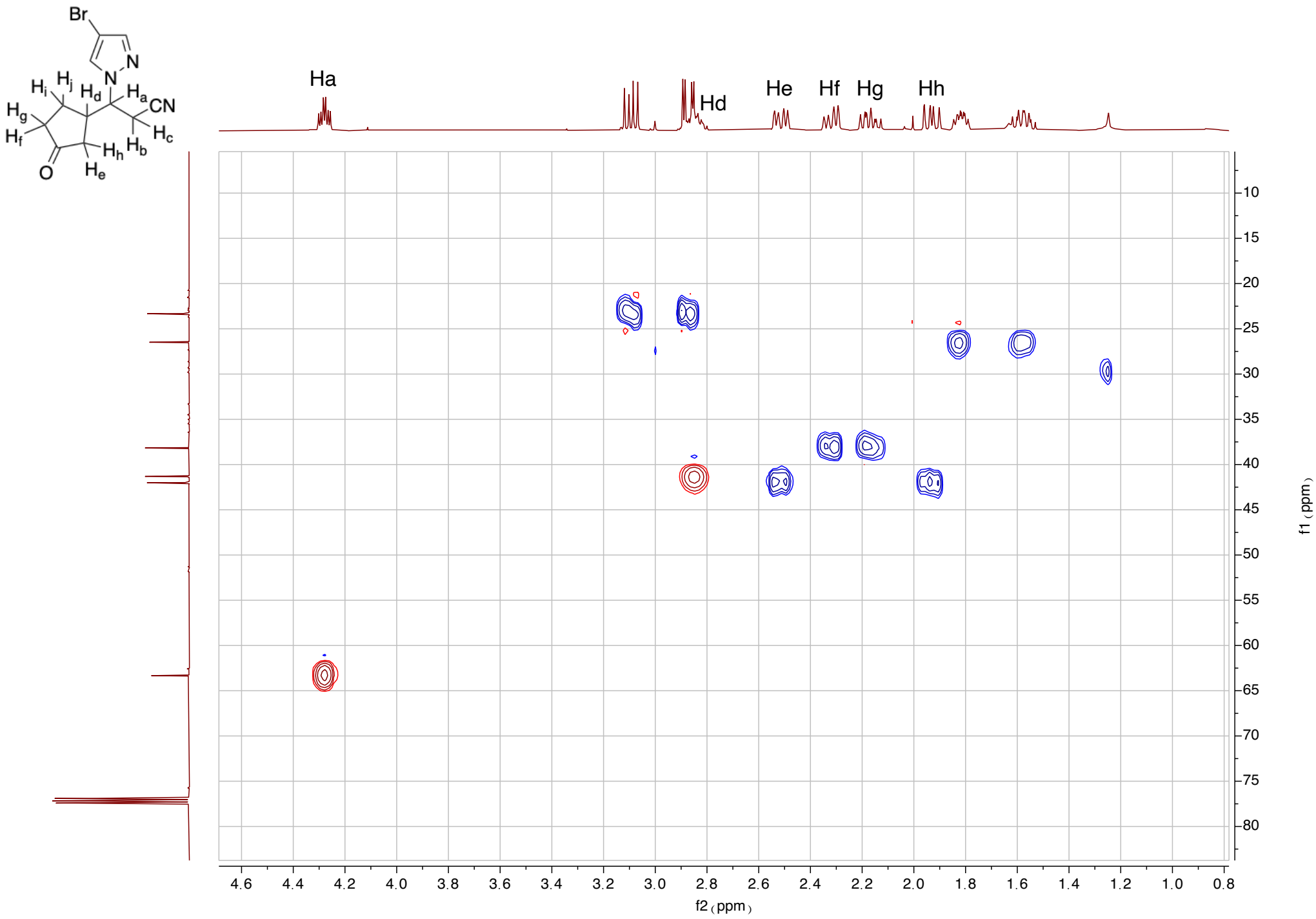




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4310.3
14	Lowest Frequency	-73.7
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


Br
N
N
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CN
Hg
Hf
Hc
Hh
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O
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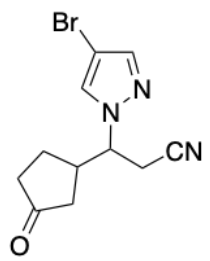
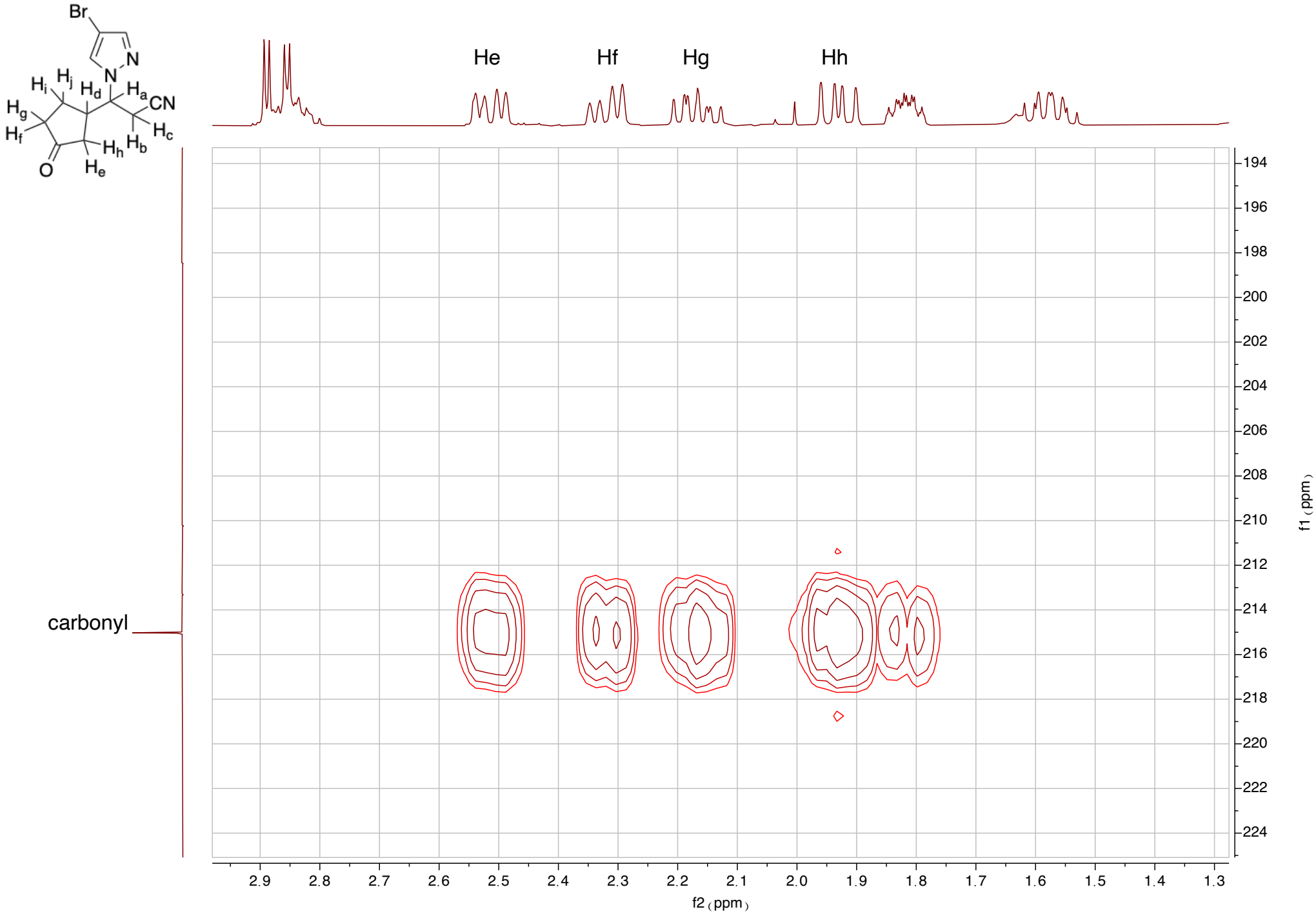
Ha
Hd
He
Hf
Hg
Hh
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
f1 (ppm)
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
f2 (ppm)



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4310.3
14	Lowest Frequency	-76.7
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


Br
N
N
Hi
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Hd
Ha
CN
Hg
Hf
Hc
Hh
Hb
O
He
He
Hf
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Hh
carbonyl
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202
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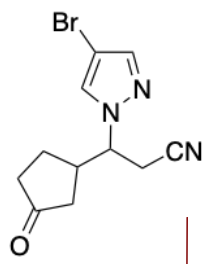
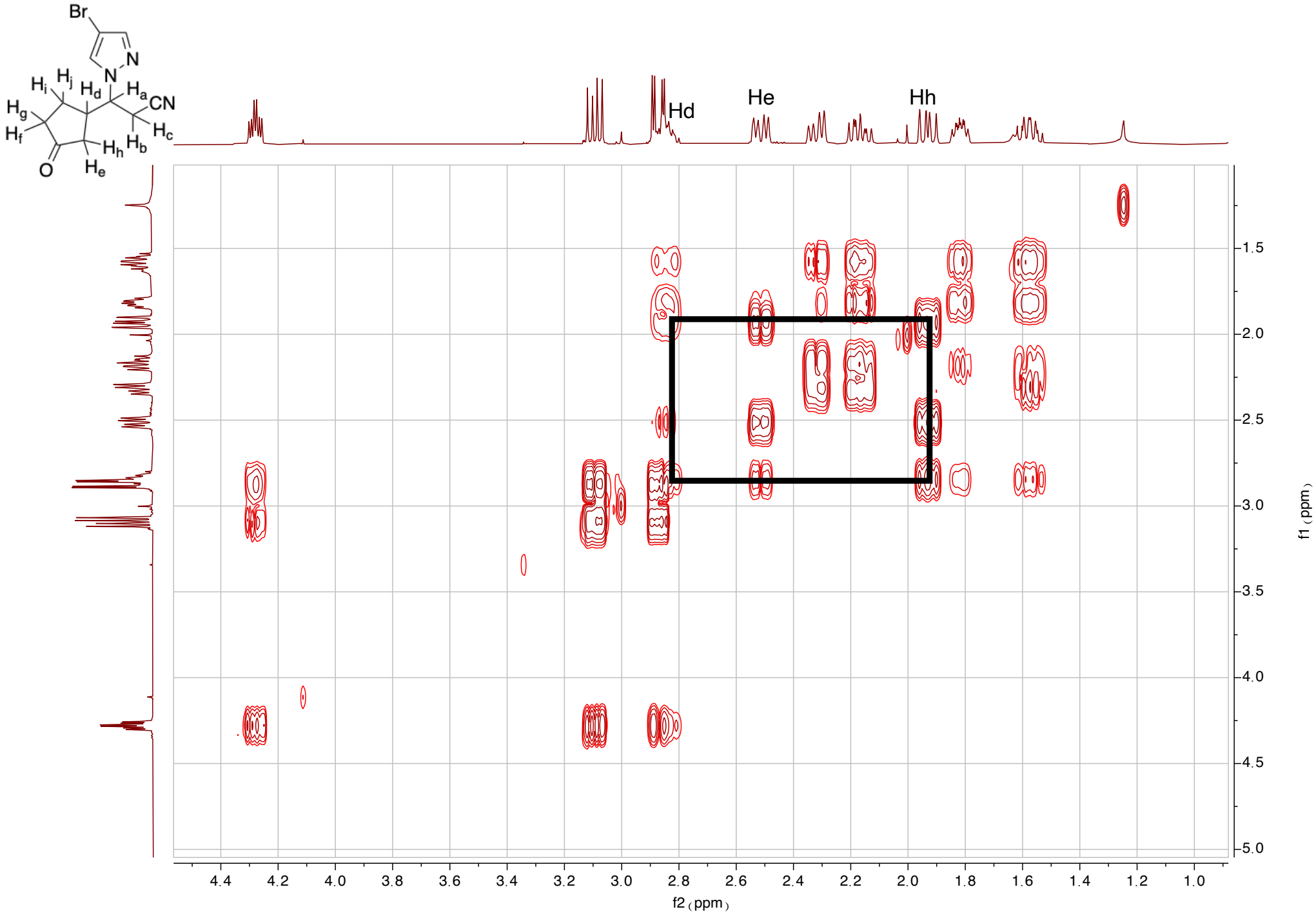
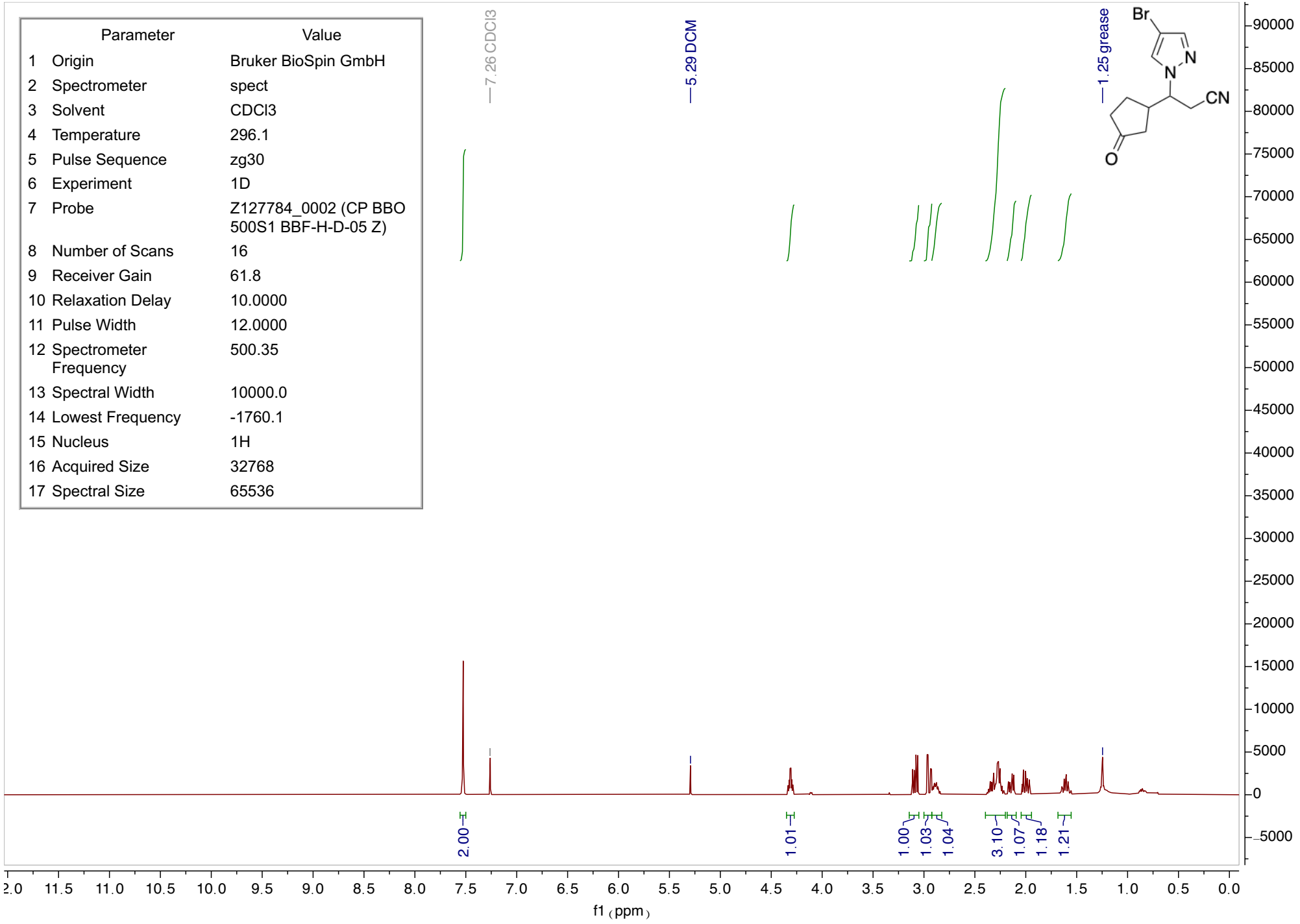
216
218
220
222
224
f1 (ppm)
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
f2 (ppm)

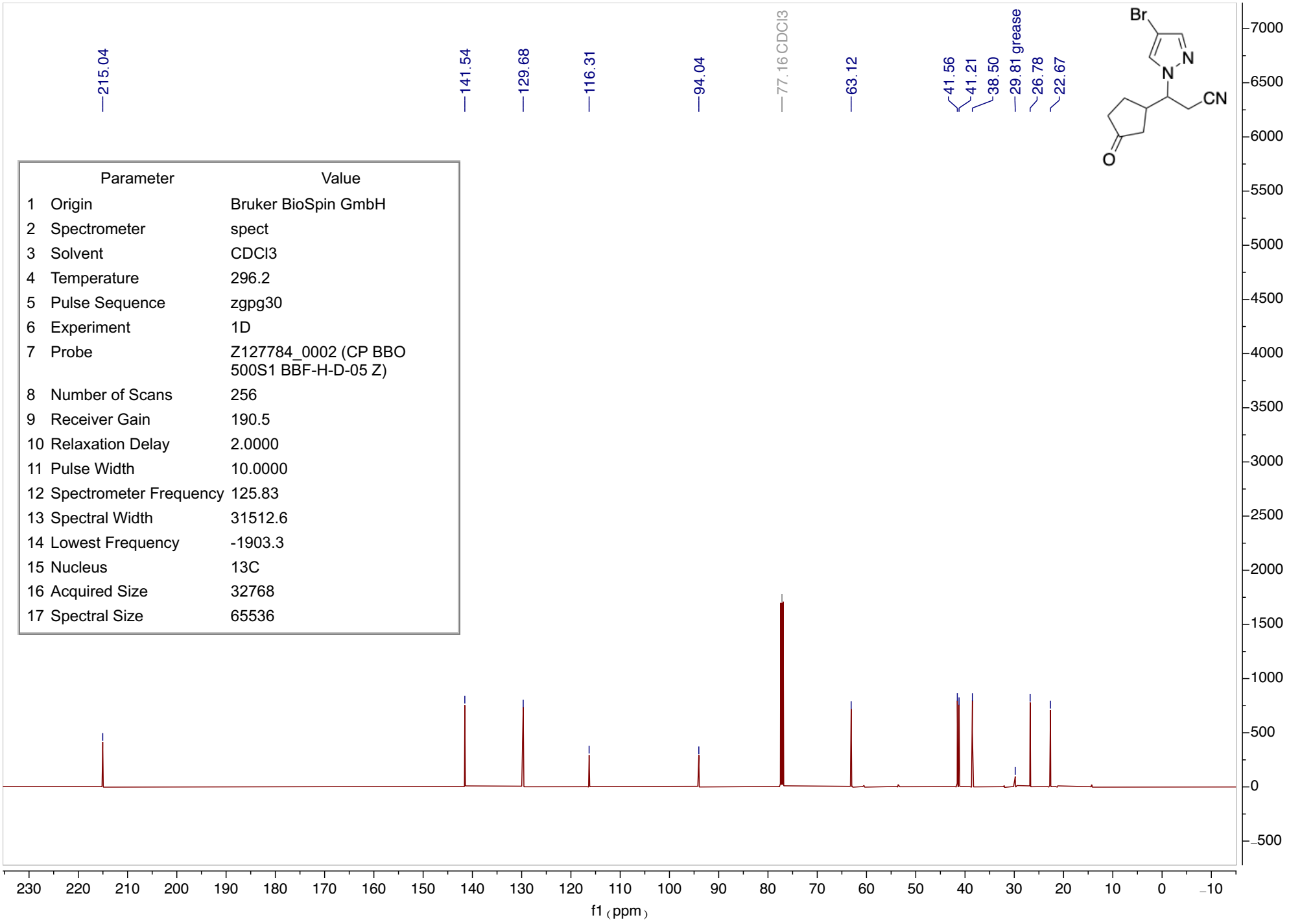


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.9197
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4310.3
14	Lowest Frequency	-76.0
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

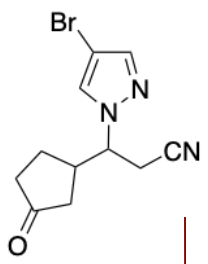

Br
N
N
Hi
Hj
Hd
Ha
CN
Hg
Hf
Hc
Hh
Hb
O
He
Hd
He
Hh
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
f1 (ppm)
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



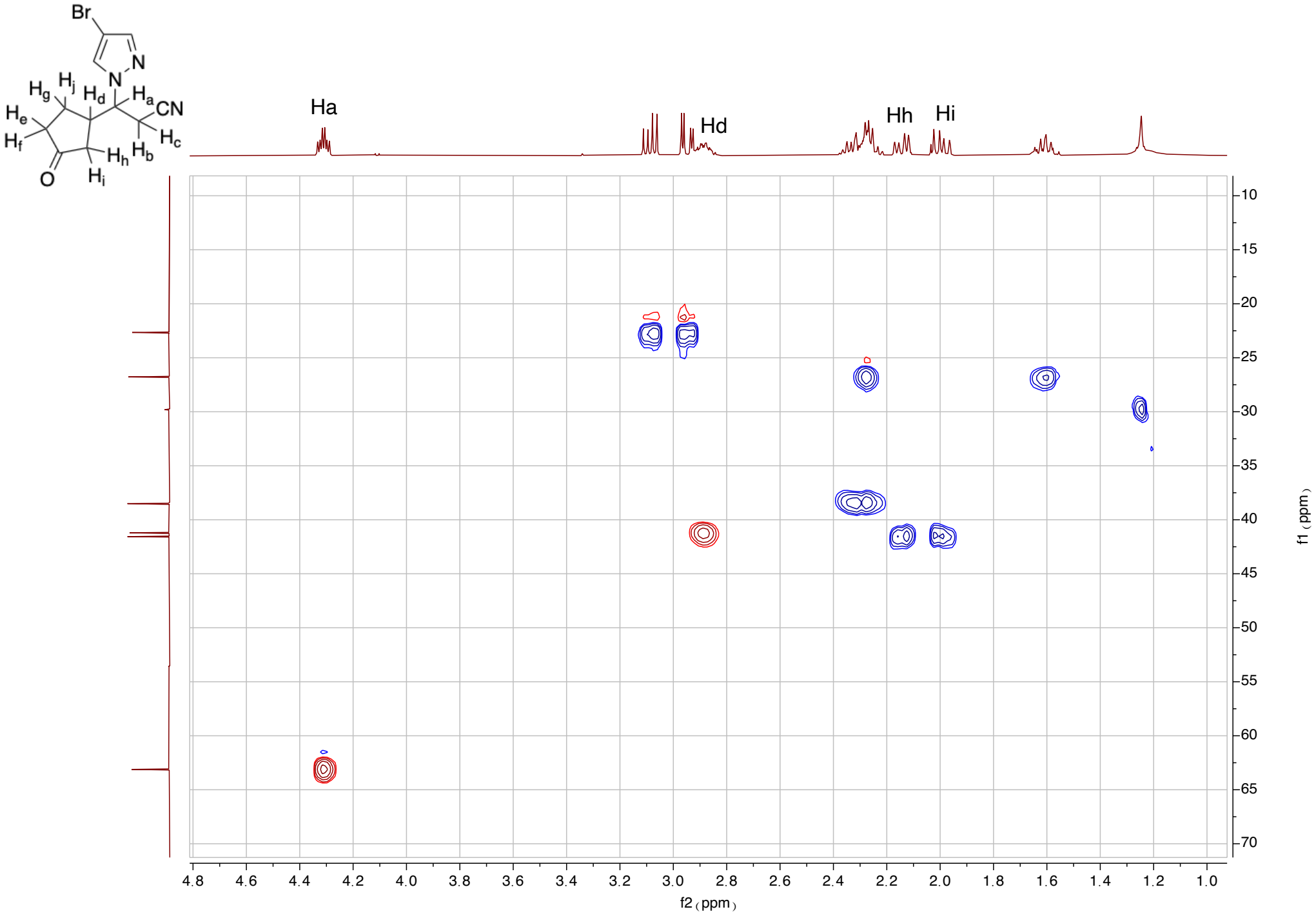


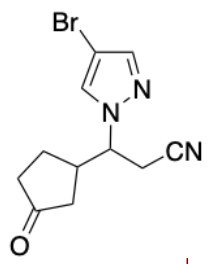
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



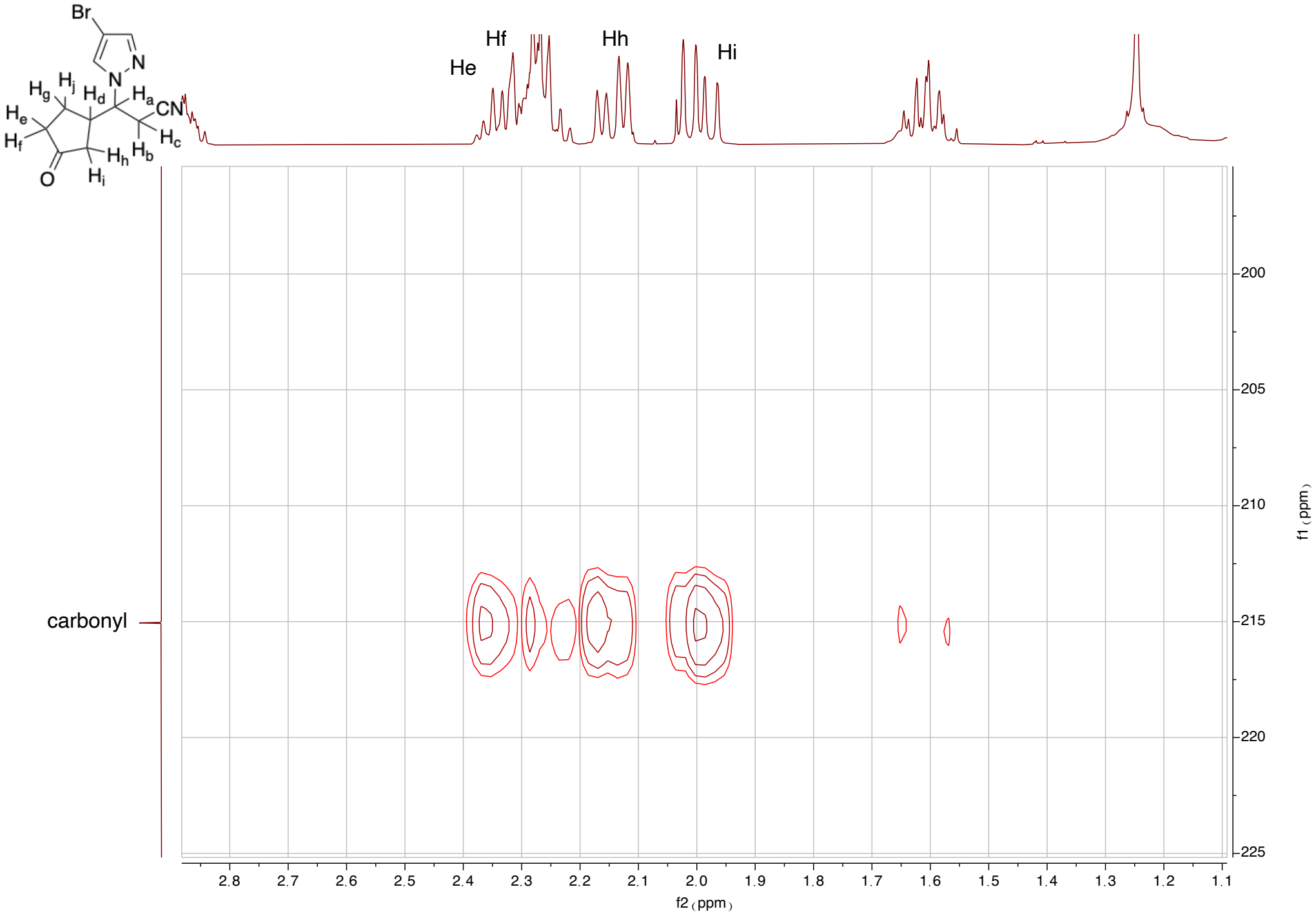
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4347.8
14	Lowest Frequency	-125.6
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

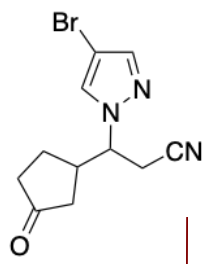
500


Br
N
N
Hg
Hj
Hd
Ha
CN
He
Hf
Hc
Hh
Hb
O
Hi
Ha
Hd
Hh
Hi
f2 (ppm)
f1 (ppm)
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
10
15
20
25
30
35
40
45
50
55
60
65
70

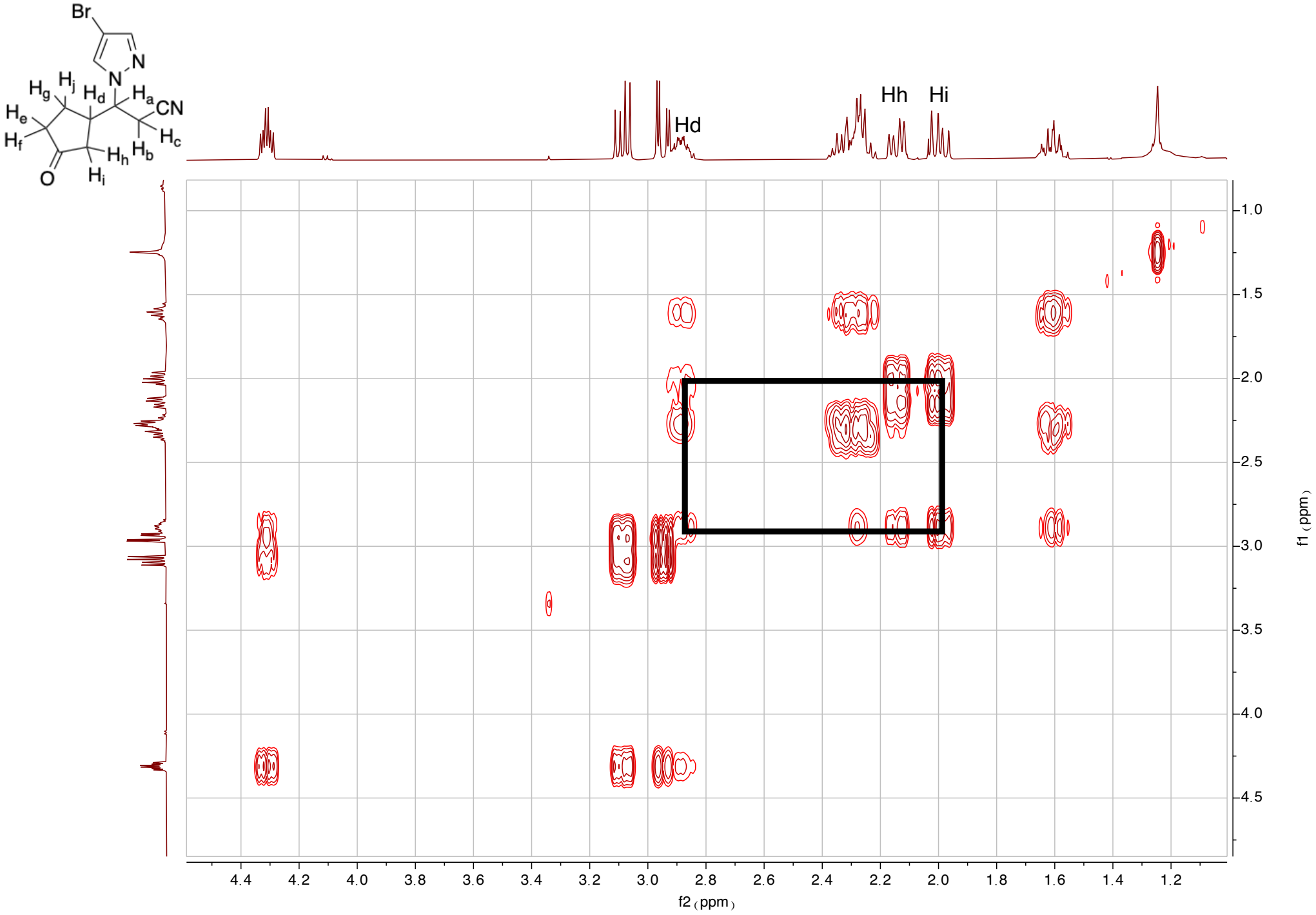


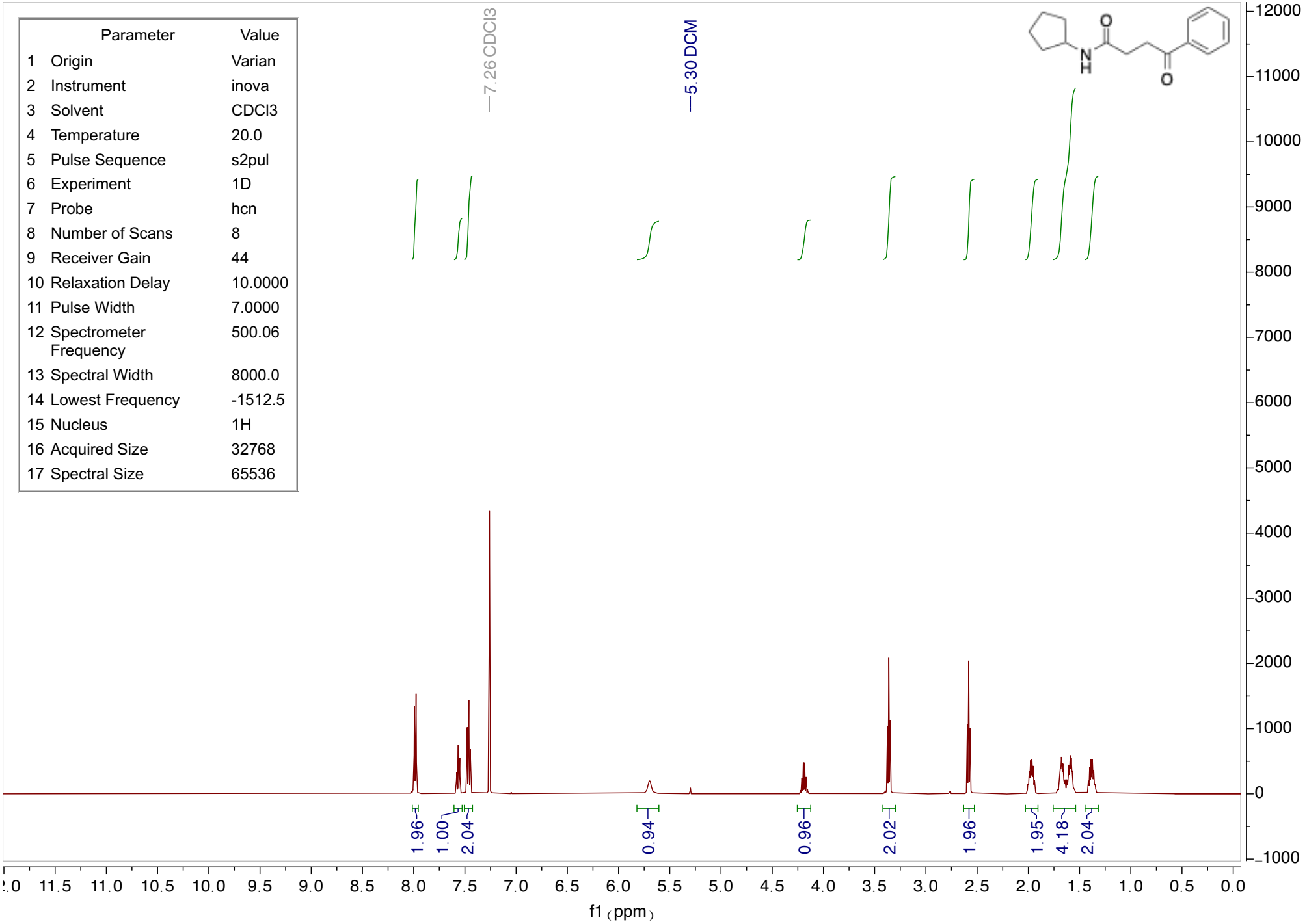
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4273.5
14	Lowest Frequency	-74.8
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


Br
N
N
Hg
Hj
Hd
Ha
CN
He
Hf
Hc
Hh
Hb
O
Hi
He
Hf
Hh
Hi
carbonyl
200
205
210
215
220
225
f1 (ppm)
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
f2 (ppm)



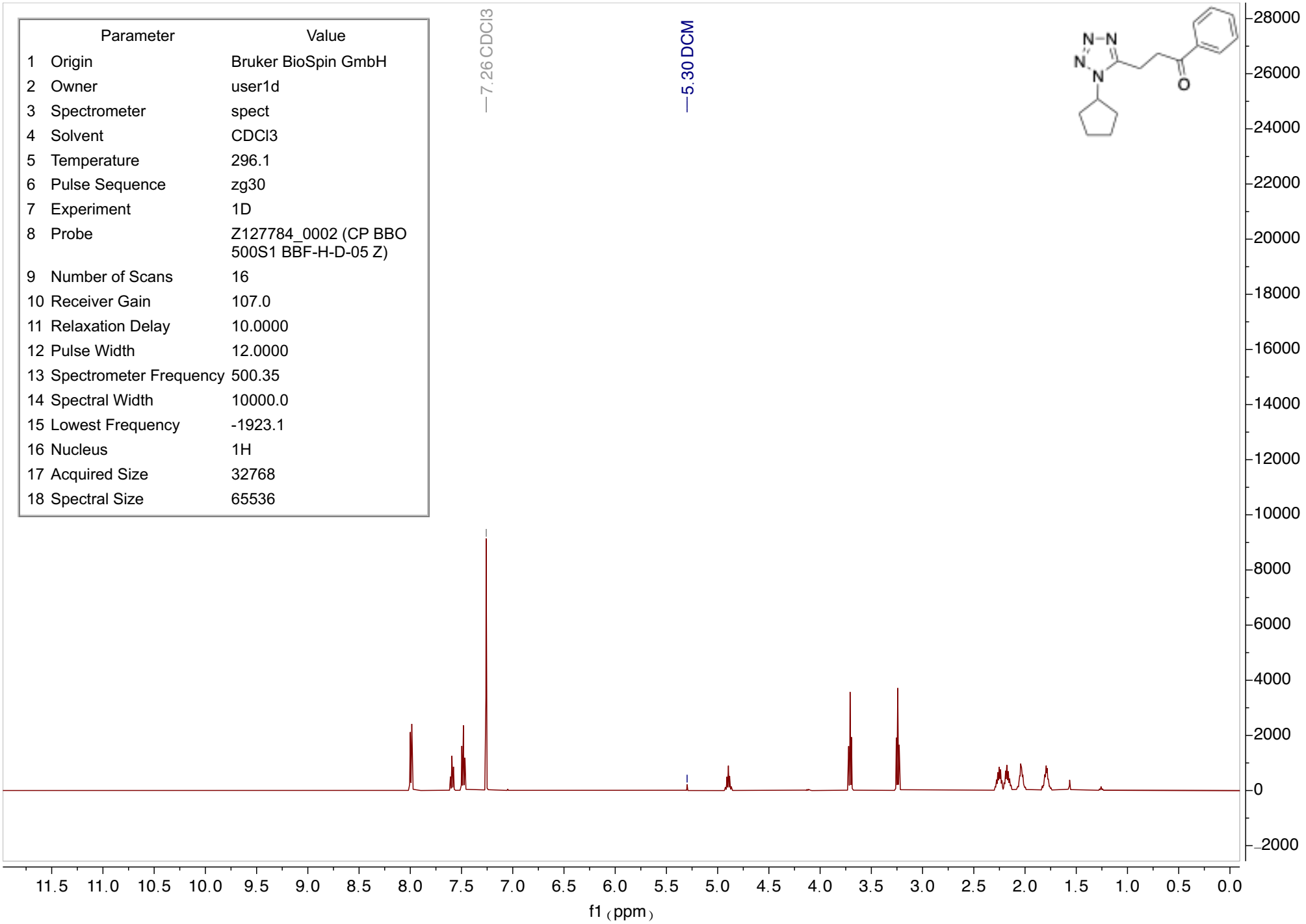
Parameter		Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	42.7
10	Relaxation Delay	1.9218
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4347.8
14	Lowest Frequency	-126.4
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

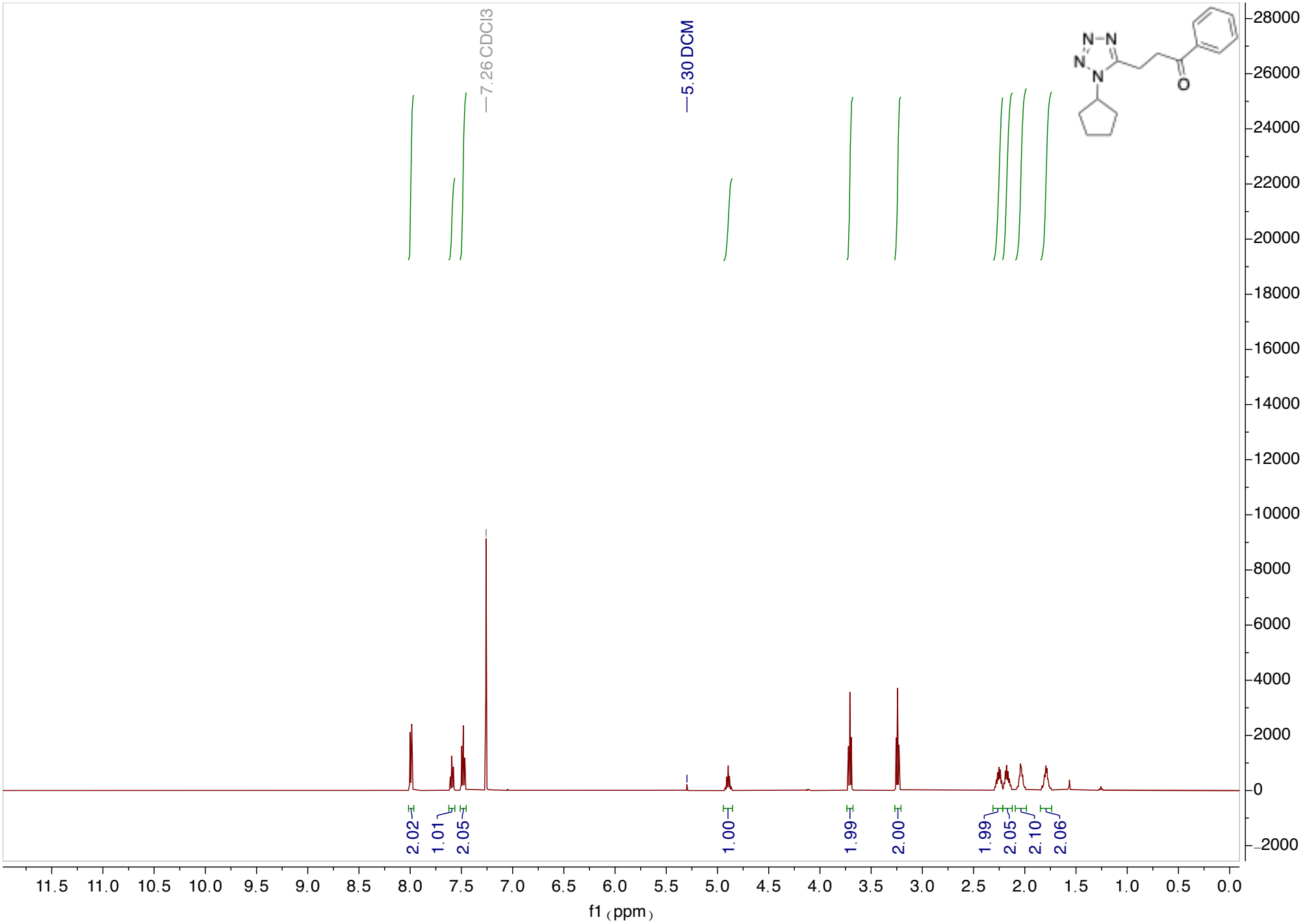

Br
N
N
Hg
Hj
Hd
Ha
CN
He
Hf
Hc
Hh
Hb
O
Hi
Hd
Hh
Hi
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
f2 (ppm)

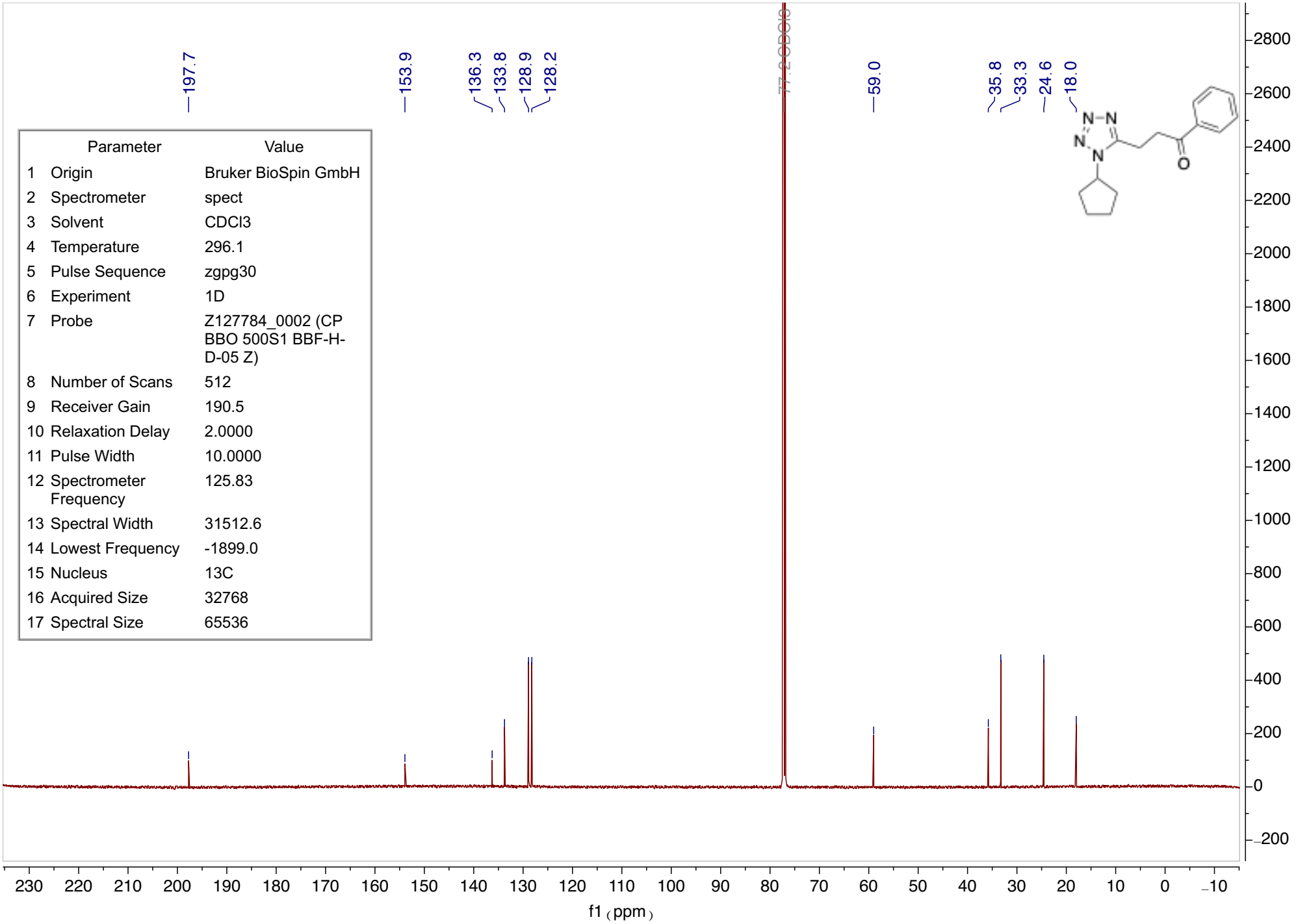


	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	hcn
8	Number of Scans	8
9	Receiver Gain	44
10	Relaxation Delay	10.0000
11	Pulse Width	7.0000
12	Spectrometer Frequency	500.06
13	Spectral Width	8000.0
14	Lowest Frequency	-1512.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

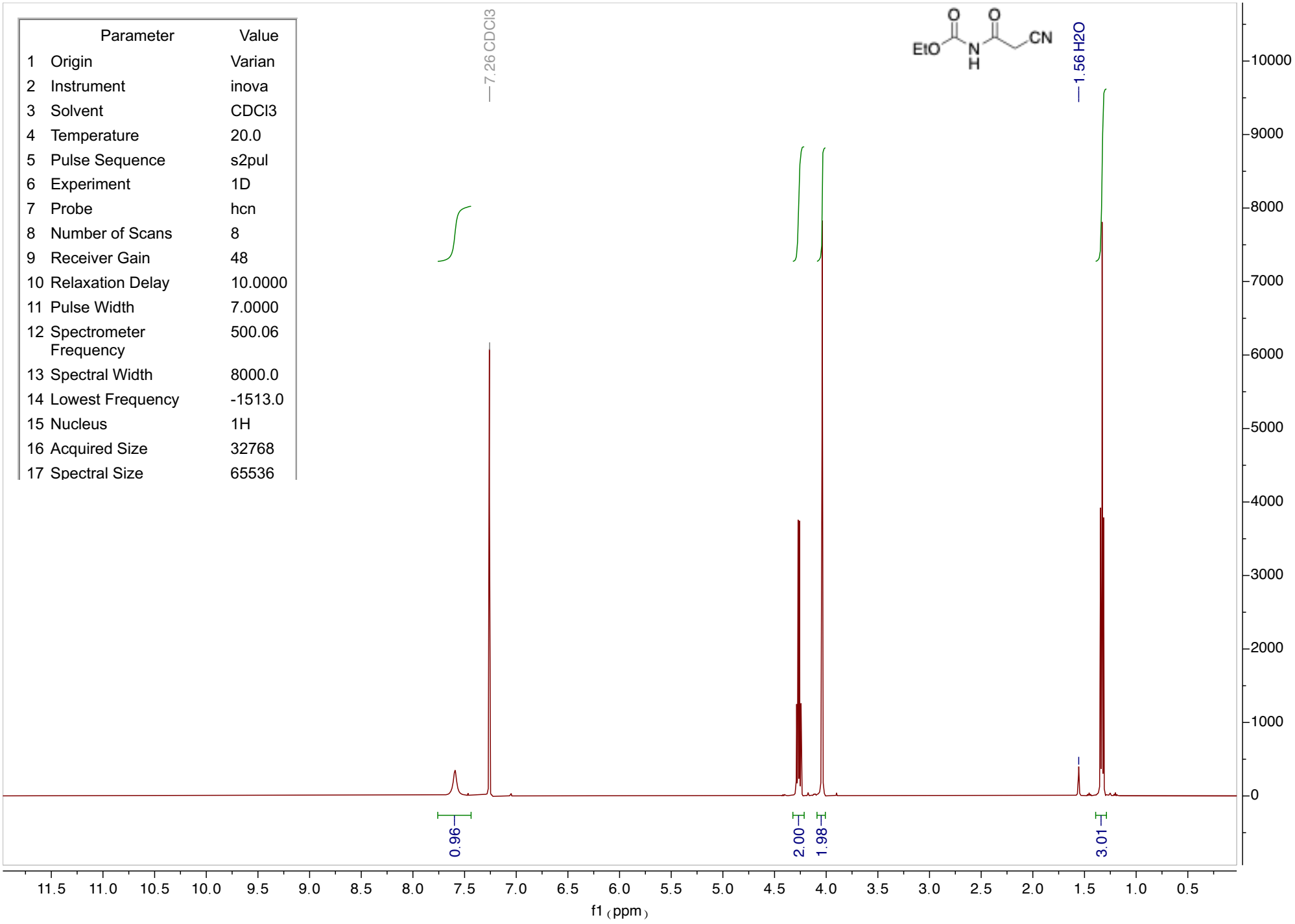
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Owner	user1d
3	Spectrometer	spect
4	Solvent	CDCl3
5	Temperature	296.1
6	Pulse Sequence	zg30
7	Experiment	1D
8	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
9	Number of Scans	16
10	Receiver Gain	107.0
11	Relaxation Delay	10.0000
12	Pulse Width	12.0000
13	Spectrometer Frequency	500.35
14	Spectral Width	10000.0
15	Lowest Frequency	-1923.1
16	Nucleus	1H
17	Acquired Size	32768
18	Spectral Size	65536

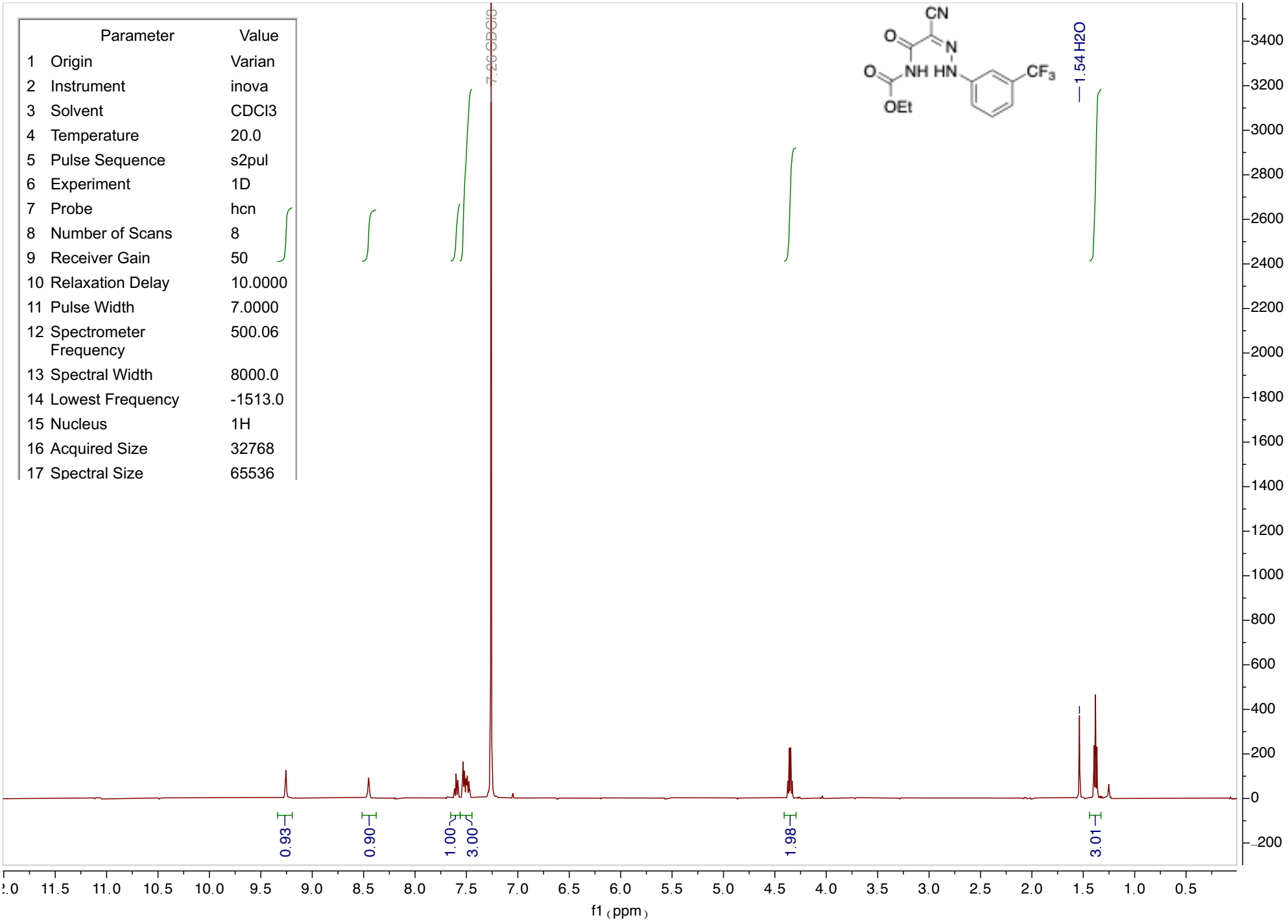


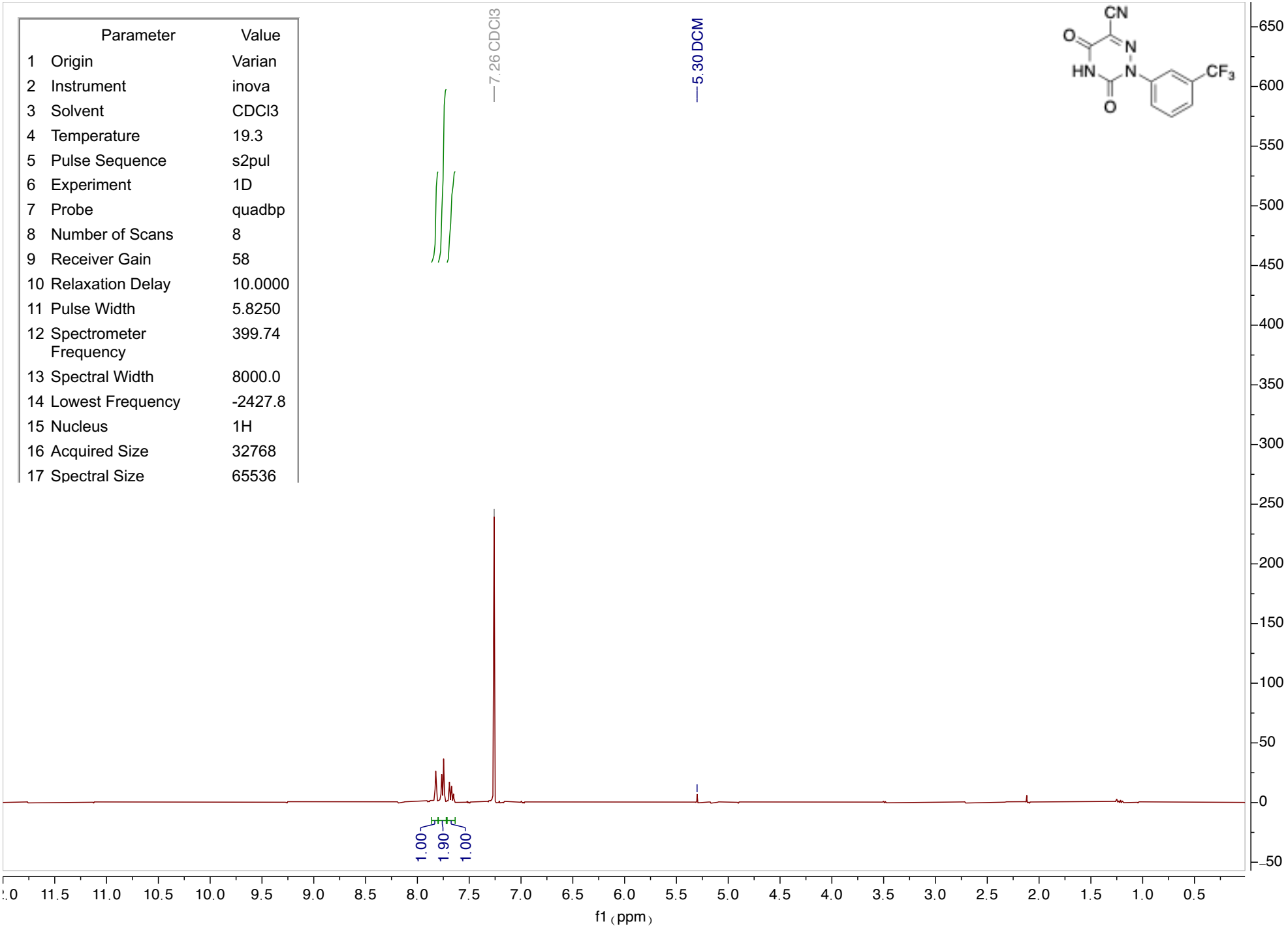

7.26 CDCl3
5.30 DCM
2.02
1.01
2.05
1.00
1.99
2.00
1.99
2.05
2.10
2.06
f1 (ppm)



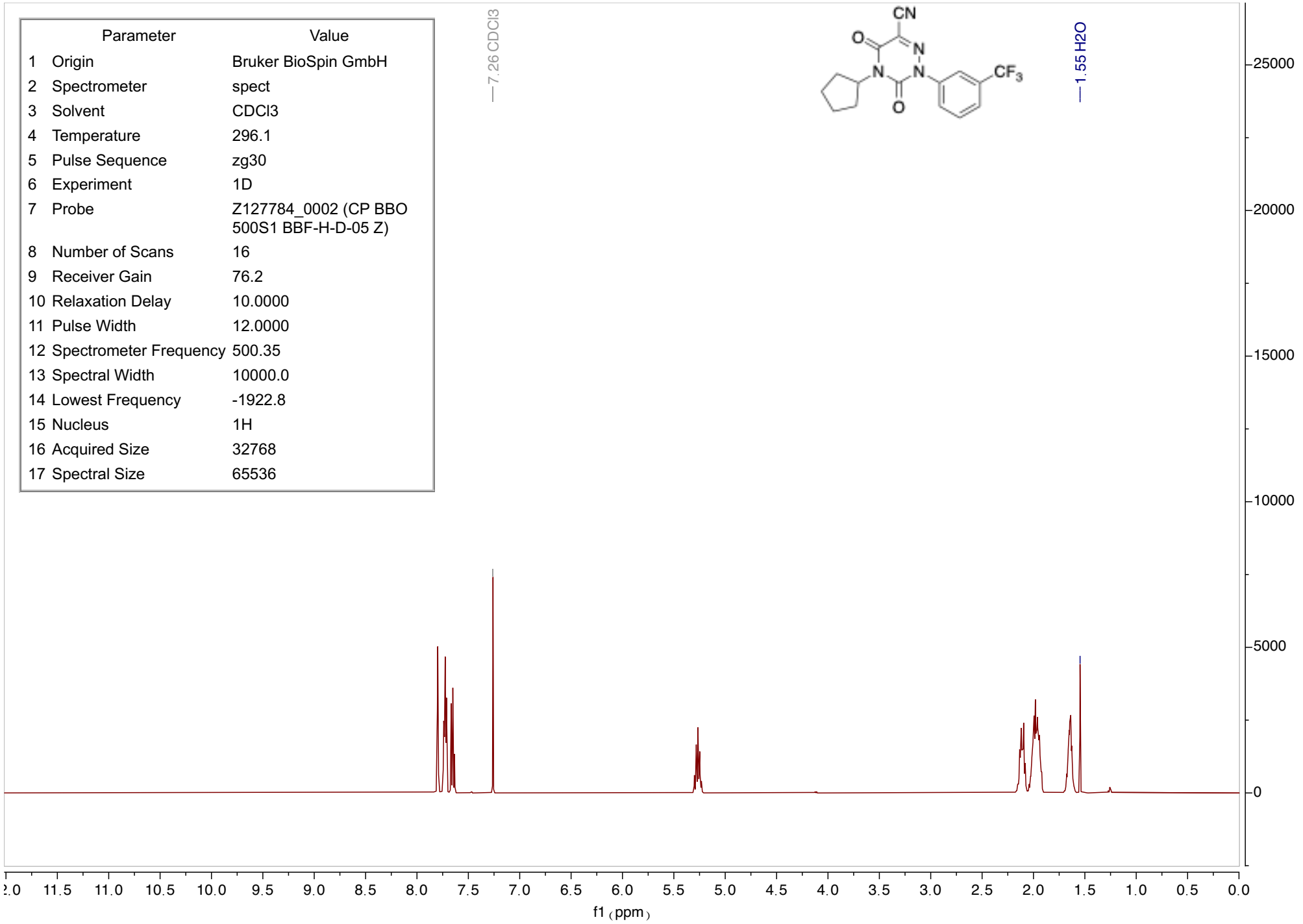
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

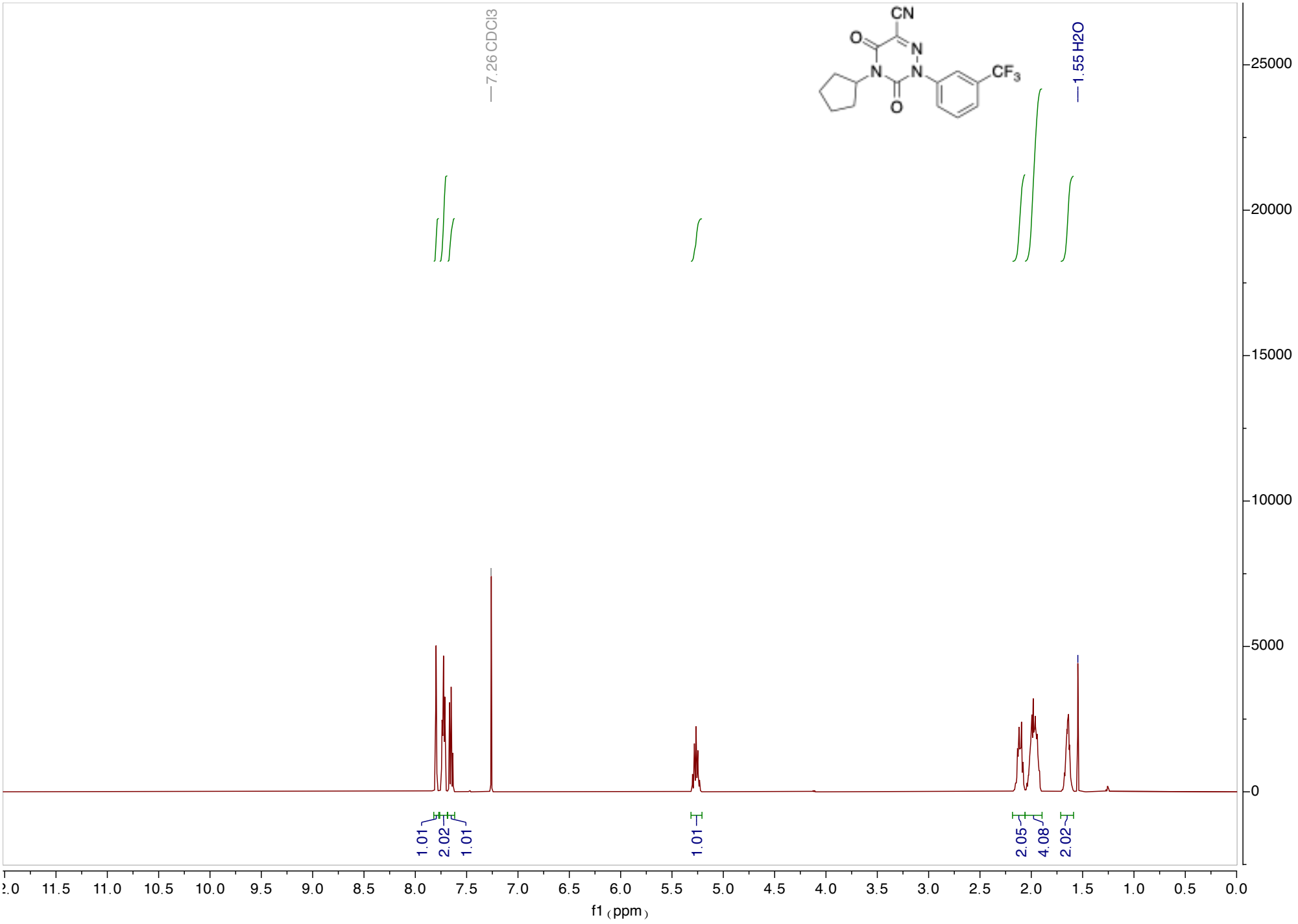

Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 48
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1513.0
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
1.56 H2O
EtO
N
H
CN
0.96
2.00
1.98
3.01
f1 (ppm)

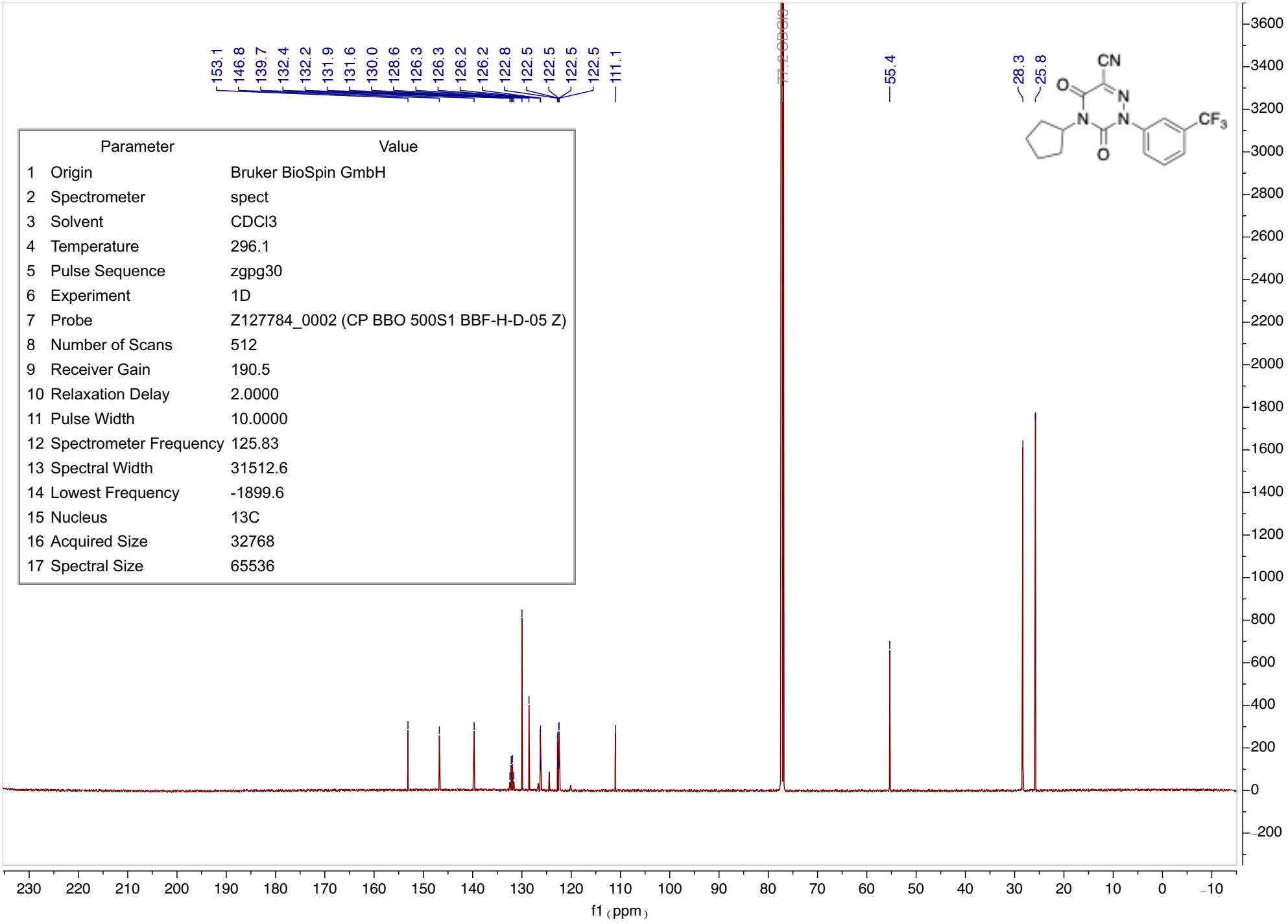

Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 50
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1513.0
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
1.54 H2O
CN
O
N
O
NH HN
CF3
OEt
0.93
0.90
1.00
3.00
1.98
3.01
f1 (ppm)


Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 19.3
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe quadbp
8 Number of Scans 8
9 Receiver Gain 58
10 Relaxation Delay 10.0000
11 Pulse Width 5.8250
12 Spectrometer Frequency 399.74
13 Spectral Width 8000.0
14 Lowest Frequency -2427.8
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
5.30 DCM
CN
O
N
HN
N
CF3
O
1.00
1.90
1.00
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	76.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

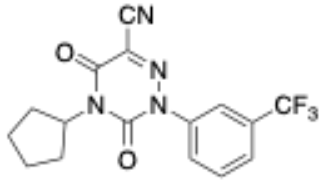



7.26 CDCl3
1.55 H2O
CN
O
N
N
N
O
CF3
25000
20000
15000
10000
5000
0
1.01
2.02
1.01
1.01
2.05
4.08
2.02
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

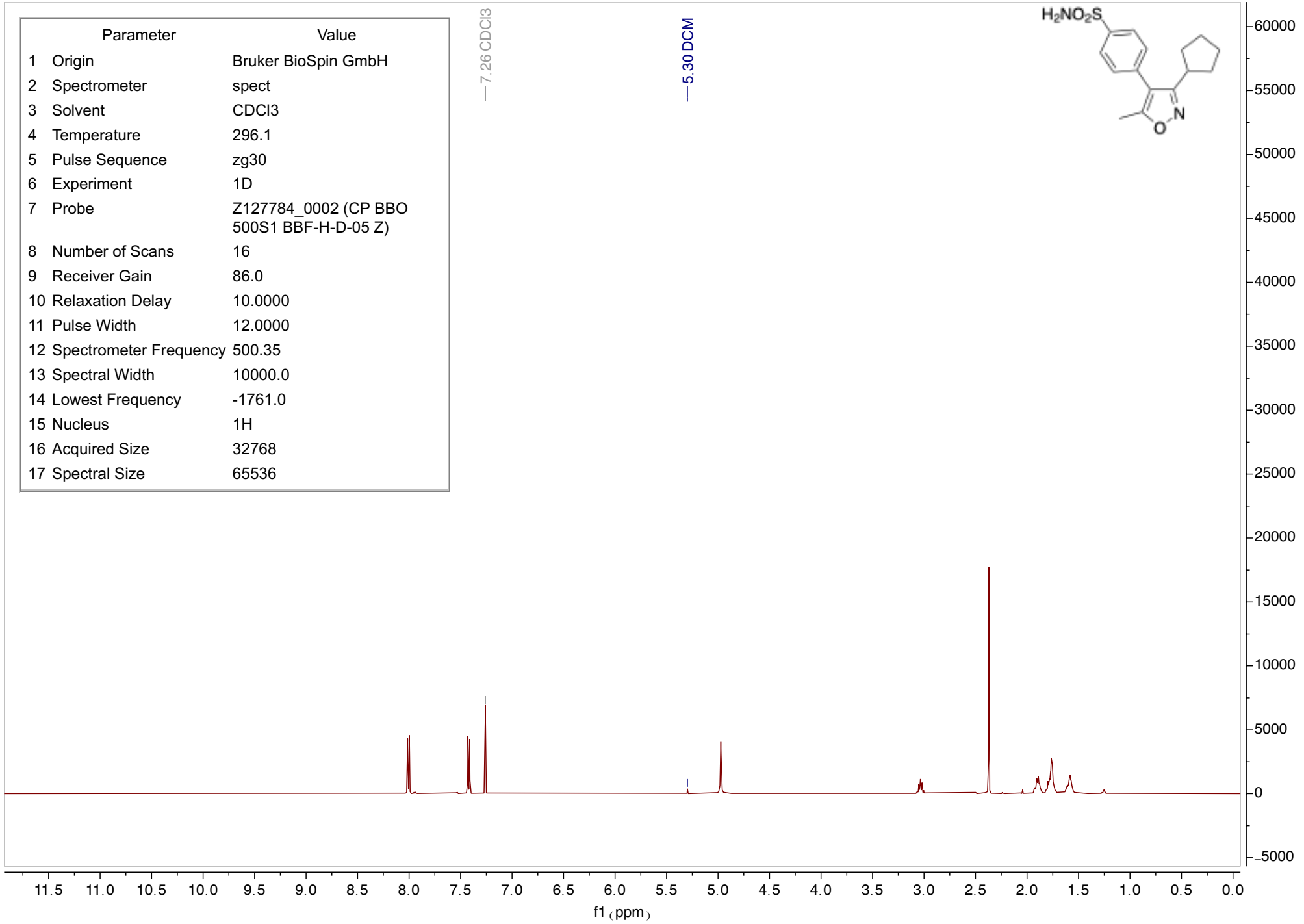


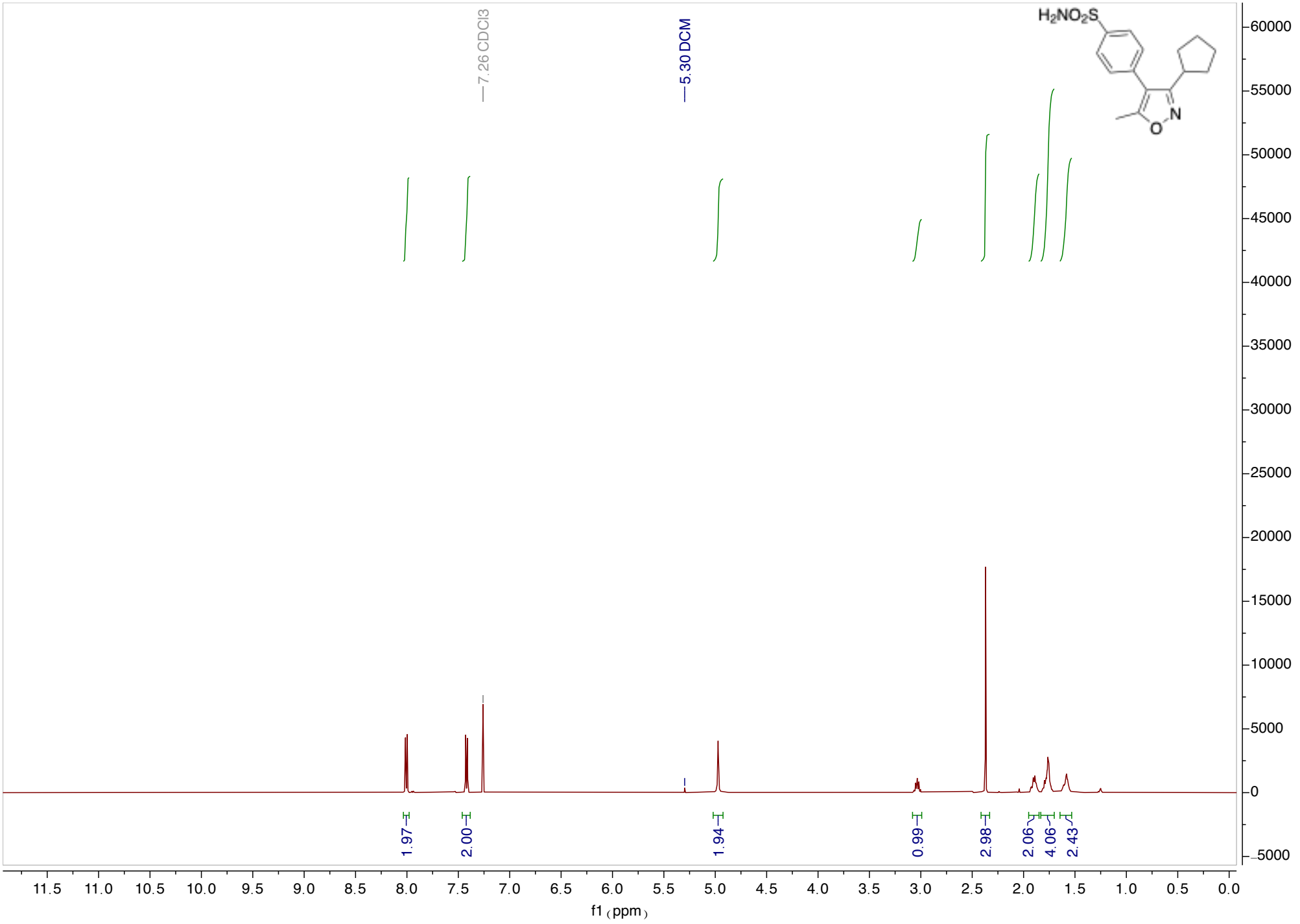
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

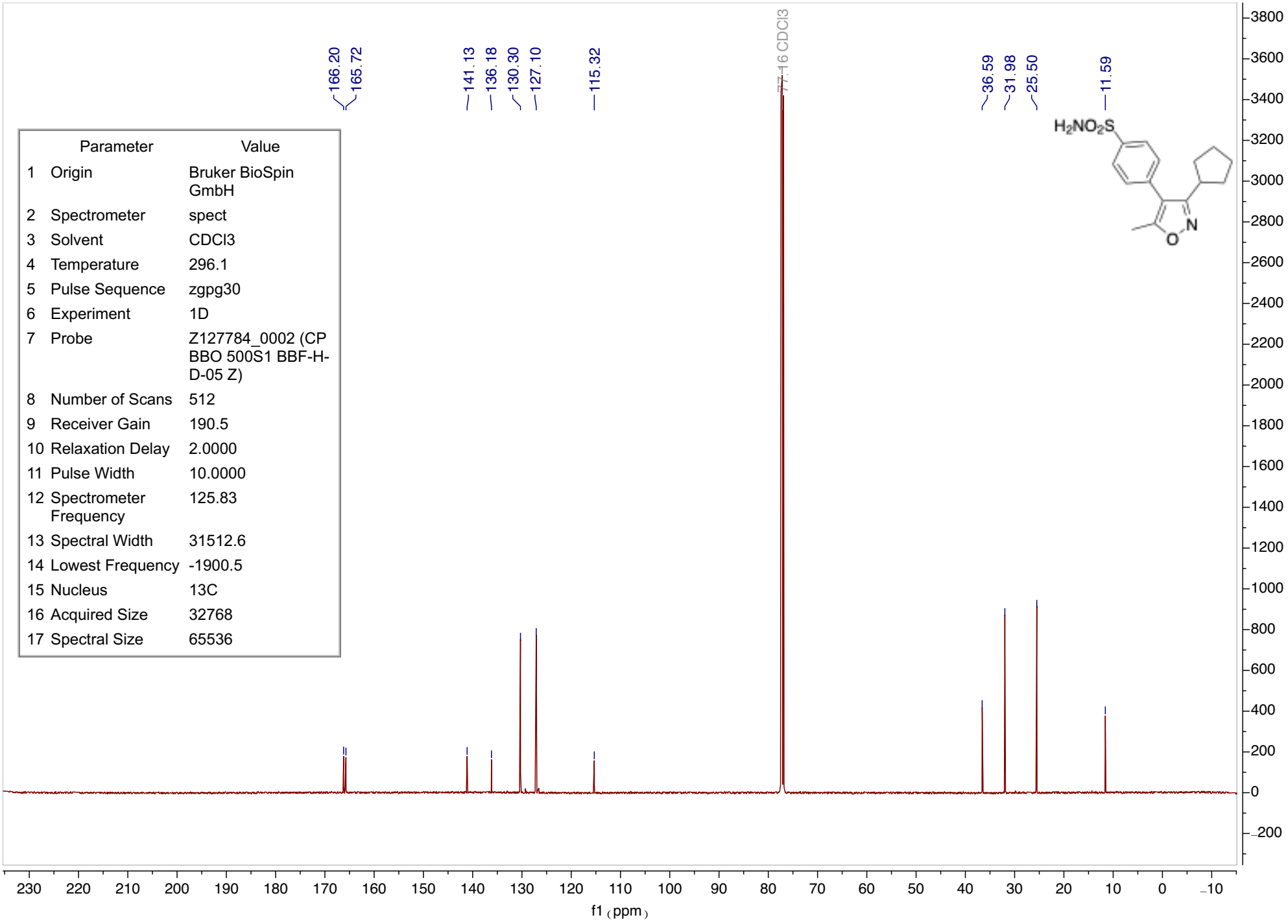
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1761.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

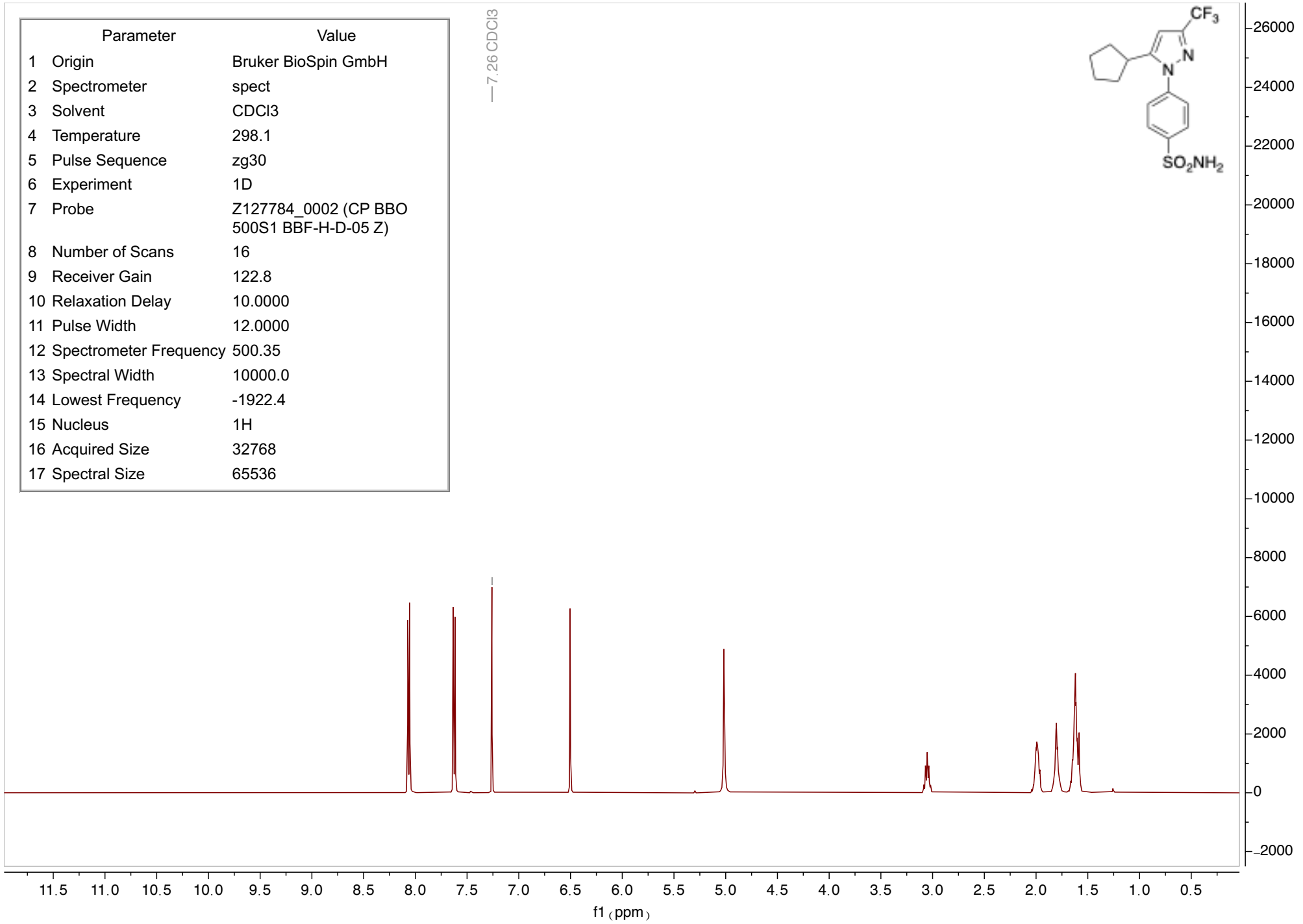


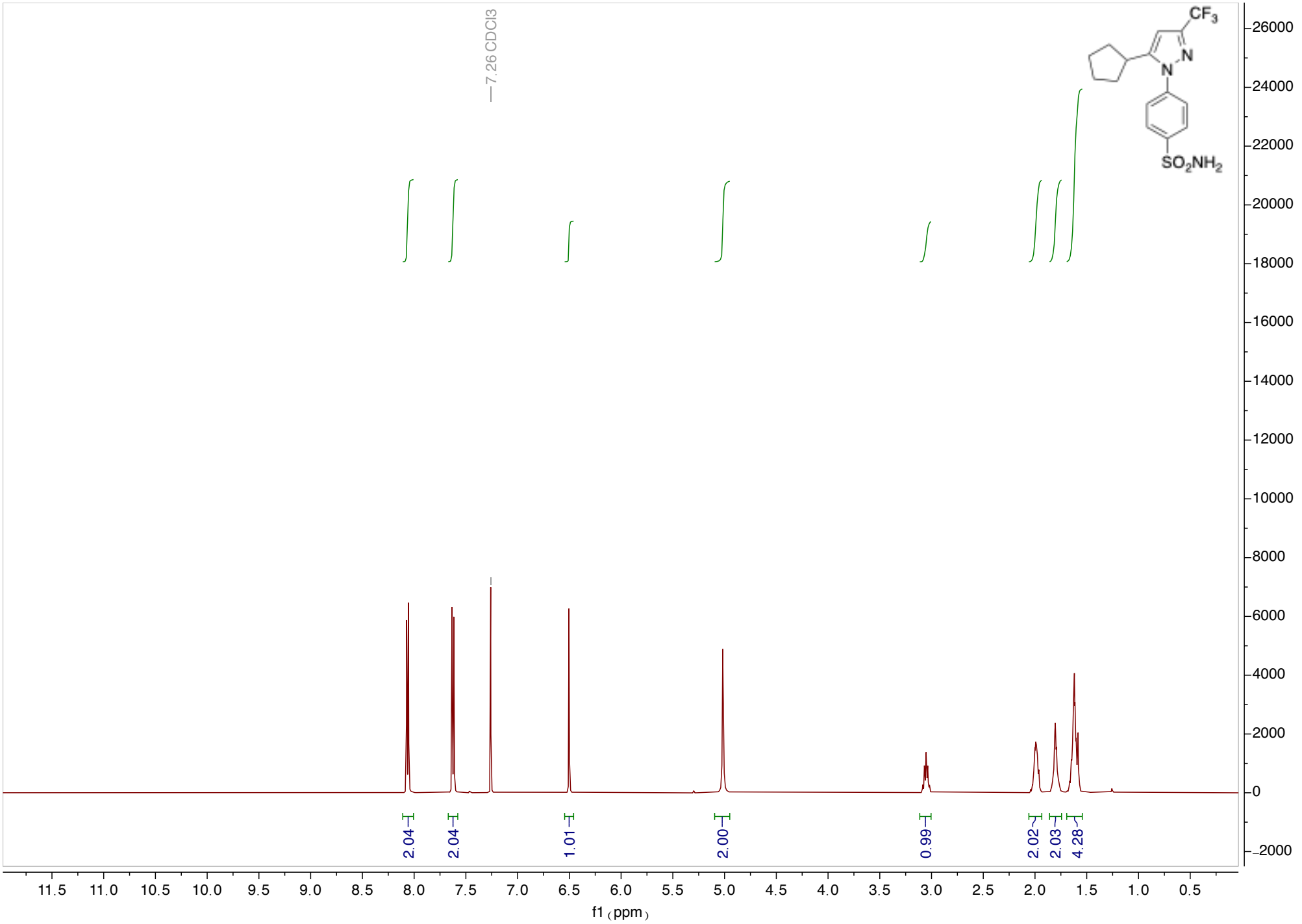

7.26 CDCl3
5.30 DCM
H2NO2S
O
N
1.97
2.00
1.94
0.99
2.98
2.06
4.06
2.43
f1 (ppm)



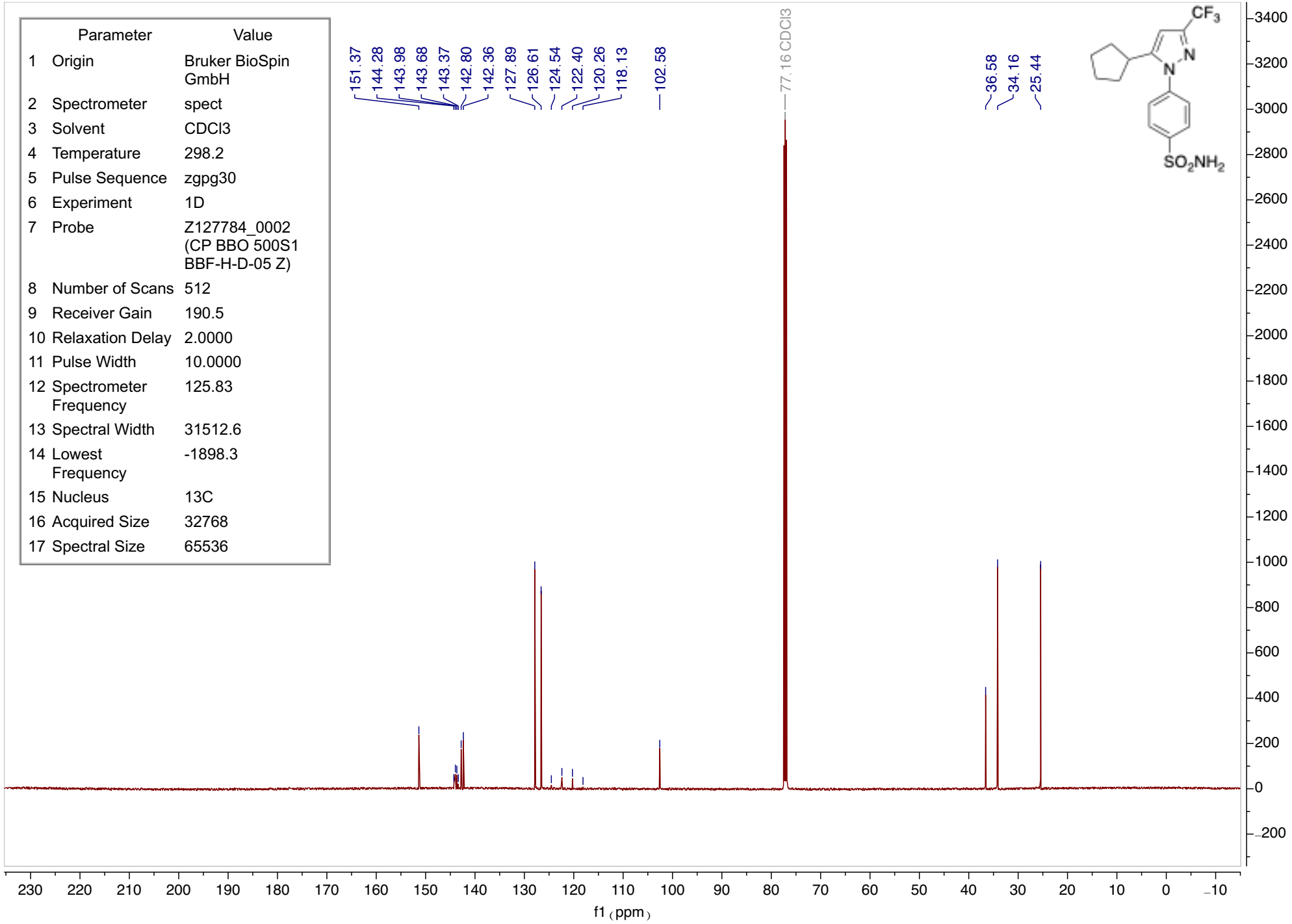
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	122.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

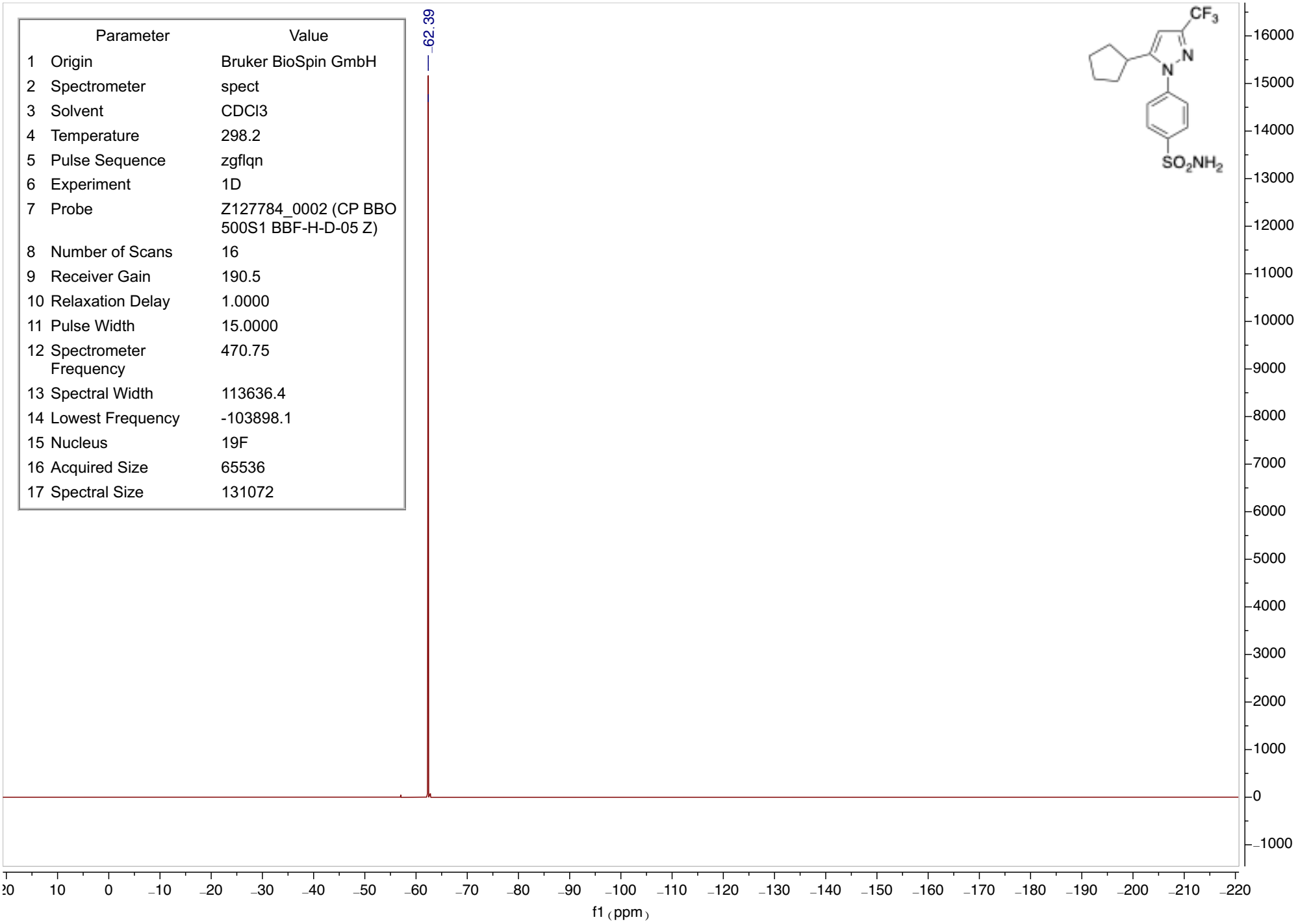


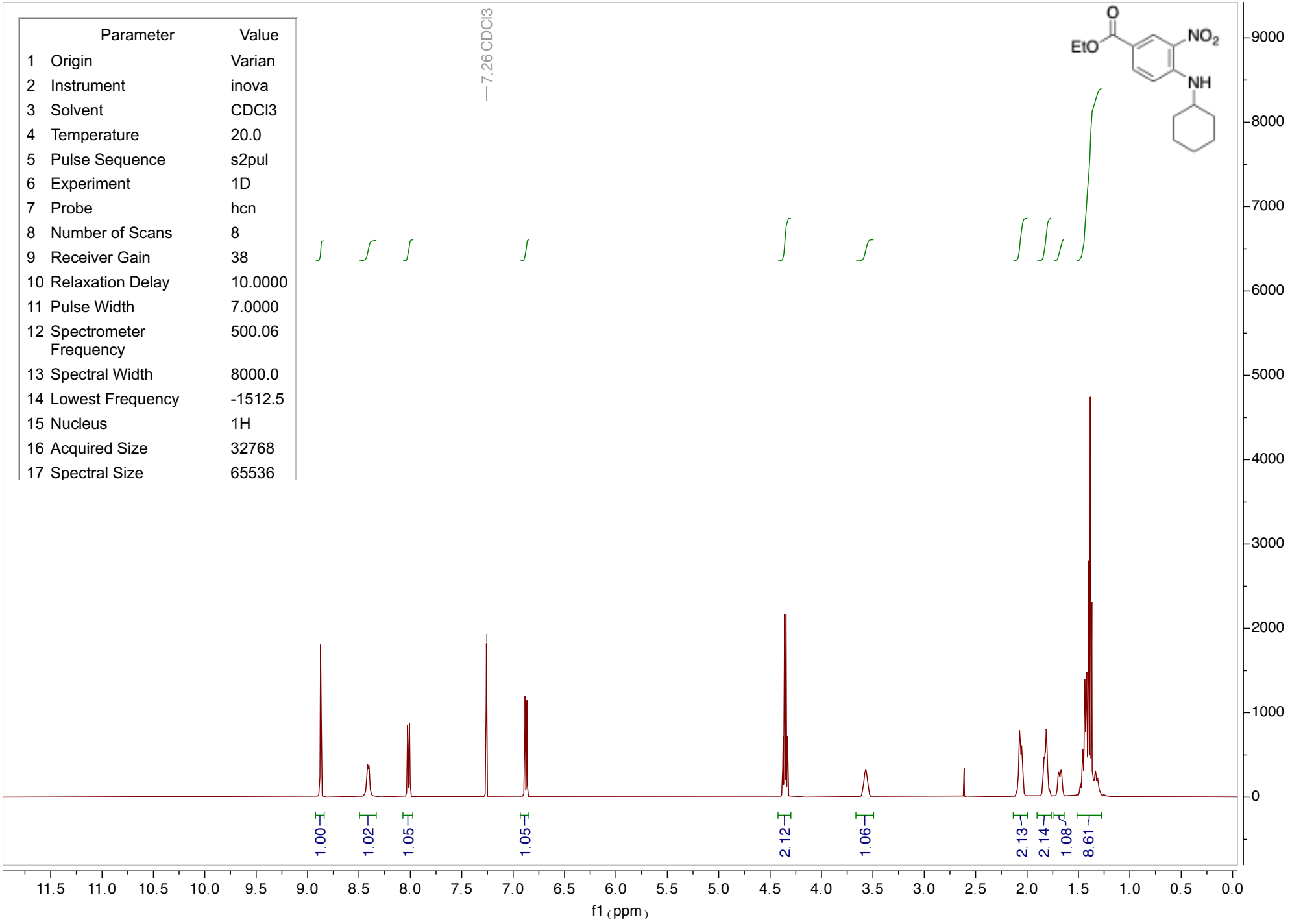

7.26 CDCl3
CF3
N
N
SO2NH2
2.04
2.04
1.01
2.00
0.99
2.02
2.03
4.28
f1 (ppm)

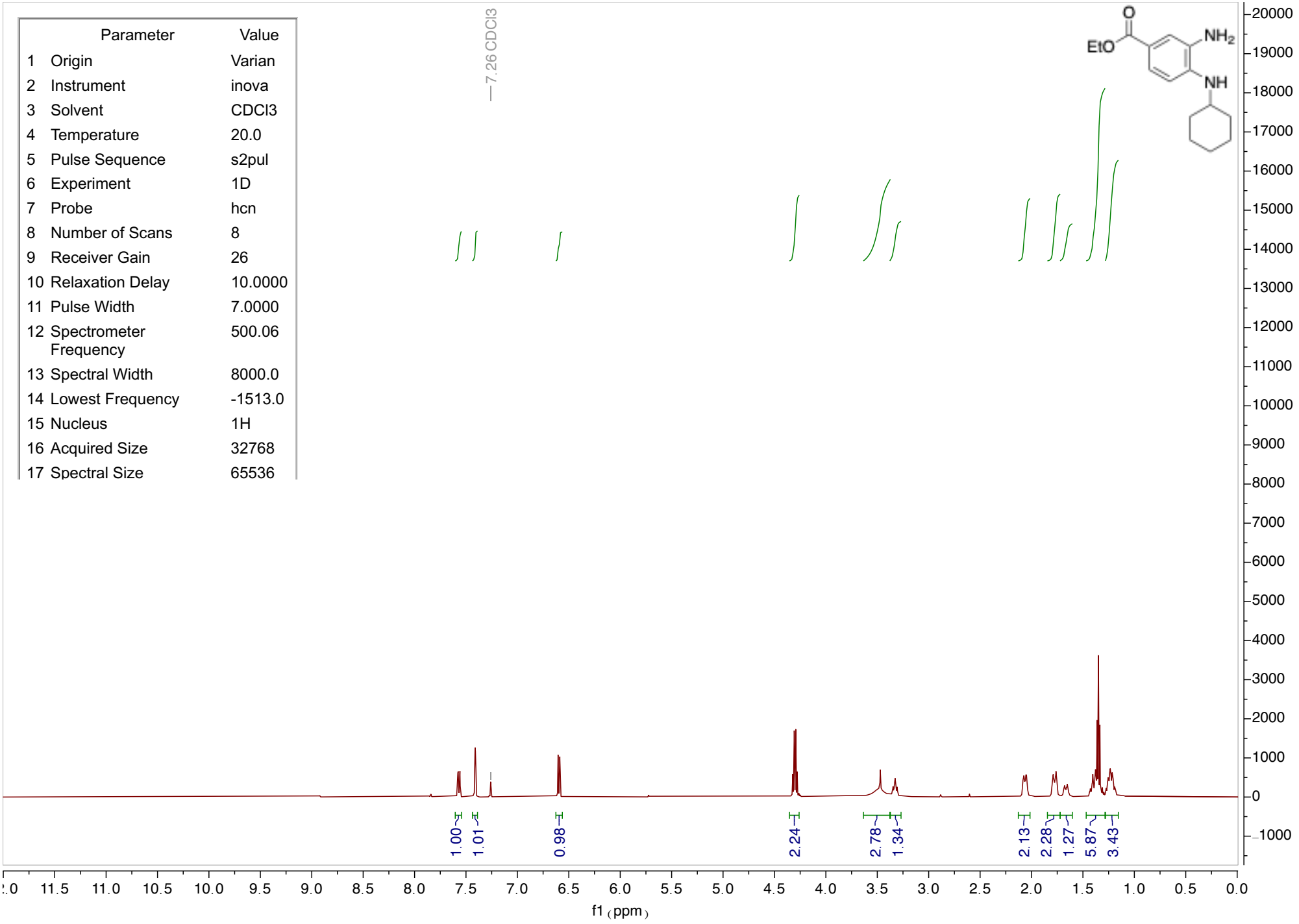
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



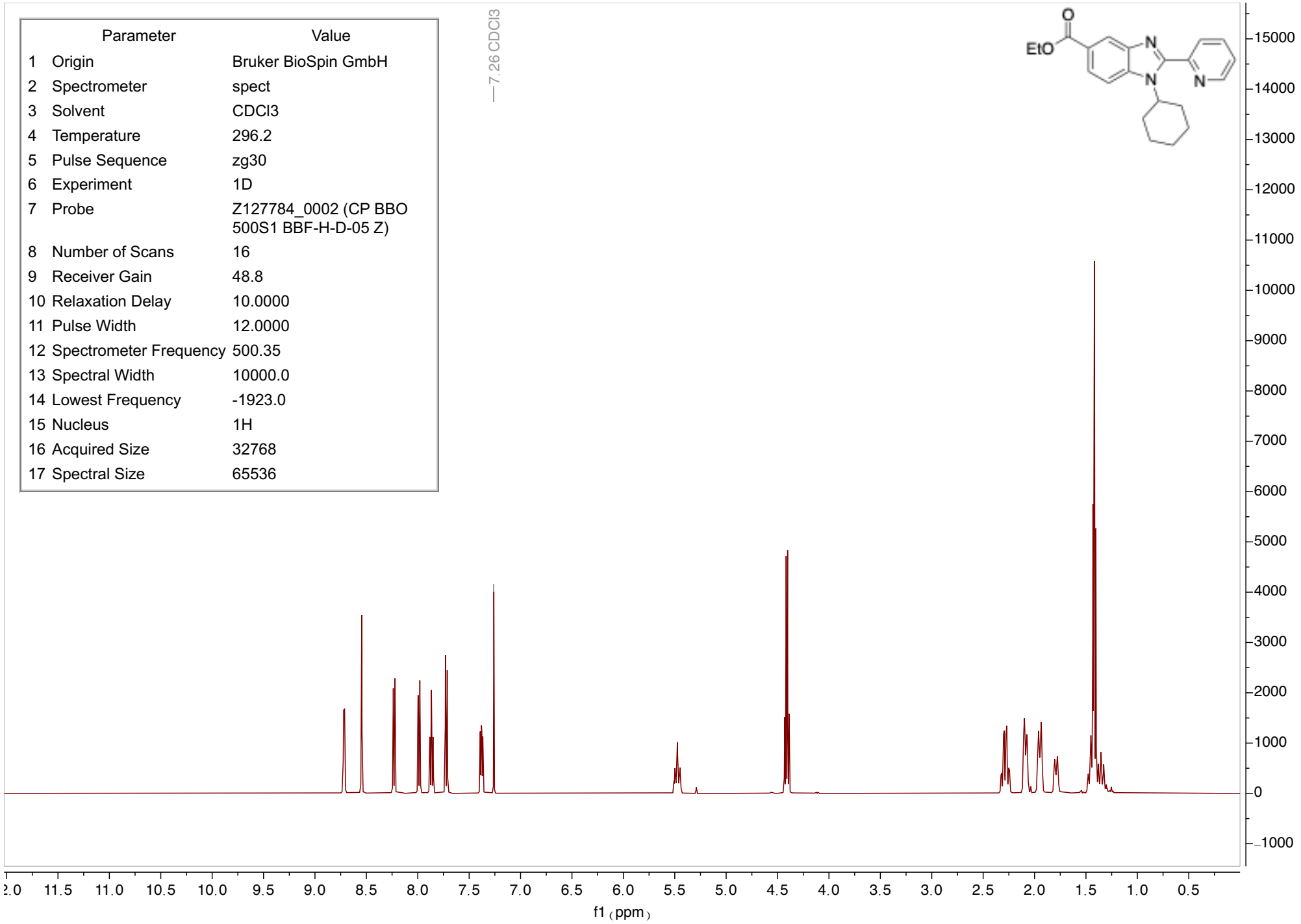
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

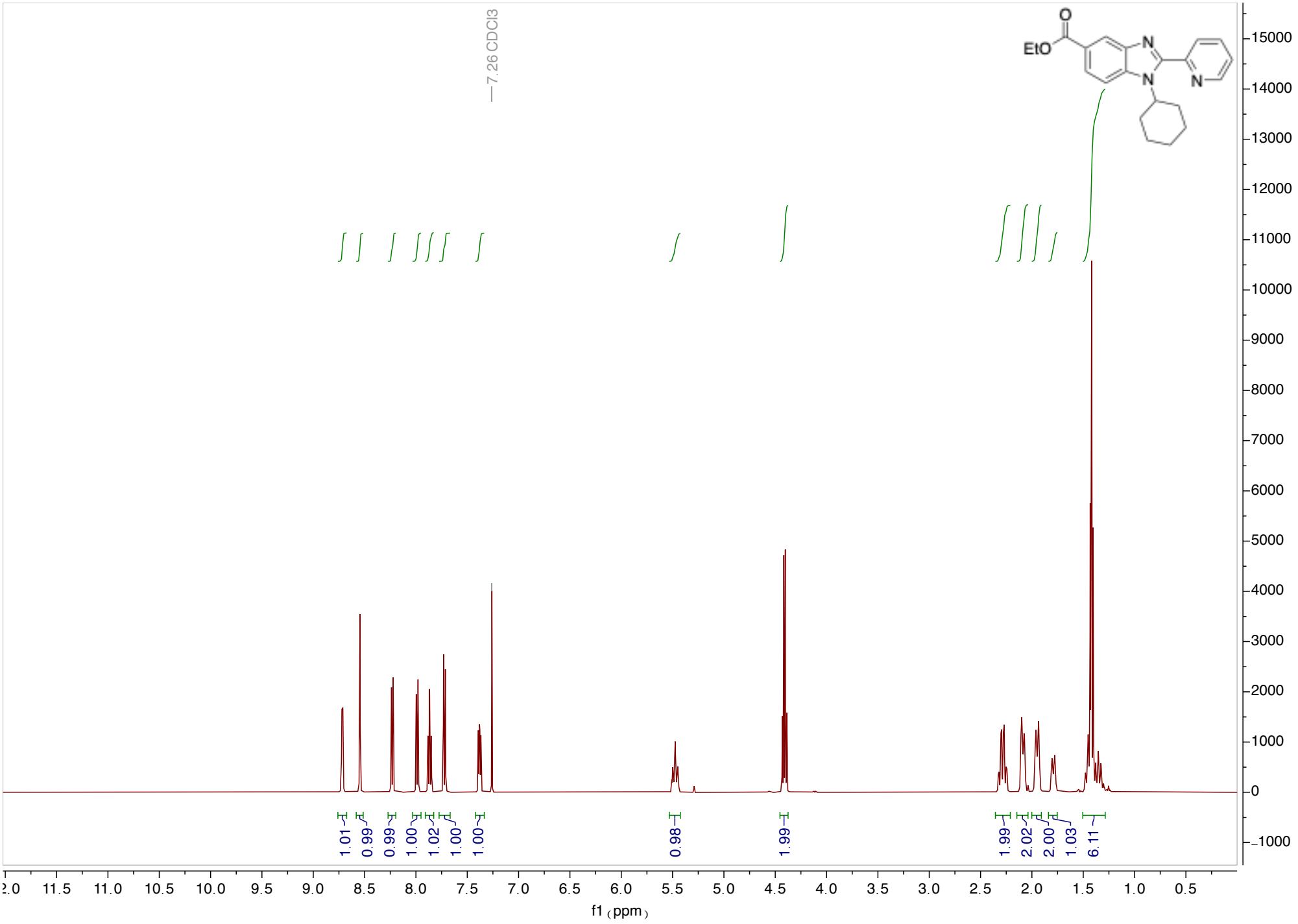



Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 38
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1512.5
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
EtO
O
NO2
NH
1.00
1.02
1.05
1.05
2.12
1.06
2.13
2.14
1.08
8.61
f1 (ppm)

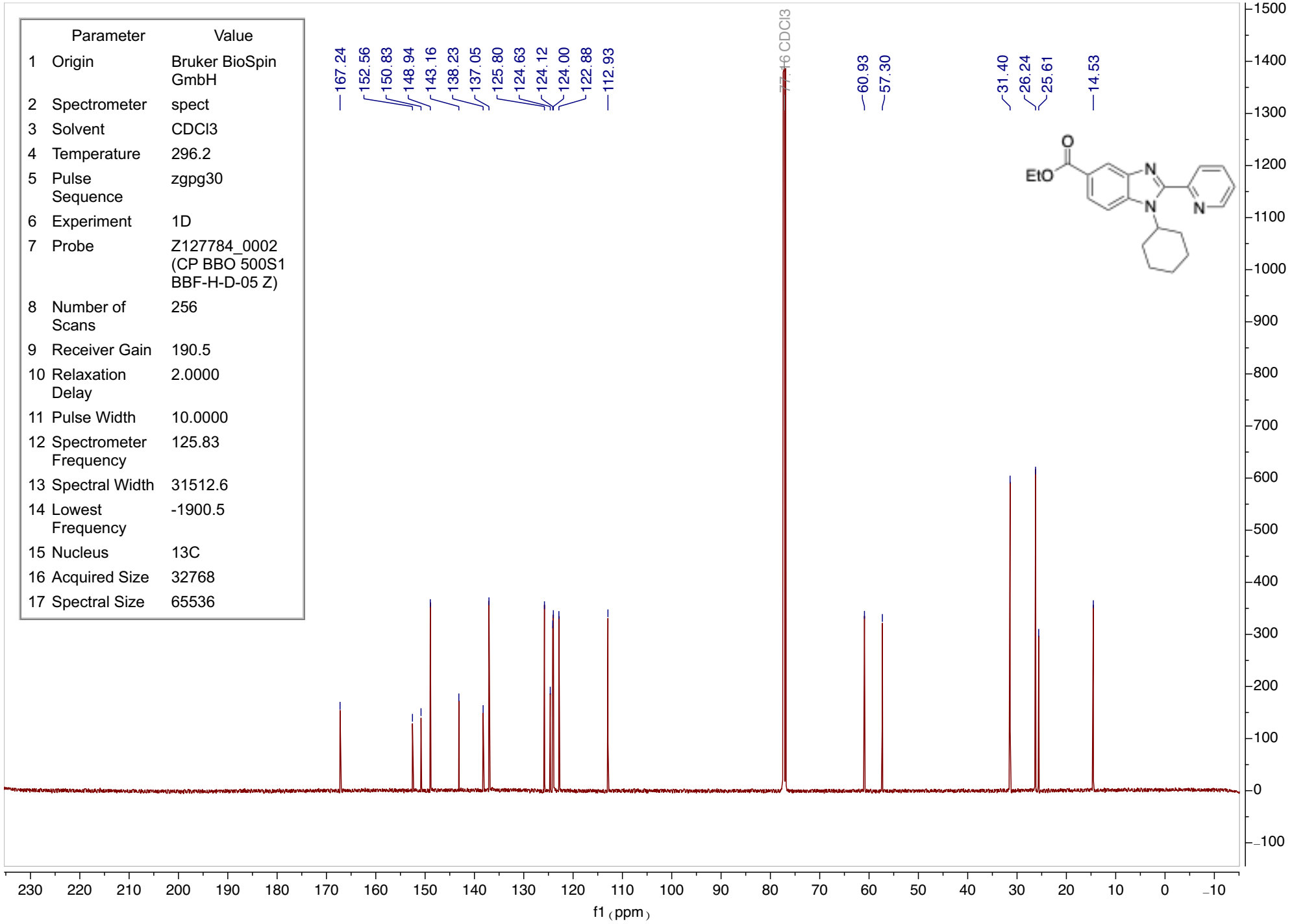

Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 26
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1513.0
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
EtO
O
NH2
NH
1.00
1.01
0.98
2.24
2.78
1.34
2.13
2.28
1.27
5.87
3.43
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	48.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

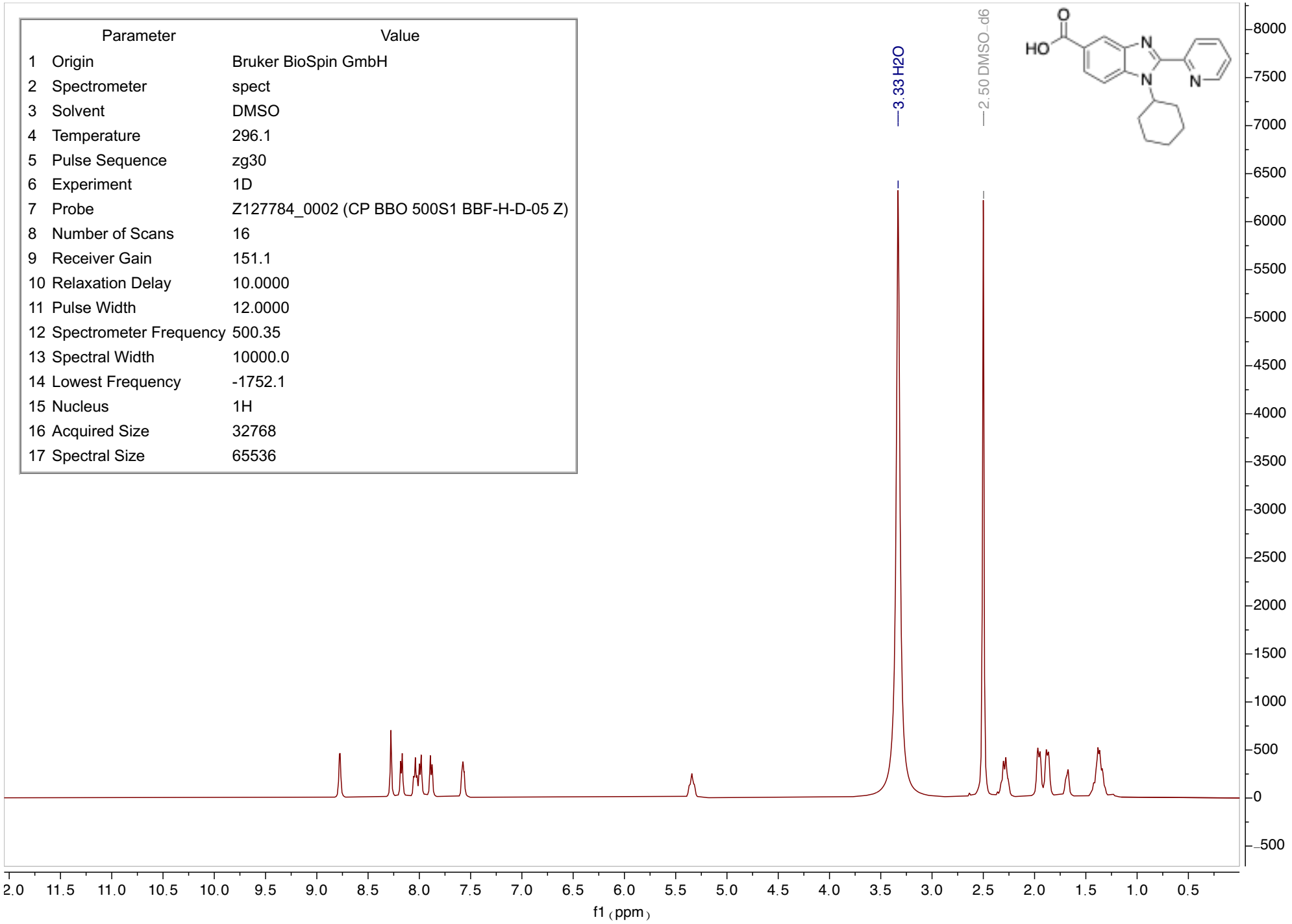


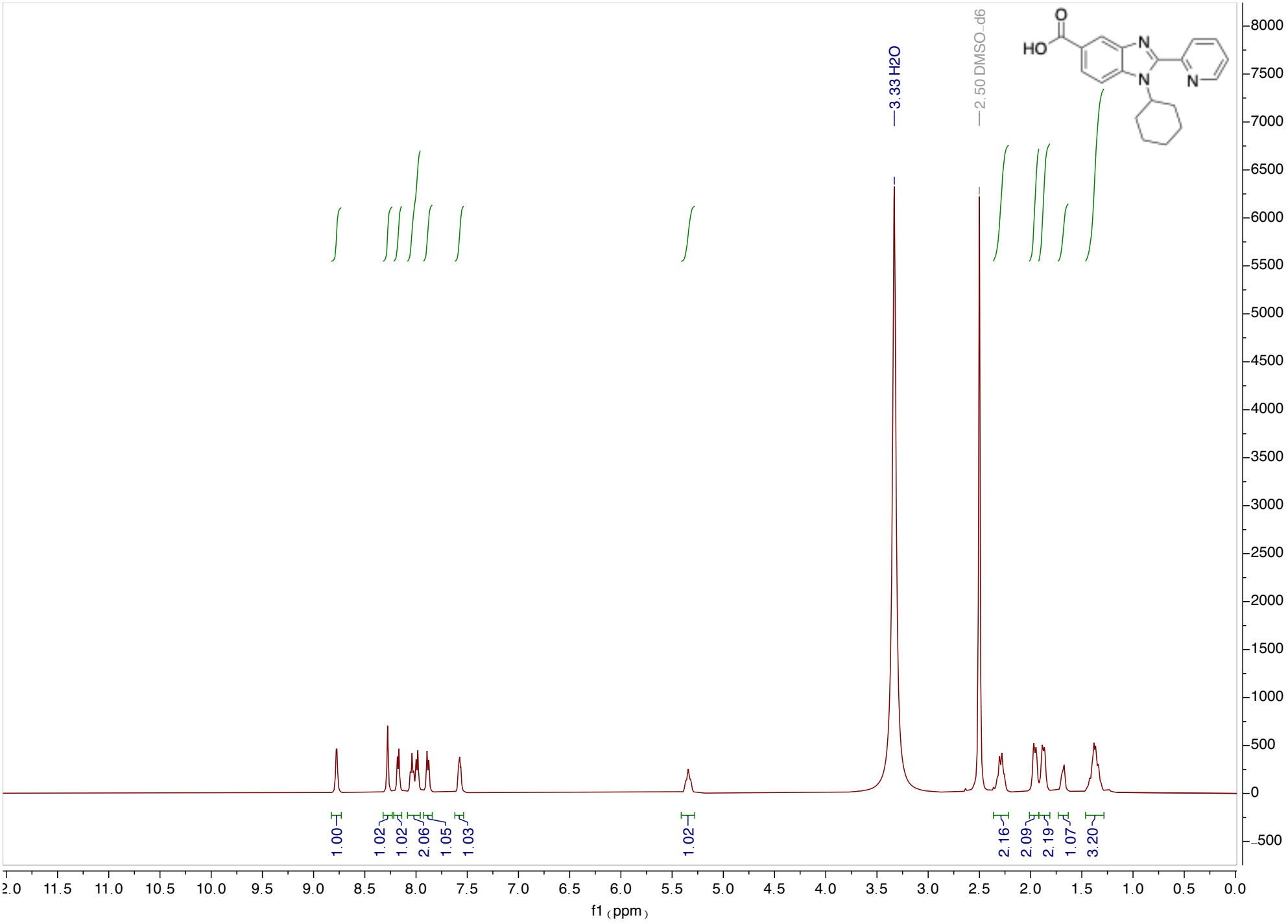

7.26 CDCl3
EtO
O
N
N
N
1.01
0.99
0.99
1.00
1.02
1.00
1.00
0.98
1.99
1.99
2.02
2.00
1.03
6.11
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

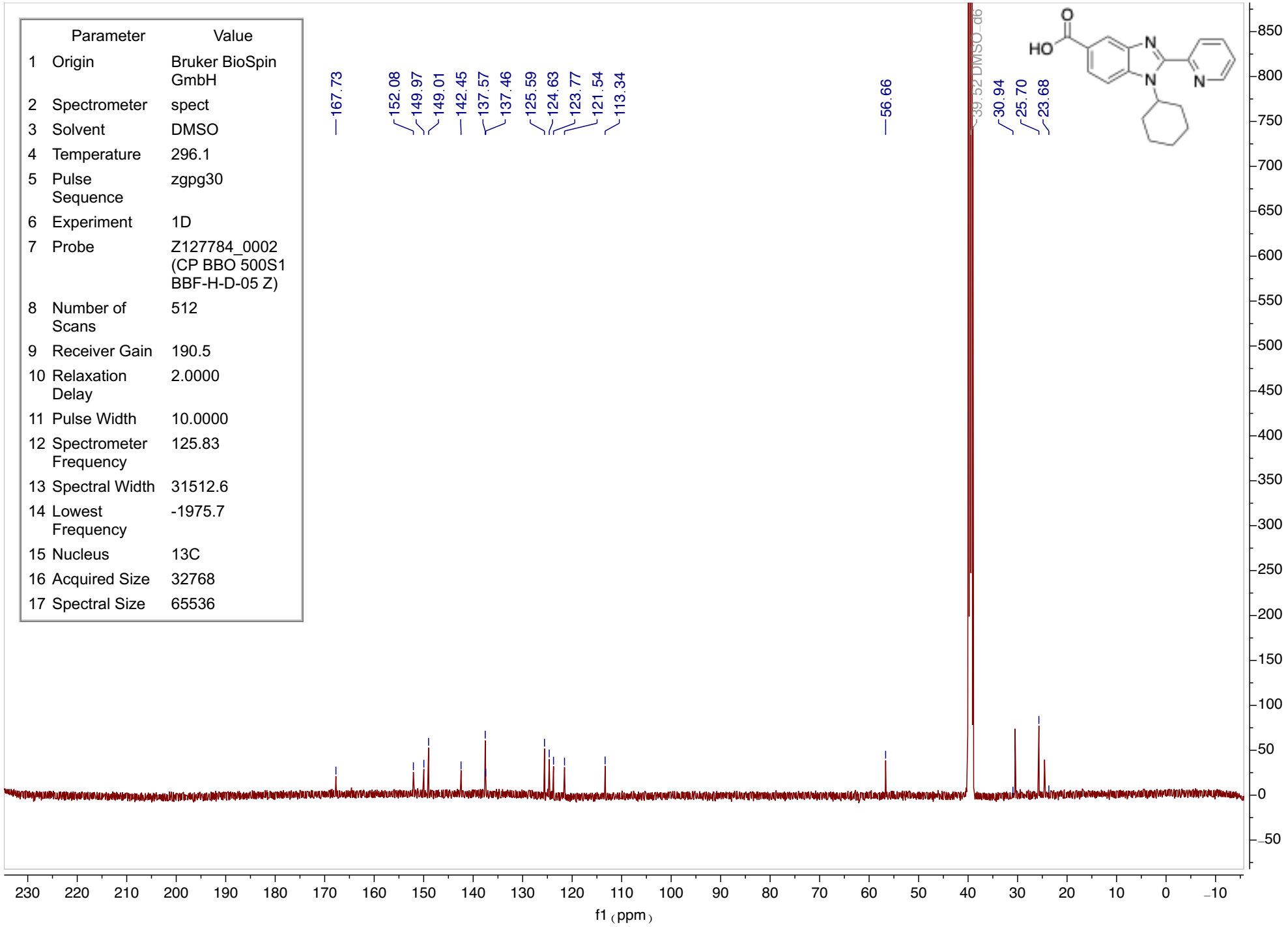


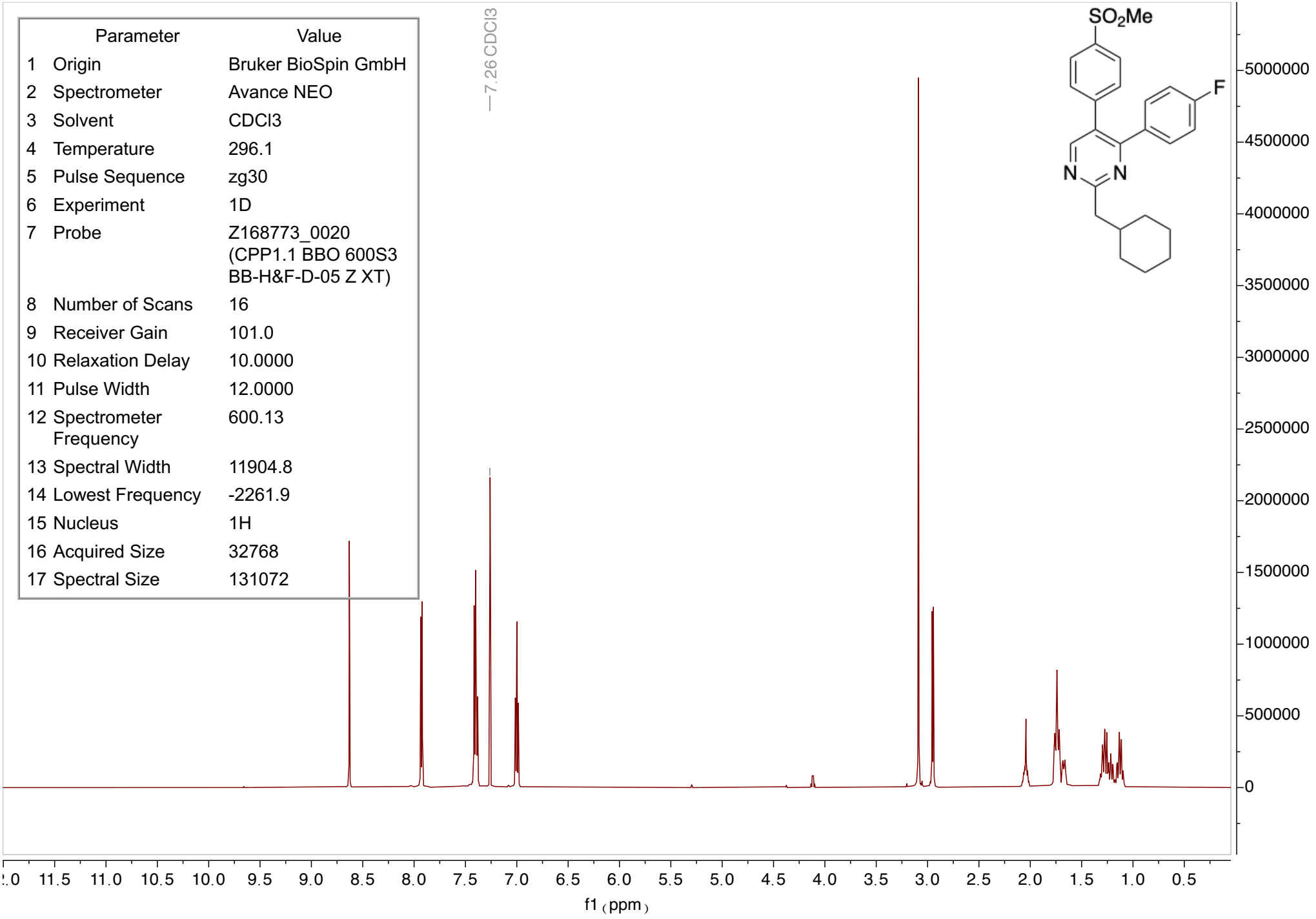
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	151.1
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1752.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

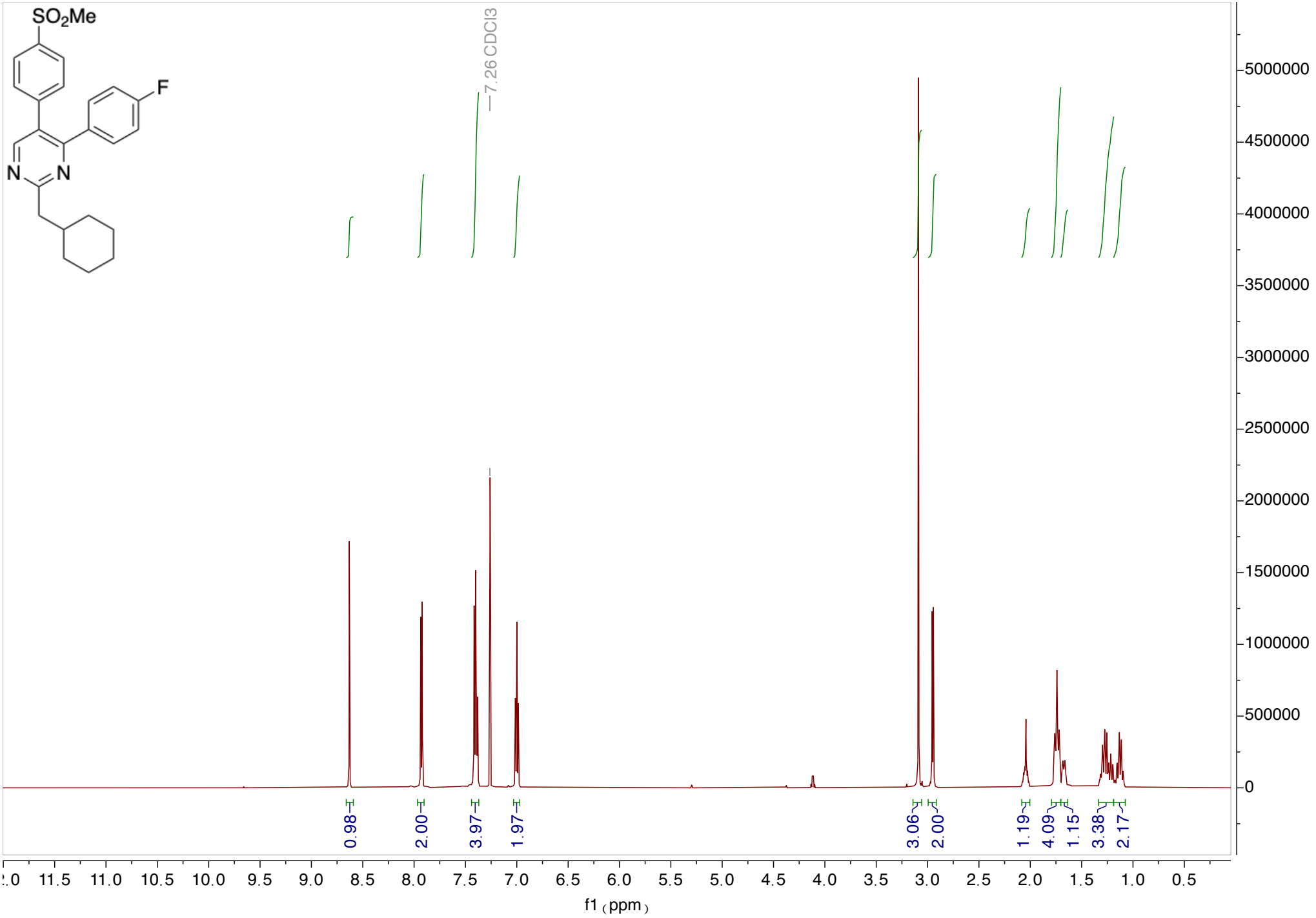


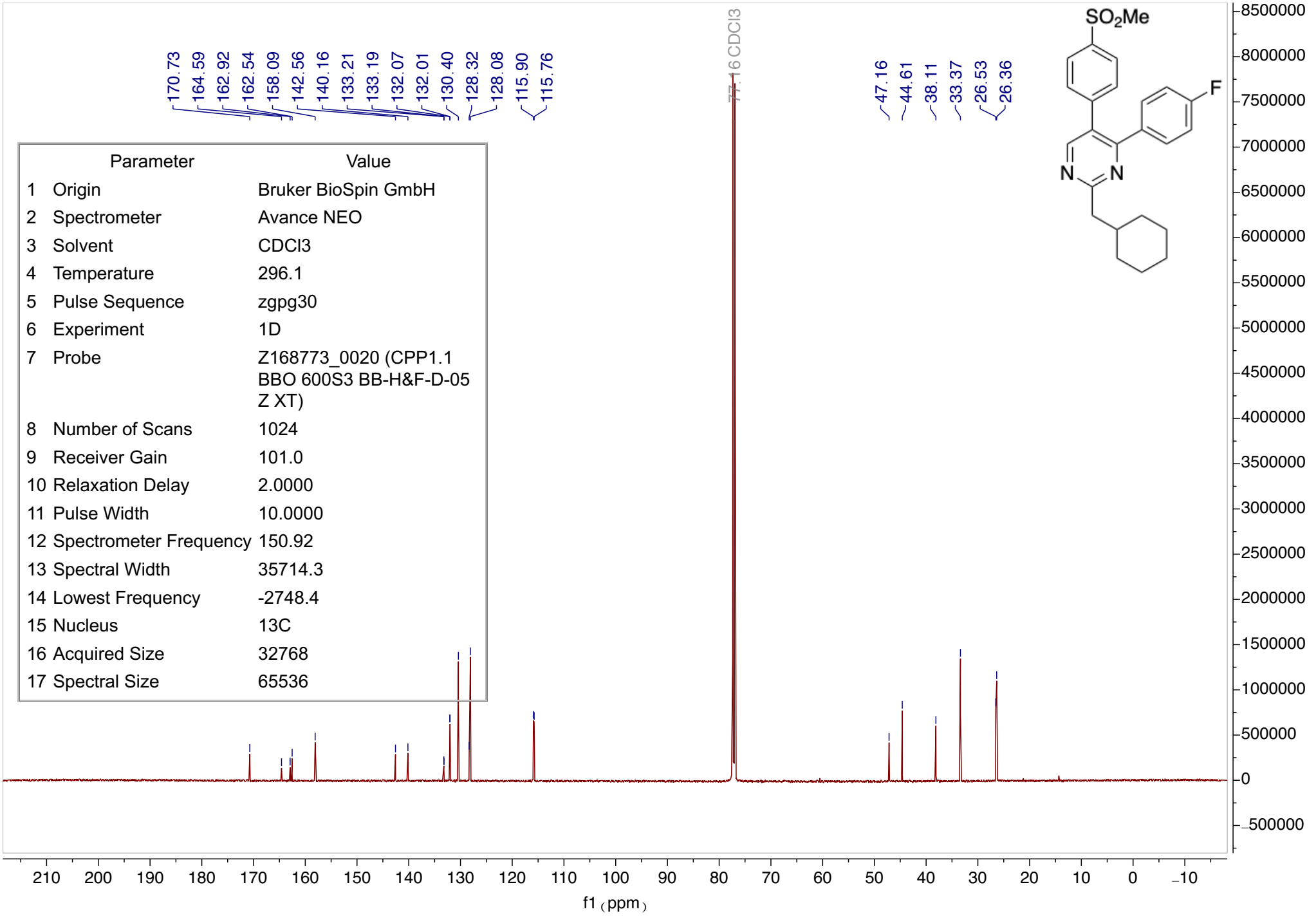

3.33 H2O
2.50 DMSO-d6
HO
O
N
N
N
1.00
1.02
1.02
2.06
1.05
1.03
1.02
2.16
2.09
2.19
1.07
3.20
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1975.7
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



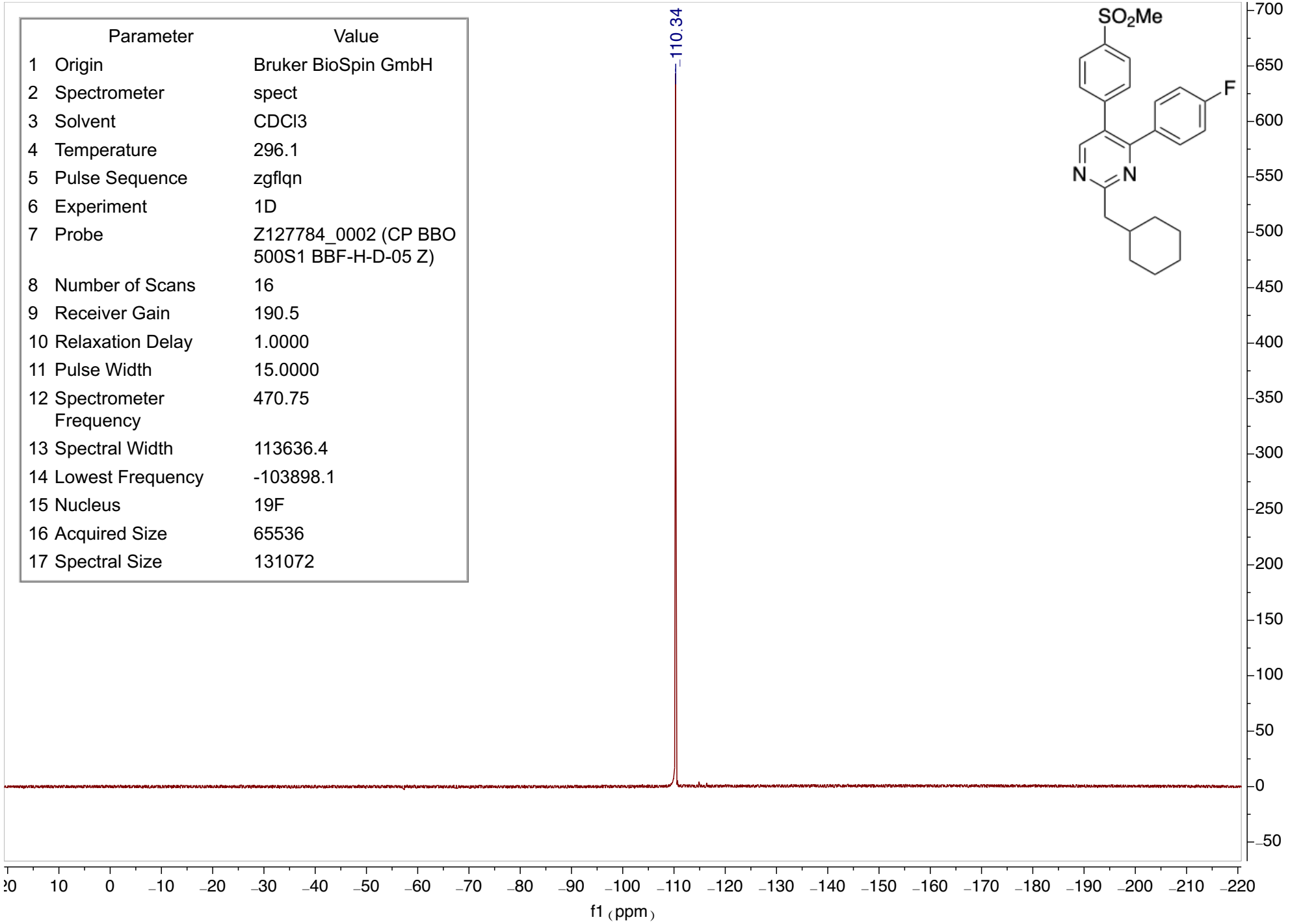

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 101.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2261.9
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.26 CDCl3
SO2Me
F
N
N
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
11.5 11.0 10.5 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
f1 (ppm)


SO2Me
F
N
N
7.26 CDCl3
0.98
2.00
3.97
1.97
3.06
2.00
1.19
4.09
1.15
3.38
2.17
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
f1 (ppm)

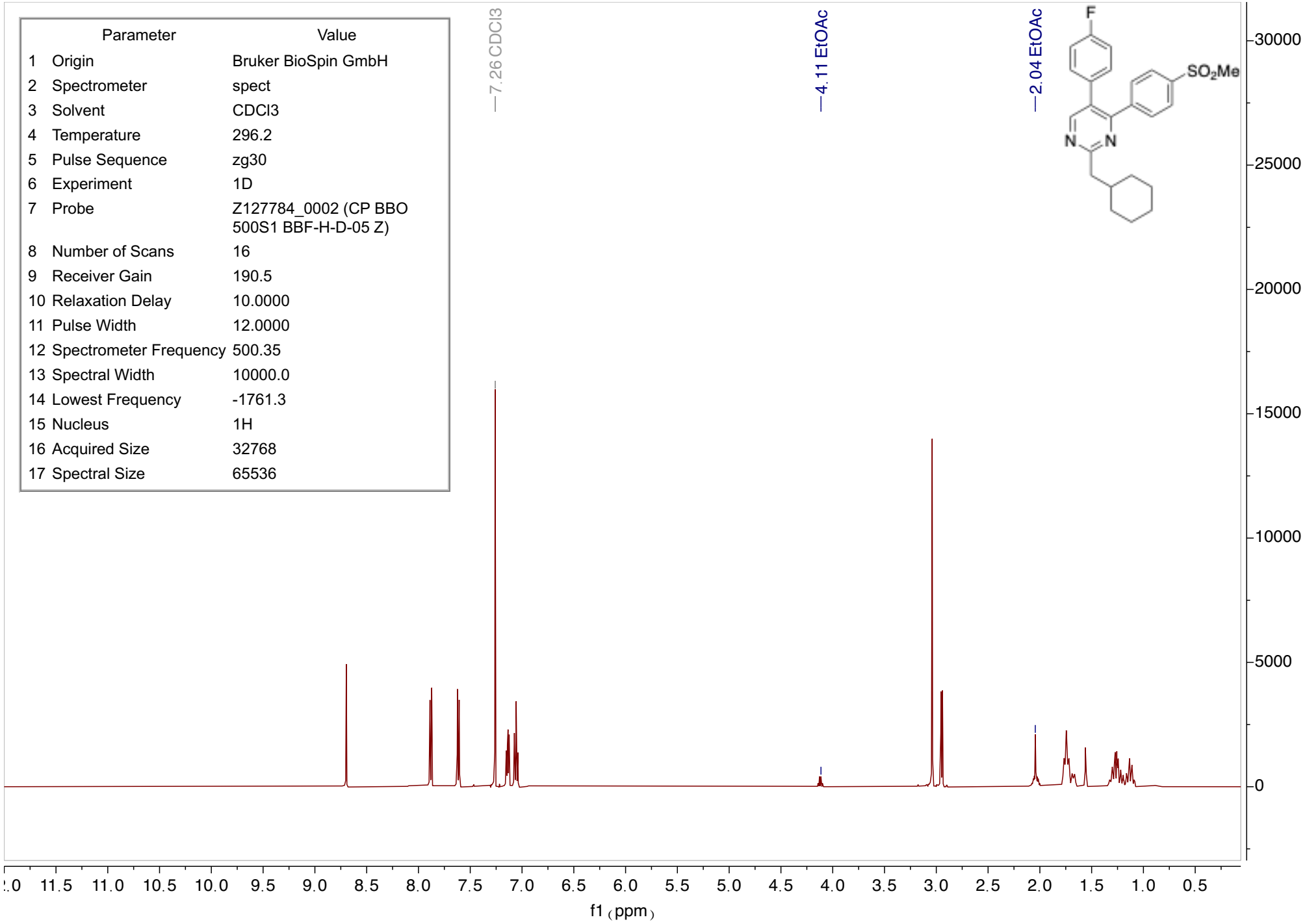


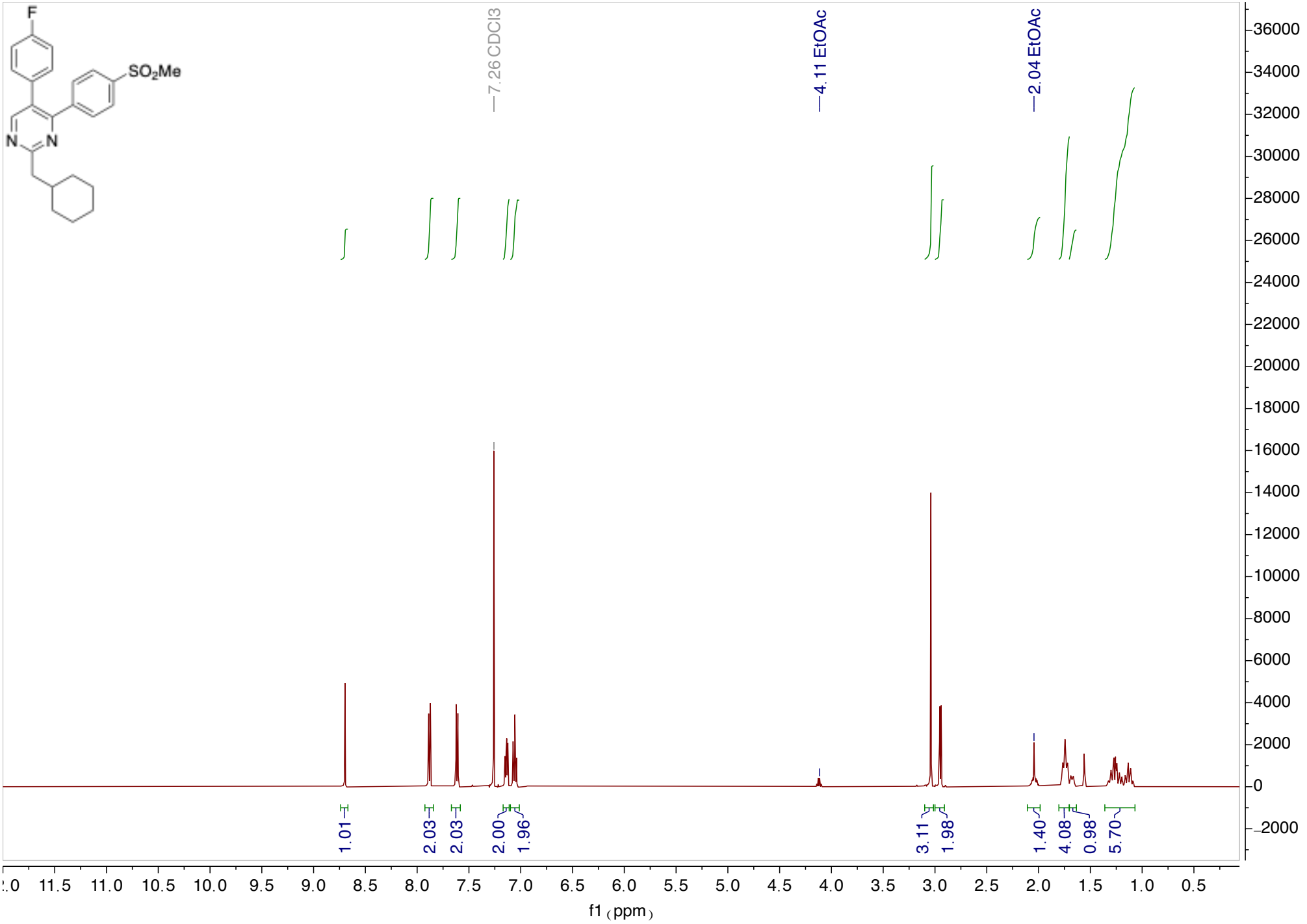
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2748.4
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

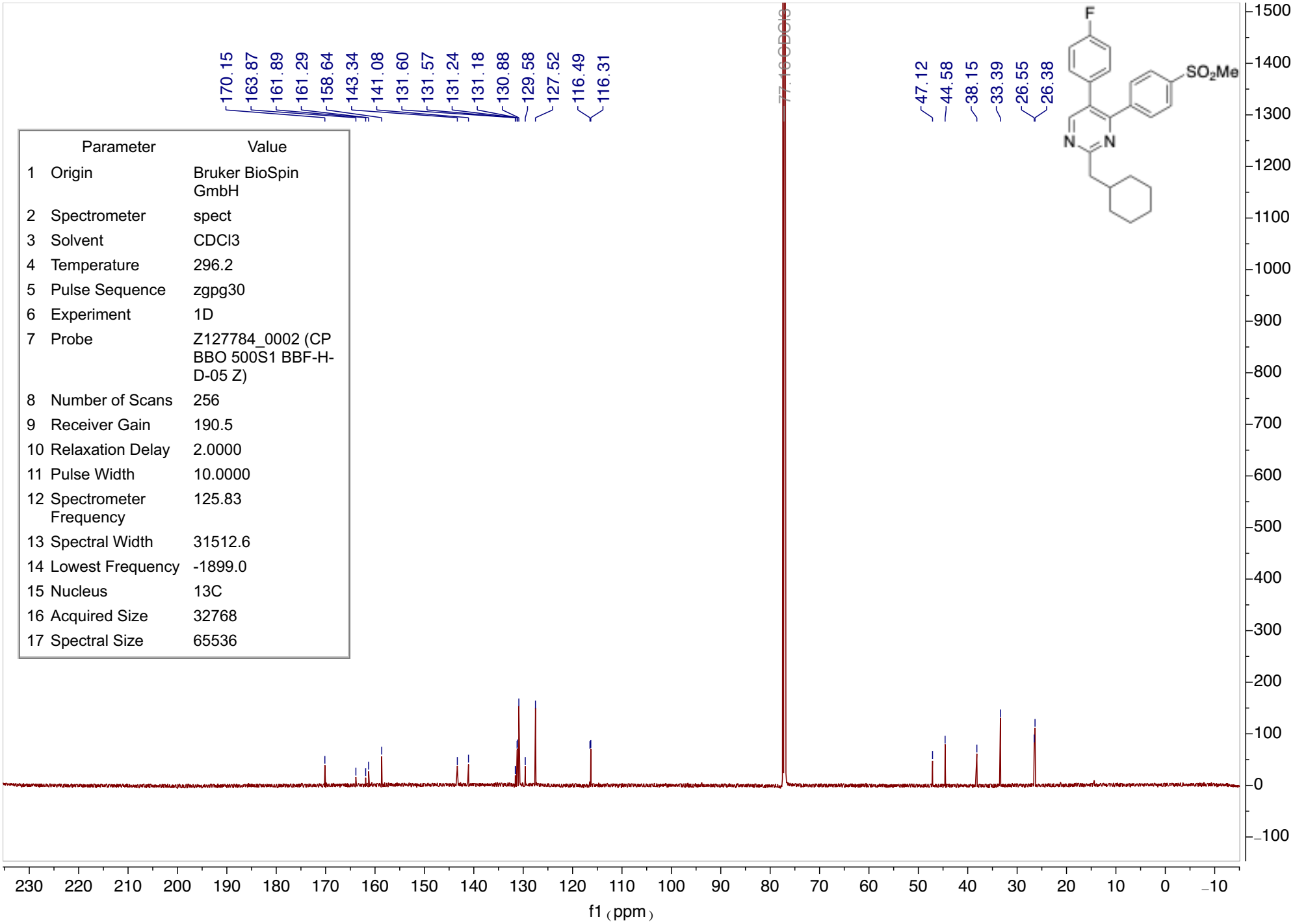
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1761.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

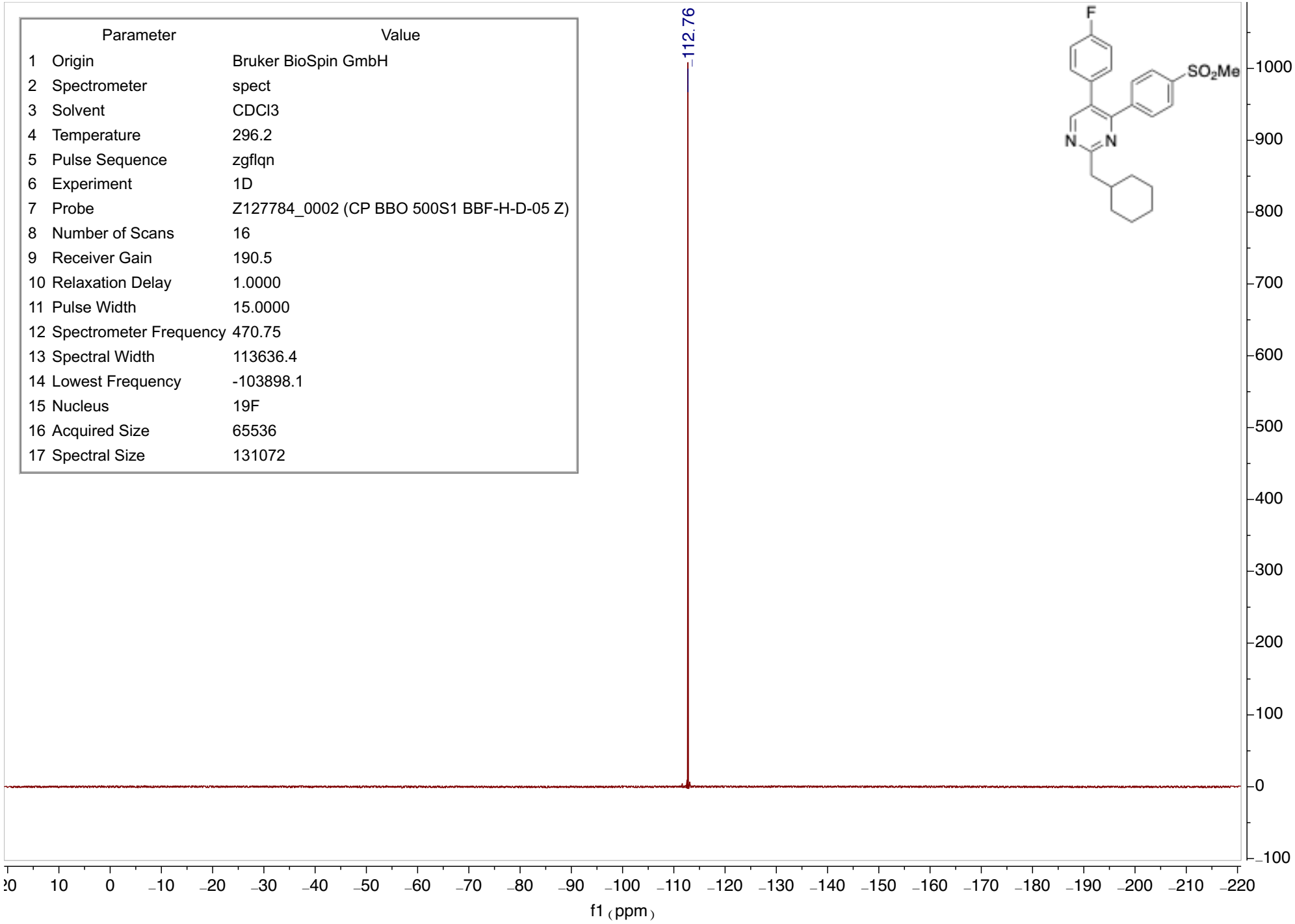



F
SO2Me
N
N
7.26 CDCl3
4.11 EtOAc
2.04 EtOAc
1.01
2.03
2.03
2.00
1.96
3.11
1.98
1.40
4.08
0.98
5.70
f1 (ppm)

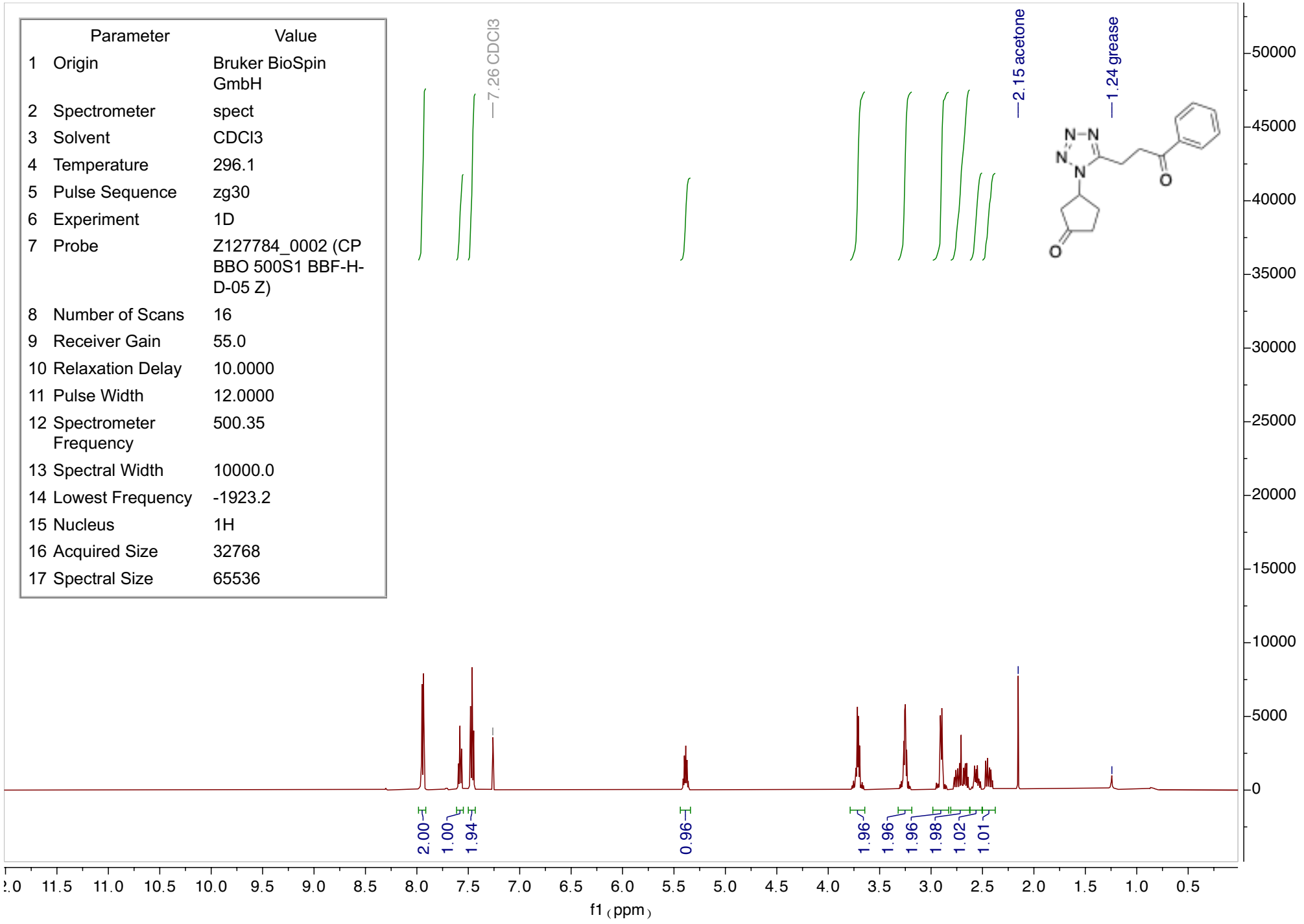


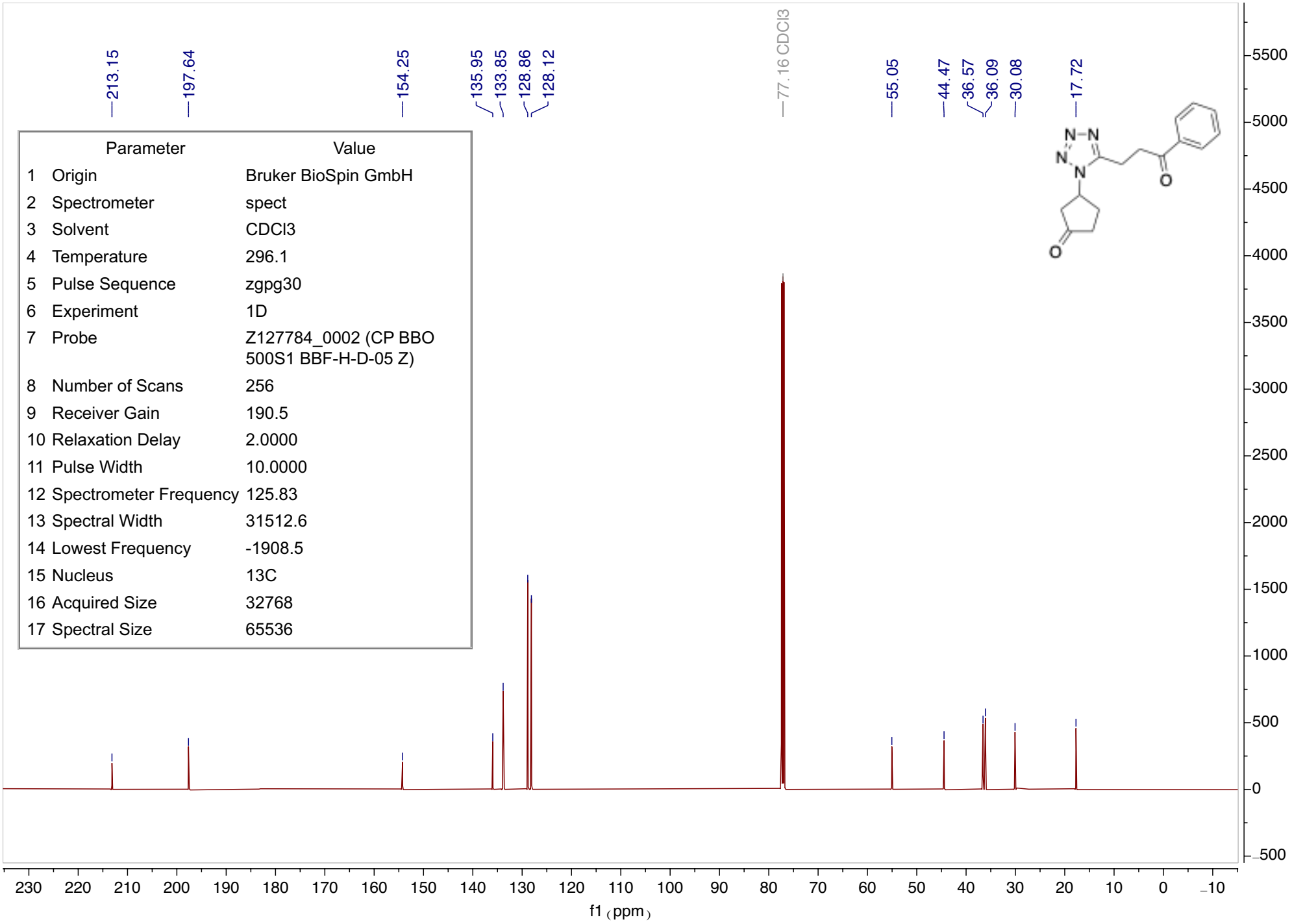
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

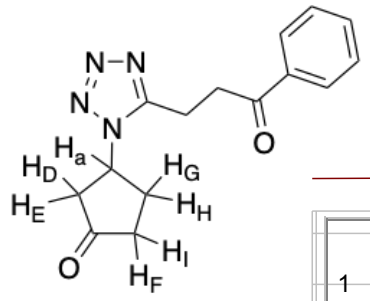


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	55.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

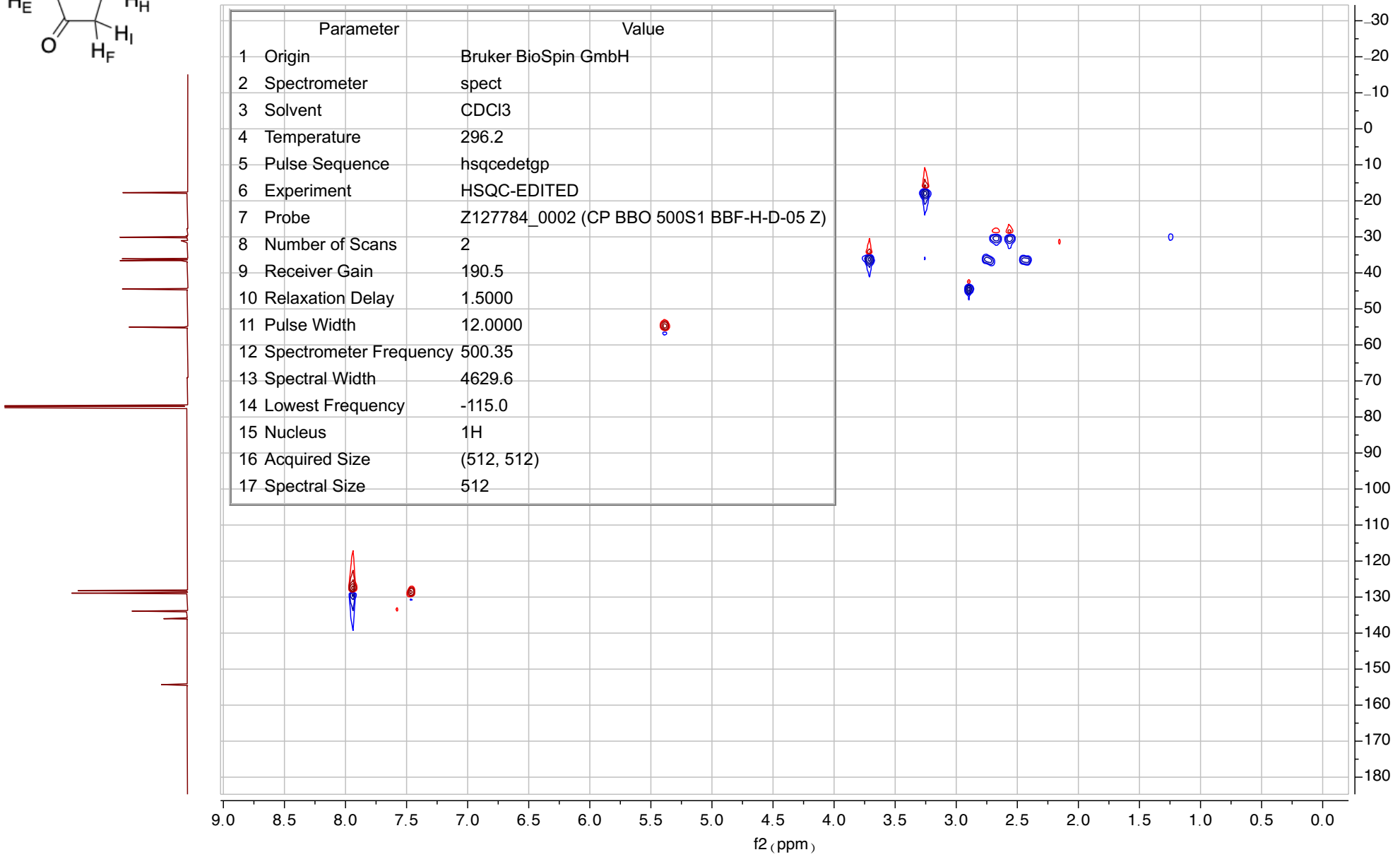


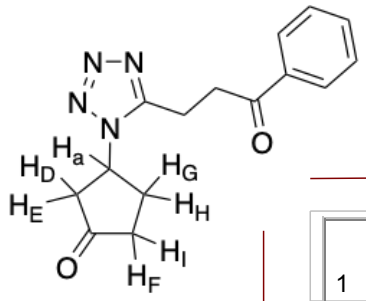


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1908.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

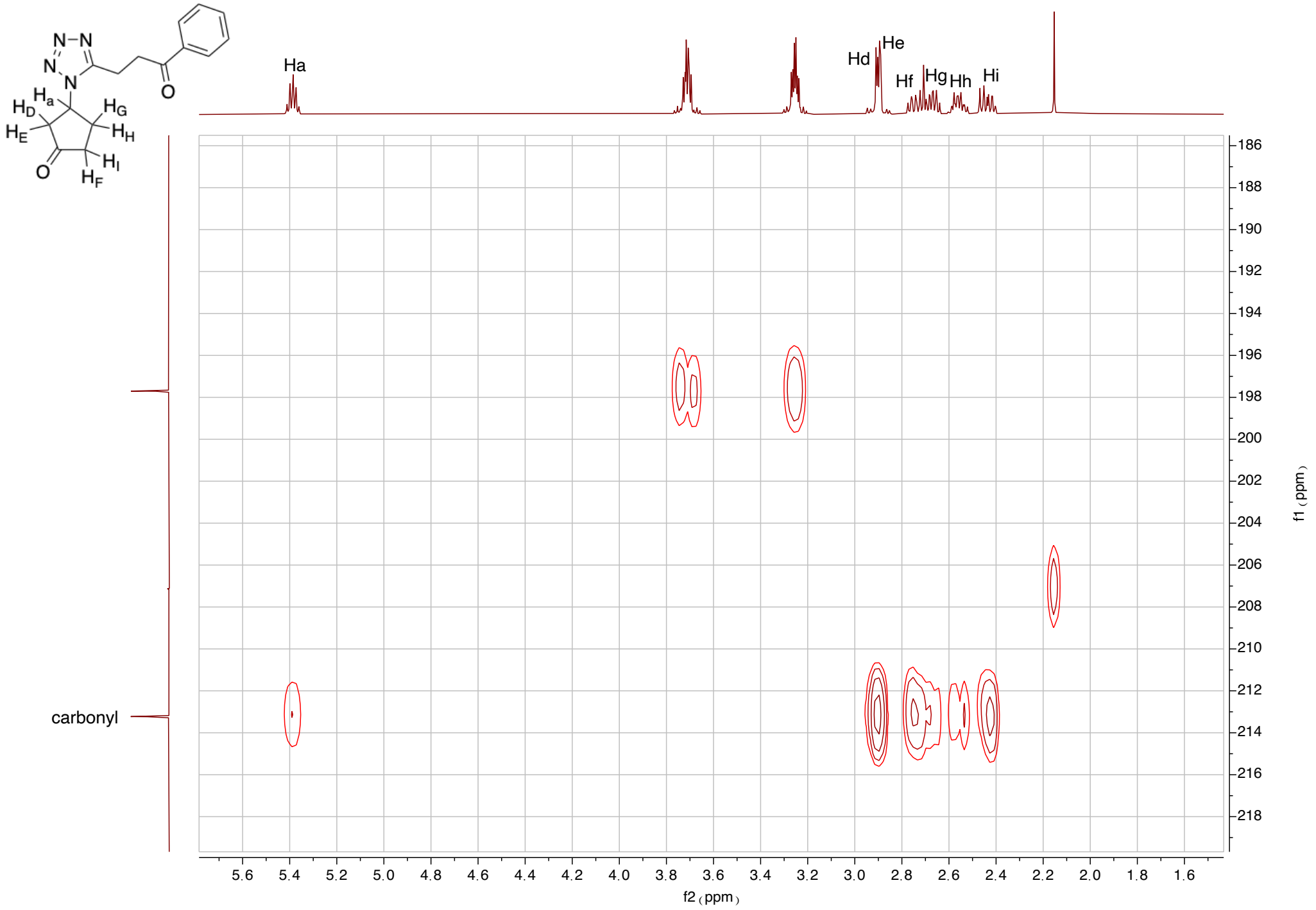


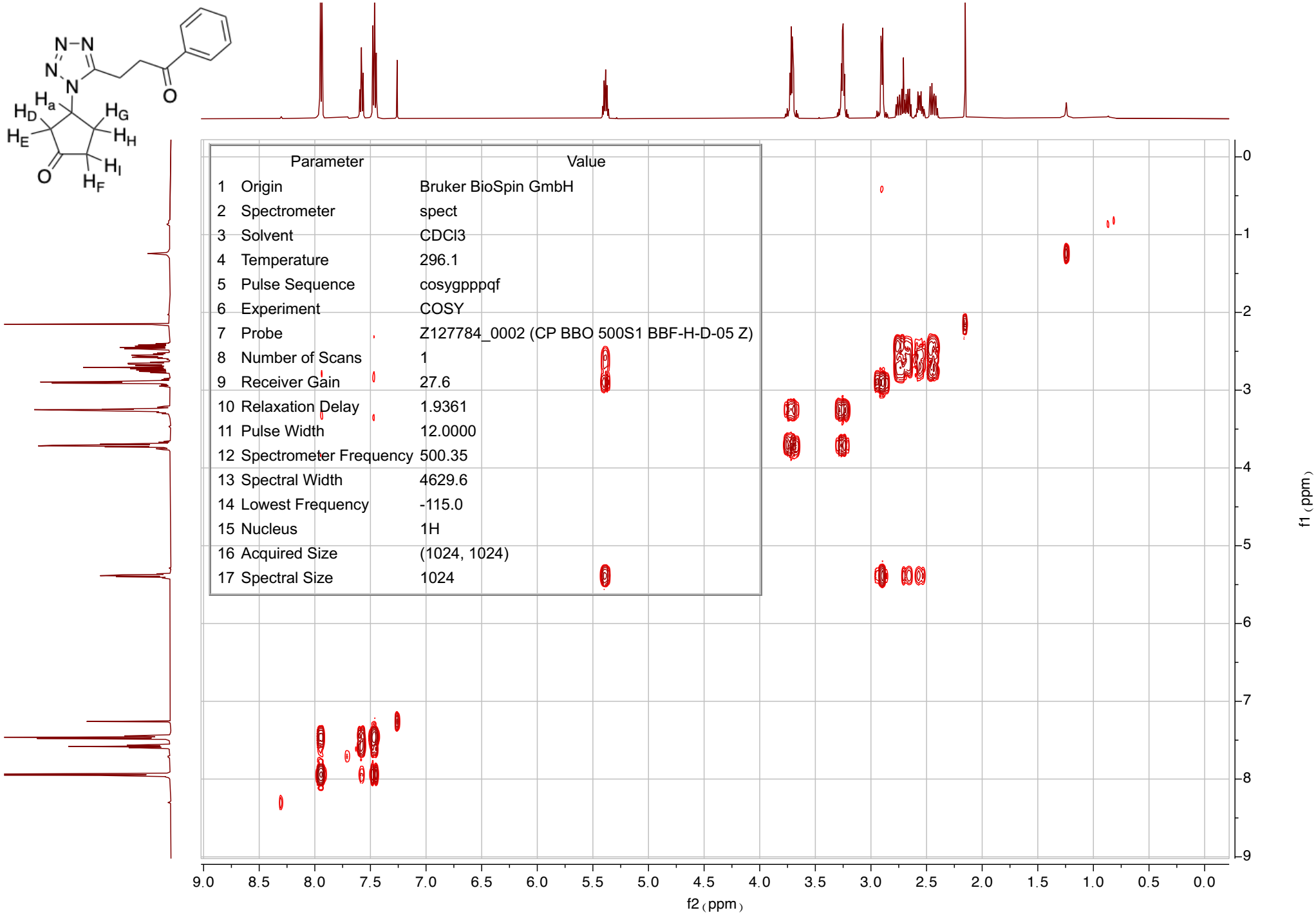
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4629.6
14	Lowest Frequency	-115.0
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

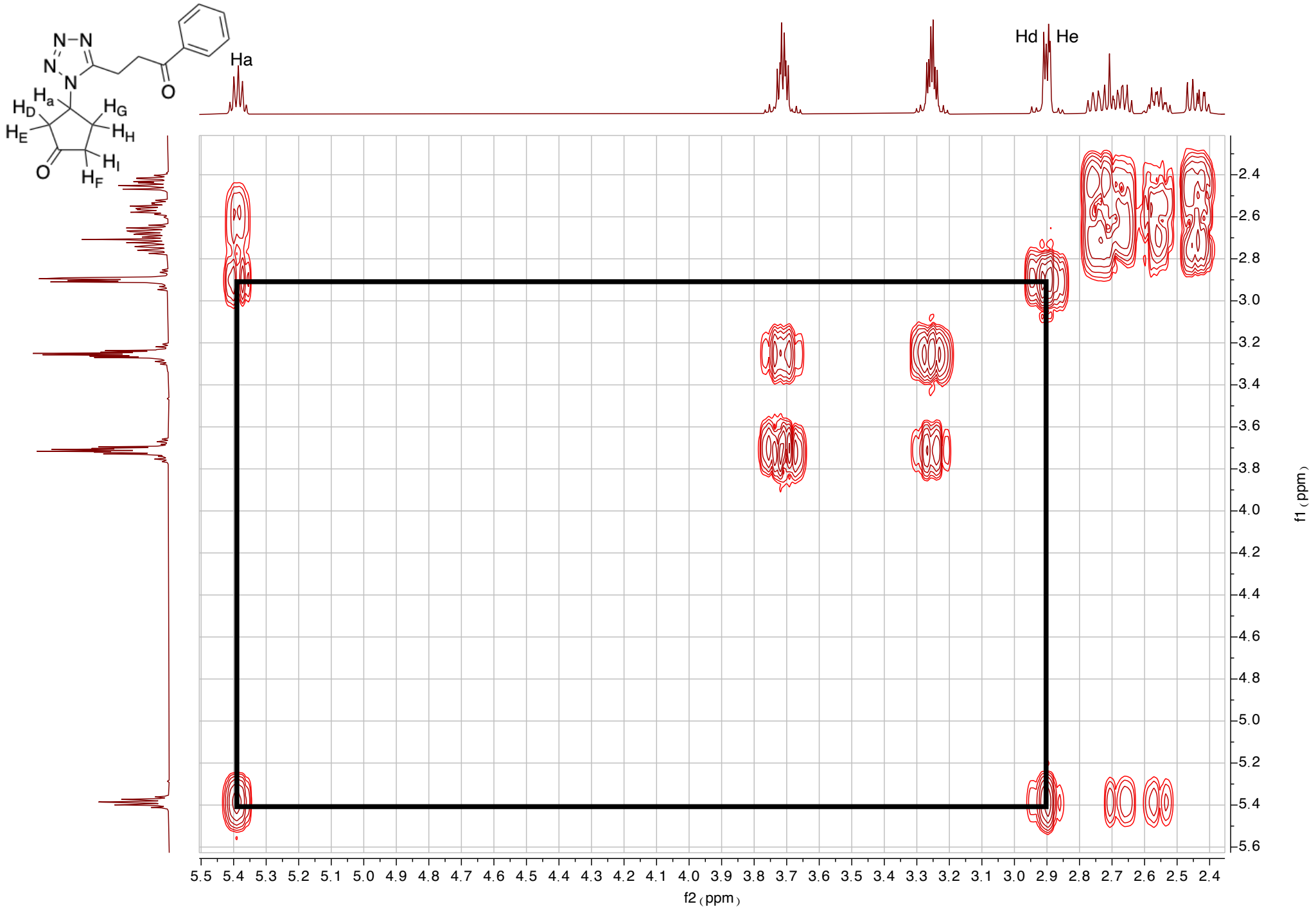




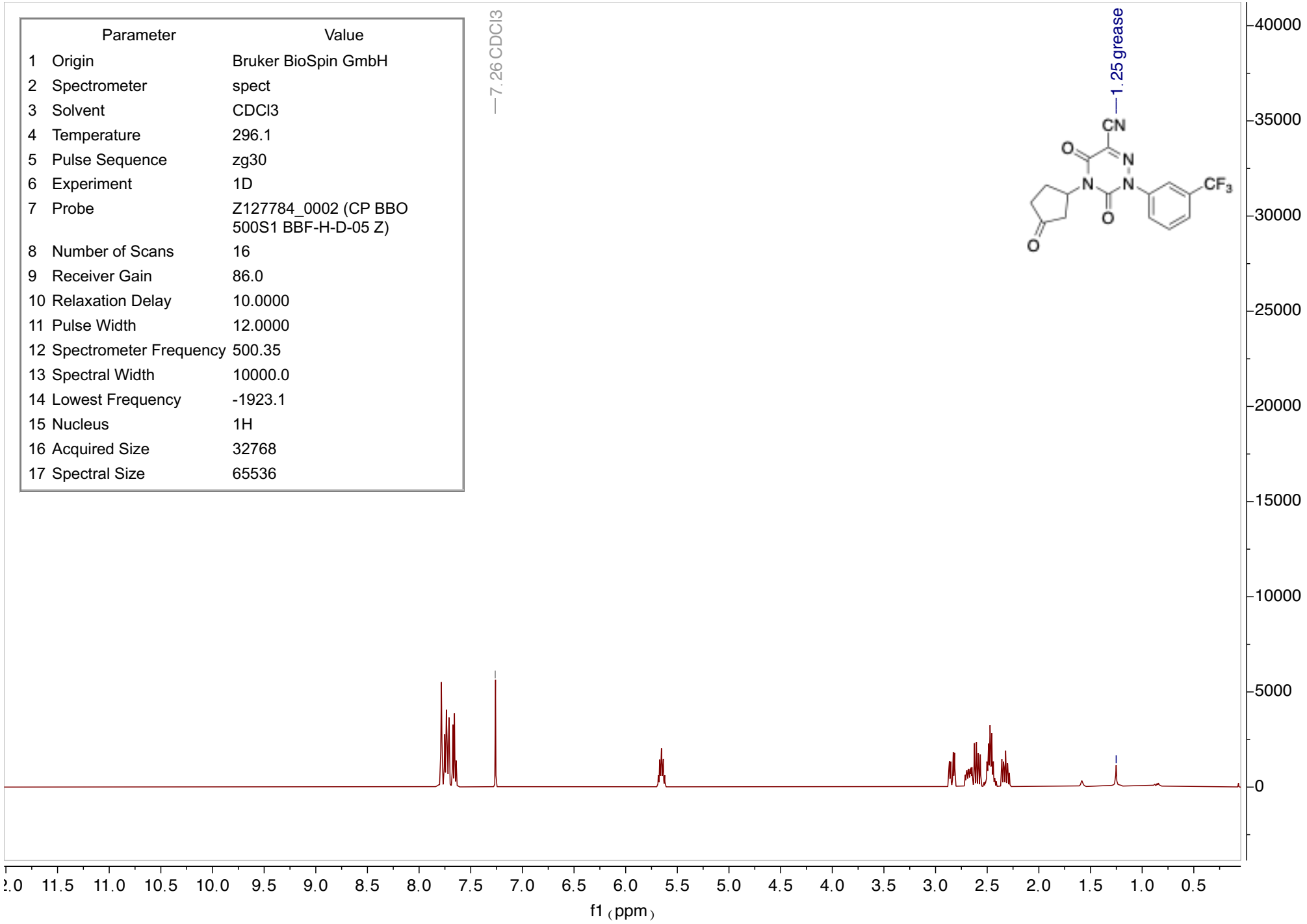
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4629.6
14	Lowest Frequency	-115.0
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

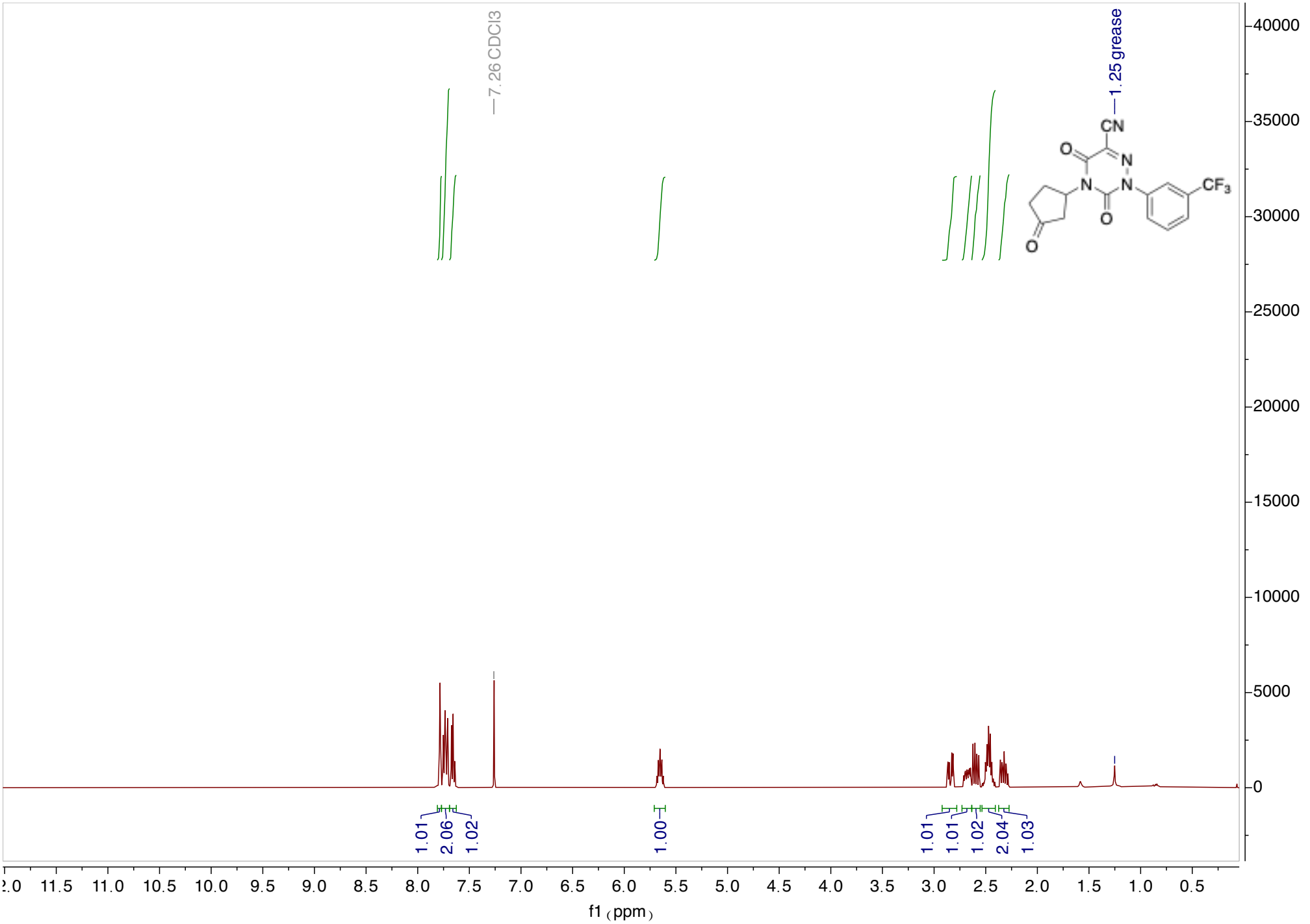

Ha
Hd
He
Hf
Hg
Hh
Hi
carbonyl
f2 (ppm)
f1 (ppm)

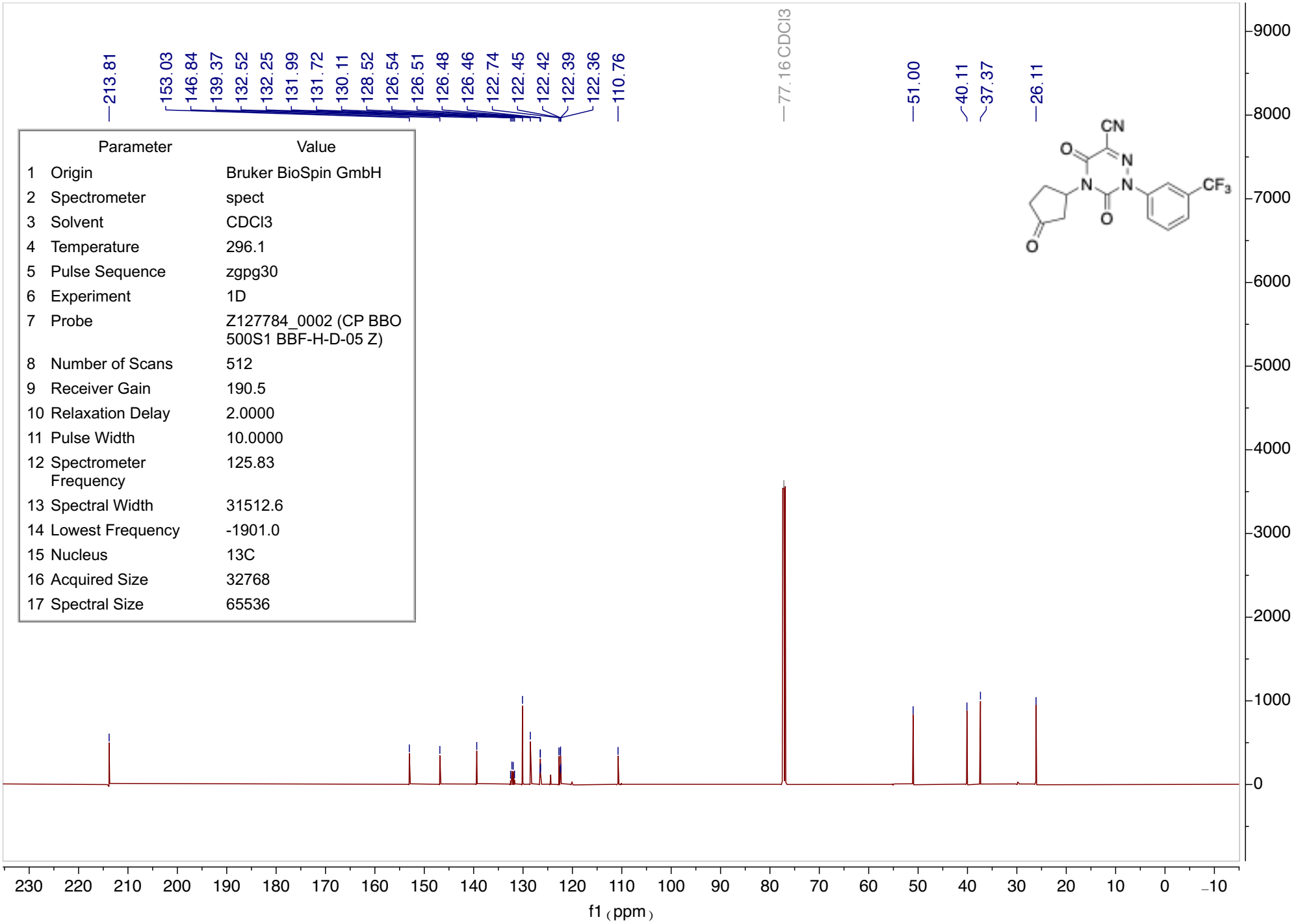

N–N
N
N
O
Ha
HD
HG
HE
HH
HI
O
HF
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 1
9 Receiver Gain 27.6
10 Relaxation Delay 1.9361
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4629.6
14 Lowest Frequency -115.0
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)


Ha
Hd
He
f2 (ppm)
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

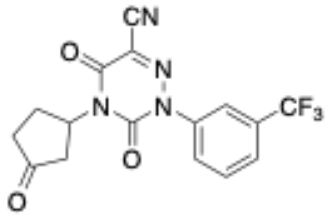



7.26 CDCl3
1.25 grease
CN
O
N
N
N
O
O
CF3
40000
35000
30000
25000
20000
15000
10000
5000
0
1.01
2.06
1.02
1.00
1.01
1.01
1.02
2.04
1.03
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

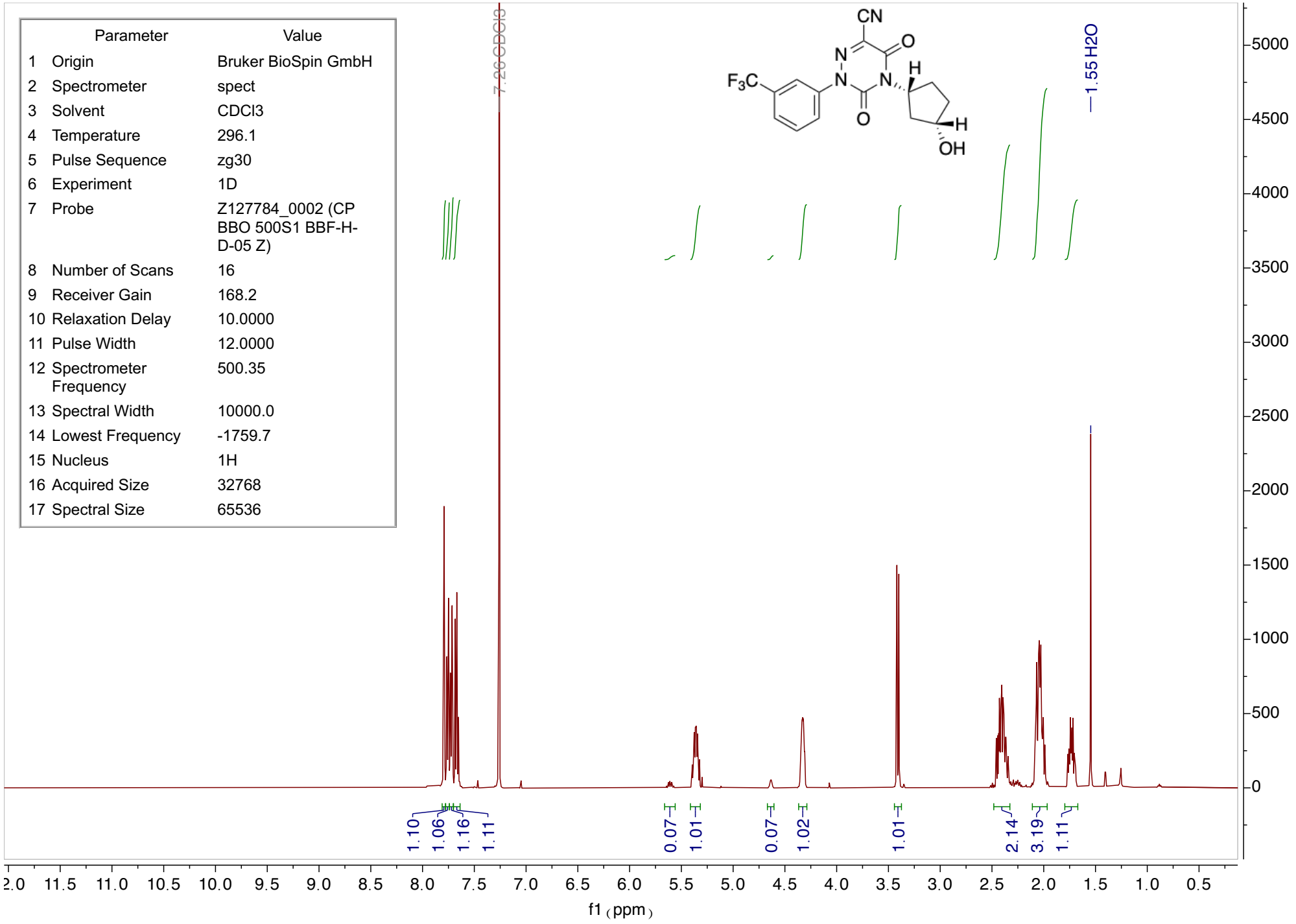


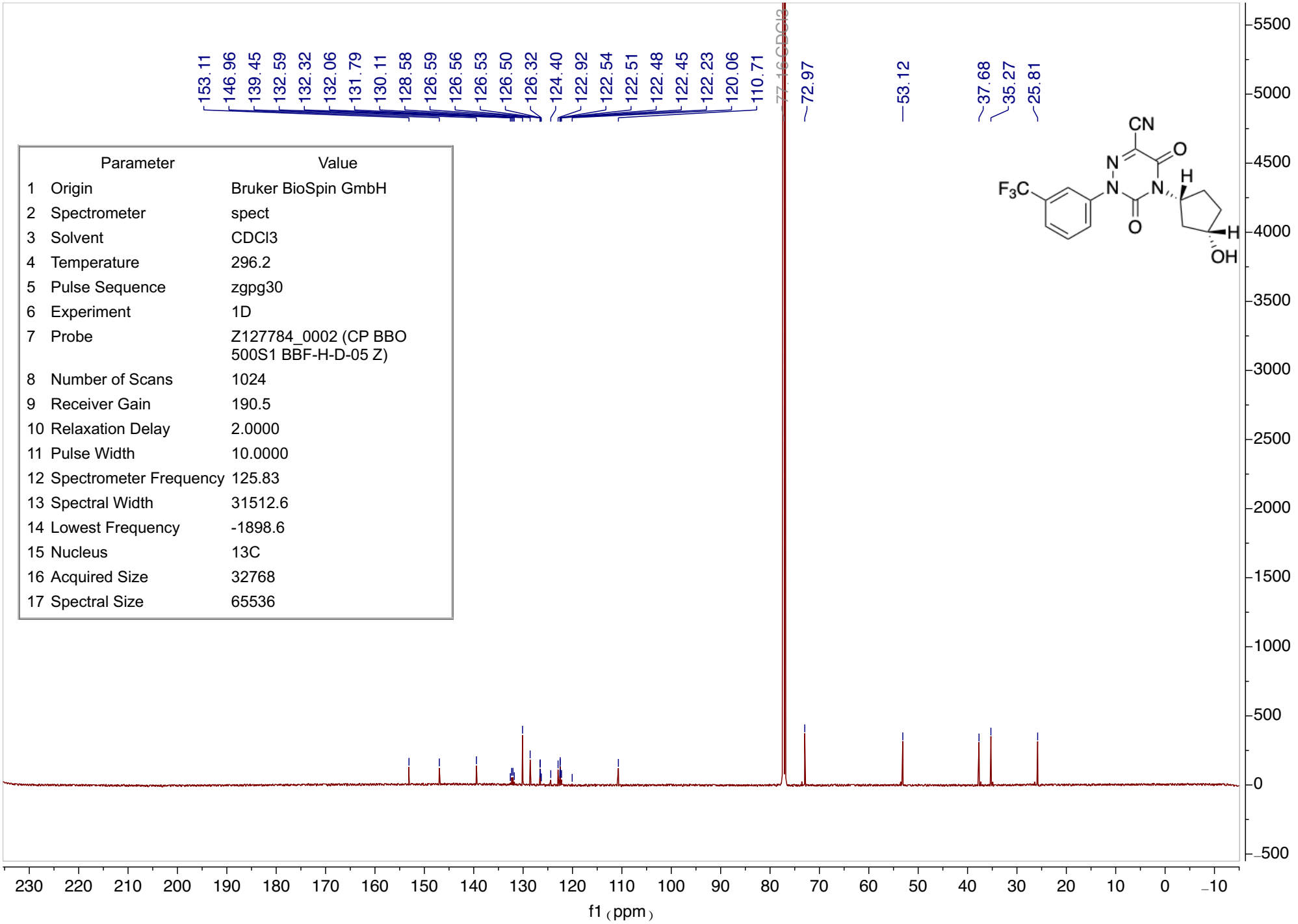
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



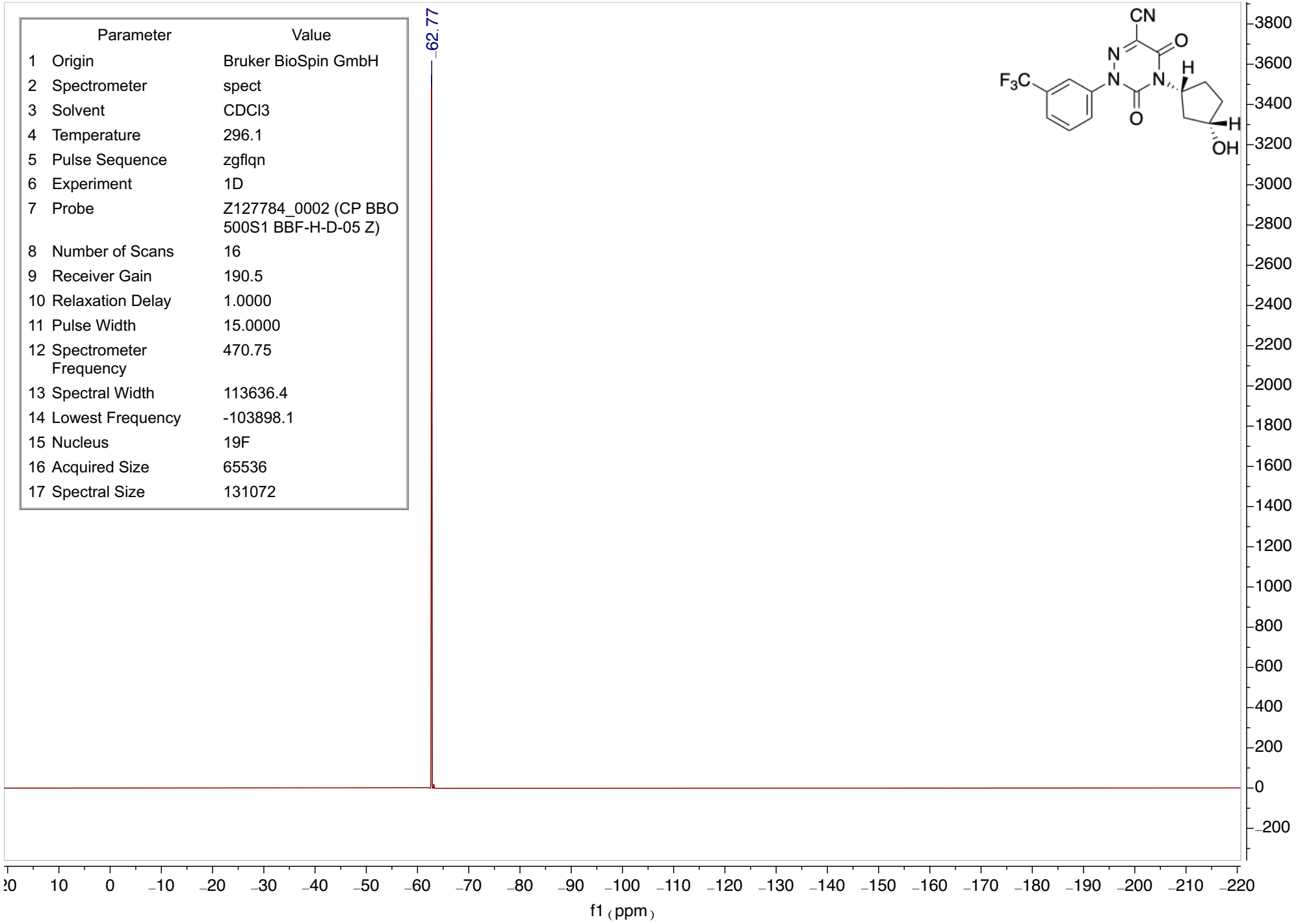
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	168.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

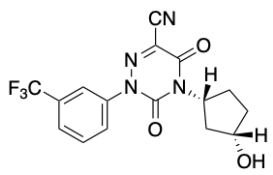




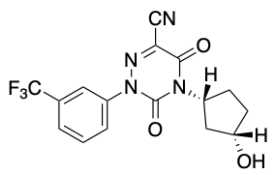
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



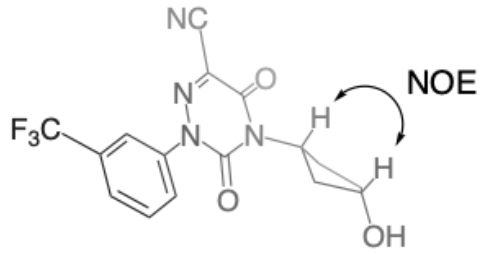


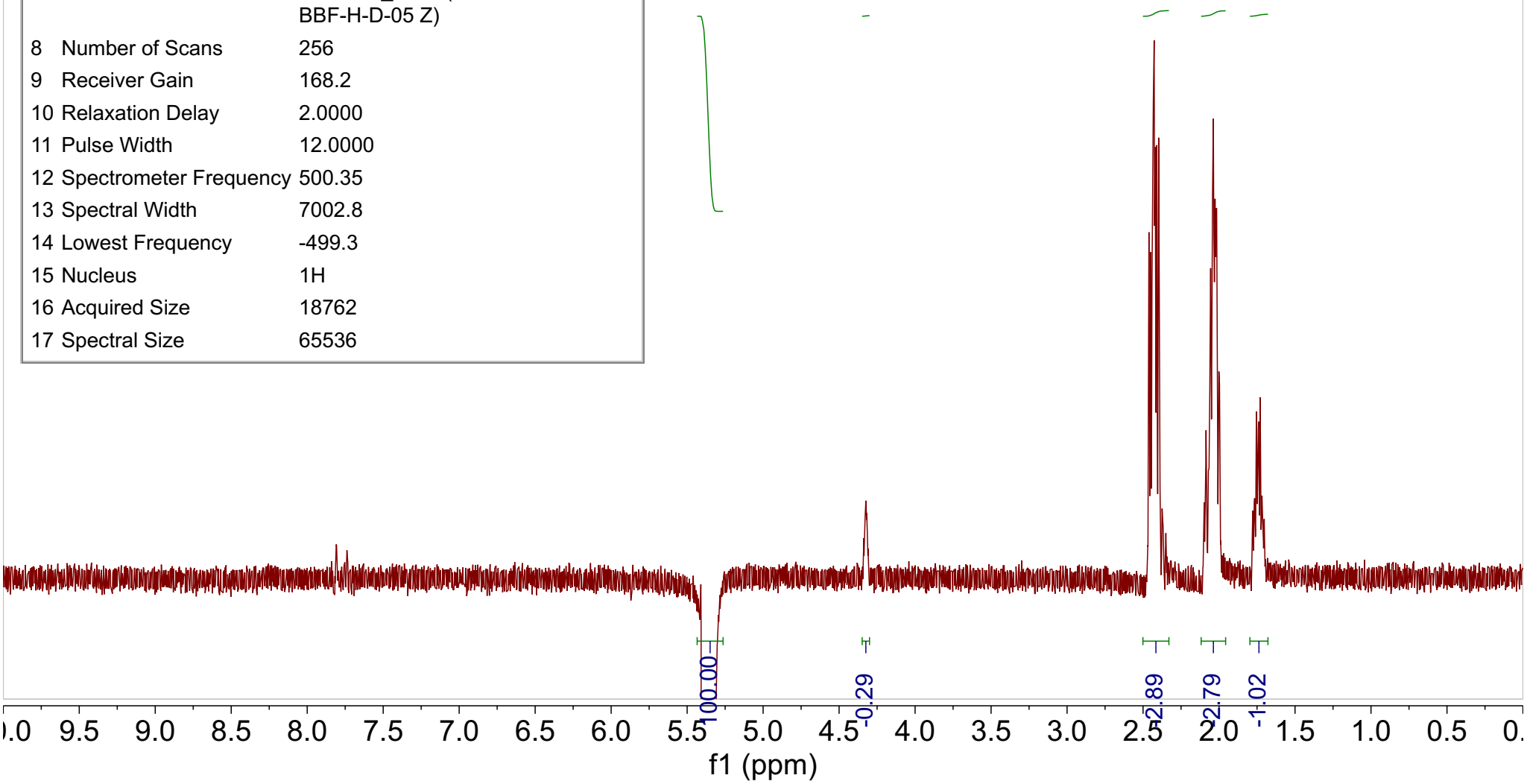
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	27.6
10	Relaxation Delay	1.9259
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4424.8
14	Lowest Frequency	-111.3
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024



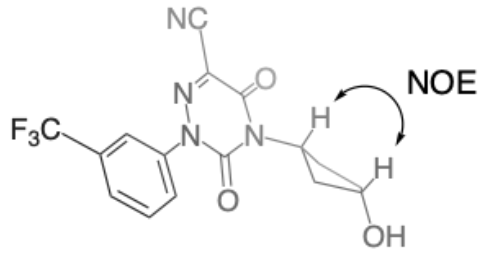
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4424.8
14	Lowest Frequency	-64.9
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

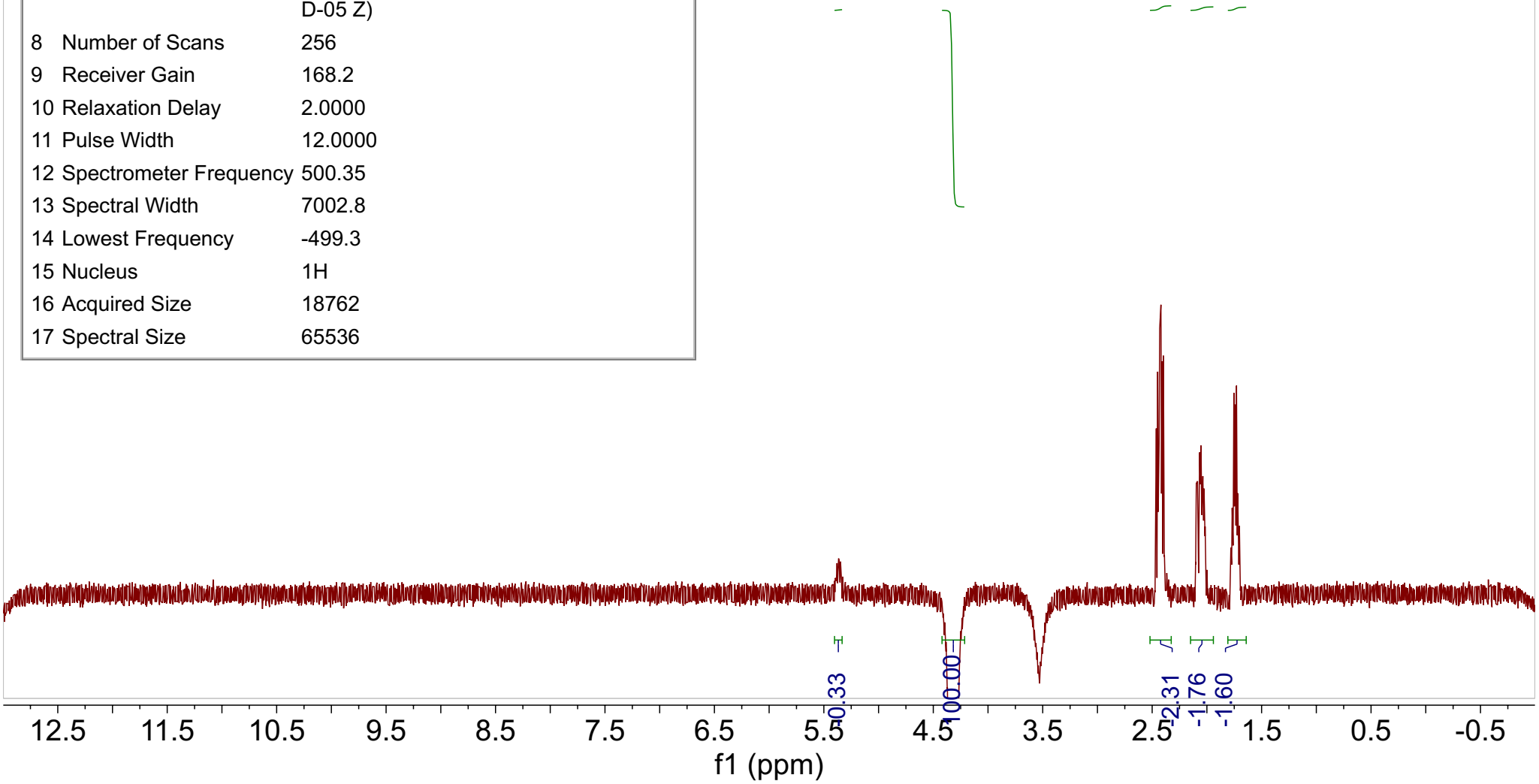
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	168.2
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	7002.8
14	Lowest Frequency	-499.3
15	Nucleus	1H
16	Acquired Size	18762
17	Spectral Size	65536



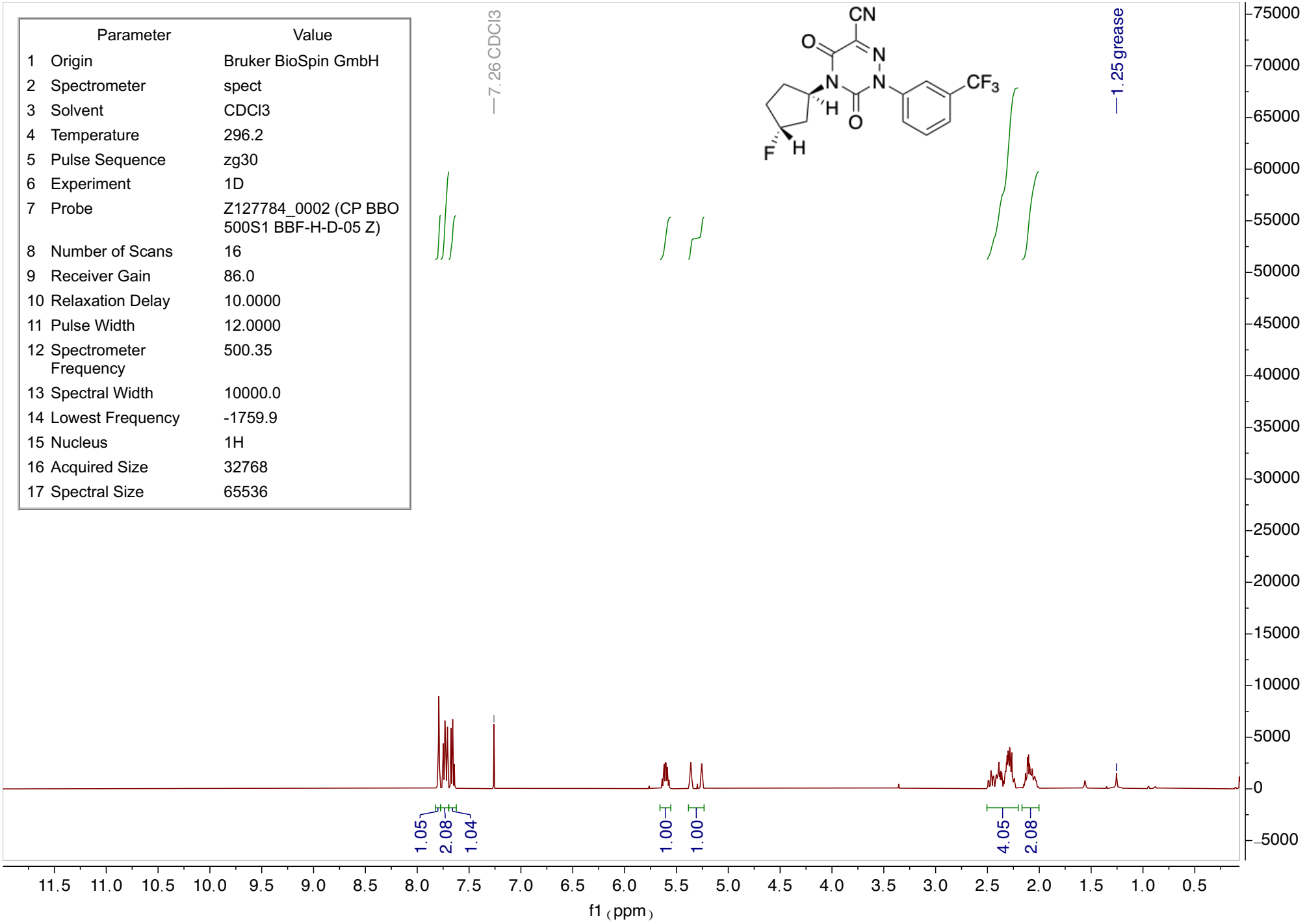


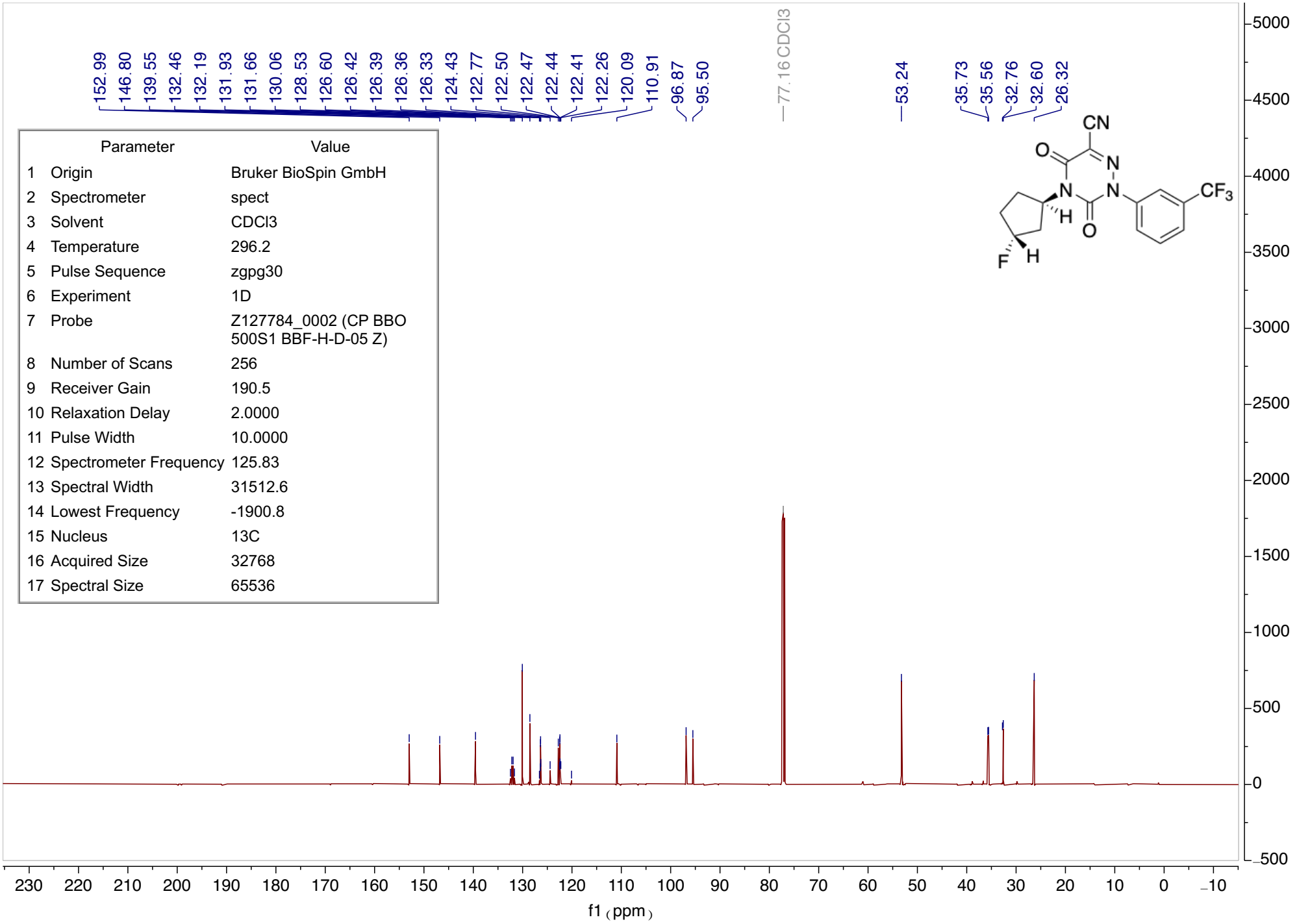
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	168.2
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	7002.8
14	Lowest Frequency	-499.3
15	Nucleus	1H
16	Acquired Size	18762
17	Spectral Size	65536





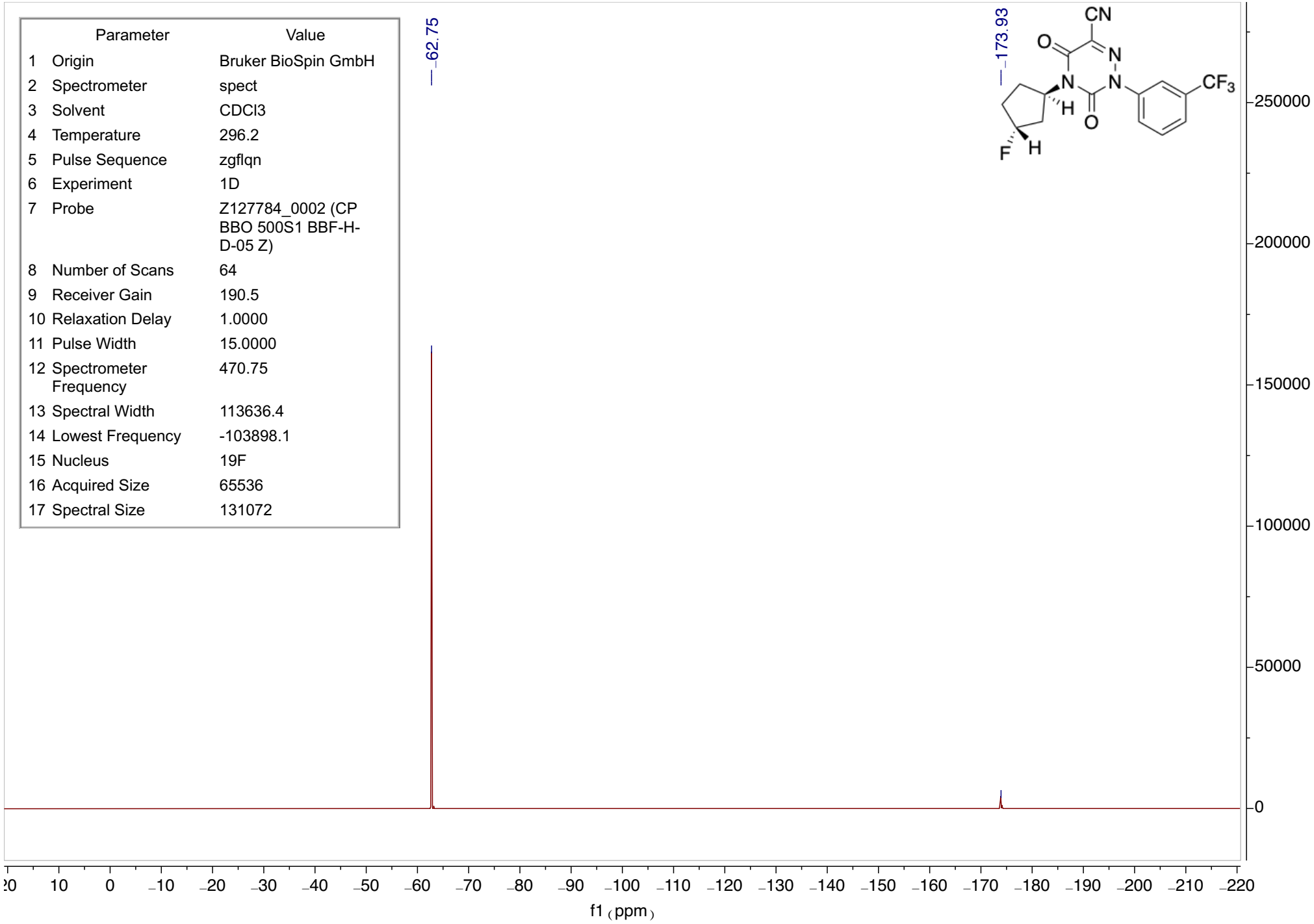
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



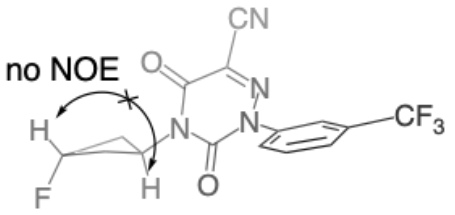


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

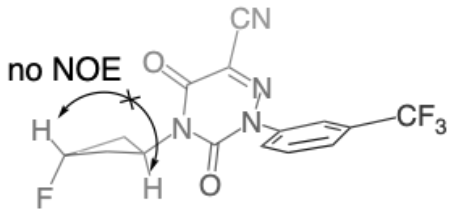
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	64
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

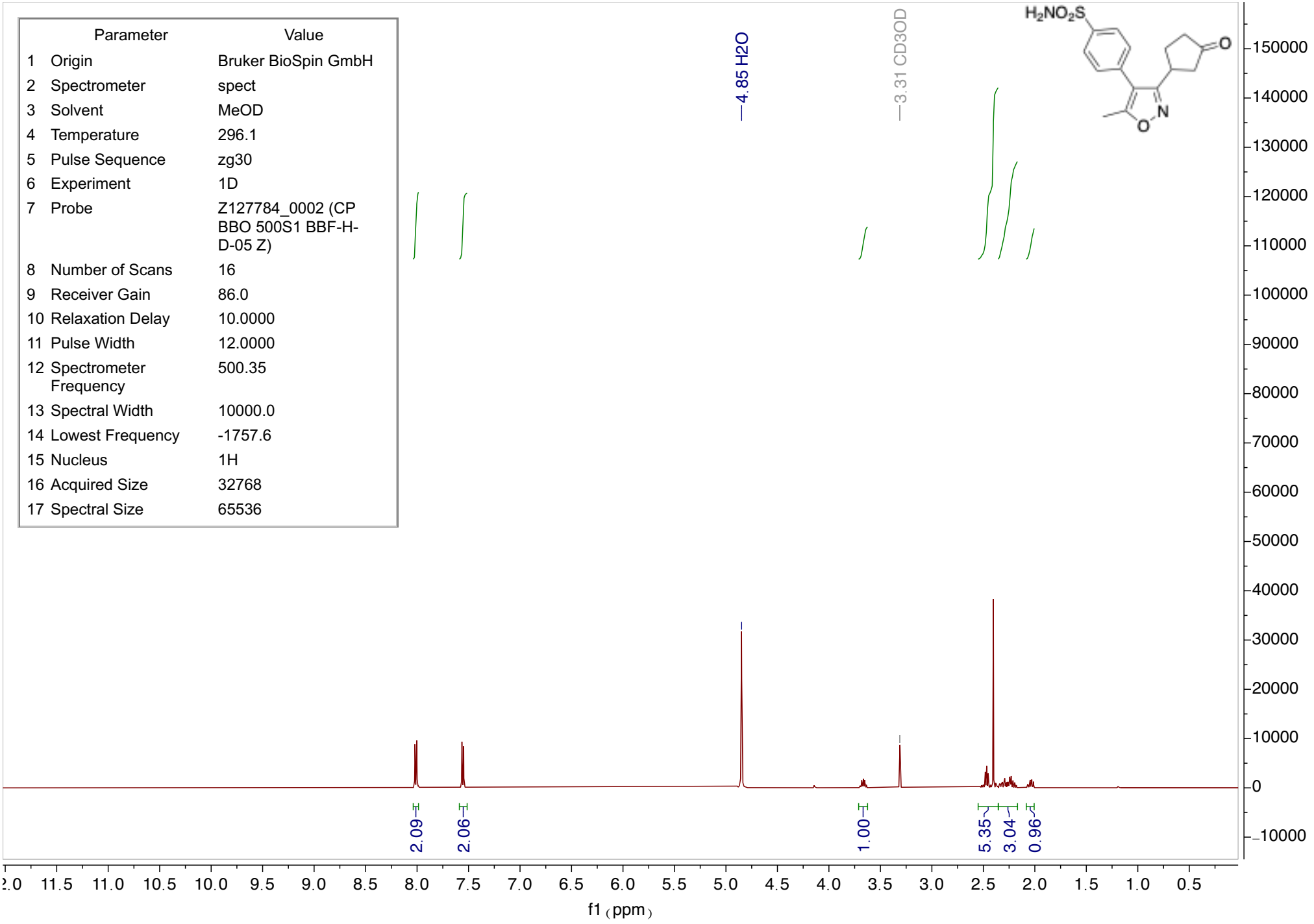


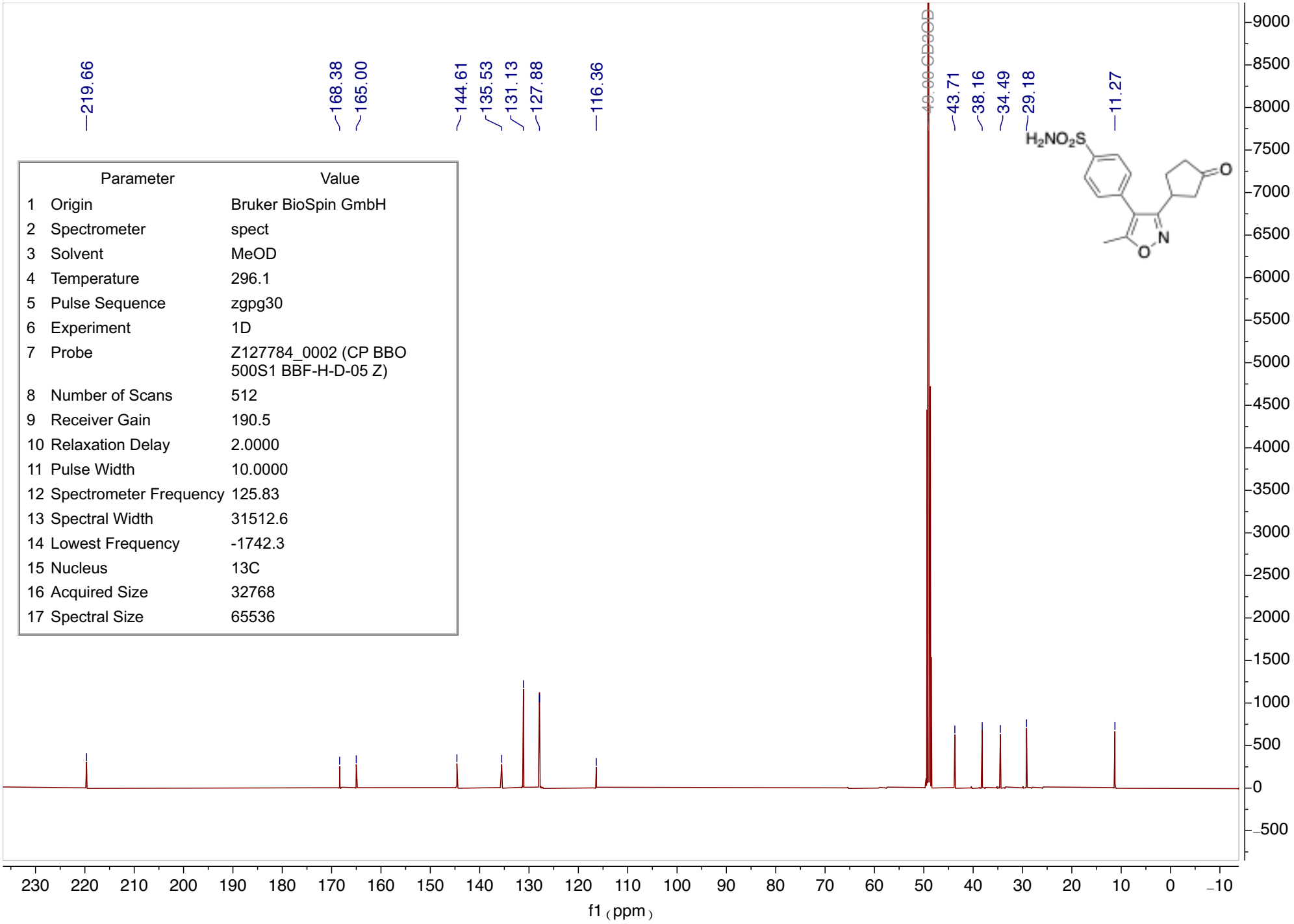
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	128
9	Receiver Gain	32.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2246.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



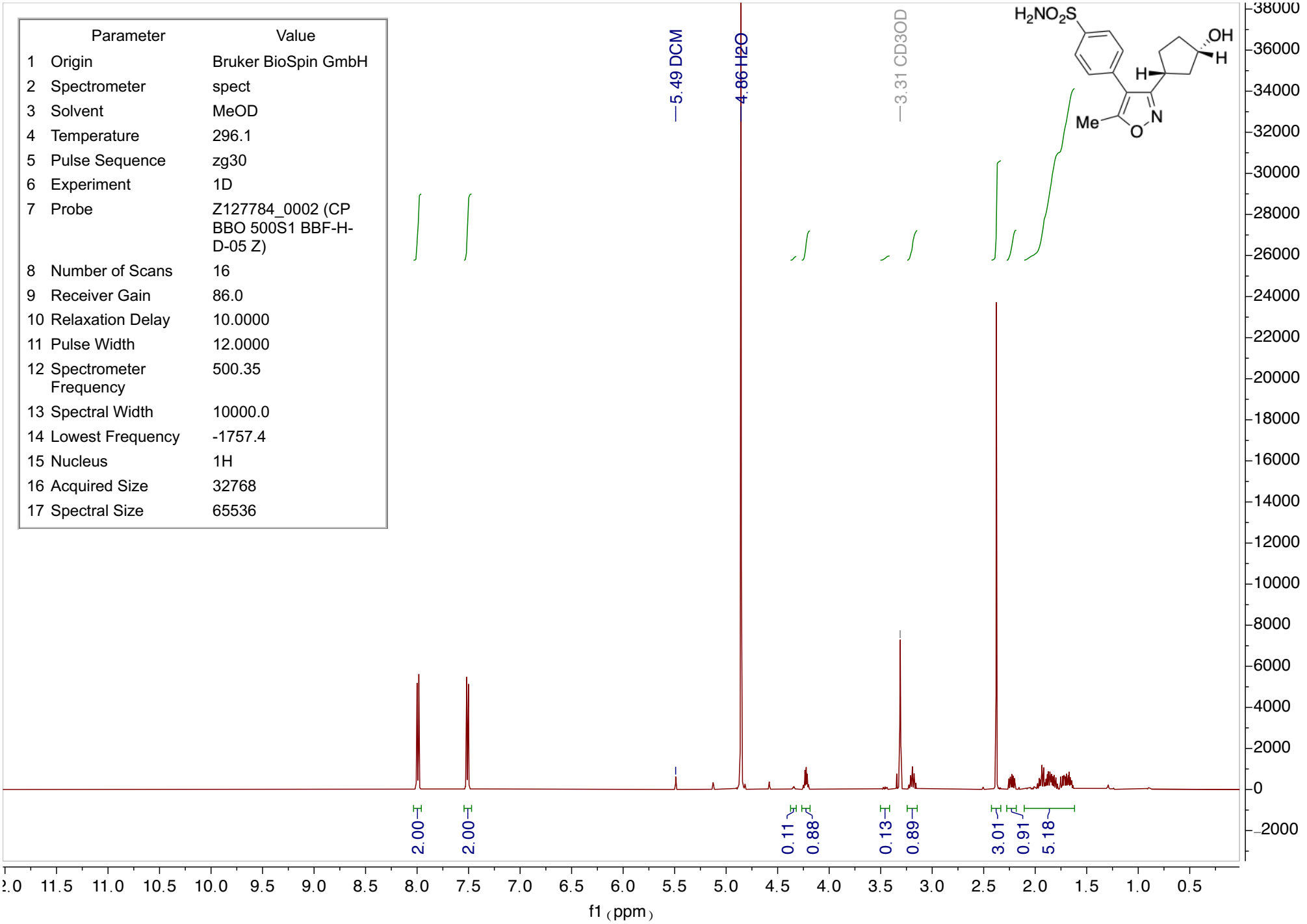
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	128
9	Receiver Gain	32.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2246.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

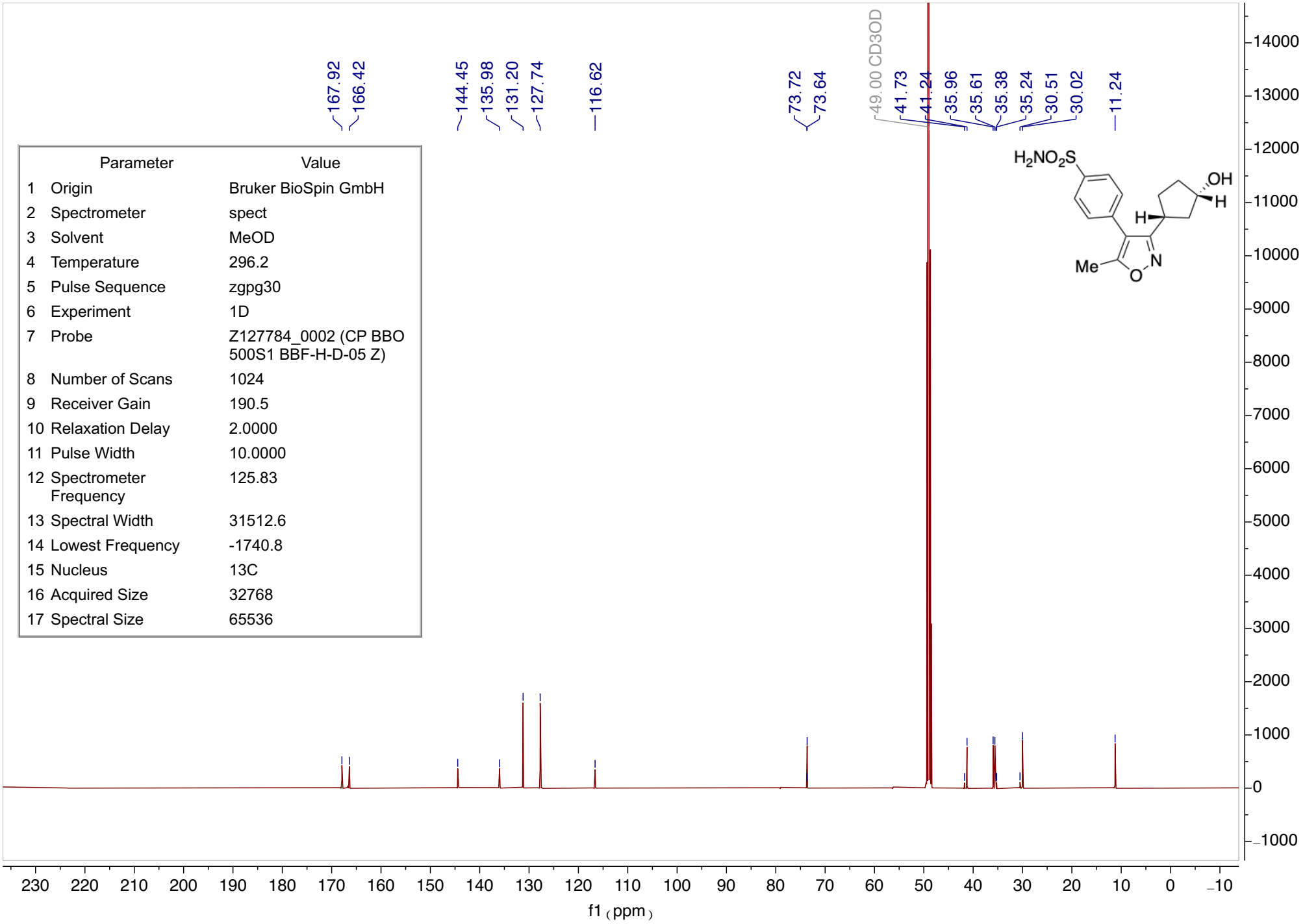



Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent MeOD
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 16
9 Receiver Gain 86.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 10000.0
14 Lowest Frequency -1757.6
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
4.85 H2O
3.31 CD3OD
H2NO2S
O
N
O
2.09
2.06
1.00
5.35
3.04
0.96
f1 (ppm)

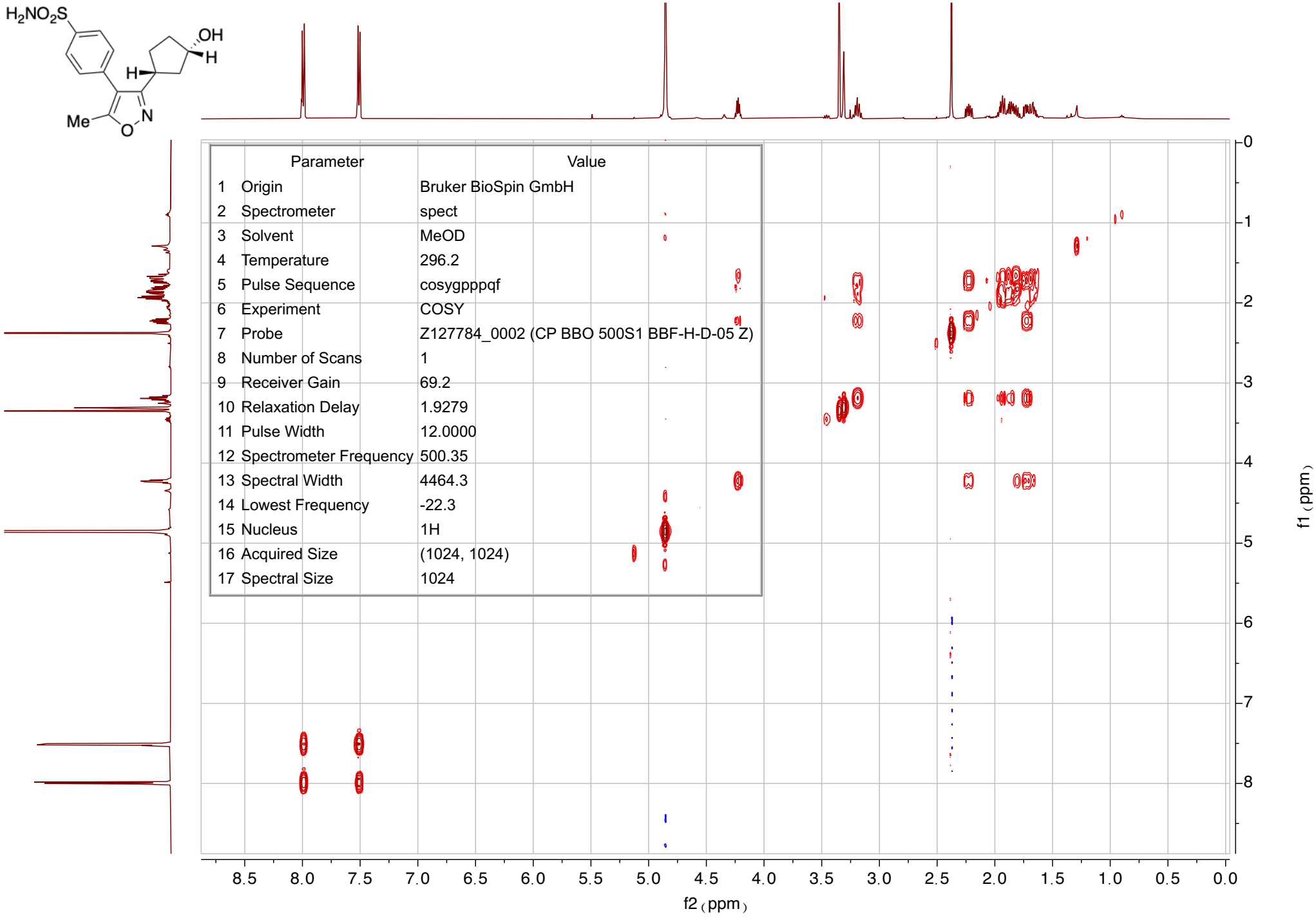


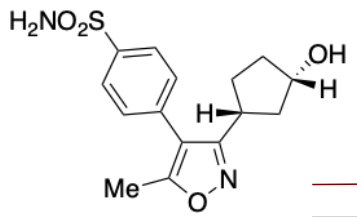
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1742.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent MeOD
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 16
9 Receiver Gain 86.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 10000.0
14 Lowest Frequency -1757.4
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
5.49 DCM
4.86 H2O
3.31 CD3OD
H2NO2S
OH
H
Me
N
O
2.00
2.00
0.11
0.88
0.13
0.89
3.01
0.91
5.18
f1 (ppm)

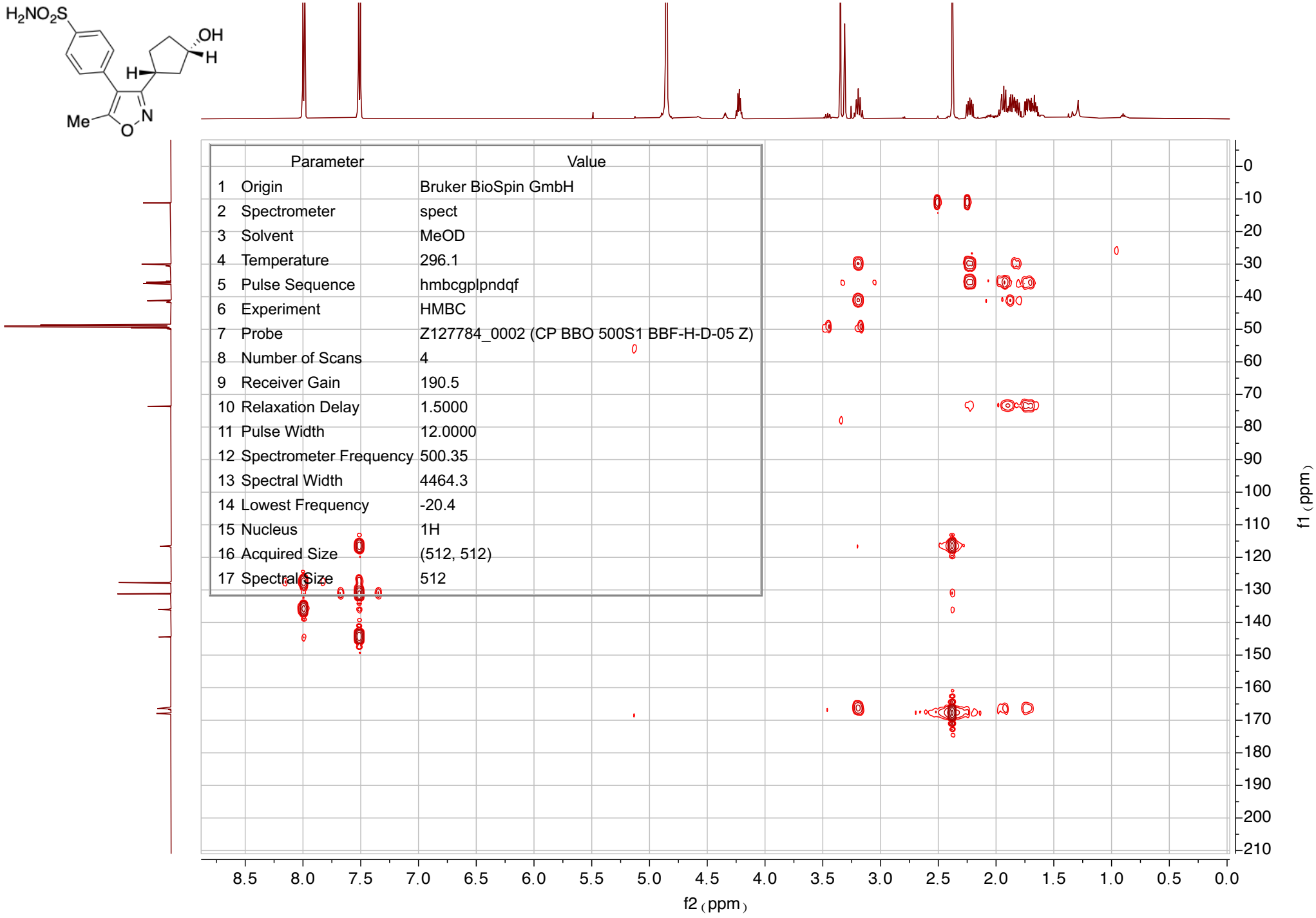


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1740.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

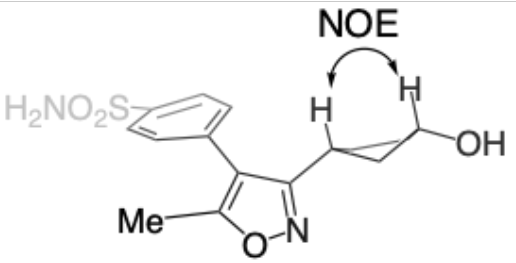

H_2NO_2S
OH
H
H
Me
O
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent MeOD
4 Temperature 296.2
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 1
9 Receiver Gain 69.2
10 Relaxation Delay 1.9279
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4464.3
14 Lowest Frequency -22.3
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8
f1 (ppm)



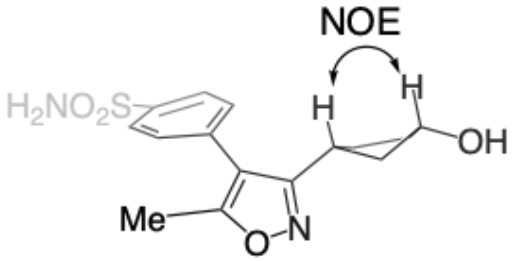
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4464.3
14	Lowest Frequency	-23.5
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


H_2NO_2S
OH
H
H
Me
N
O
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent MeOD
4 Temperature 296.1
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4464.3
14 Lowest Frequency -20.4
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
f2 (ppm)
f1 (ppm)

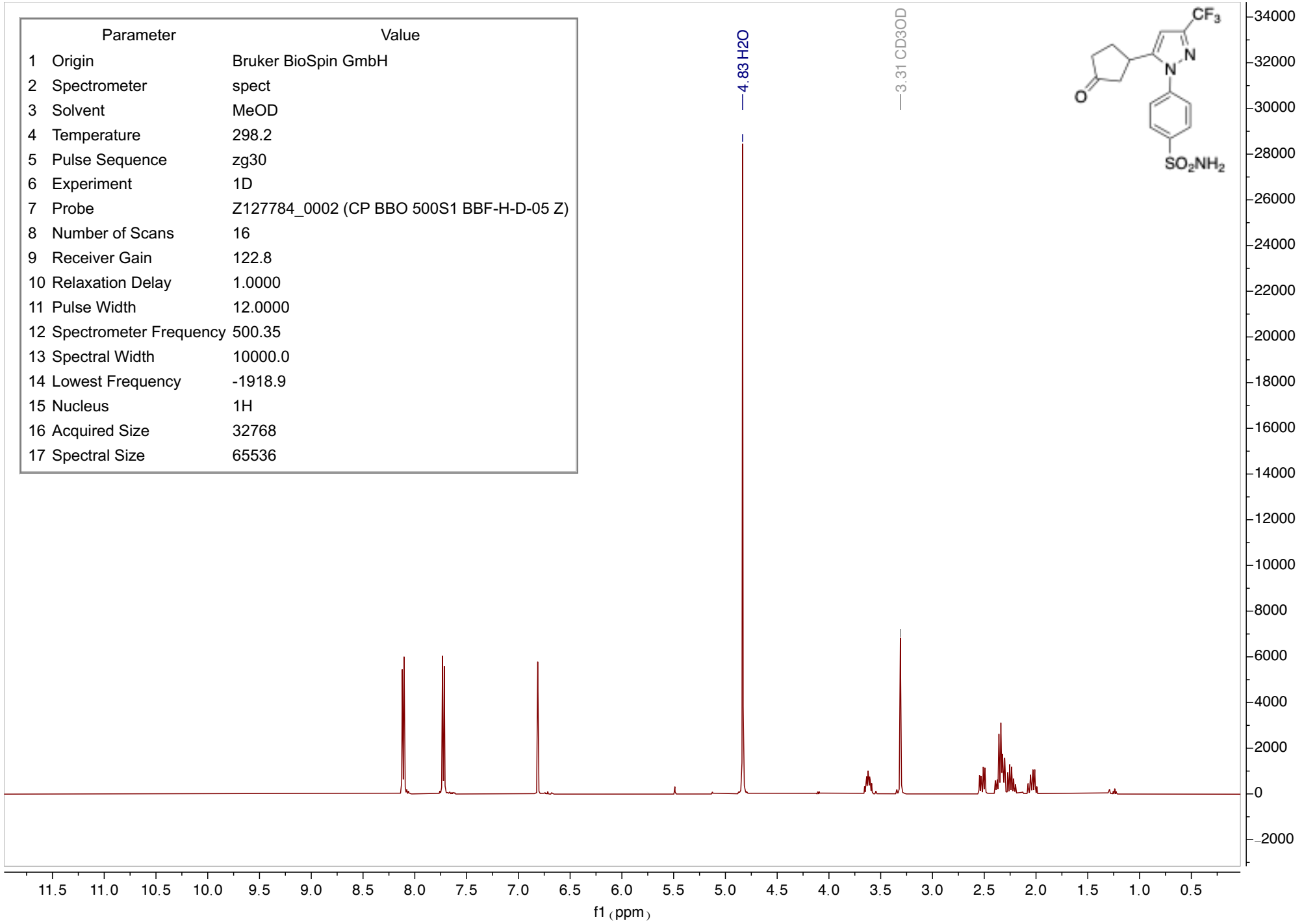
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	64
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	7002.8
14	Lowest Frequency	-499.3
15	Nucleus	1H
16	Acquired Size	18762
17	Spectral Size	65536

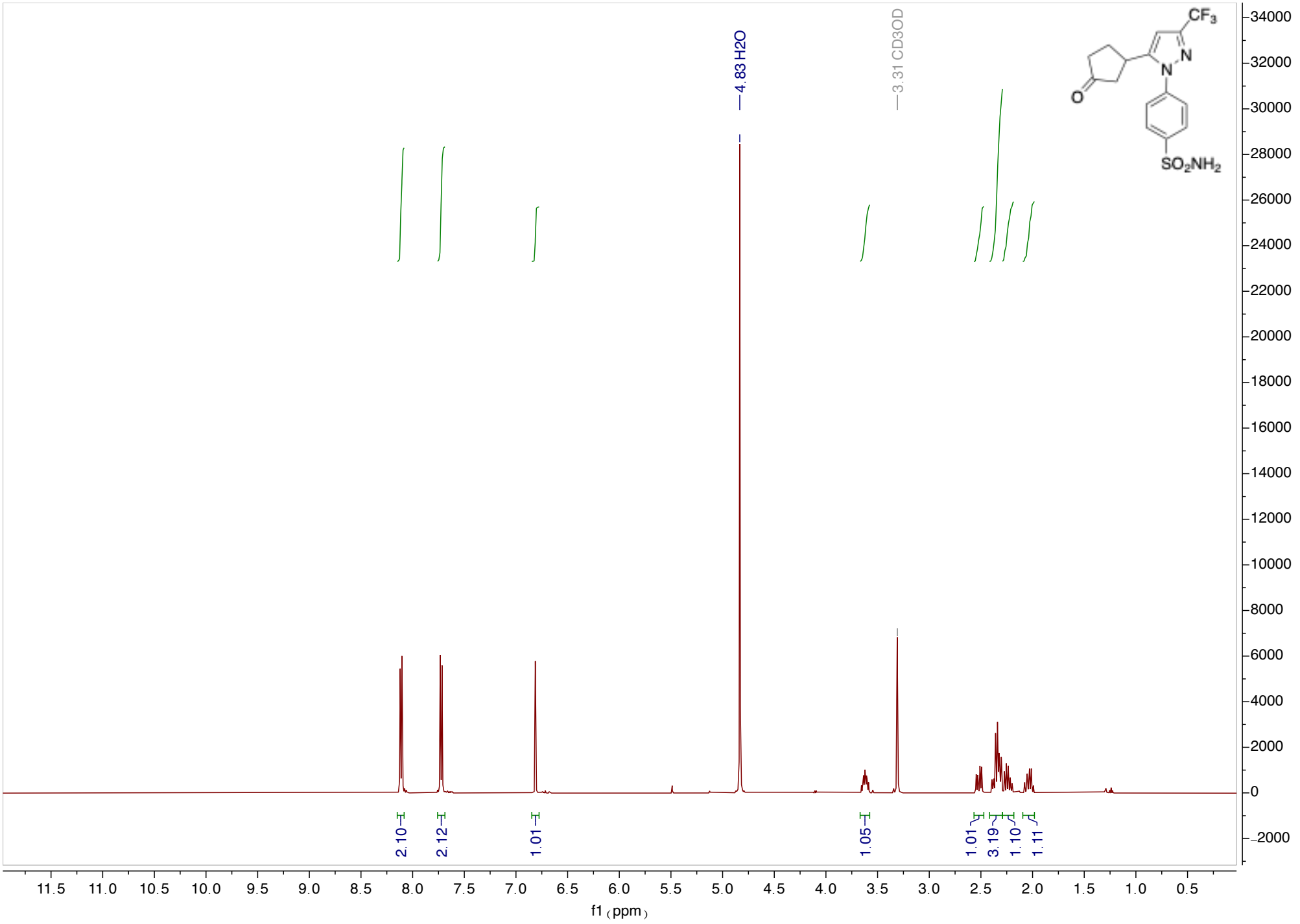


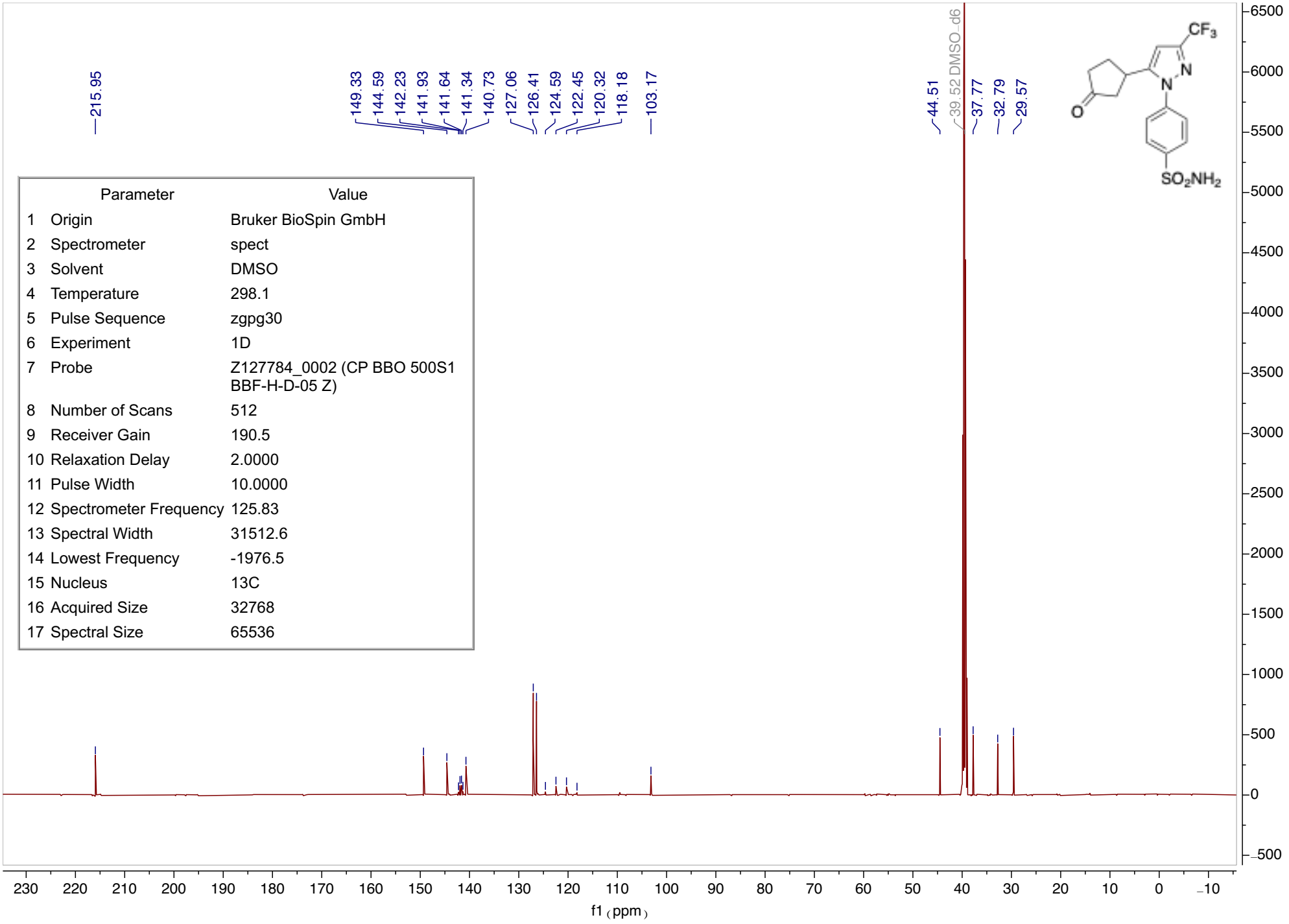
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	64
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	7002.8
14	Lowest Frequency	-499.3
15	Nucleus	1H
16	Acquired Size	18762
17	Spectral Size	65536



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	298.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	122.8
10	Relaxation Delay	1.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1918.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

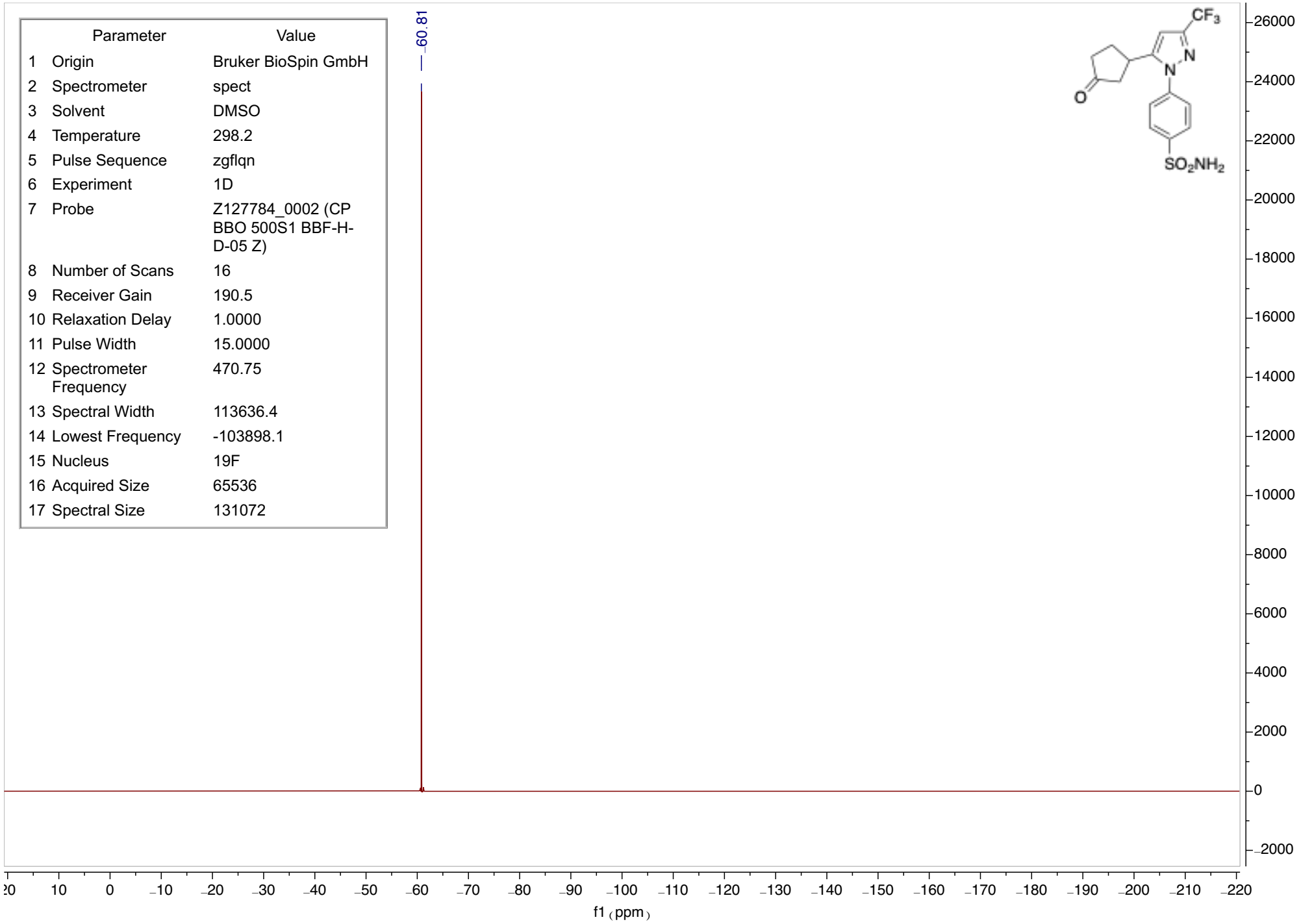



4.83 H2O
3.31 CD3OD
CF3
N
N
O
SO2NH2
2.10
2.12
1.01
1.05
1.01
3.19
1.10
1.11
f1 (ppm)

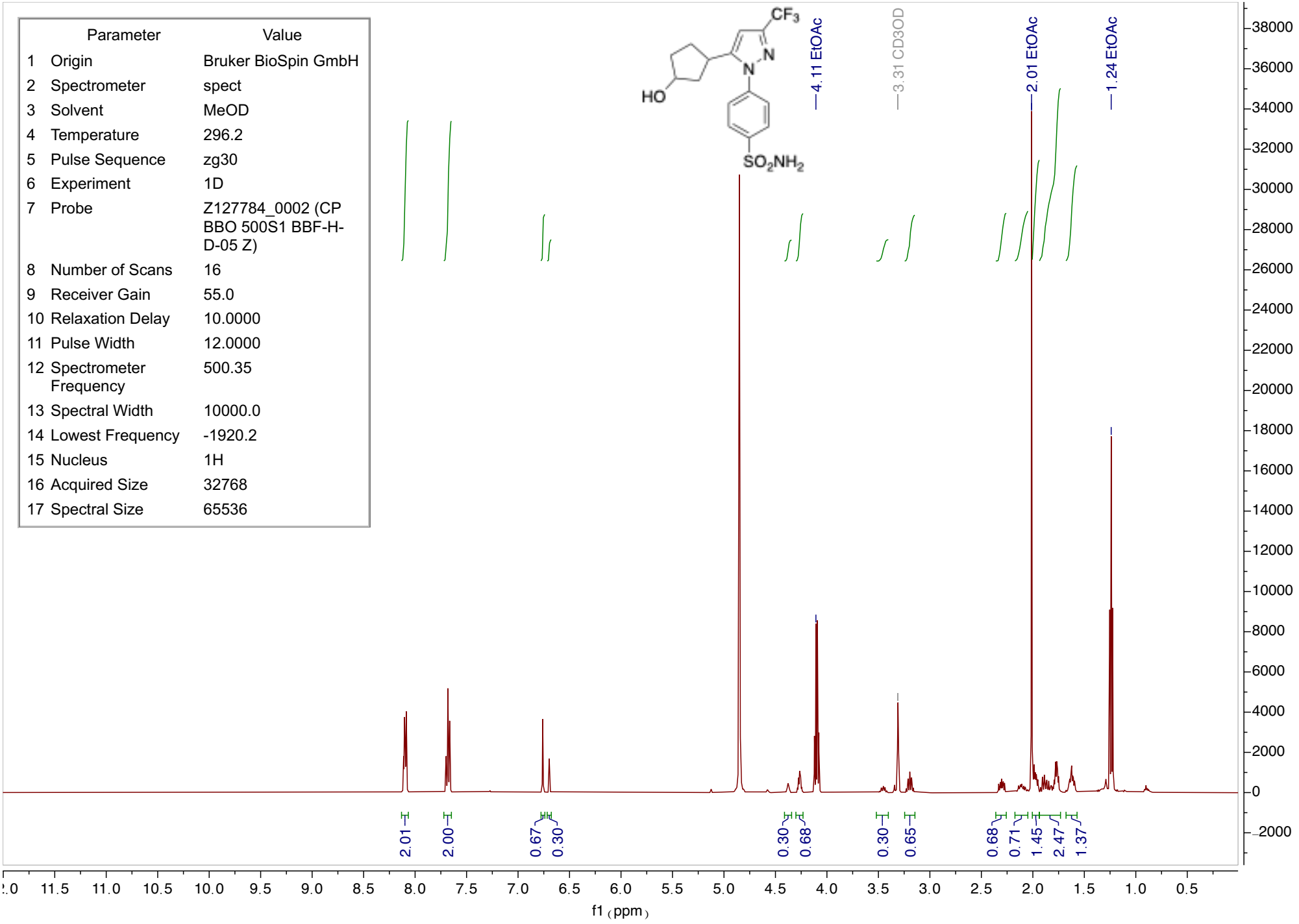


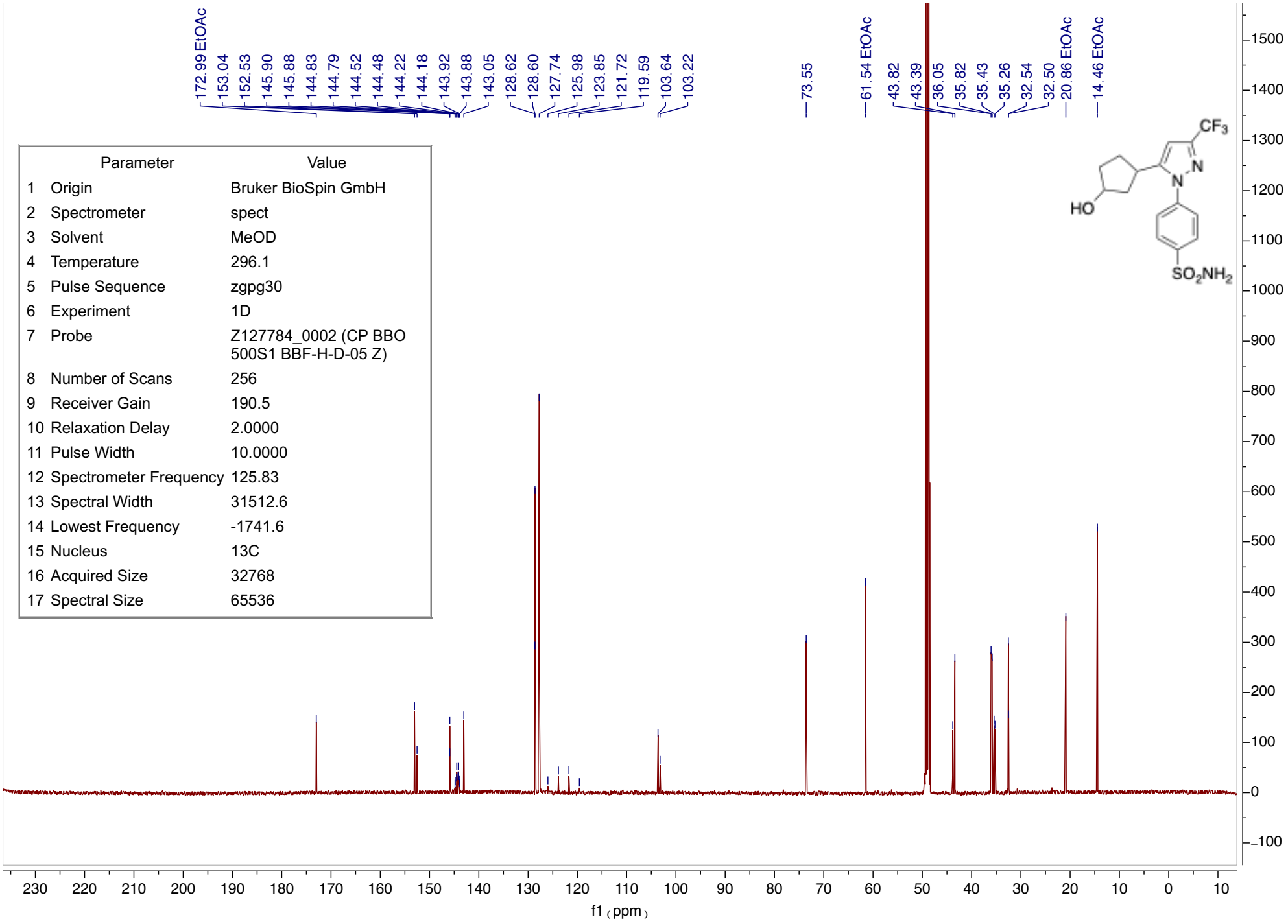
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1976.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	DMSO
4	Temperature	298.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



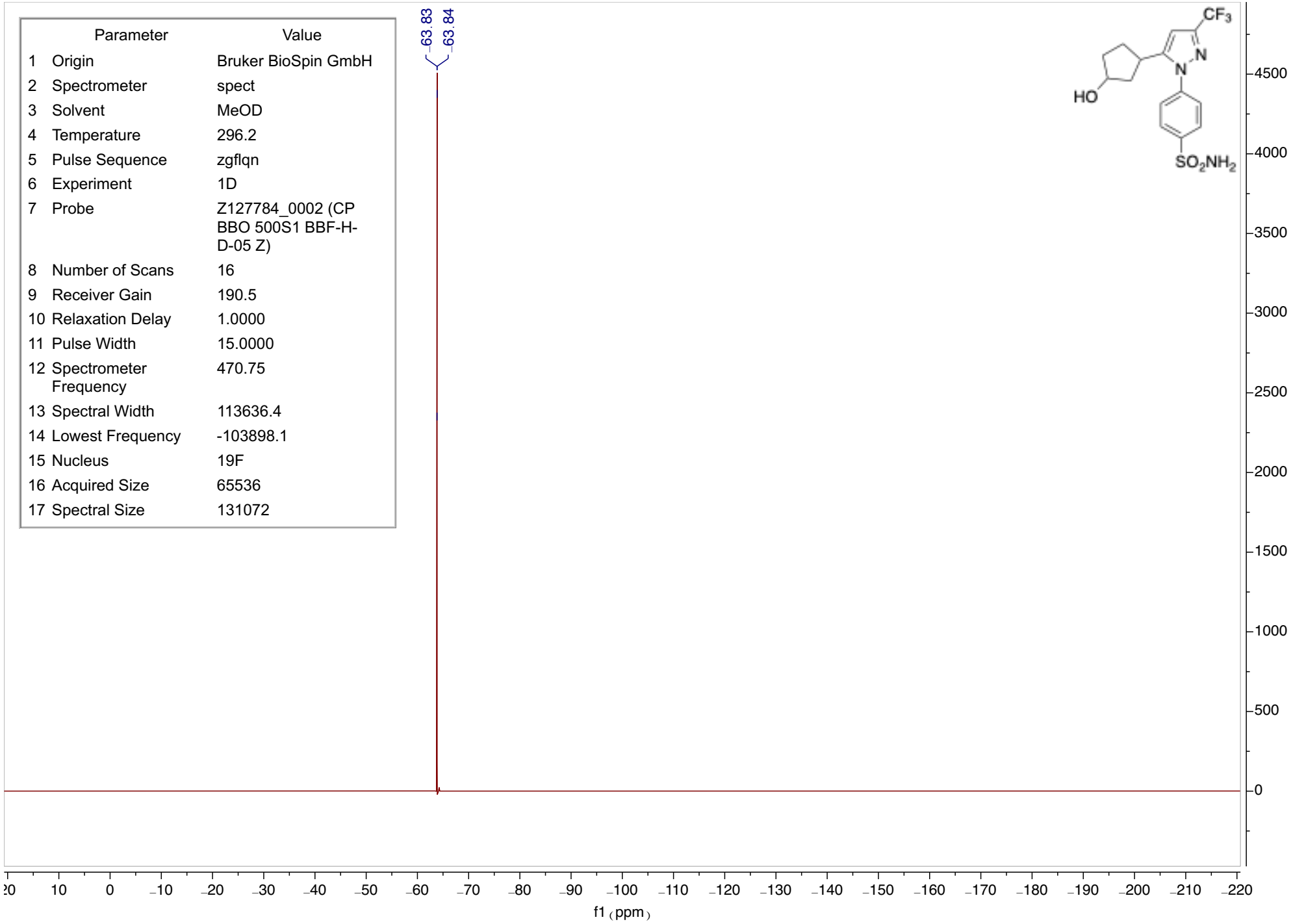
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	55.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1920.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



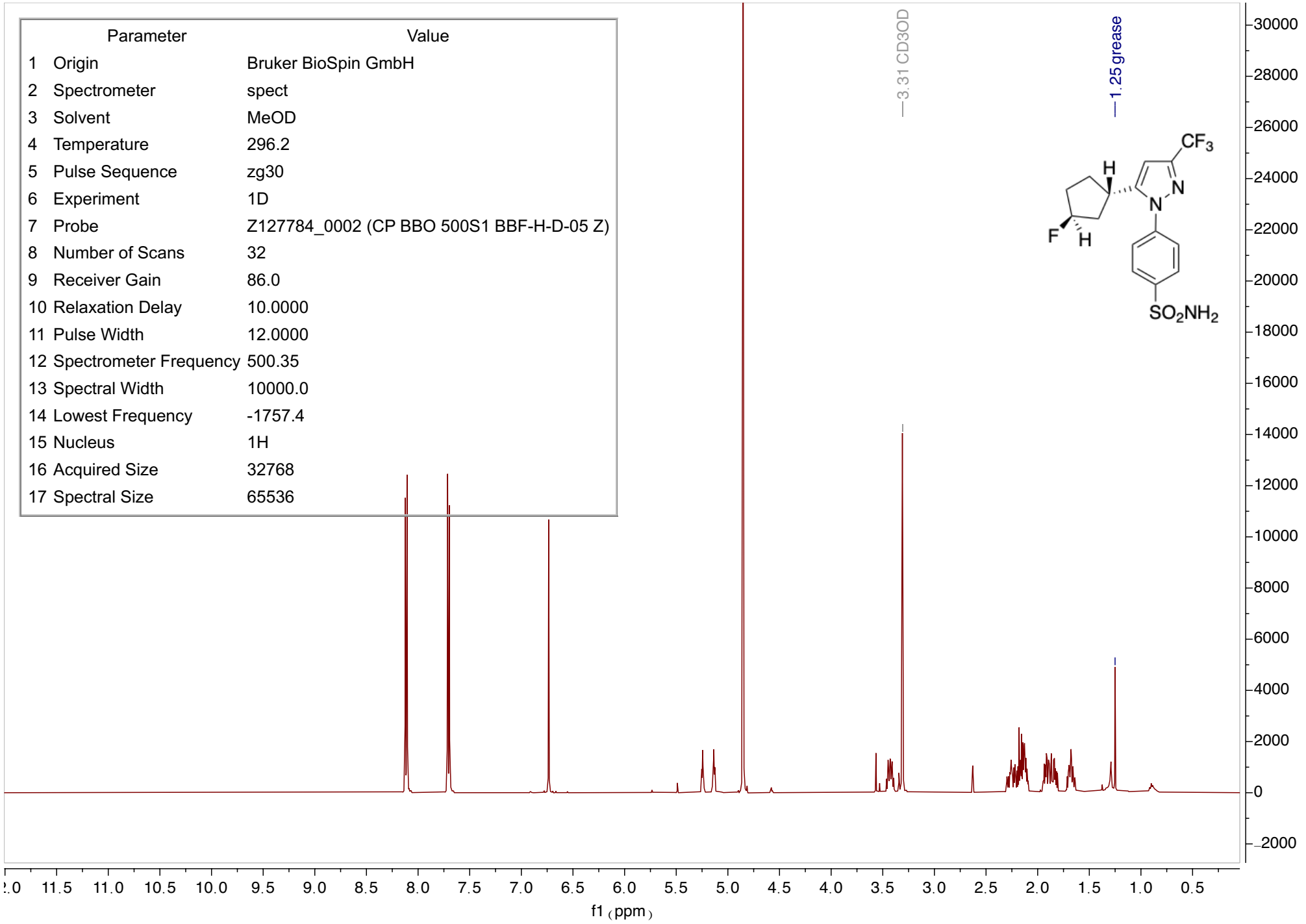


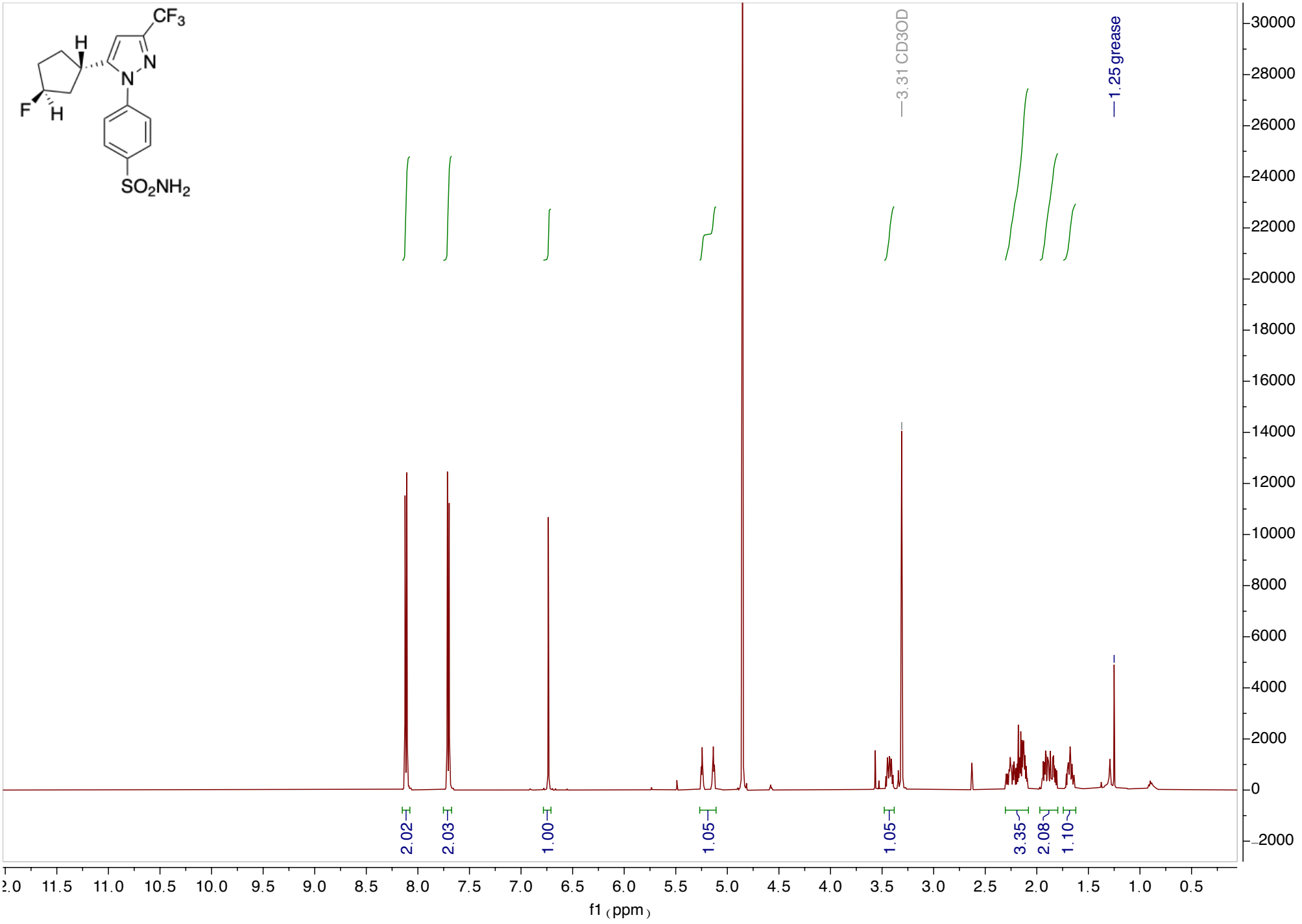
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1741.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

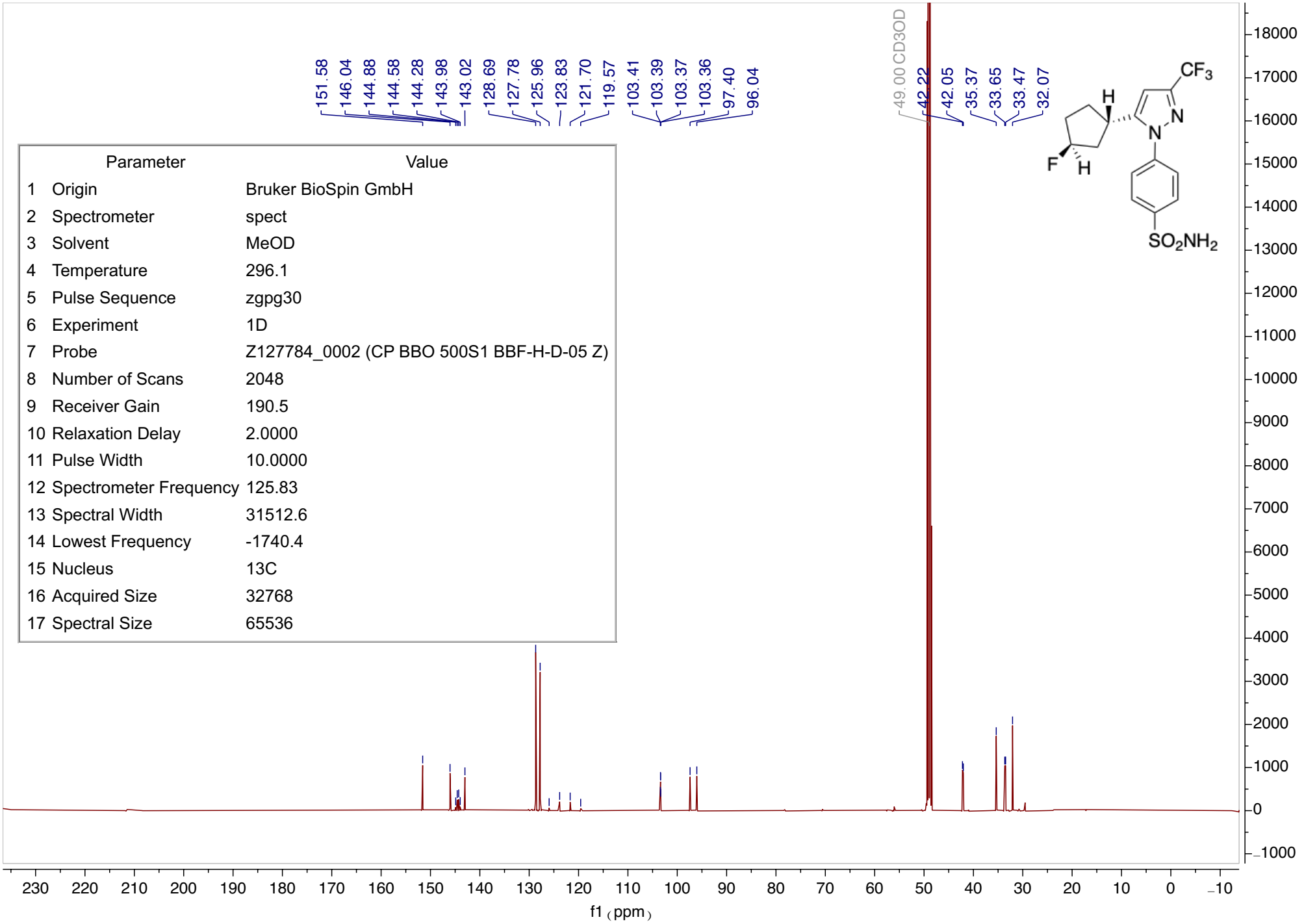
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



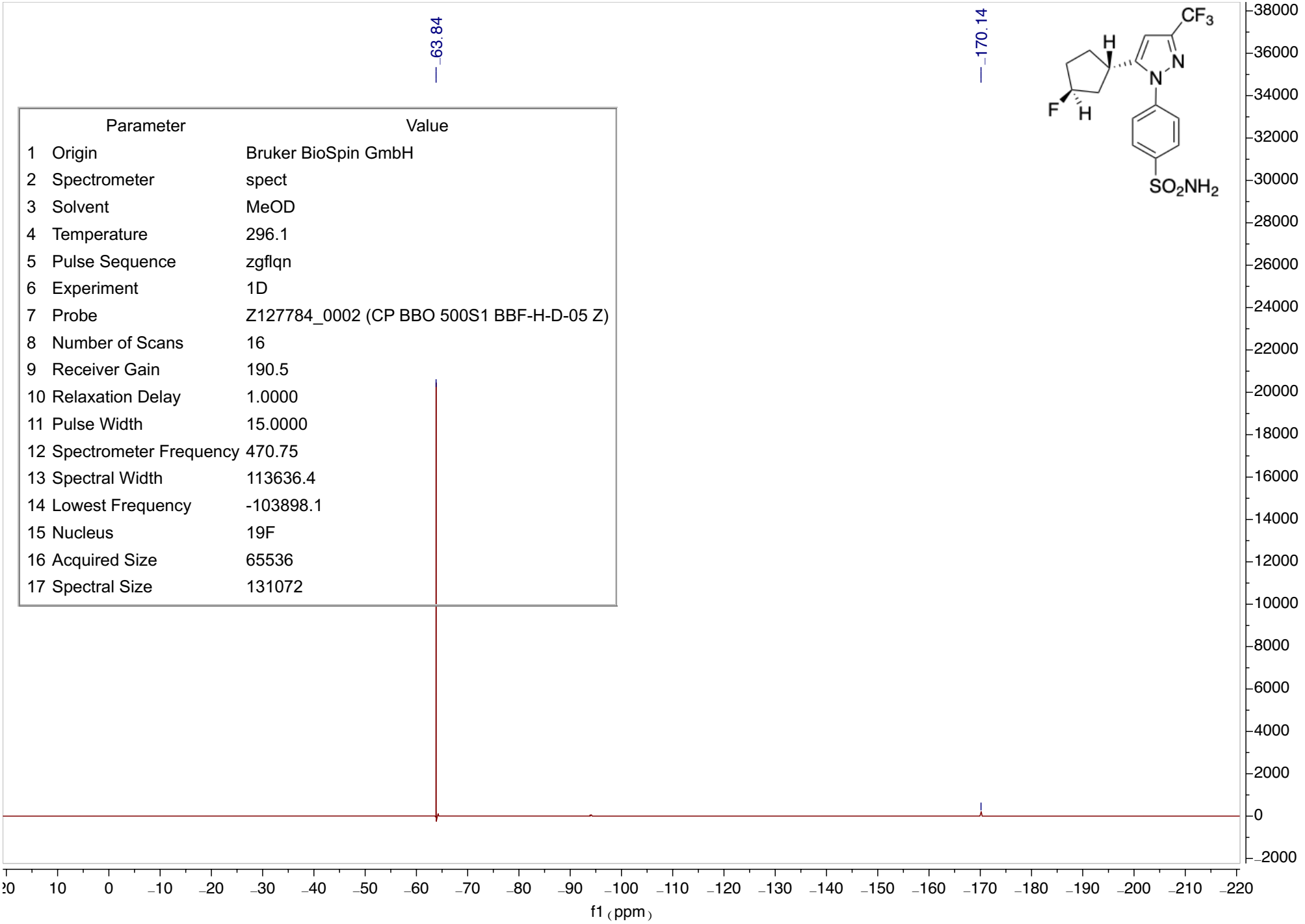
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	32
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1757.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



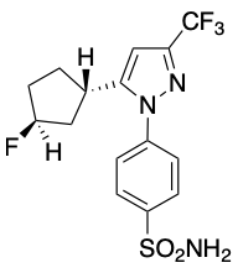

CF3
H
N
N
F
H
SO2NH2
3.31 CD3OD
1.25 grease
2.02
2.03
1.00
1.05
1.05
3.35
2.08
1.10
f1 (ppm)



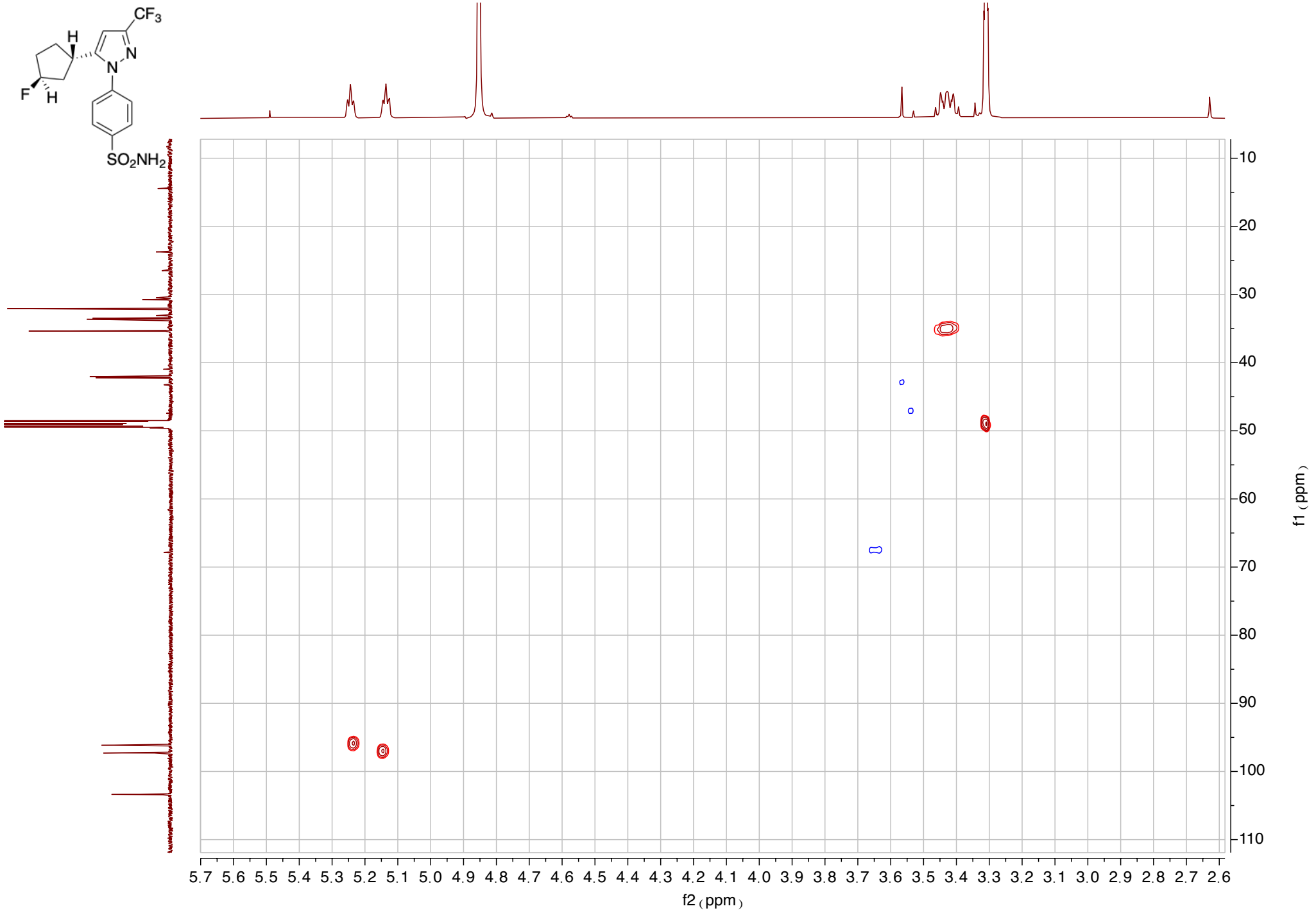
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2048
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1740.4
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



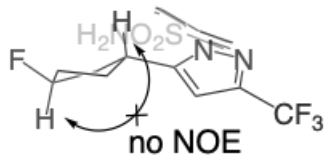
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

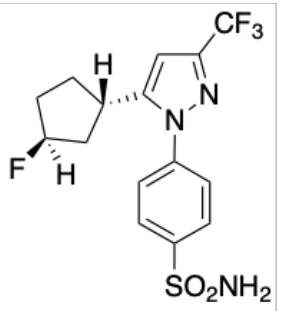


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5555.6
14	Lowest Frequency	-65.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

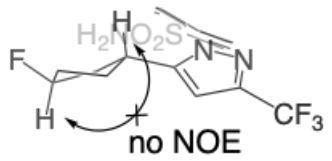

CF3
H
N
N
F
H
SO2NH2
10
20
30
40
50
60
70
80
90
100
110
f1 (ppm)
5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6
f2 (ppm)

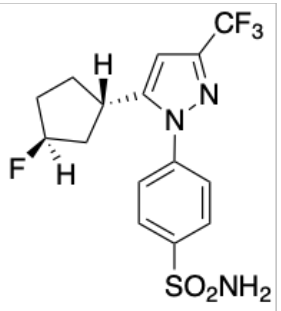
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	32.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2246.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



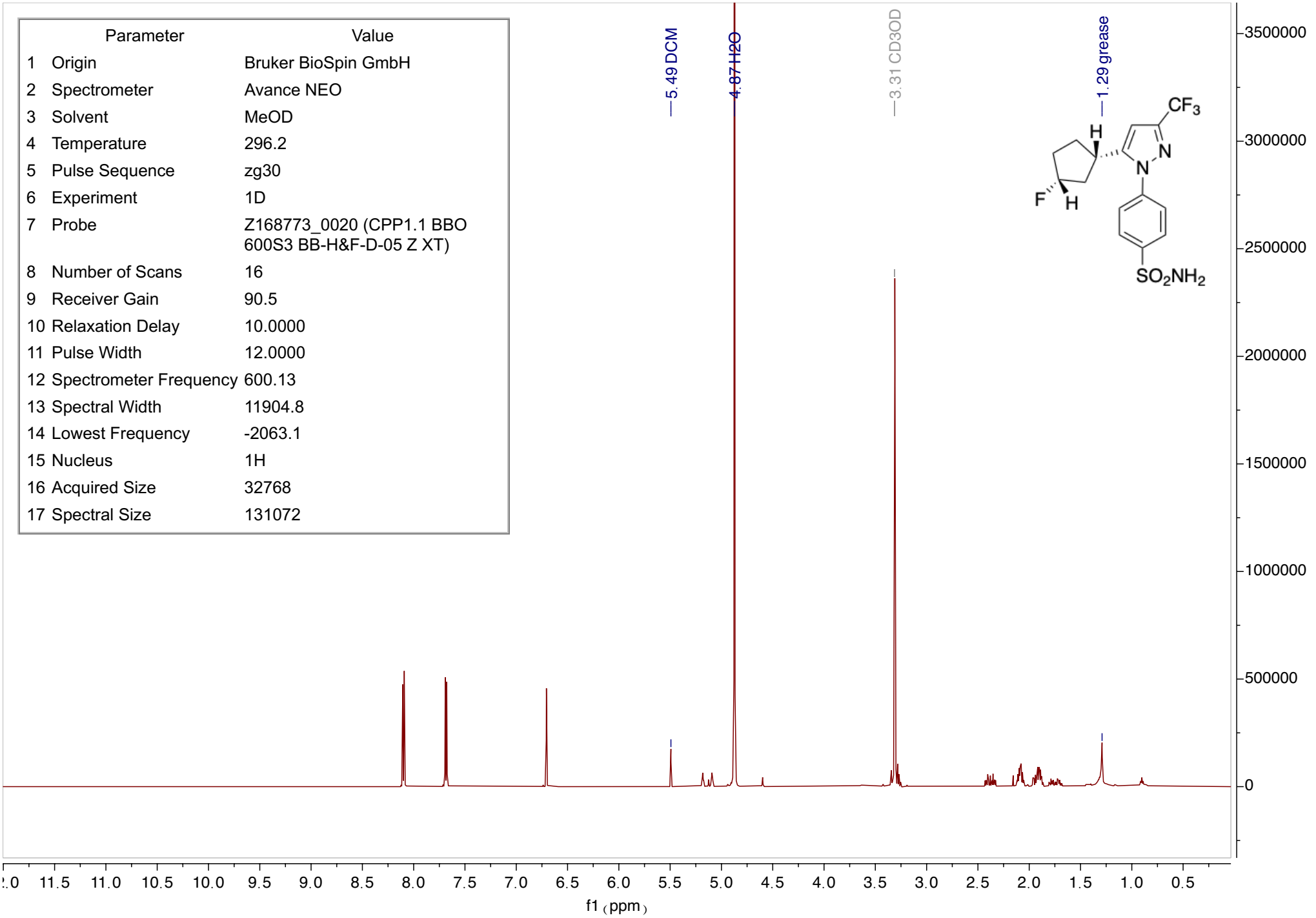


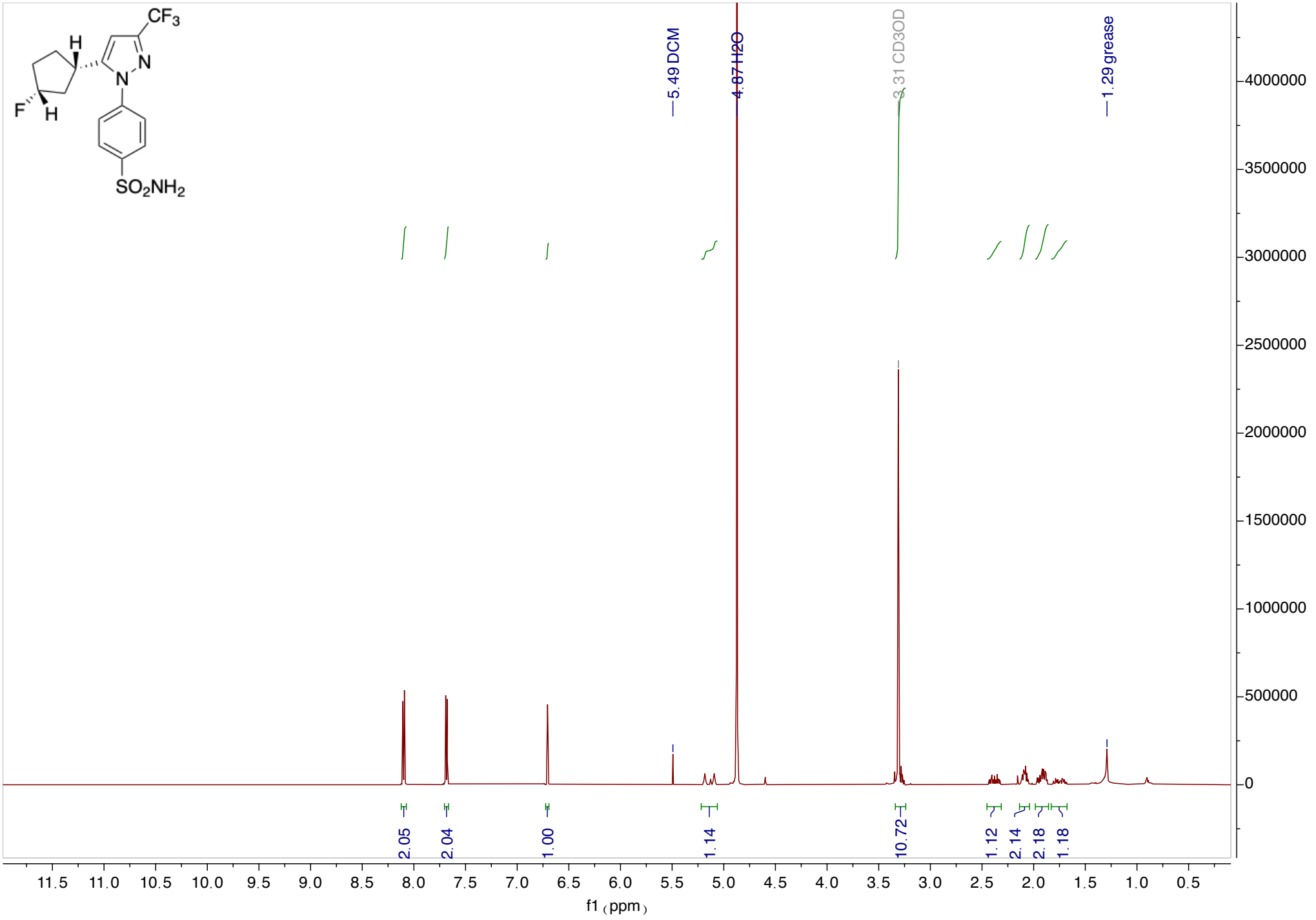
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	32.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2246.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

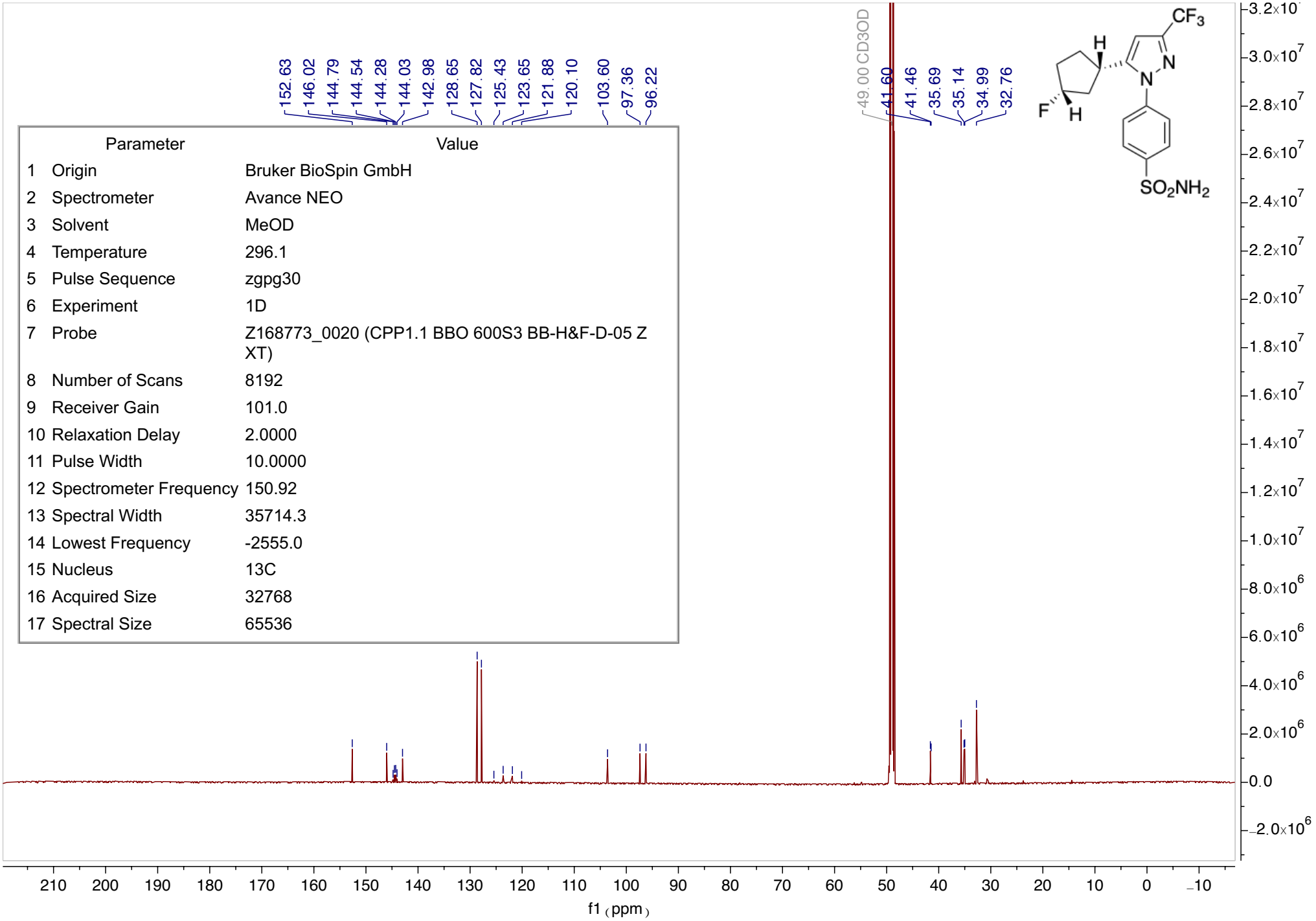




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	90.5
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2063.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

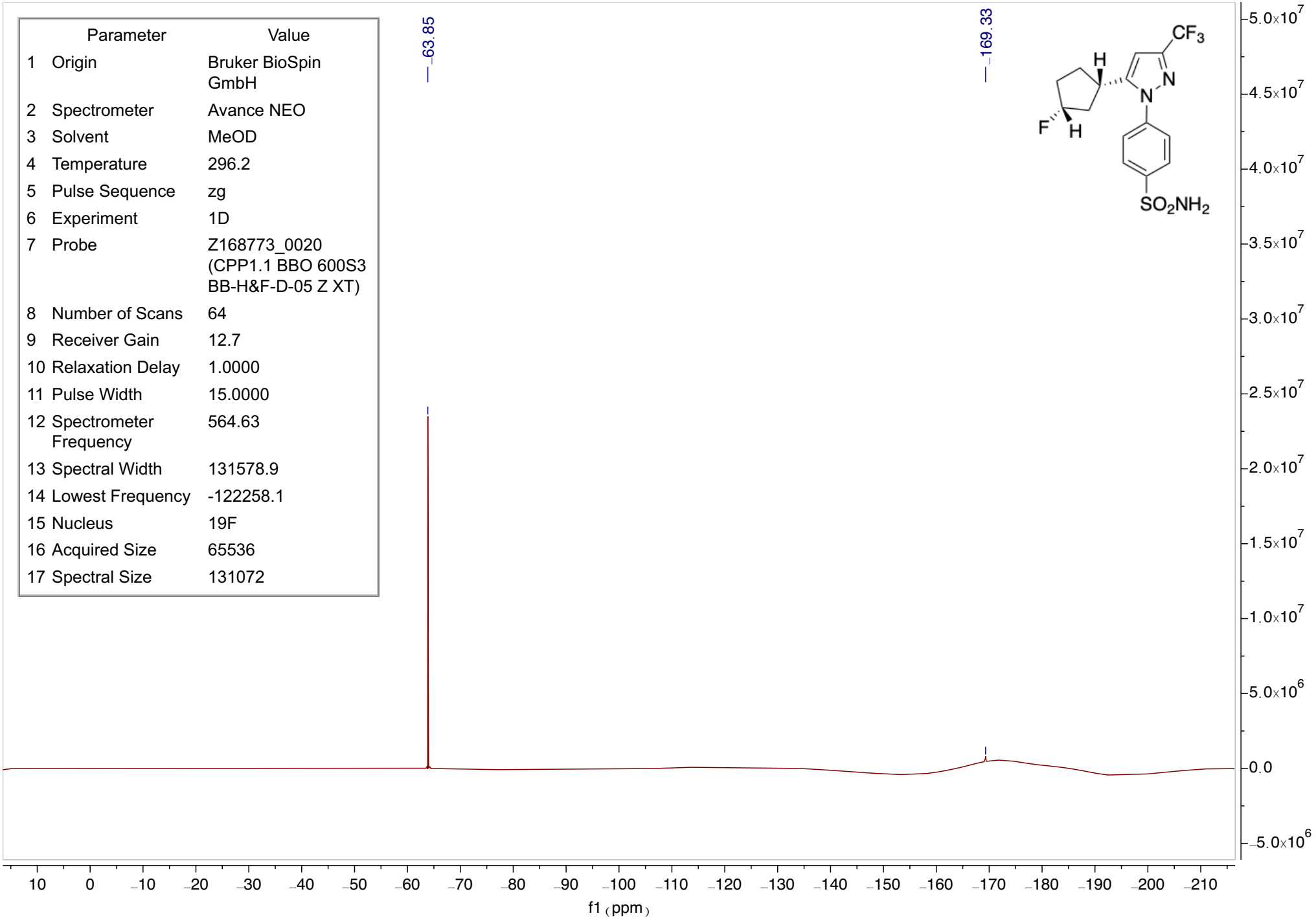


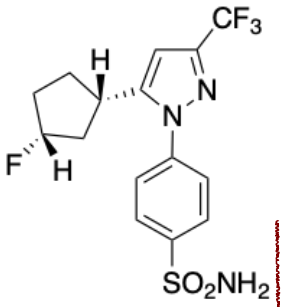

CF3
H
N
N
F
H
SO2NH2
5.49 DCM
4.87 H2O
3.31 CD3OD
1.29 grease
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
2.05
2.04
1.00
1.14
10.72
1.12
2.14
2.18
1.18
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



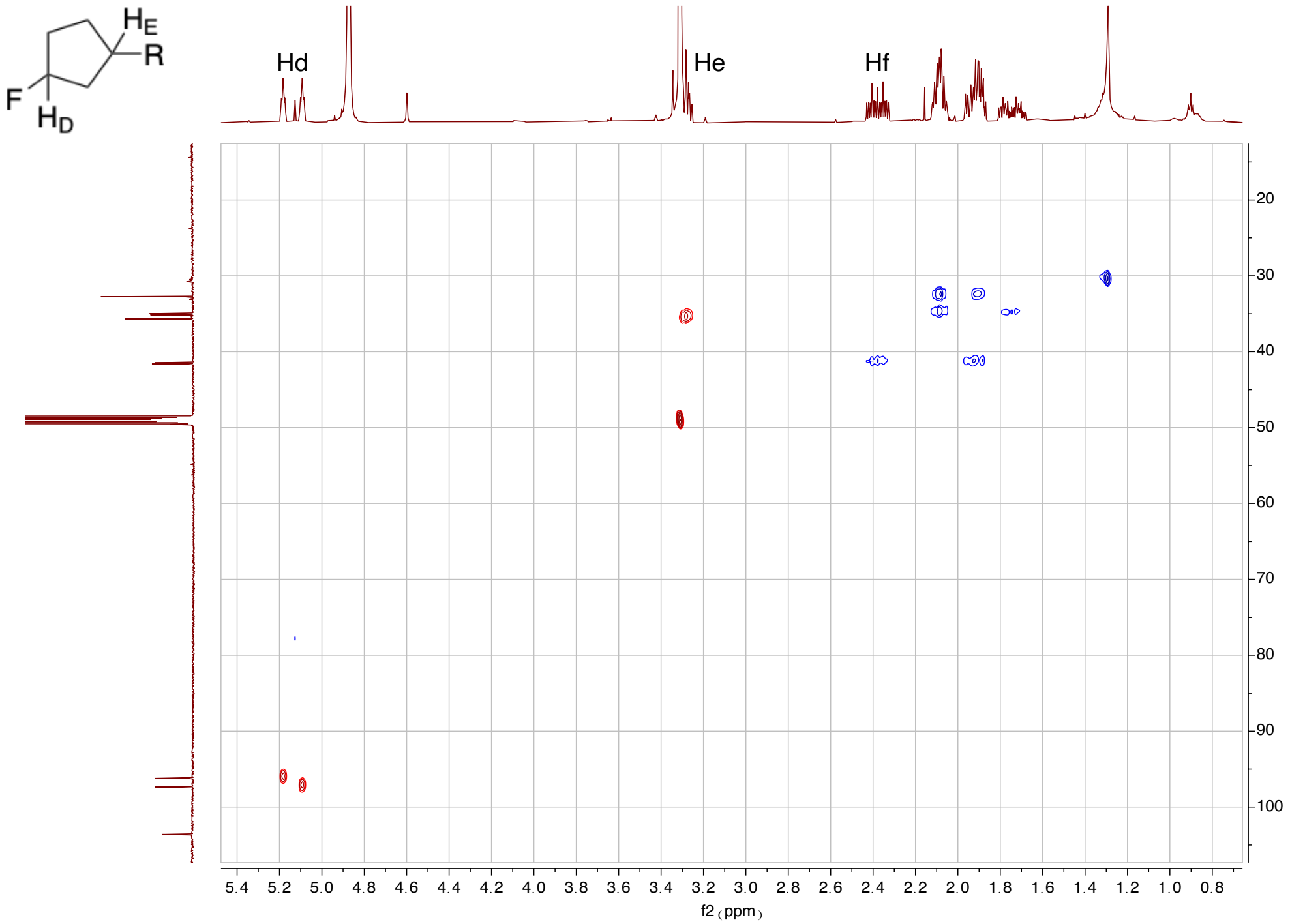
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	8192
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2555.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

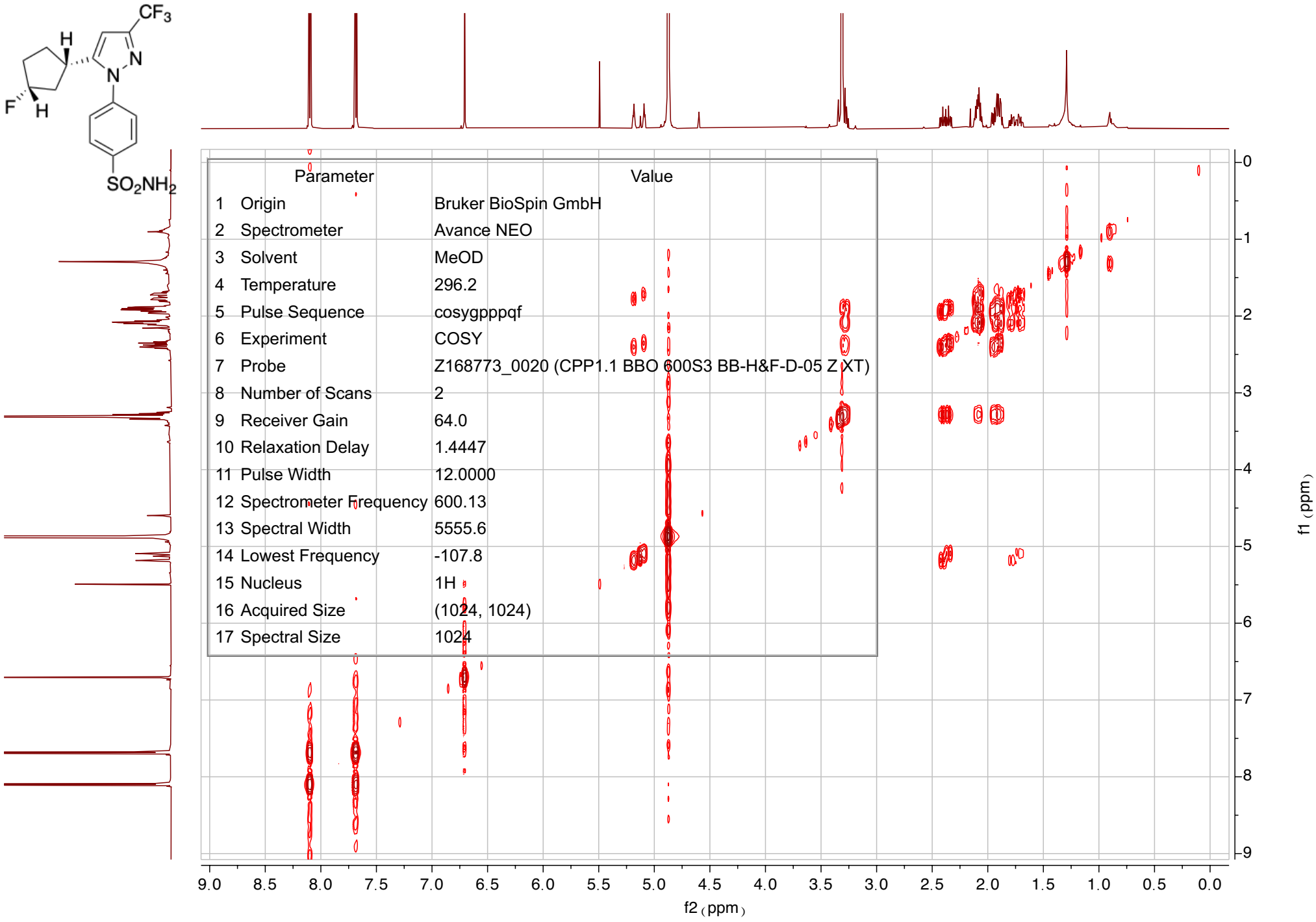
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	64
9	Receiver Gain	12.7
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

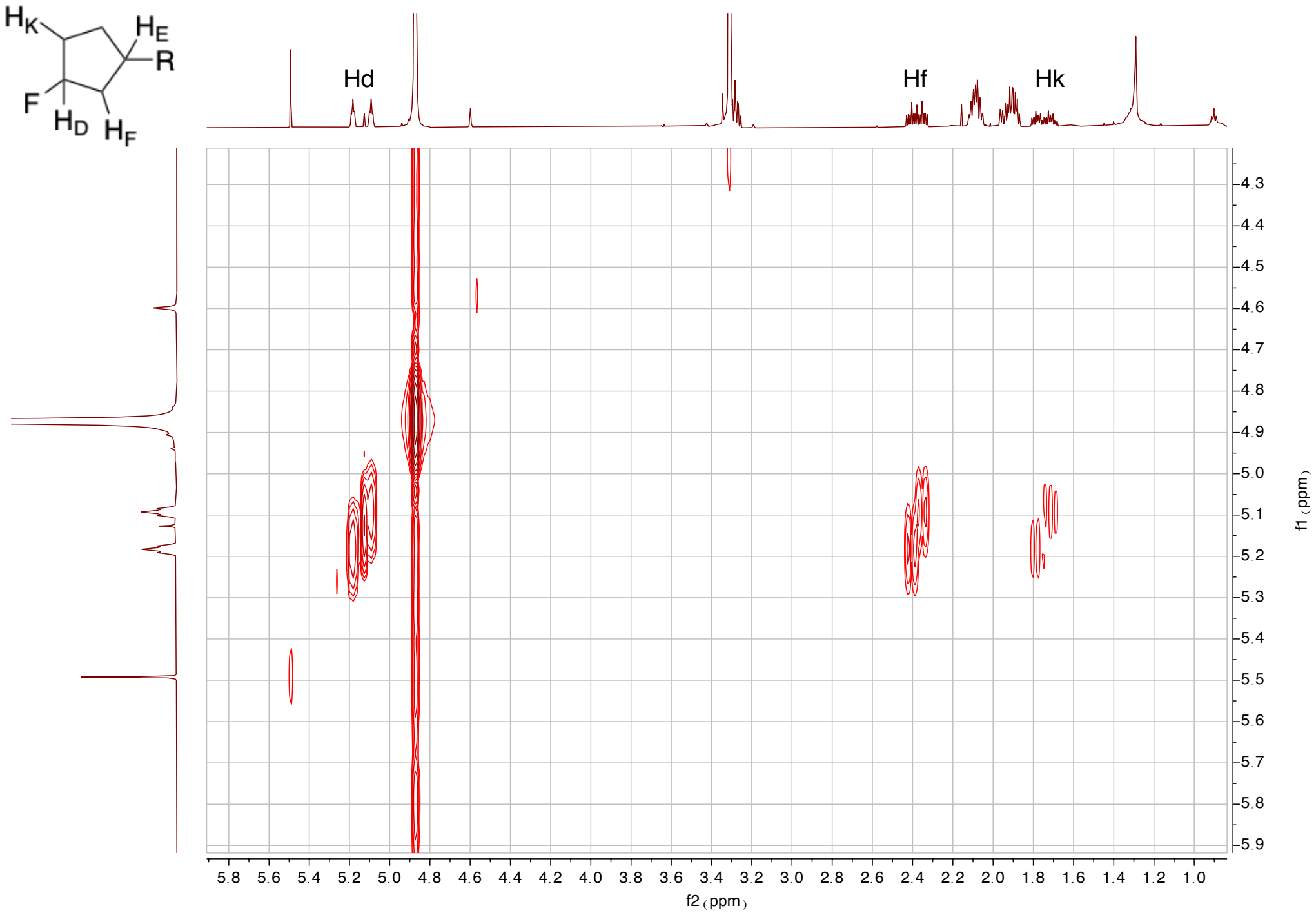




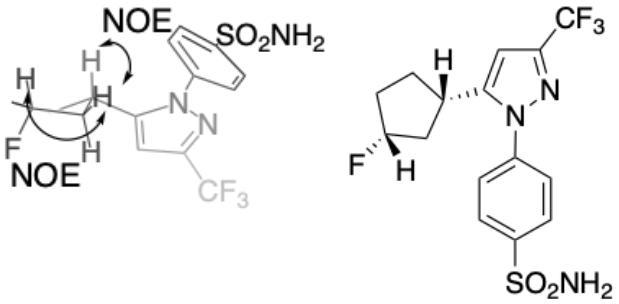
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5555.6
14	Lowest Frequency	-91.8
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


H_E
R
F
H_D
Hd
He
Hf
20
30
40
50
60
70
80
90
100
f1 (ppm)
5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
f2 (ppm)

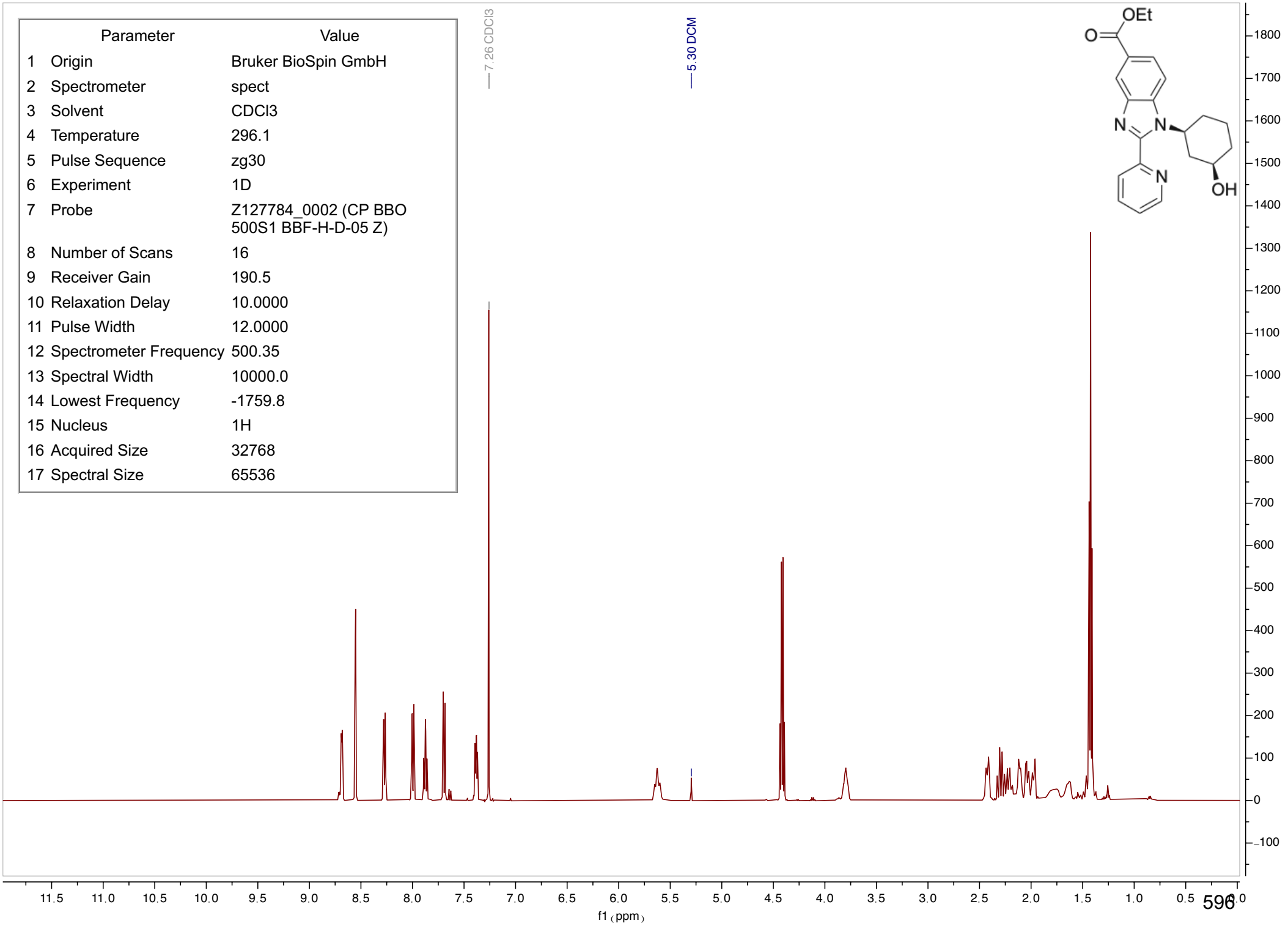

CF3
H
N
N
F
H
SO2NH2
Parameter
Value
1 Origin
Bruker BioSpin GmbH
2 Spectrometer
Avance NEO
3 Solvent
MeOD
4 Temperature
296.2
5 Pulse Sequence
cosygpppqf
6 Experiment
COSY
7 Probe
Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans
2
9 Receiver Gain
64.0
10 Relaxation Delay
1.4447
11 Pulse Width
12.0000
12 Spectrometer Frequency
600.13
13 Spectral Width
5555.6
14 Lowest Frequency
-107.8
15 Nucleus
1H
16 Acquired Size
(1024, 1024)
17 Spectral Size
1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)

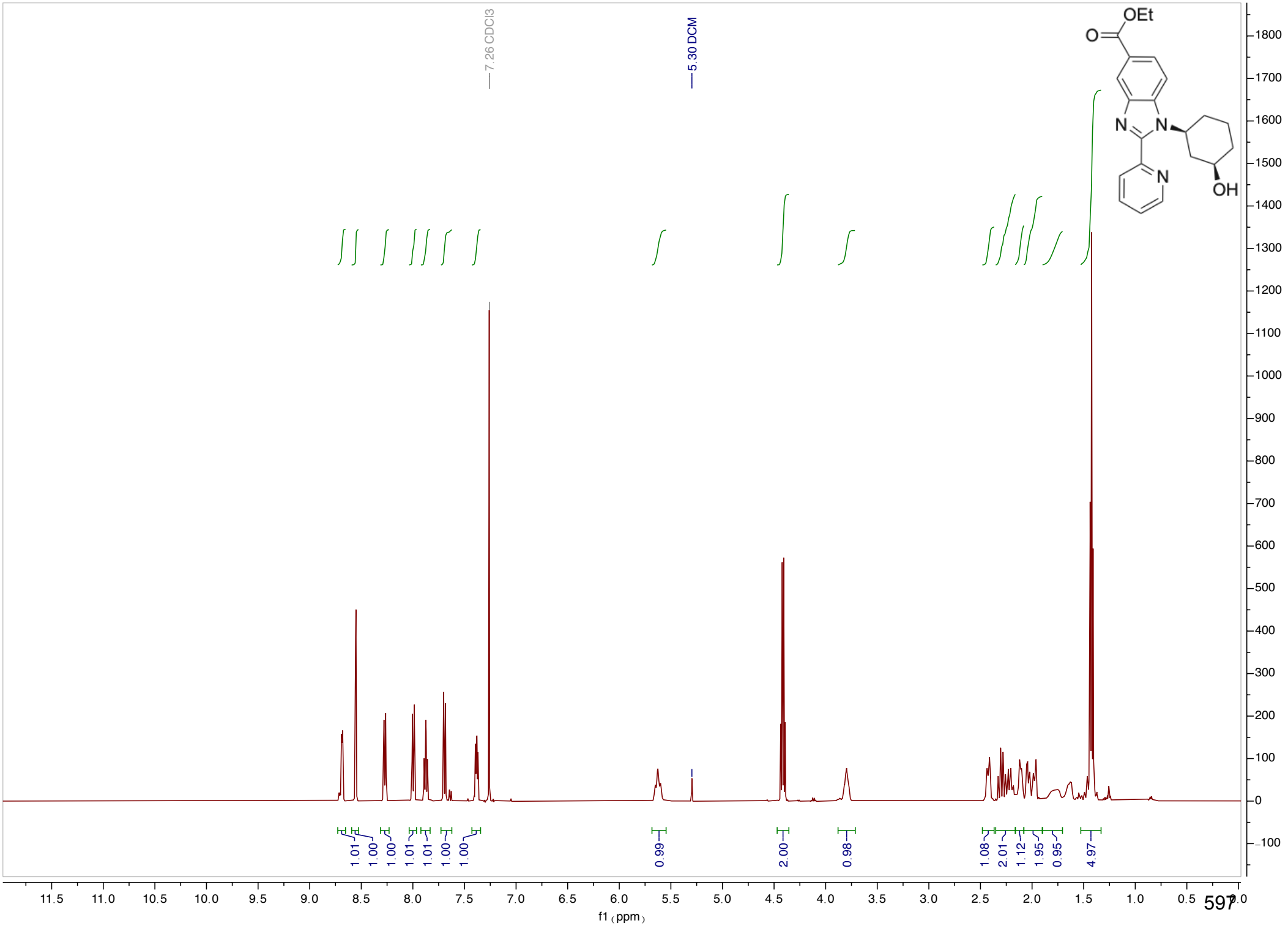

H_K
H_E
R
F
H_D
H_F
Hd
Hf
Hk
4.3
4.4
4.5
4.6
4.7
4.8
4.9
5.0
5.1
5.2
5.3
5.4
5.5
5.6
5.7
5.8
5.9
f1 (ppm)
5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f2 (ppm)

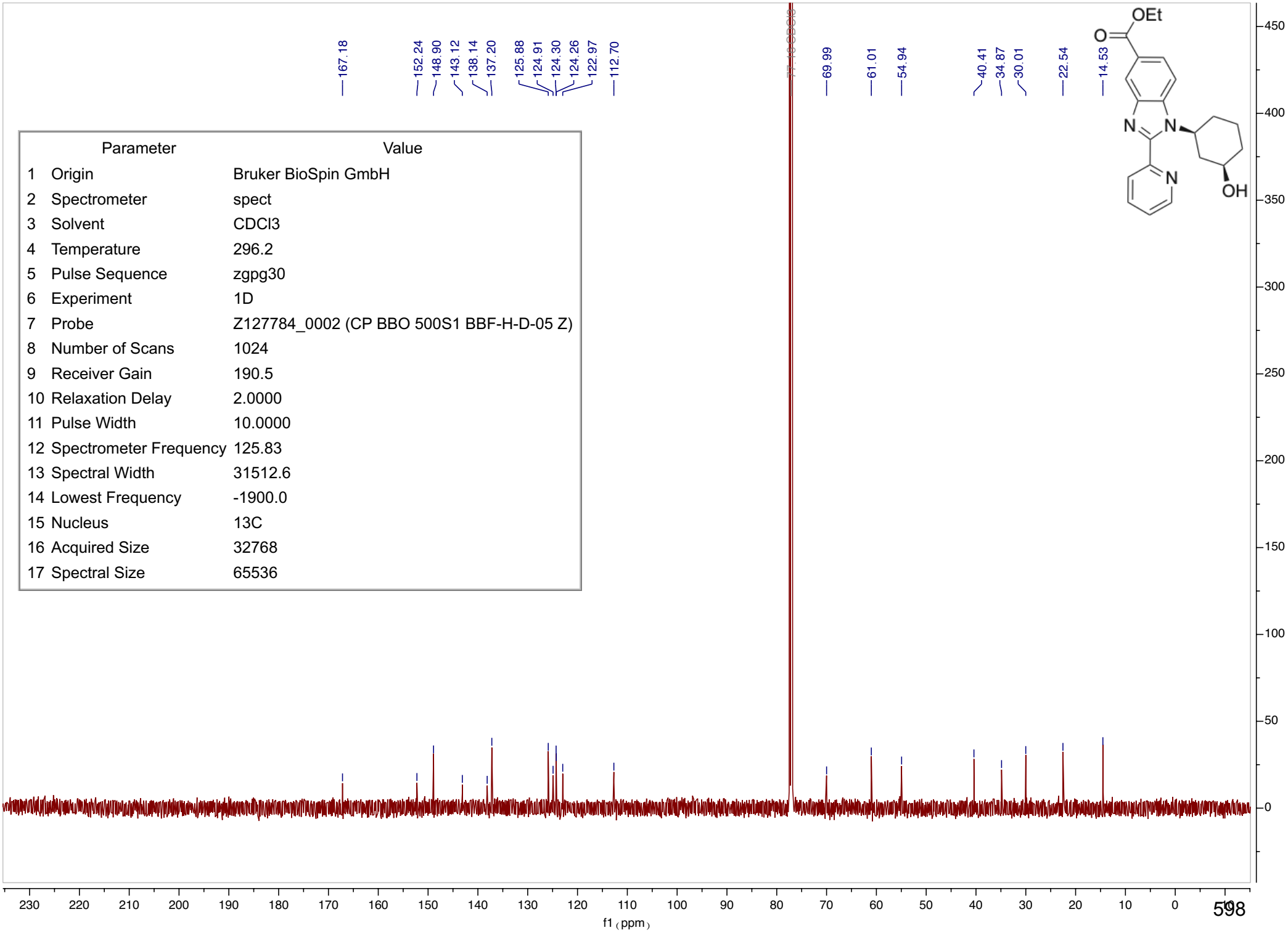
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	selnogpzs.2
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	32.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2246.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



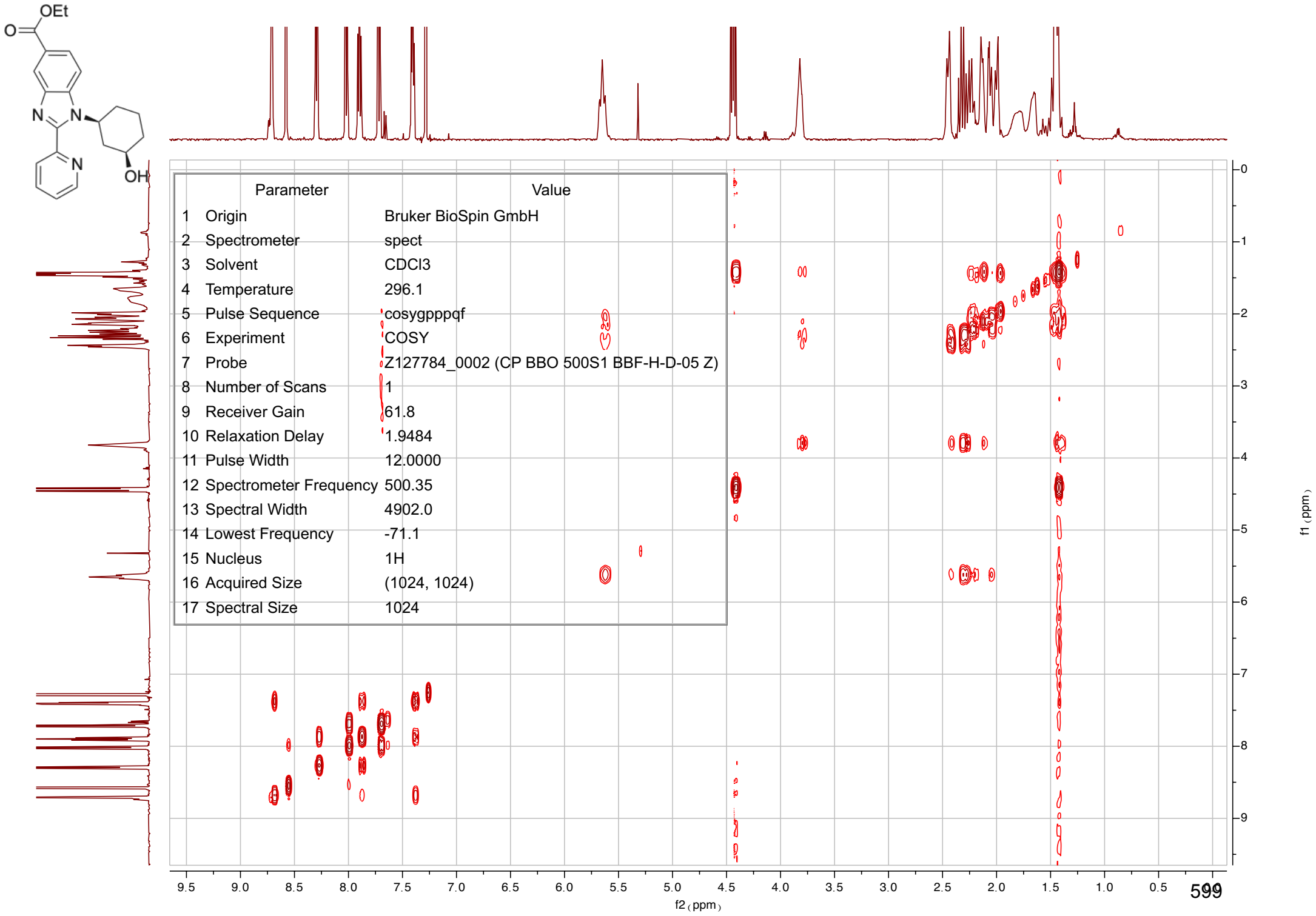
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

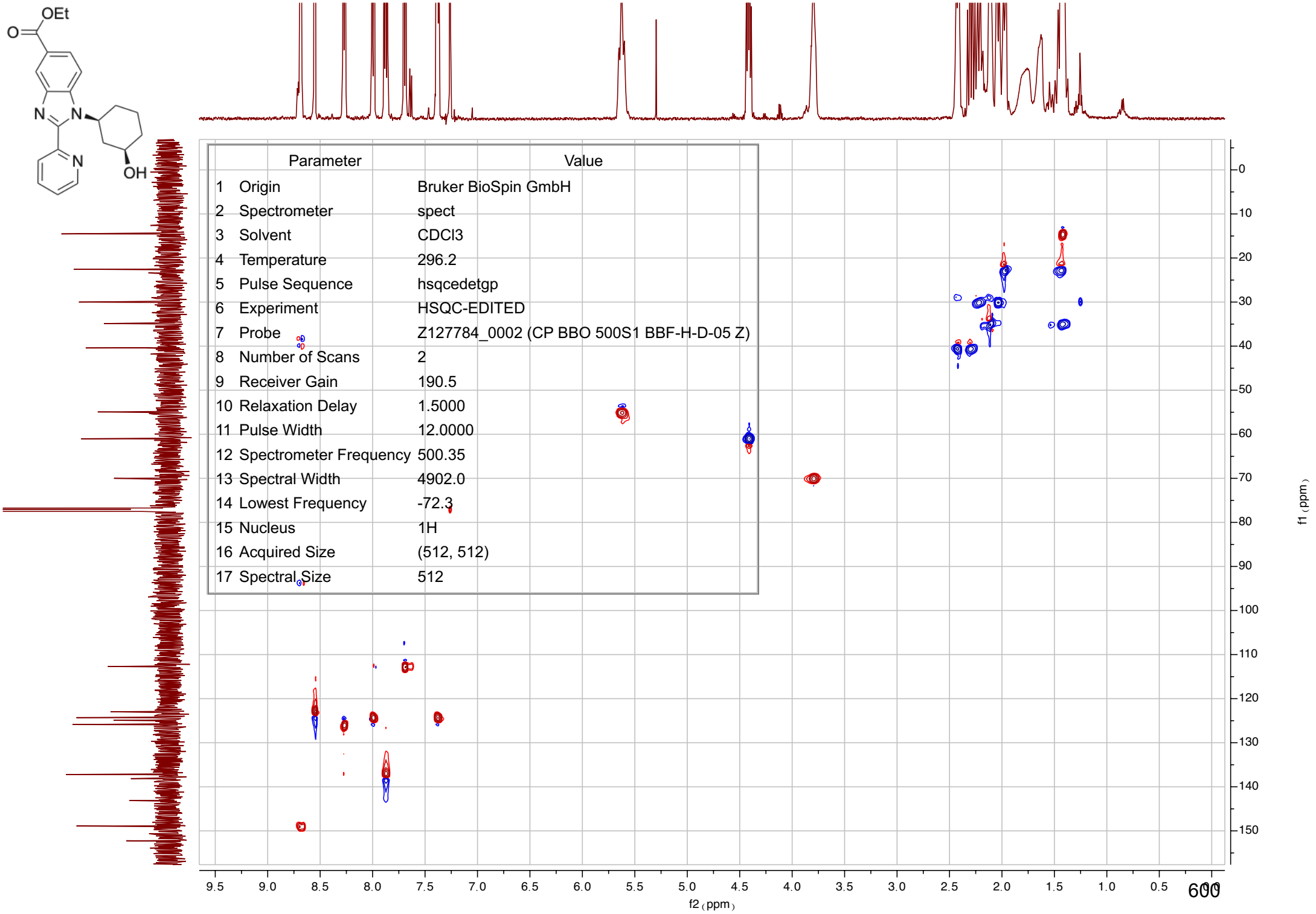


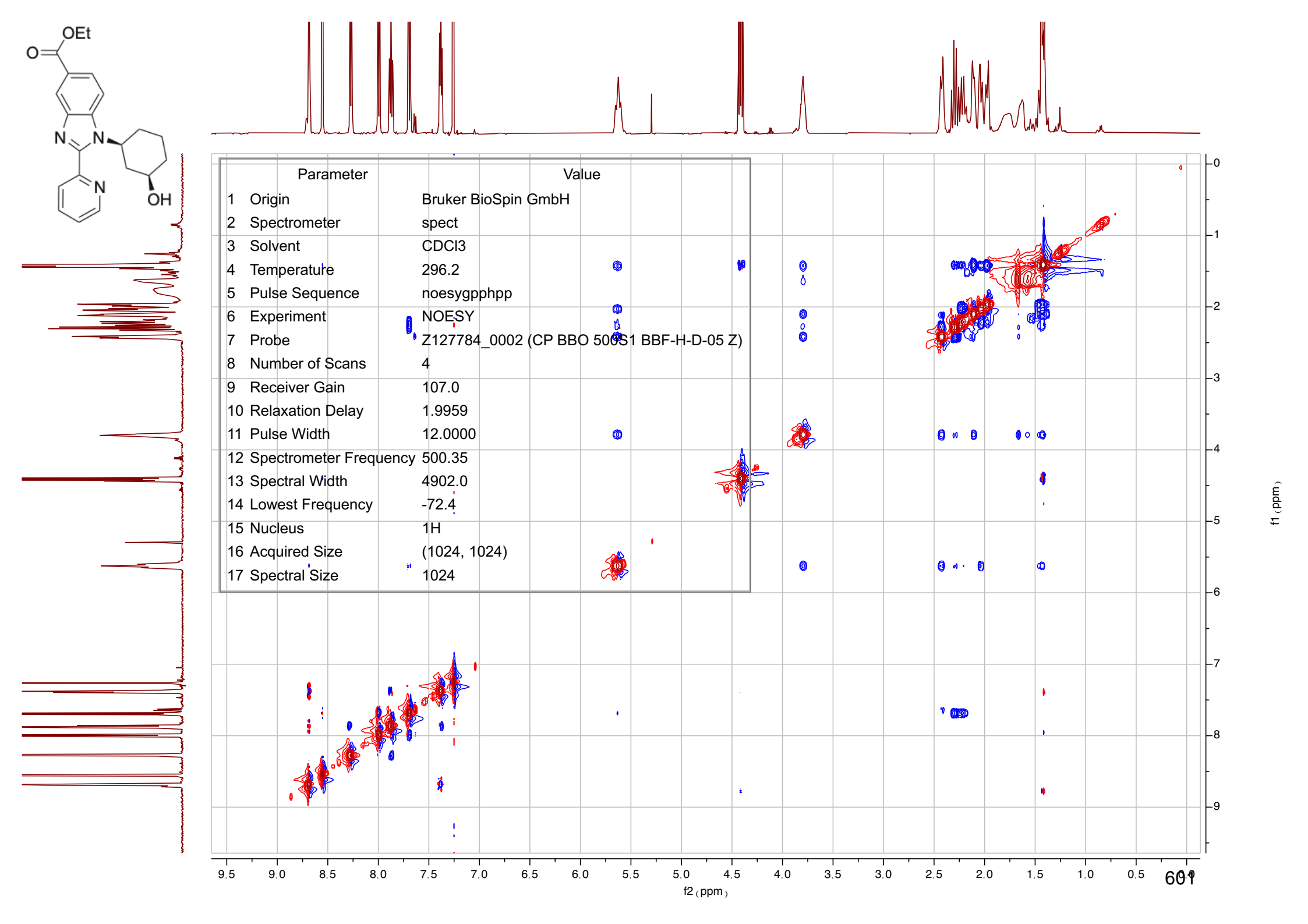

7.26 CDCl3
5.30 DCM
OEt
O
N
N
N
OH
1.01
1.00
1.00
1.01
1.01
1.00
1.00
0.99
2.00
0.98
1.08
2.01
1.12
1.95
0.95
4.97
f1 (ppm)

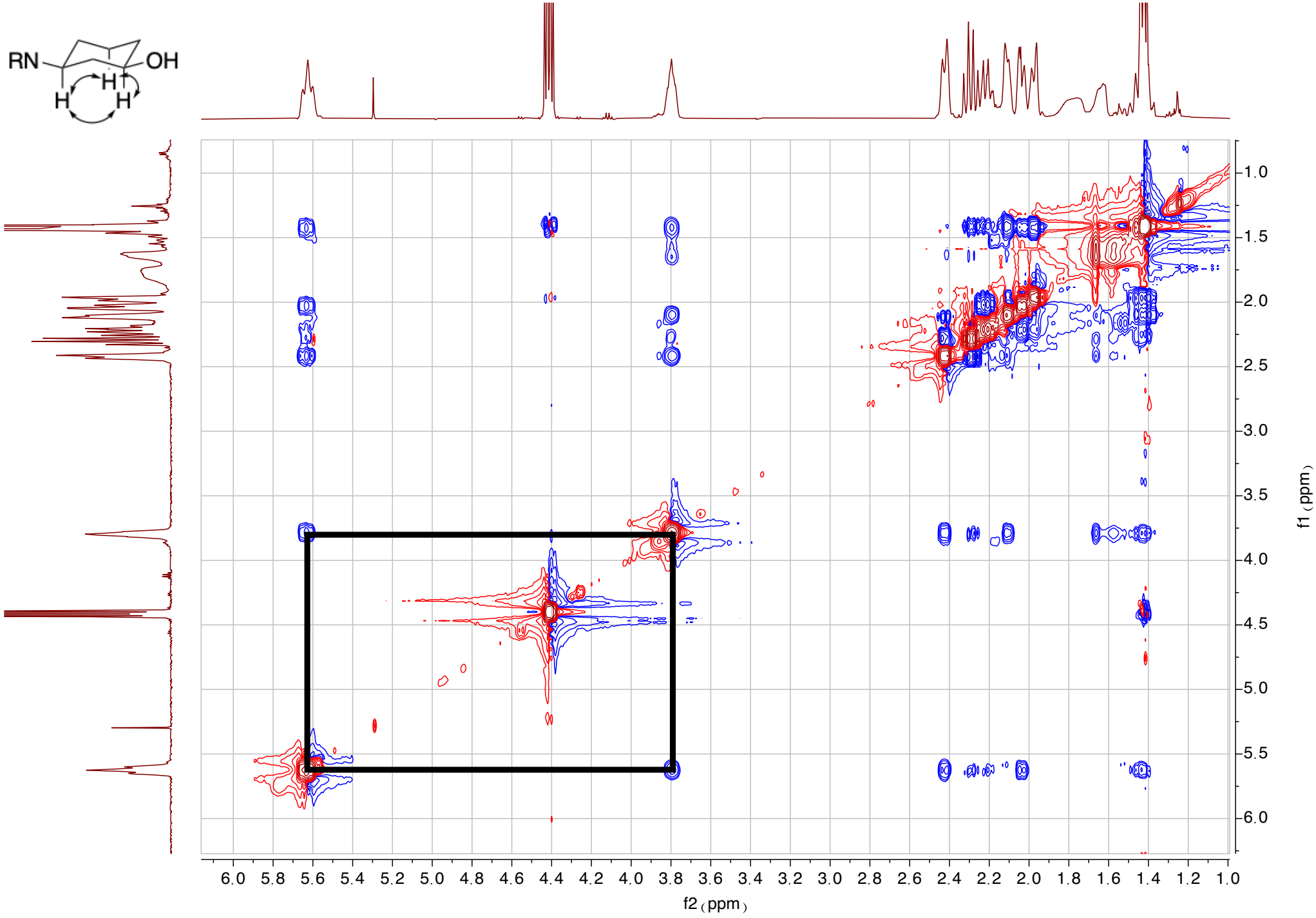


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


OEt
O
N
N
N
OH
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 1
9 Receiver Gain 61.8
10 Relaxation Delay 1.9484
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4902.0
14 Lowest Frequency -71.1
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)

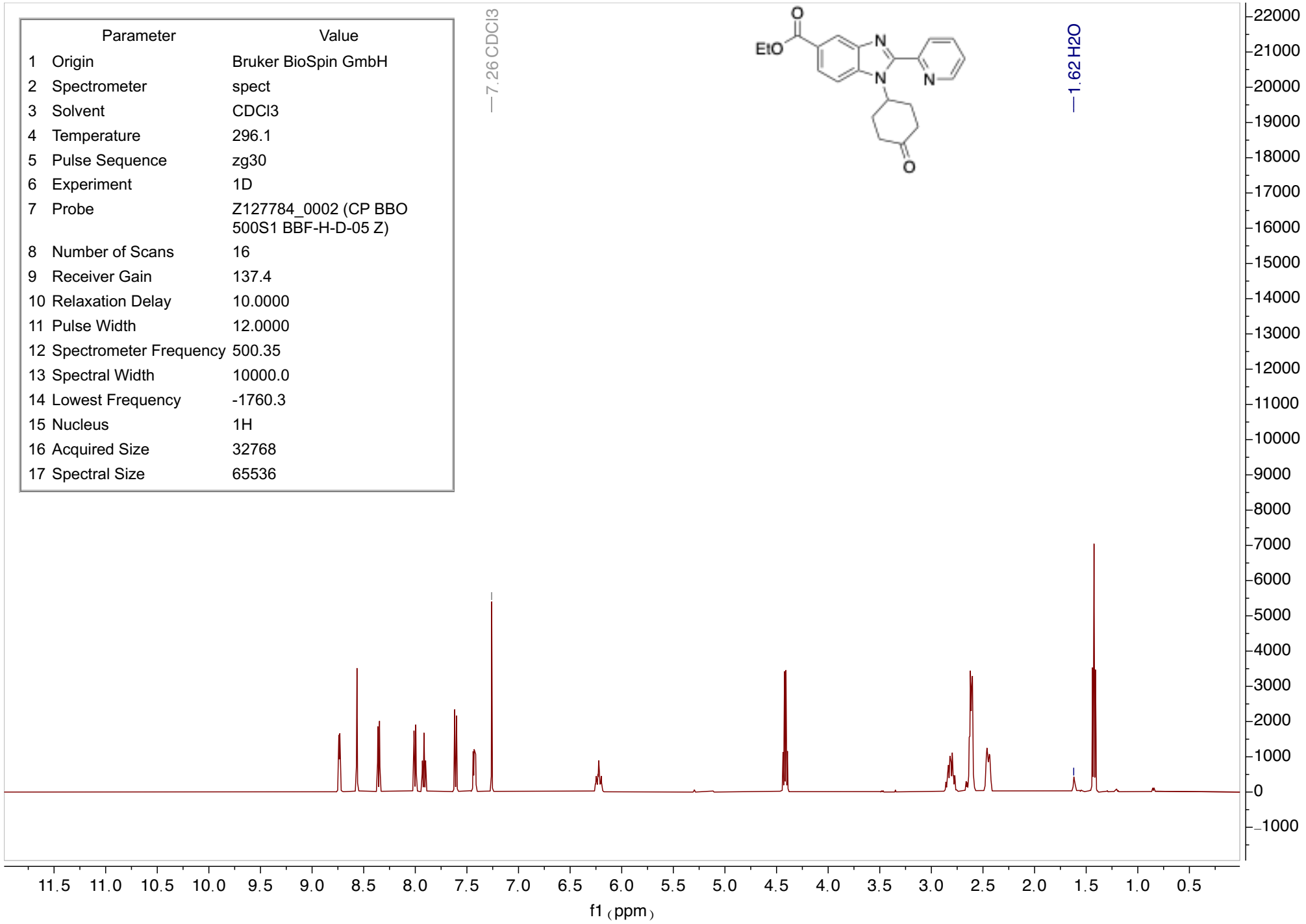

OEt
O
N
N
N
OH
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hsqcedetgp
6 Experiment HSQC-EDITED
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 2
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4902.0
14 Lowest Frequency -72.3
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
f2 (ppm)
f1 (ppm)

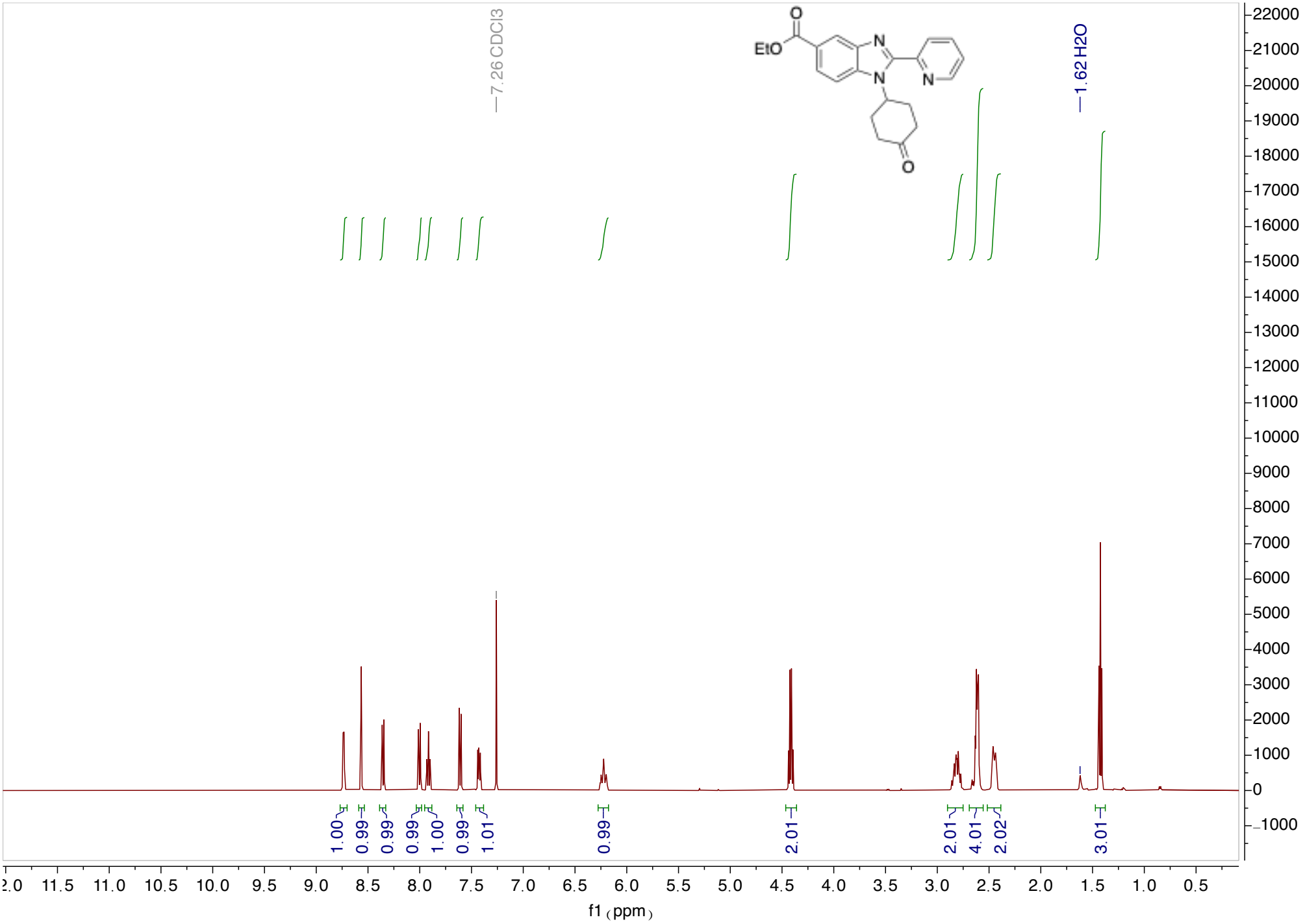

OEt
O
N
N
N
OH
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence noesygpphpp
6 Experiment NOESY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 107.0
10 Relaxation Delay 1.9959
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4902.0
14 Lowest Frequency -72.4
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
f2 (ppm)
f1 (ppm)
601

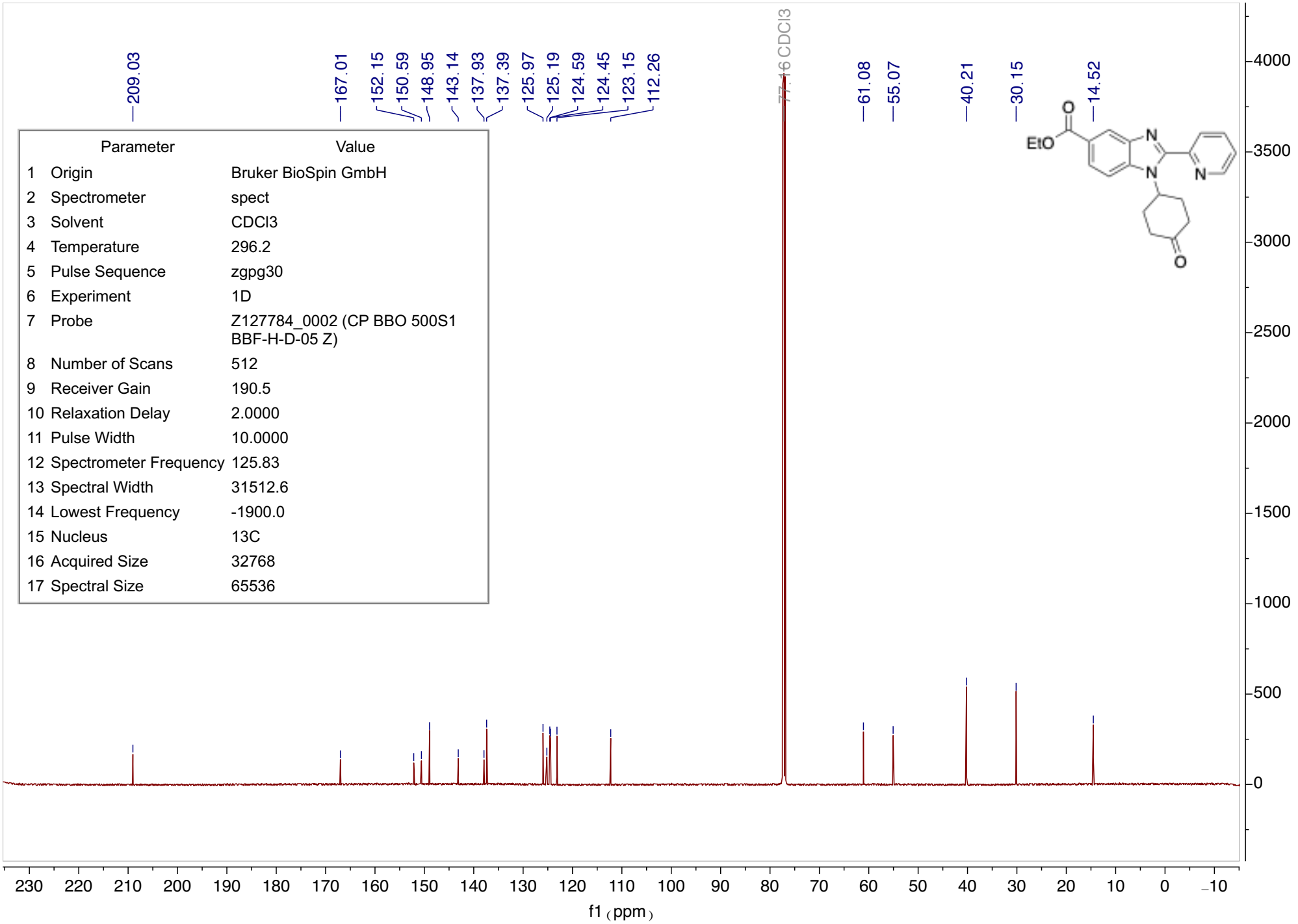

RN
OH
H
H
H
f2 (ppm)
f1 (ppm)
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0

602

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	137.4
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

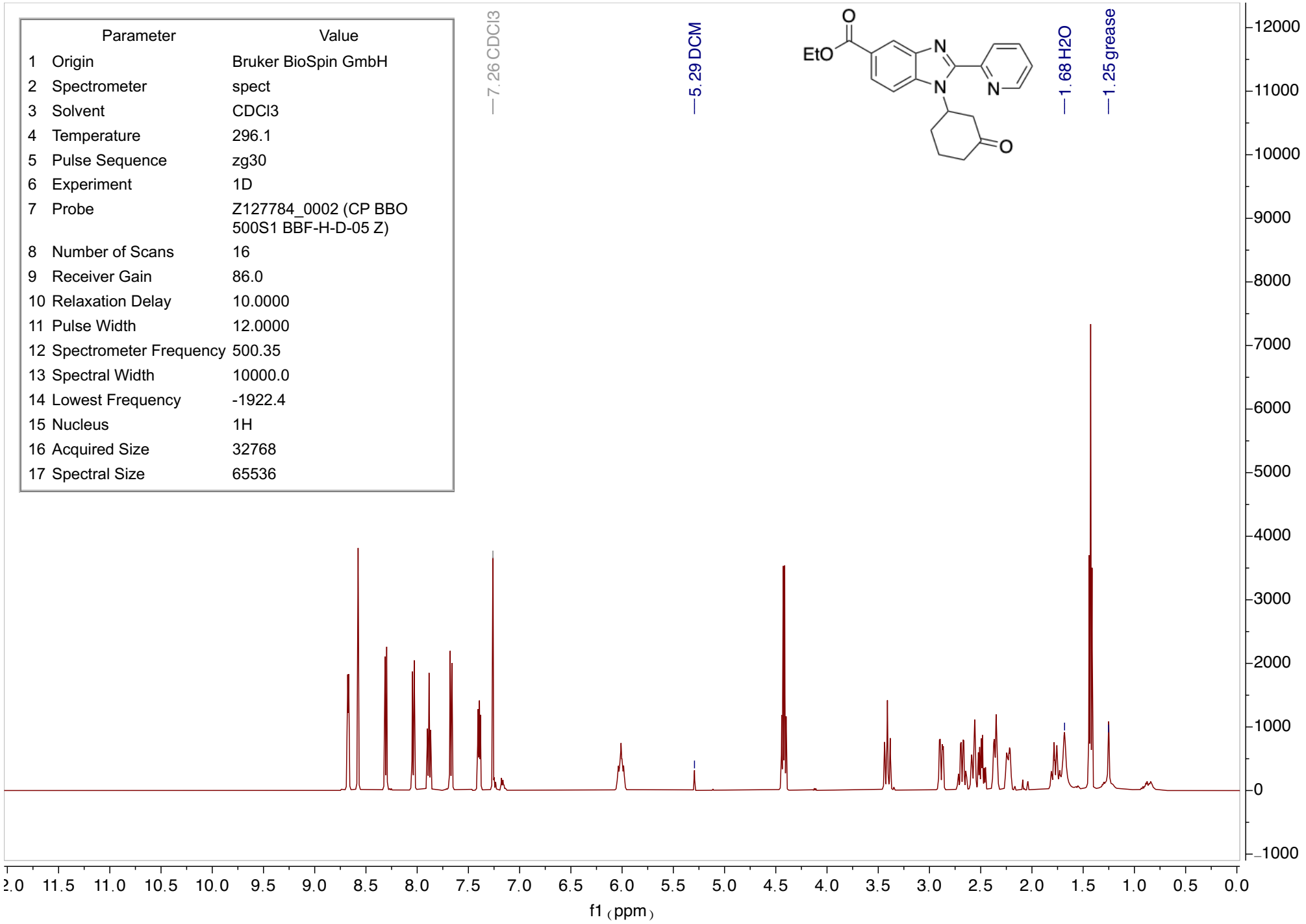


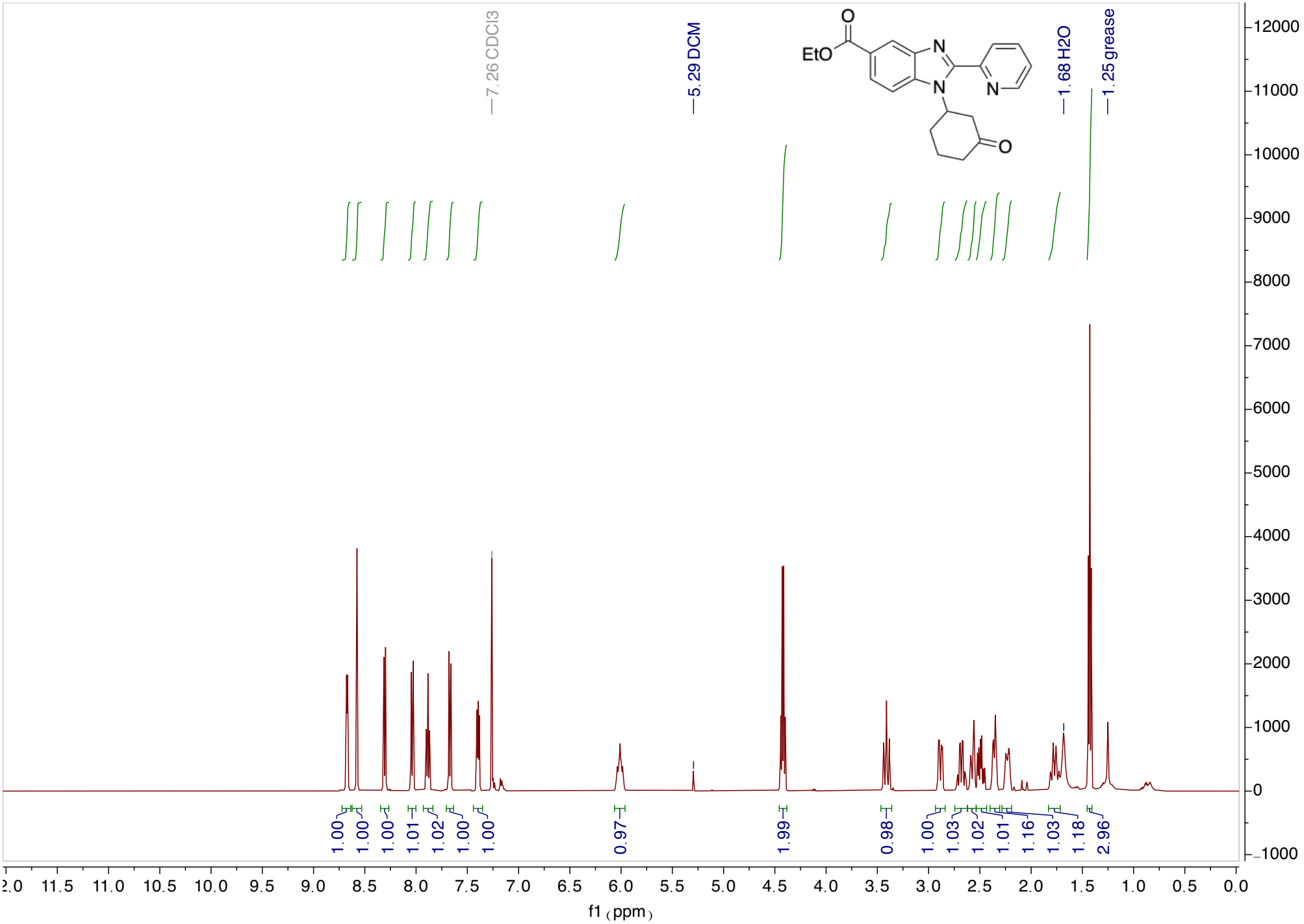

7.26 CDCl3
1.62 H2O
EtO
O
N
N
N
O
1.00
0.99
0.99
0.99
1.00
0.99
1.01
0.99
2.01
2.01
4.01
2.02
3.01
f1 (ppm)

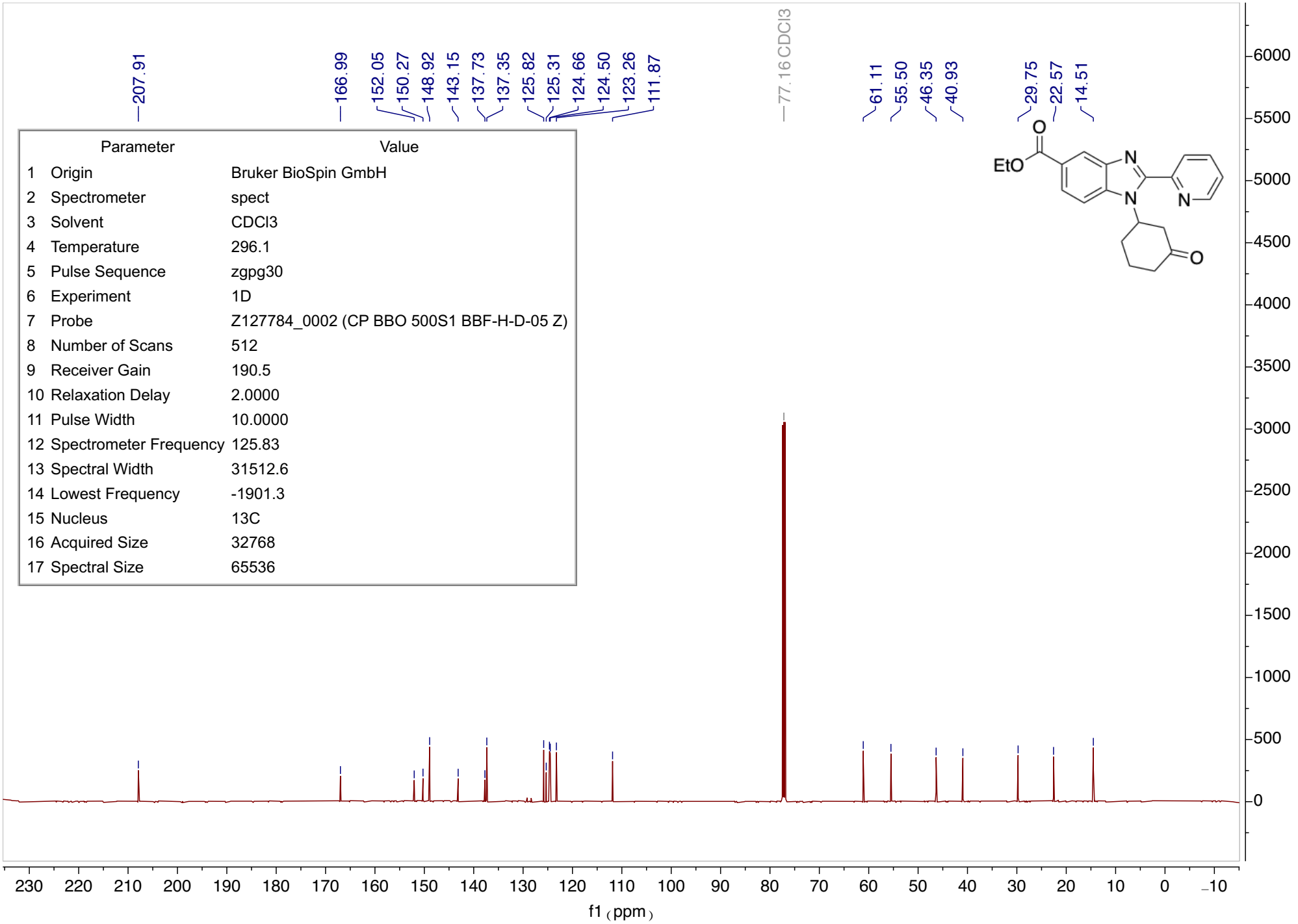


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

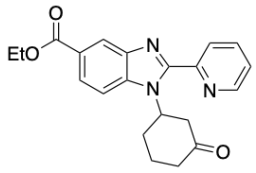
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



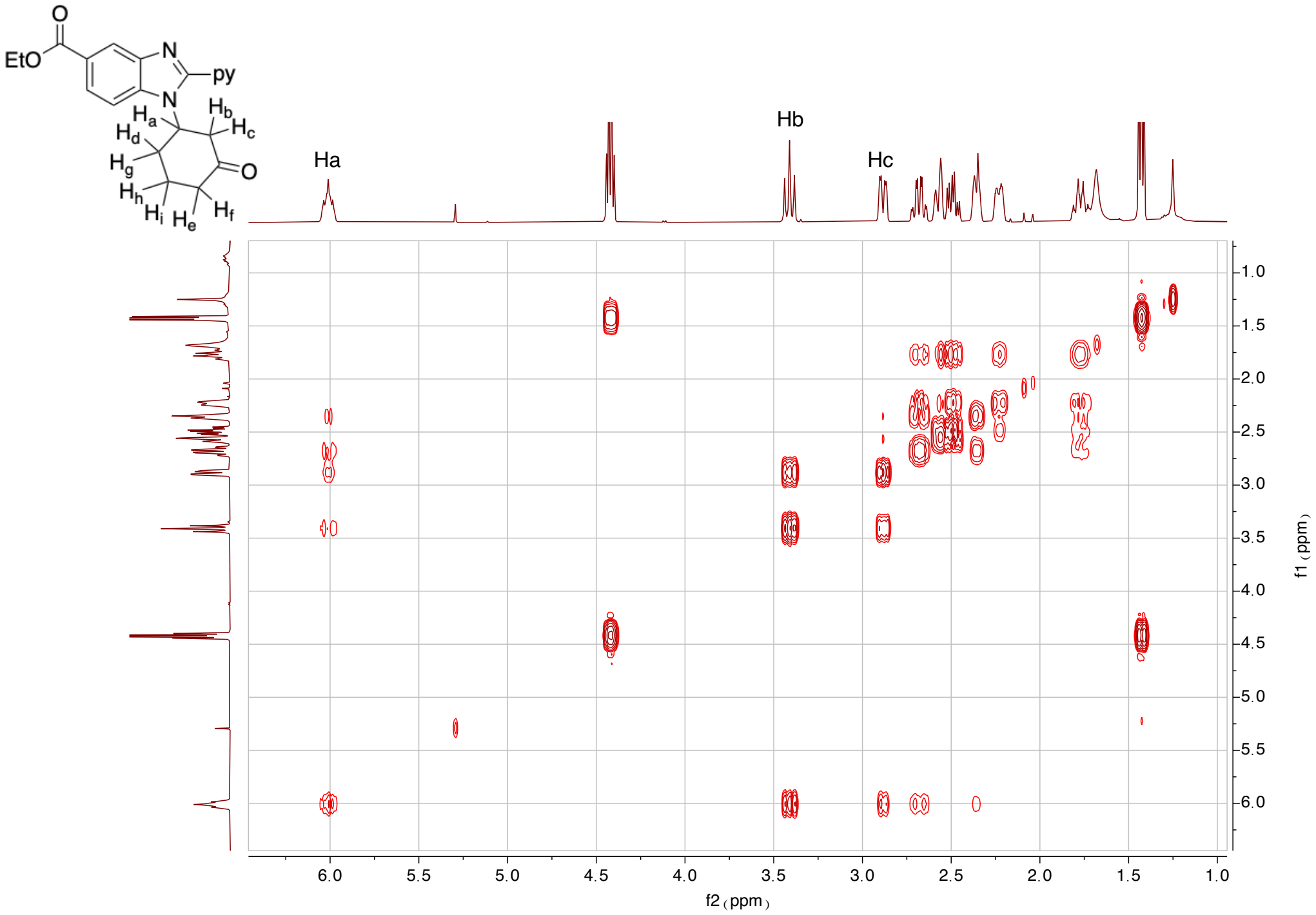

7.26 CDCl3
5.29 DCM
1.68 H2O
1.25 grease
EtO
O
N
N
N
O
1.00
1.00
1.00
1.01
1.02
1.00
1.00
0.97
1.99
0.98
1.00
1.03
1.02
1.01
1.16
1.03
1.18
2.96
f1 (ppm)

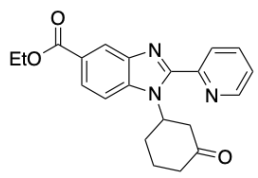


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

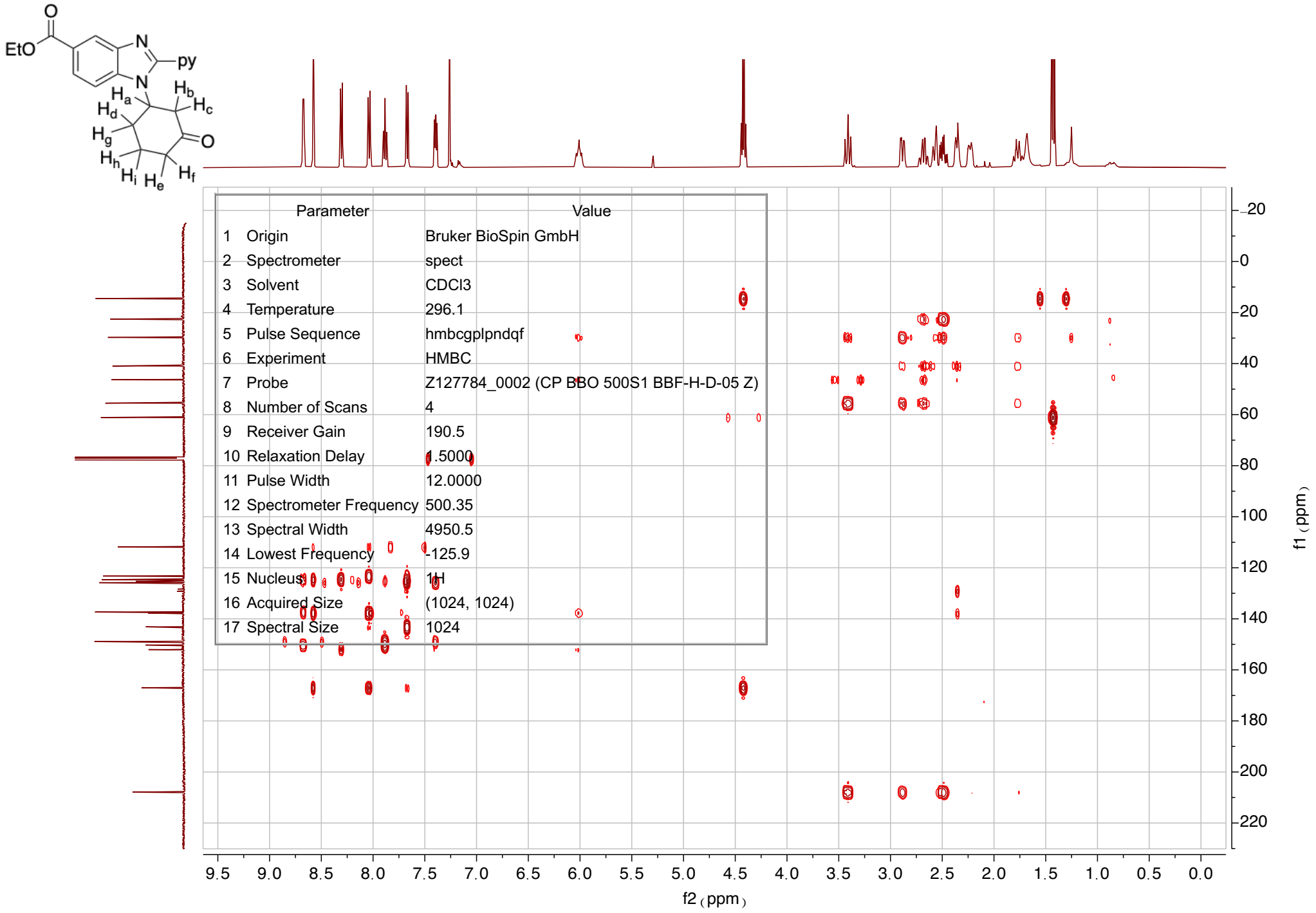


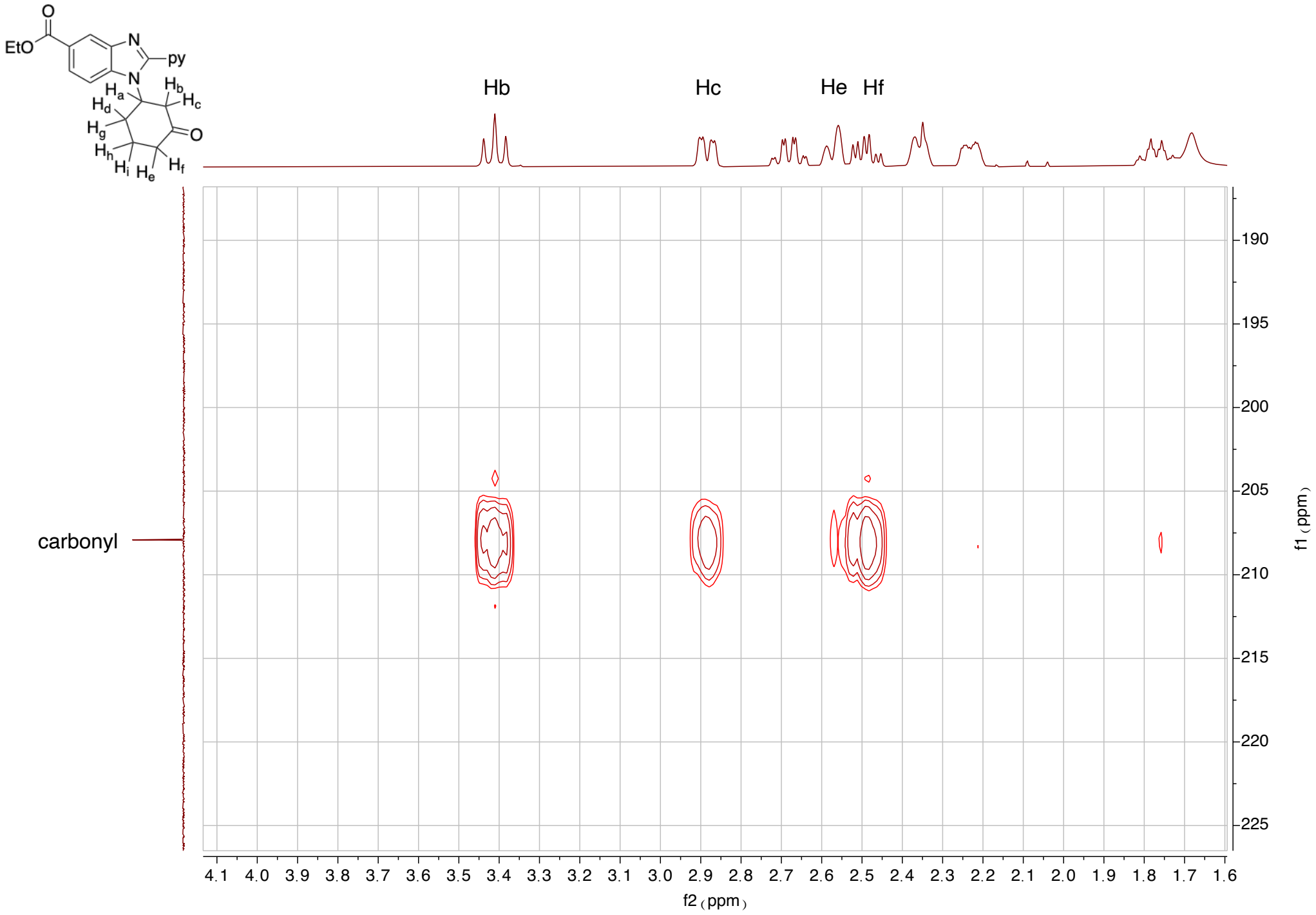
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	34.8
10	Relaxation Delay	1.9504
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4950.5
14	Lowest Frequency	-127.8
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


O
EtO
N
py
N
Ha
Hb
Hc
Hd
Hg
O
Hh
Hi
He
Hf
Ha
Hb
Hc
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
f1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)

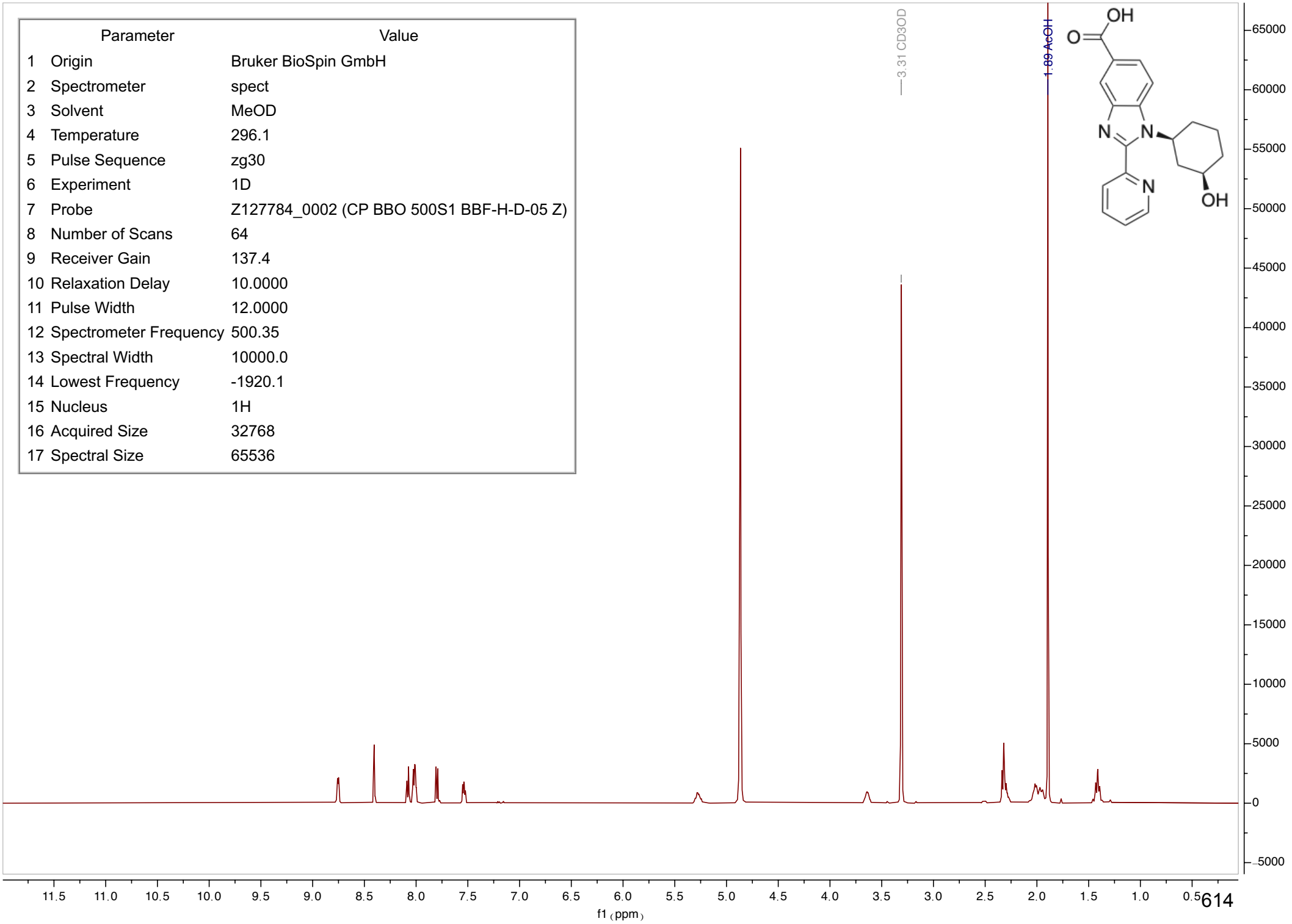


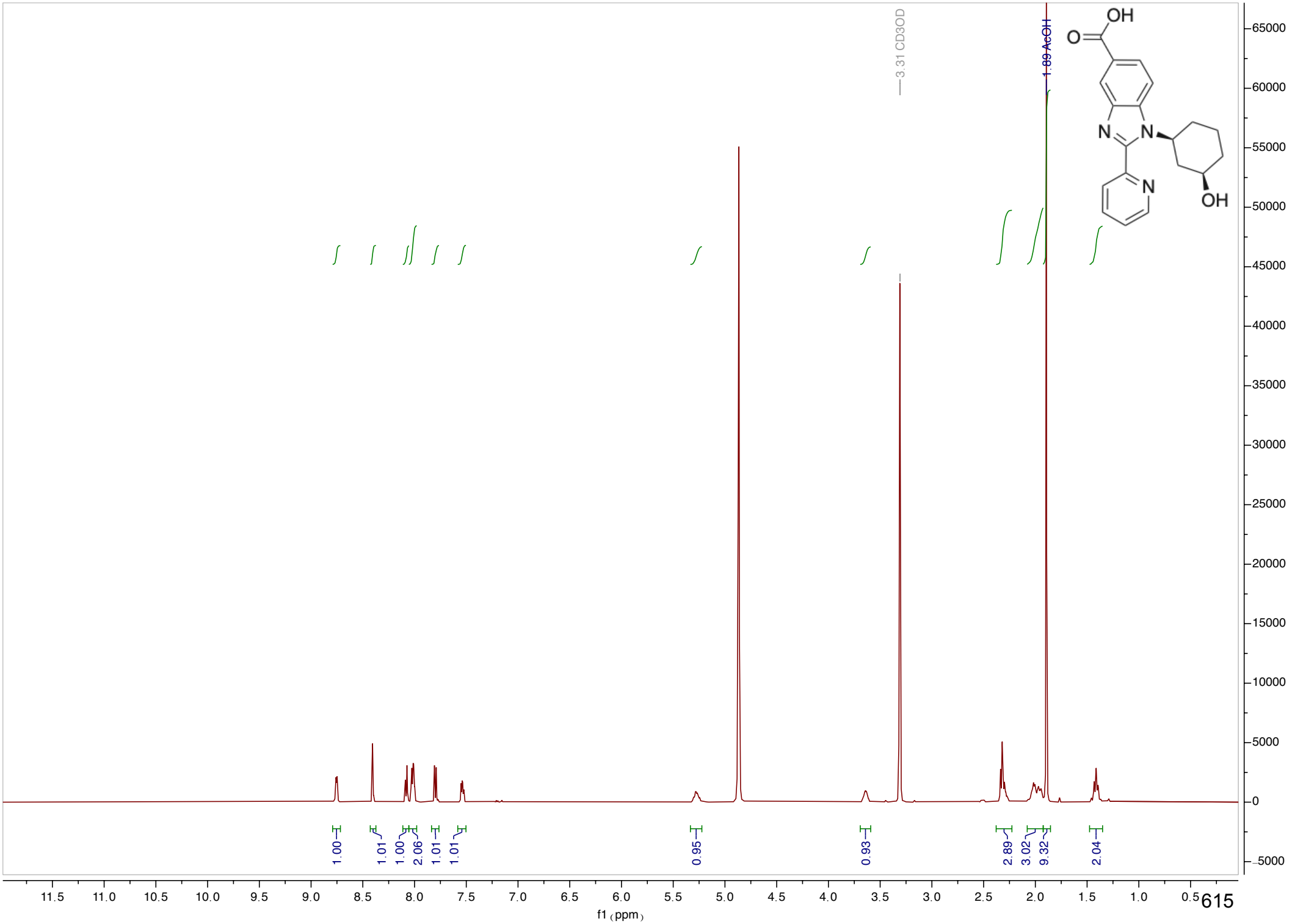
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4950.5
14	Lowest Frequency	-125.4
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

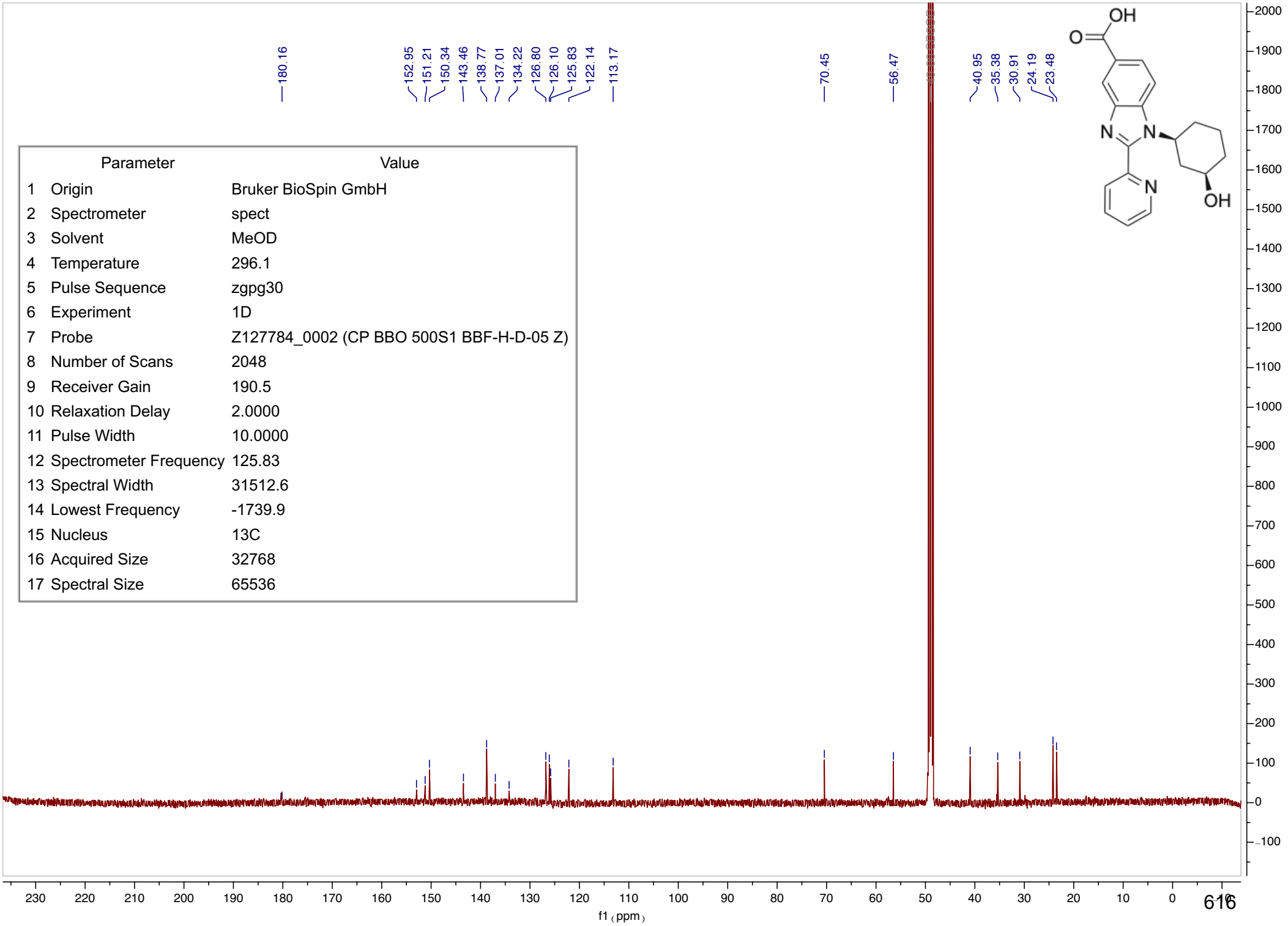

EtO
O
N
N
py
Ha
Hb
Hc
Hd
Hg
Hh
Hi
He
Hf
O
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4950.5
14 Lowest Frequency -125.9
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
-20 0 20 40 60 80 100 120 140 160 180 200 220
f1 (ppm)


EtO
O
N
N
py
Ha
Hb
Hc
Hd
Hg
Hh
Hi
He
Hf
O
Hb
Hc
He
Hf
carbonyl
190
195
200
205
210
215
220
225
f1 (ppm)
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	64
9	Receiver Gain	137.4
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1920.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

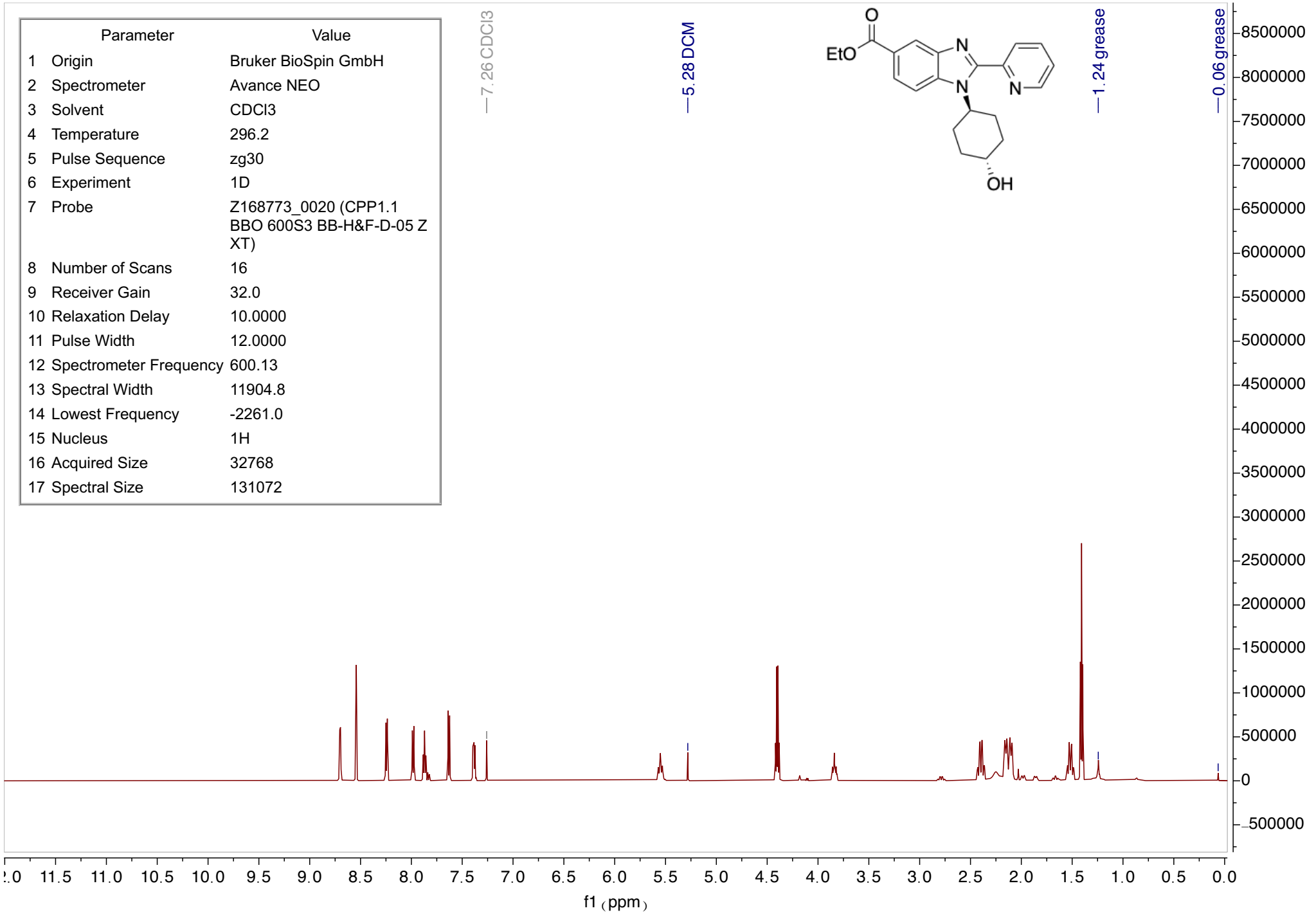


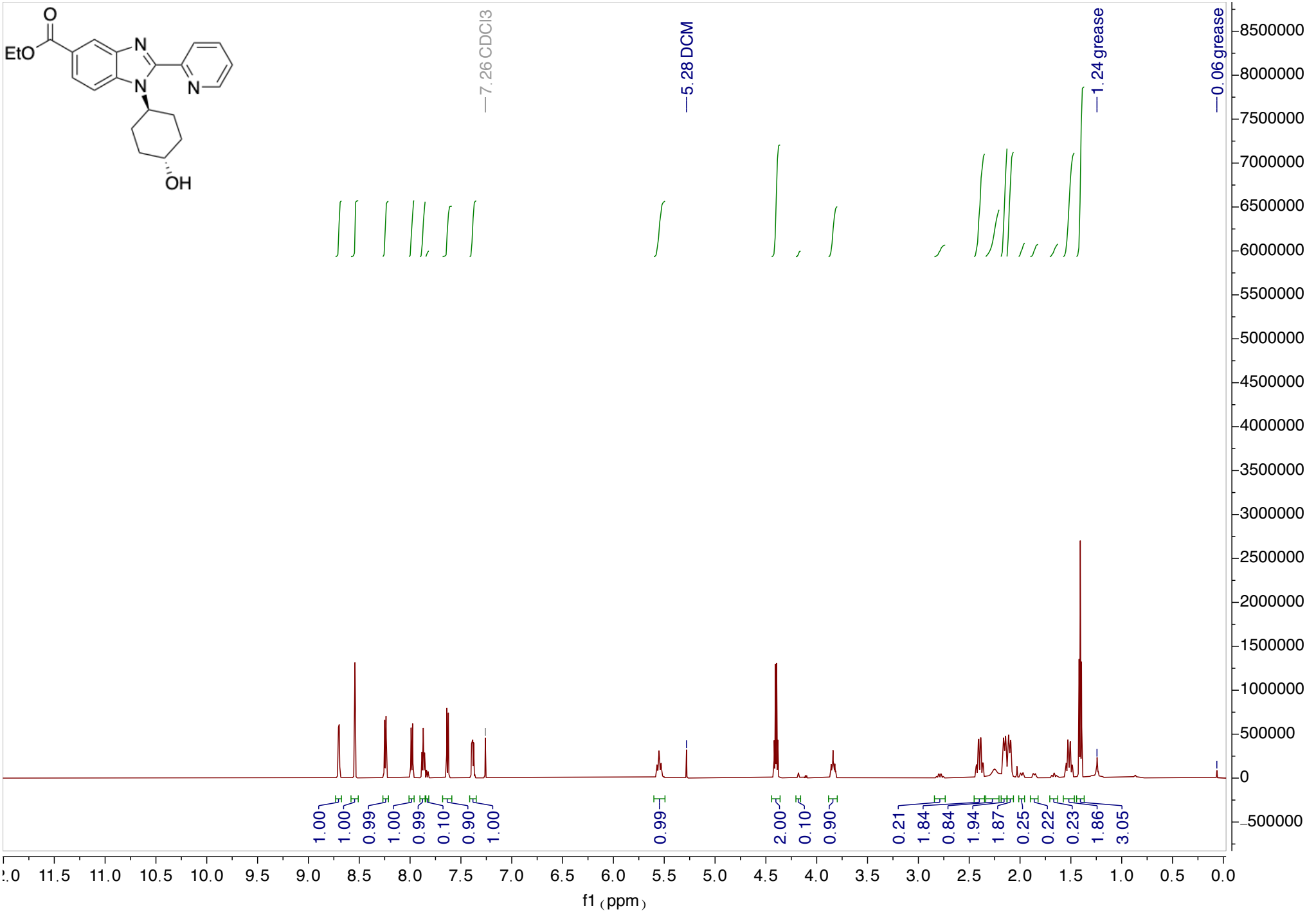

3.31 CD3OD
1.89 AcOH
OH
O
N
N
N
OH
1.00
1.01
1.00
2.06
1.01
1.01
0.95
0.93
2.89
3.02
9.32
2.04
f1 (ppm)

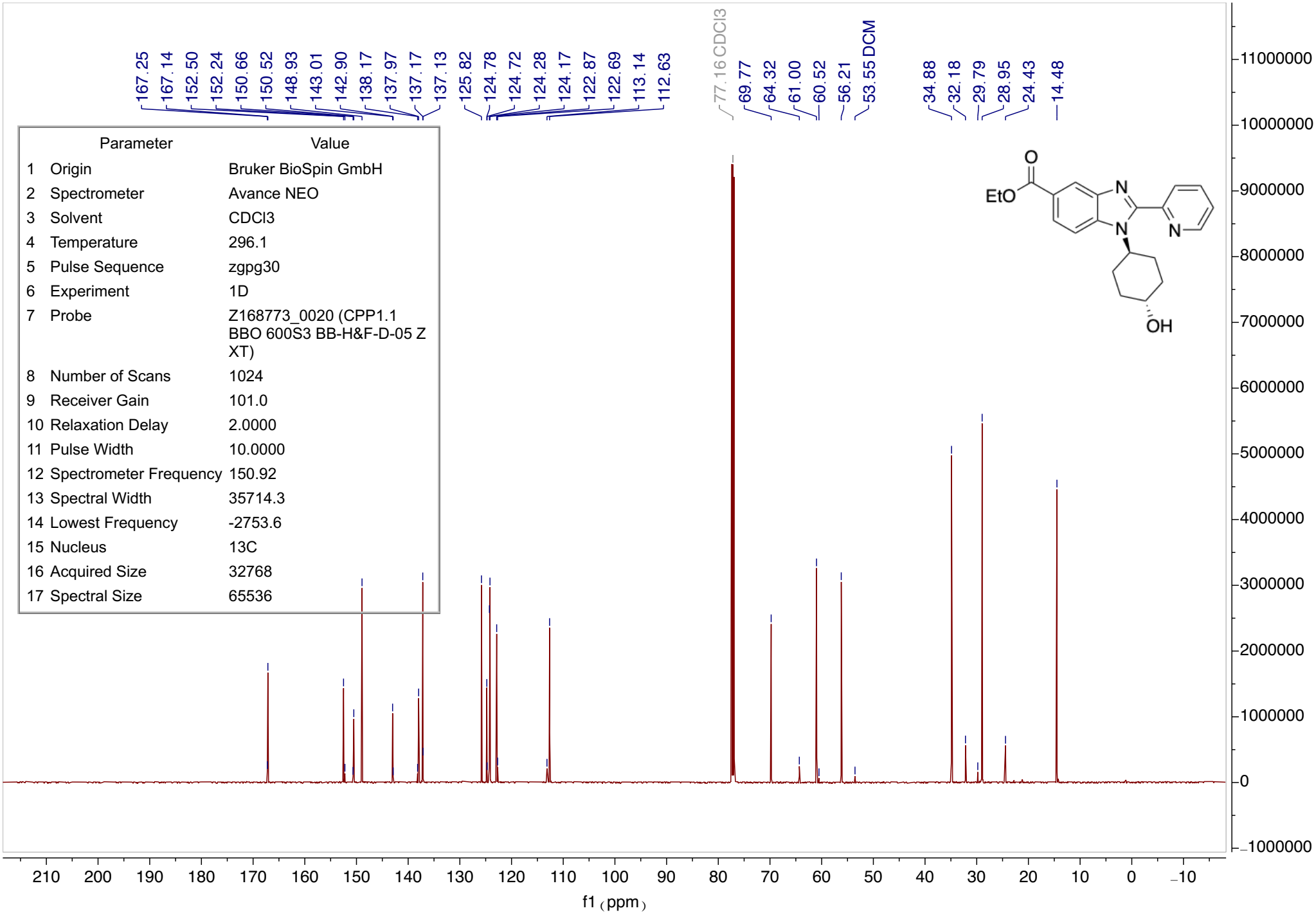


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2048
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1739.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

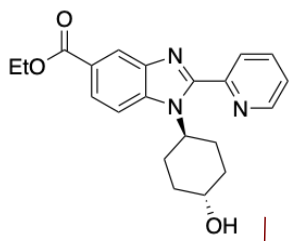
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2261.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



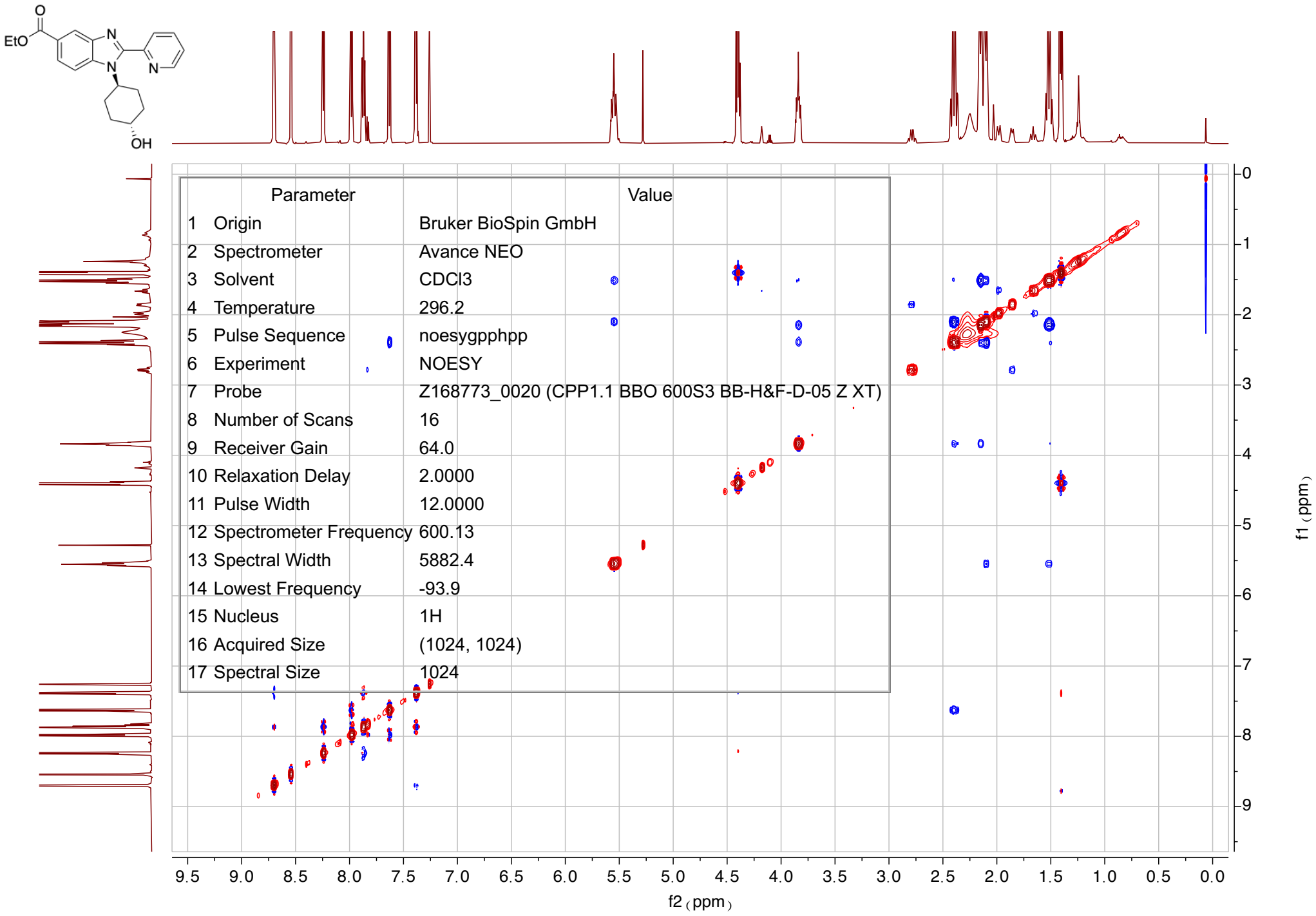

O
EtO
N
N
N
OH
7.26 CDCl3
5.28 DCM
1.24 grease
0.06 grease
1.00
1.00
0.99
1.00
0.99
0.10
0.90
1.00
0.99
2.00
0.10
0.90
0.21
1.84
0.84
1.94
1.87
0.25
0.22
0.23
1.86
3.05
f1 (ppm)

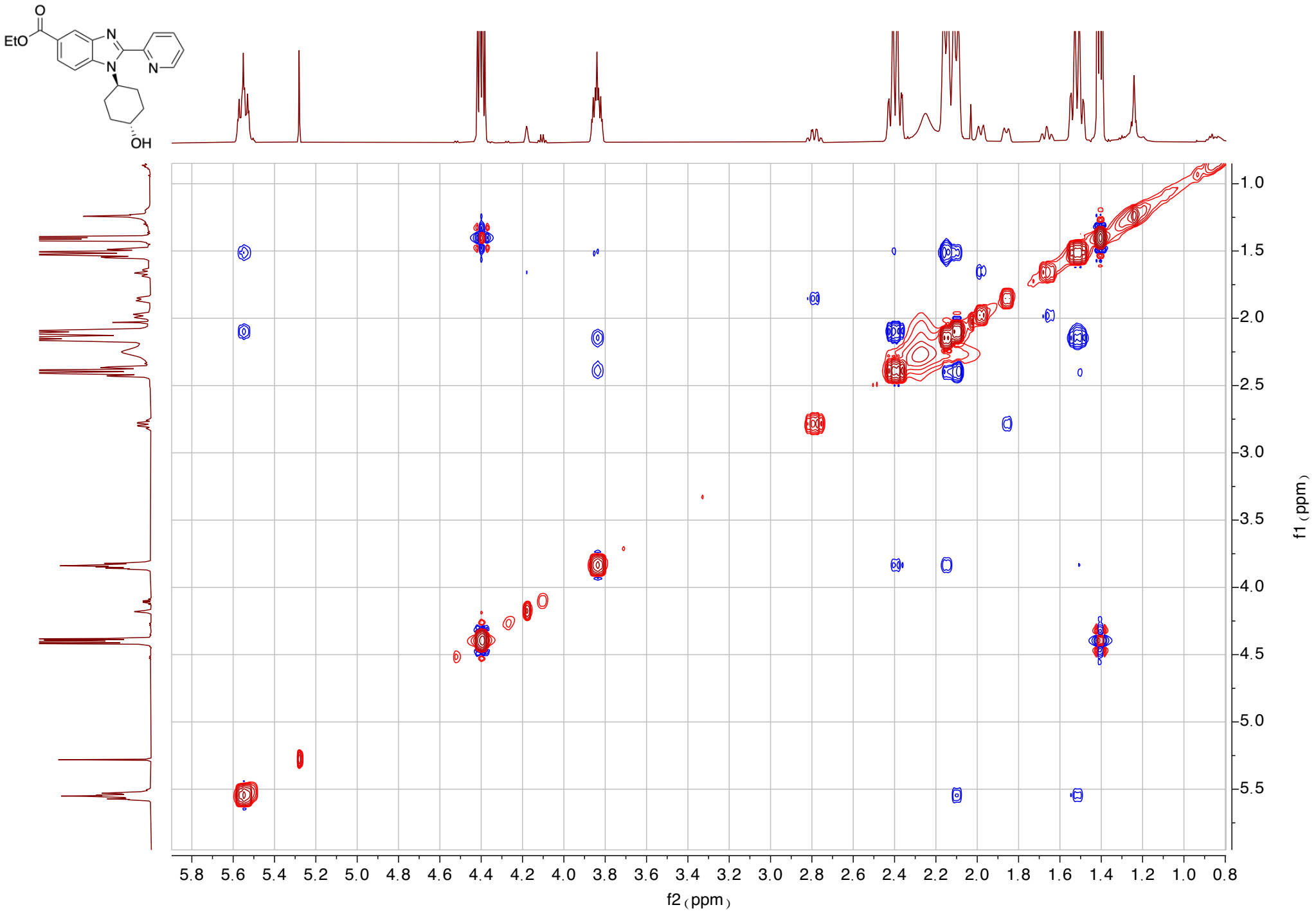


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2753.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

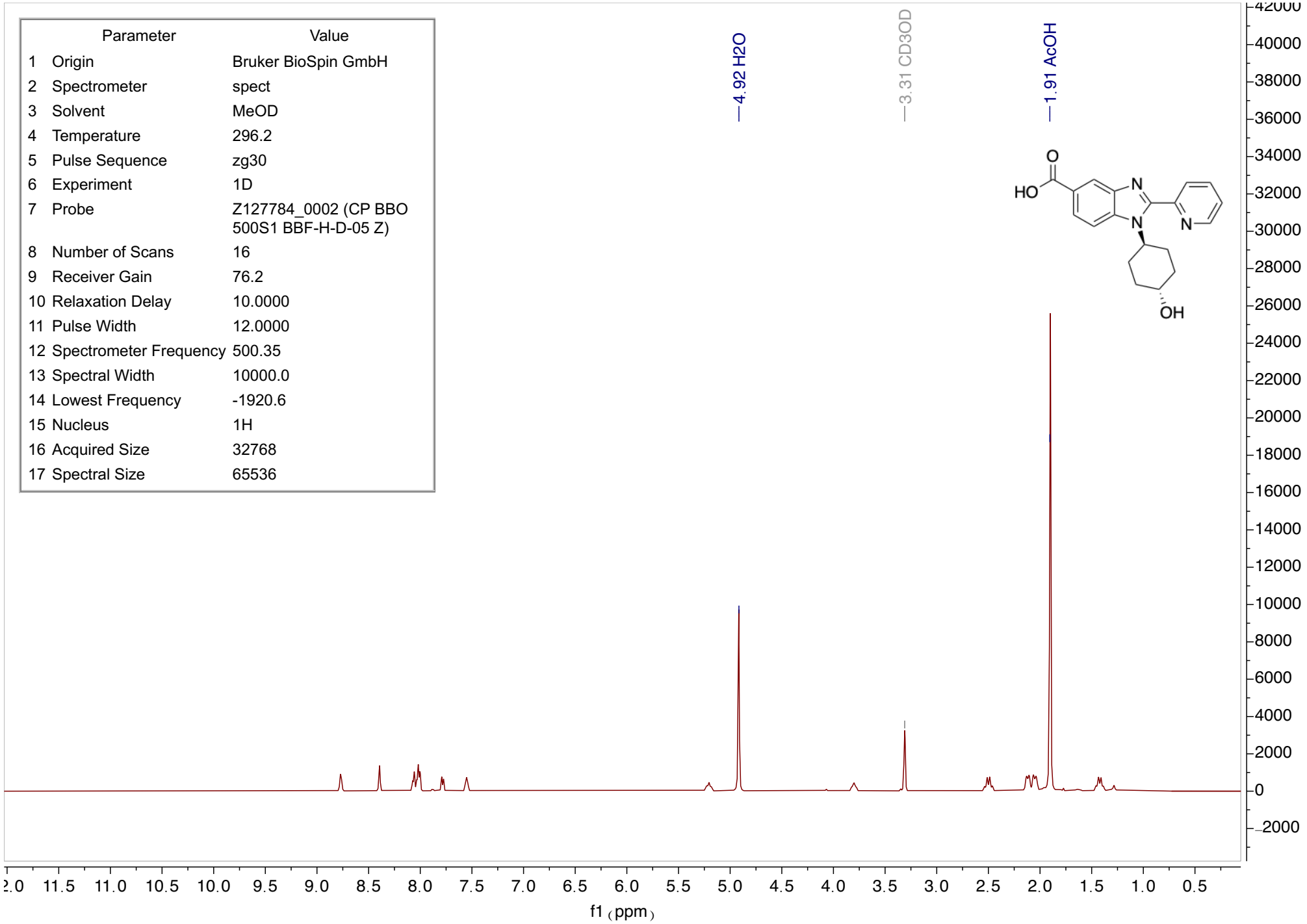


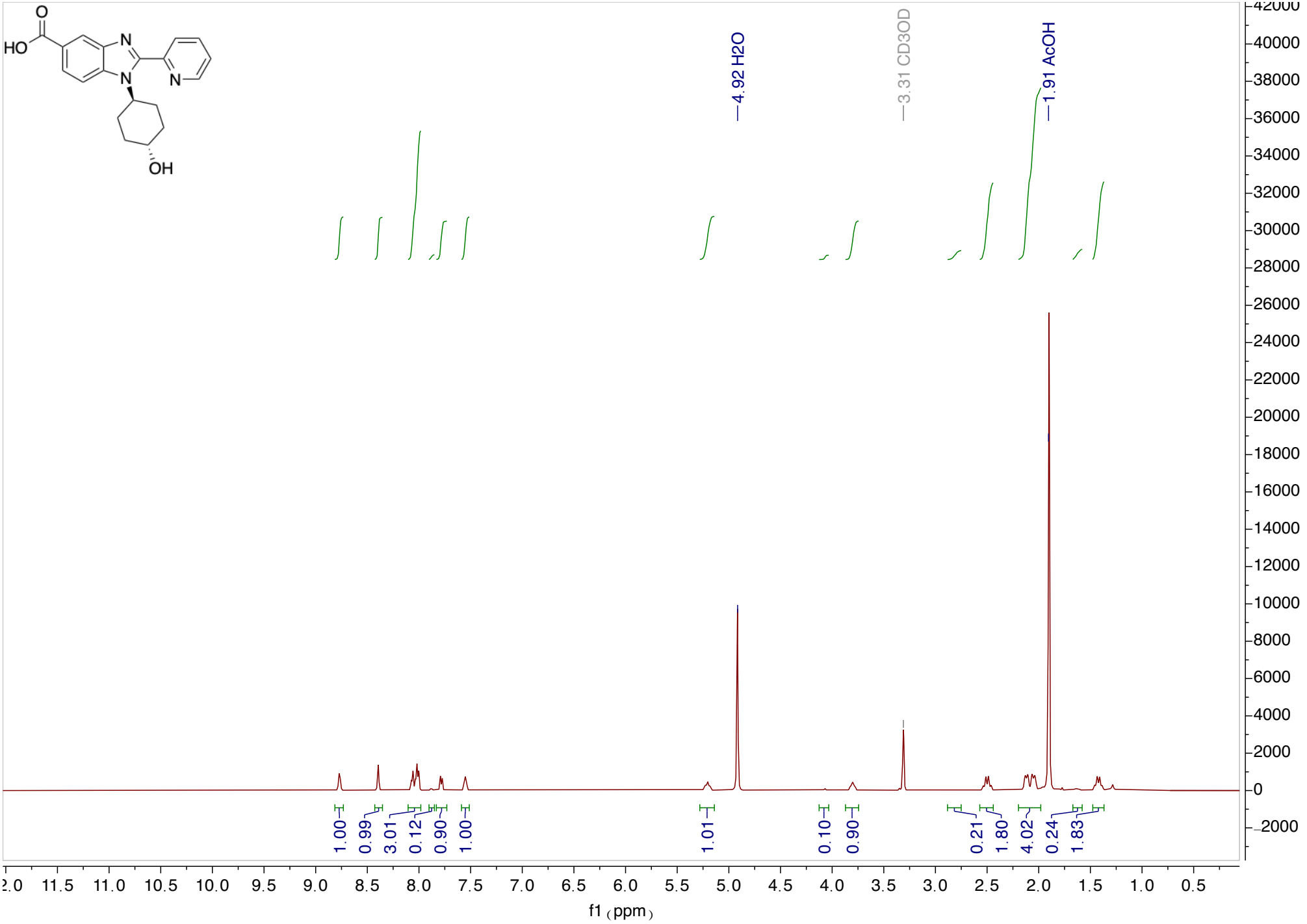
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-90.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

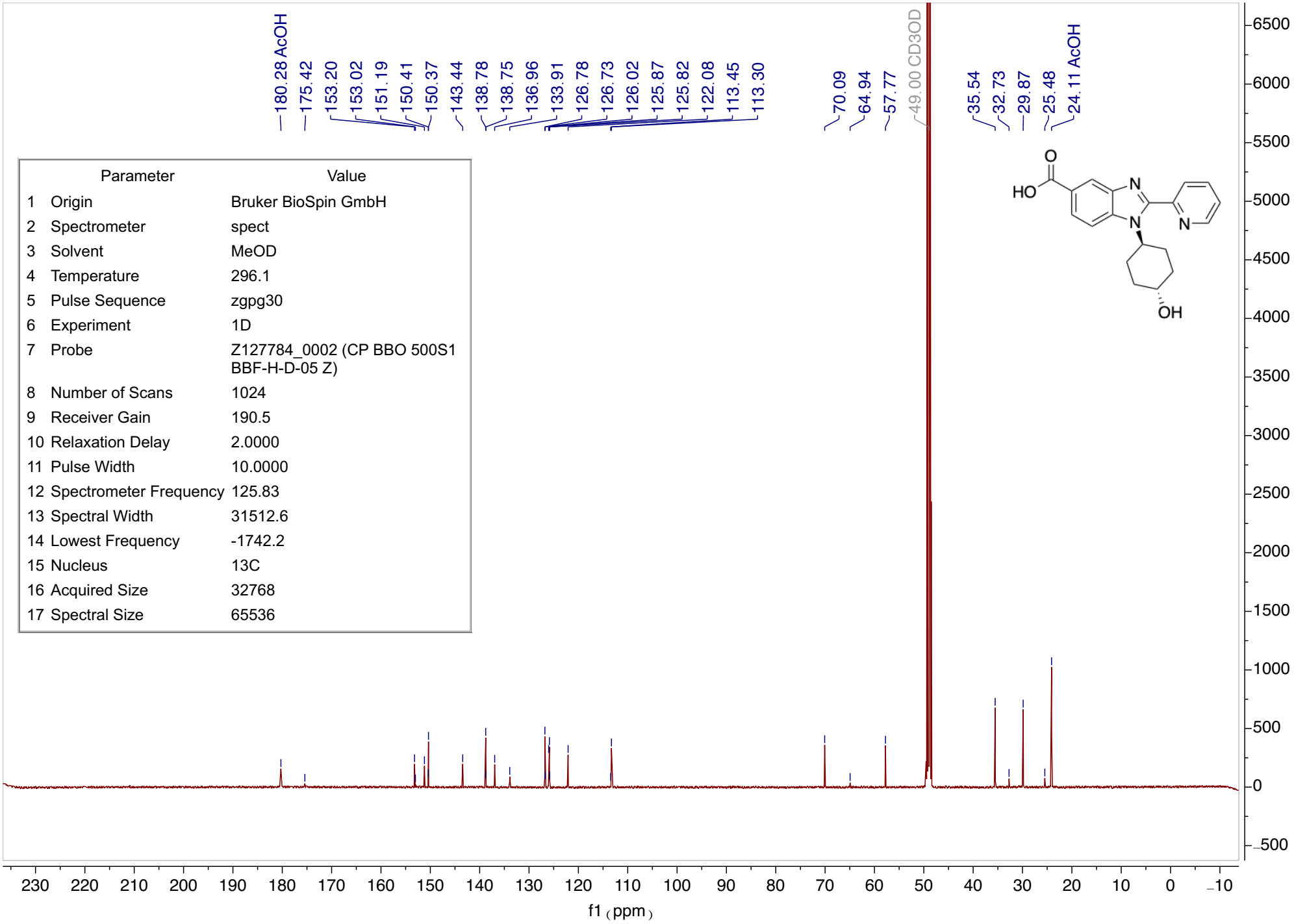

EtO
O
N
N
N
OH
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence noesygpphpp
6 Experiment NOESY
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 64.0
10 Relaxation Delay 2.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5882.4
14 Lowest Frequency -93.9
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)


O
EtO
N
N
N
OH
5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
f2 (ppm)
1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	76.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1920.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

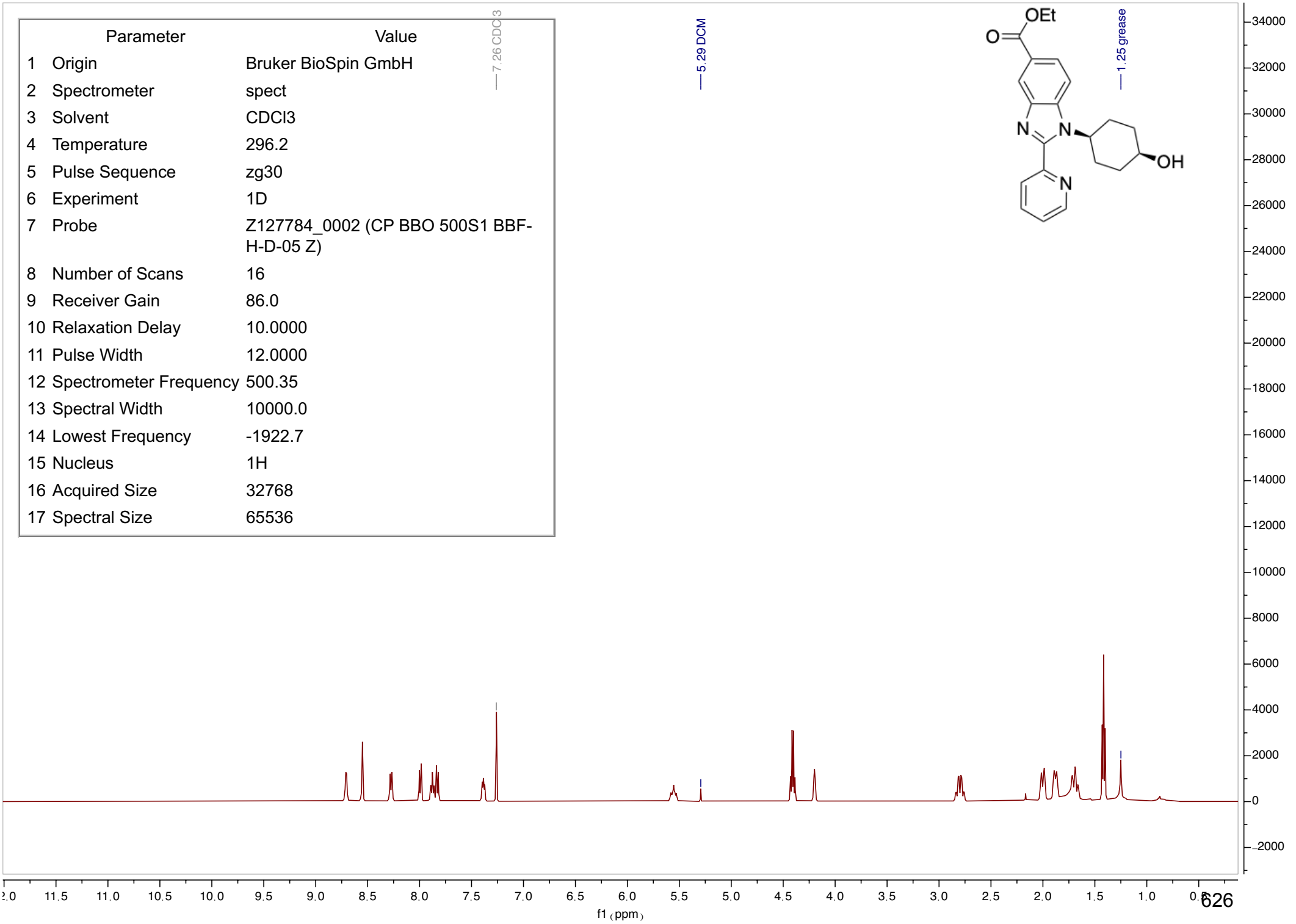


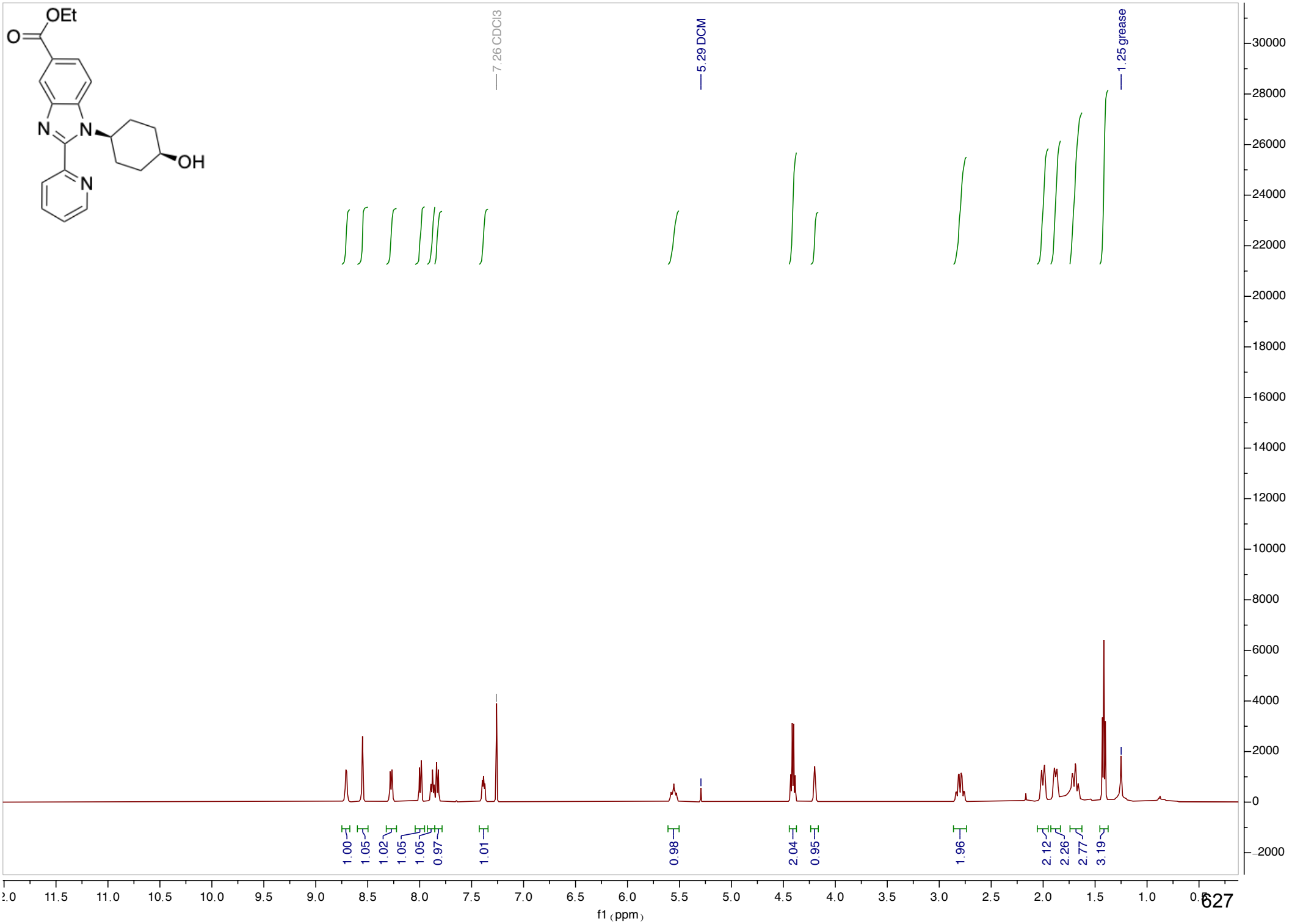

HO
O
N
N
N
OH
4.92 H2O
3.31 CD3OD
1.91 AcOH
1.00
0.99
3.01
0.12
0.90
1.00
1.01
0.10
0.90
0.21
1.80
4.02
0.24
1.83
f1 (ppm)

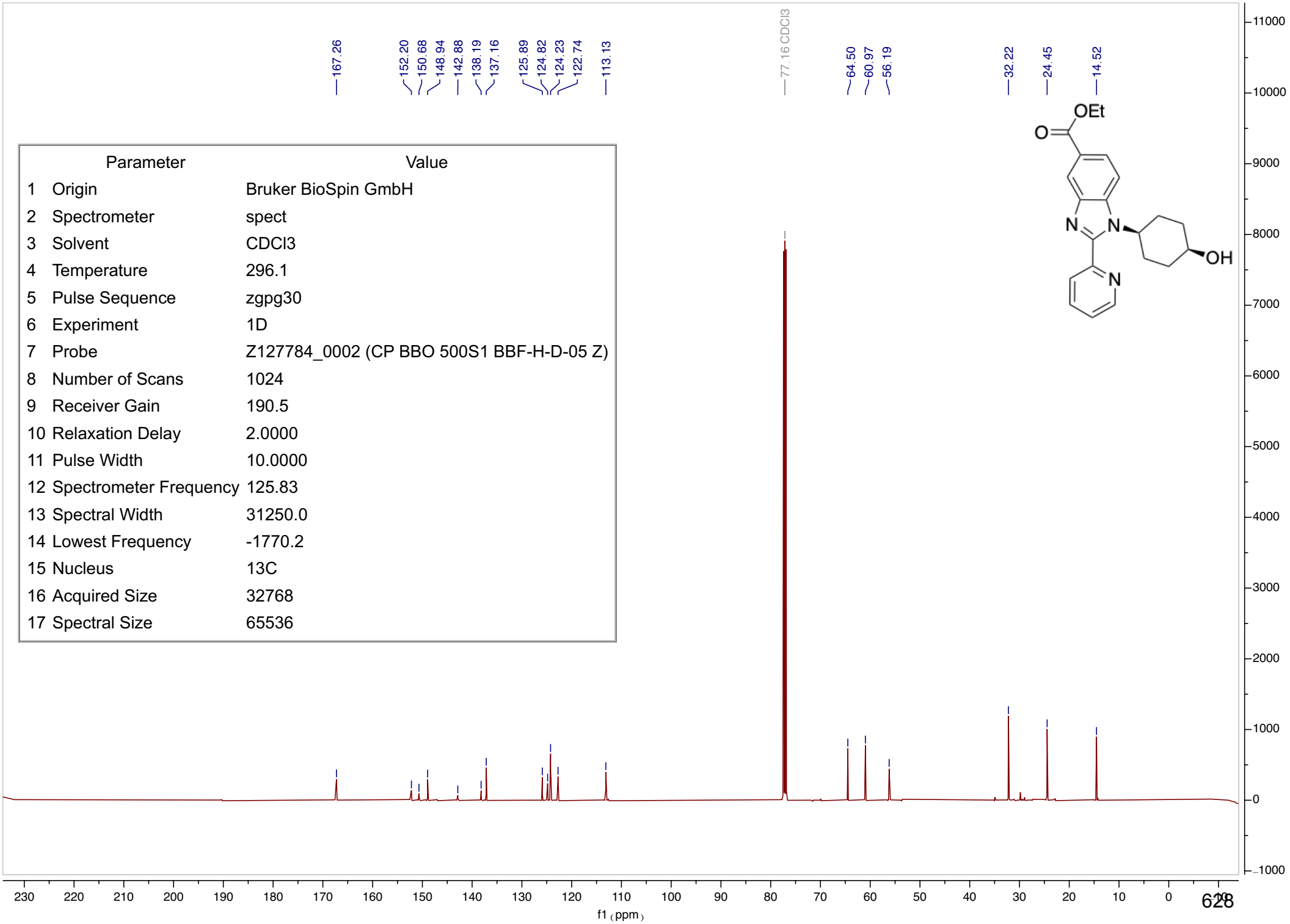


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1742.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

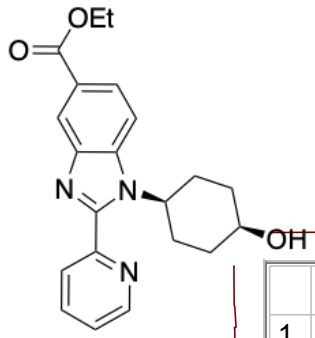
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



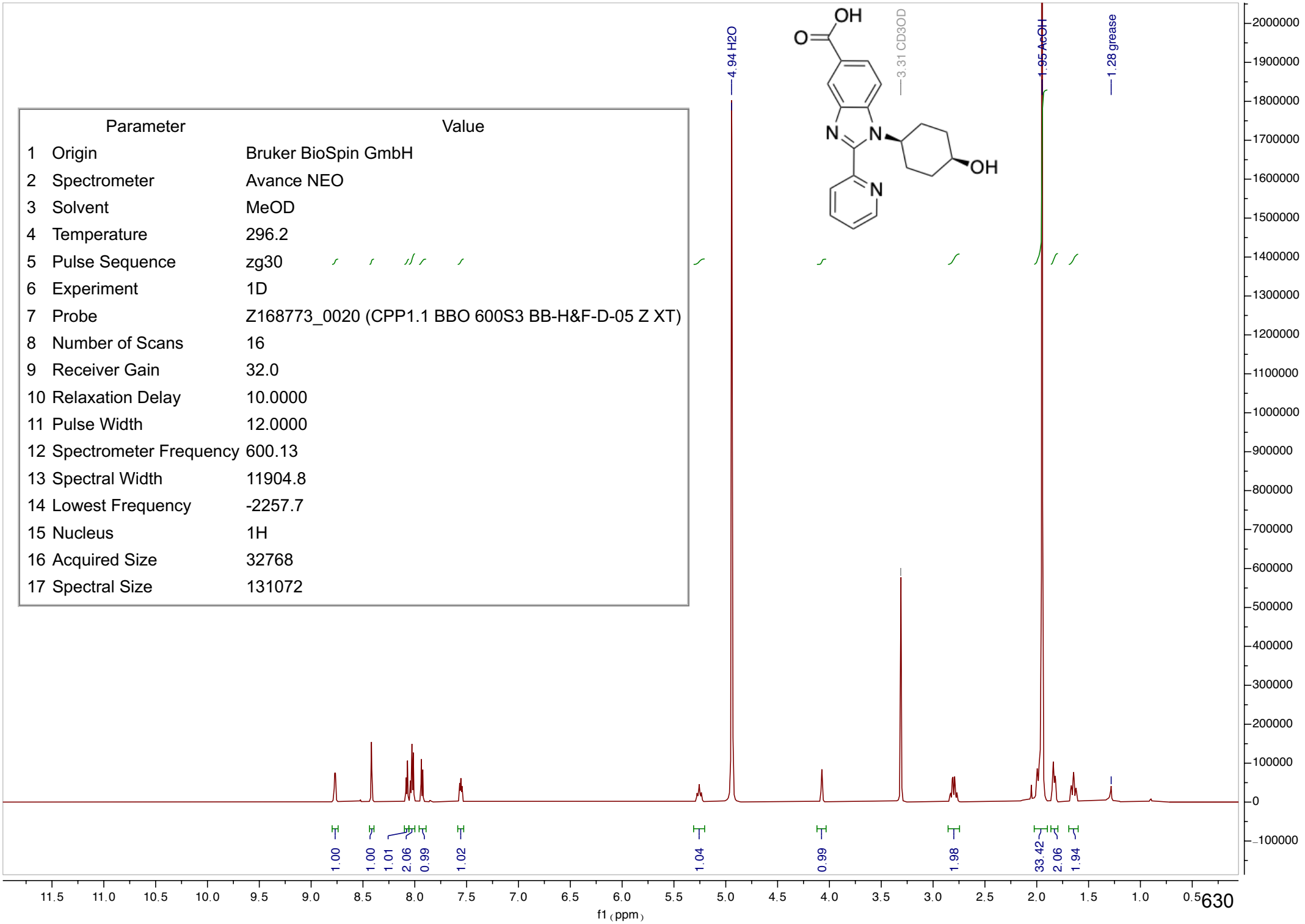

OEt
O
N
N
OH
N
7.26 CDCl3
5.29 DCM
1.25 grease
1.00
1.05
1.02
1.05
1.05
0.97
1.01
0.98
2.04
0.95
1.96
2.12
2.26
2.77
3.19
f1 (ppm)



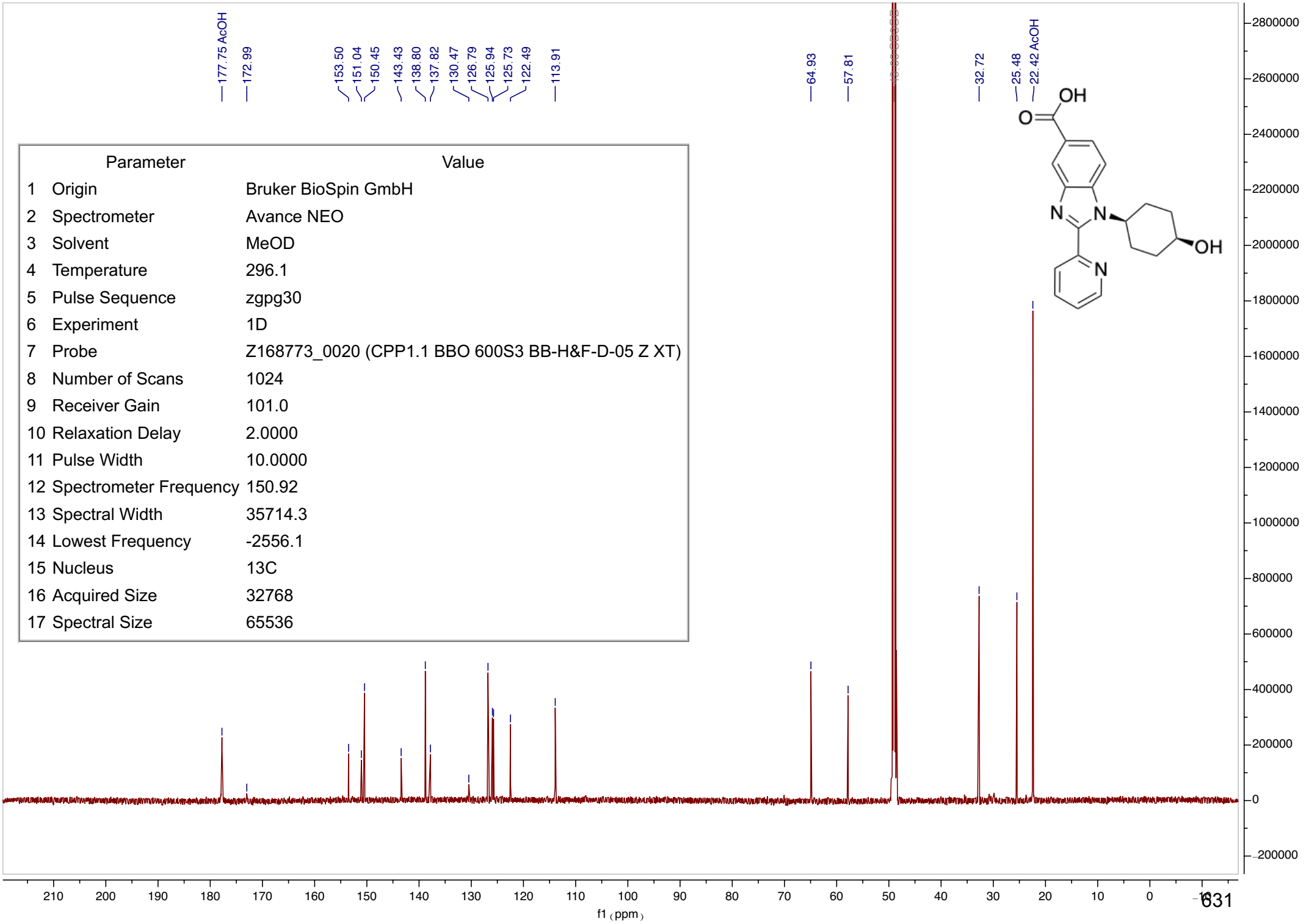
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31250.0
14	Lowest Frequency	-1770.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



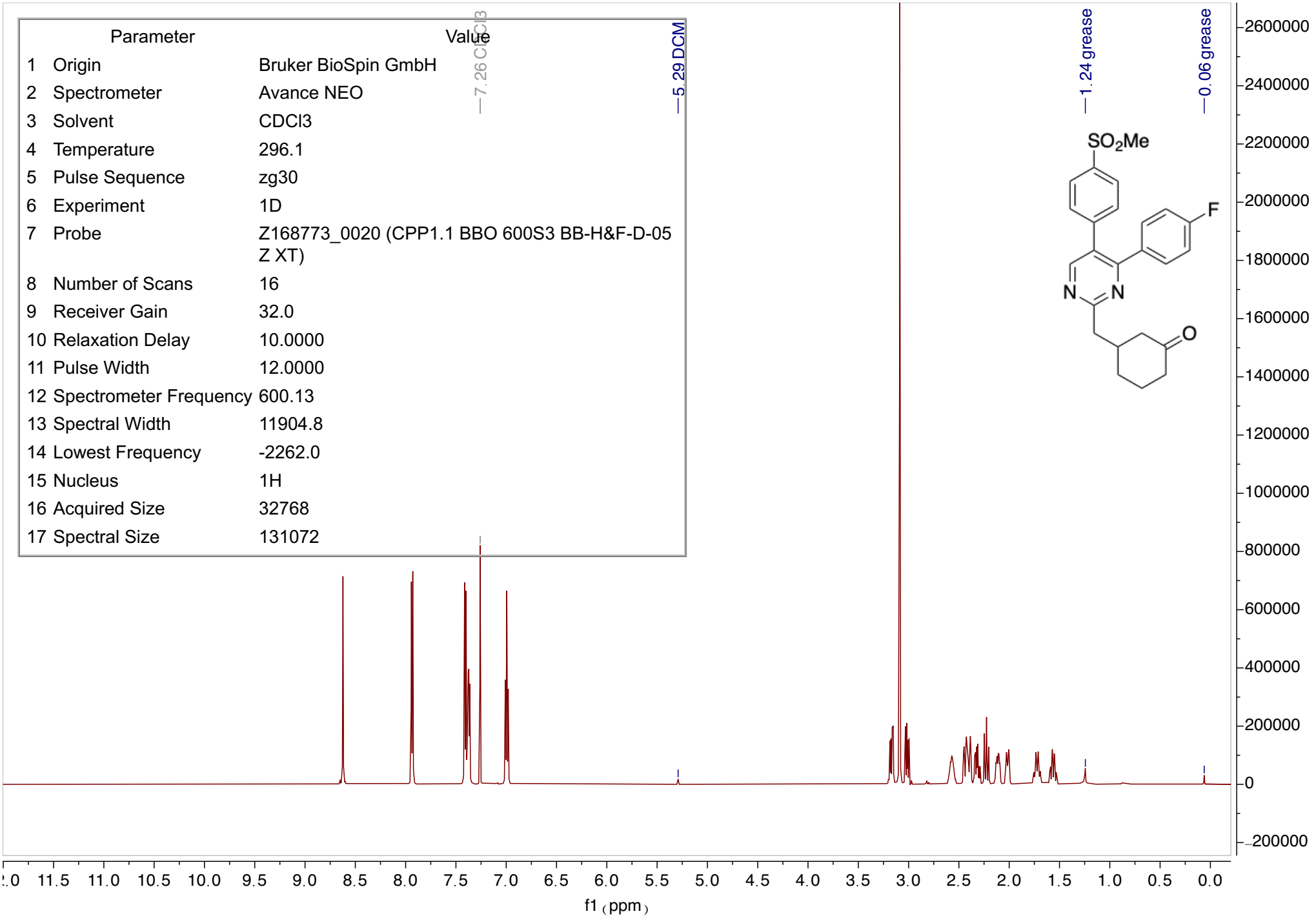
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	5000.0
14	Lowest Frequency	-129.1
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

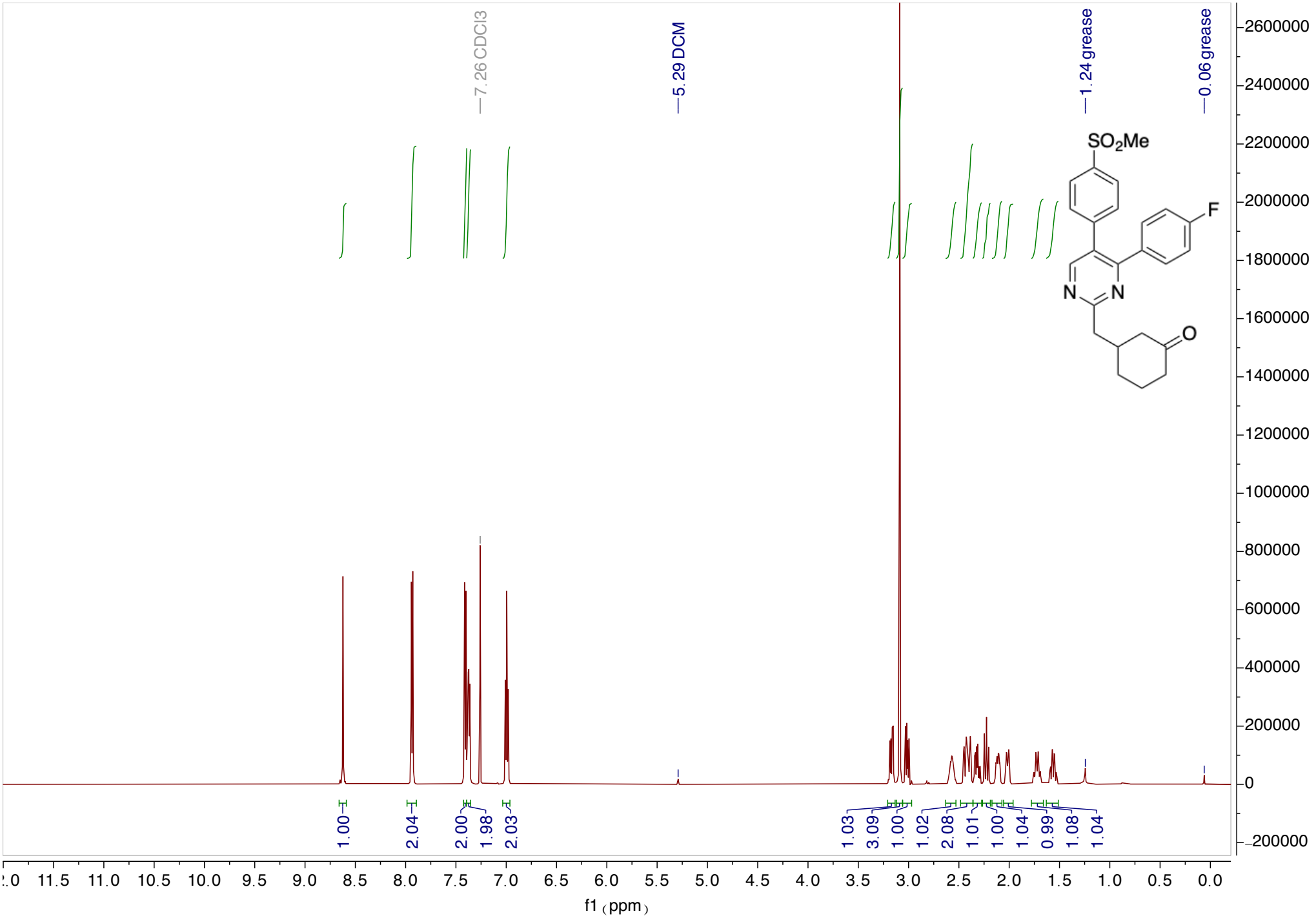


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2257.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

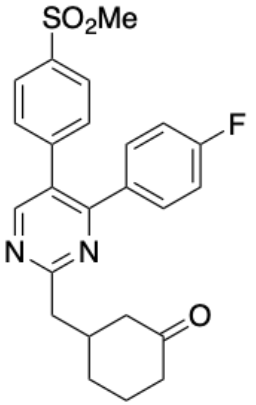


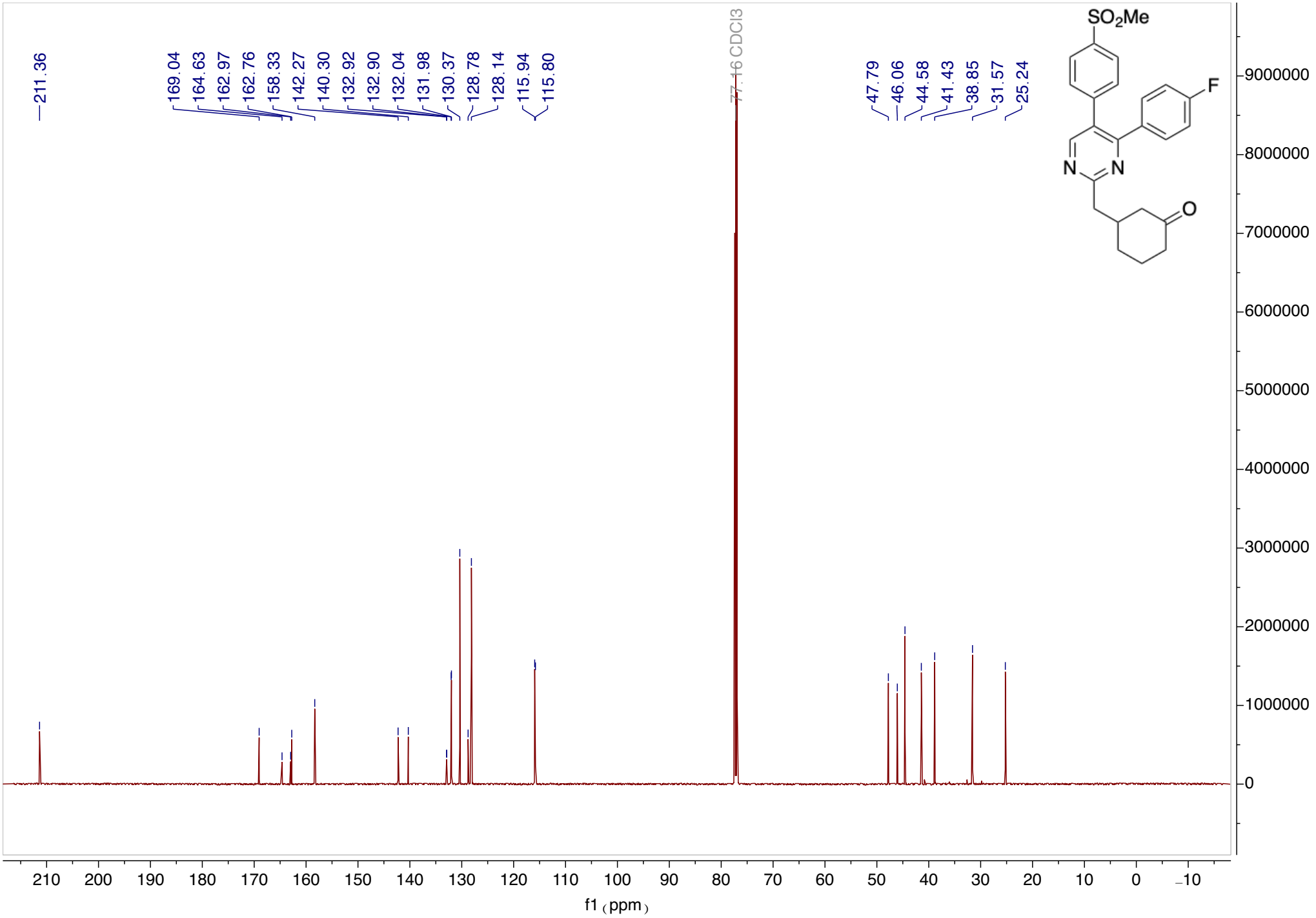
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	MeOD
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2556.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 32.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2262.0
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.26 CHCl3
5.29 DCM
1.24 grease
0.06 grease
SO2Me
F
N
N
O
f1 (ppm)

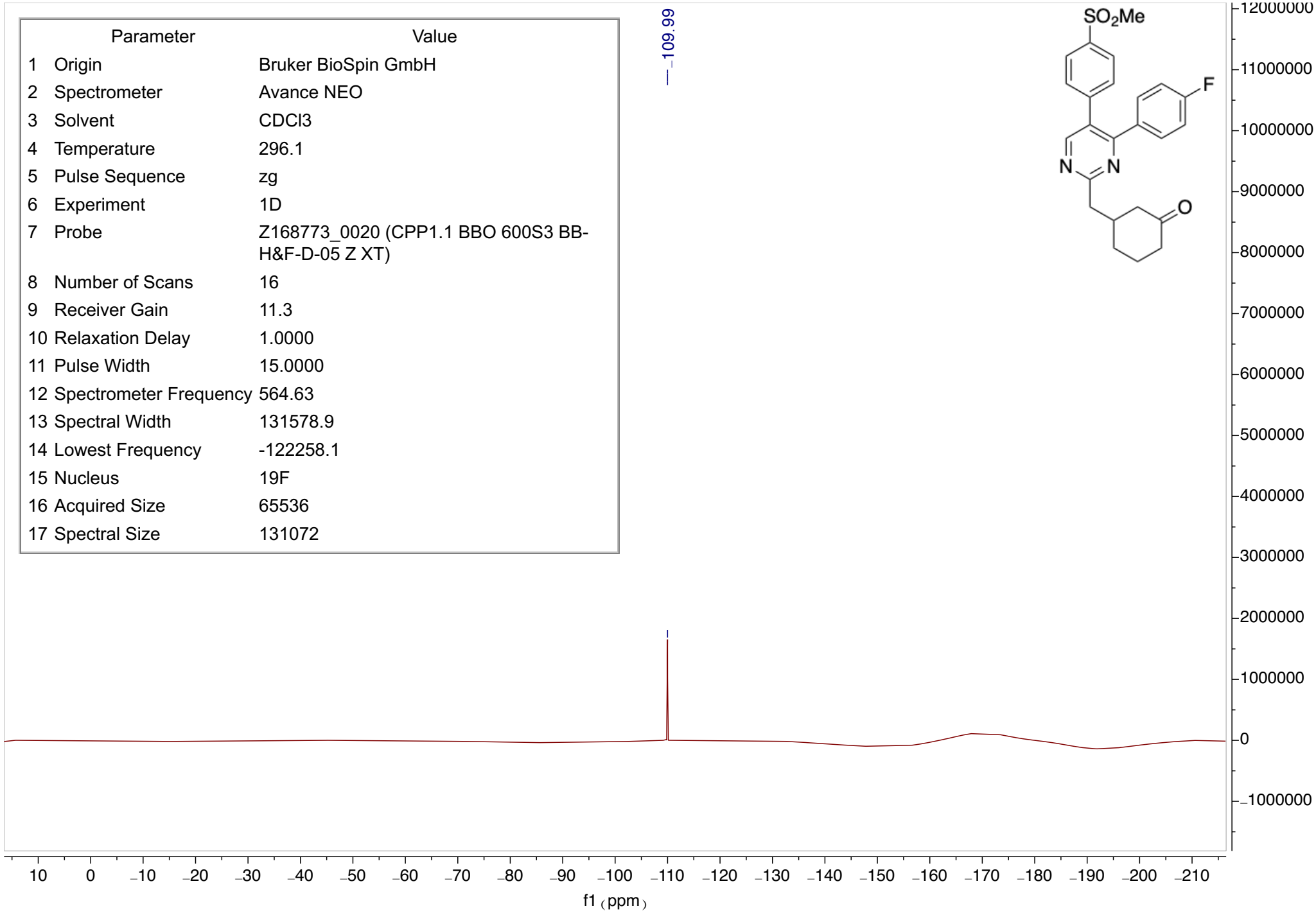

7.26 CDCl3
5.29 DCM
1.24 grease
0.06 grease
SO2Me
F
N
N
O
1.00
2.04
2.00
1.98
2.03
1.03
3.09
1.00
1.02
2.08
1.01
1.00
1.04
0.99
1.08
1.04
f1 (ppm)

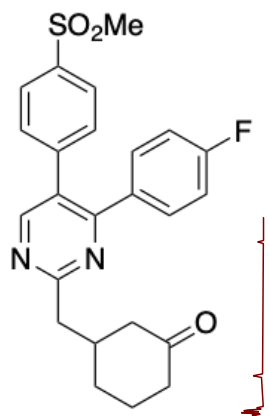
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2750.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



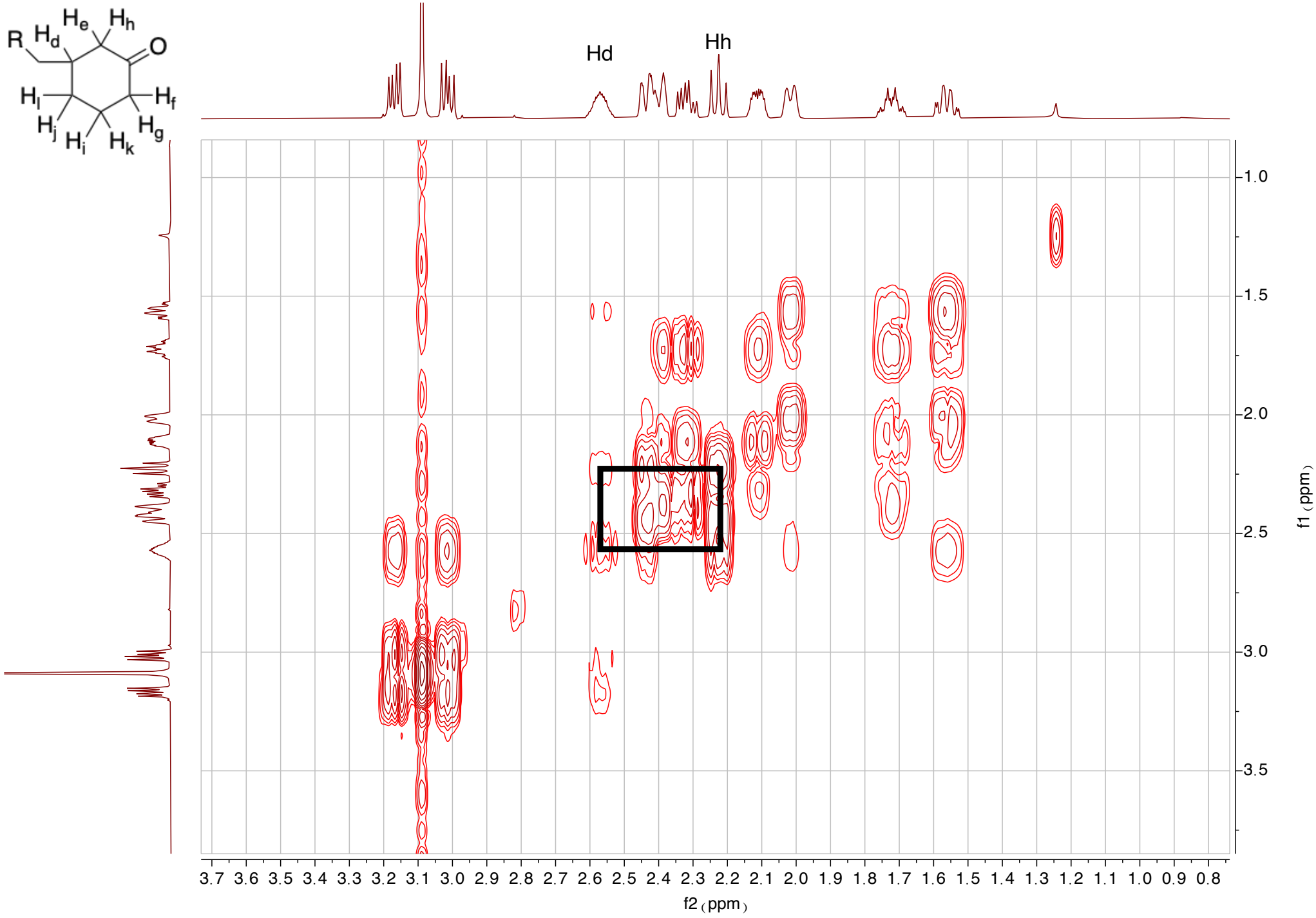

211.36
169.04
164.63
162.97
162.76
158.33
142.27
140.30
132.92
132.90
132.04
131.98
130.37
128.78
128.14
115.94
115.80
77.16 CDCl3
47.79
46.06
44.58
41.43
38.85
31.57
25.24
SO2Me
F
N
N
O
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

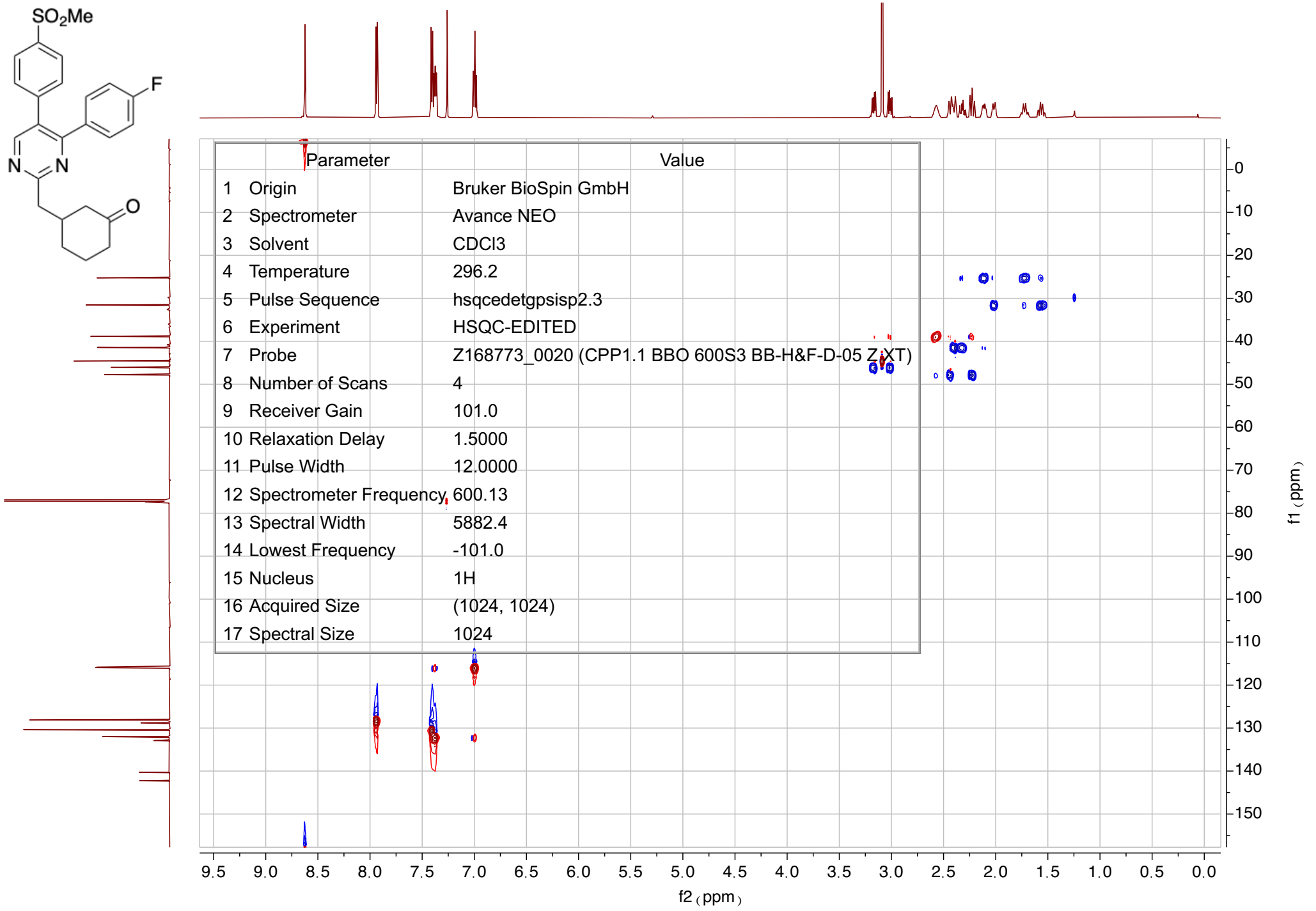
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	11.3
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

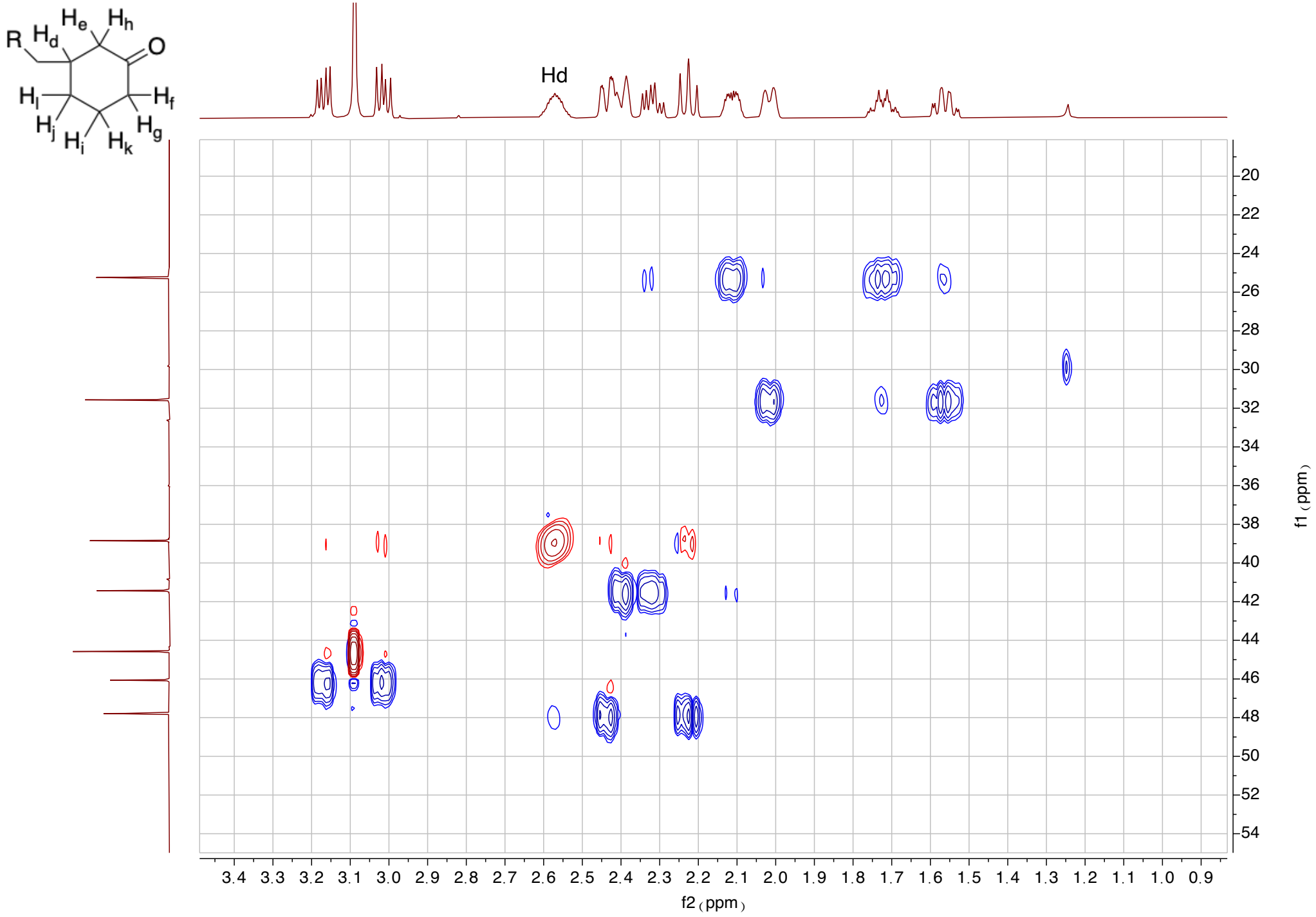


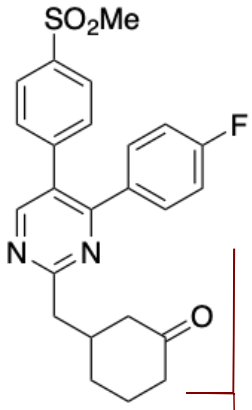


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	2
9	Receiver Gain	101.0
10	Relaxation Delay	1.4570
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-104.1
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

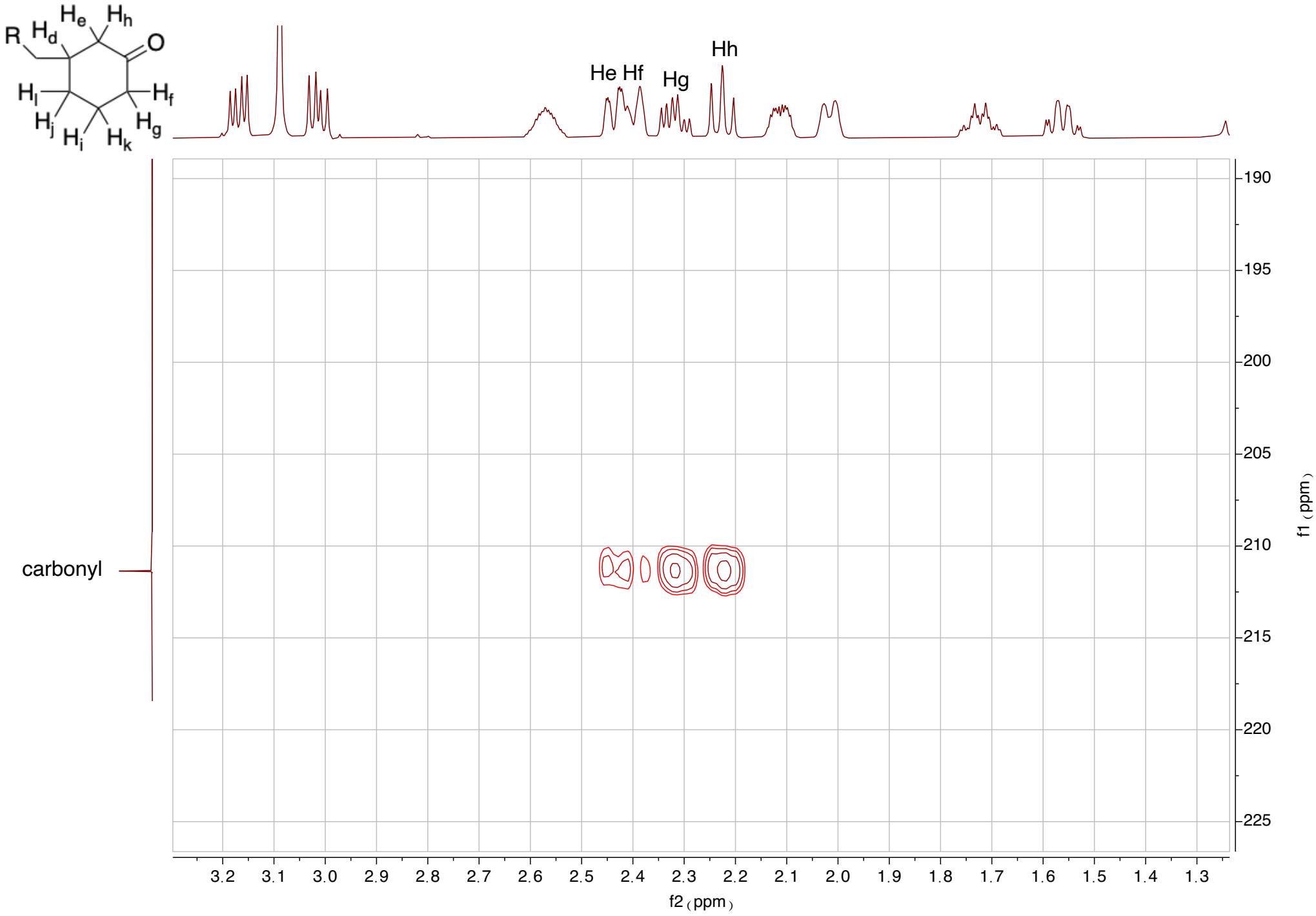

R
Hd
He
Hh
O
Hl
Hf
Hj
Hi
Hk
Hg
Hd
Hh
1.0
1.5
2.0
2.5
3.0
3.5
f1 (ppm)
3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8
f2 (ppm)


SO2Me
F
N
N
O
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hsqcedetgpsisp2.3
6 Experiment HSQC-EDITED
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 4
9 Receiver Gain 101.0
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5882.4
14 Lowest Frequency -101.0
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)

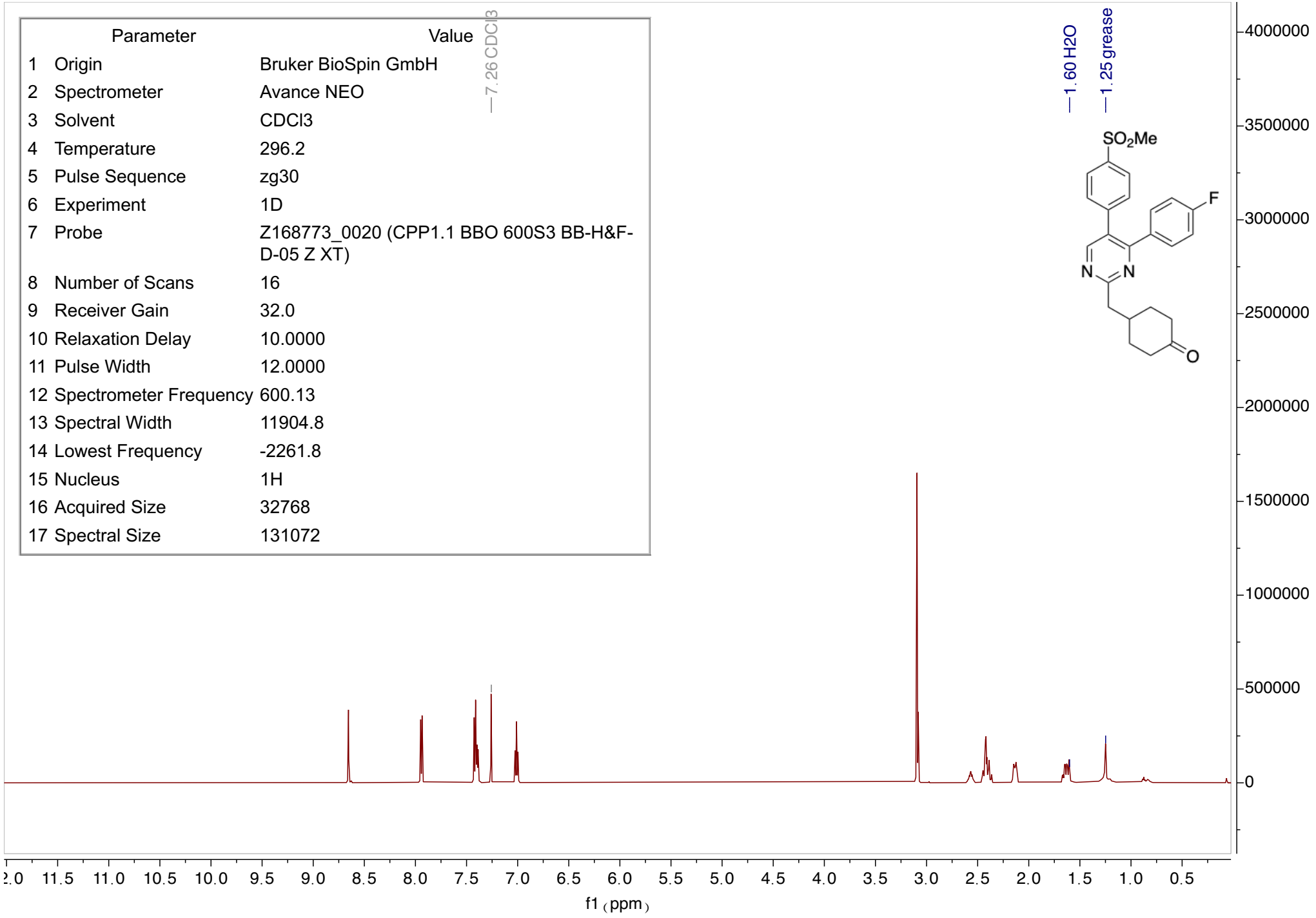

R
Hd
He
Hh
O
Hf
Hg
Hk
Hi
Hj
Hl
Hd
f2 (ppm)
f1 (ppm)
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9
20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54

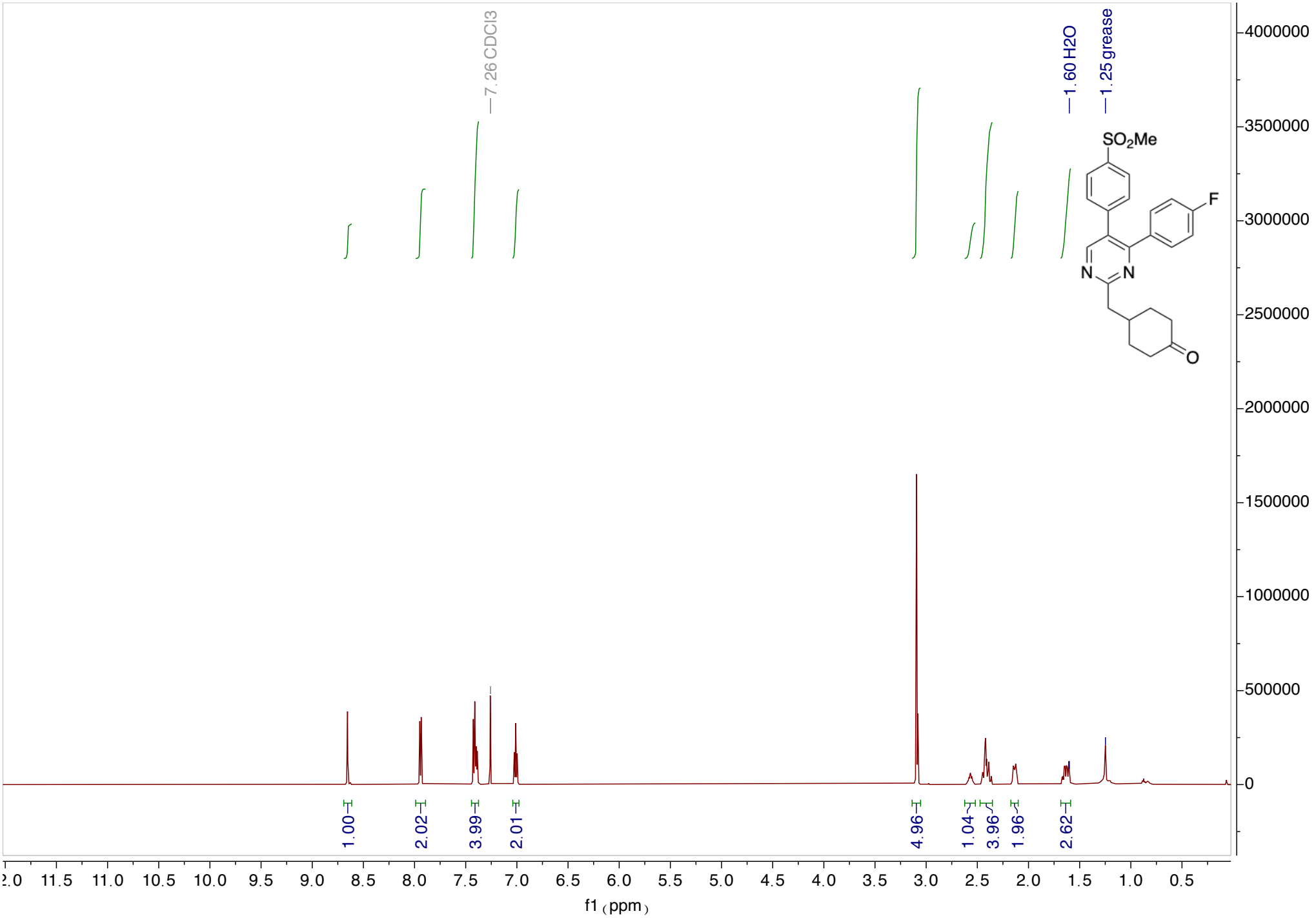


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgpndqf
6	Experiment	HMBC
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	8
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-105.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

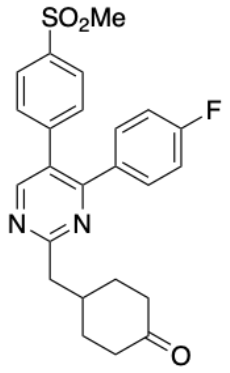

R
Hd
He
Hh
O
Hl
Hf
Hj
Hi
Hk
Hg
He Hf
Hg
Hh
carbonyl
190
195
200
205
210
215
220
225
f1 (ppm)
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
f2 (ppm)

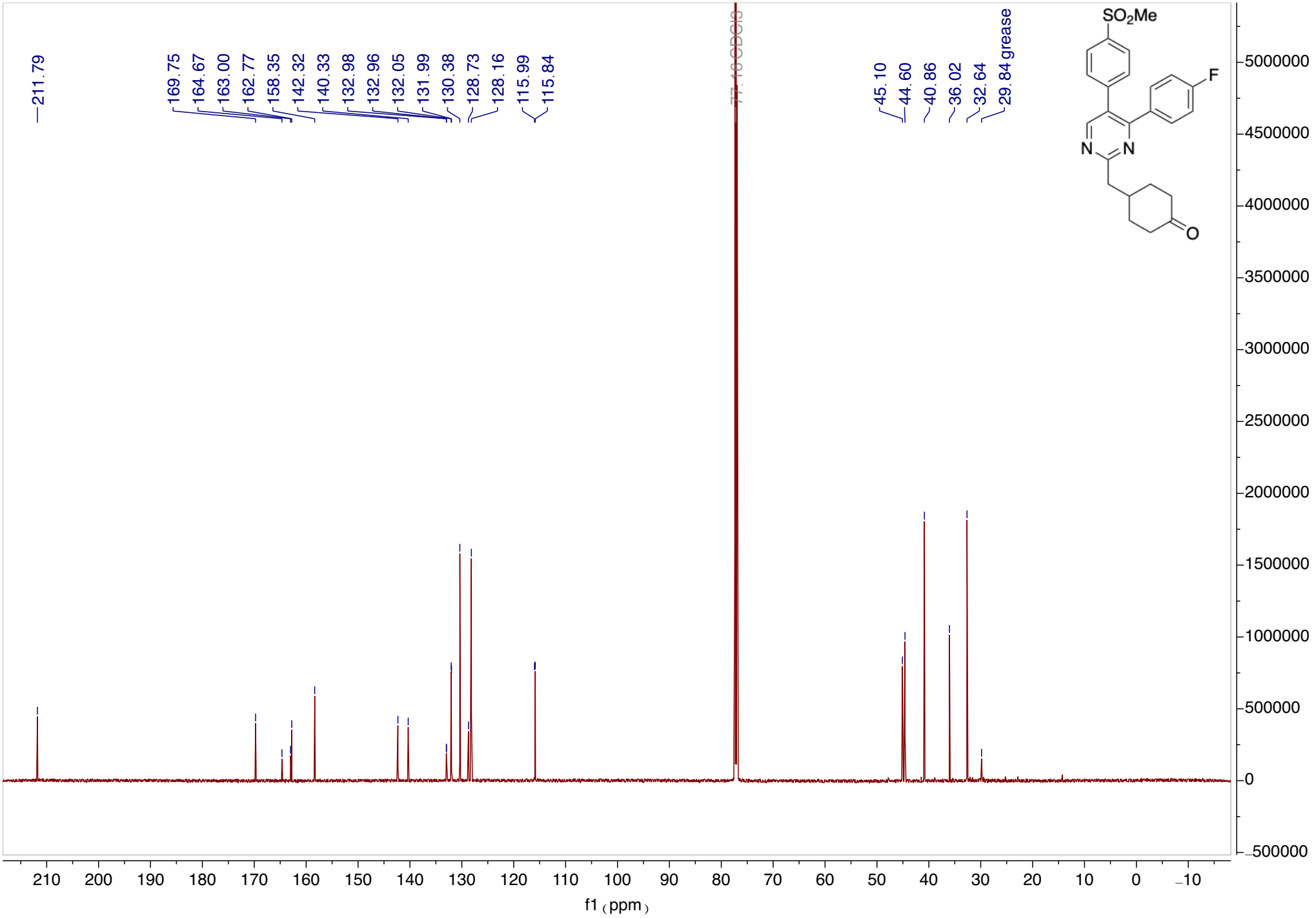
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2261.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



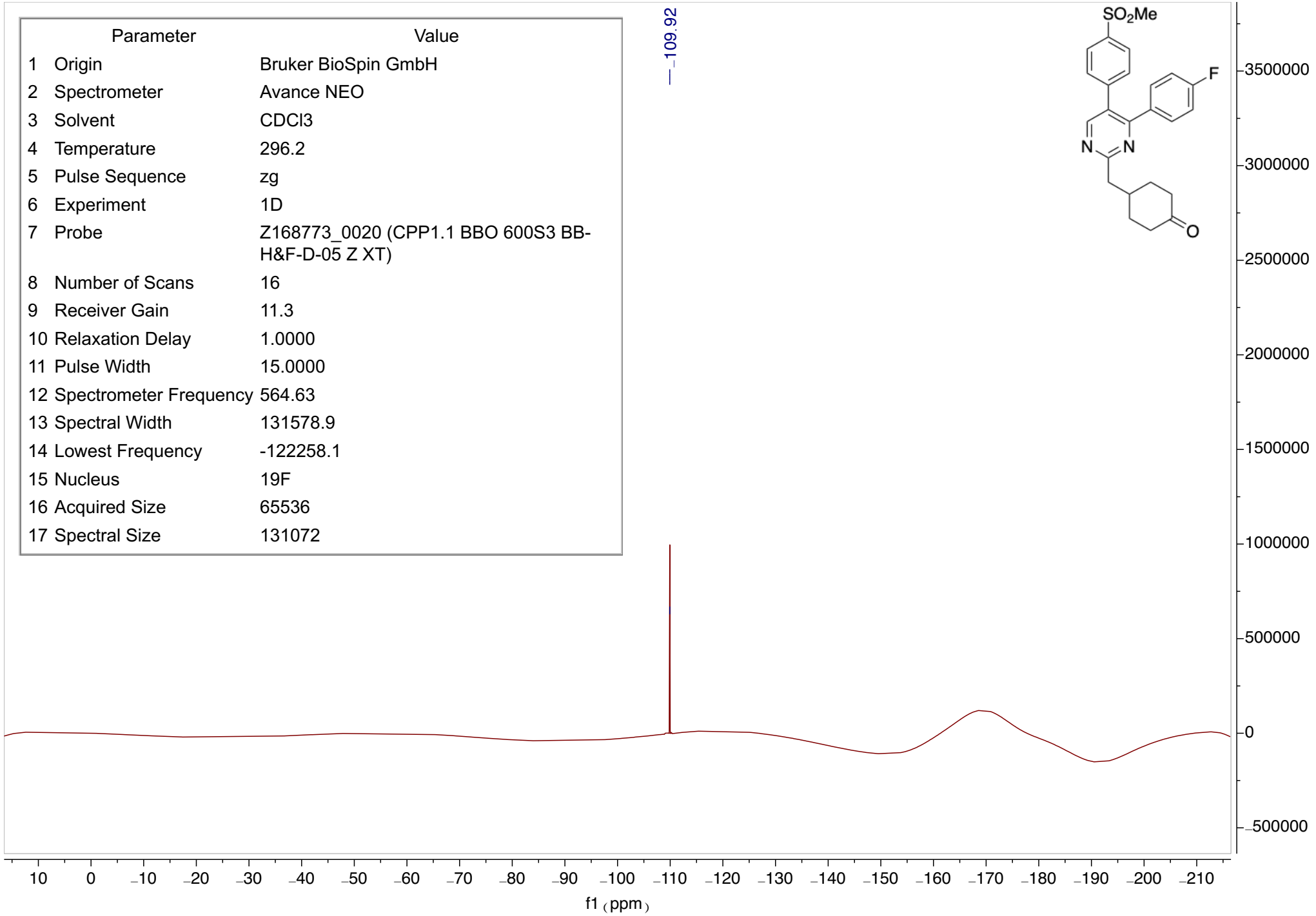

7.26 CDCl3
1.60 H2O
1.25 grease
SO2Me
F
N
N
O
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
1.00
2.02
3.99
2.01
4.96
1.04
3.96
1.96
2.62
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2748.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

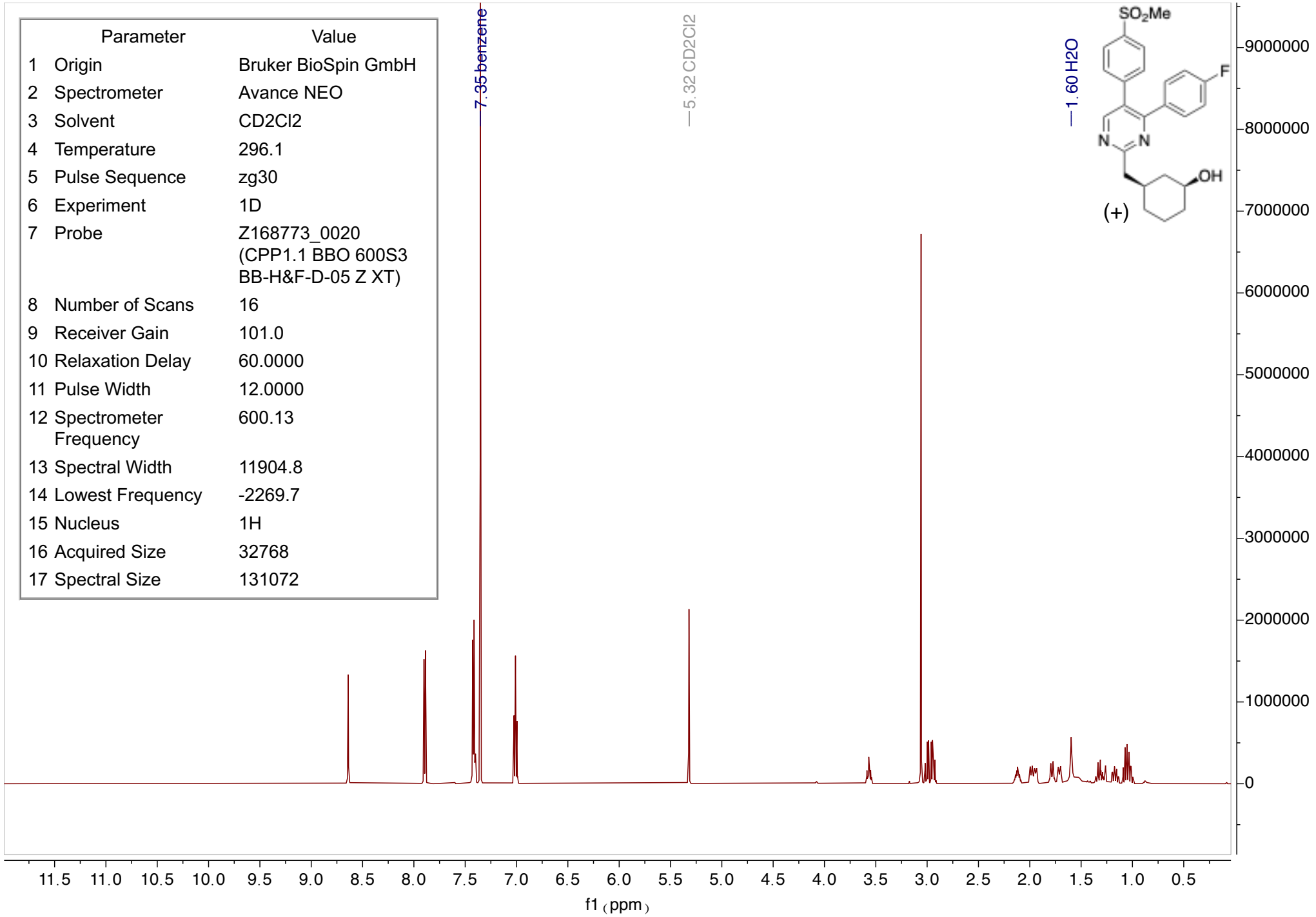


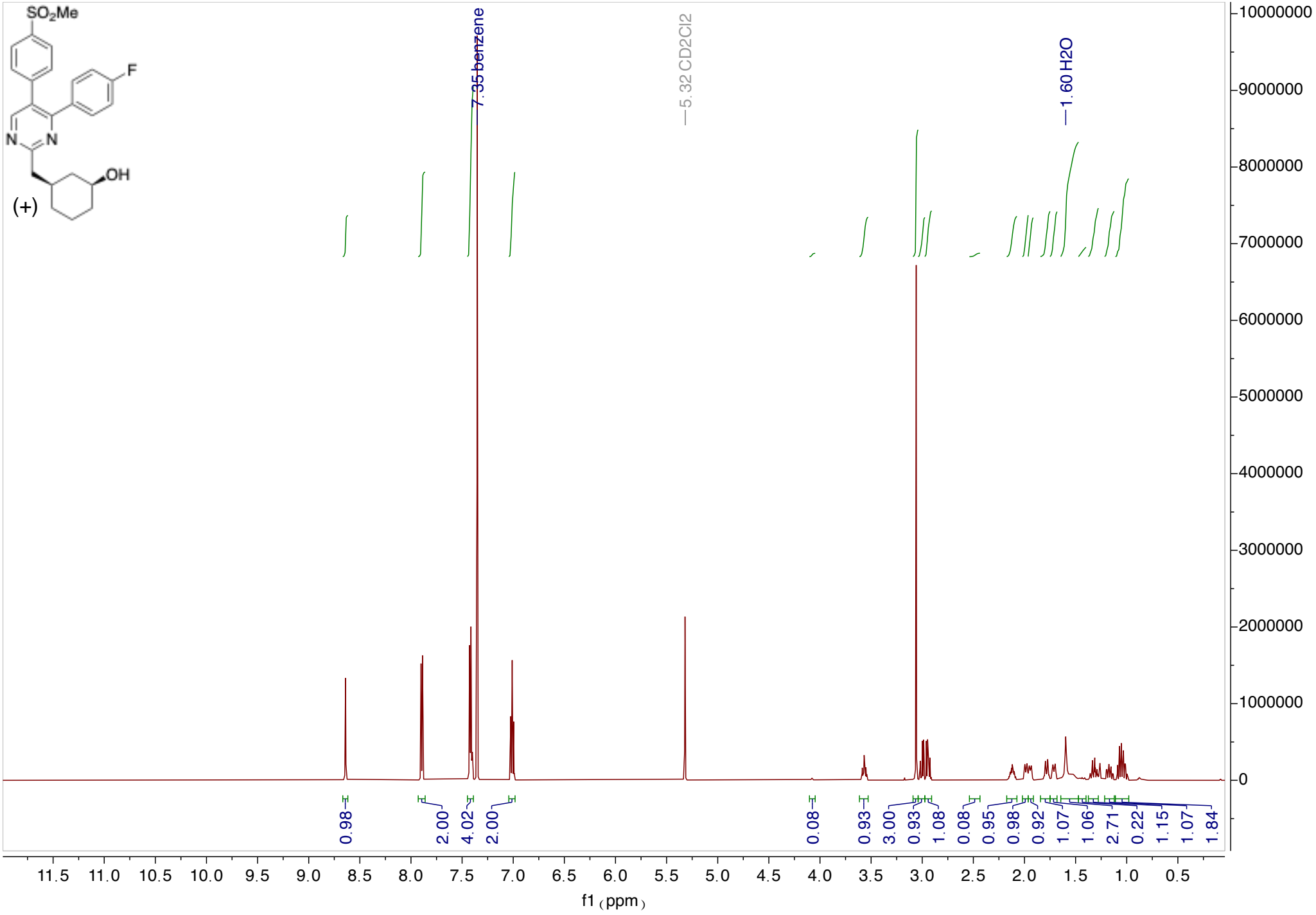

211.79
169.75
164.67
163.00
162.77
158.35
142.32
140.33
132.98
132.96
132.05
131.99
130.38
128.73
128.16
115.99
115.84
77.16 CDCl3
45.10
44.60
40.86
36.02
32.64
29.84 grease
SO2Me
F
N
N
O
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	11.3
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

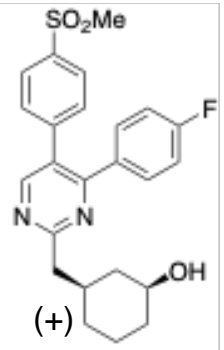


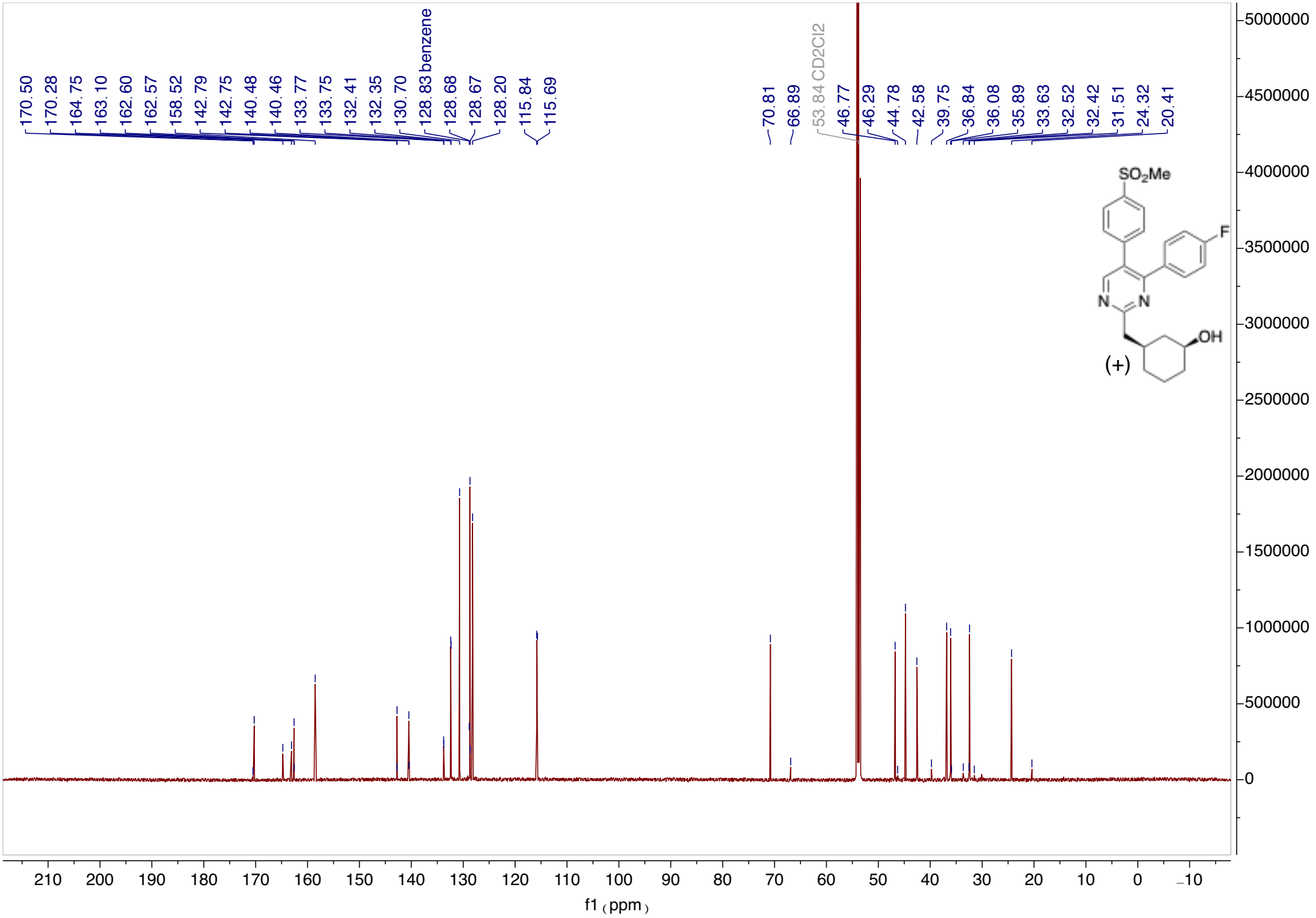
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CD2Cl2
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	101.0
10	Relaxation Delay	60.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2269.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



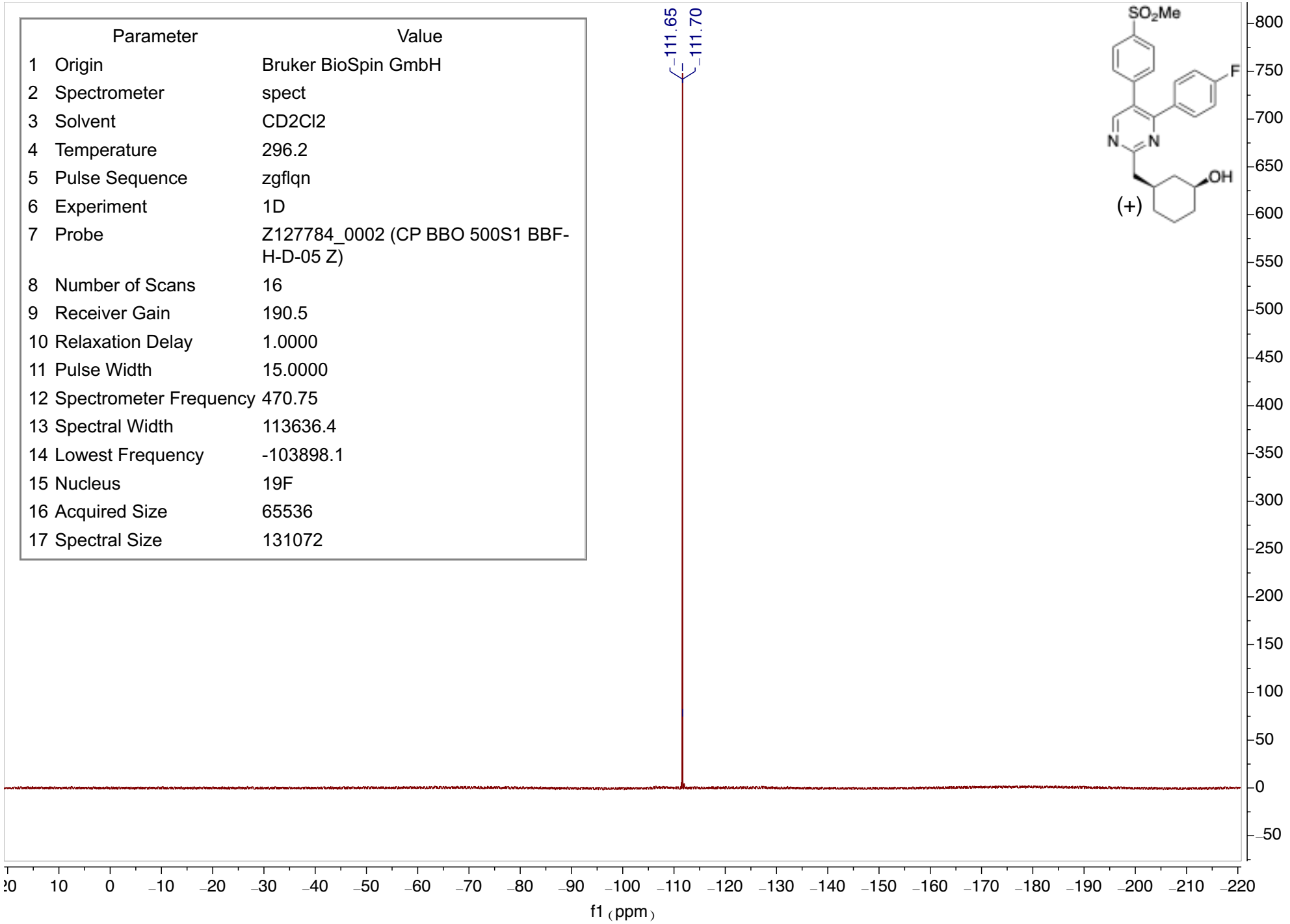

SO2Me
F
N
N
OH
(+)
7.35 benzene
5.32 CD2Cl2
1.60 H2O
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
0.98
2.00
4.02
2.00
0.08
0.93
3.00
0.93
1.08
0.08
0.95
0.98
0.92
1.07
1.06
2.71
0.22
1.15
1.07
1.84
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

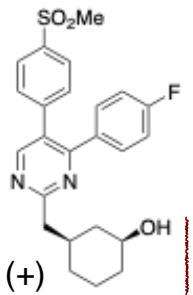
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CD2Cl2
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2708.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



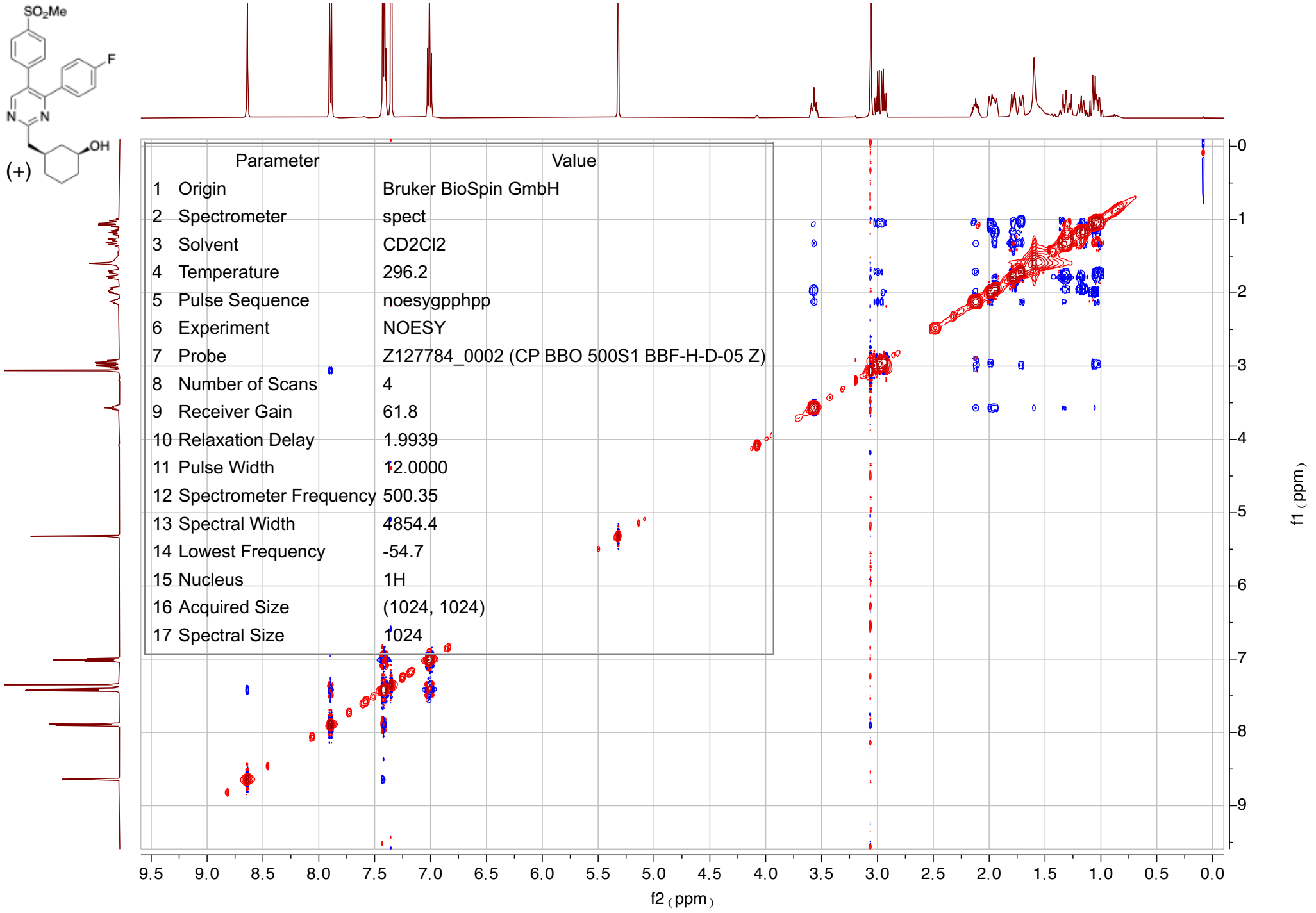

170.50
170.28
164.75
163.10
162.60
162.57
158.52
142.79
142.75
140.48
140.46
133.77
133.75
132.41
132.35
130.70
128.83 benzene
128.68
128.67
128.20
115.84
115.69
70.81
66.89
53.84 CD2Cl2
46.77
46.29
44.78
42.58
39.75
36.84
36.08
35.89
33.63
32.52
32.42
31.51
24.32
20.41
SO2Me
F
N
N
OH
(+)
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
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)

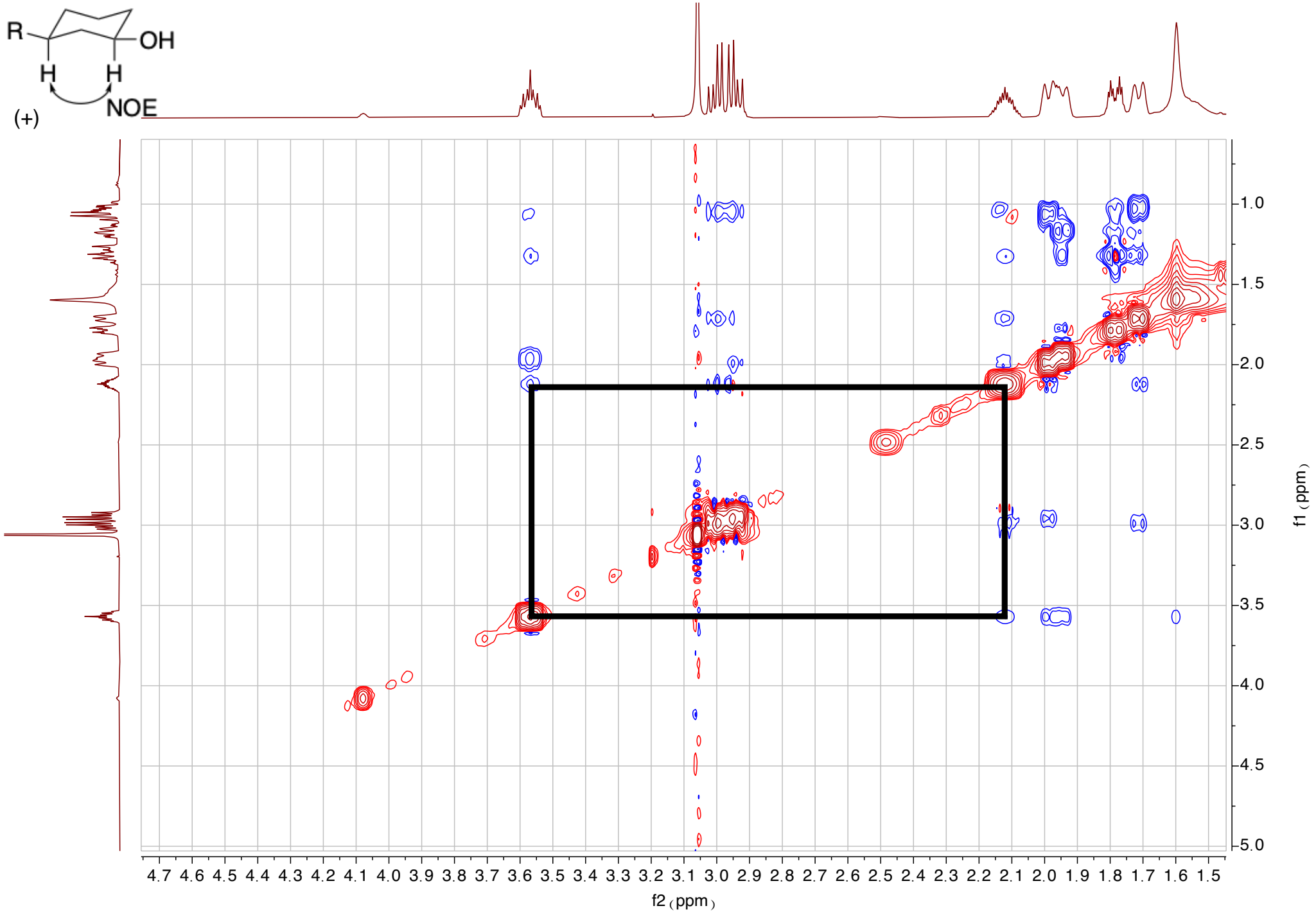
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CD2Cl2
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

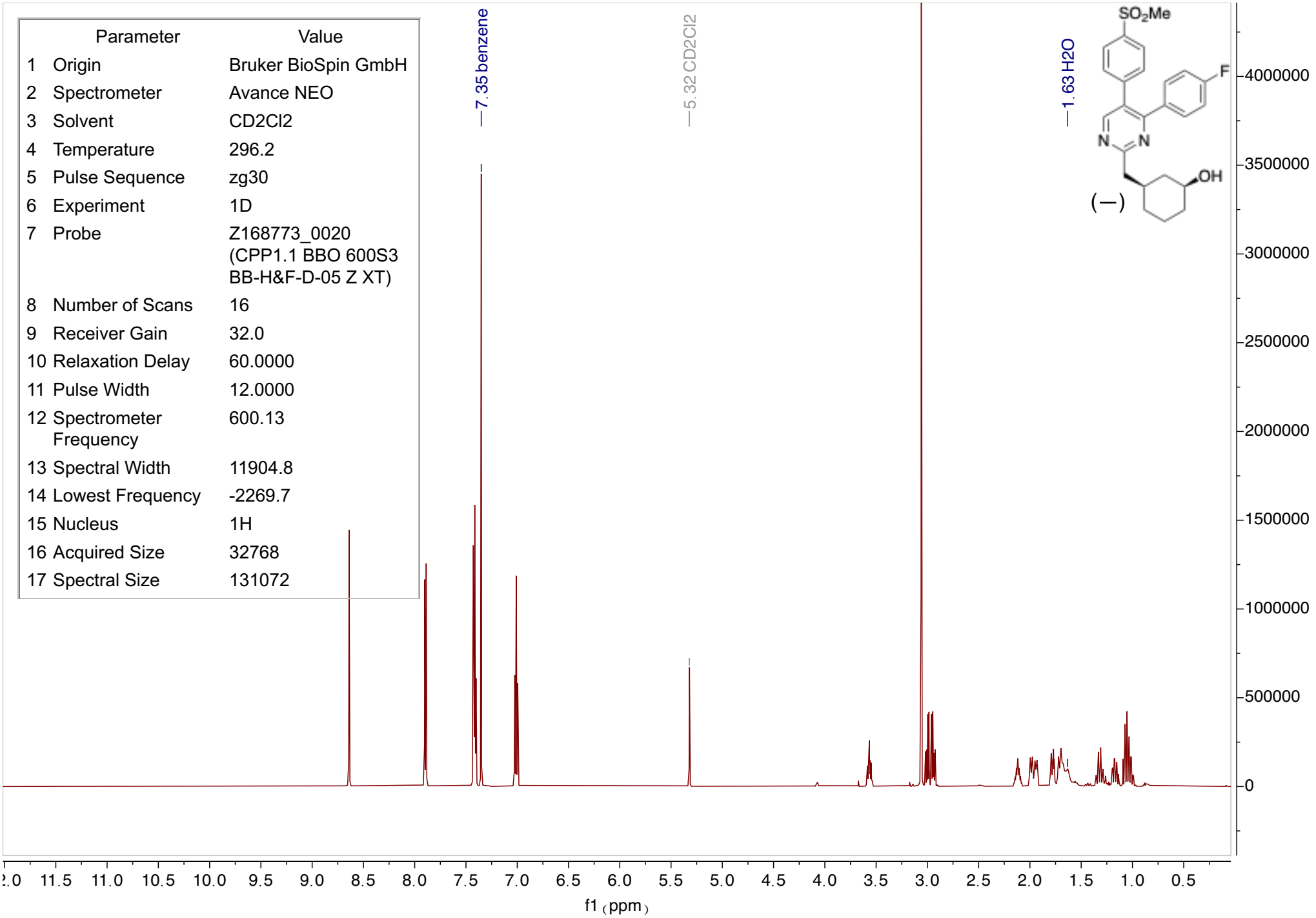


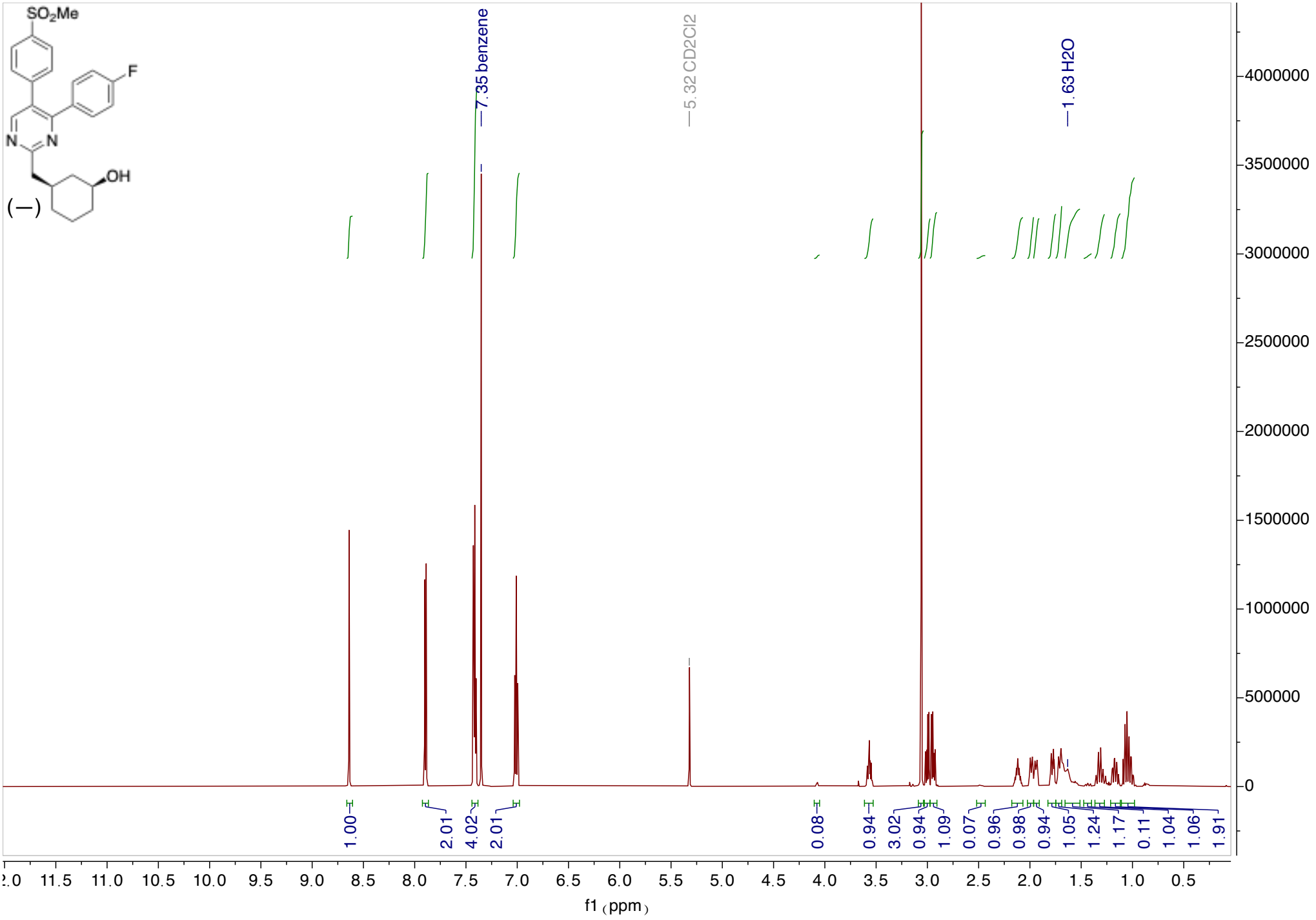


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CD2Cl2
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-96.5
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

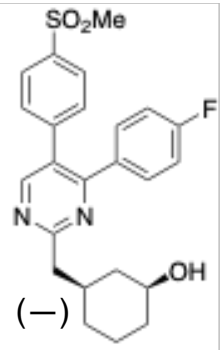

SO2Me
F
N
N
OH
(+)
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CD2Cl2
4 Temperature 296.2
5 Pulse Sequence noesygpphpp
6 Experiment NOESY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 61.8
10 Relaxation Delay 1.9939
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4854.4
14 Lowest Frequency -54.7
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)

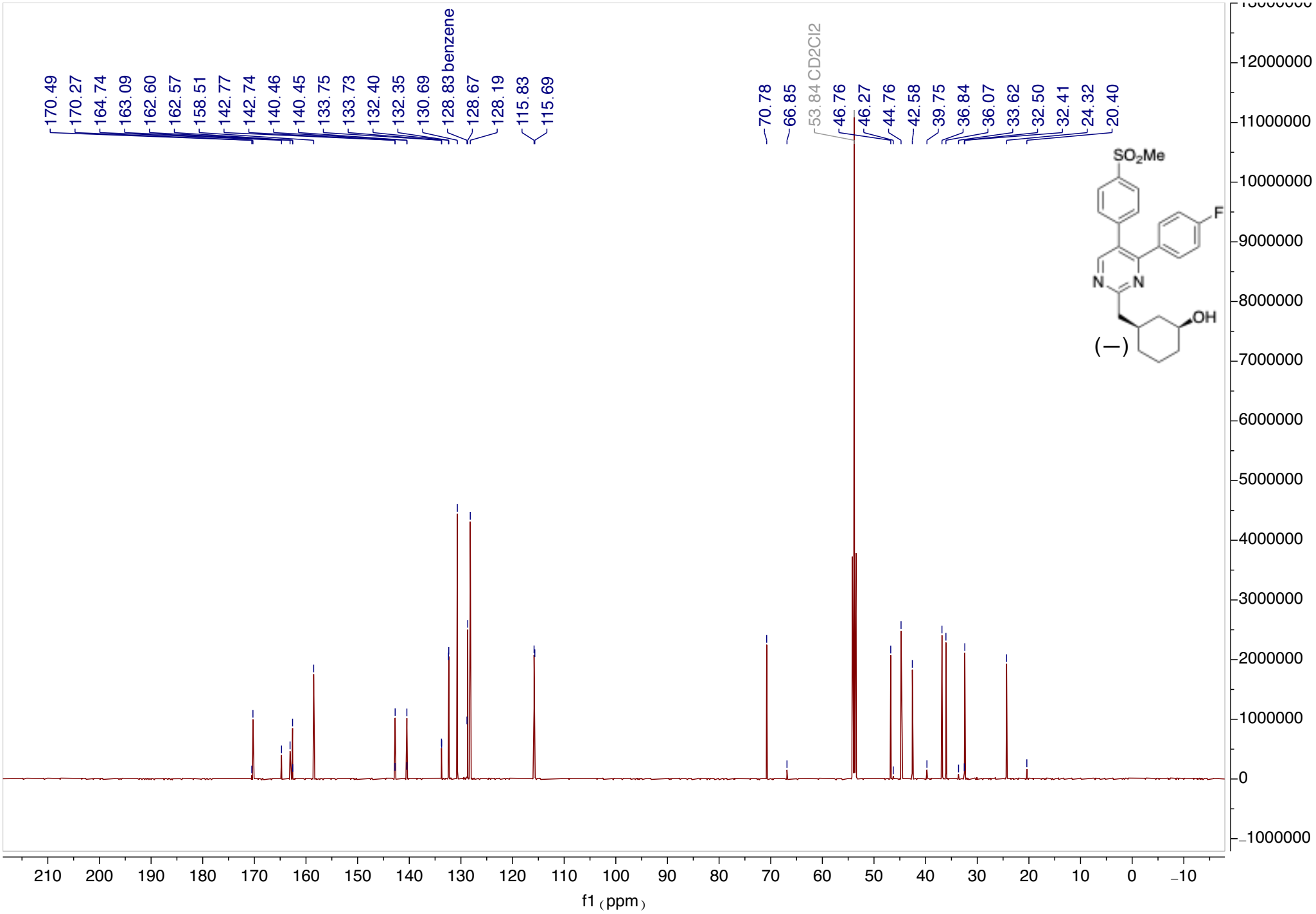

R
OH
H
H
NOE
(+)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
f1 (ppm)
4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5
f2 (ppm)


Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CD2Cl2
4 Temperature 296.2
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 32.0
10 Relaxation Delay 60.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2269.7
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.35 benzene
5.32 CD2Cl2
1.63 H2O
SO2Me
F
N
N
OH
(—)
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
11.5 11.0 10.5 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
f1 (ppm)

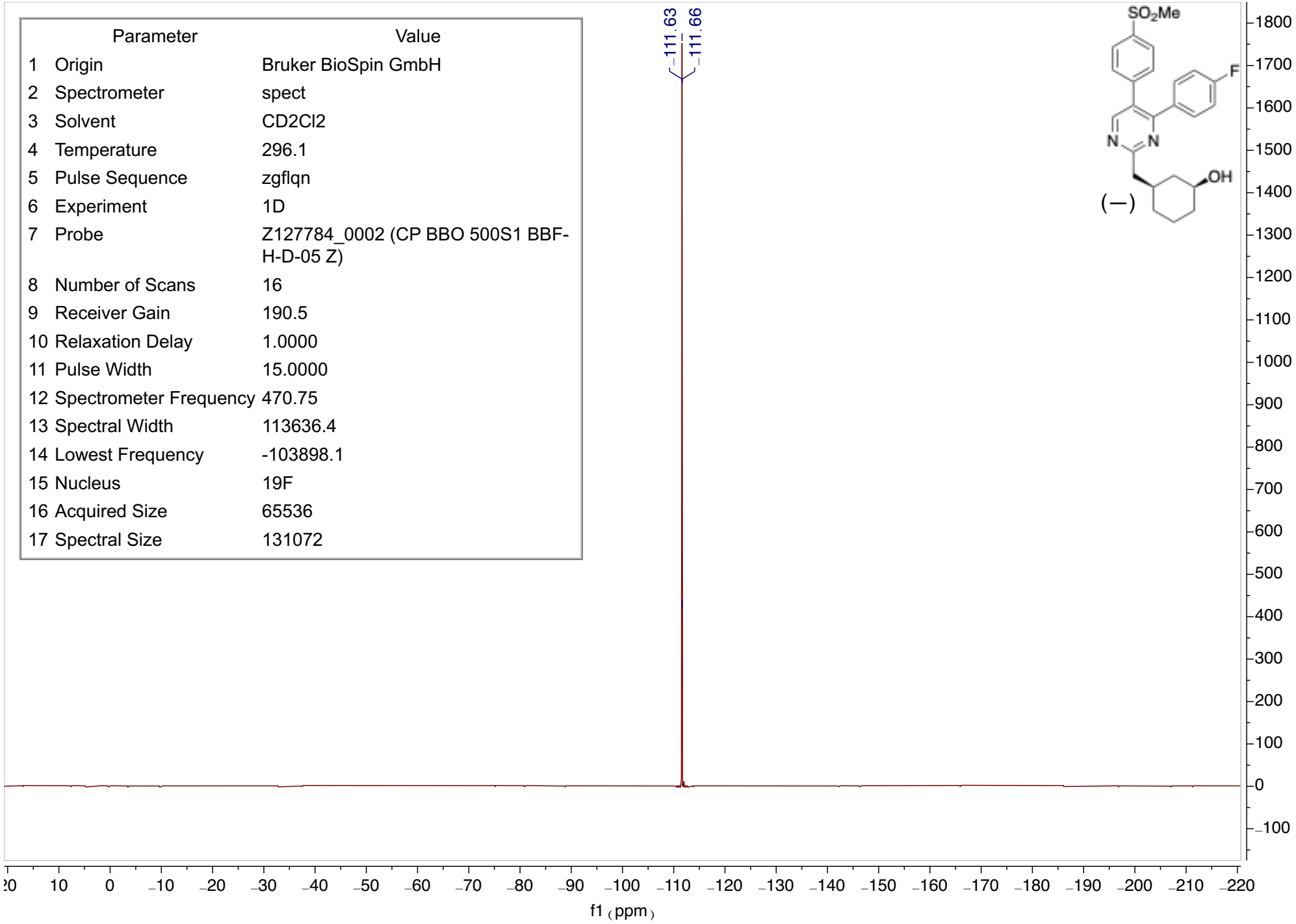

SO2Me
F
N
N
OH
(—)
7.35 benzene
5.32 CD2Cl2
1.63 H2O
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
1.00
2.01
4.02
2.01
0.08
0.94
3.02
0.94
1.09
0.07
0.96
0.98
0.94
1.05
1.24
1.17
0.11
1.04
1.06
1.91
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

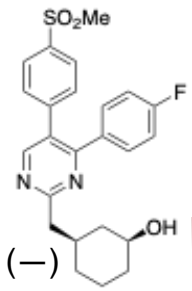
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CD2Cl2
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2709.7
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



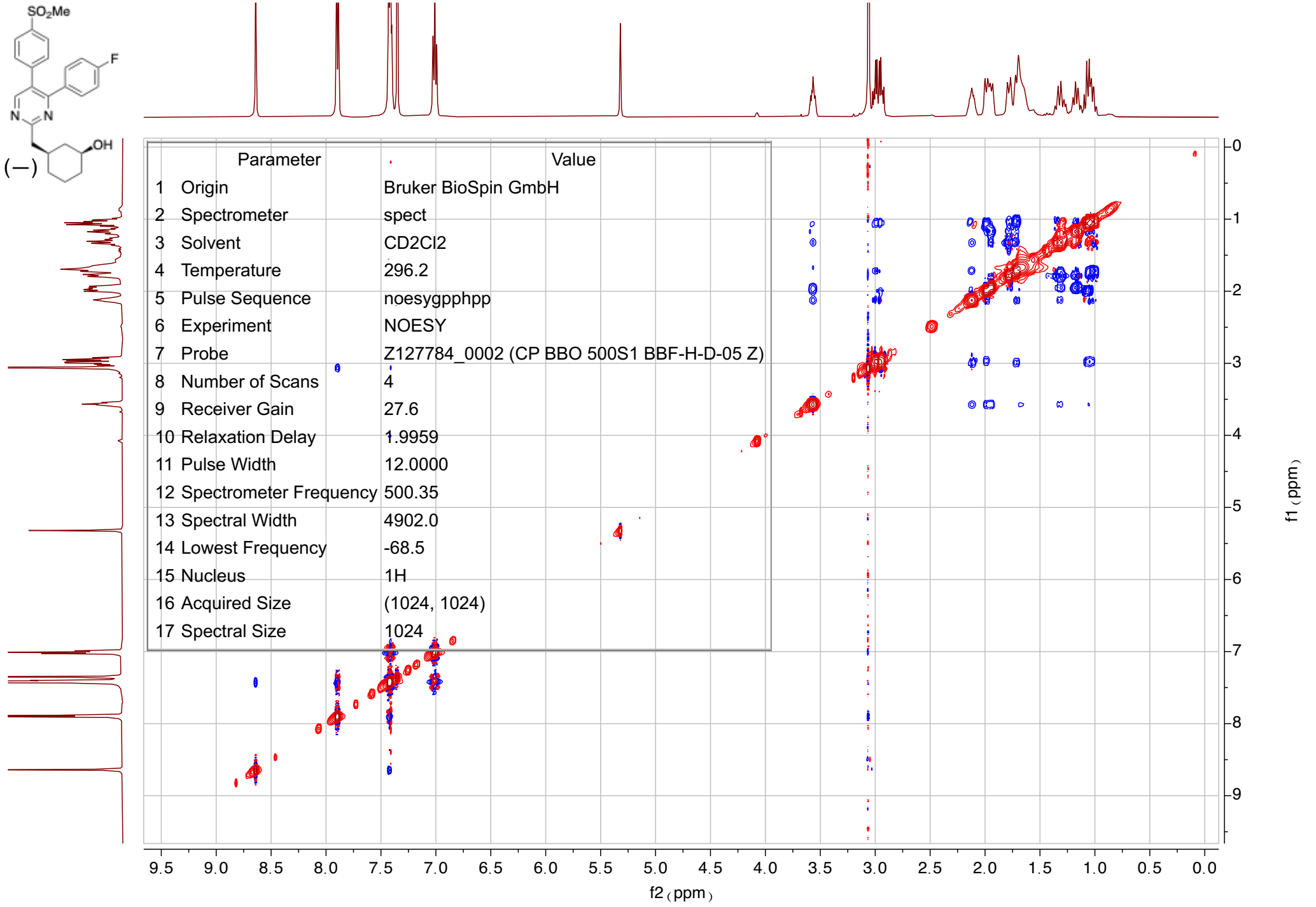

170.49
170.27
164.74
163.09
162.60
162.57
158.51
142.77
142.74
140.46
140.45
133.75
133.73
132.40
132.35
130.69
128.83 benzene
128.67
128.19
115.83
115.69
70.78
66.85
53.84 CD2Cl2
46.76
46.27
44.76
42.58
39.75
36.84
36.07
33.62
32.50
32.41
24.32
20.40
SO2Me
F
N
N
OH
(—)
12000000
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000
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)

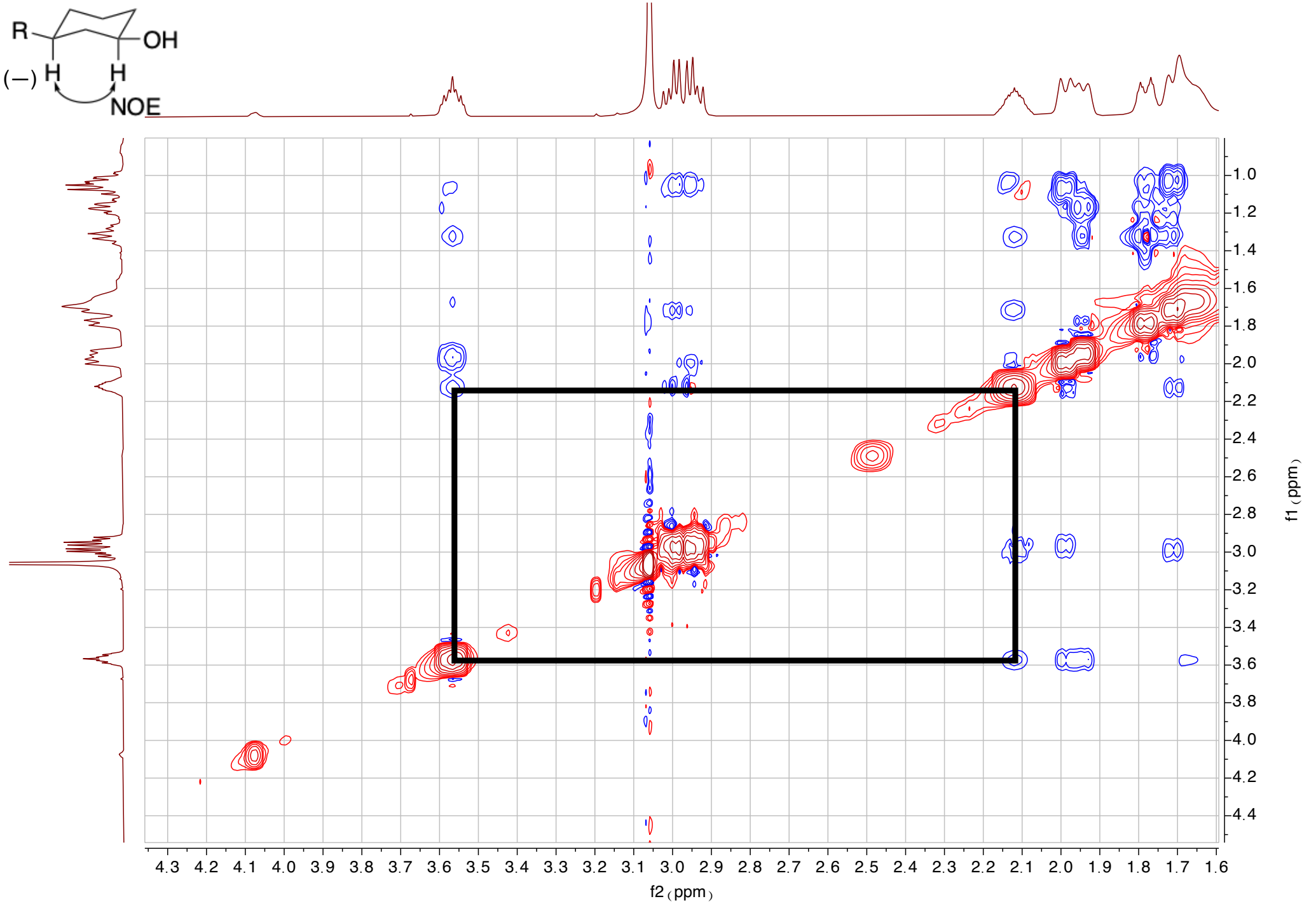
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CD2Cl2
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



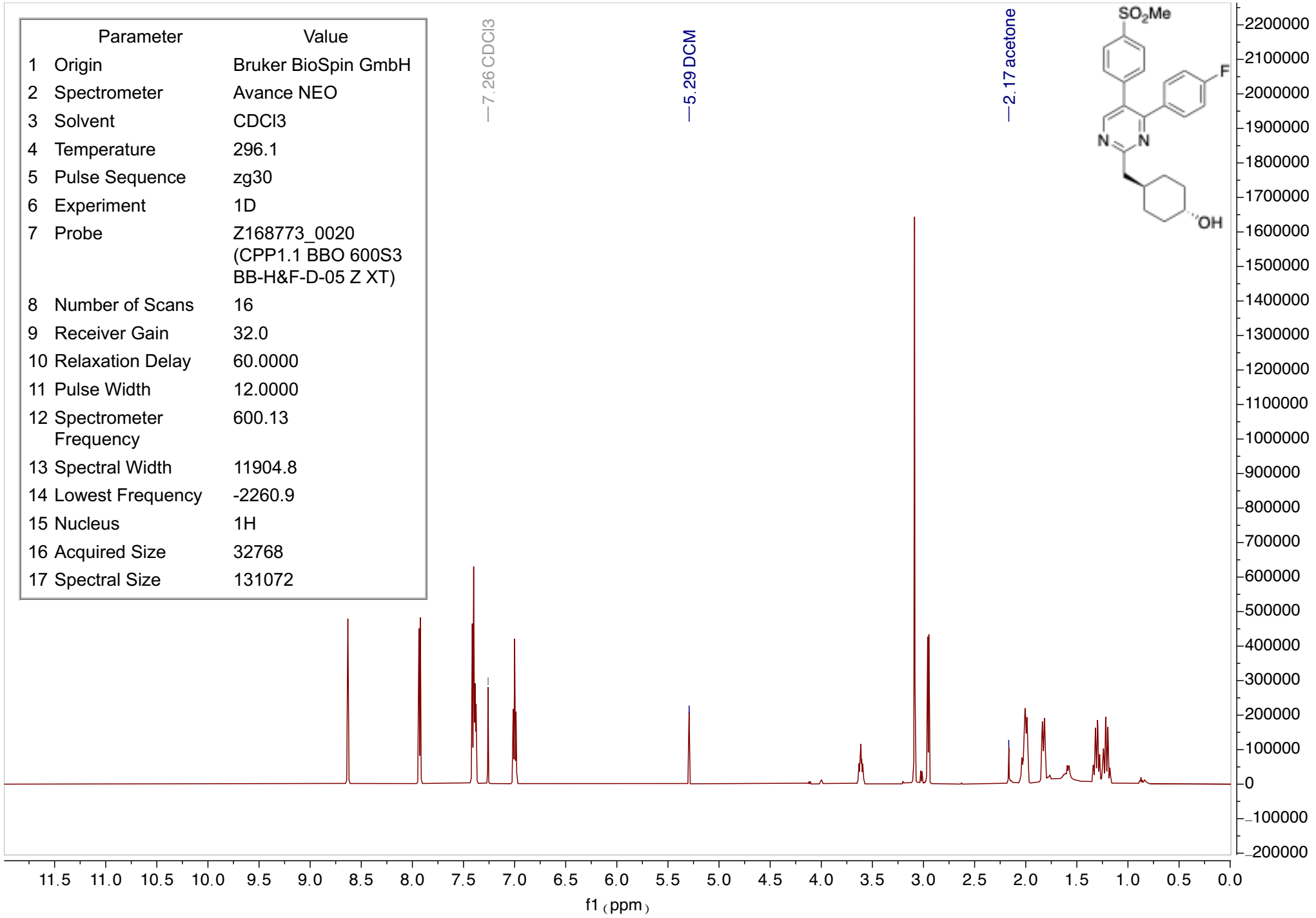


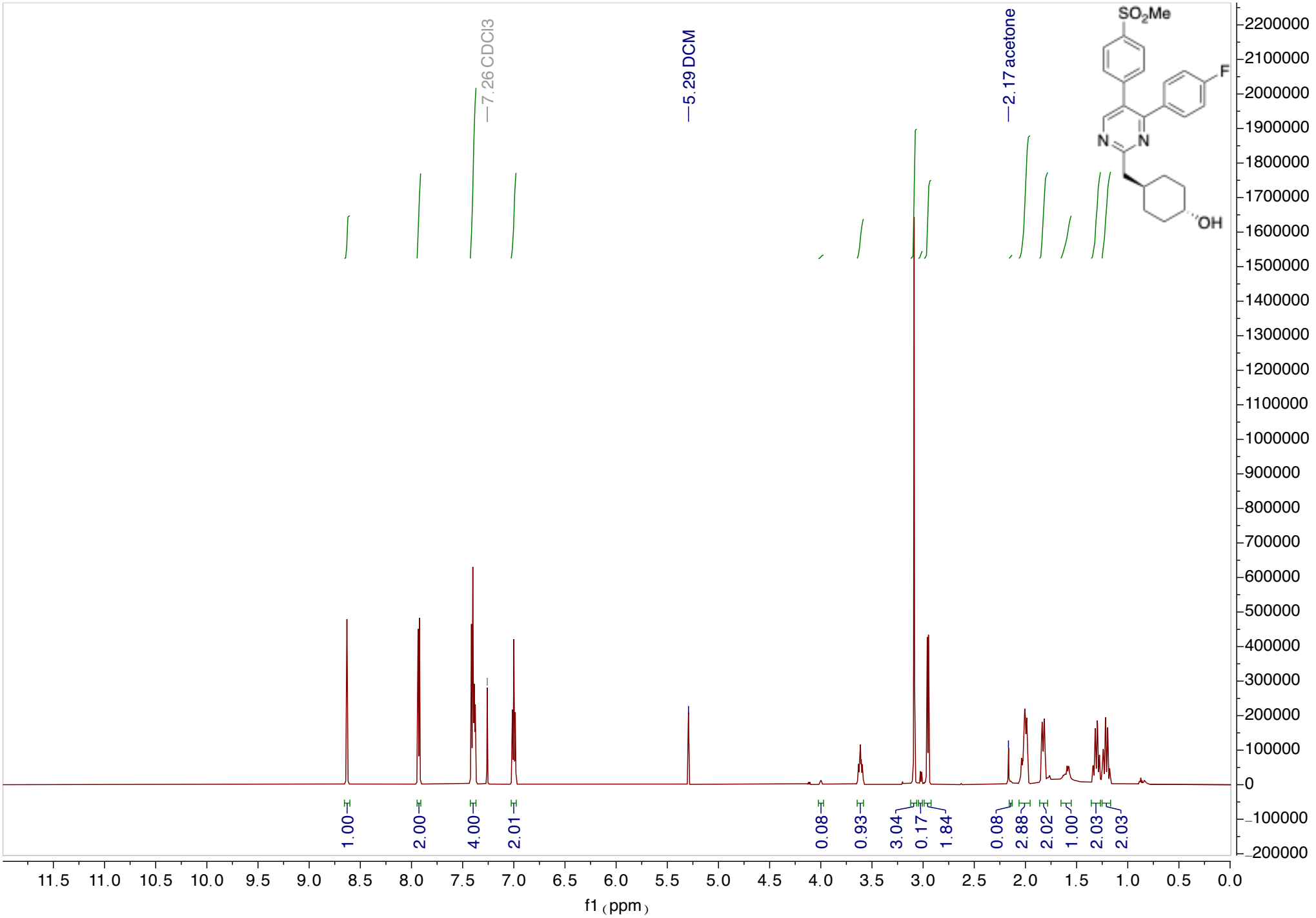
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CD2Cl2
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-70.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


SO2Me
F
N
N
OH
(—)
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CD2Cl2
4 Temperature 296.2
5 Pulse Sequence noesygpphpp
6 Experiment NOESY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 27.6
10 Relaxation Delay 1.9959
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4902.0
14 Lowest Frequency -68.5
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)

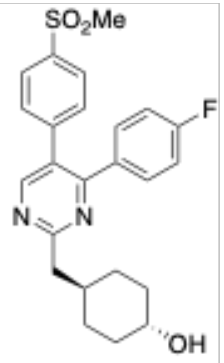

R
OH
(–) H
H
NOE
f2 (ppm)
f1 (ppm)

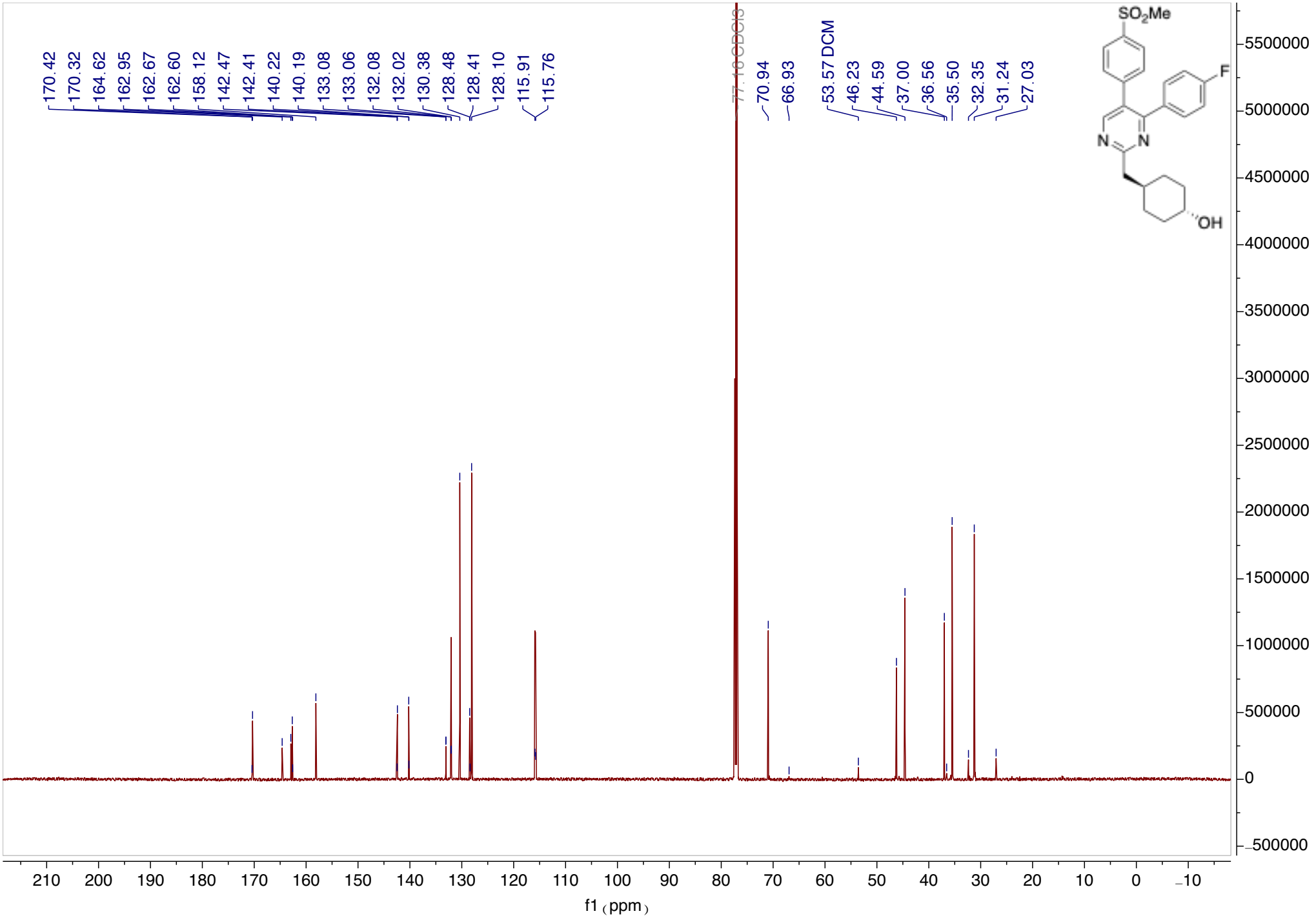
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	60.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2260.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072



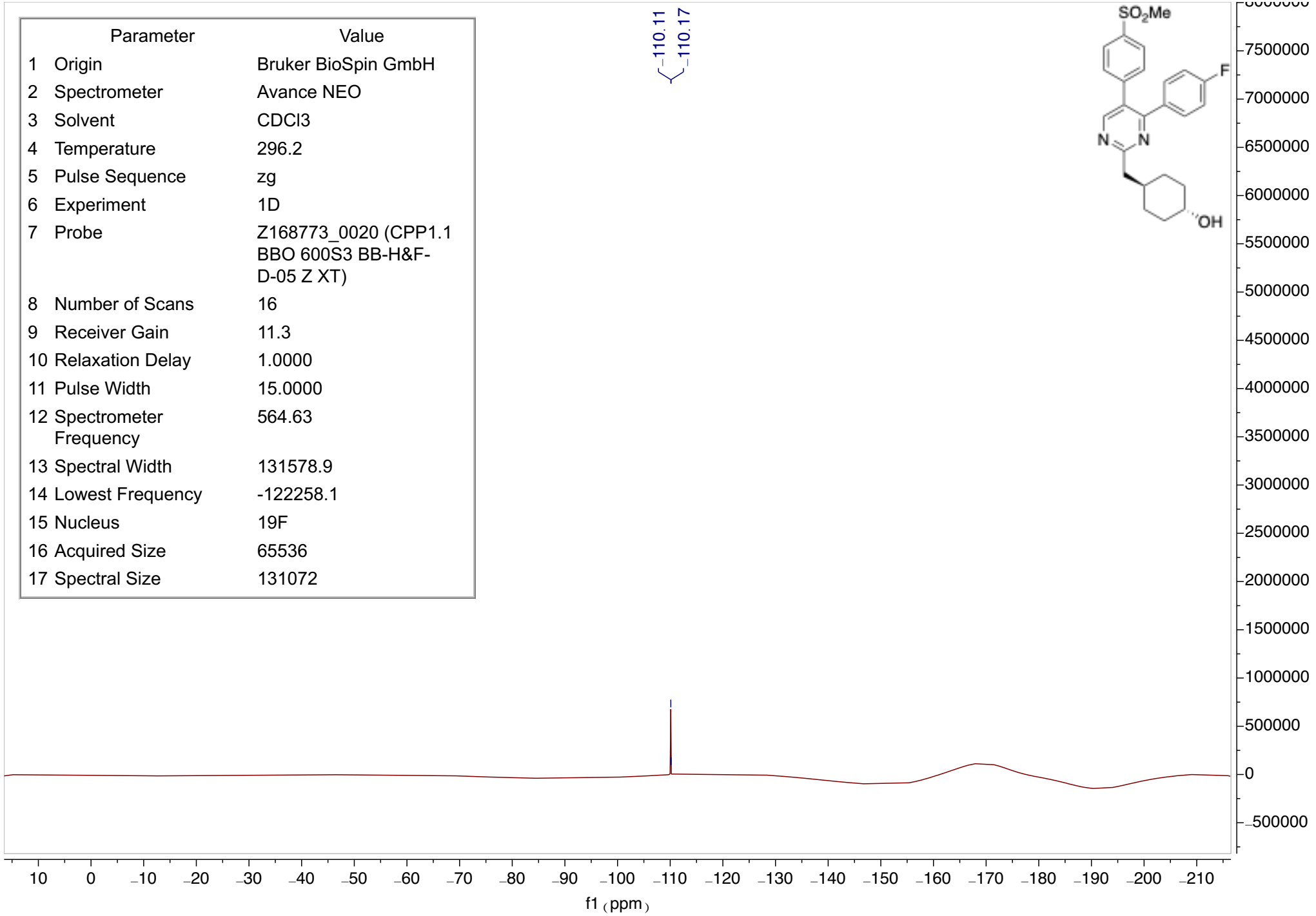

7.26 CDCl3
5.29 DCM
2.17 acetone
SO2Me
F
N
N
OH
1.00
2.00
4.00
2.01
0.08
0.93
3.04
0.17
1.84
0.08
2.88
2.02
1.00
2.03
2.03
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2749.7
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

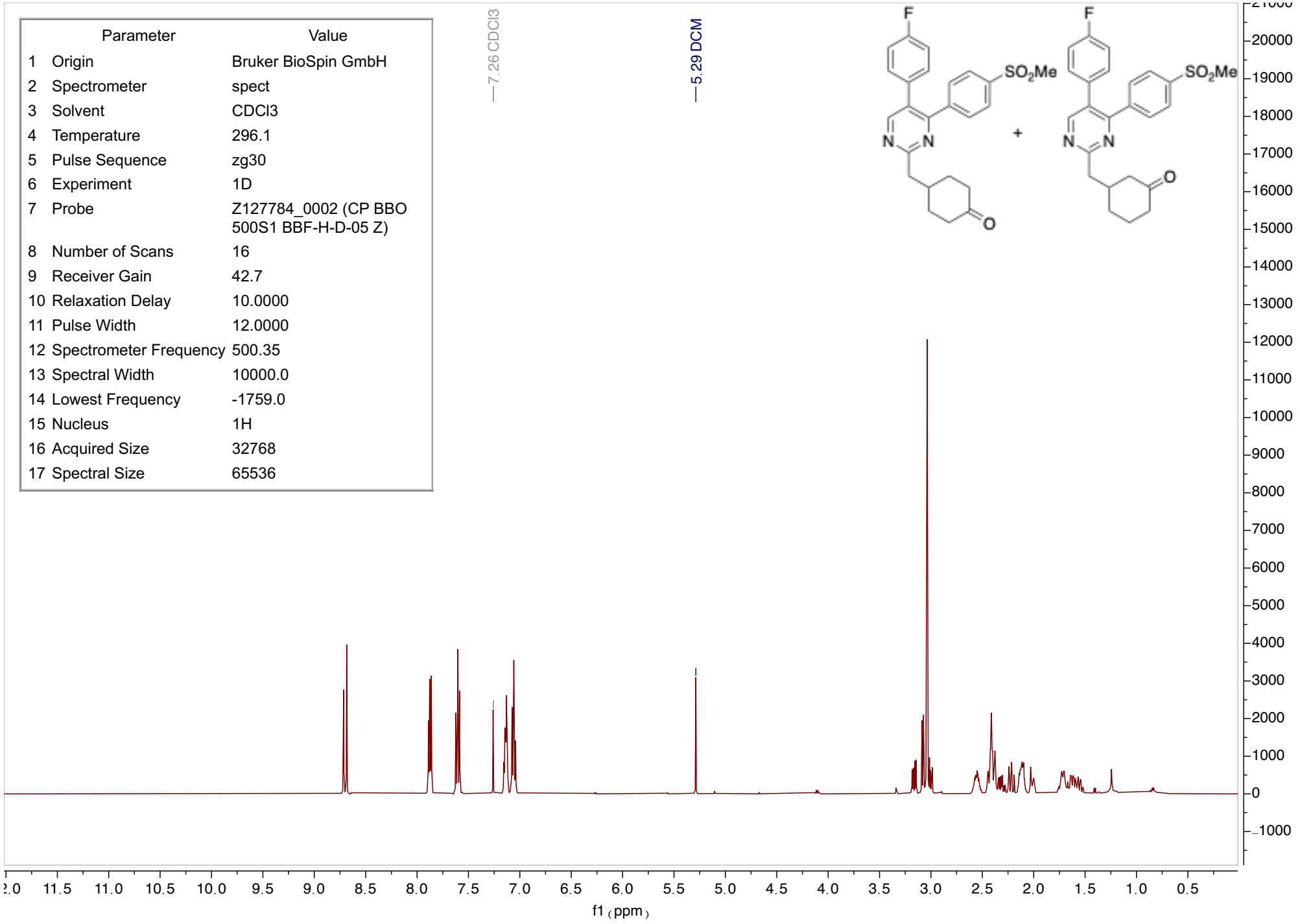


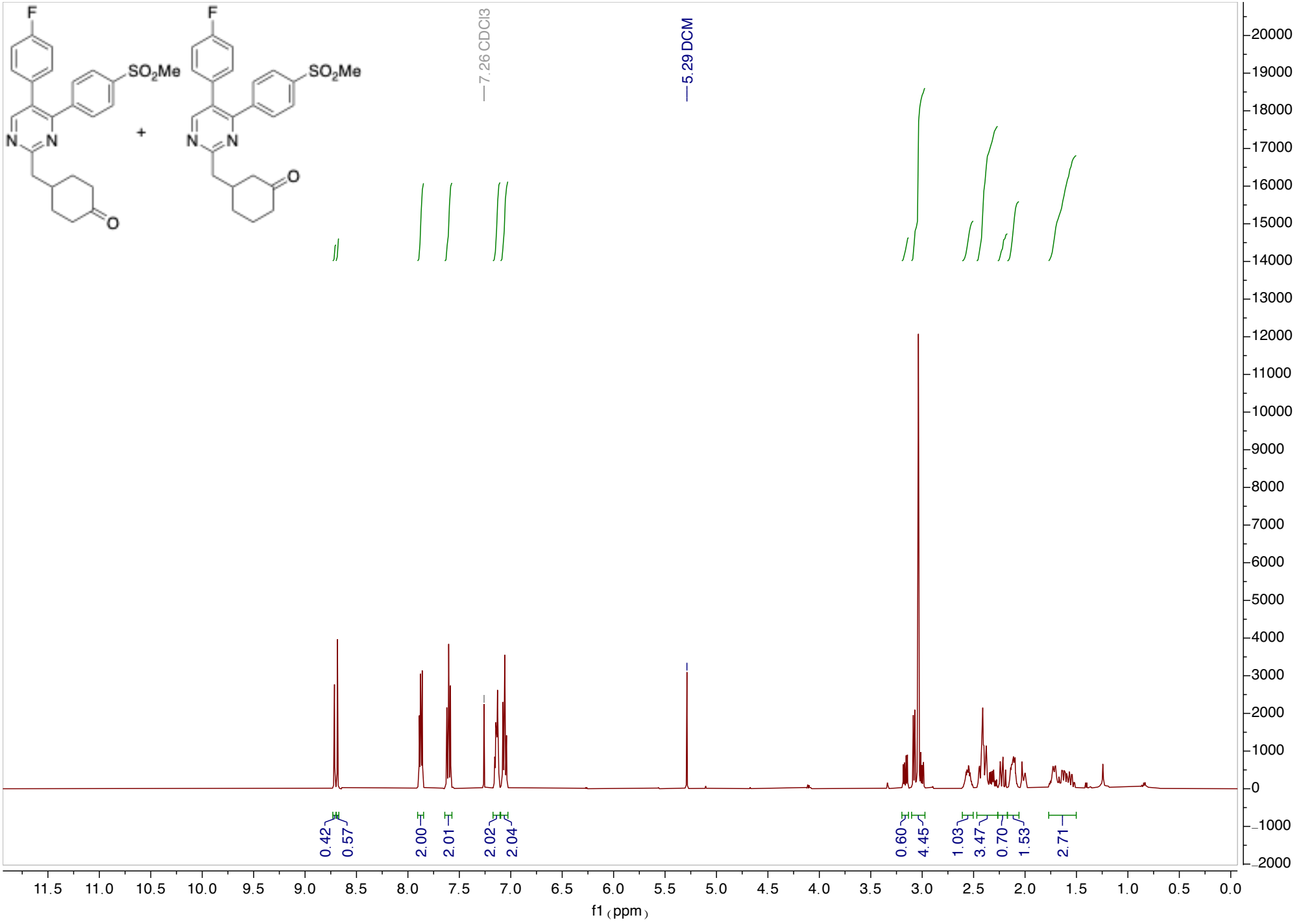

170.42
170.32
164.62
162.95
162.67
162.60
158.12
142.47
142.41
140.22
140.19
133.08
133.06
132.08
132.02
130.38
128.48
128.41
128.10
115.91
115.76
77.16 CDCl3
70.94
66.93
53.57 DCM
46.23
44.59
37.00
36.56
35.50
32.35
31.24
27.03
SO2Me
F
N
N
OH
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
−500000
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)

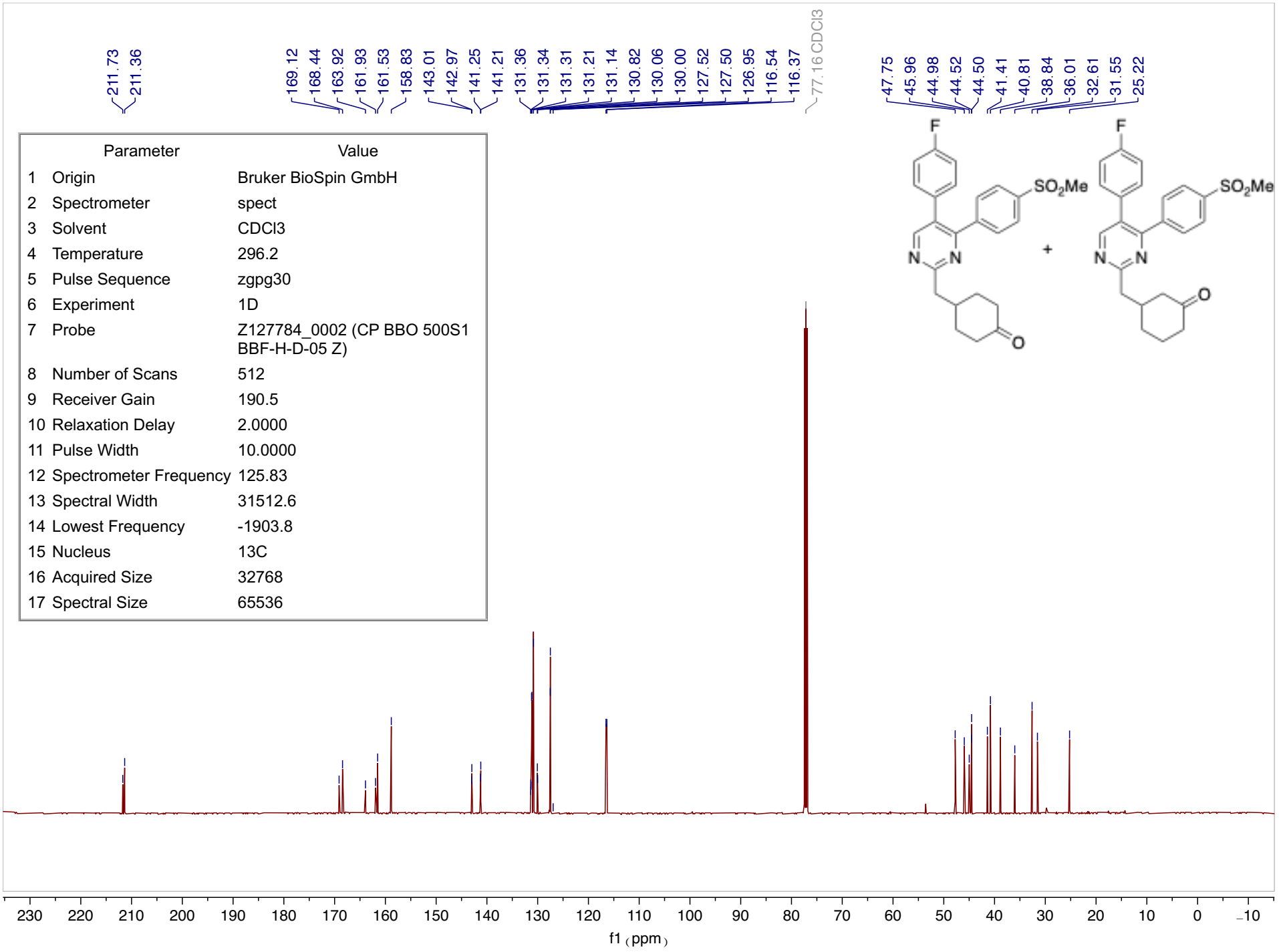
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	11.3
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	42.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

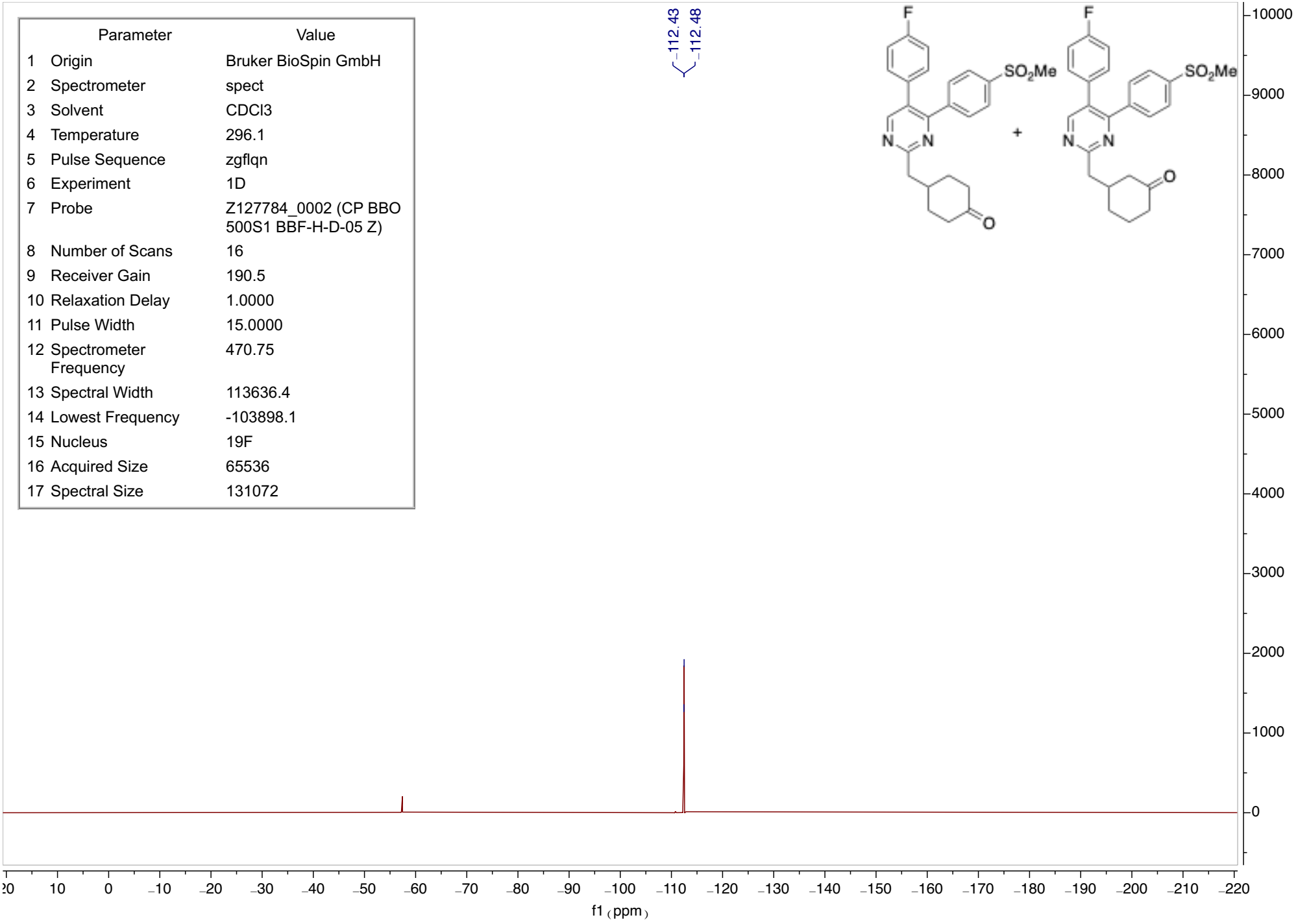



F
SO2Me
N
N
O
+
F
SO2Me
N
N
O
7.26 CDCl3
5.29 DCM
0.42
0.57
2.00
2.01
2.02
2.04
0.60
4.45
1.03
3.47
0.70
1.53
2.71
f1 (ppm)

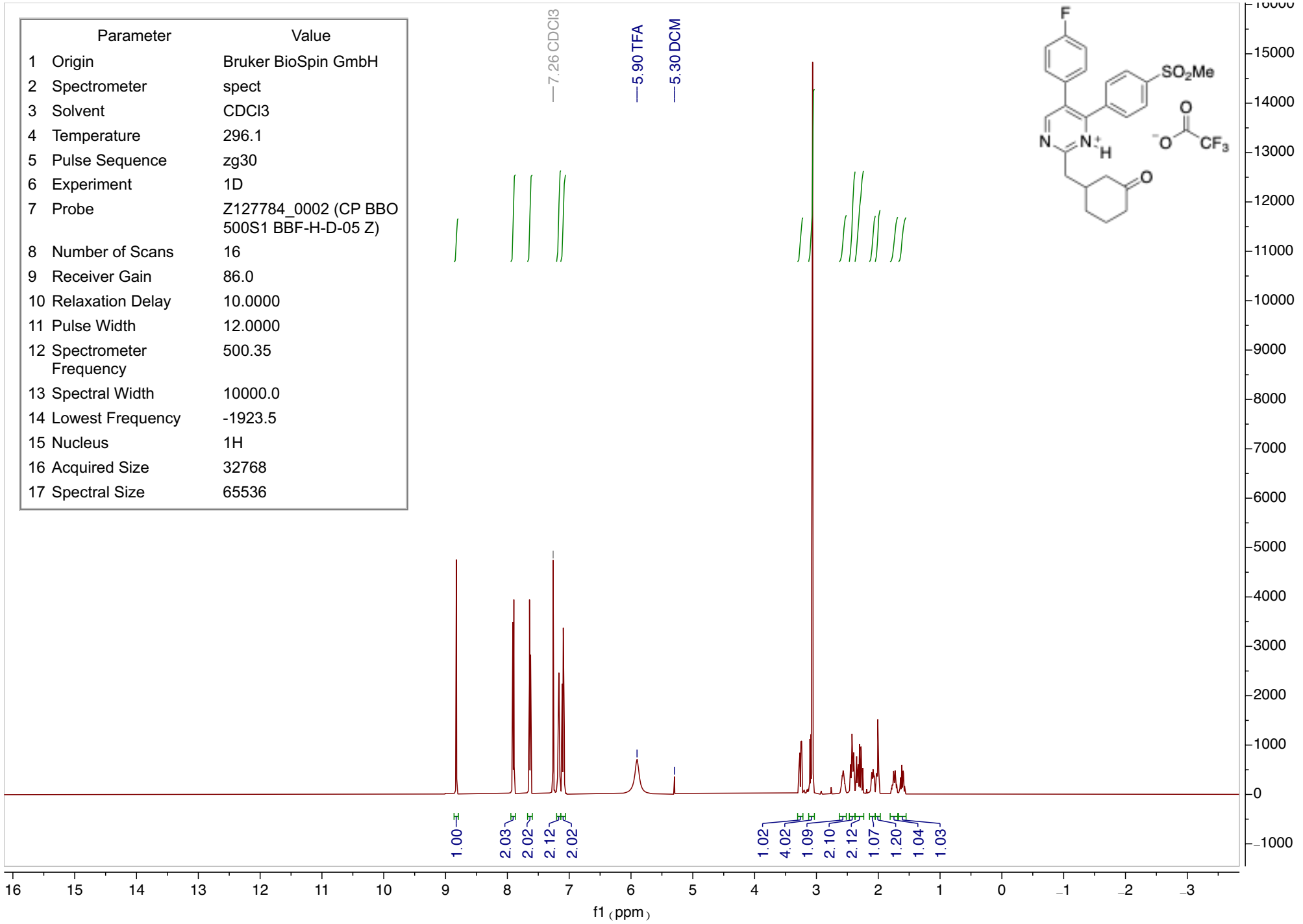


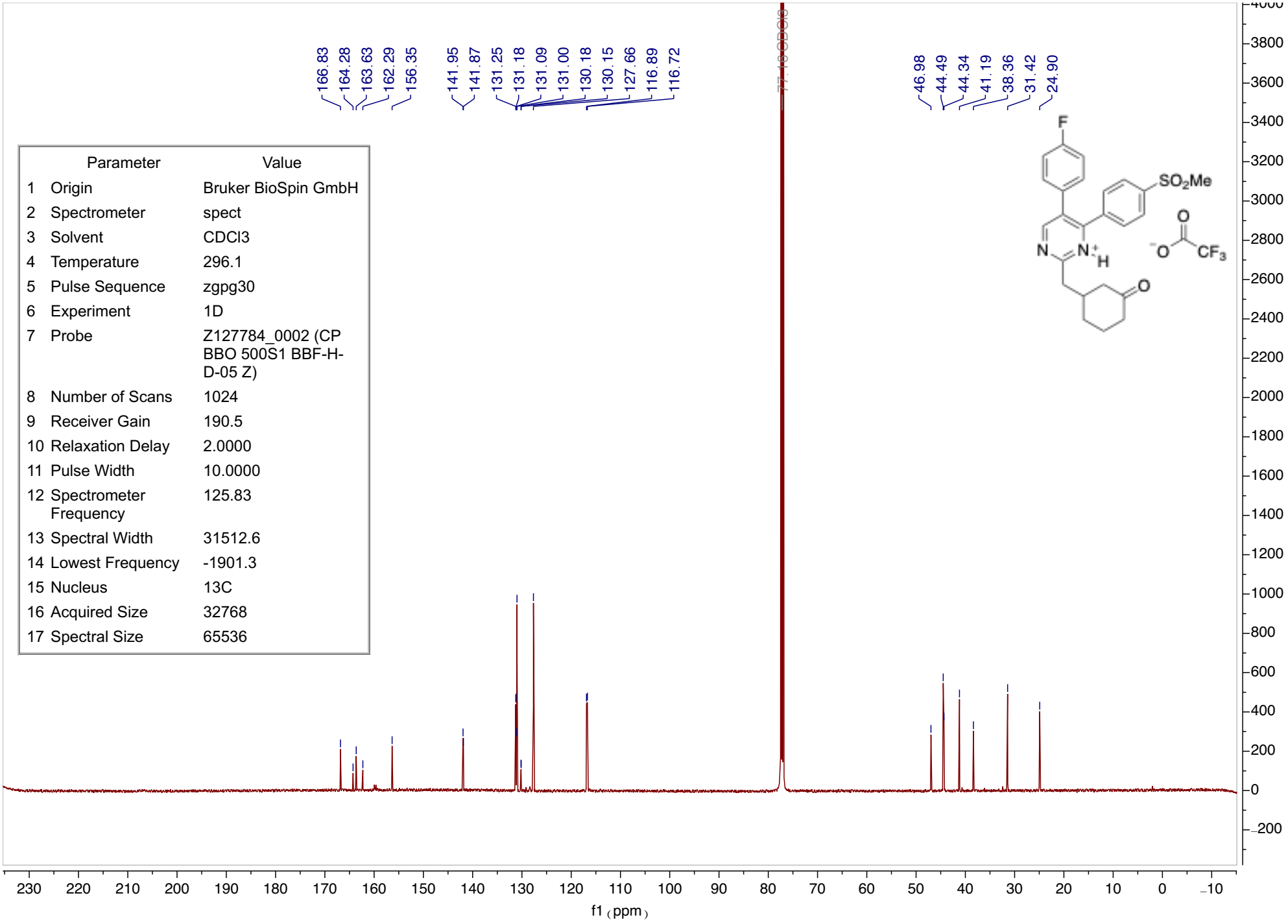
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



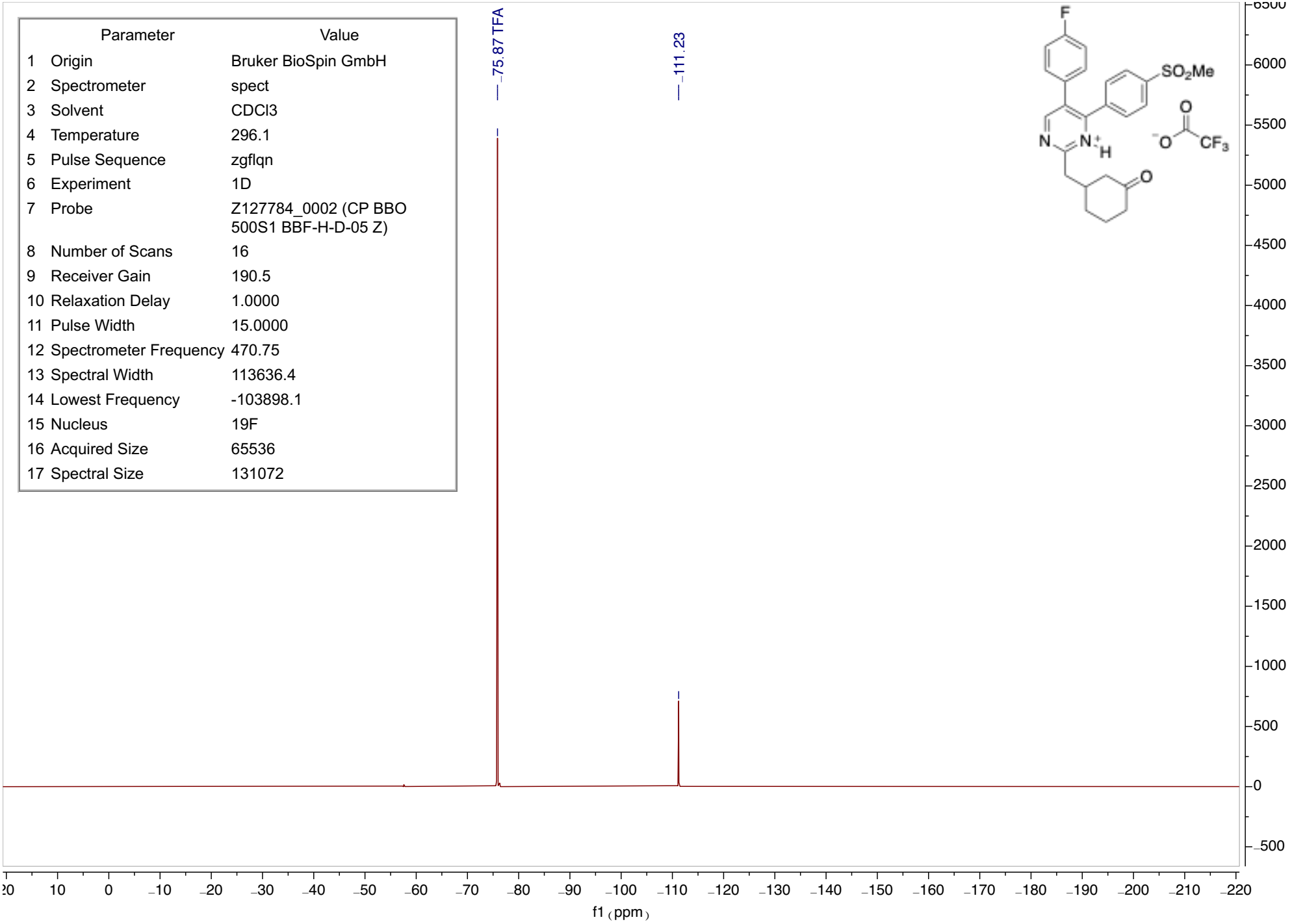
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

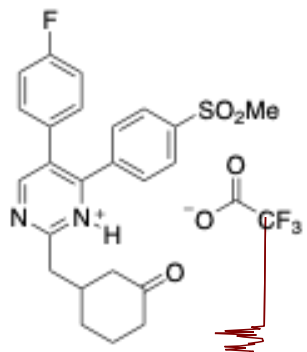




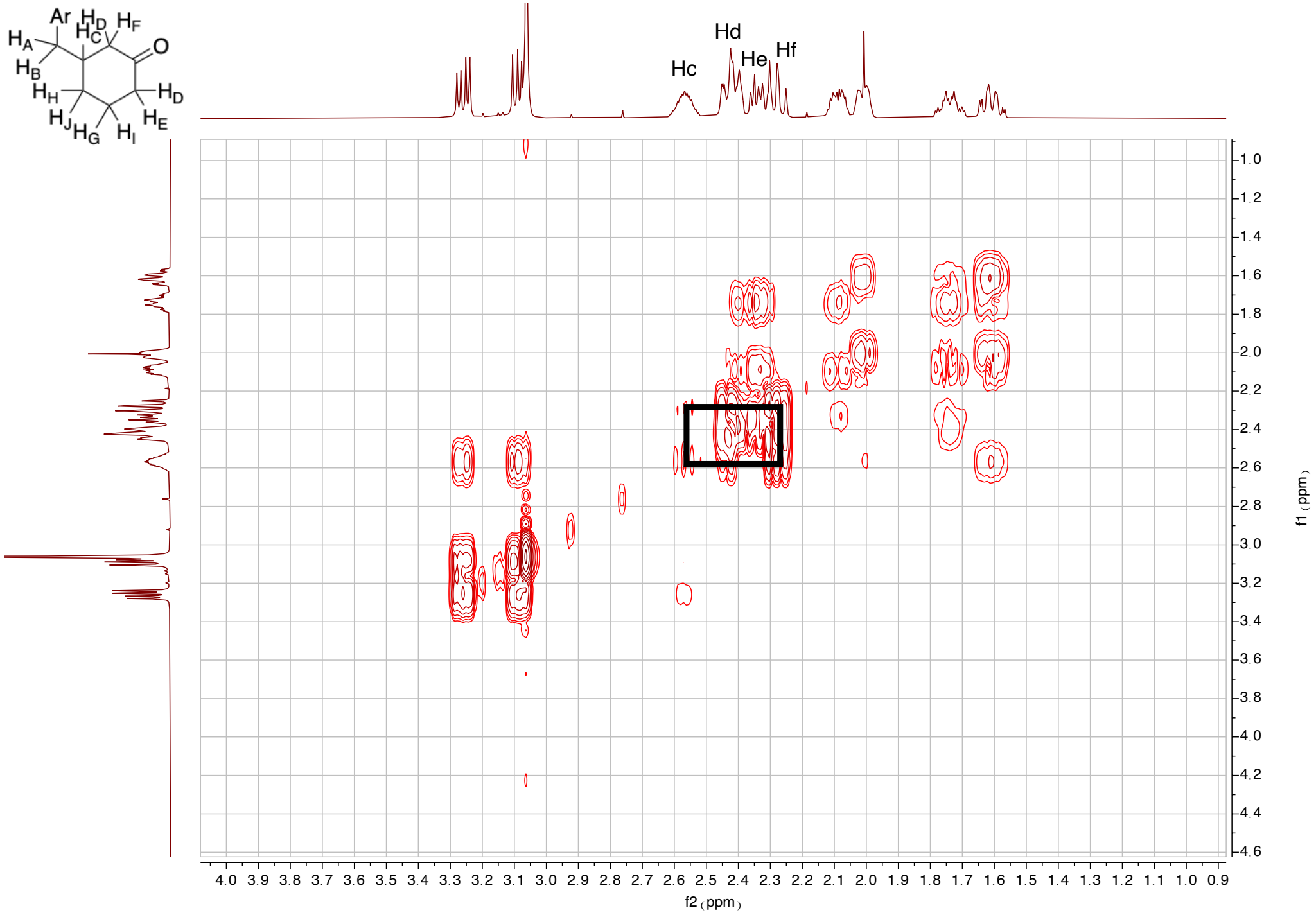
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

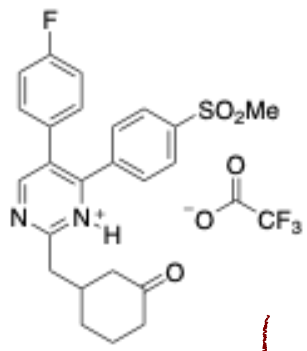
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



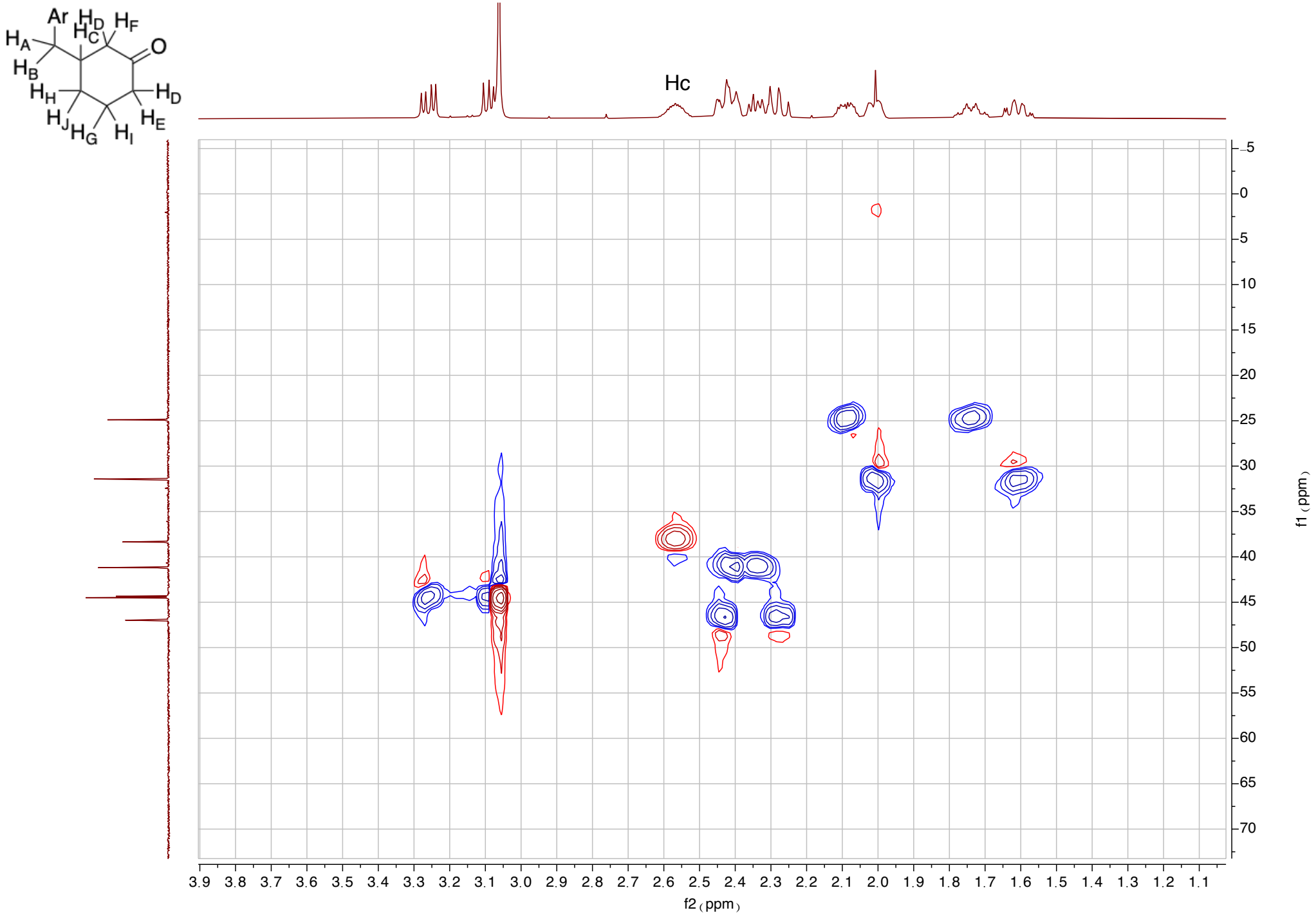


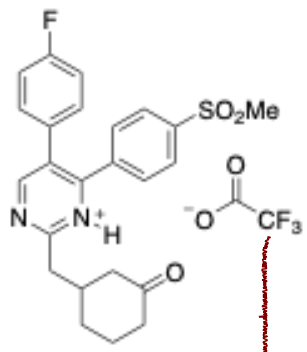
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.9341
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4587.2
14	Lowest Frequency	327.9
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


Ar
H_D
H_F
H_C
H_A
O
H_B
H_H
H_D
H_J
H_E
H_G
H_I
Hc
Hd
He
Hf
4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9
f2 (ppm)
1.0 1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8 4.0 4.2 4.4 4.6
f1 (ppm)

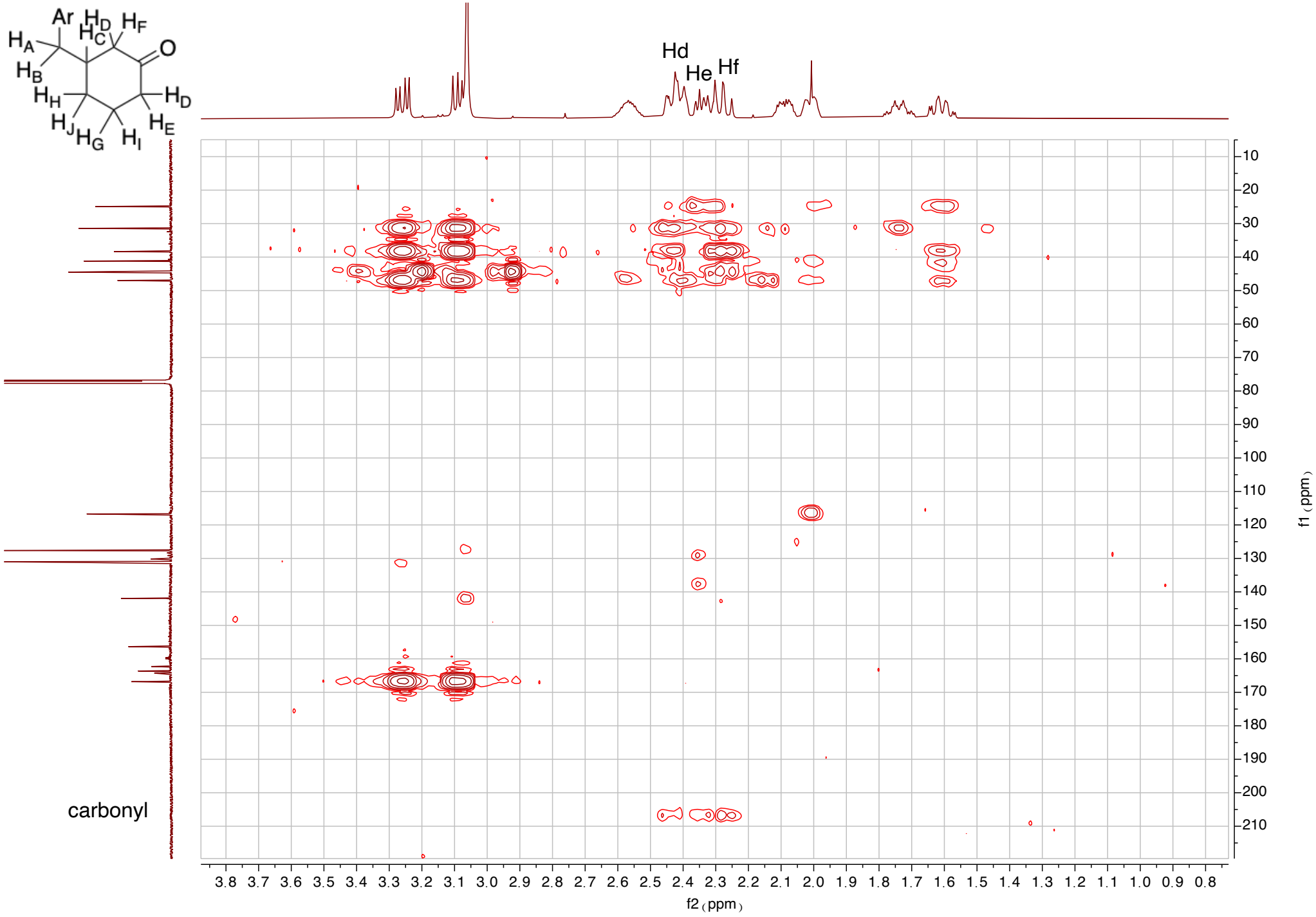


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4587.2
14	Lowest Frequency	327.9
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

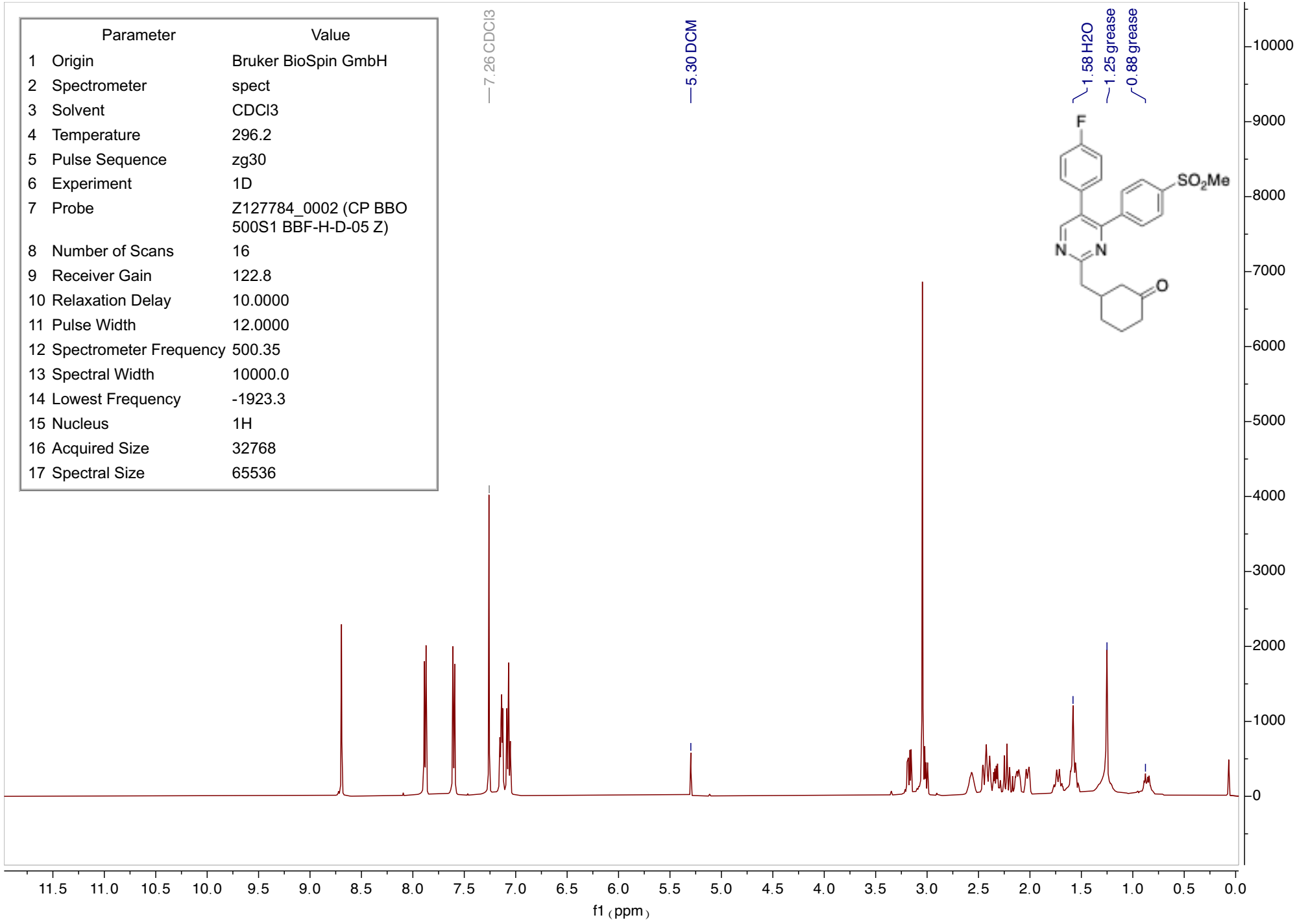

Ar
H_D
H_F
H_A
H_C
O
H_B
H_H
H_D
H_J
H_E
H_G
H_I
Hc
f2 (ppm)
f1 (ppm)

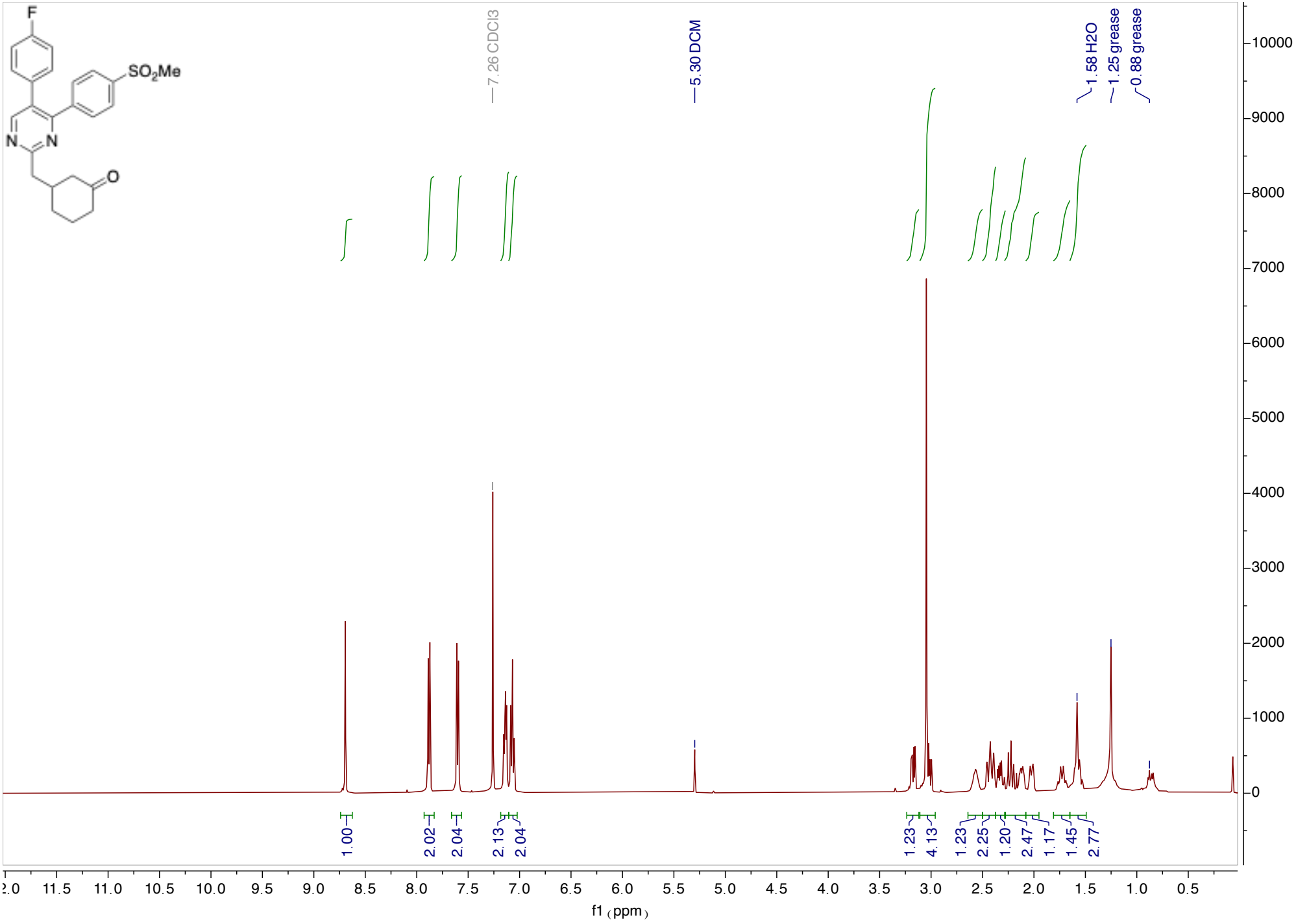


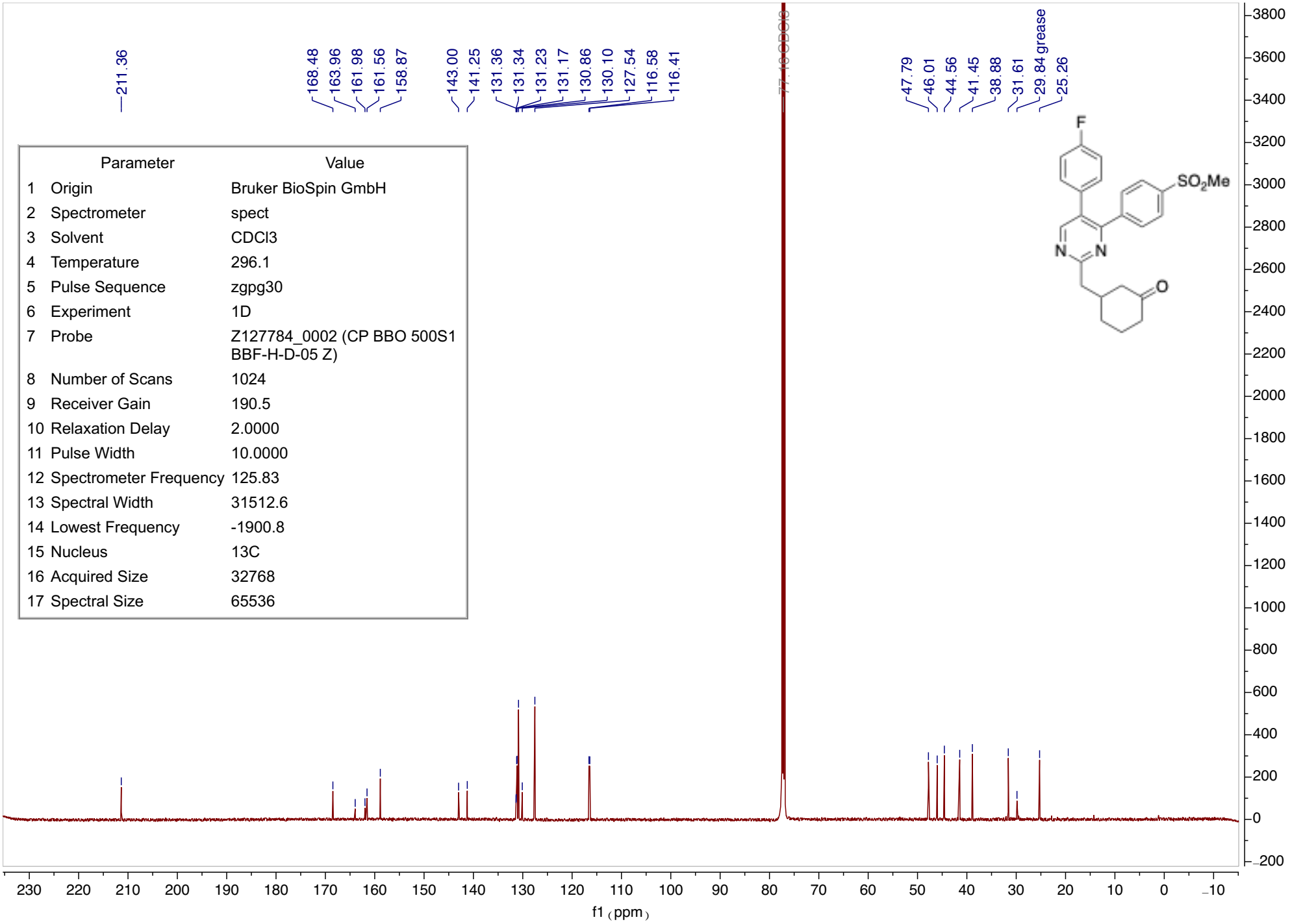
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4587.2
14	Lowest Frequency	327.9
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	0512


Ar
H_D
H_F
H_C
H_A
O
H_B
H_H
H_D
H_J
H_G
H_I
H_E
Hd
He
Hf
carbonyl
3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8
f2 (ppm)
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	122.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

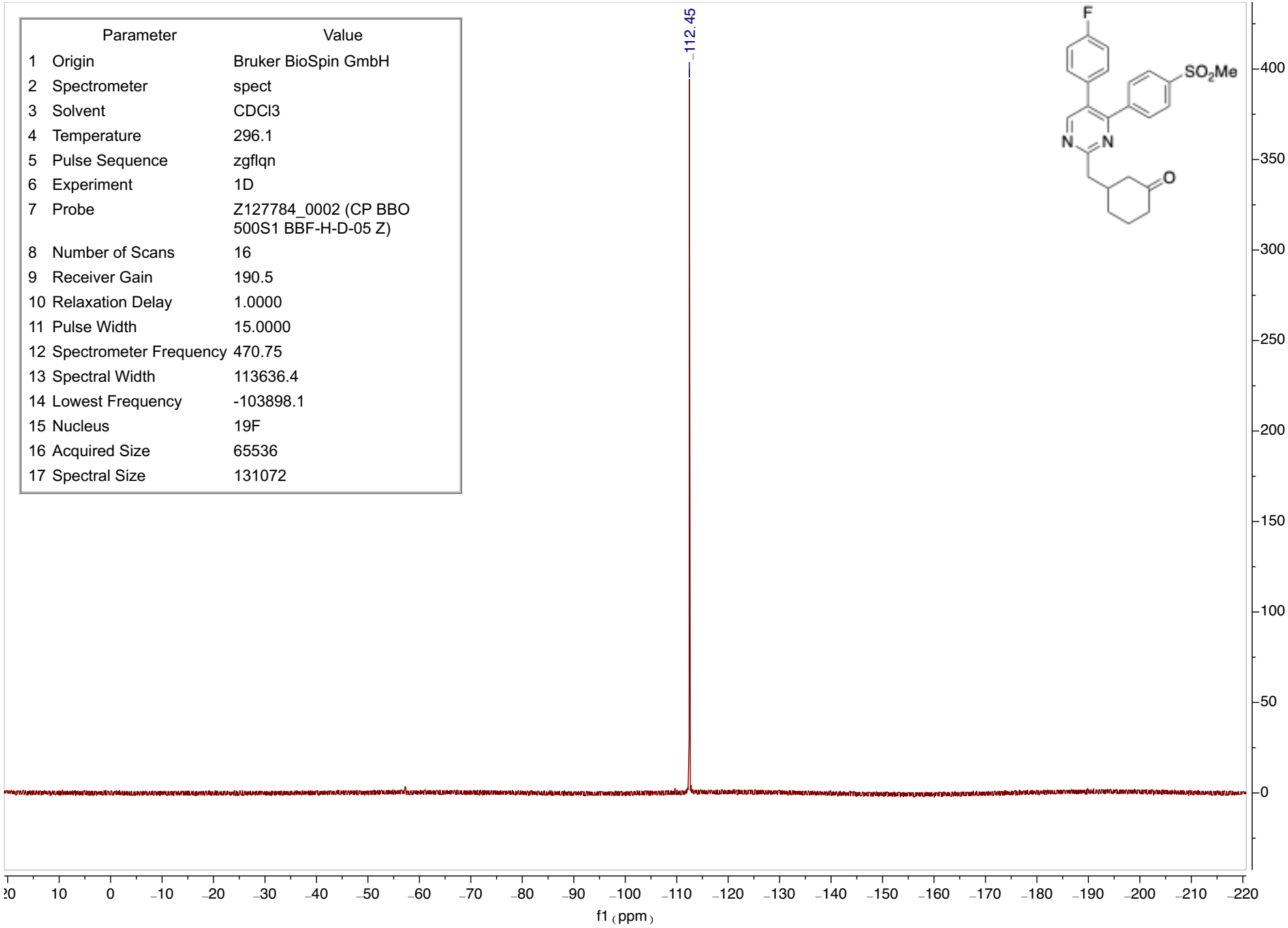



F
SO2Me
N
N
O
7.26 CDCl3
5.30 DCM
1.58 H2O
1.25 grease
0.88 grease
1.00
2.02
2.04
2.13
2.04
1.23
4.13
1.23
2.25
1.20
2.47
1.17
1.45
2.77
f1 (ppm)

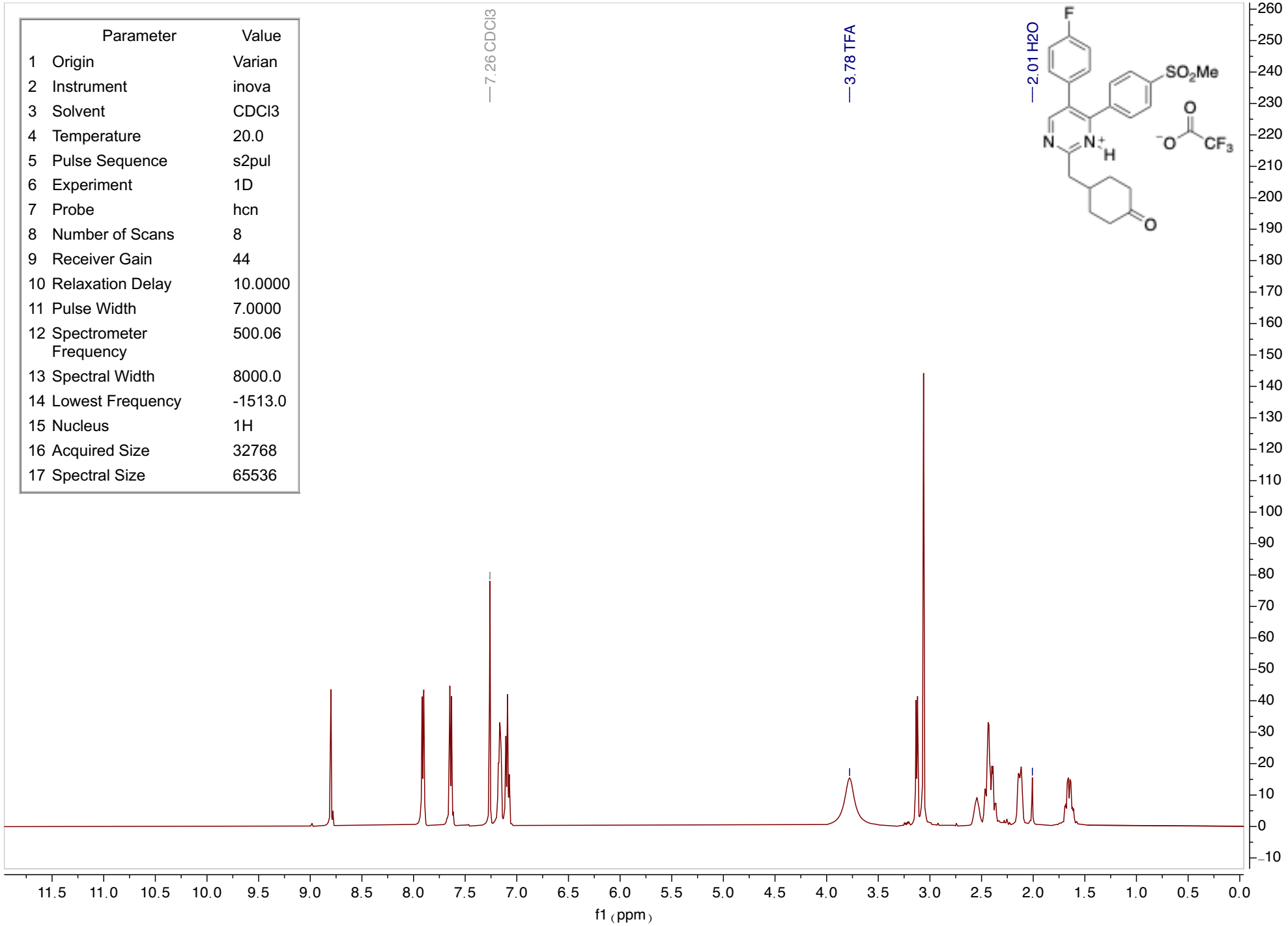


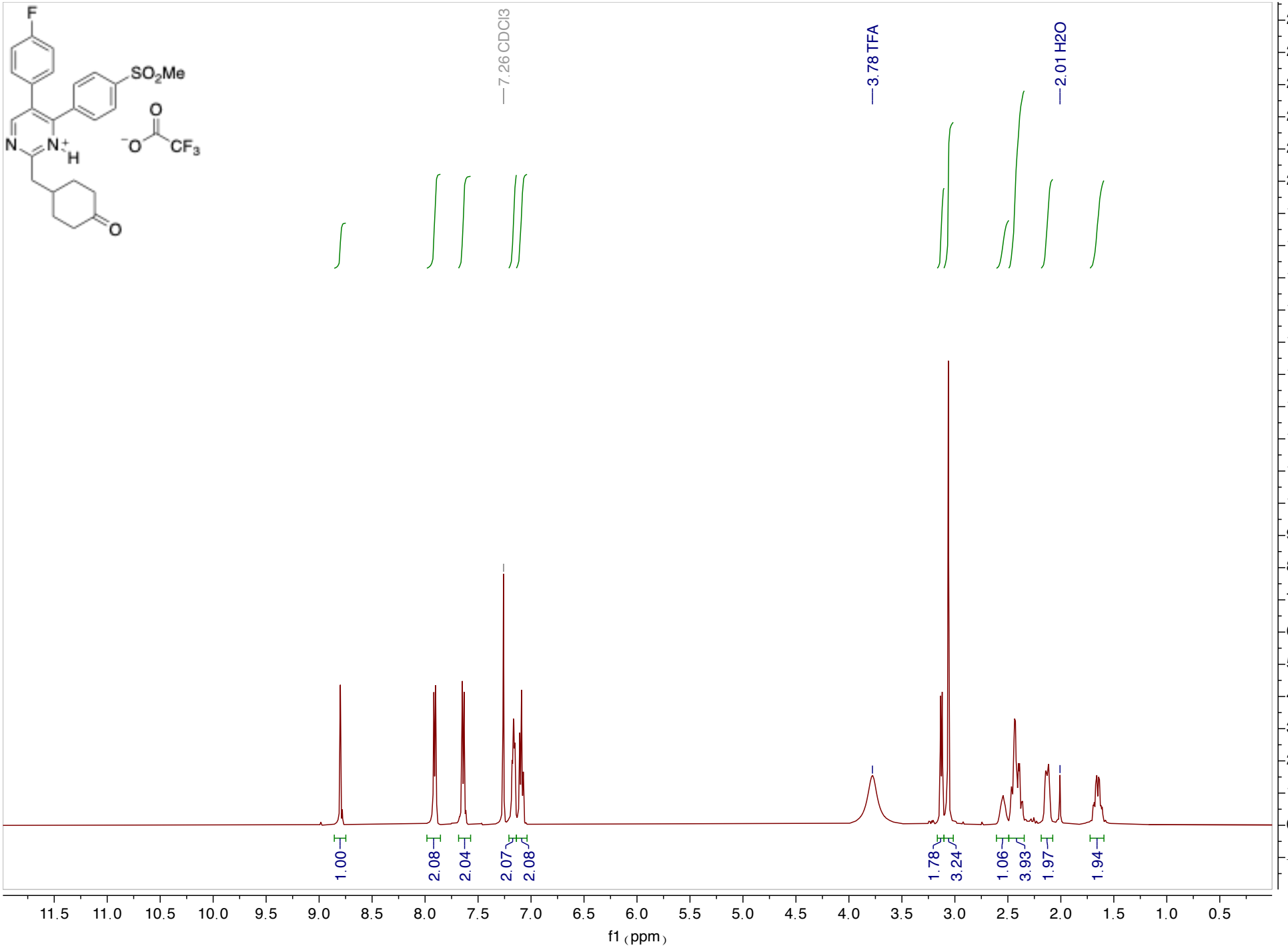
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

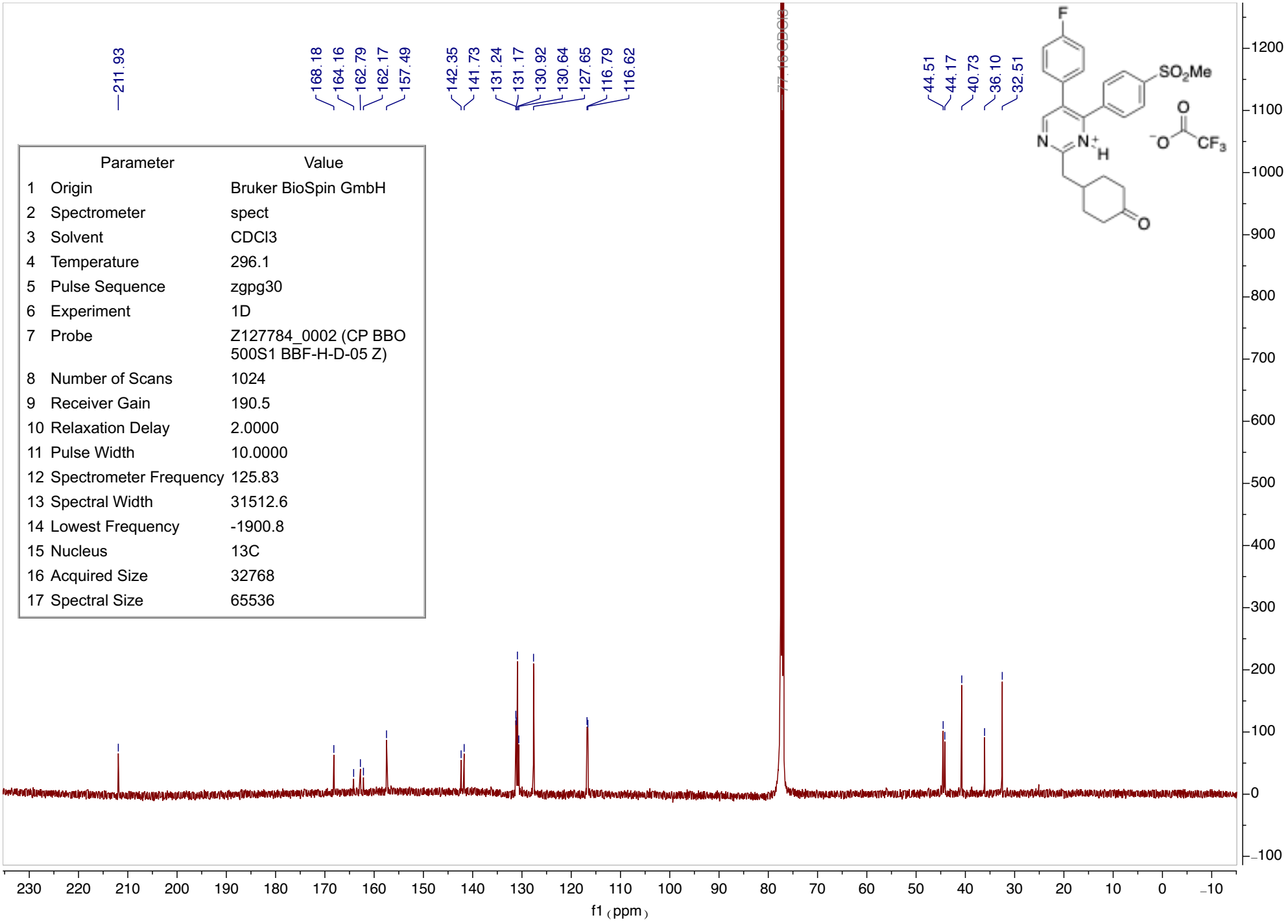
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	hcn
8	Number of Scans	8
9	Receiver Gain	44
10	Relaxation Delay	10.0000
11	Pulse Width	7.0000
12	Spectrometer Frequency	500.06
13	Spectral Width	8000.0
14	Lowest Frequency	-1513.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

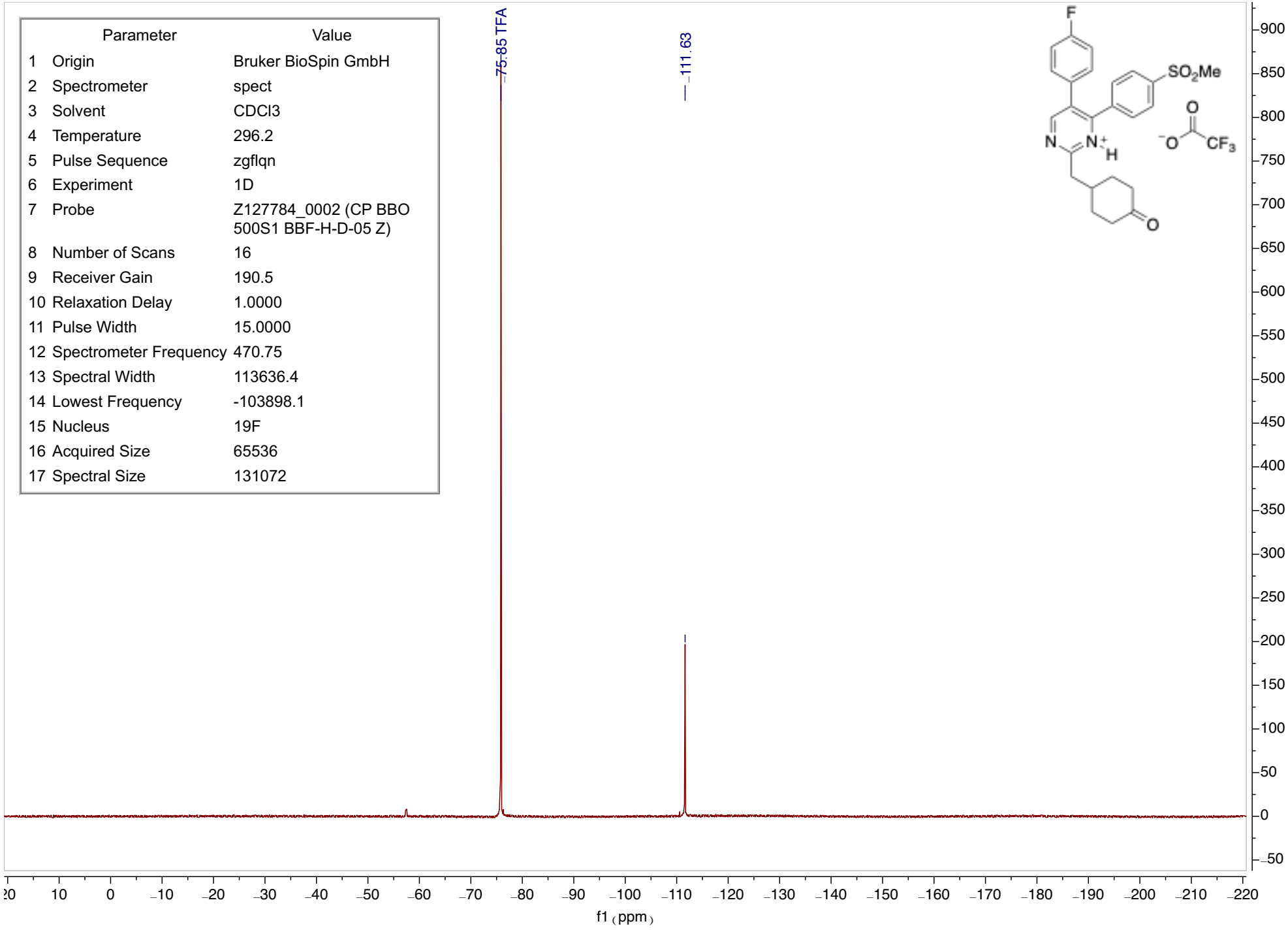



F
SO2Me
O
O
CF3
N
N+
H
O
7.26 CDCl3
3.78 TFA
2.01 H2O
1.00
2.08
2.04
2.07
2.08
1.78
3.24
1.06
3.93
1.97
1.94
f1 (ppm)

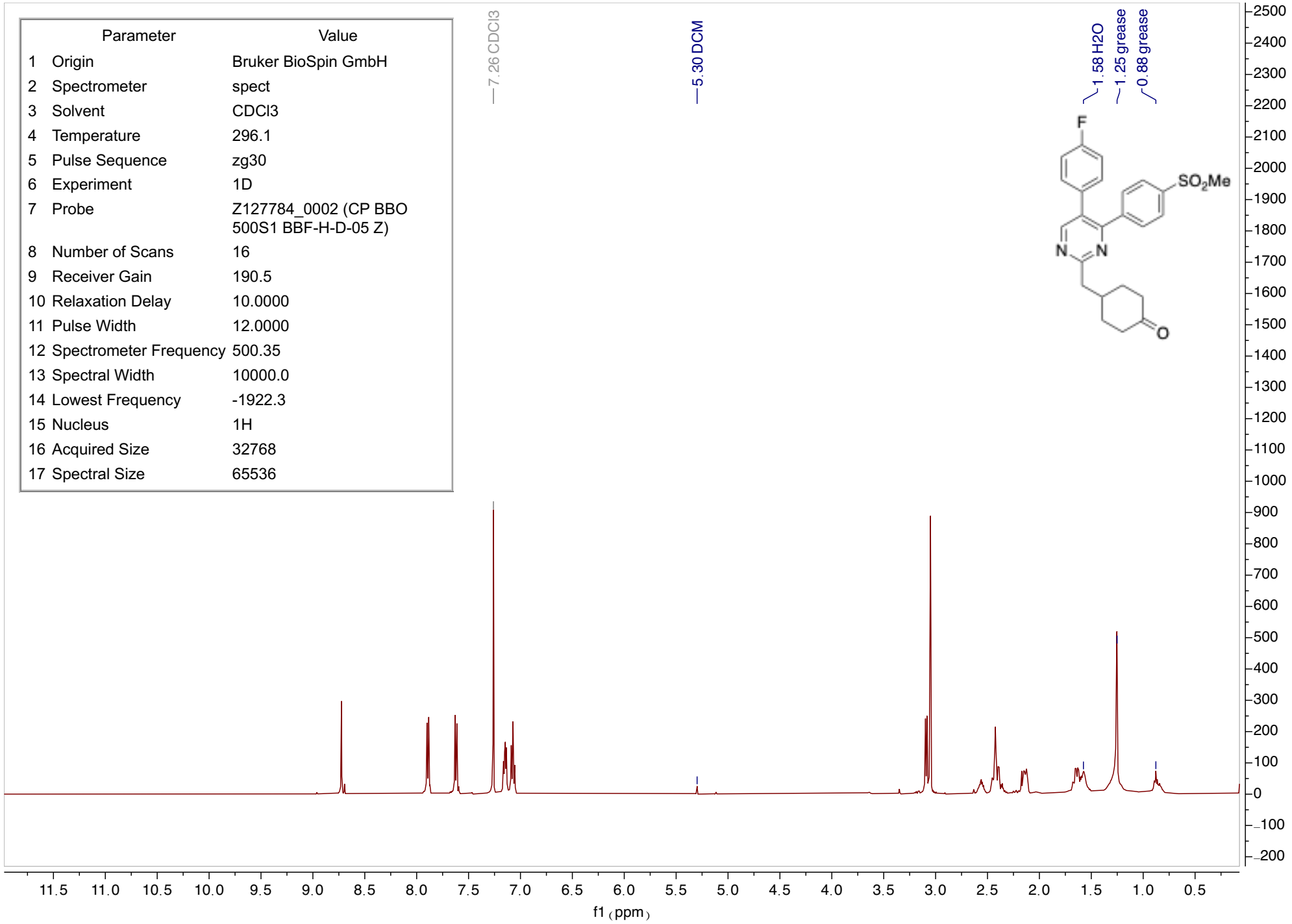


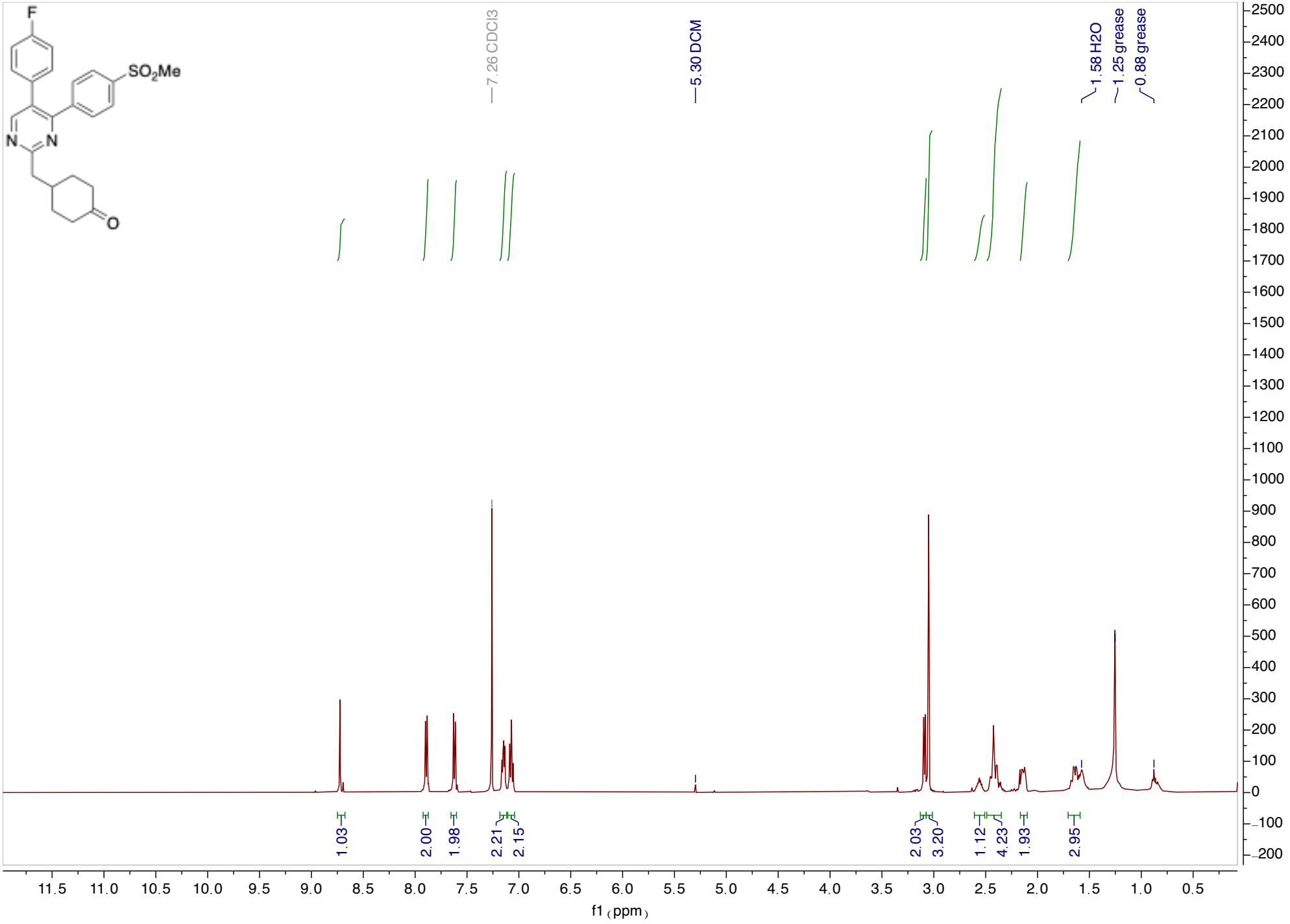
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

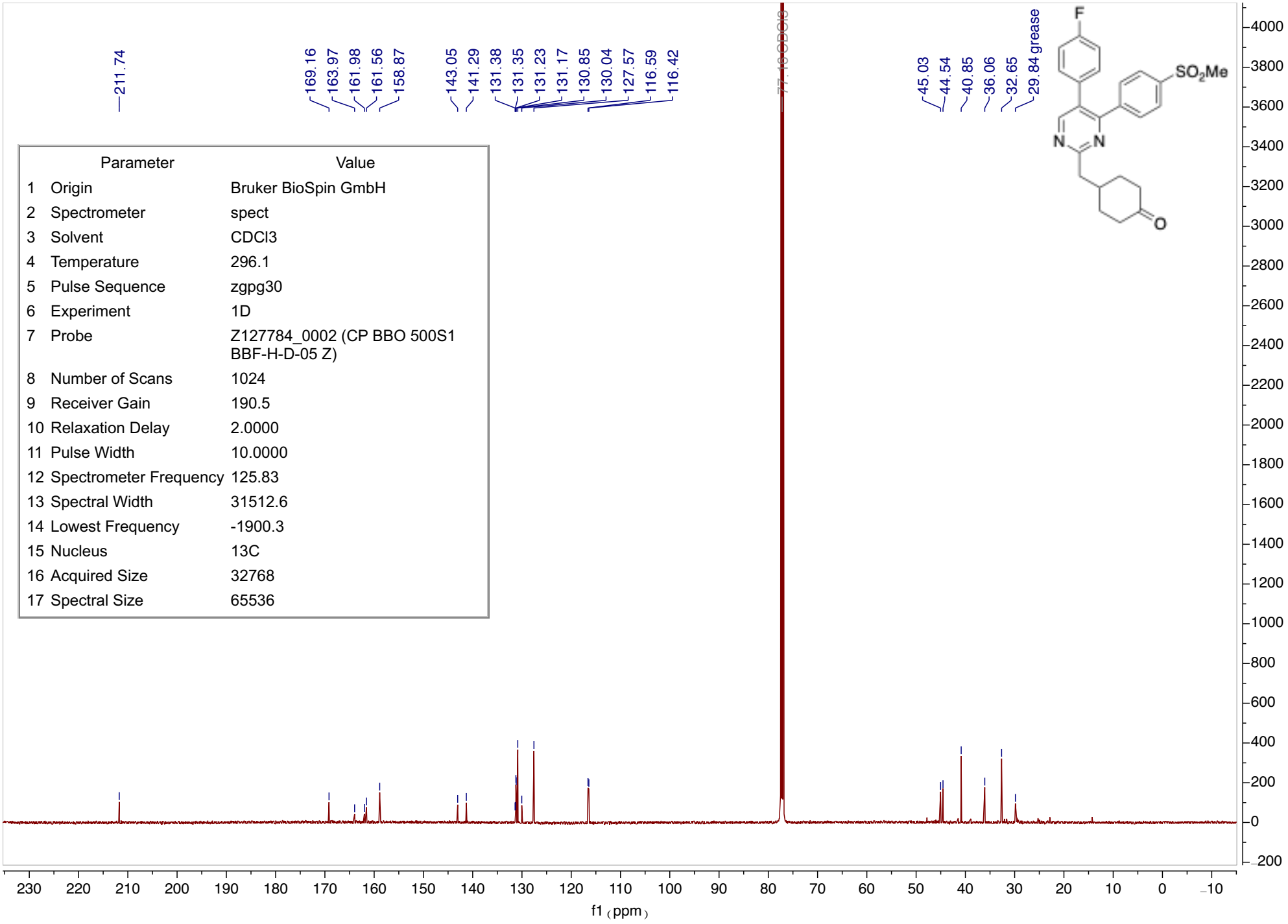
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

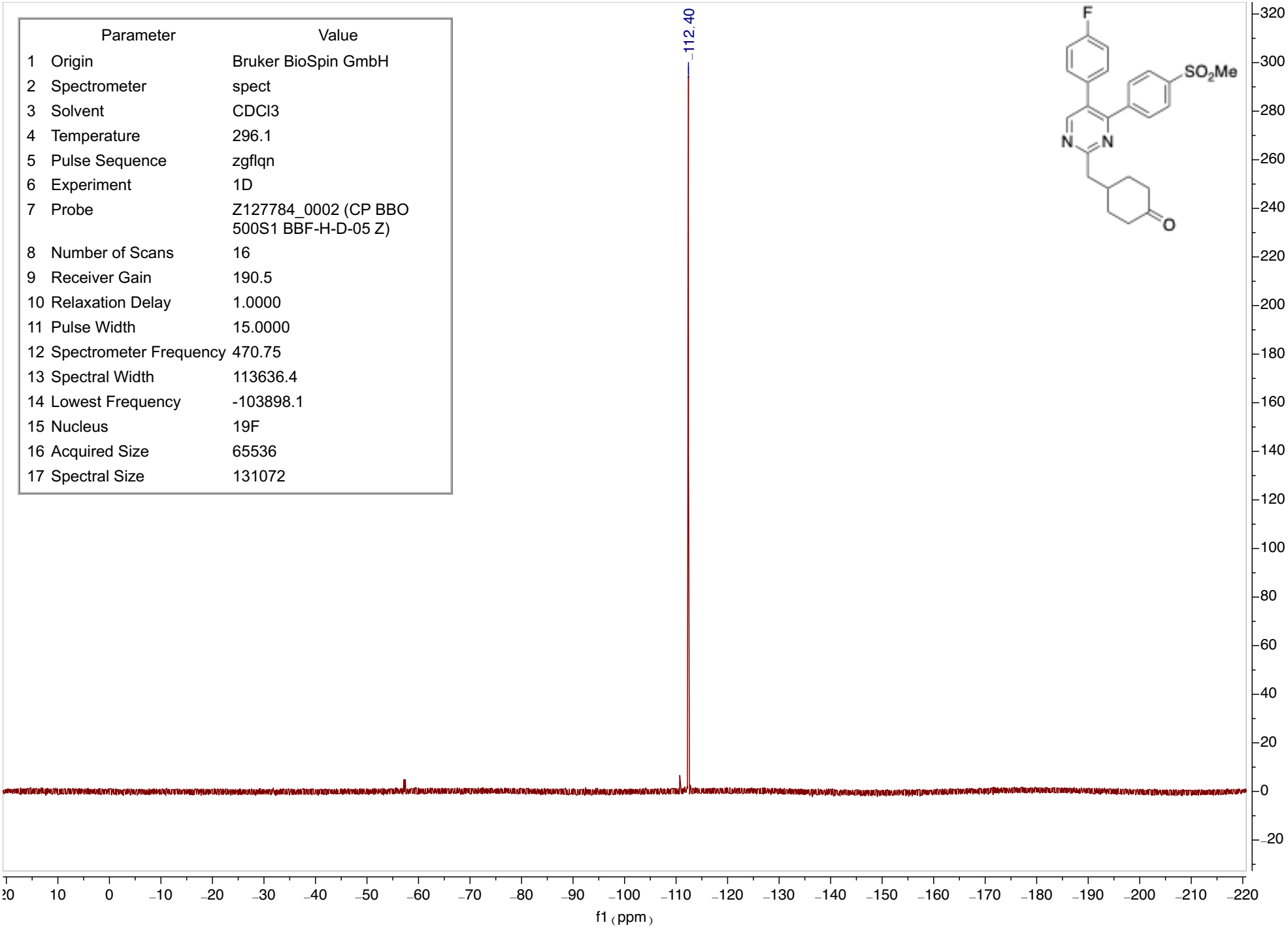



F
SO2Me
N
N
O
7.26 CDCl3
5.30 DCM
1.58 H2O
1.25 grease
0.88 grease
1.03
2.00
1.98
2.21
2.15
2.03
3.20
1.12
4.23
1.93
2.95
f1 (ppm)

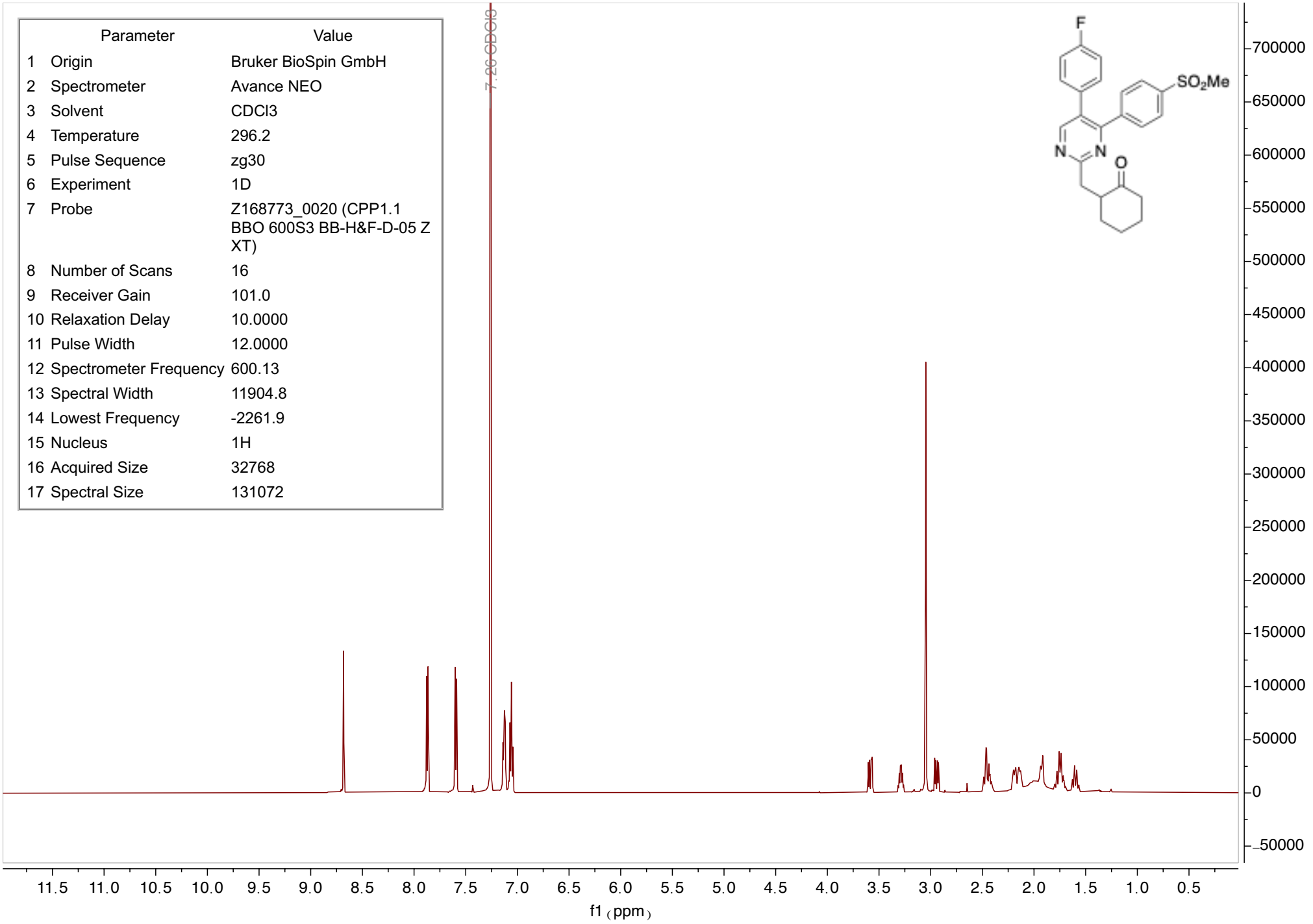


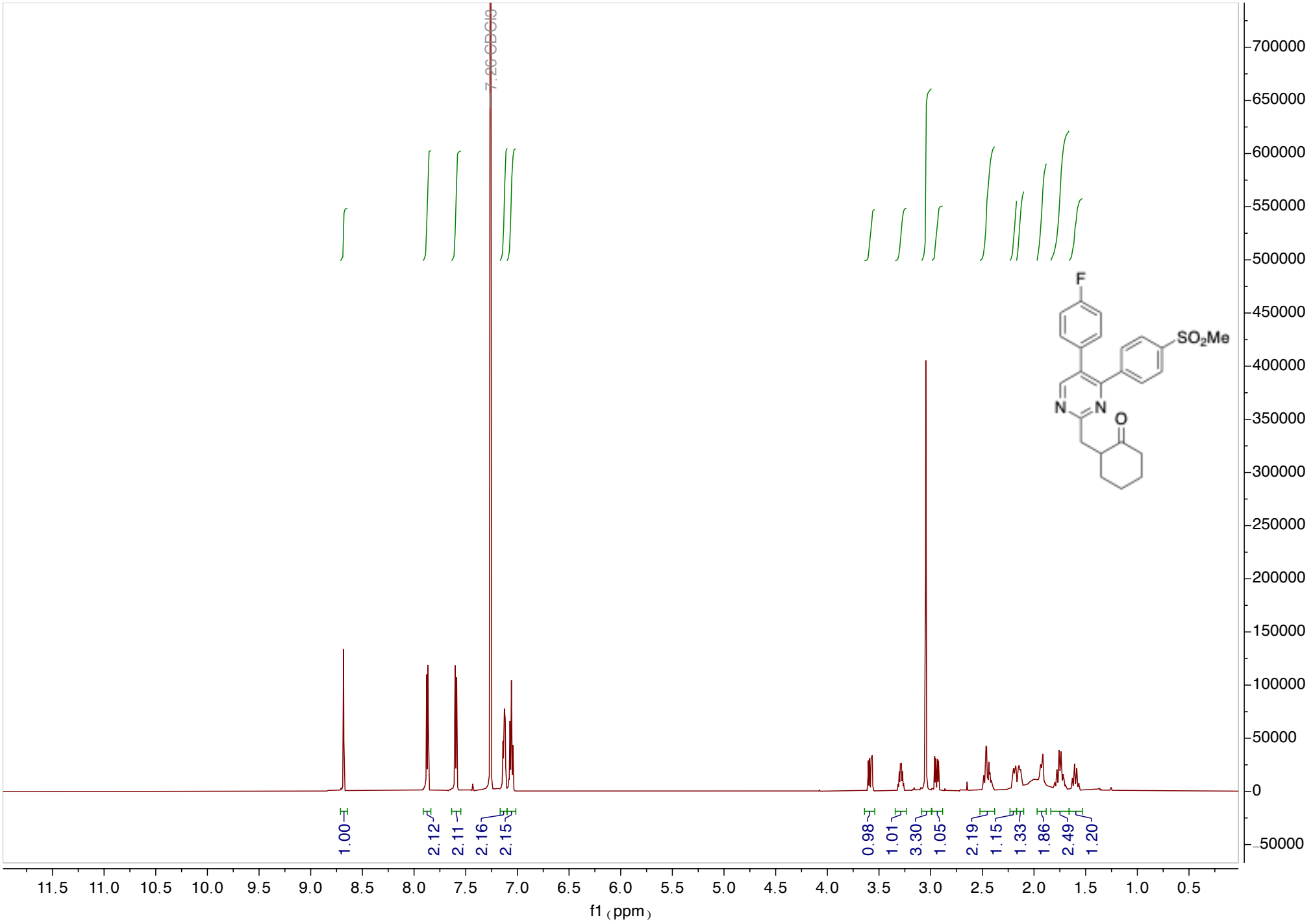
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

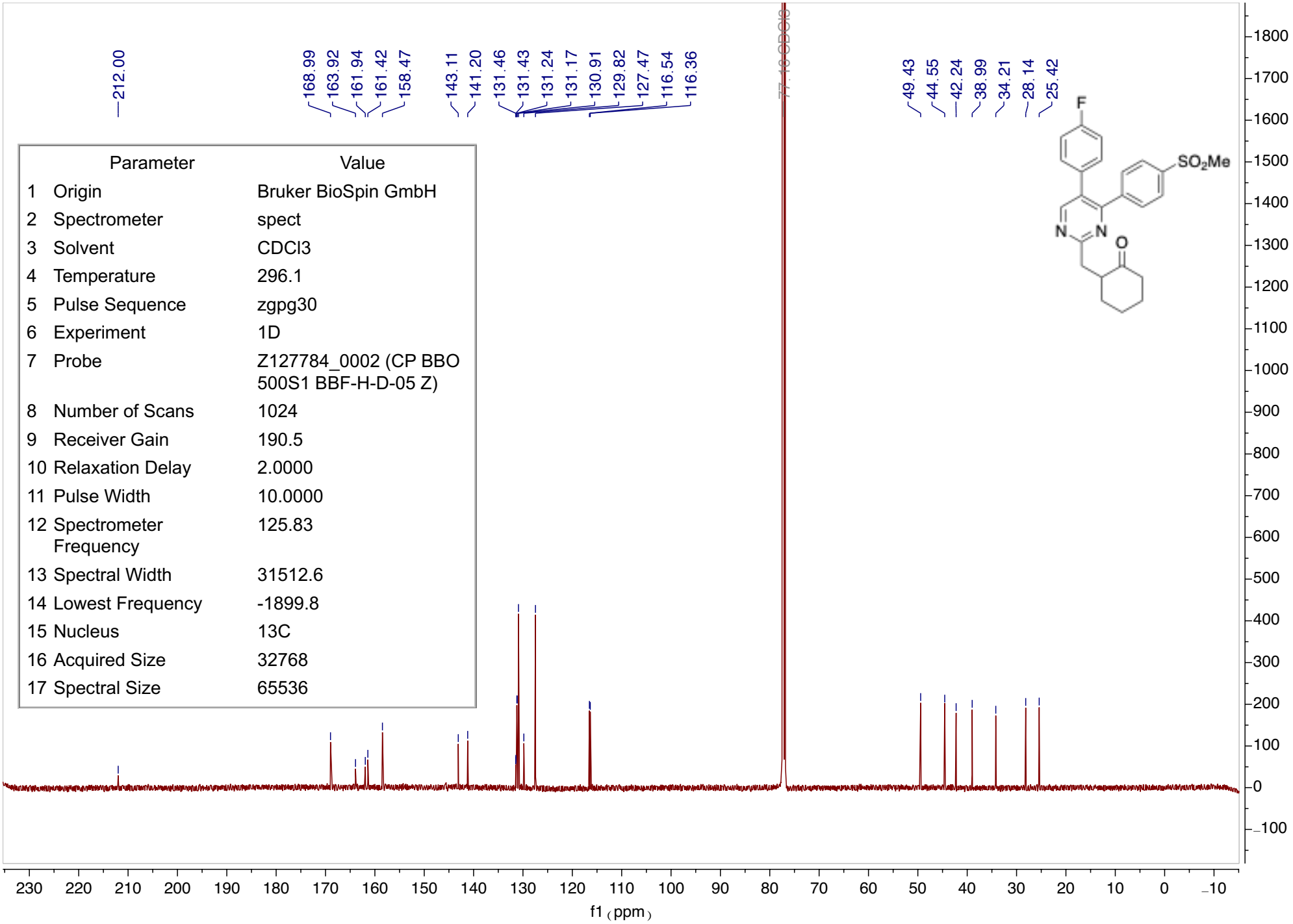
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



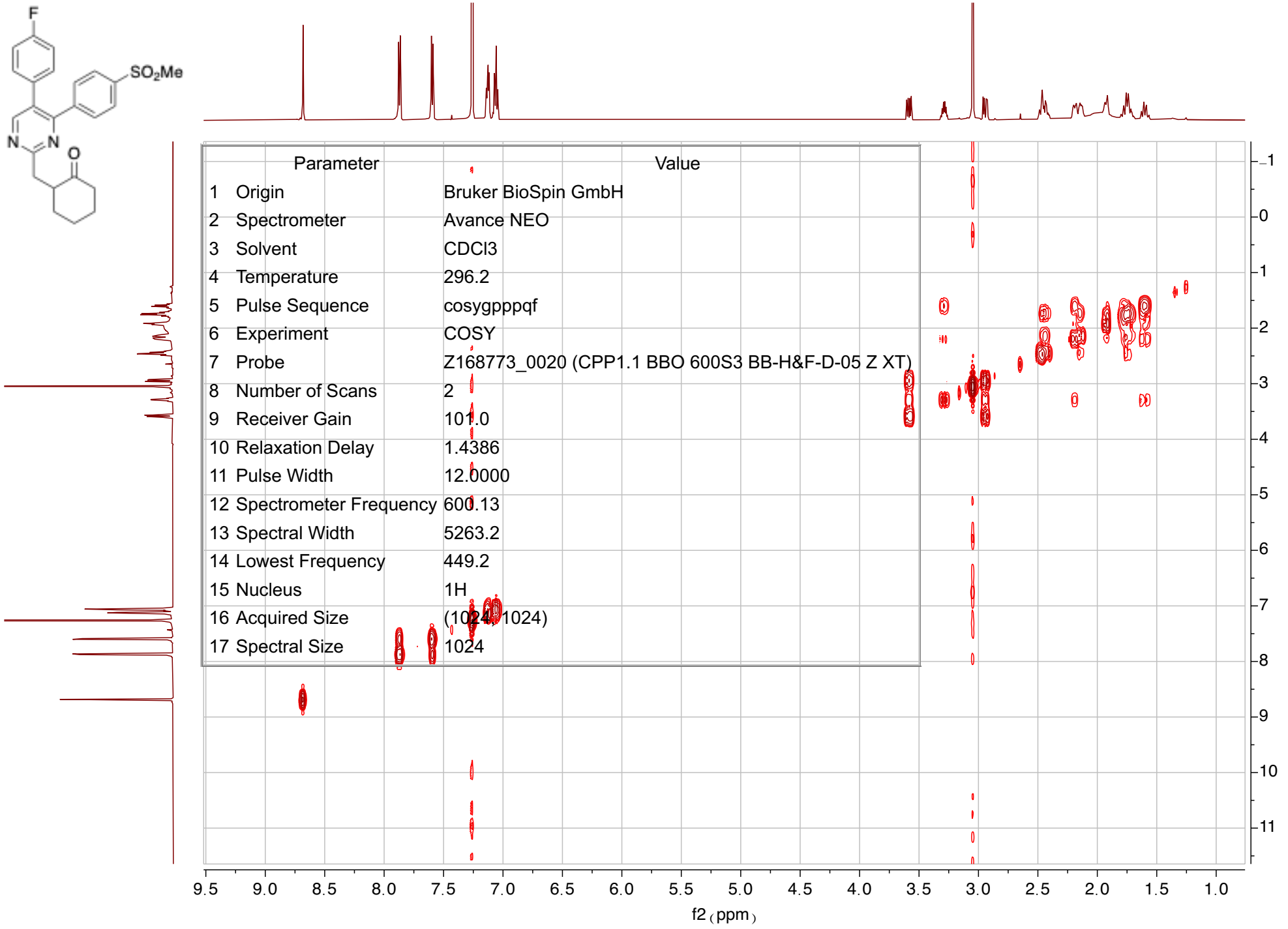
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	101.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2261.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

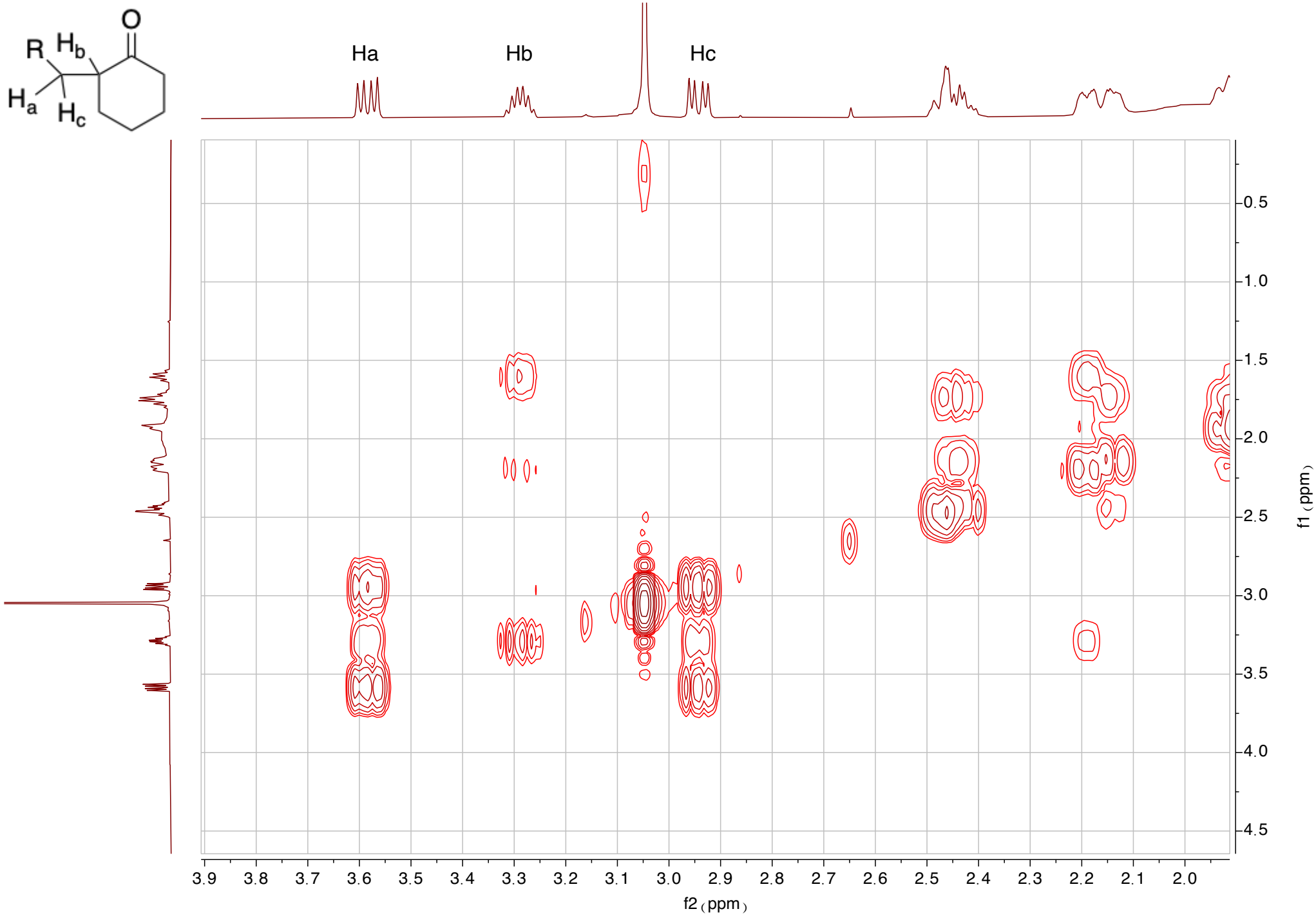


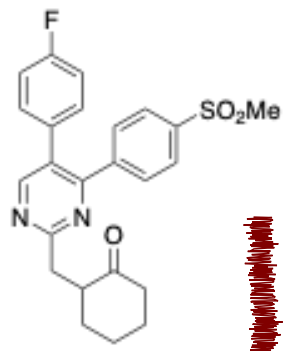

7.26 CDCl3
F
SO2Me
N
N
O
1.00
2.12
2.11
2.16
2.15
0.98
1.01
3.30
1.05
2.19
1.15
1.33
1.86
2.49
1.20
700000
650000
600000
550000
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
-50000
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



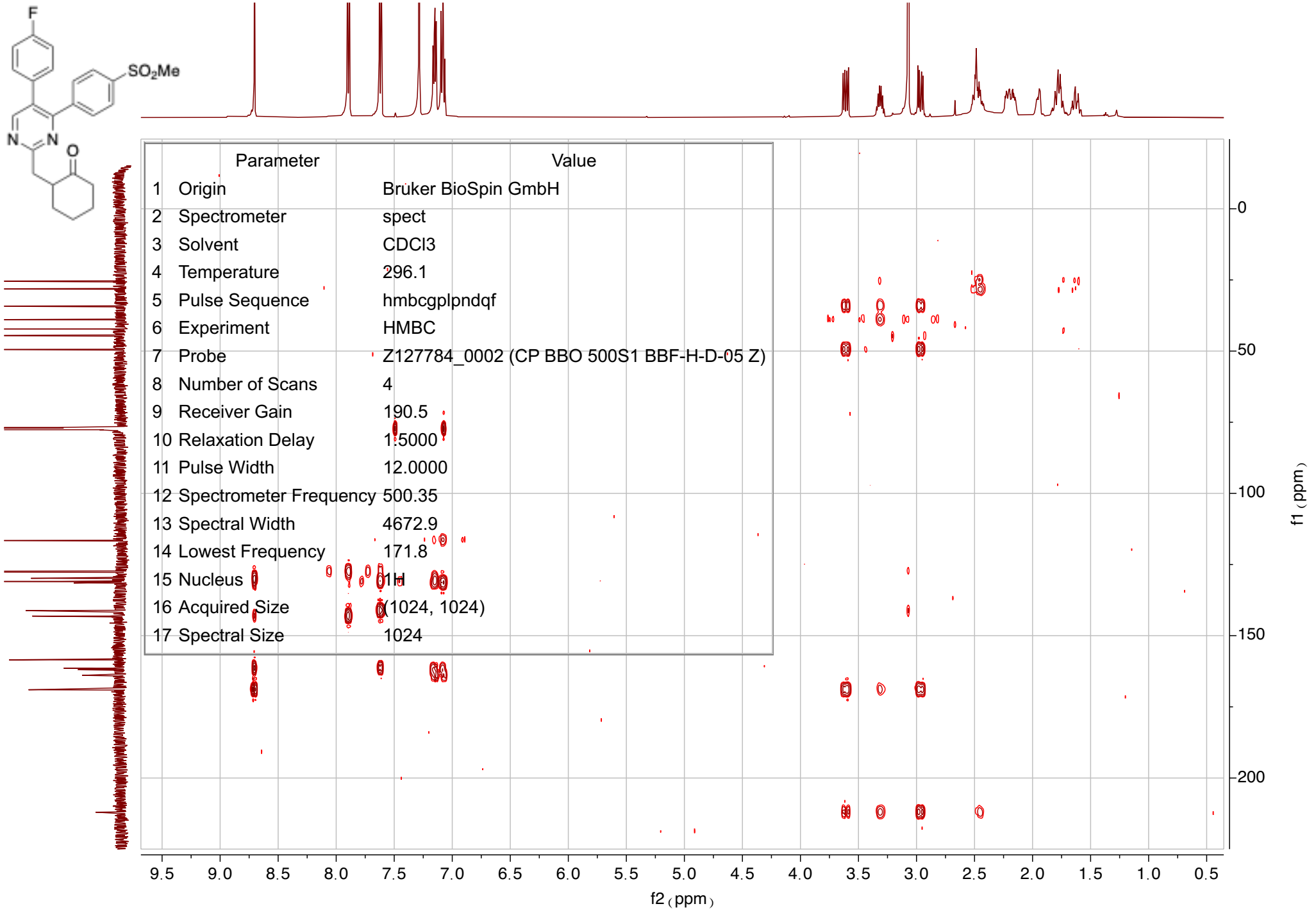
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


F
SO2Me
N
N
O
Parameter
Value
1 Origin
Bruker BioSpin GmbH
2 Spectrometer
Avance NEO
3 Solvent
CDCl3
4 Temperature
296.2
5 Pulse Sequence
cosygpppqf
6 Experiment
COSY
7 Probe
Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans
2
9 Receiver Gain
101.0
10 Relaxation Delay
1.4386
11 Pulse Width
12.0000
12 Spectrometer Frequency
600.13
13 Spectral Width
5263.2
14 Lowest Frequency
449.2
15 Nucleus
1H
16 Acquired Size
(1024, 1024)
17 Spectral Size
1024
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
f2 (ppm)
-1 0 1 2 3 4 5 6 7 8 9 10 11
f1 (ppm)

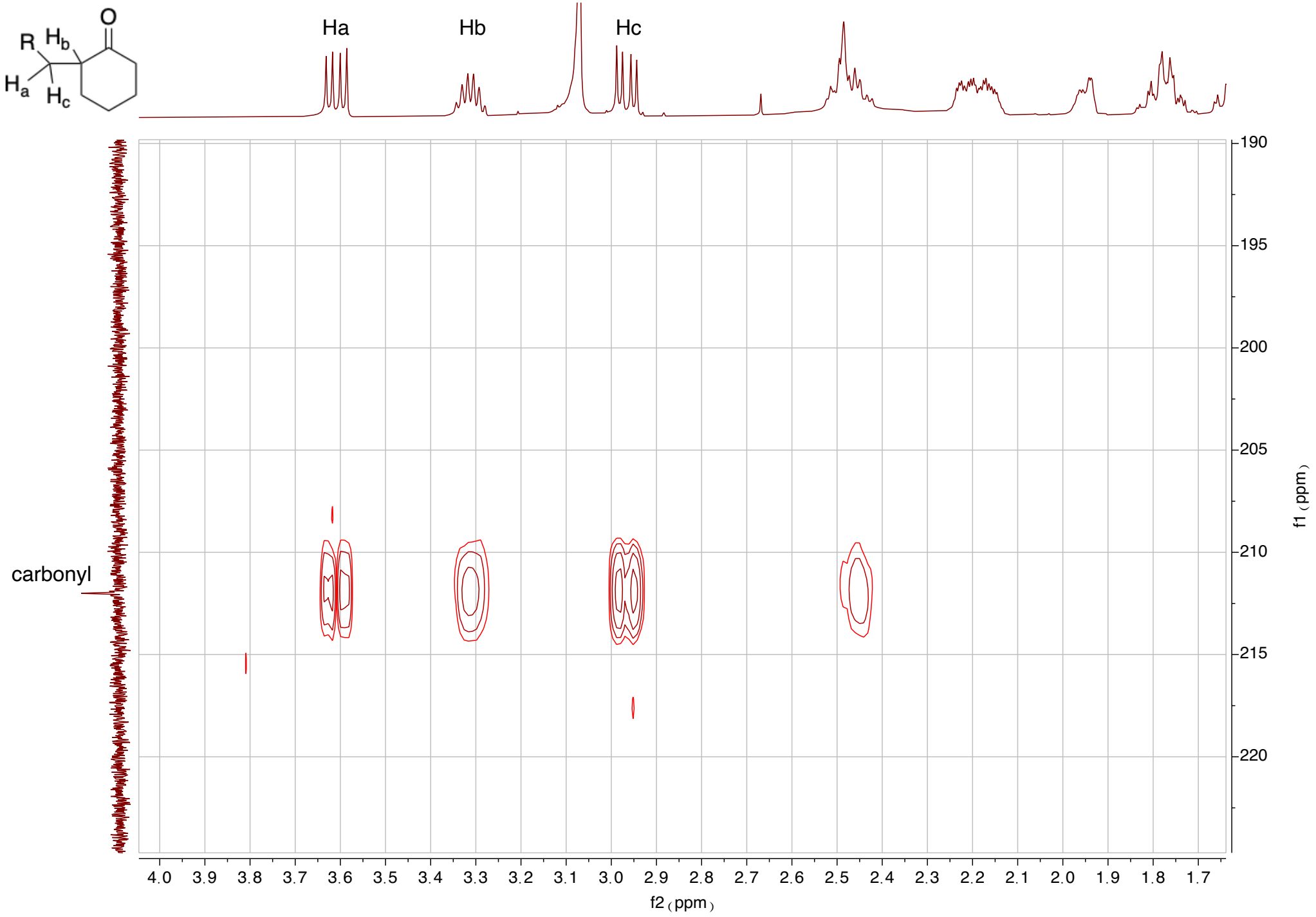

O
R
Hb
Ha
Hc
Ha
Hb
Hc
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
f2 (ppm)



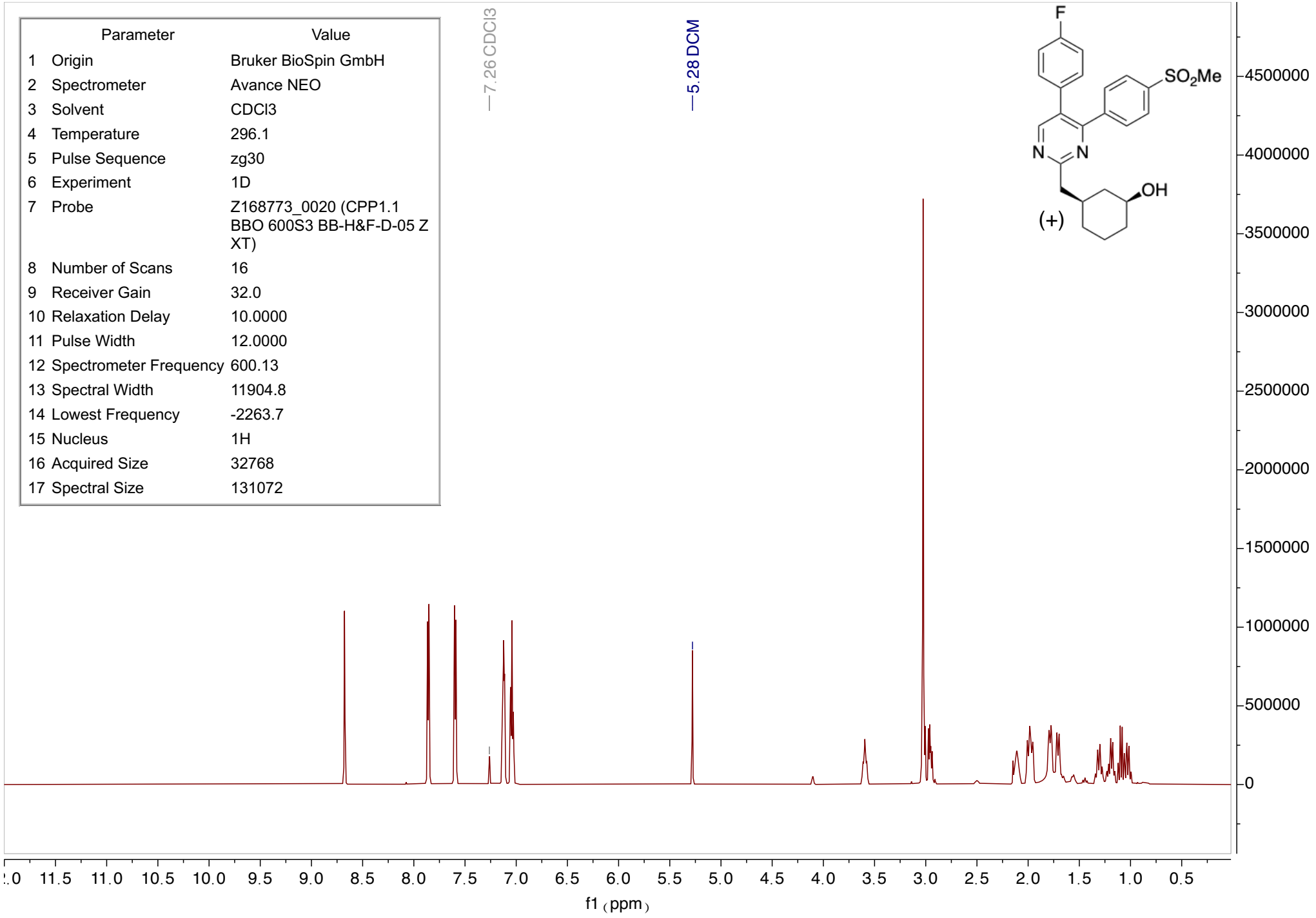
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5263.2
14	Lowest Frequency	447.8
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

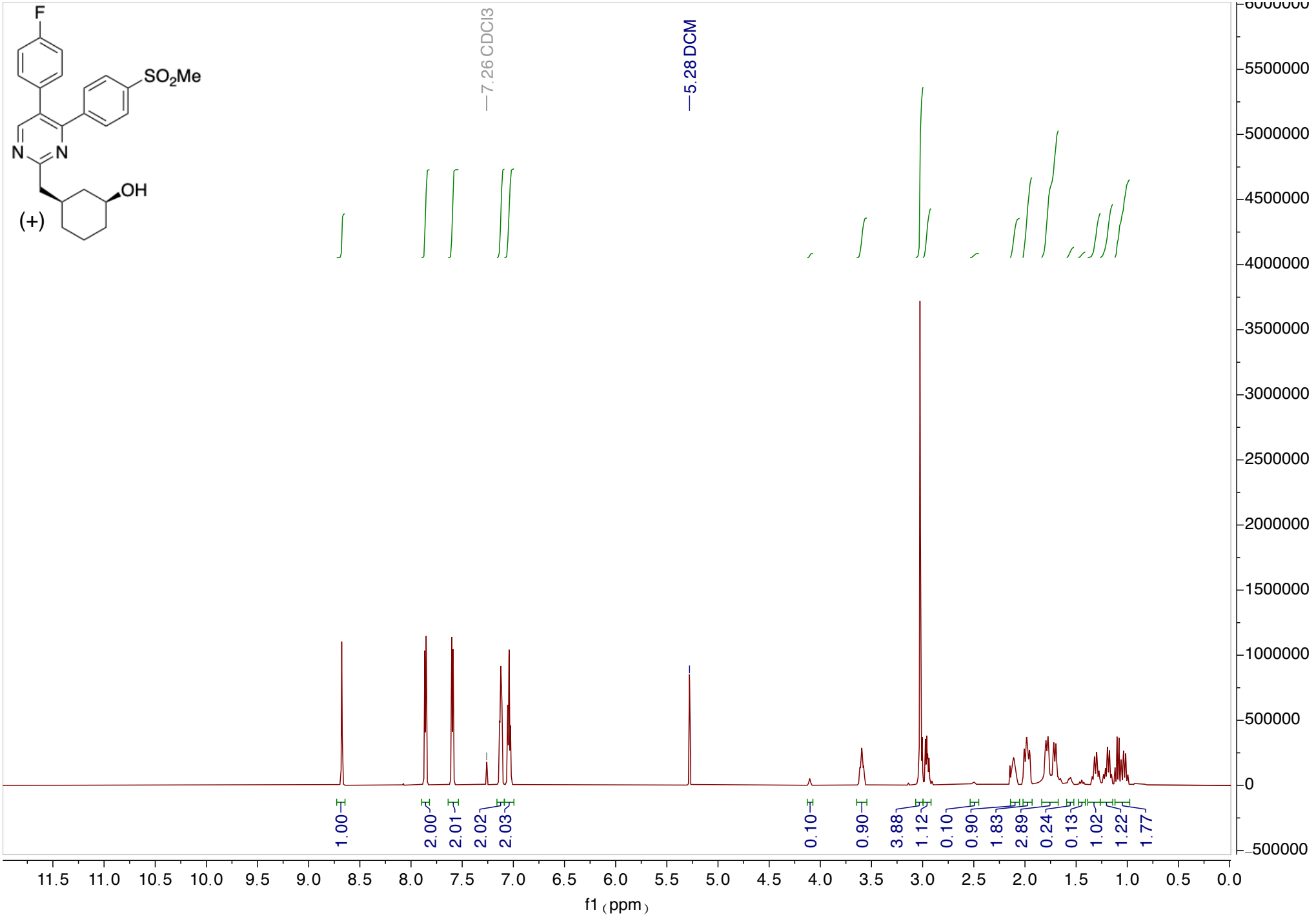

F
SO2Me
N
N
O
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4672.9
14 Lowest Frequency 171.8
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
0
50
100
150
200
f1 (ppm)
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
f2 (ppm)

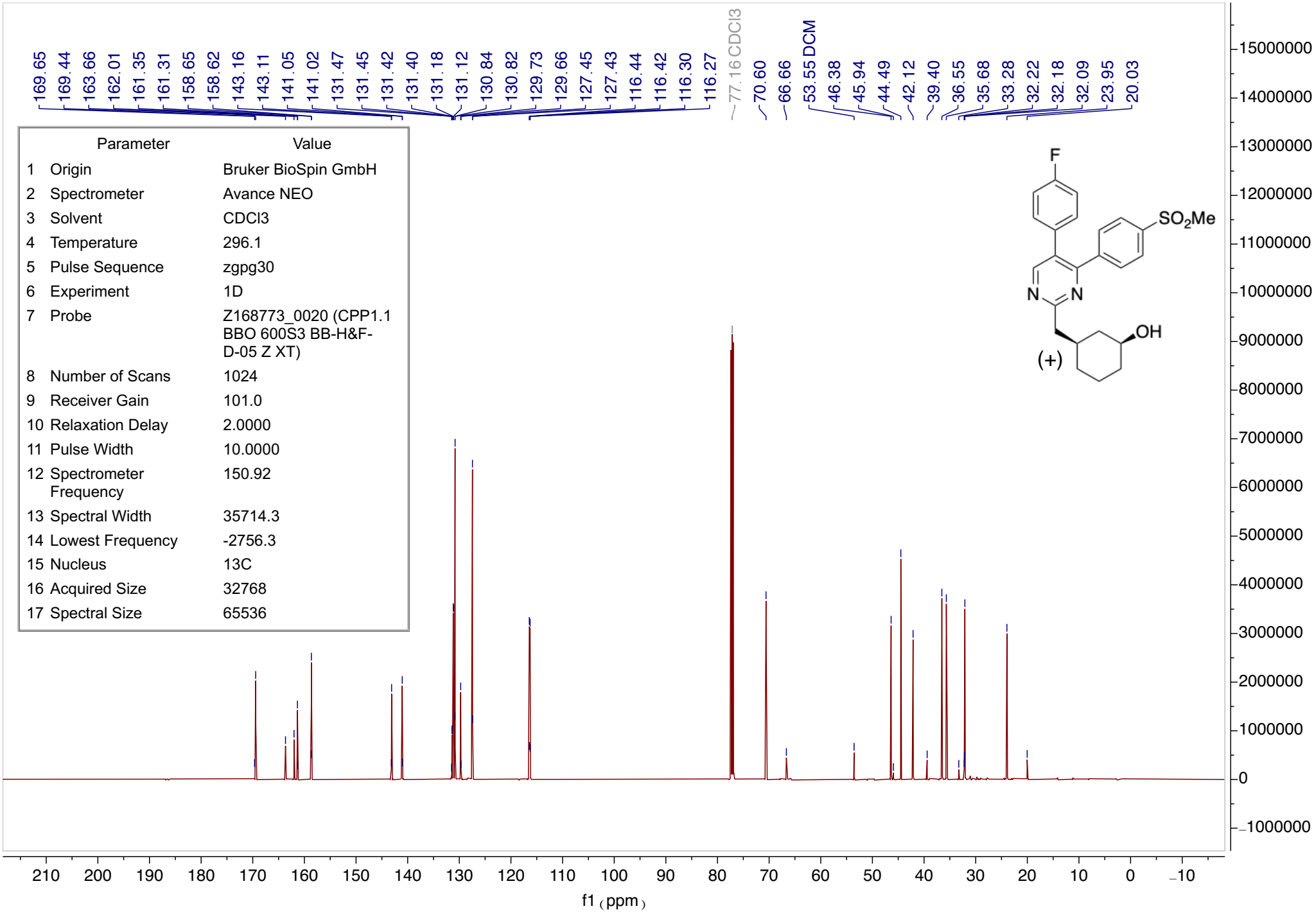
700


O
R
Hb
Ha
Hc
Ha
Hb
Hc
carbonyl
190
195
200
205
210
215
220
f1 (ppm)
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2263.7
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

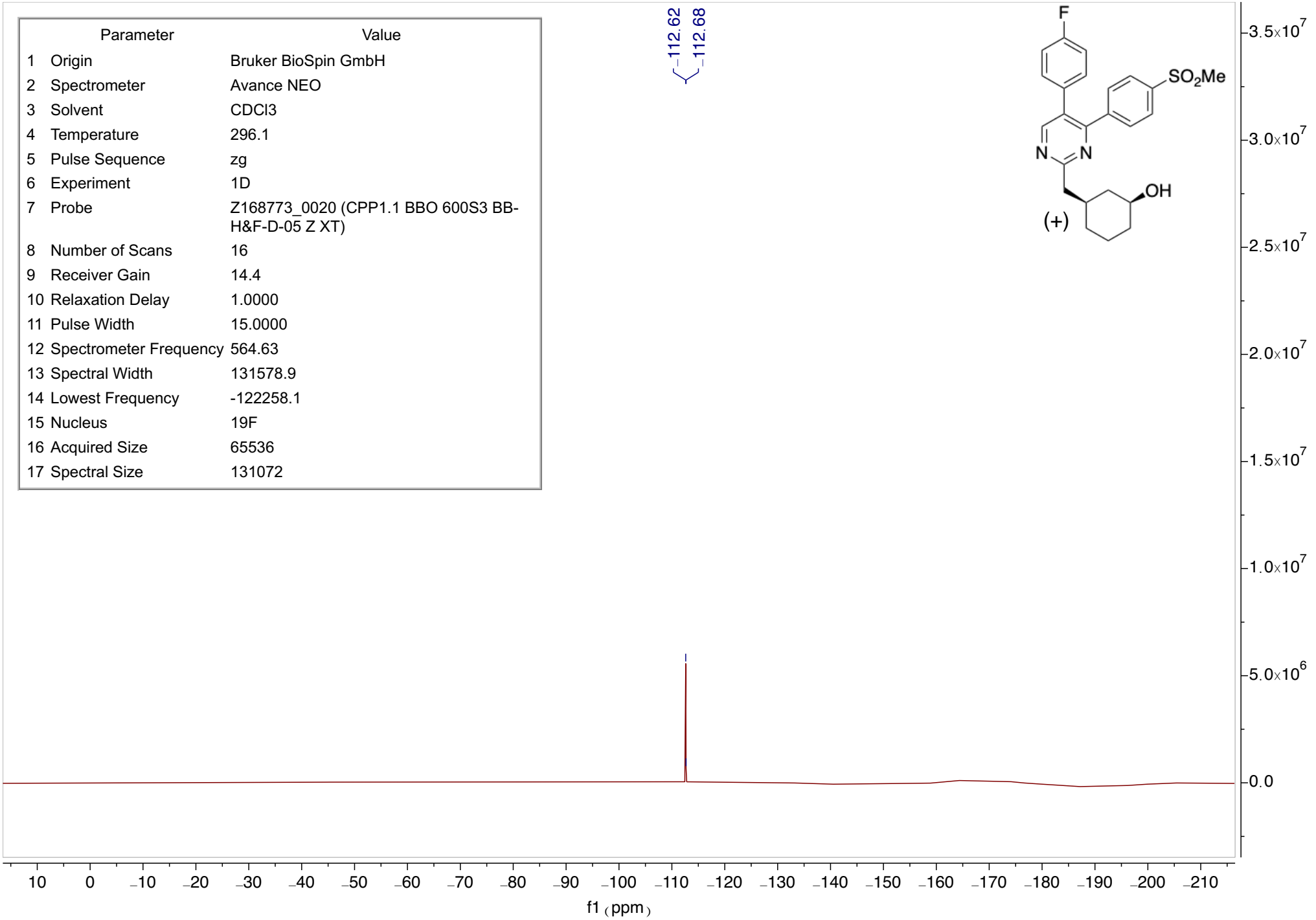


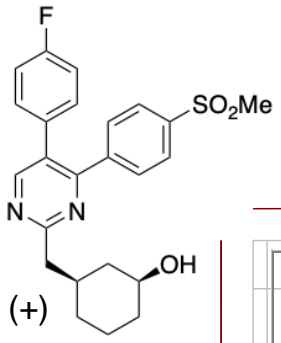

F
SO2Me
N
N
OH
(+)
7.26 CDCl3
5.28 DCM
1.00
2.00
2.01
2.02
2.03
0.10
0.90
3.88
1.12
0.10
0.90
1.83
2.89
0.24
0.13
1.02
1.22
1.77
f1 (ppm)



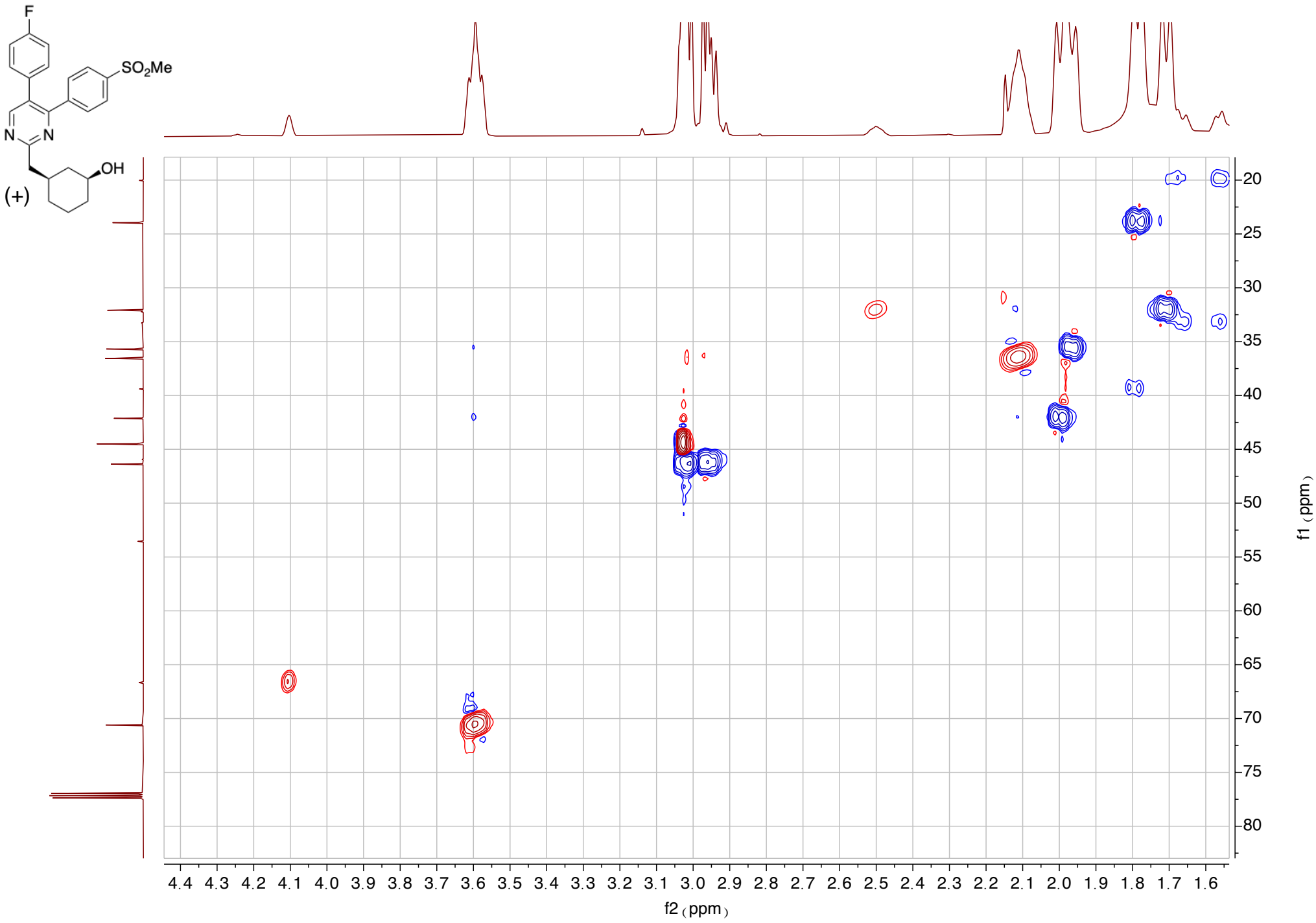
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2756.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

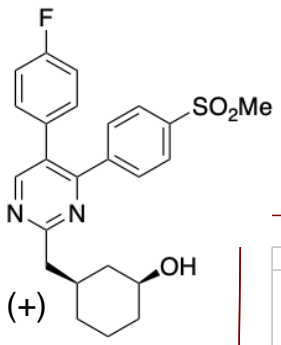
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	14.4
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



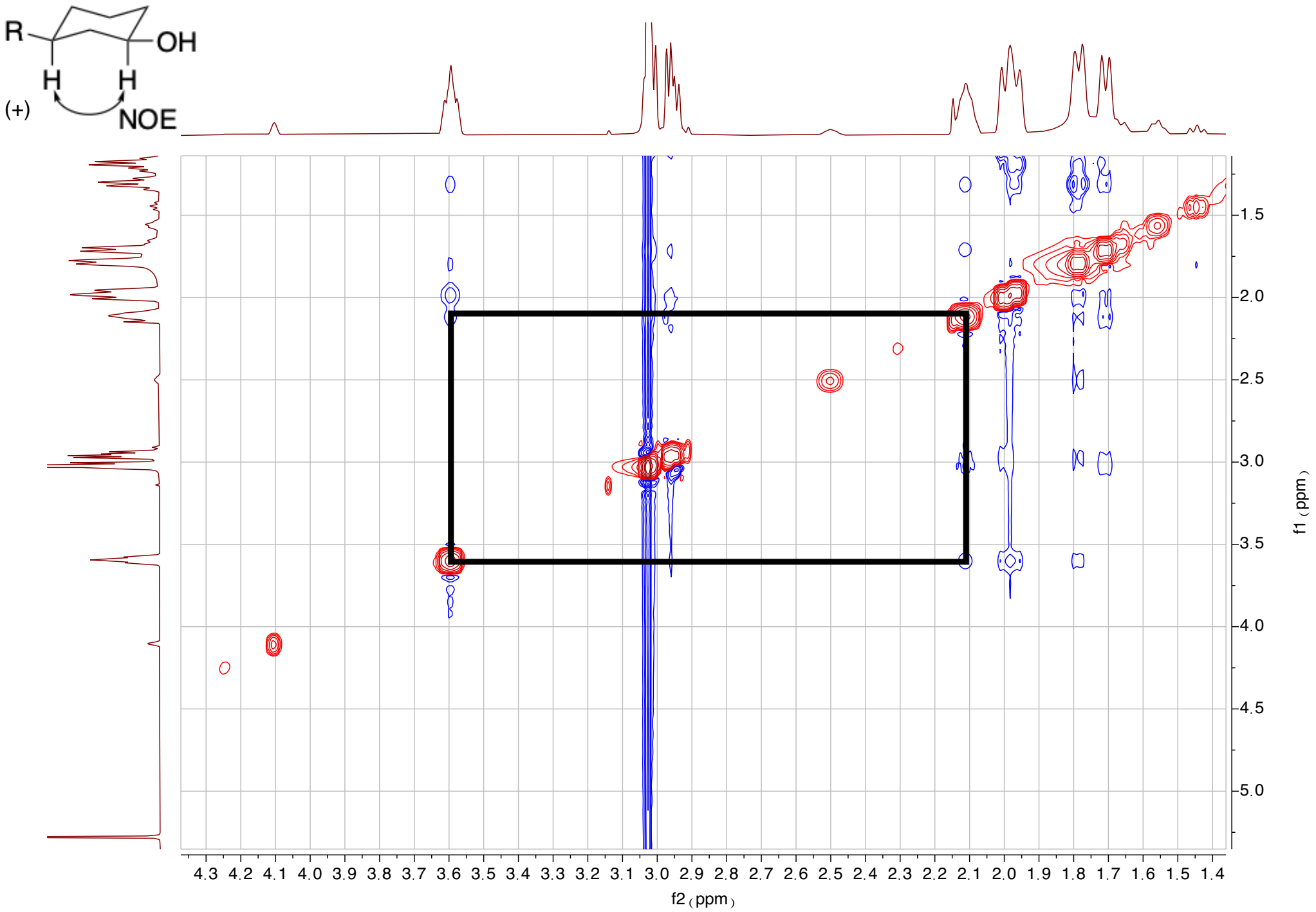


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-131.4
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

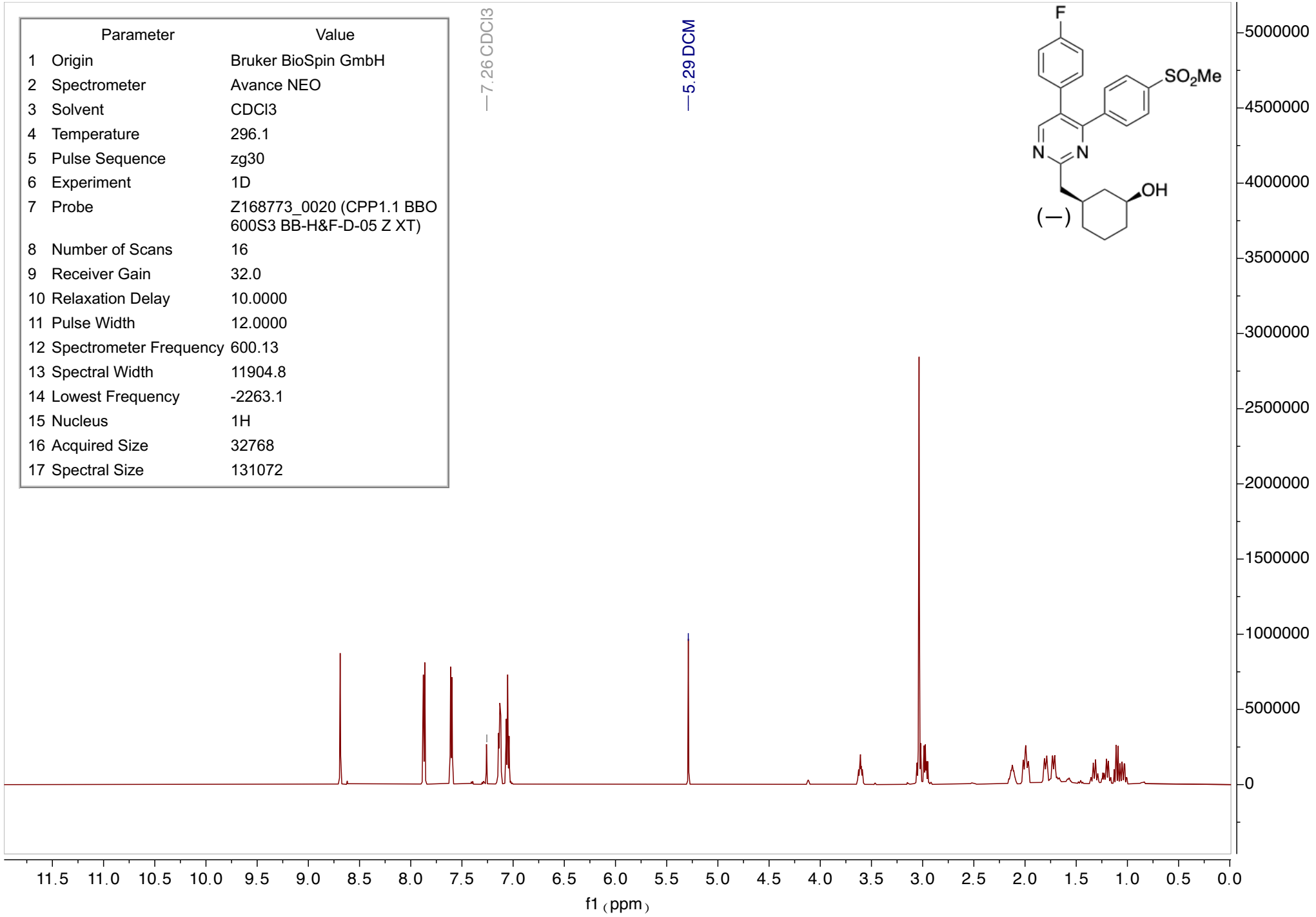

F
SO2Me
N
N
OH
(+)
4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6
f2 (ppm)
20 25 30 35 40 45 50 55 60 65 70 75 80
f1 (ppm)

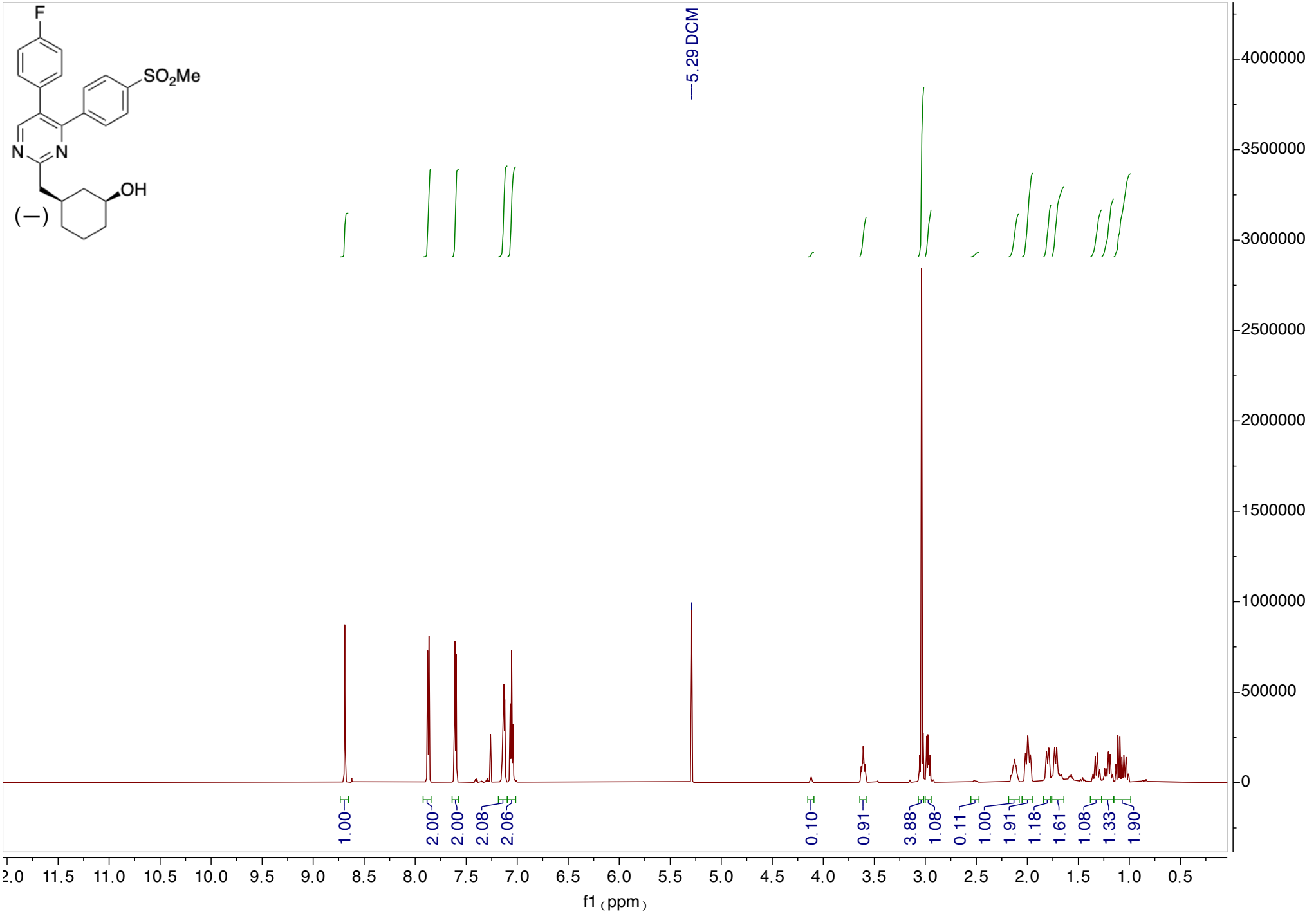


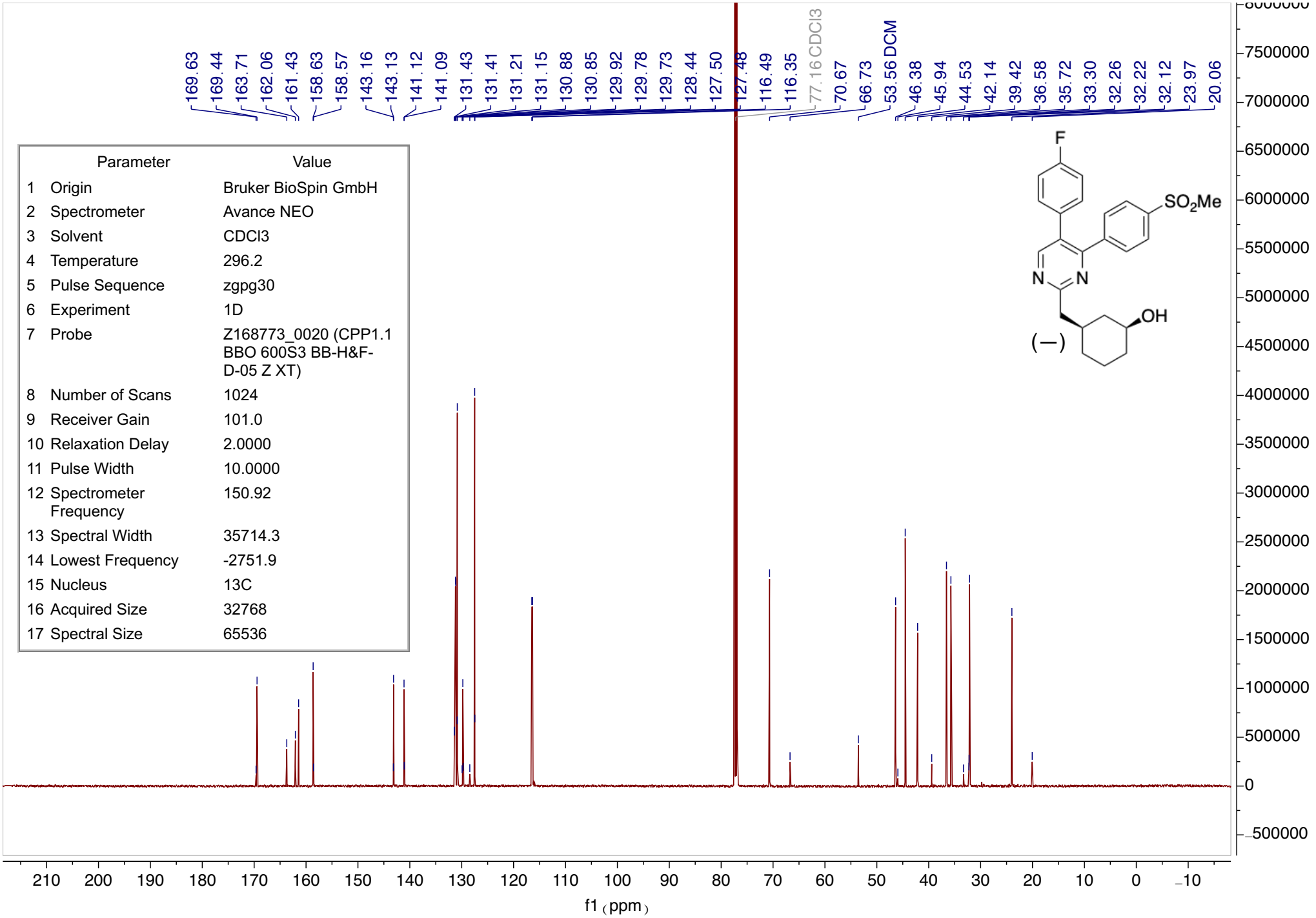
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	noesygpphpp
6	Experiment	NOESY
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-131.4
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


R
OH
H
H
(+)
NOE
f2 (ppm)
f1 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	32.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	11904.8
14	Lowest Frequency	-2263.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	131072

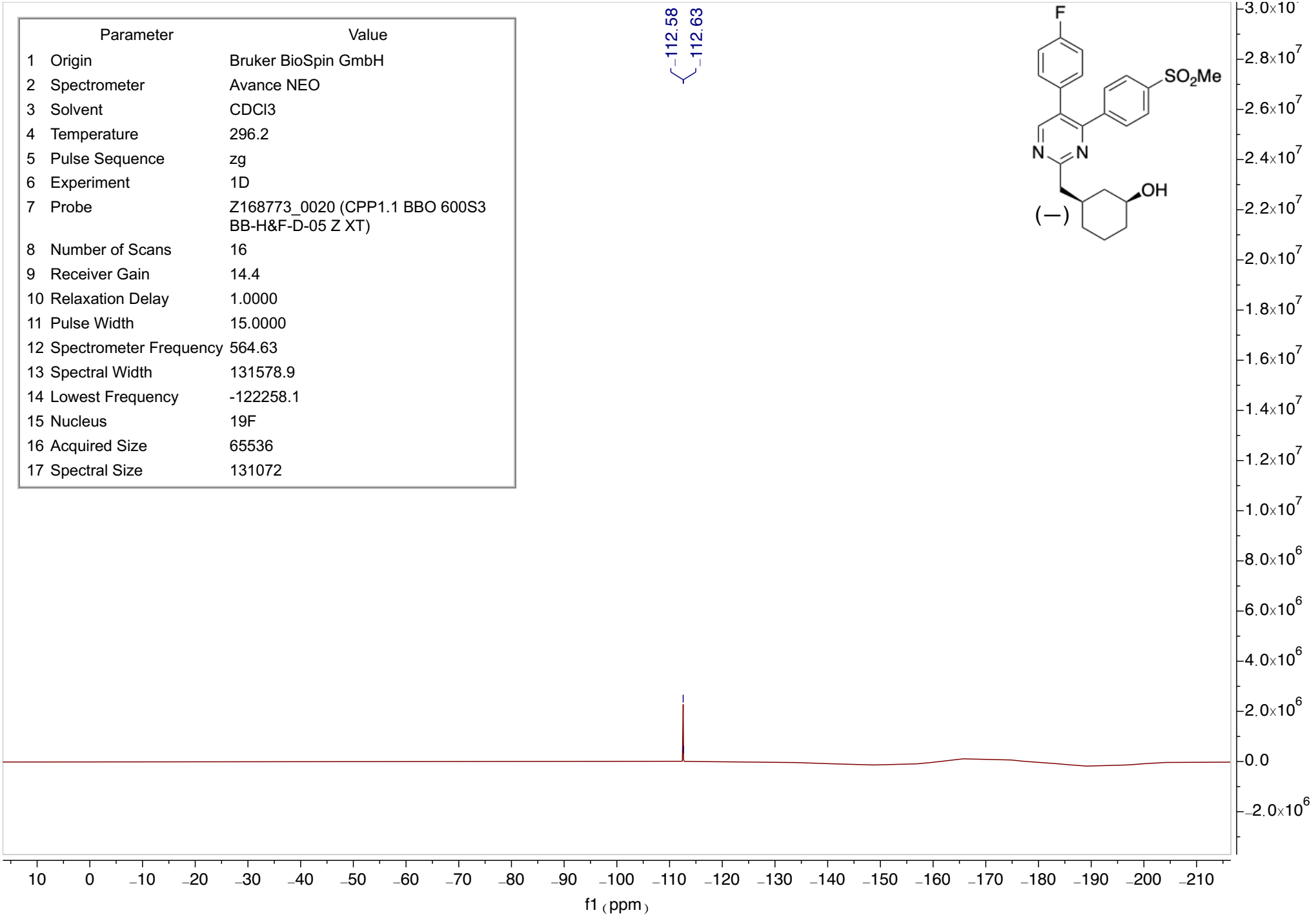


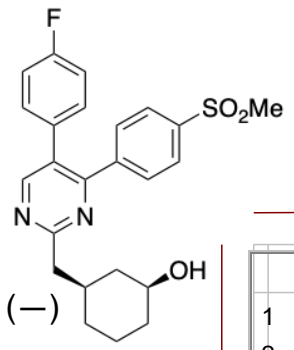

F
SO2Me
N
N
OH
(—)
5.29 DCM
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
1.00
2.00
2.00
2.08
2.06
0.10
0.91
3.88
1.08
0.11
1.00
1.91
1.18
1.61
1.08
1.33
1.90
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



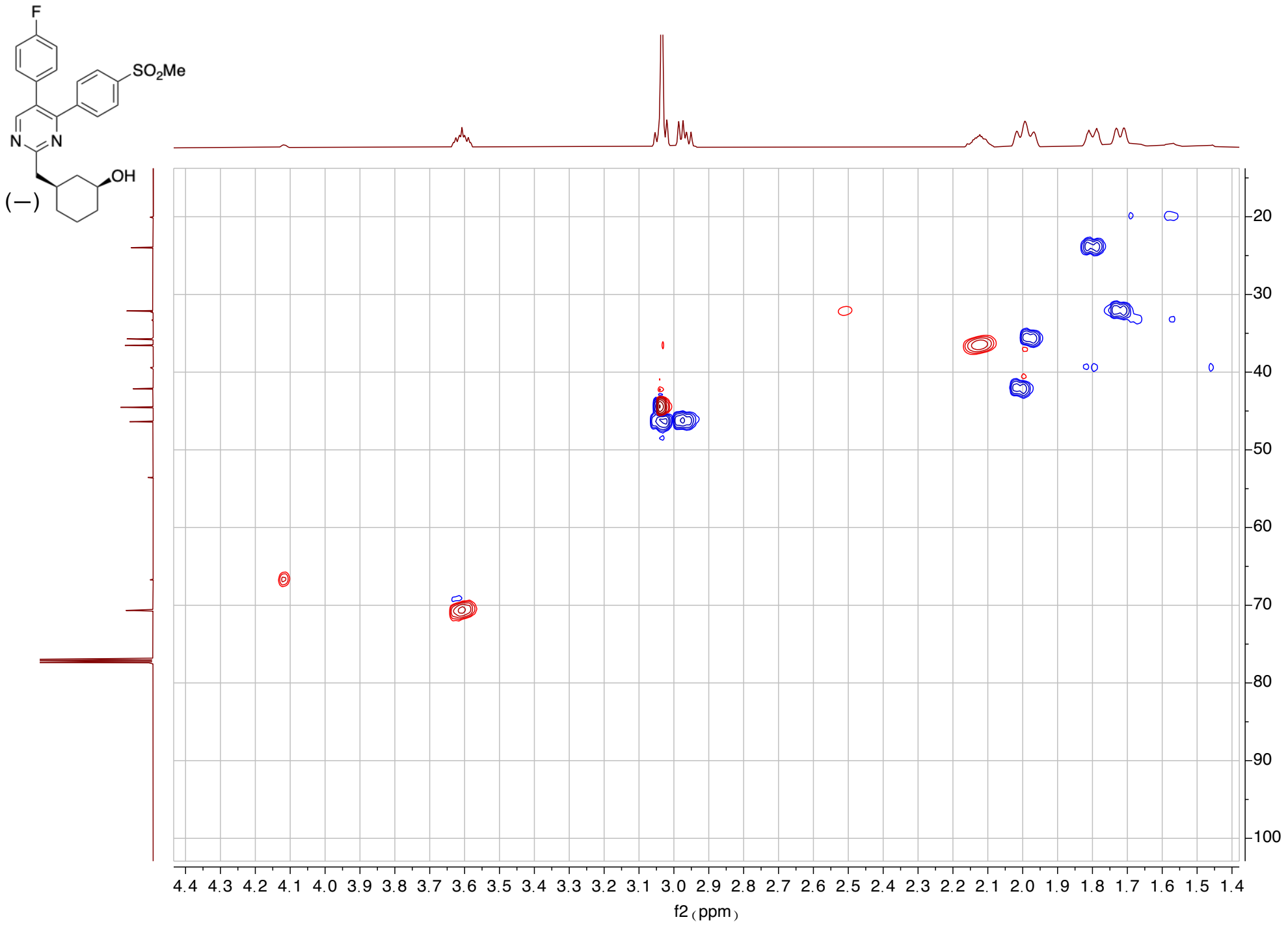
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2751.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

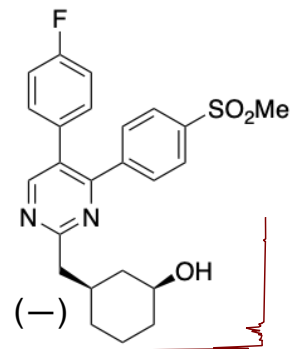
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	14.4
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



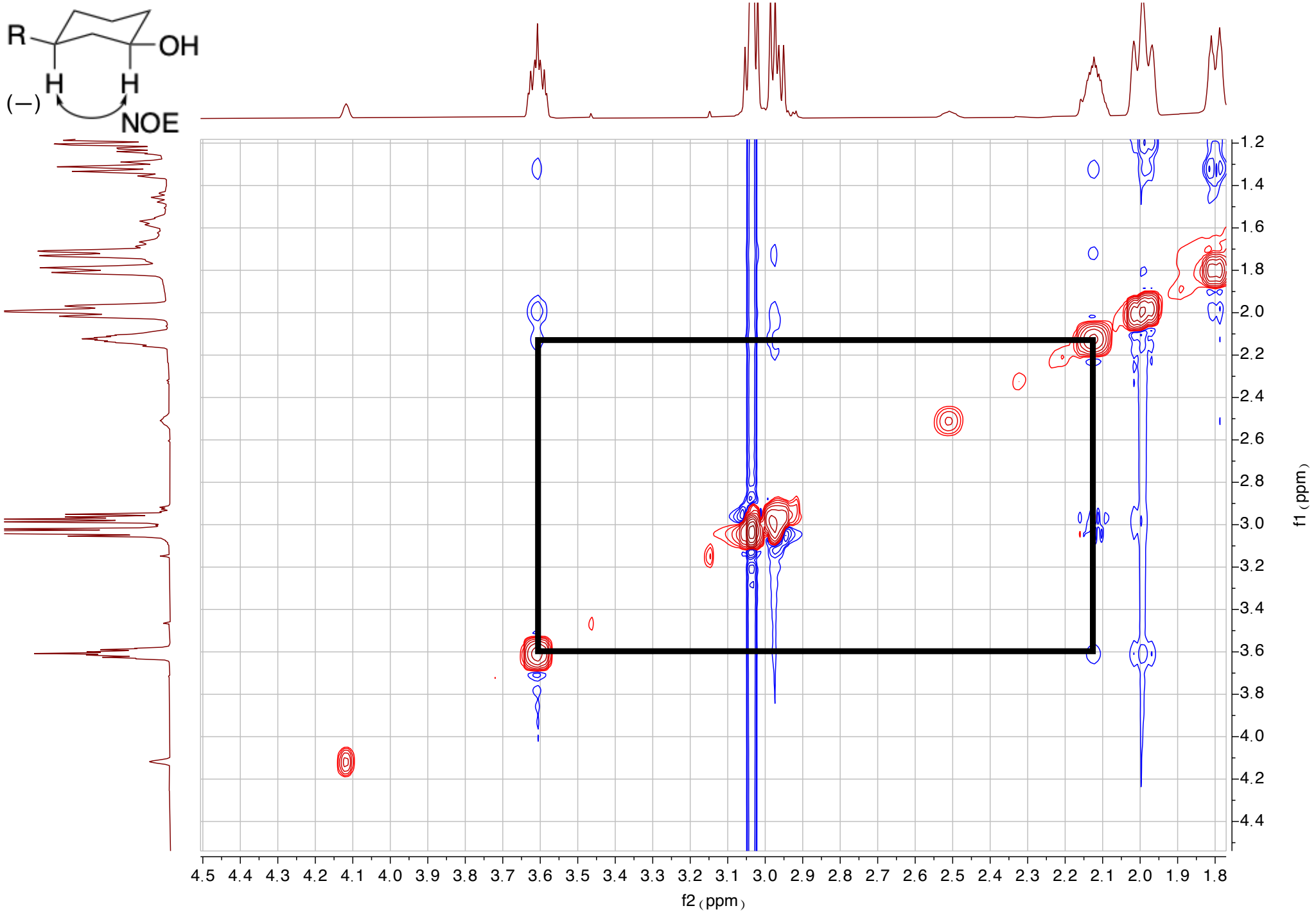


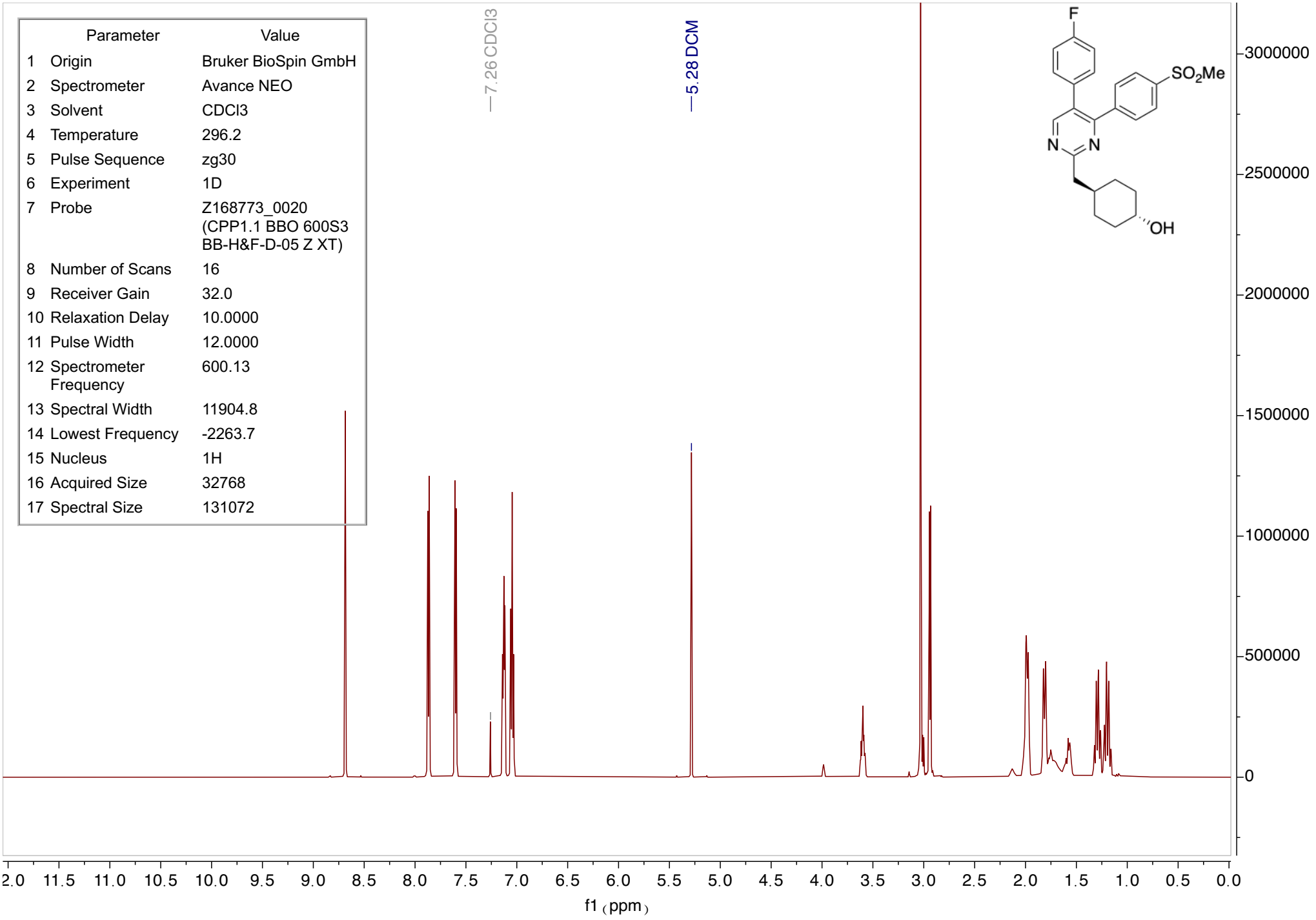
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-93.4
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

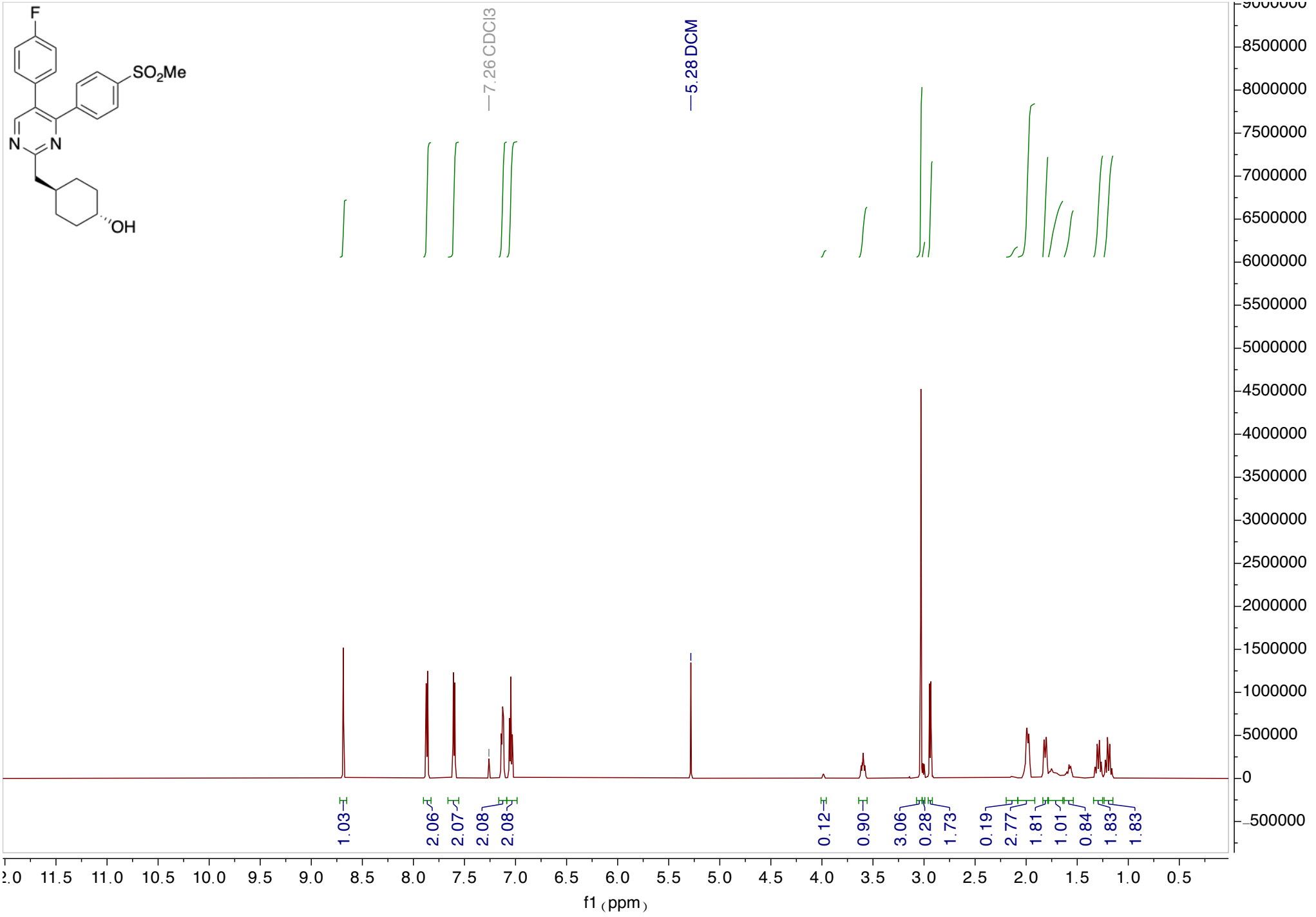

F
SO2Me
N
N
OH
(—)
f2 (ppm)
f1 (ppm)
4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4
20
30
40
50
60
70
80
90
100

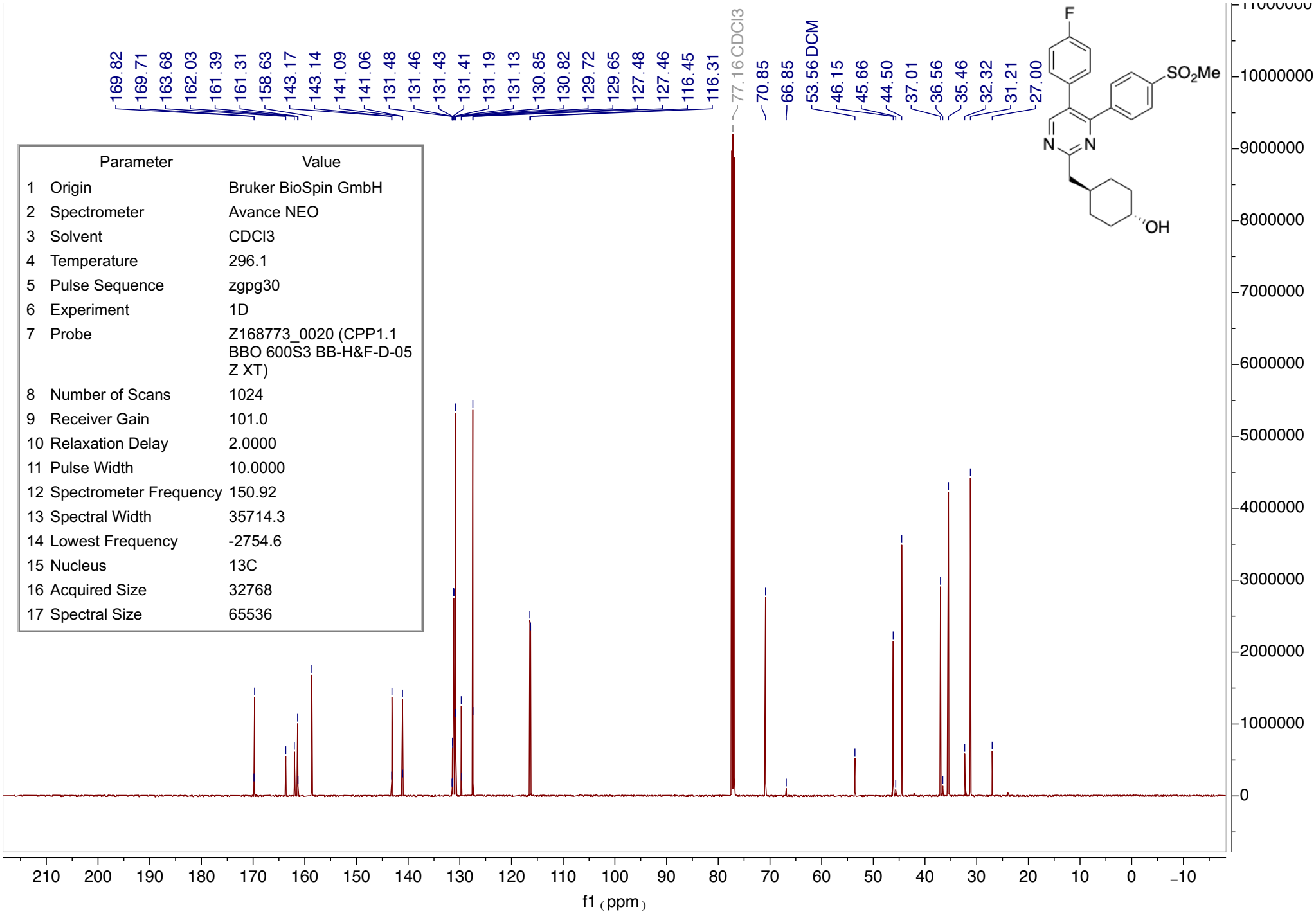


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	noesygpphpp
6	Experiment	NOESY
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	64.0
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-93.7
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

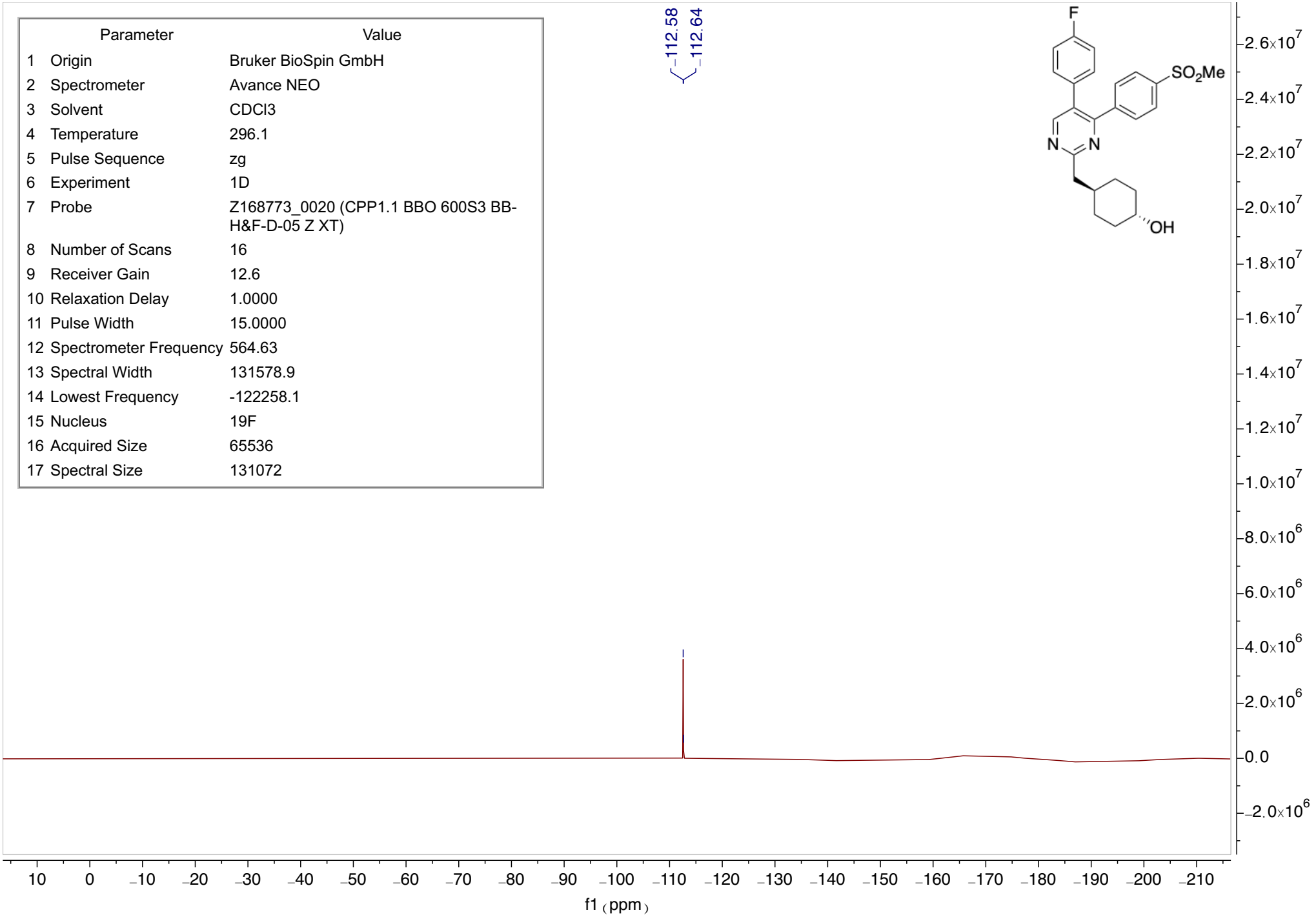

R
OH
H
H
(–)
NOE
f2 (ppm)
f1 (ppm)

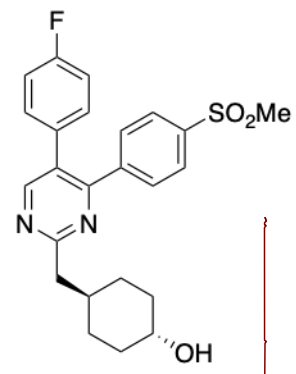

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 32.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2263.7
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.26 CDCl3
5.28 DCM
F
SO2Me
N
N
OH
3000000
2500000
2000000
1500000
1000000
500000
0
12.0 11.5 11.0 10.5 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)


F
SO2Me
N
N
OH
7.26 CDCl3
5.28 DCM
1.03
2.06
2.07
2.08
2.08
0.12
0.90
3.06
0.28
1.73
0.19
2.77
1.81
1.01
0.84
1.83
1.83
f1 (ppm)

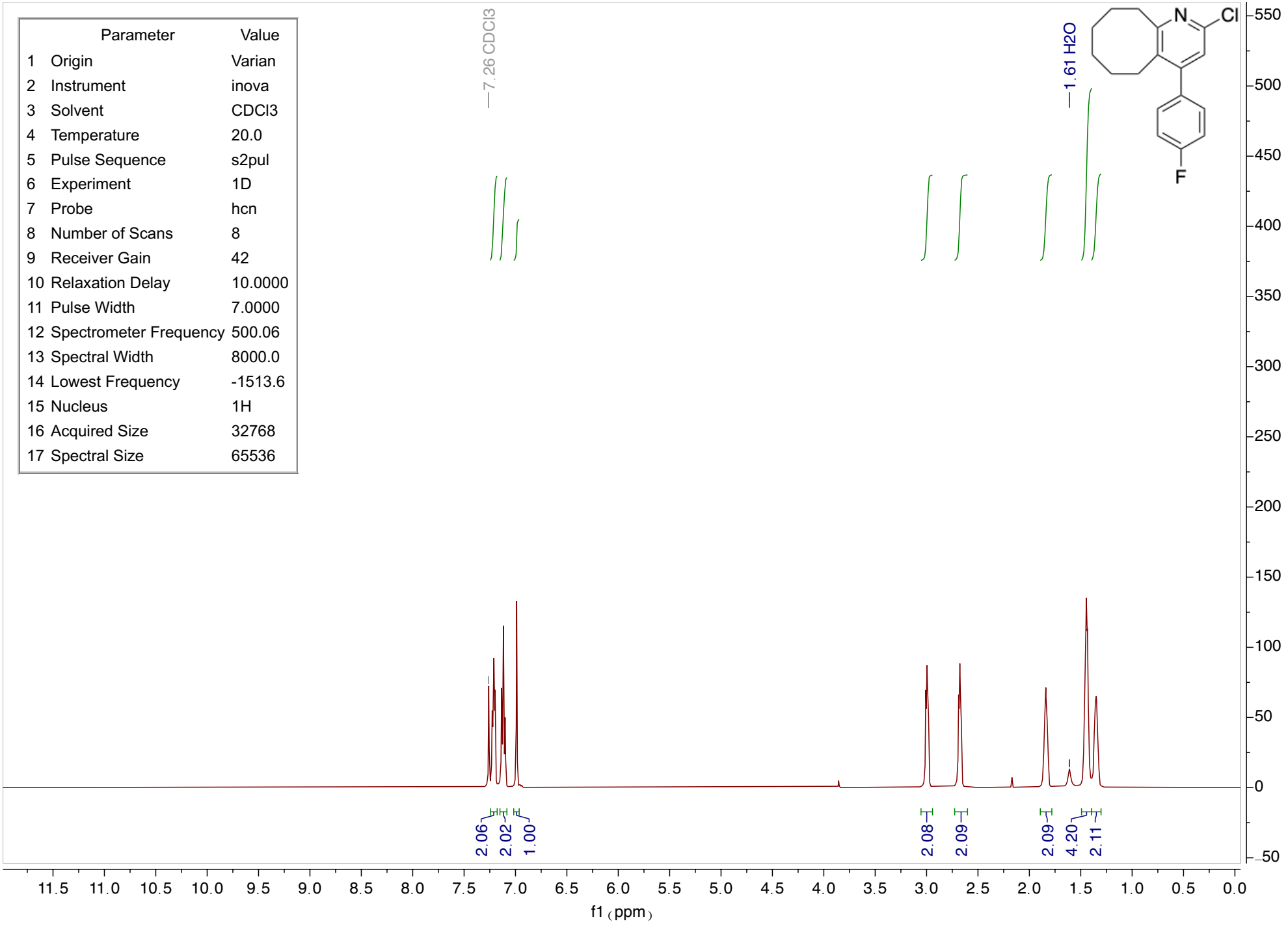

169.82
169.71
163.68
162.03
161.39
161.31
158.63
143.17
143.14
141.09
141.06
131.48
131.46
131.43
131.41
131.19
131.13
130.85
130.82
129.72
129.65
127.48
127.46
116.45
116.31
77.16 CDCl3
70.85
66.85
53.56 DCM
46.15
45.66
44.50
37.01
36.56
35.46
32.32
31.21
27.00
F
SO2Me
N
N
OH
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zgpg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 1024
9 Receiver Gain 101.0
10 Relaxation Delay 2.0000
11 Pulse Width 10.0000
12 Spectrometer Frequency 150.92
13 Spectral Width 35714.3
14 Lowest Frequency -2754.6
15 Nucleus 13C
16 Acquired Size 32768
17 Spectral Size 65536
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
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)

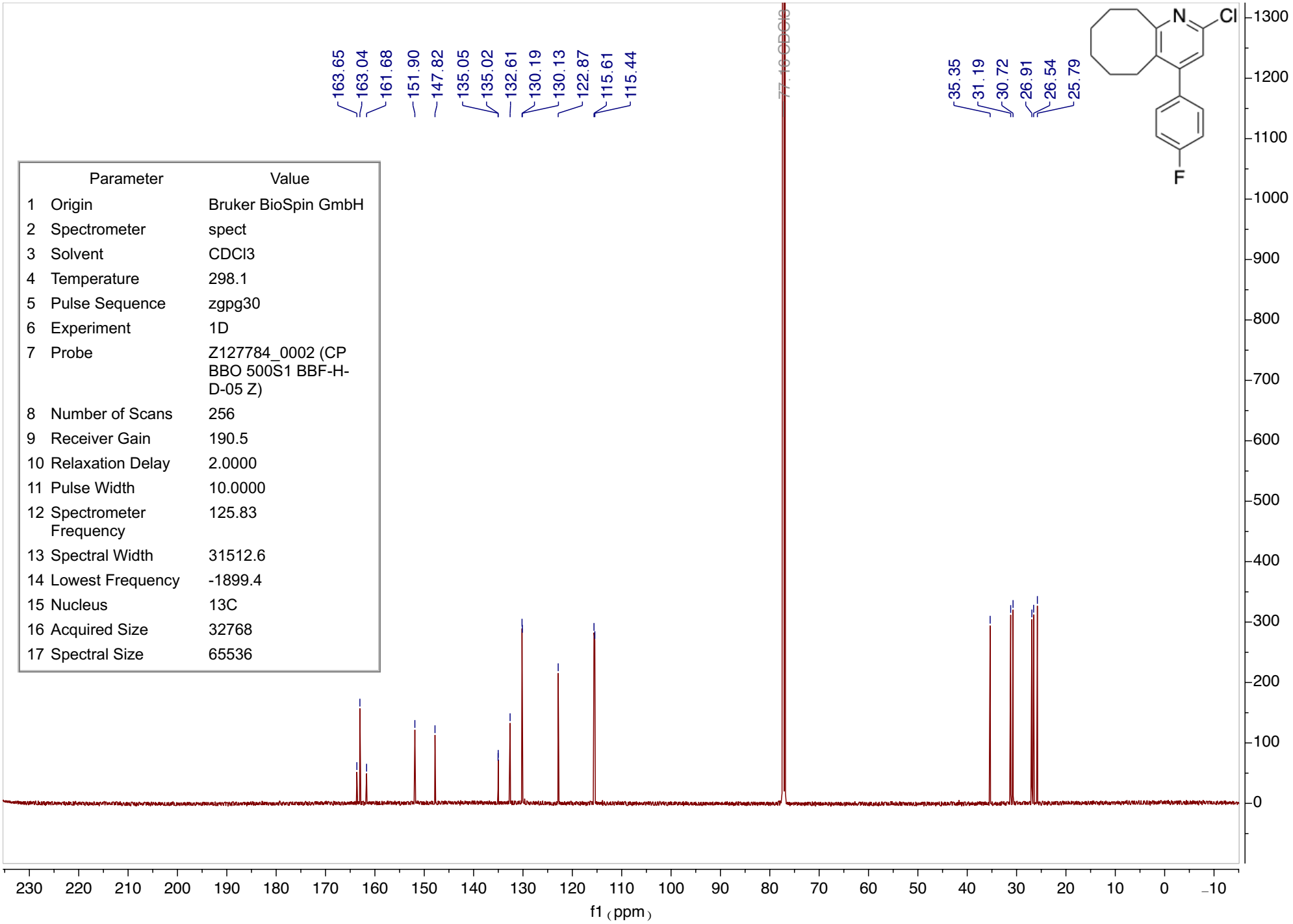
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	12.6
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072





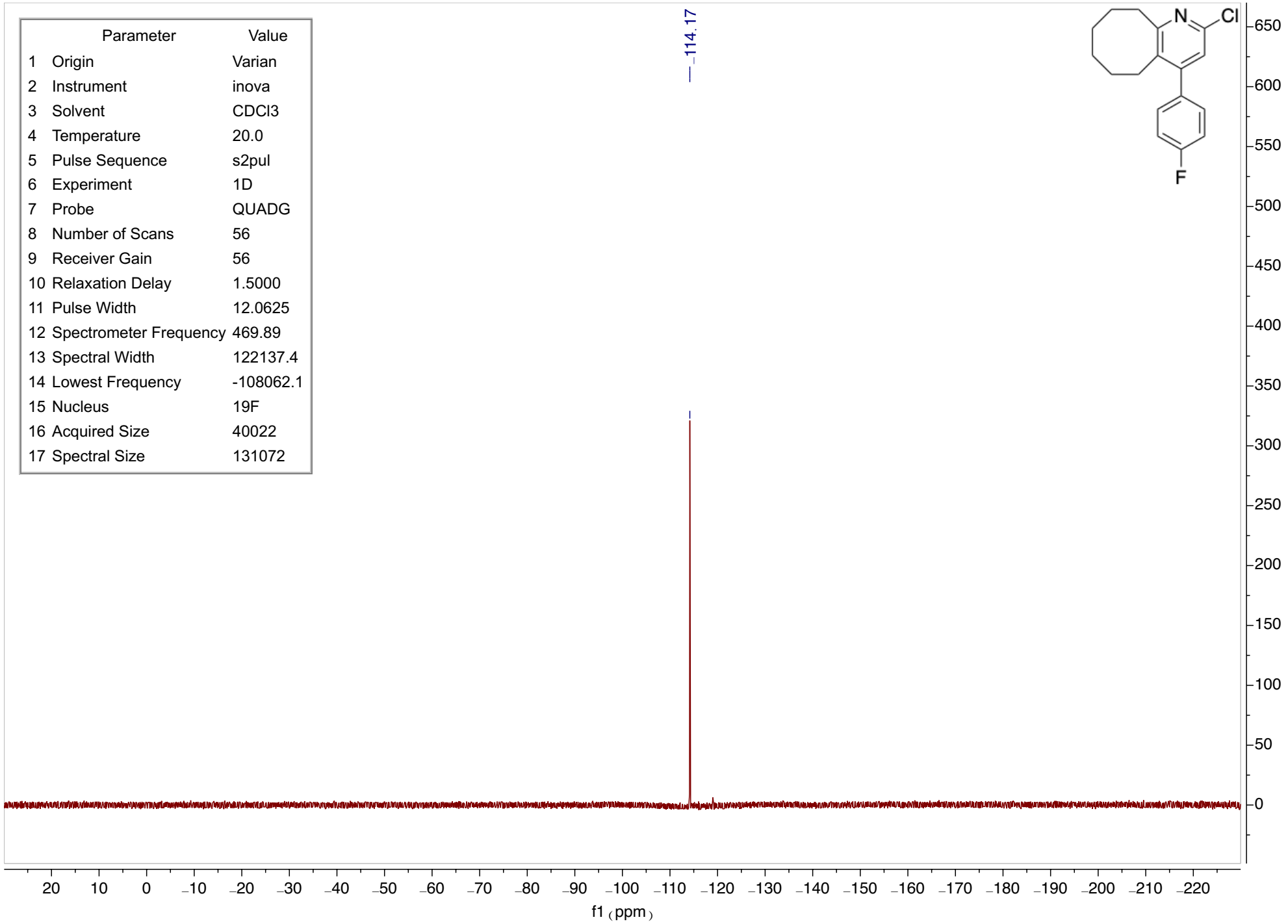
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgpsisp2.3
6	Experiment	HSQC-EDITED
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	4
9	Receiver Gain	101.0
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	600.13
13	Spectral Width	5882.4
14	Lowest Frequency	-34.5
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


Parameter Value
1 Origin Varian
2 Instrument inova
3 Solvent CDCl3
4 Temperature 20.0
5 Pulse Sequence s2pul
6 Experiment 1D
7 Probe hcn
8 Number of Scans 8
9 Receiver Gain 42
10 Relaxation Delay 10.0000
11 Pulse Width 7.0000
12 Spectrometer Frequency 500.06
13 Spectral Width 8000.0
14 Lowest Frequency -1513.6
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 65536
7.26 CDCl3
1.61 H2O
N
Cl
F
2.06
2.02
1.00
2.08
2.09
2.09
4.20
2.11
f1 (ppm)

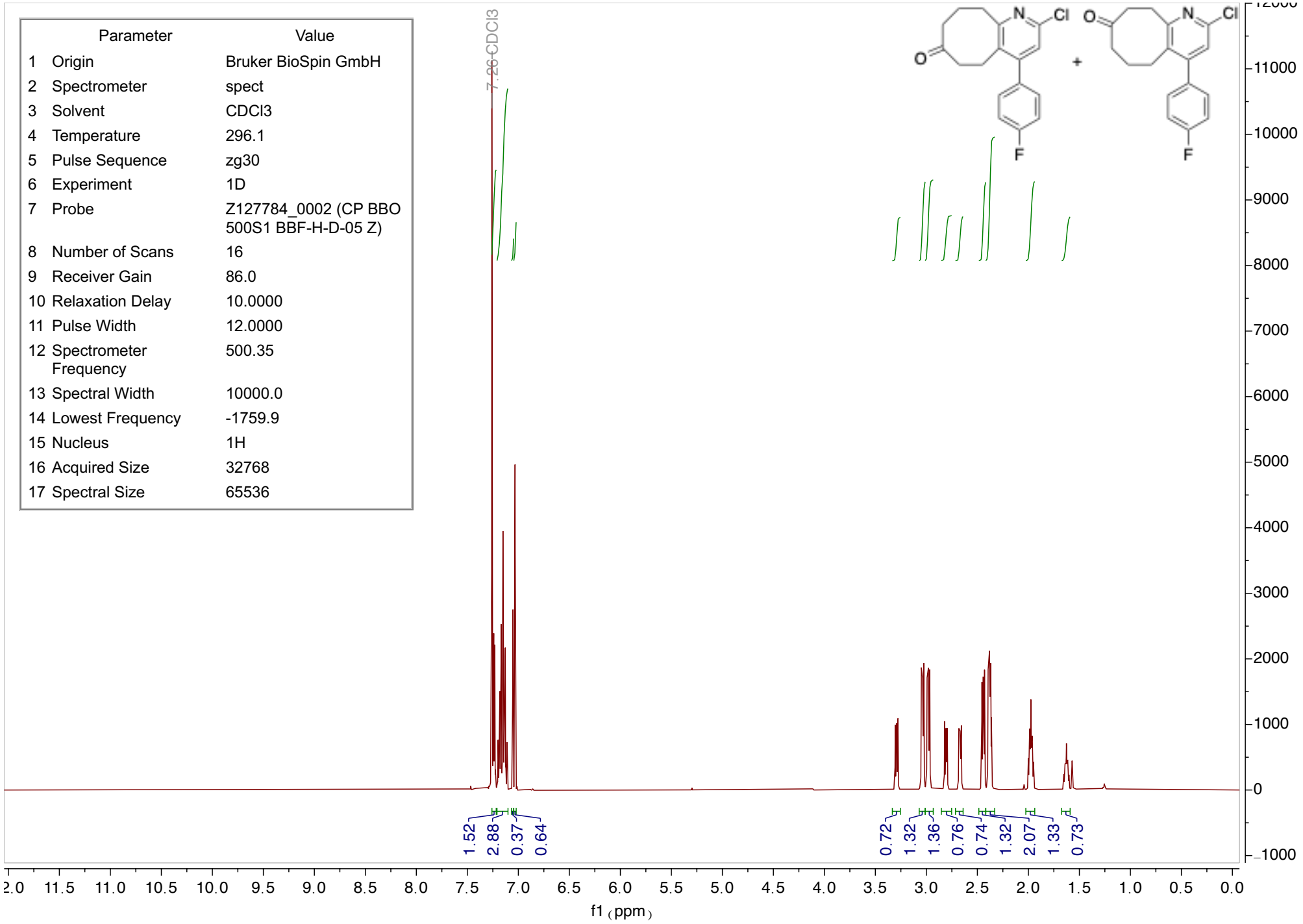


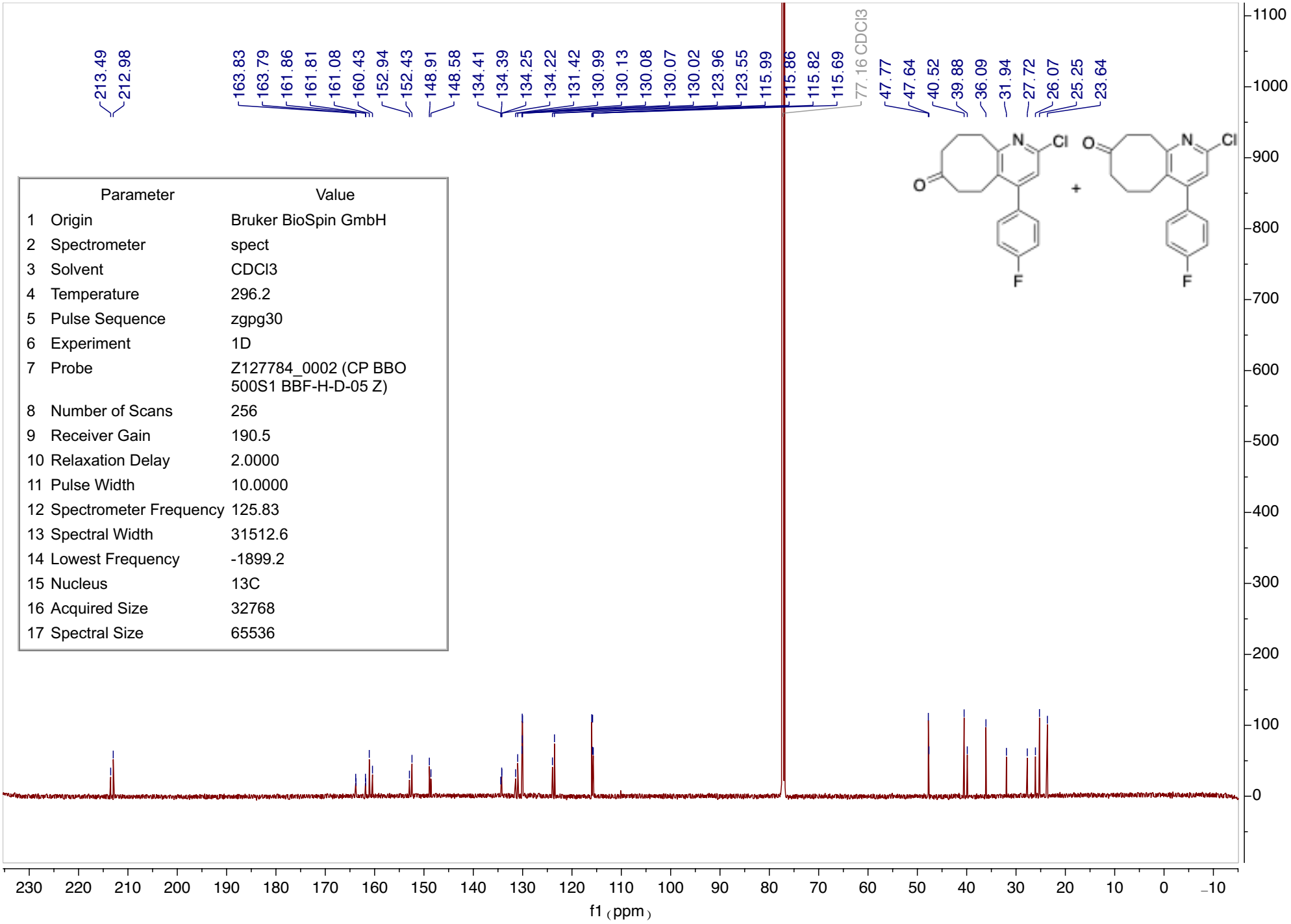
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	298.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.4
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	QUADG
8	Number of Scans	56
9	Receiver Gain	56
10	Relaxation Delay	1.5000
11	Pulse Width	12.0625
12	Spectrometer Frequency	469.89
13	Spectral Width	122137.4
14	Lowest Frequency	-108062.1
15	Nucleus	19F
16	Acquired Size	40022
17	Spectral Size	131072



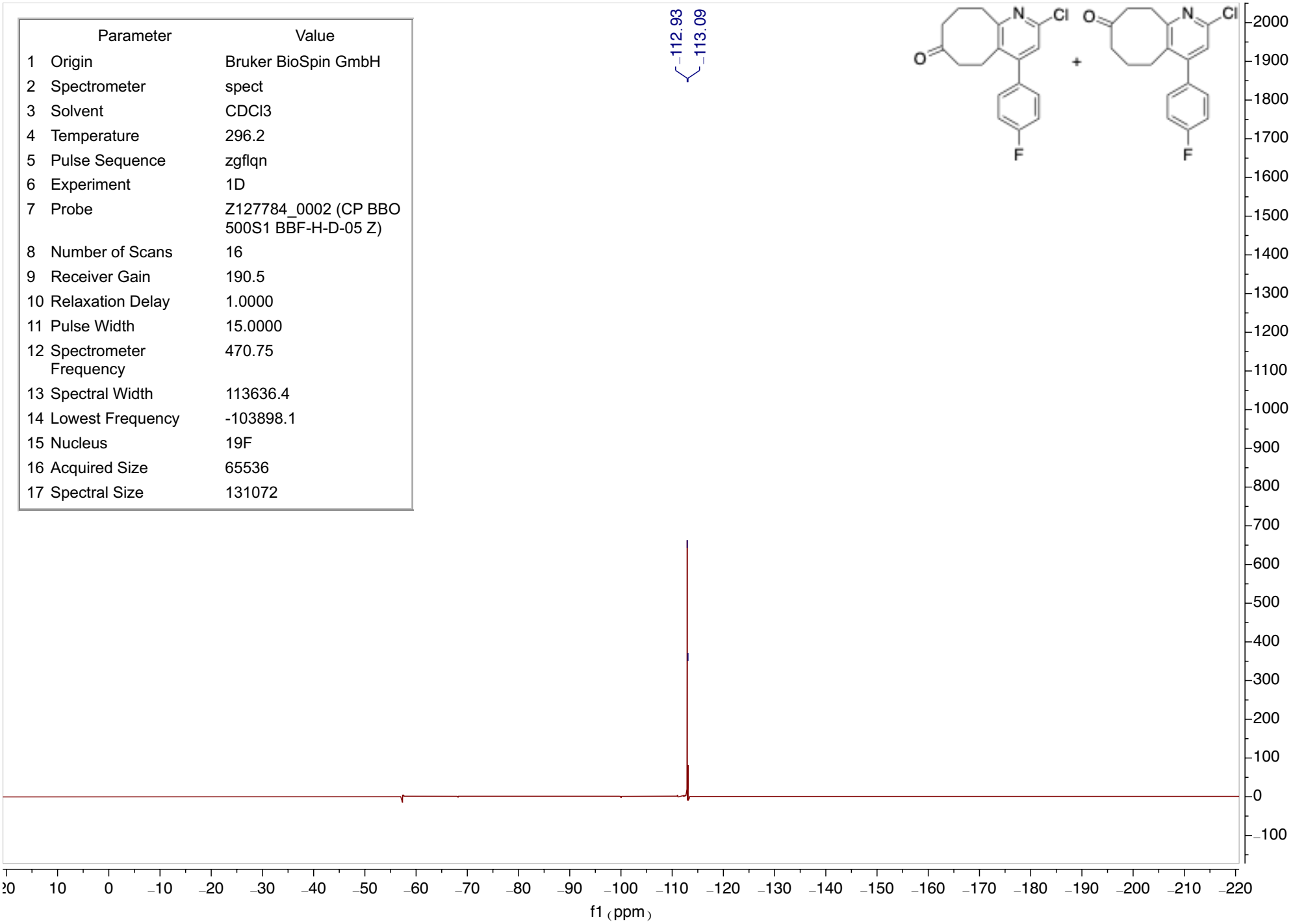
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1759.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



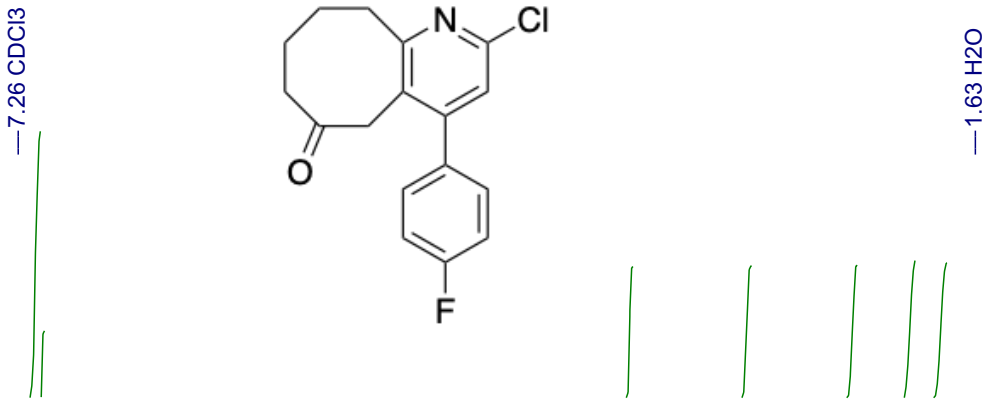


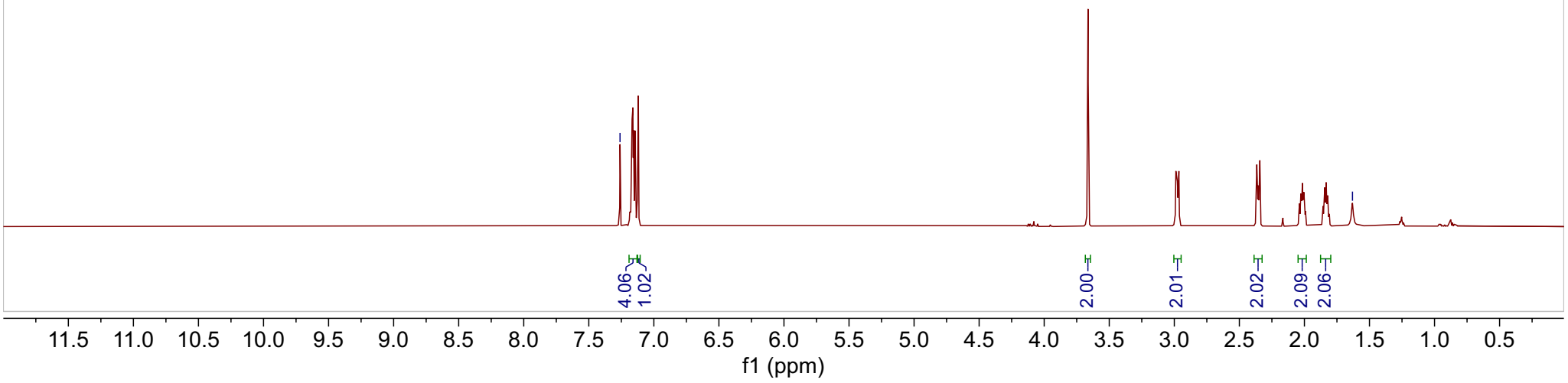
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

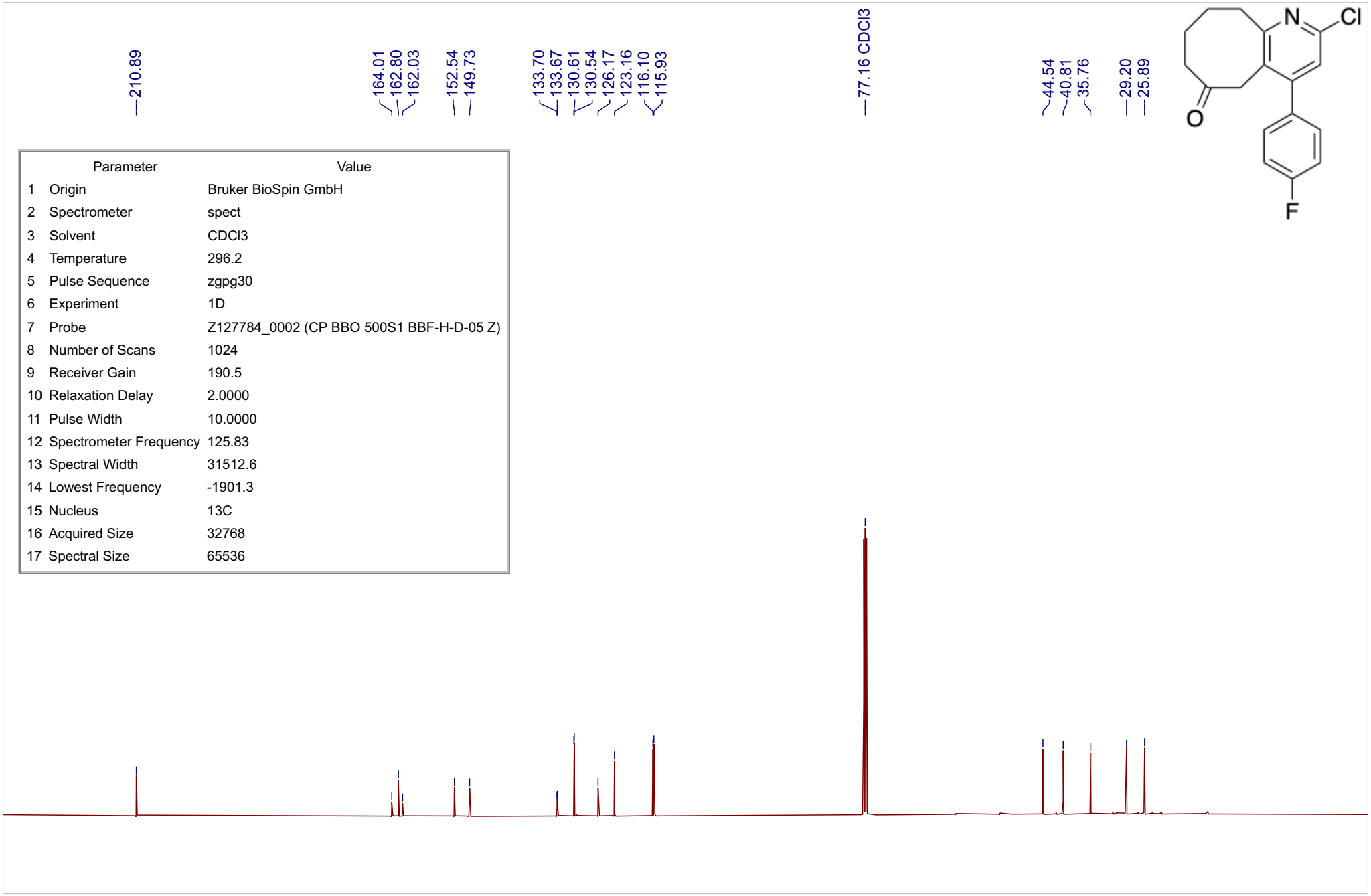
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	32
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

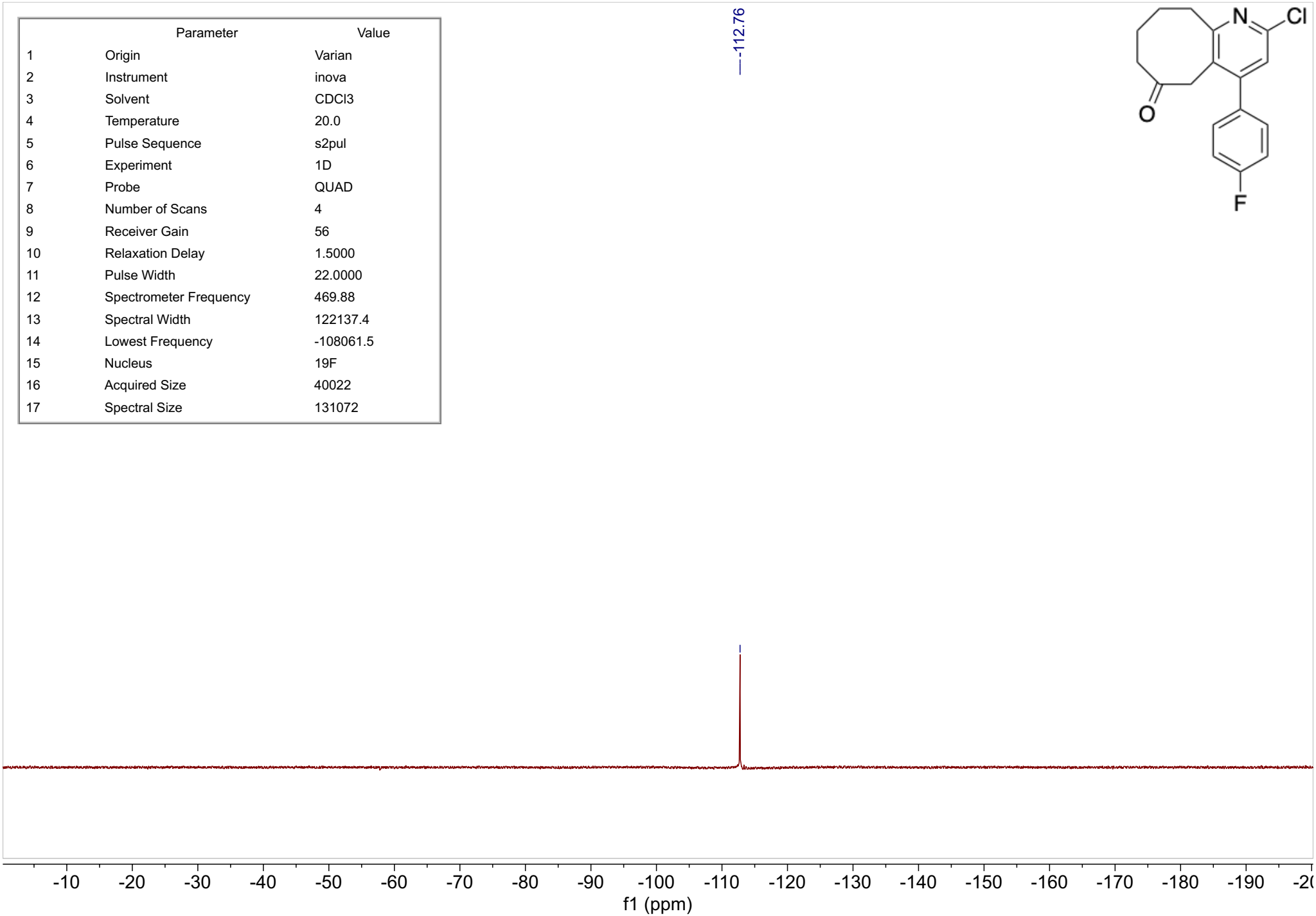


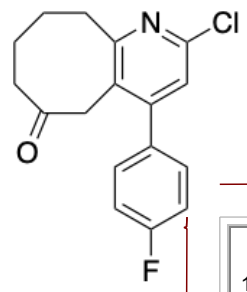




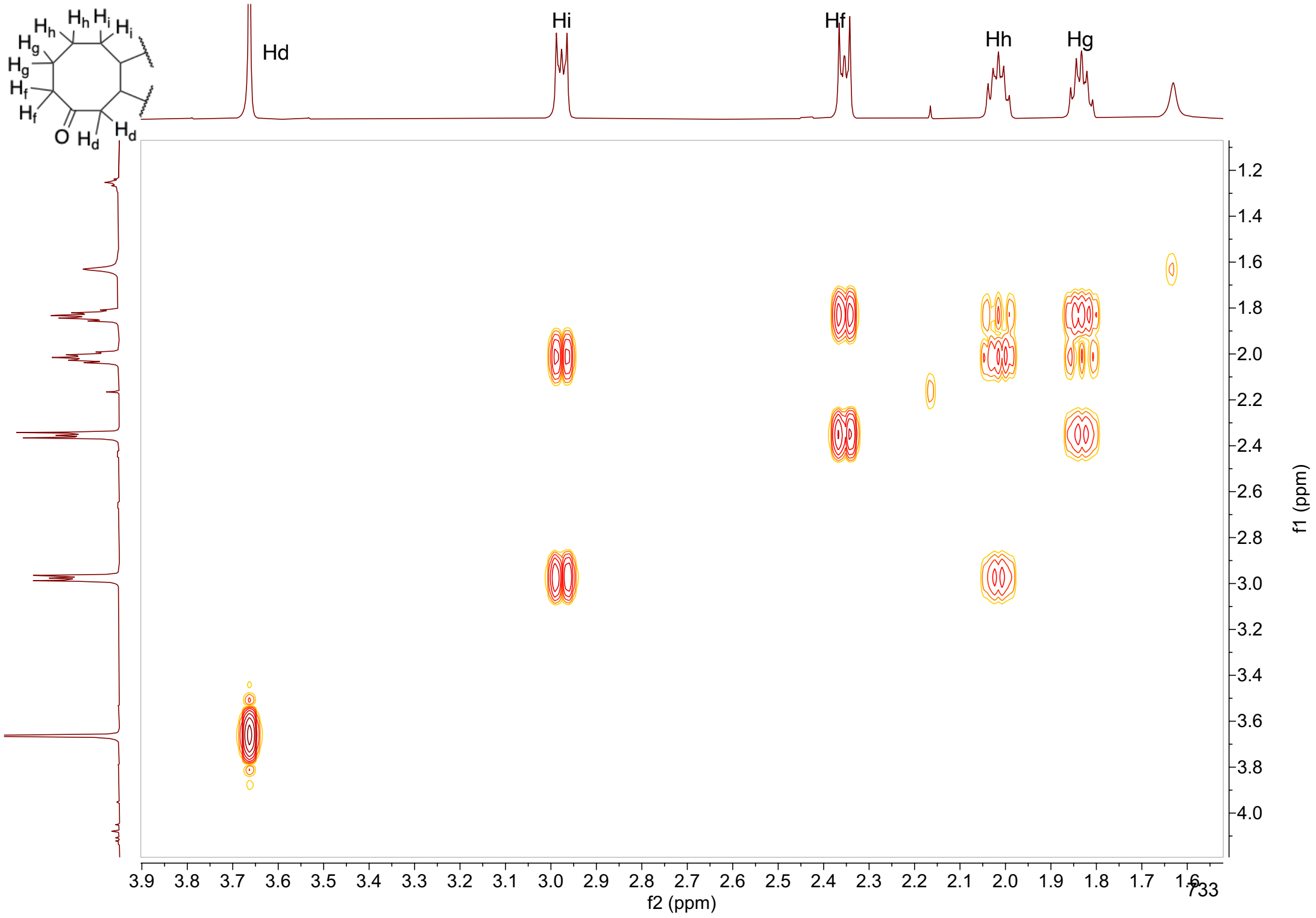
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	QUAD
8	Number of Scans	4
9	Receiver Gain	56
10	Relaxation Delay	1.5000
11	Pulse Width	22.0000
12	Spectrometer Frequency	469.88
13	Spectral Width	122137.4
14	Lowest Frequency	-108061.5
15	Nucleus	19F
16	Acquired Size	40022
17	Spectral Size	131072





	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	69.2
10	Relaxation Delay	1.9074
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-40.9
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


Hd
Hi
Hf
Hh
Hg
f2 (ppm)
f1 (ppm)
3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6
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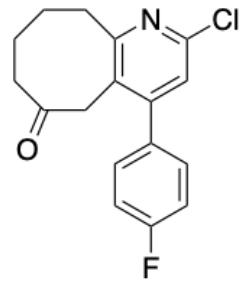
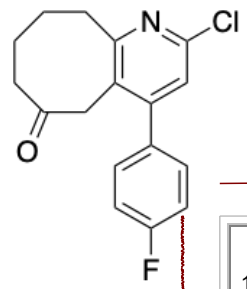
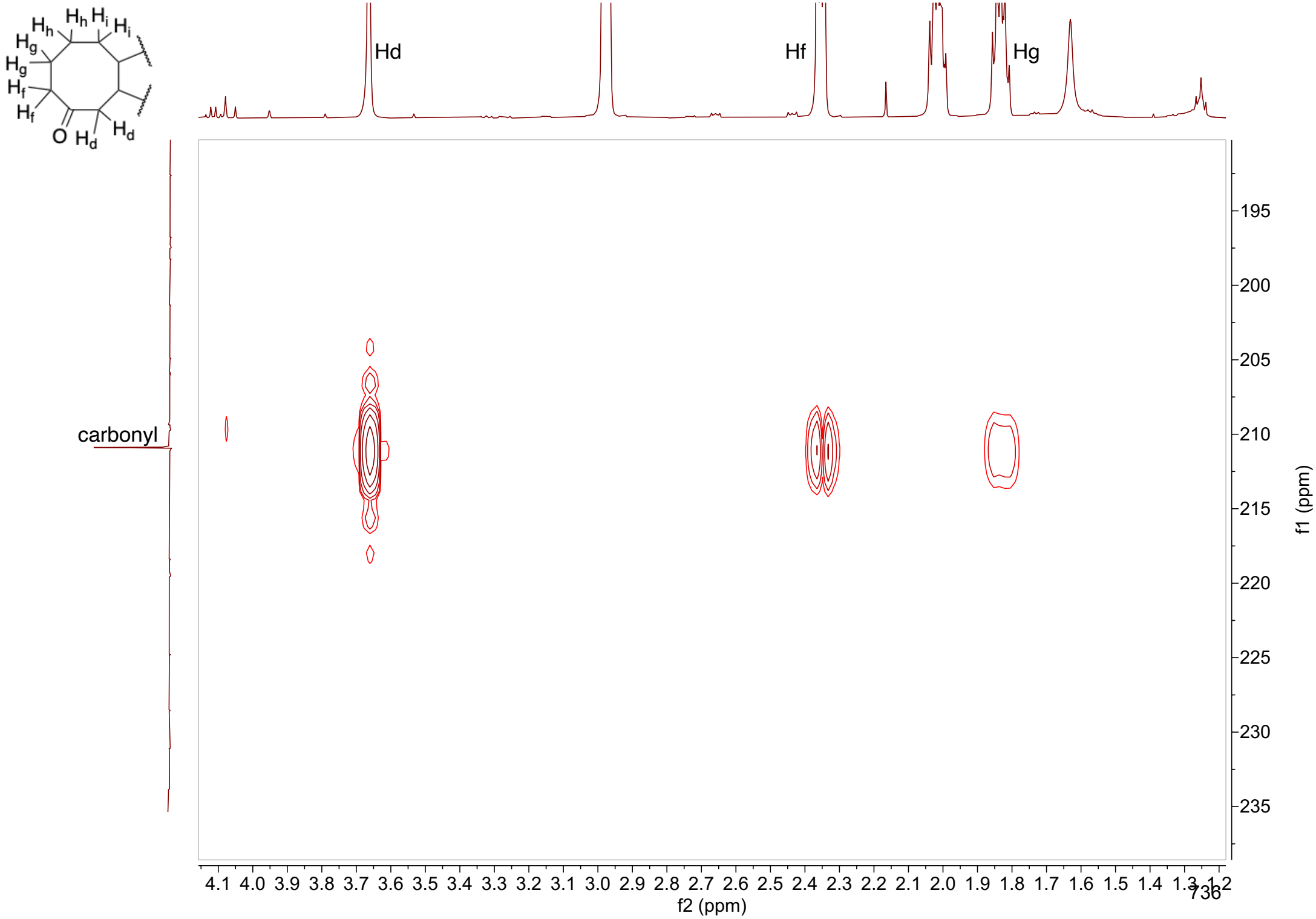


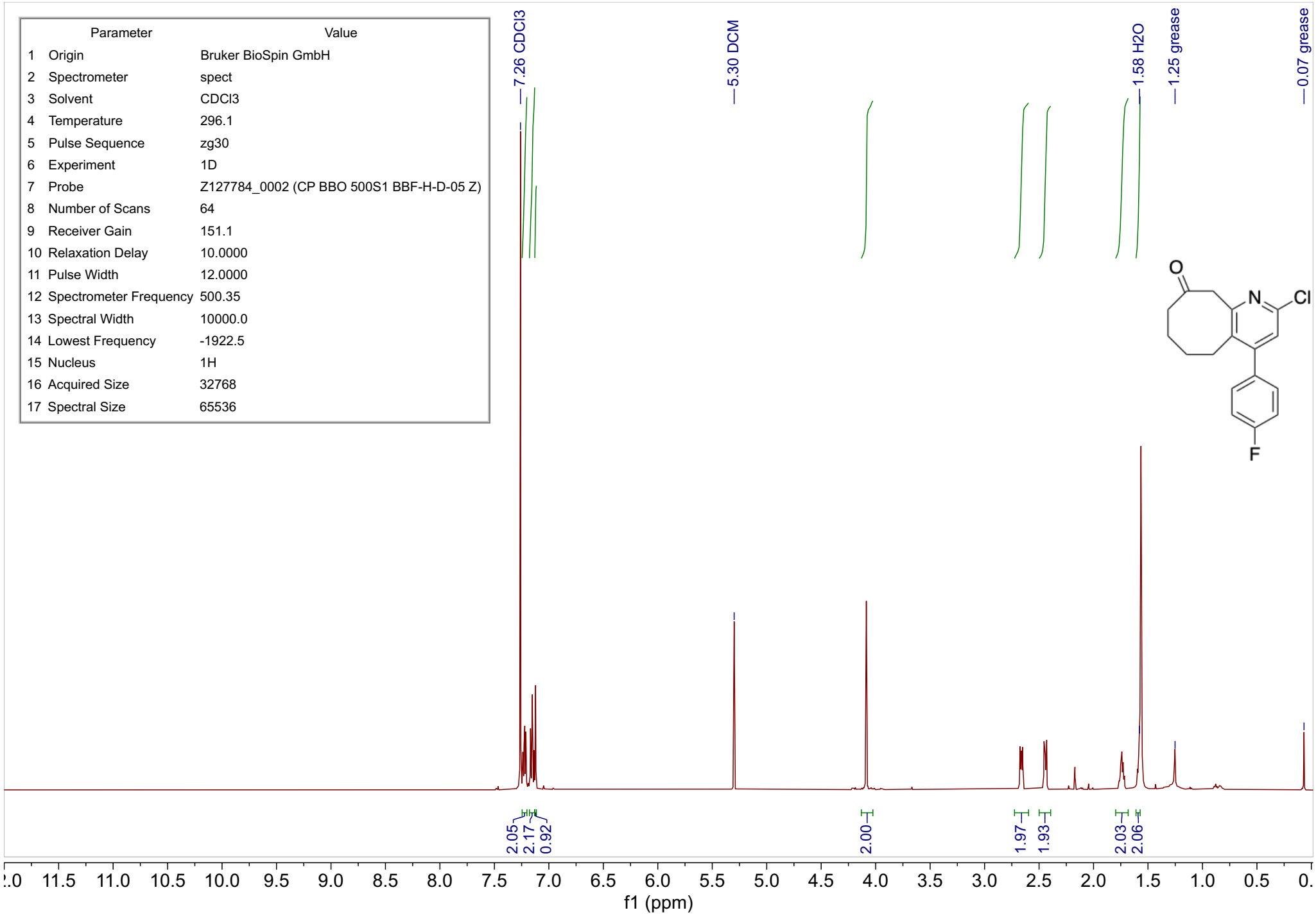
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-9.6
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

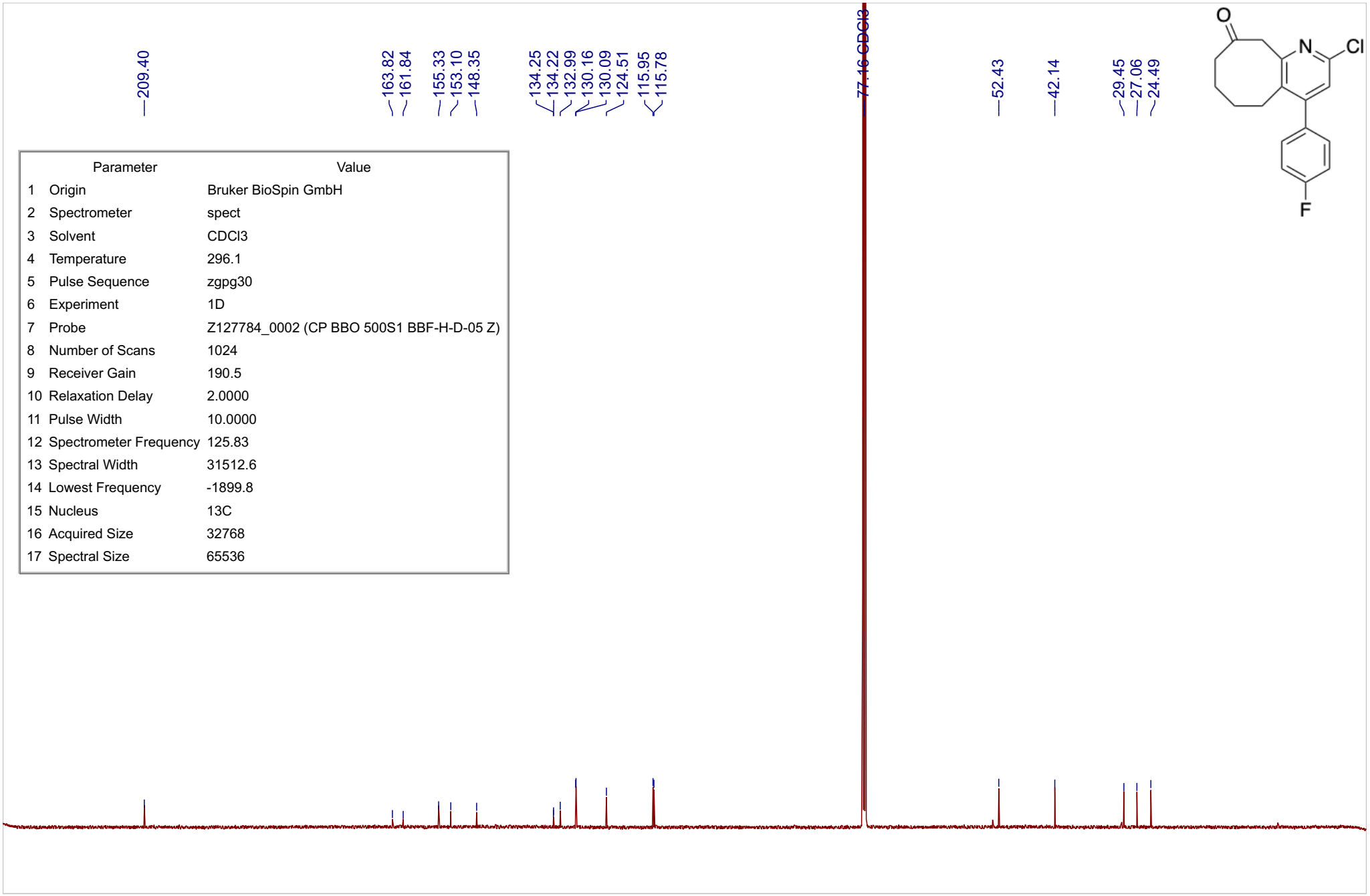


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	8
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-9.4
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


Hh
Hh
Hi
Hi
Hg
Hg
Hf
Hf
O
Hd
Hd
Hd
Hf
Hg
carbonyl
195
200
205
210
215
220
225
230
235
f1 (ppm)
4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2
f2 (ppm)

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	64
9	Receiver Gain	151.1
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

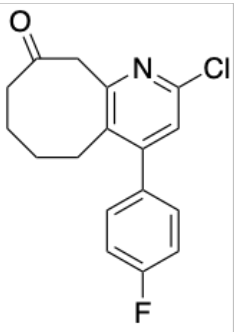


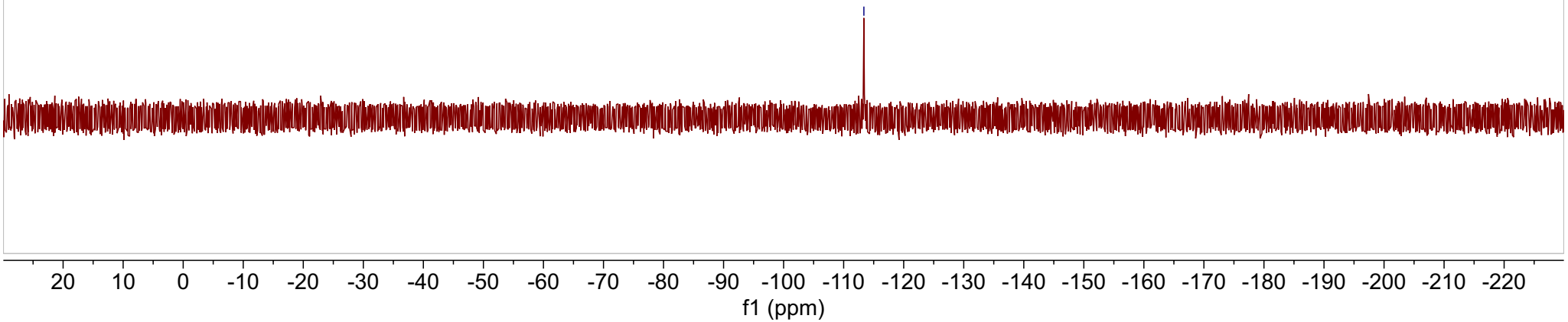


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	QUAD
8	Number of Scans	4
9	Receiver Gain	56
10	Relaxation Delay	1.5000
11	Pulse Width	22.0000
12	Spectrometer Frequency	469.88
13	Spectral Width	122137.4
14	Lowest Frequency	-108061.5
15	Nucleus	19F
16	Acquired Size	40022
17	Spectral Size	131072

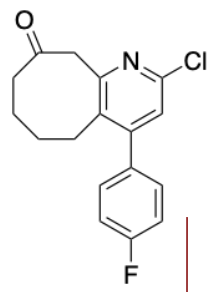
-113.37



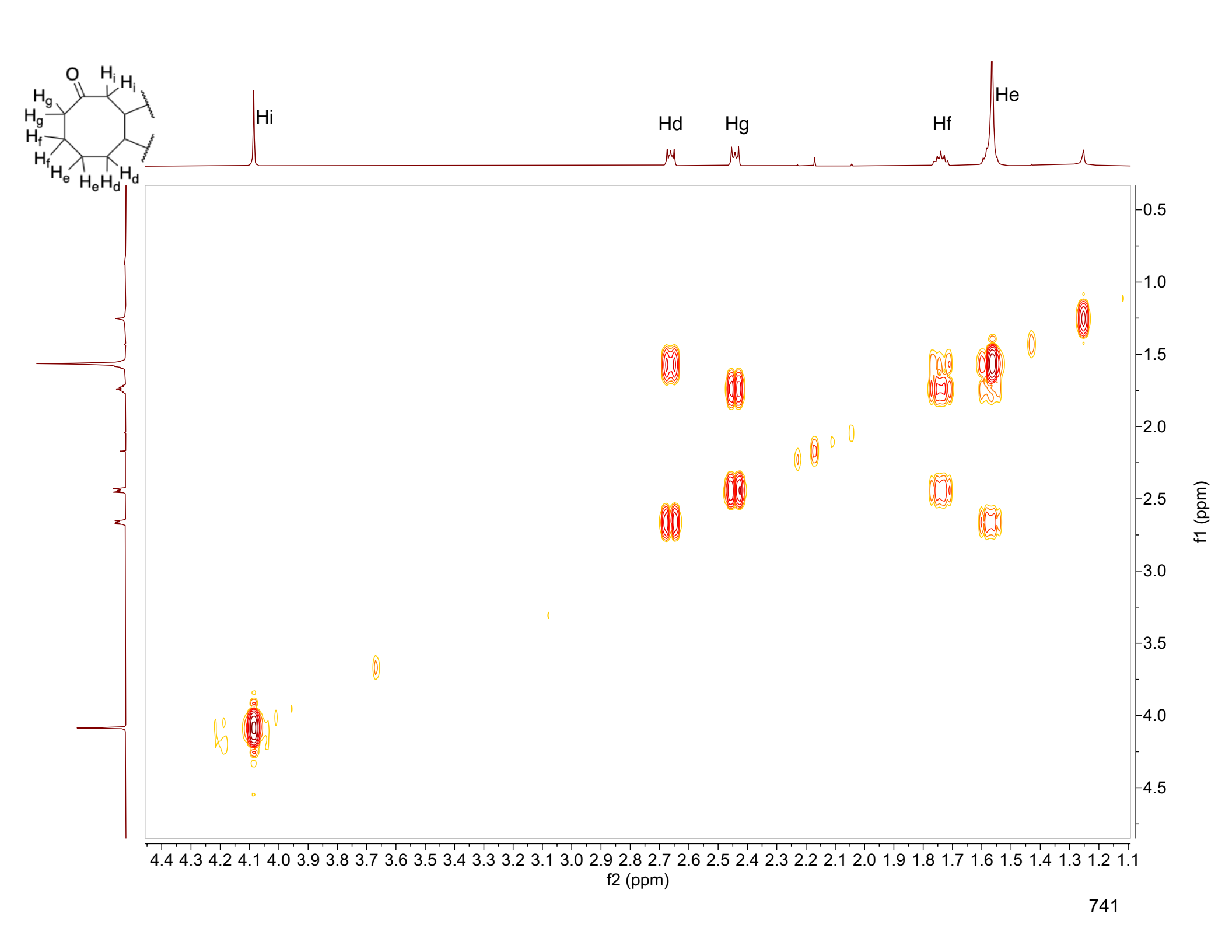


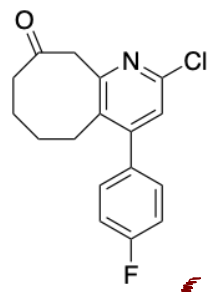
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220

f1 (ppm)

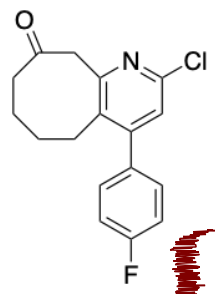


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	107.0
10	Relaxation Delay	1.9341
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4587.2
14	Lowest Frequency	-475.4
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

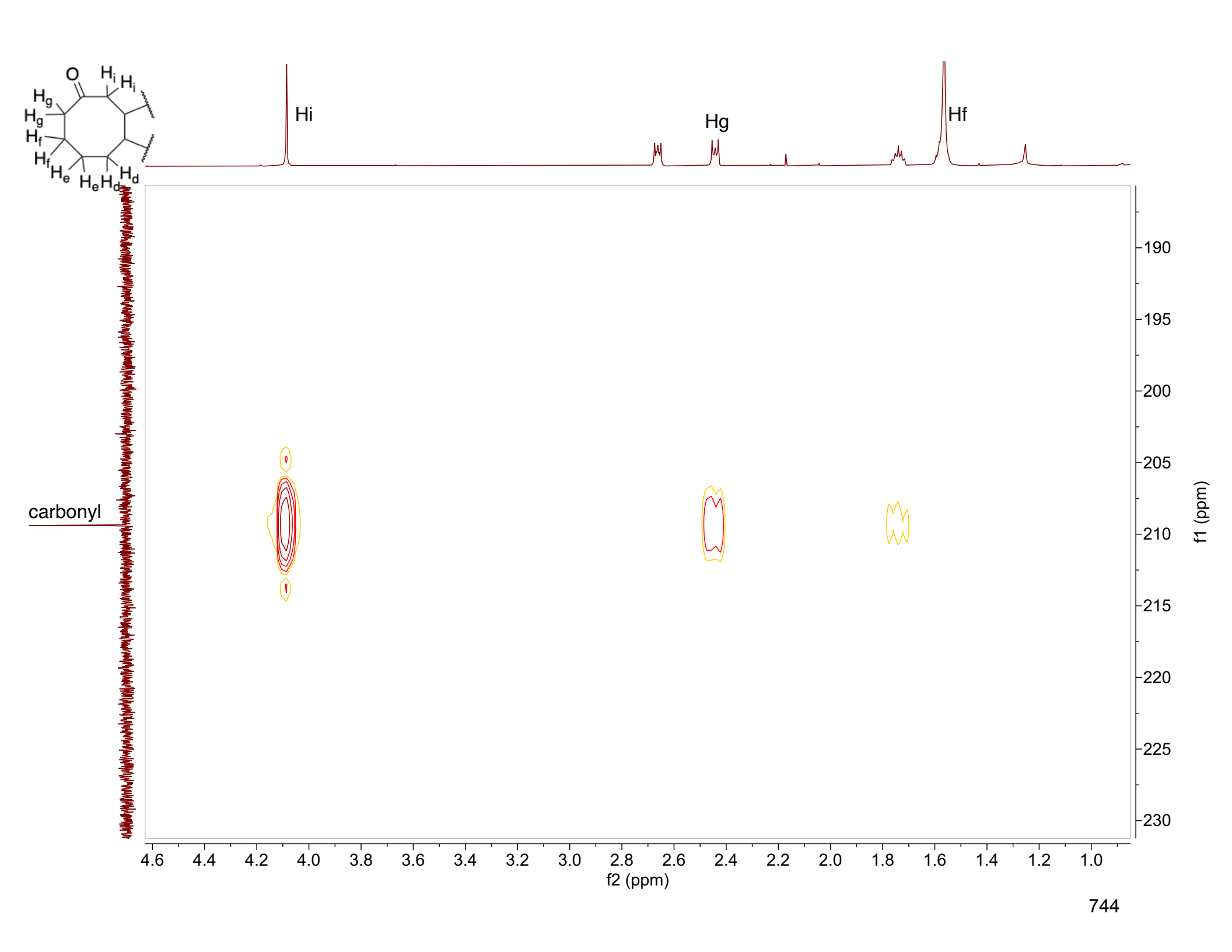

O
Hi
Hi
Hg
Hg
Hf
Hf
He
He
Hd
Hd
Hi
Hd
Hg
Hf
He
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)
4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1
f2 (ppm)



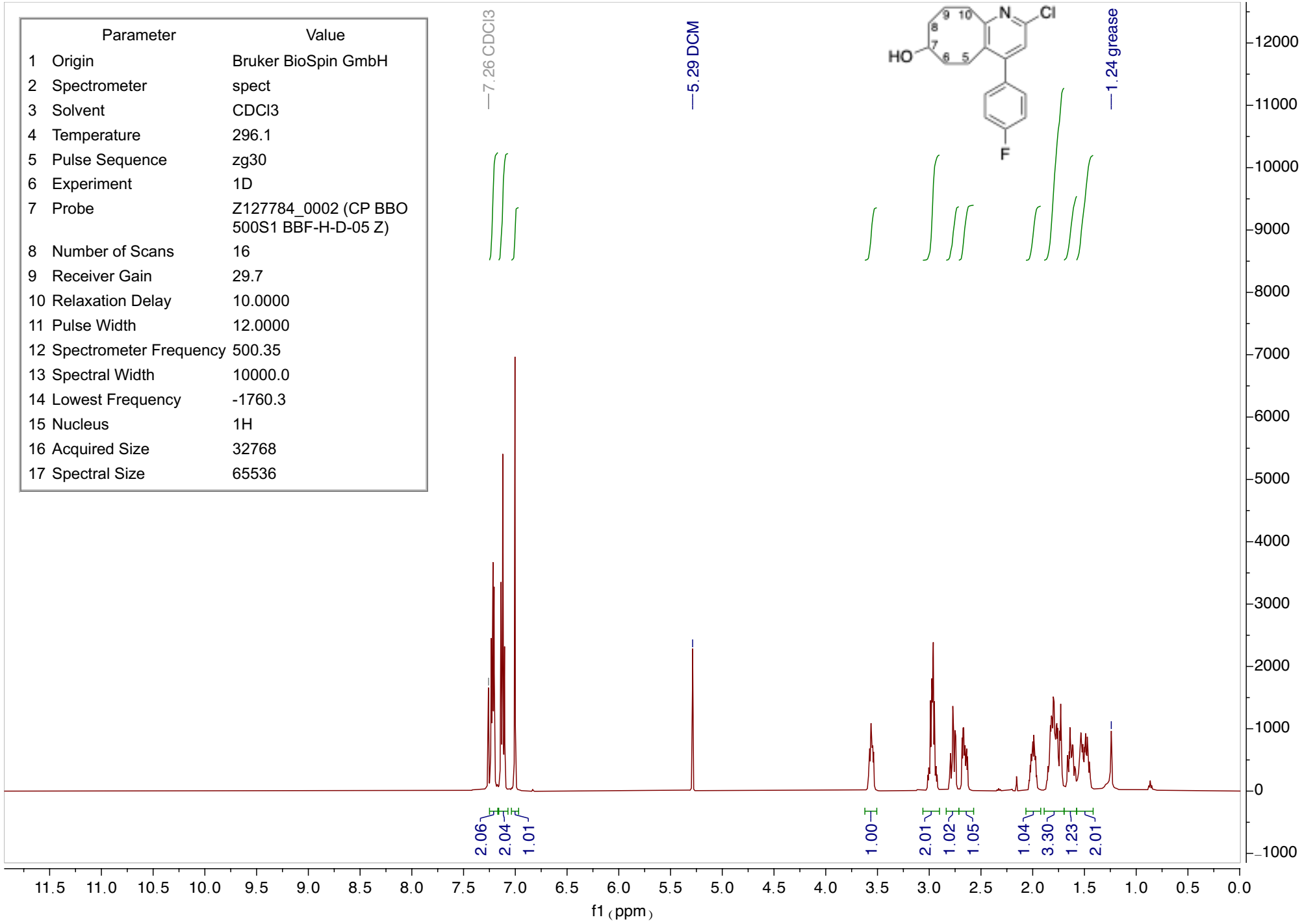
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4587.2
14	Lowest Frequency	-471.6
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

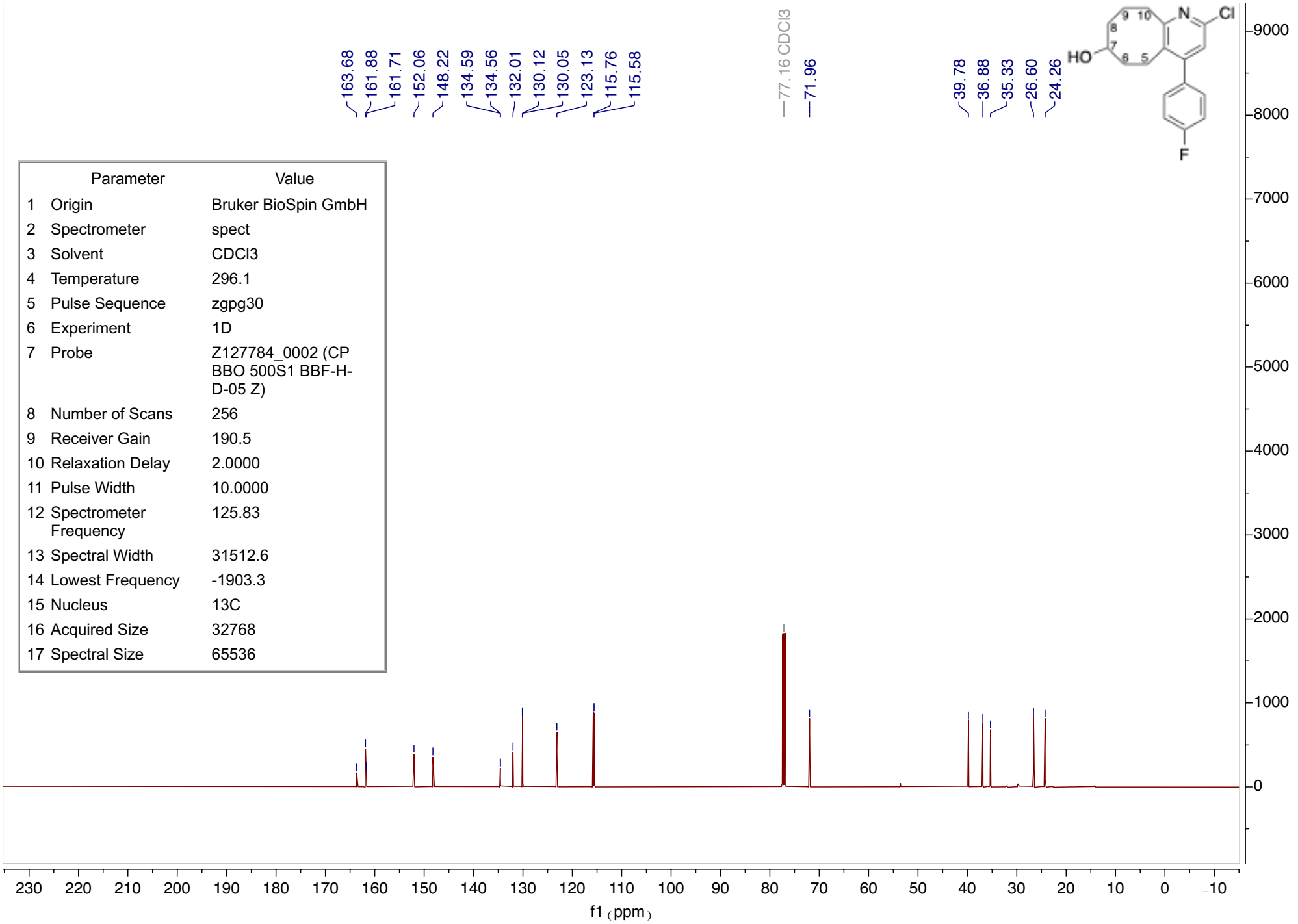


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	8
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4587.2
14	Lowest Frequency	-472.8
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


O
Hi
Hi
Hg
Hg
Hf
Hf
He
He
Hd
Hd
Hi
Hg
Hf
carbonyl
190
195
200
205
210
215
220
225
230
f1 (ppm)
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
f2 (ppm)

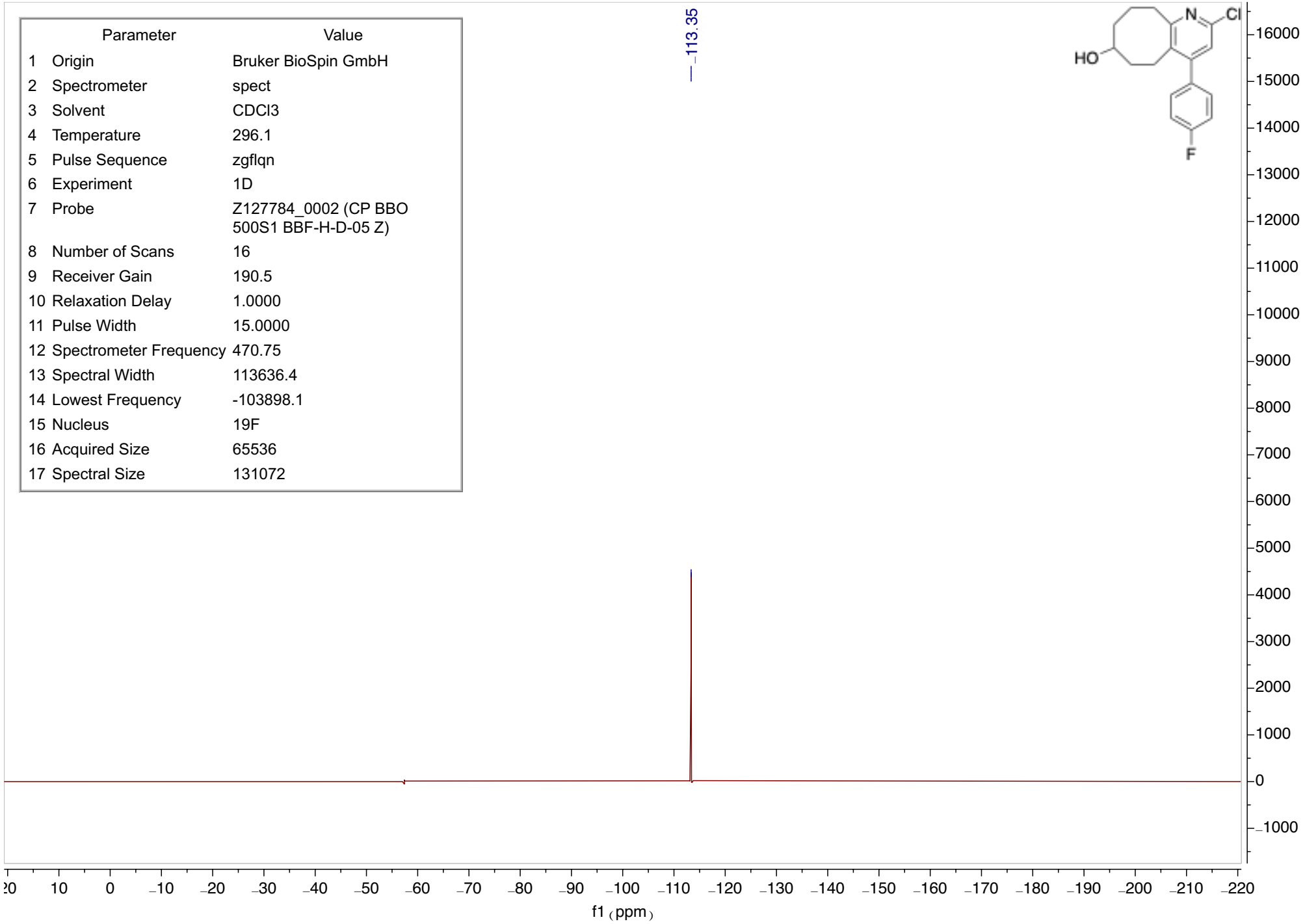
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

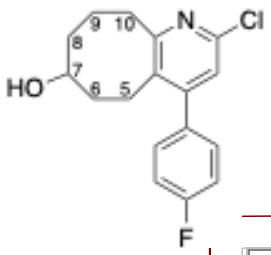




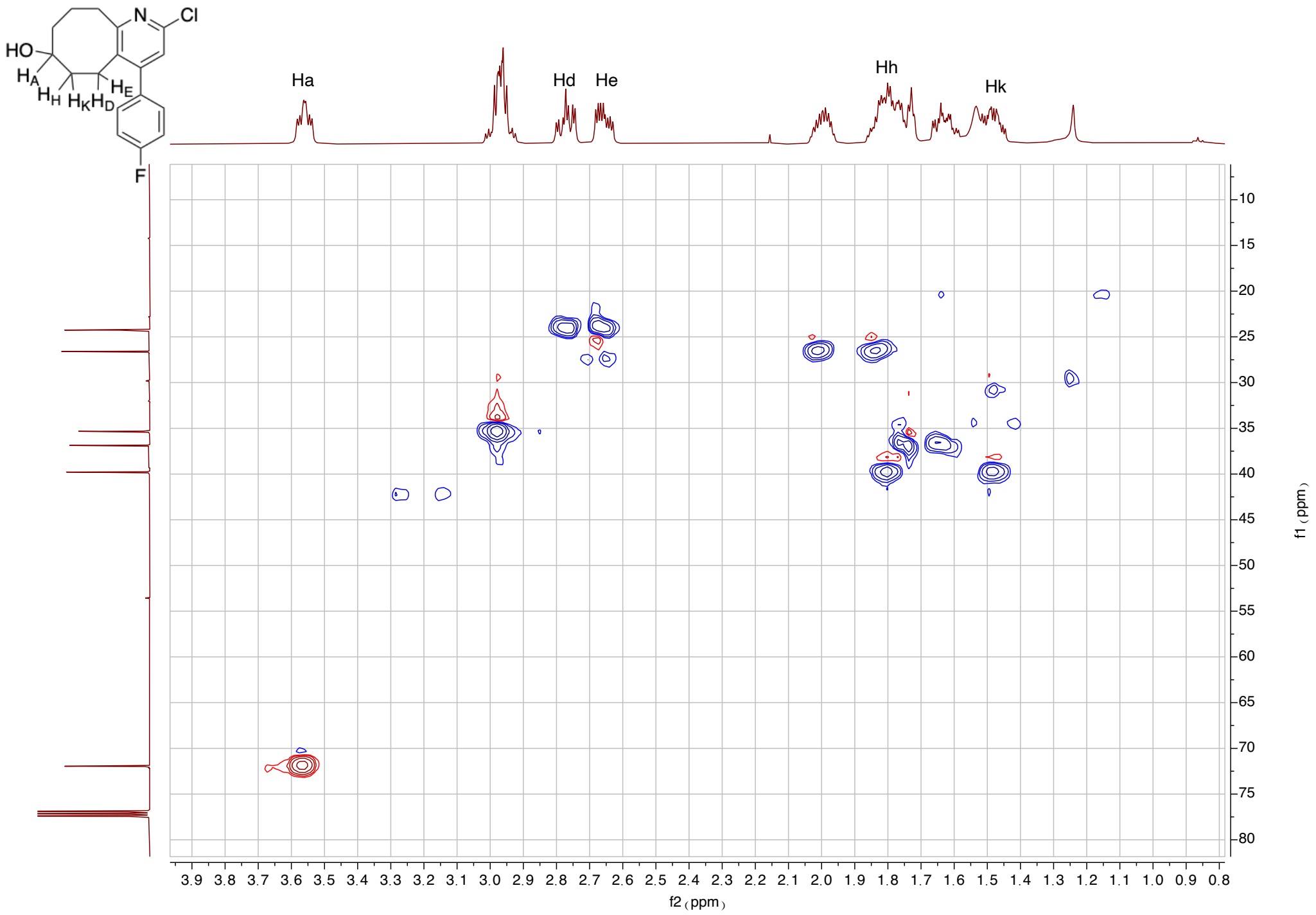
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

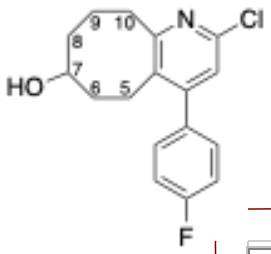
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



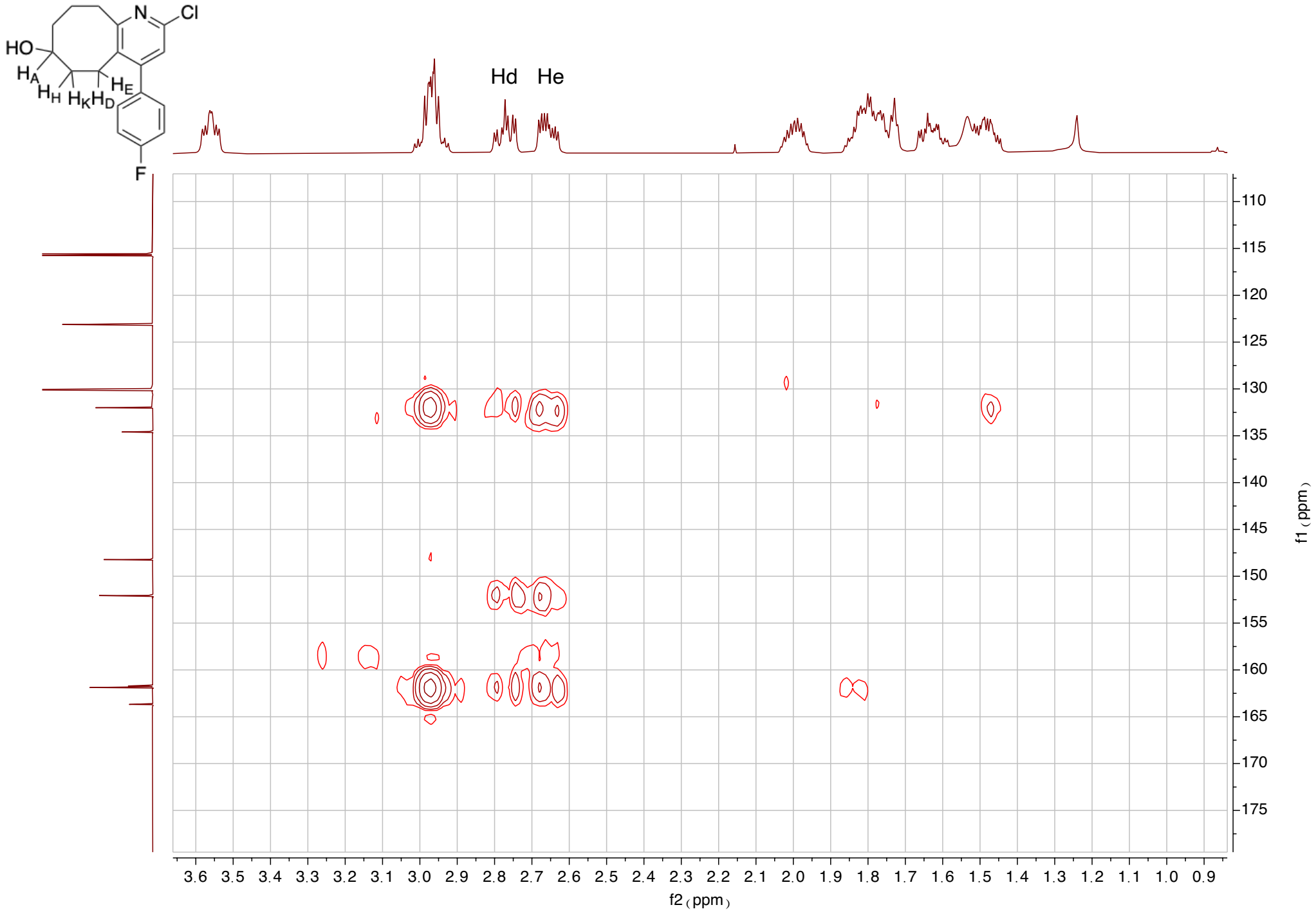


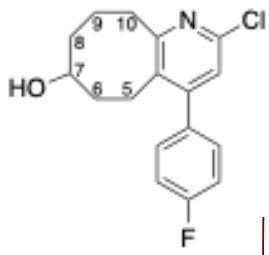
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4132.2
14	Lowest Frequency	-10.6
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


HO
N
Cl
F
HA
HH
HK
HD
HE
Ha
Hd
He
Hh
Hk
f2 (ppm)
f1 (ppm)
3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8
10 15 20 25 30 35 40 45 50 55 60 65 70 75 80

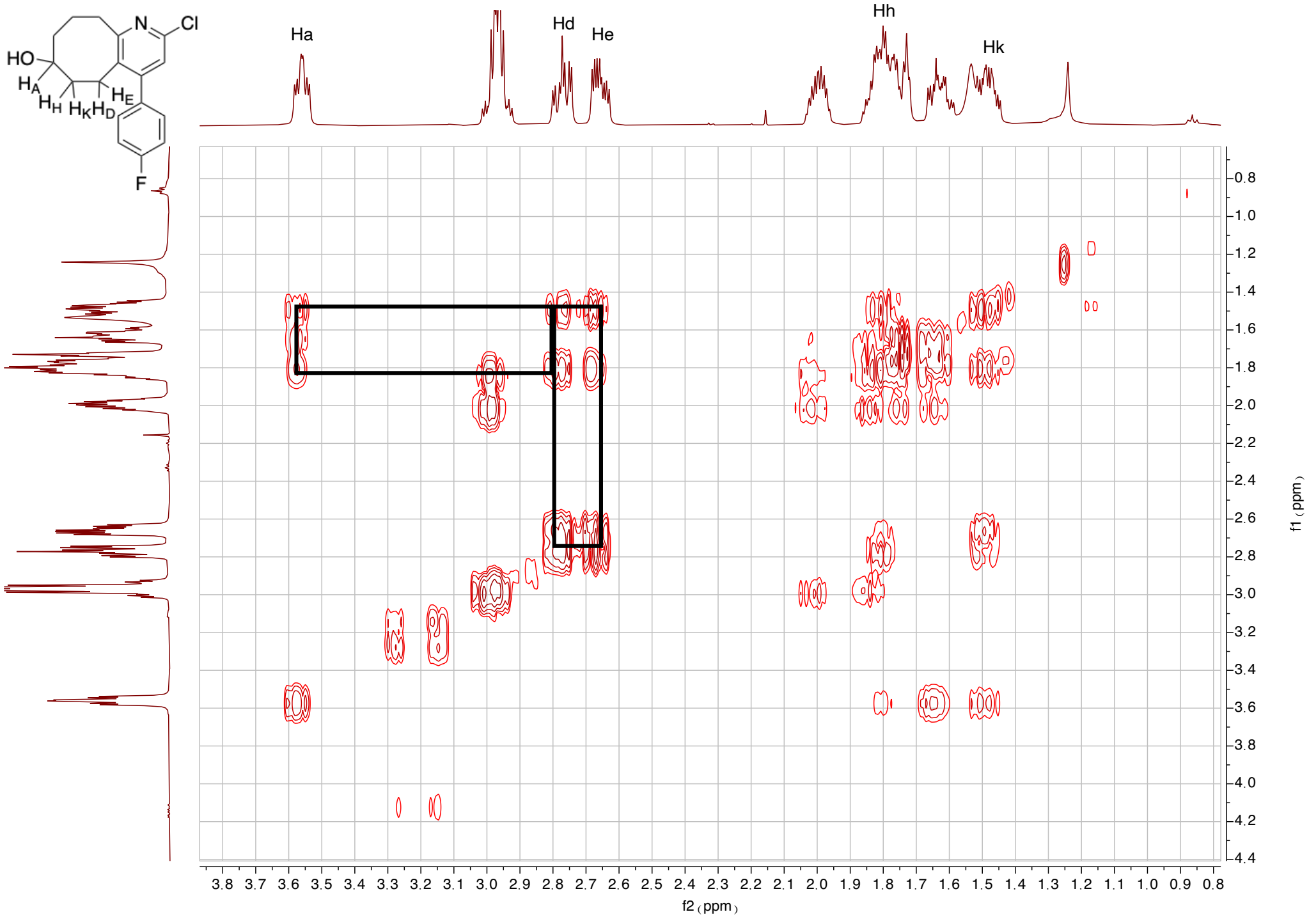


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4132.2
14	Lowest Frequency	-15.0
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

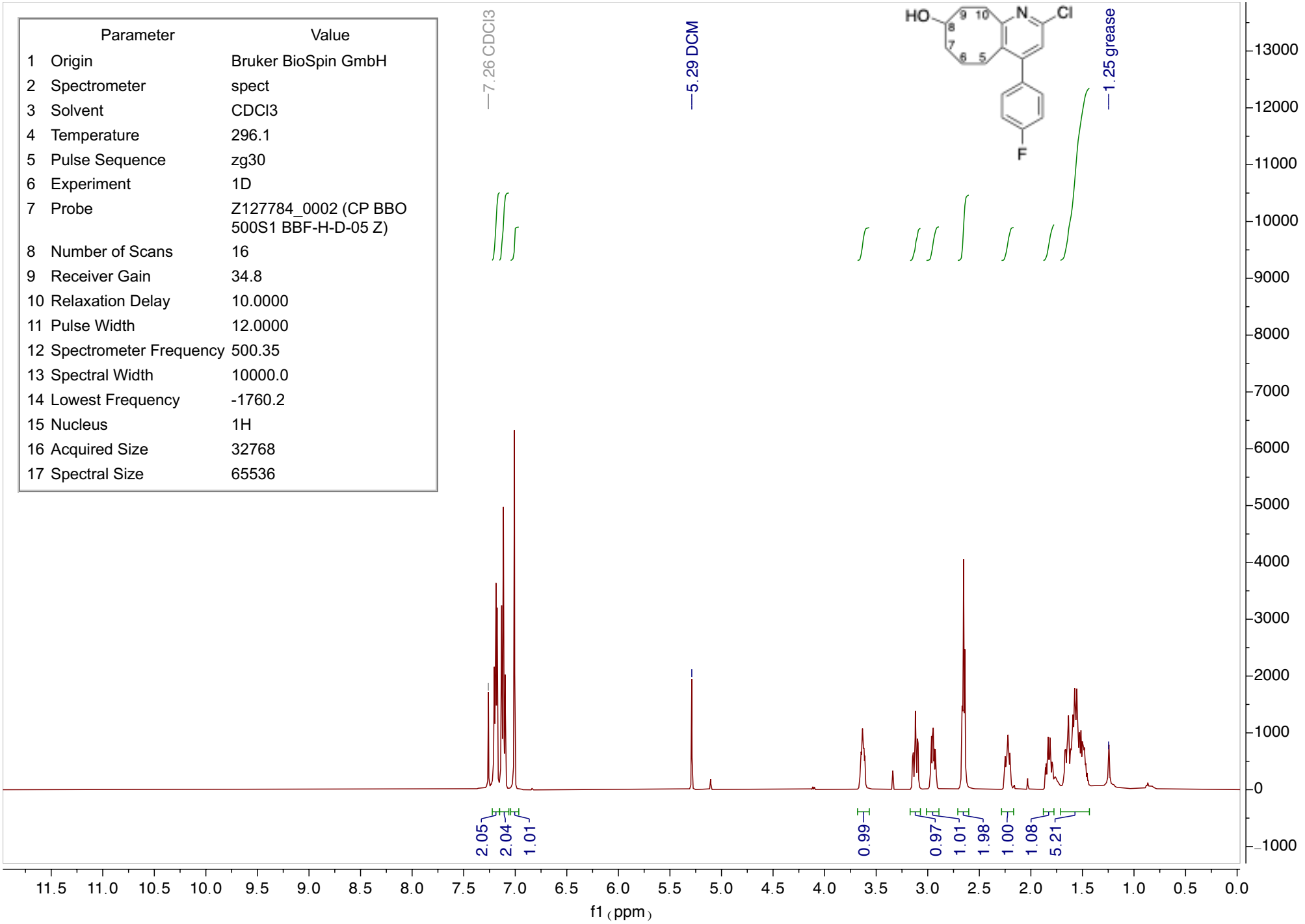

N
Cl
HO
HA
HH
HK
HD
HE
F
Hd
He
110
115
120
125
130
135
140
145
150
155
160
165
170
175
f1 (ppm)
3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9
f2 (ppm)

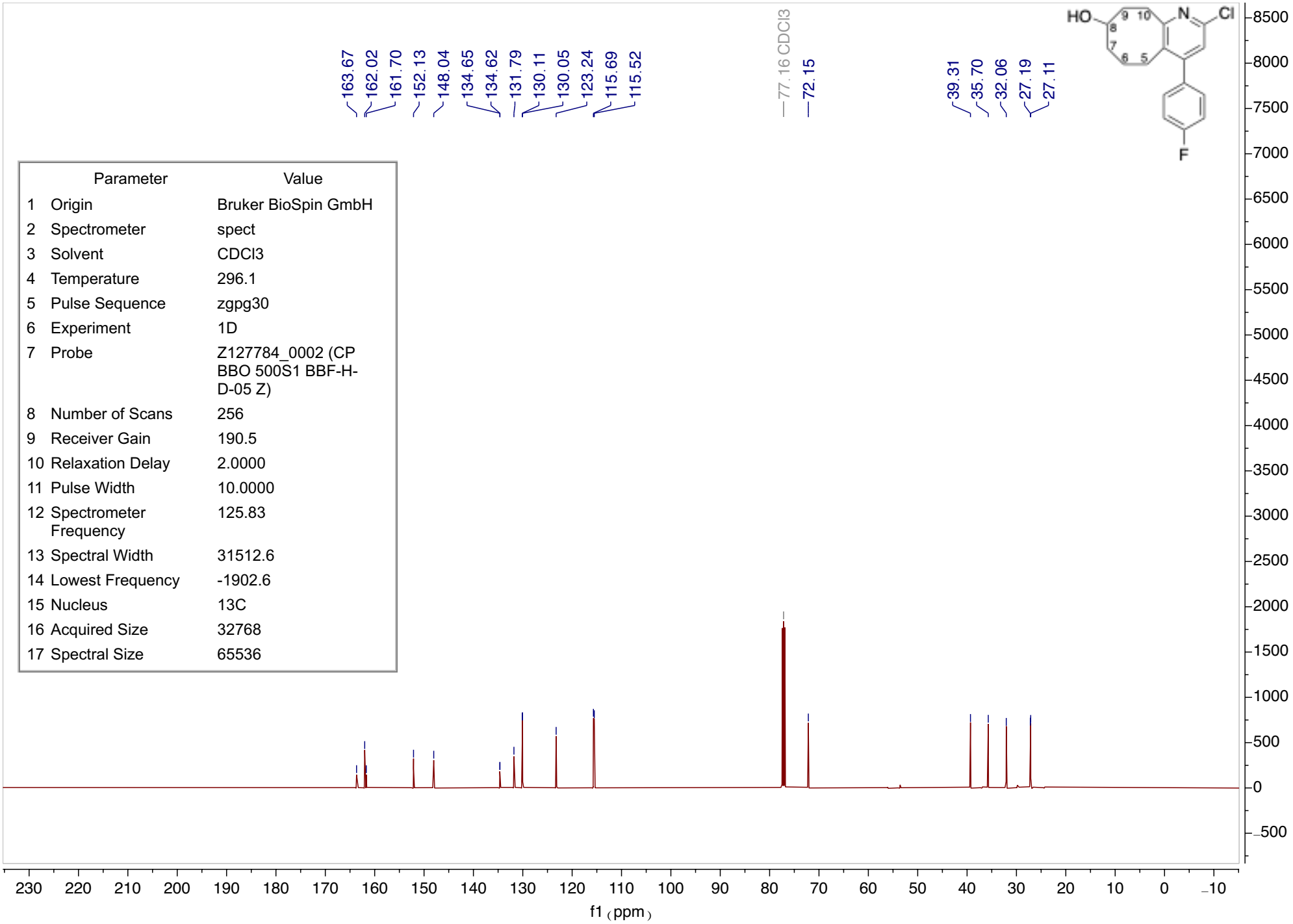


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.9095
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4132.2
14	Lowest Frequency	-7.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


HO
N
Cl
F
HA
HH
HK
HD
HE
Ha
Hd
He
Hh
Hk
f2 (ppm)
f1 (ppm)

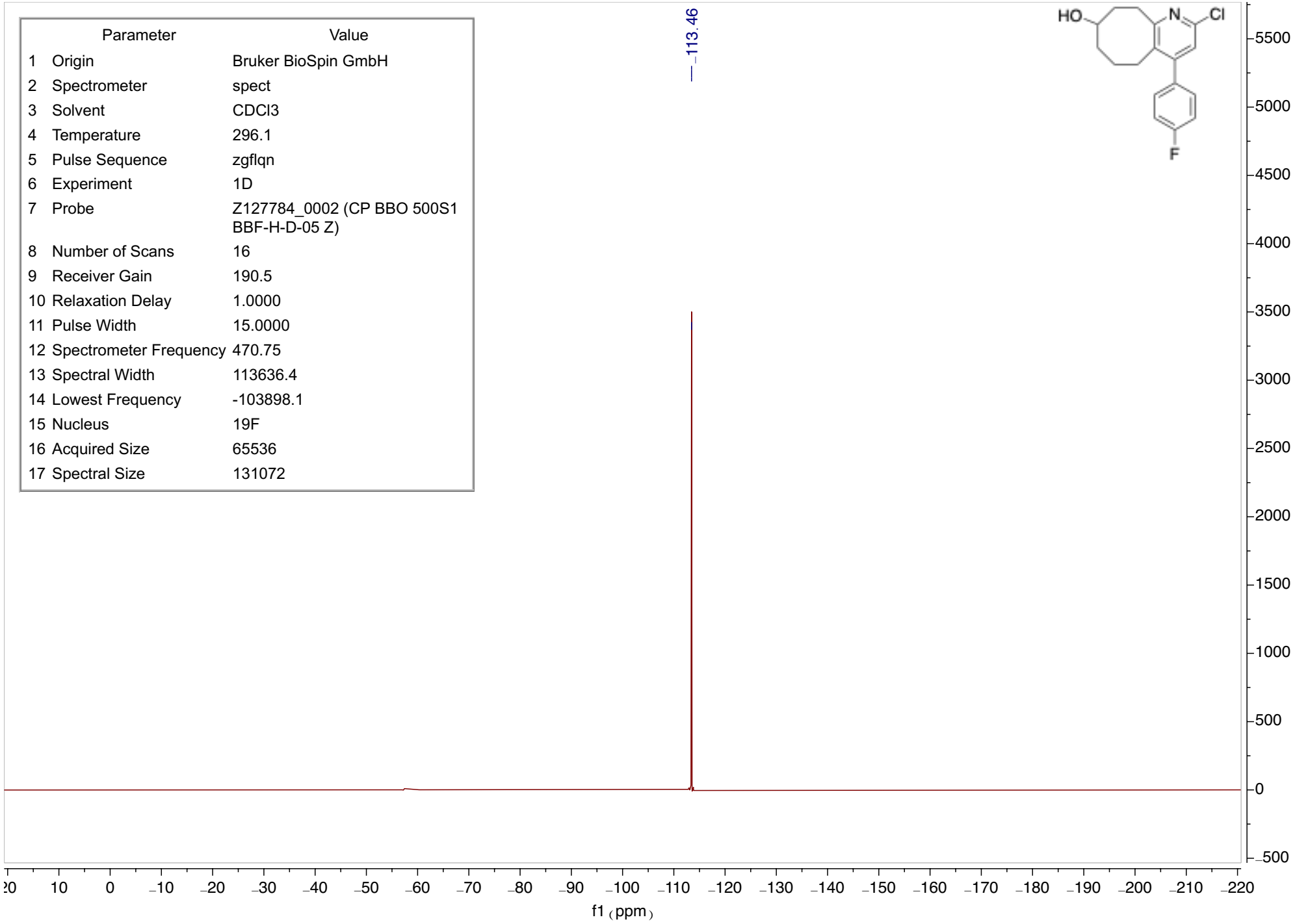
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	34.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

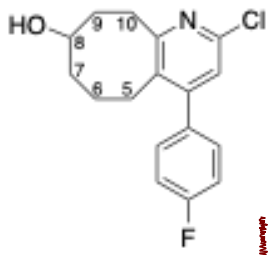




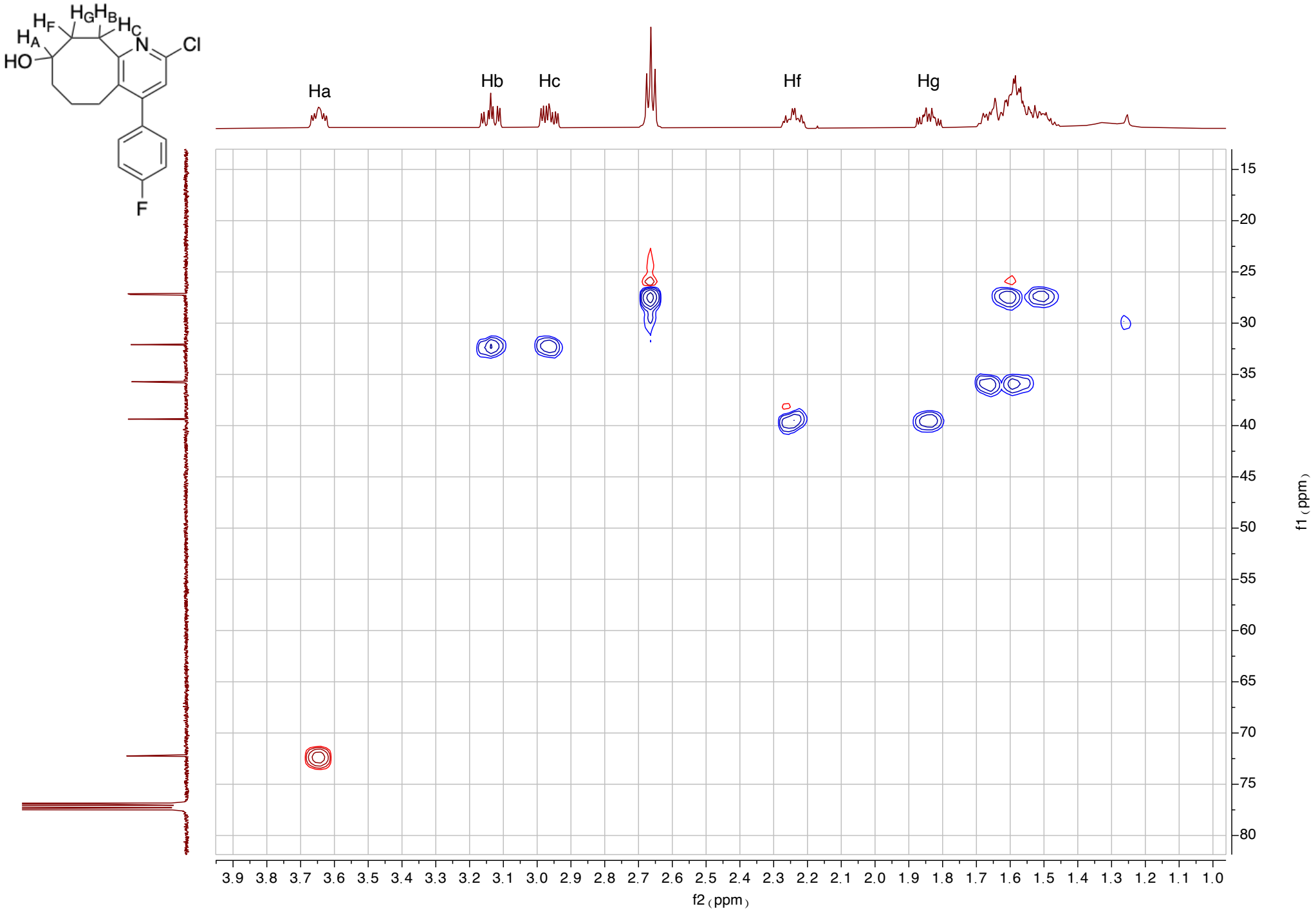
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

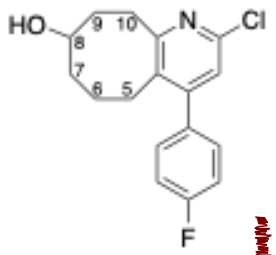
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



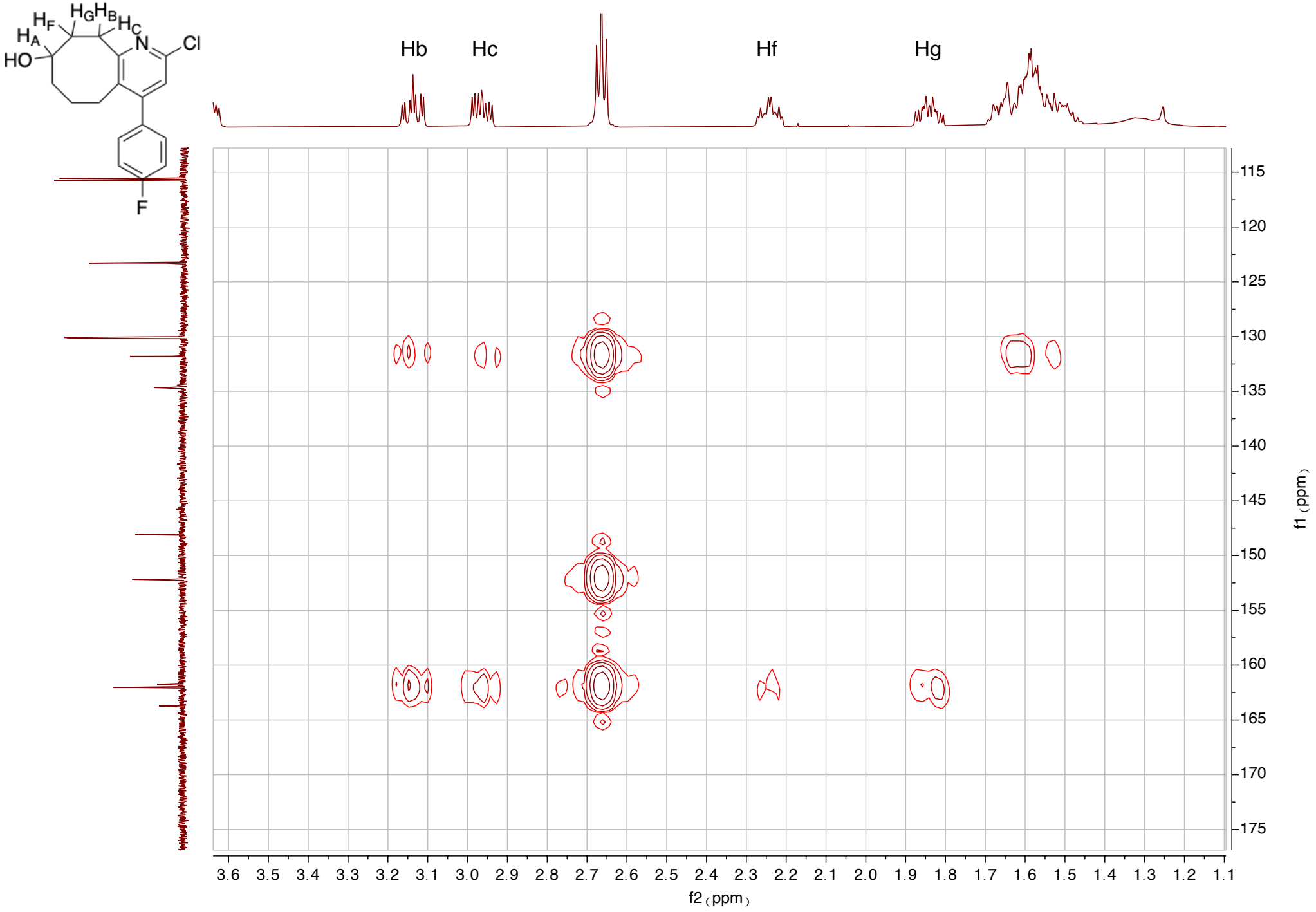


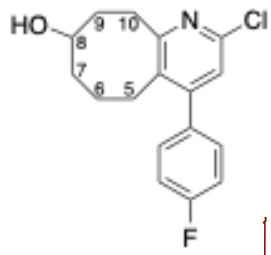
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4032.3
14	Lowest Frequency	10.1
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


HF
HG
HB
HC
HA
HO
N
Cl
F
Ha
Hb
Hc
Hf
Hg
f2 (ppm)
f1 (ppm)

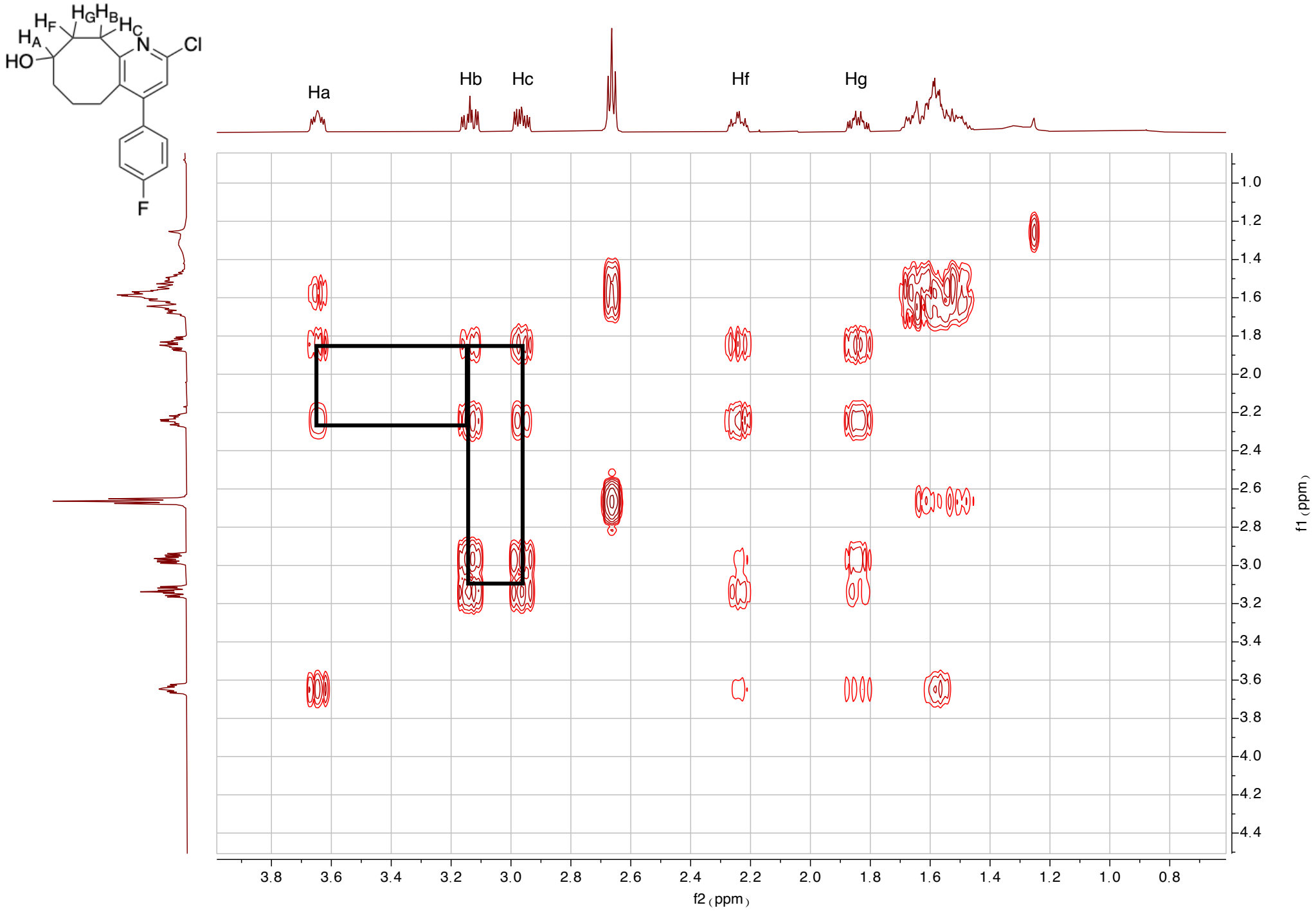


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hmbcgplpndqf
6	Experiment	HMBC
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	4
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4032.3
14	Lowest Frequency	7.7
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

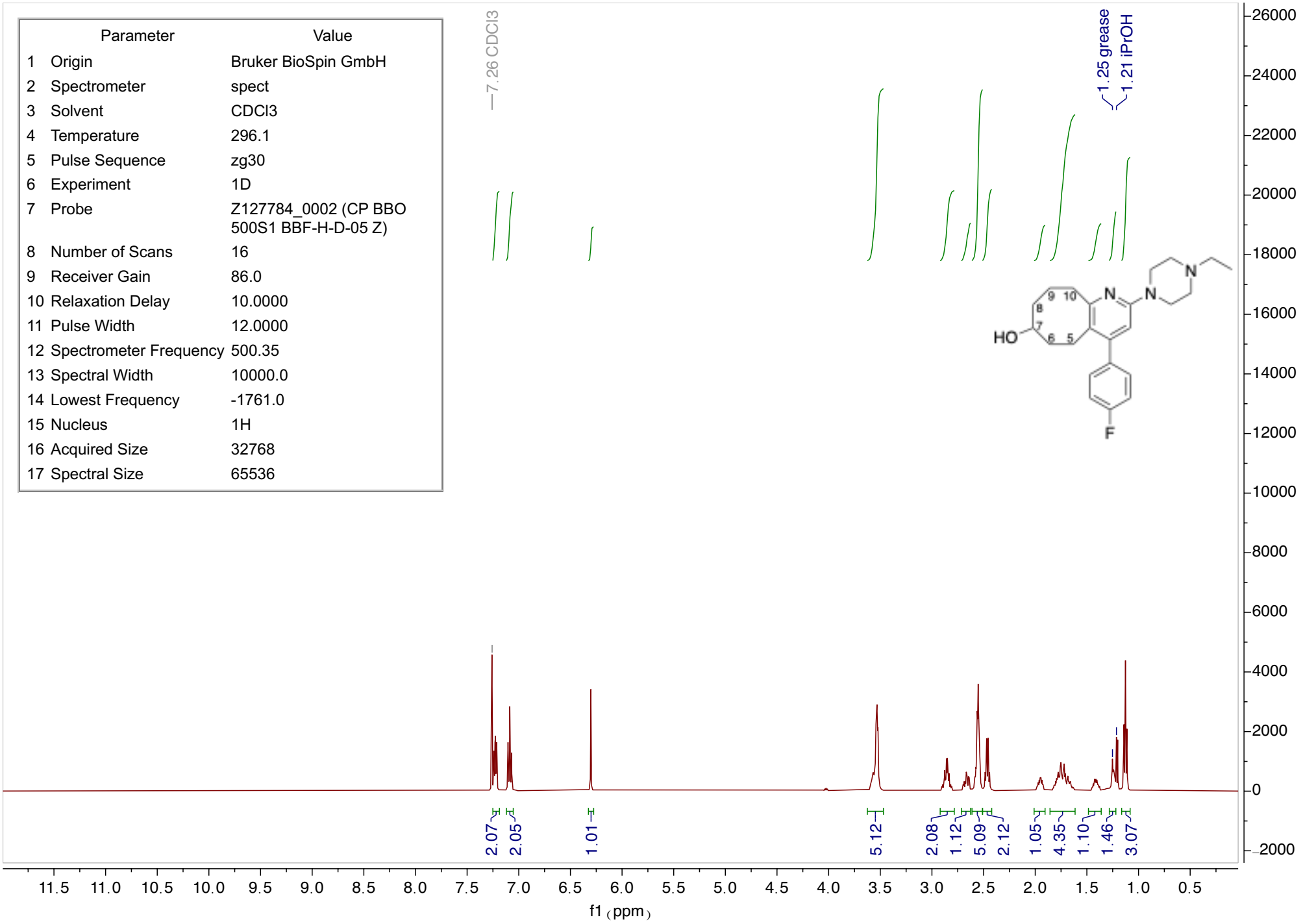

HF
HG
HB
HC
HA
HO
N
Cl
F
Hb
Hc
Hf
Hg
115
120
125
130
135
140
145
150
155
160
165
170
175
f1 (ppm)
3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1
f2 (ppm)

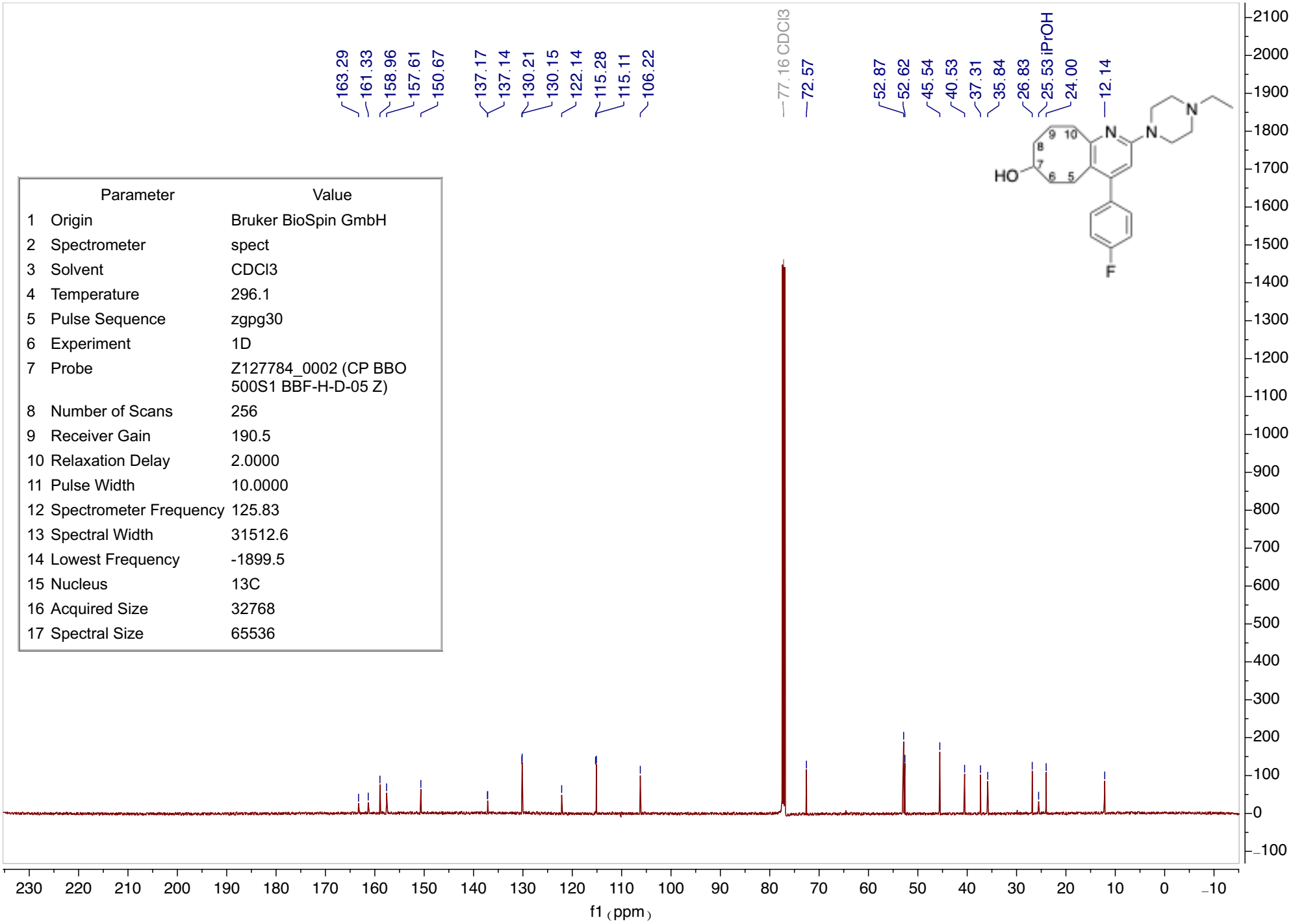


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	61.8
10	Relaxation Delay	1.9033
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4032.3
14	Lowest Frequency	7.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024


HF
HG
HB
HC
HA
HO
N
Cl
F
Ha
Hb
Hc
Hf
Hg
f2 (ppm)
f1 (ppm)

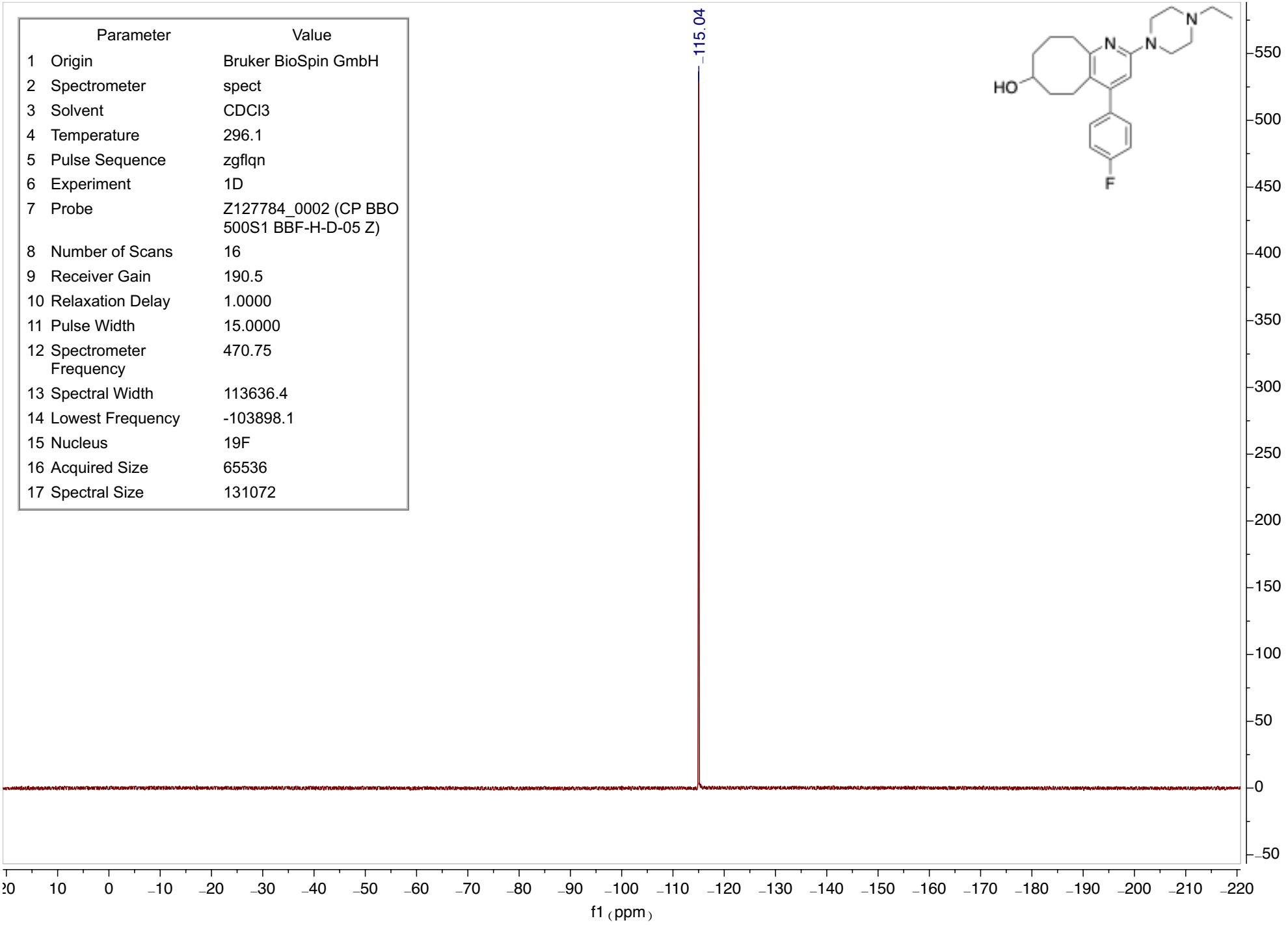
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1761.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

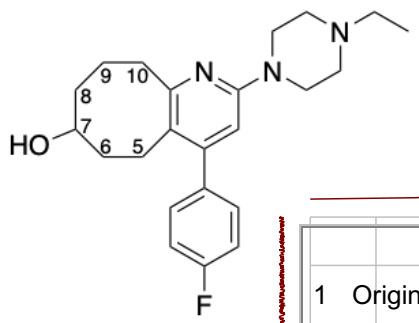




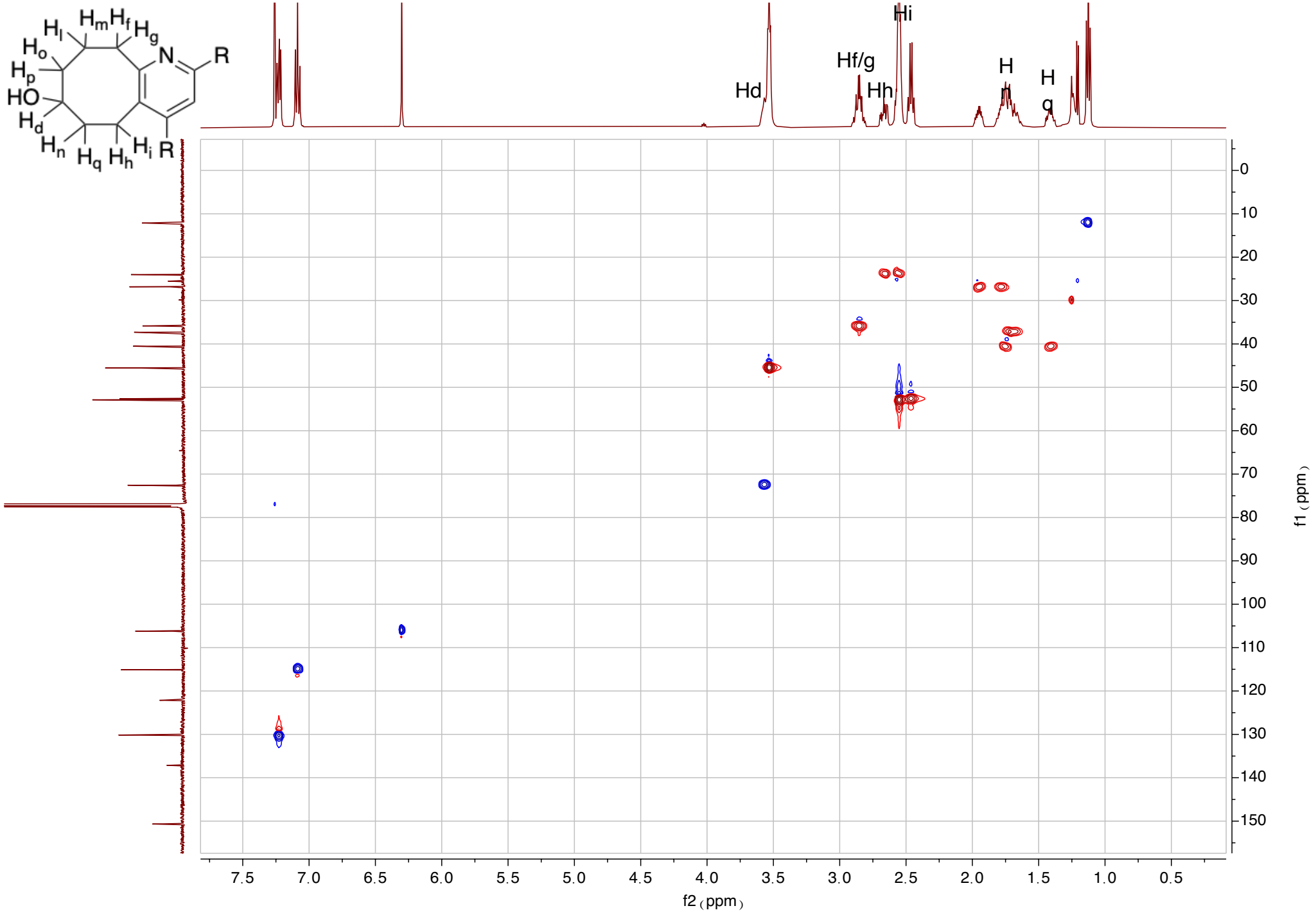
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1899.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

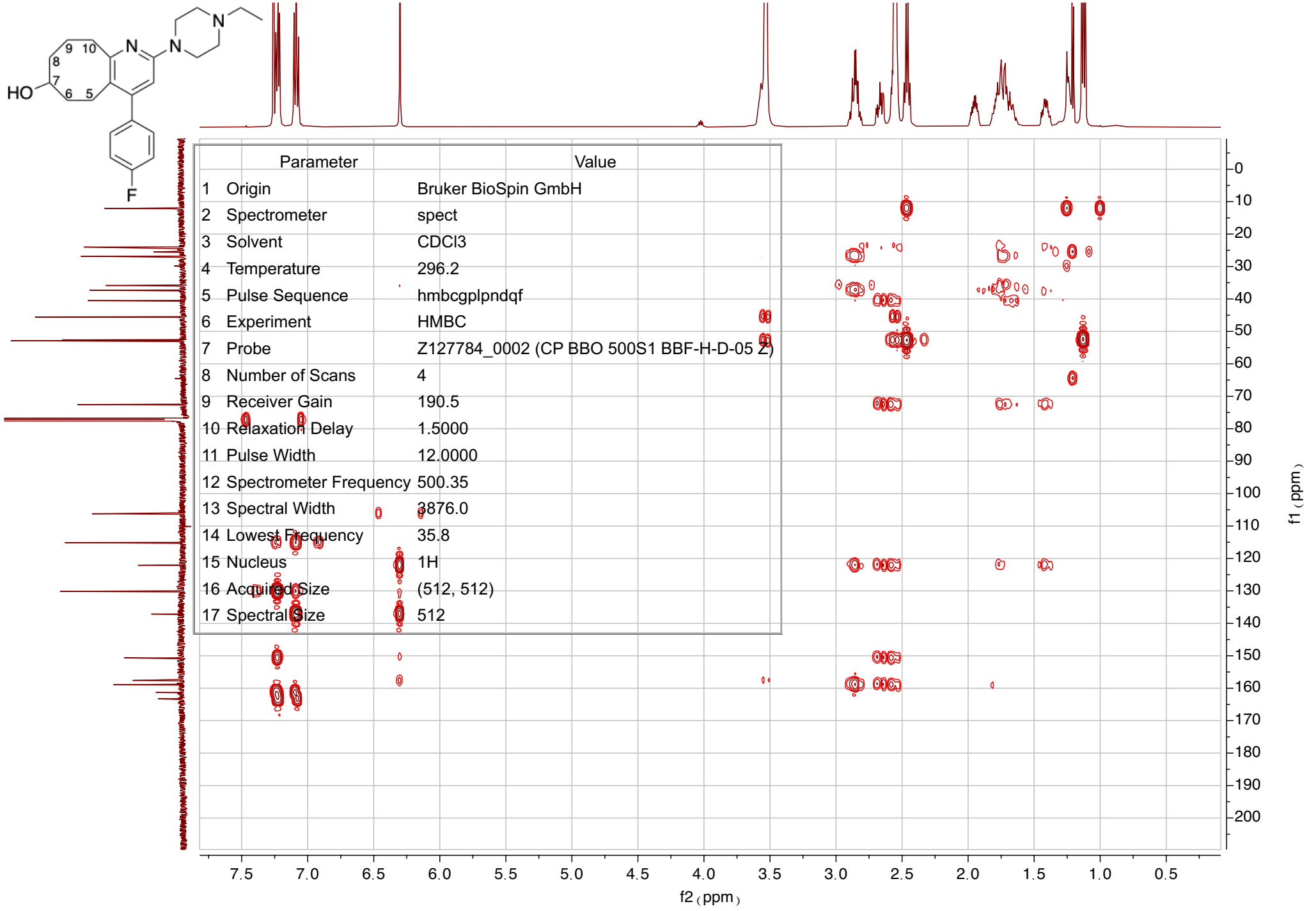
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

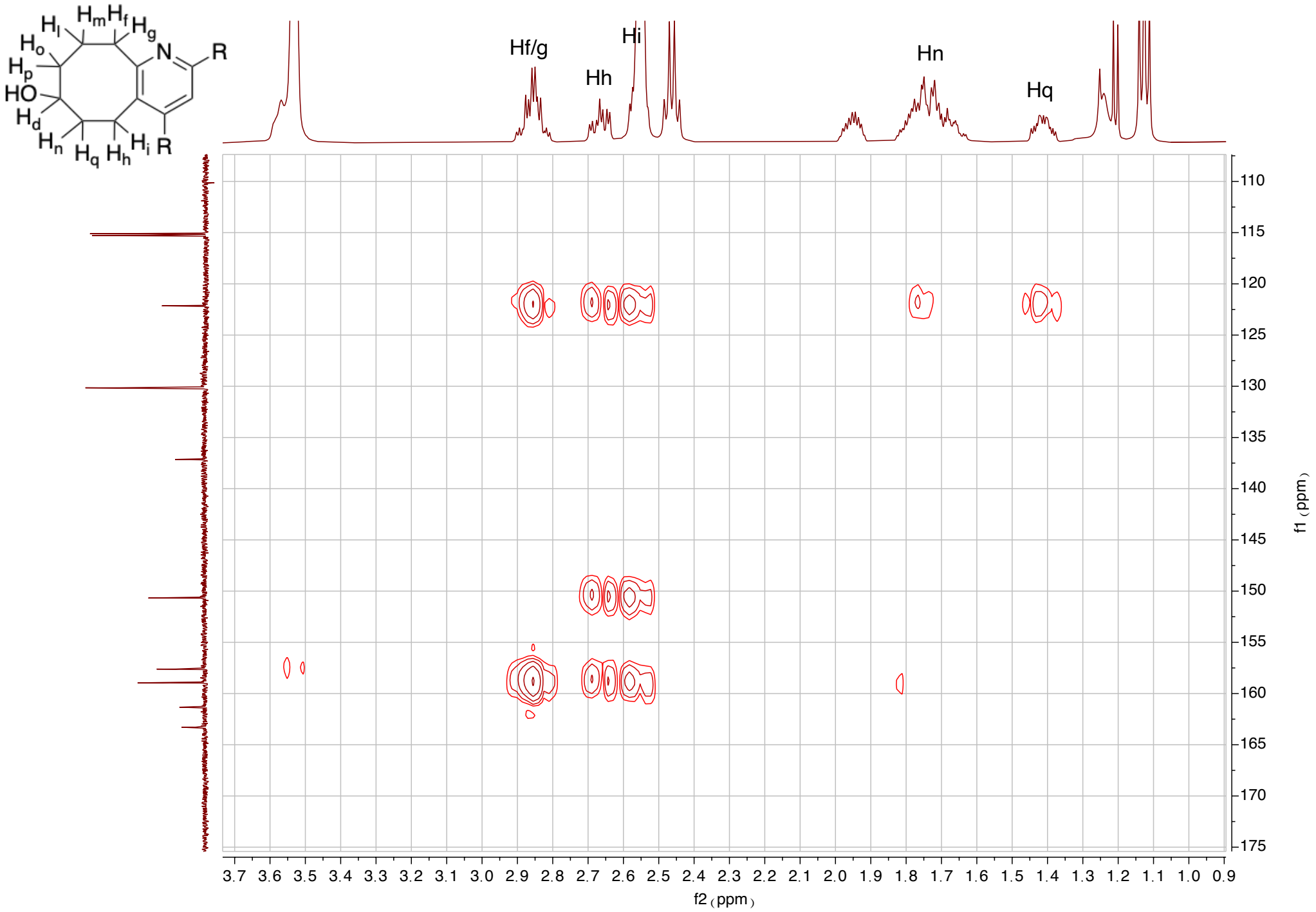


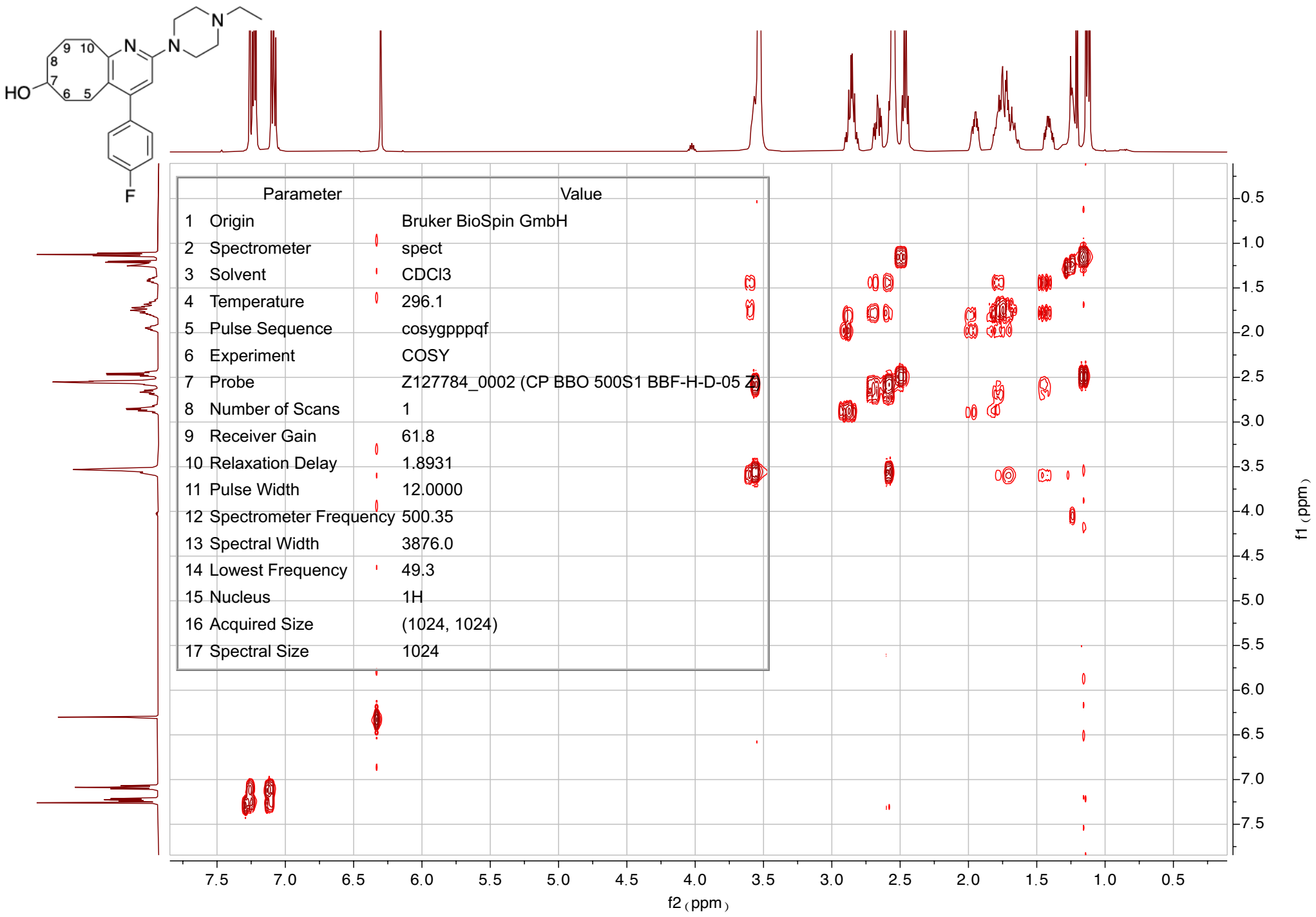


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	3876.0
14	Lowest Frequency	35.8
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512


Hd
Hf/g
Hh
Hi
H
m
H
q
f2 (ppm)
f1 (ppm)


HO
F
N
N
N
9
10
8
7
6
5
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 3876.0
14 Lowest Frequency 35.8
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
f1 (ppm)


Hf/g
Hh
Hi
Hn
Hq
f2 (ppm)
f1 (ppm)


HO
F
N
N
N
9
10
8
7
6
5
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 1
9 Receiver Gain 61.8
10 Relaxation Delay 1.8931
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 3876.0
14 Lowest Frequency 49.3
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
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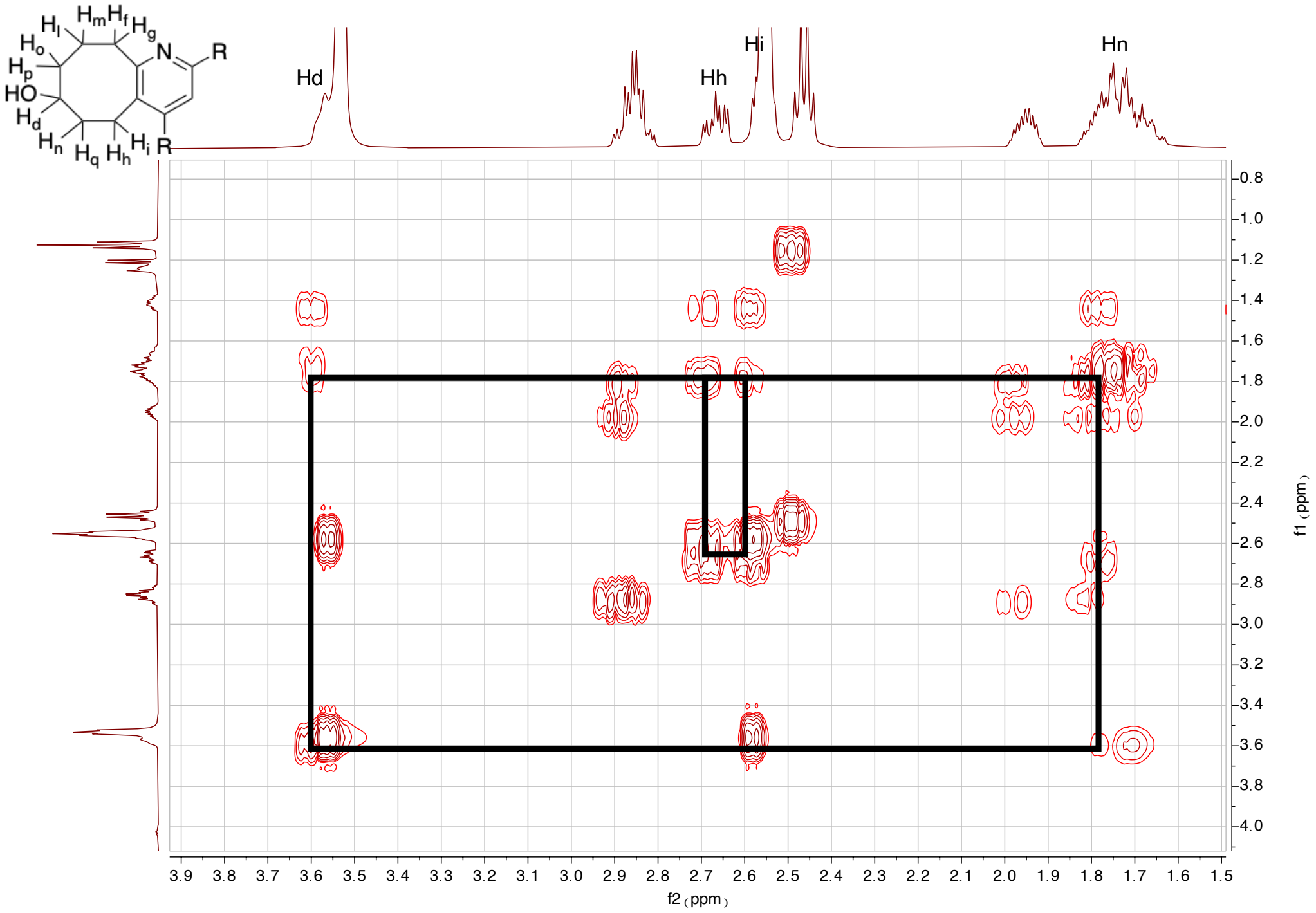
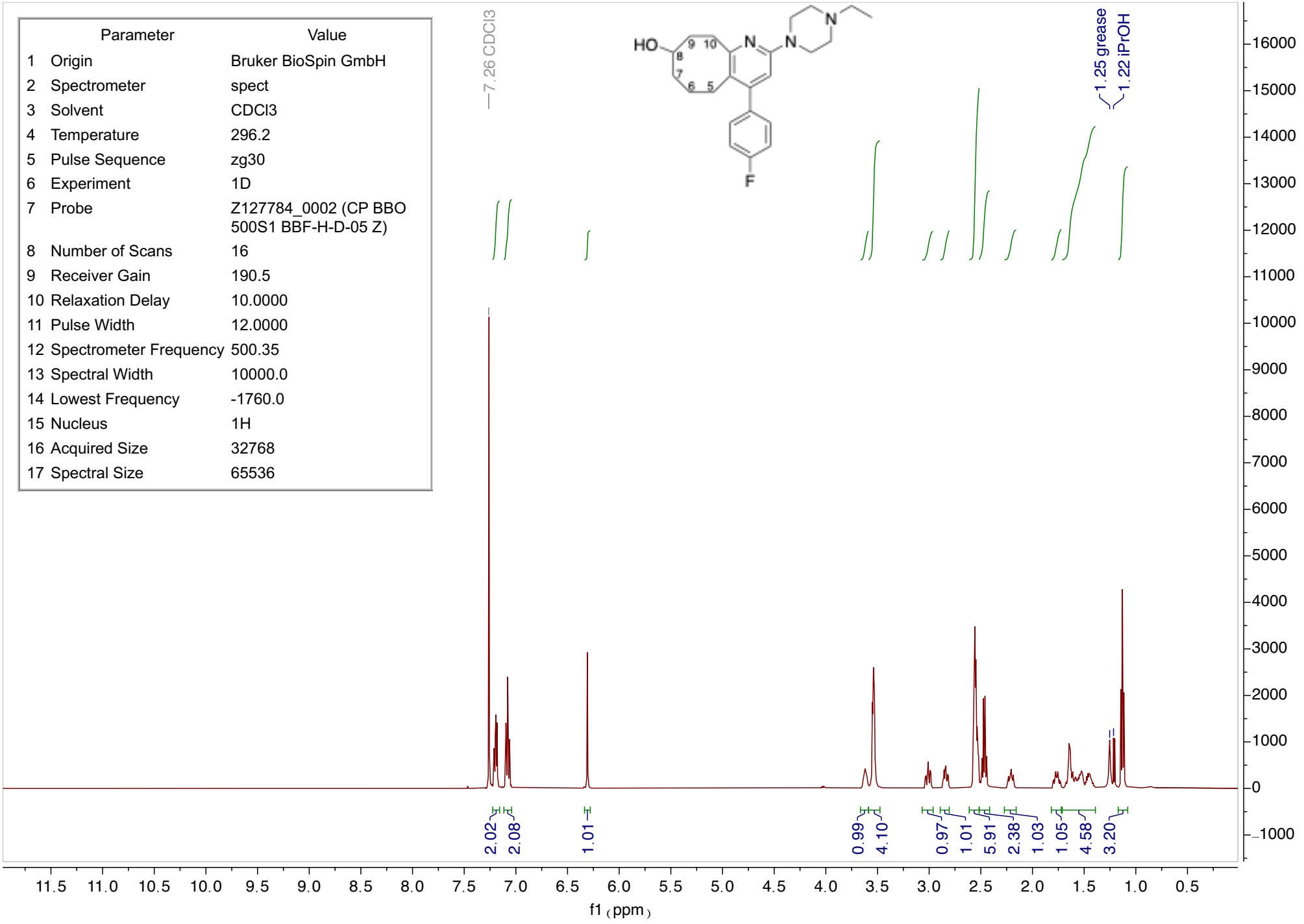
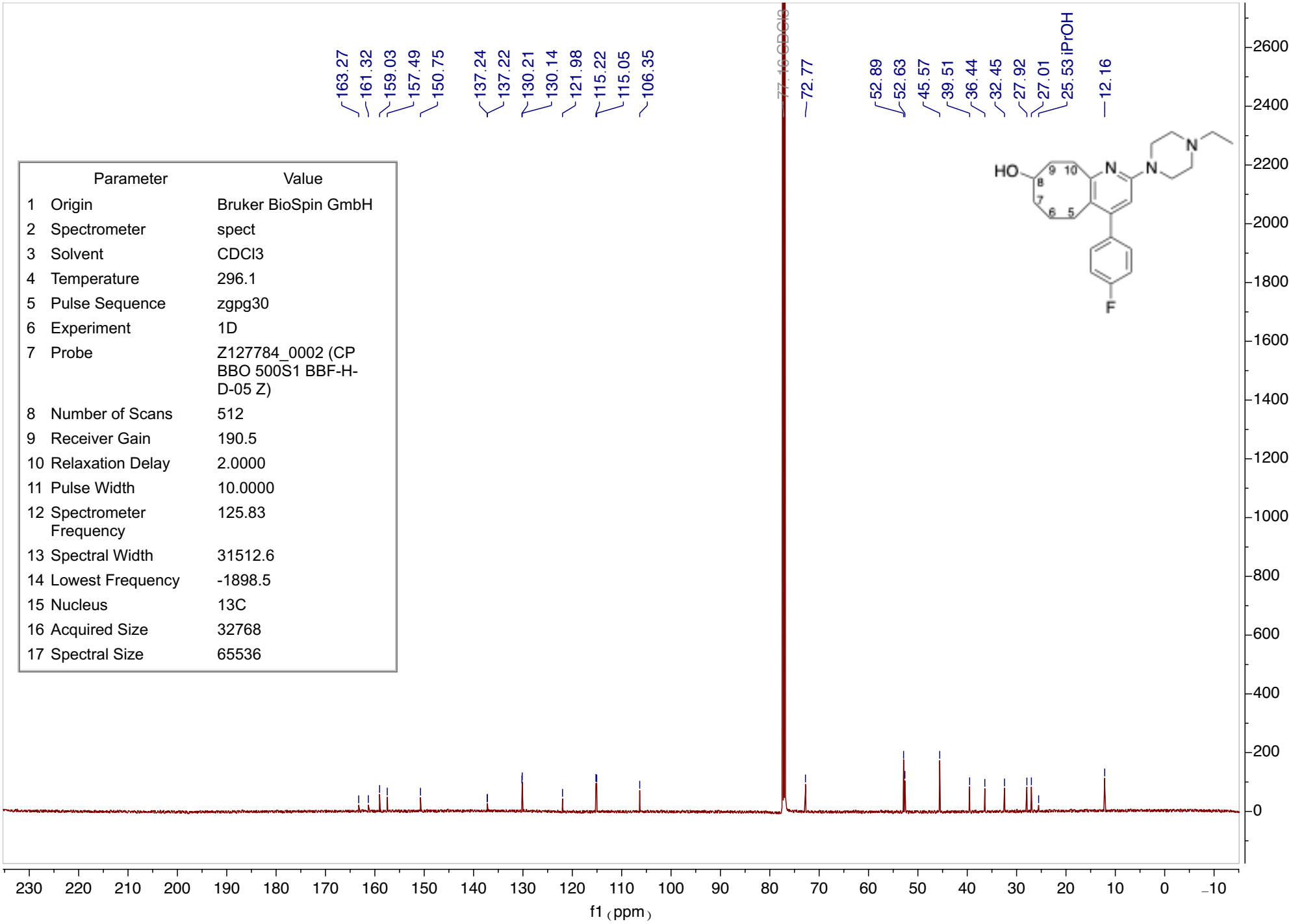
f1 (ppm)


Hd
Hh
Hi
Hn
f2 (ppm)
f1 (ppm)

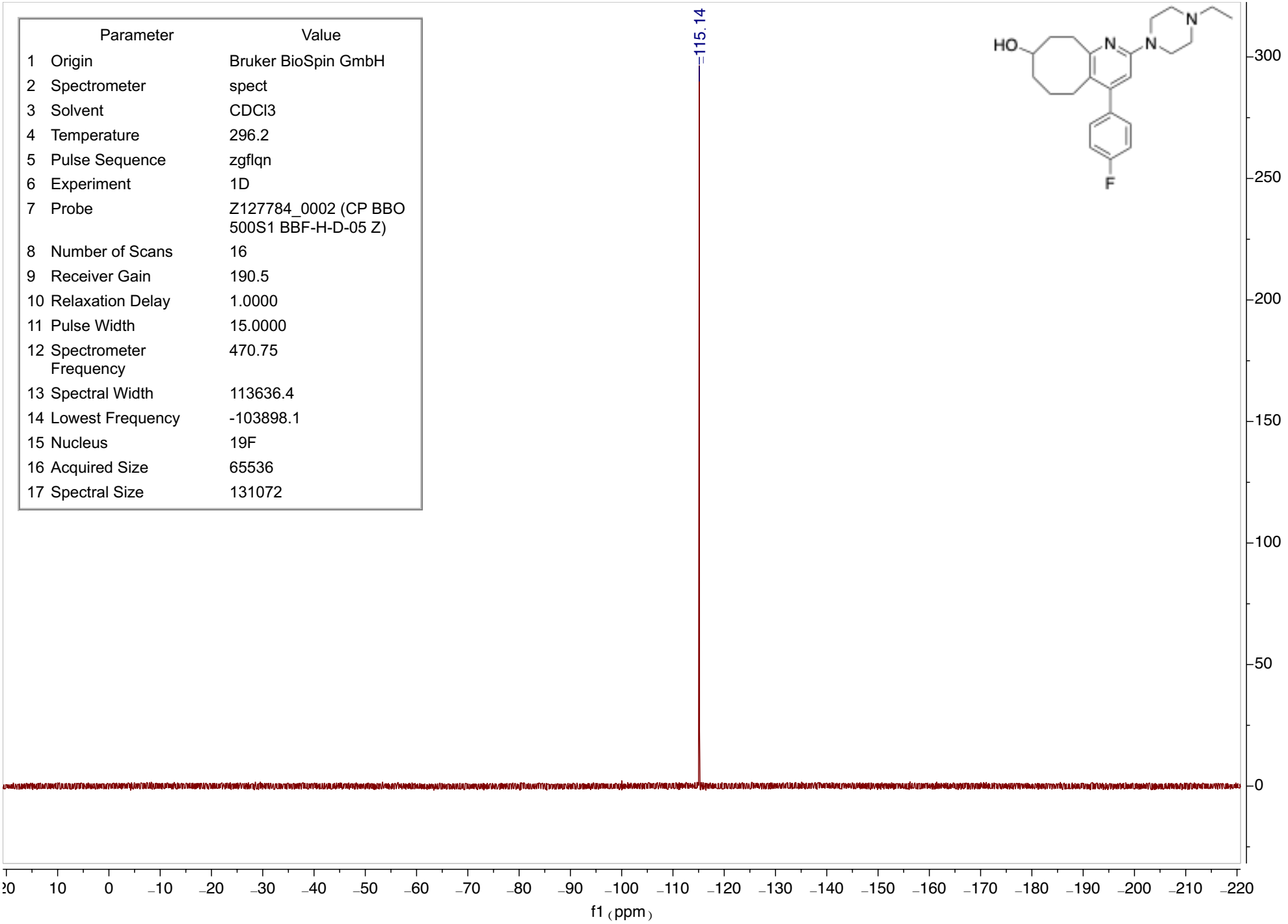
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1760.0
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

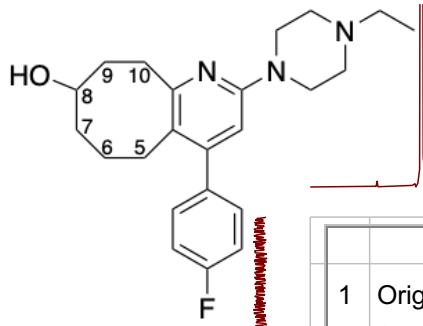




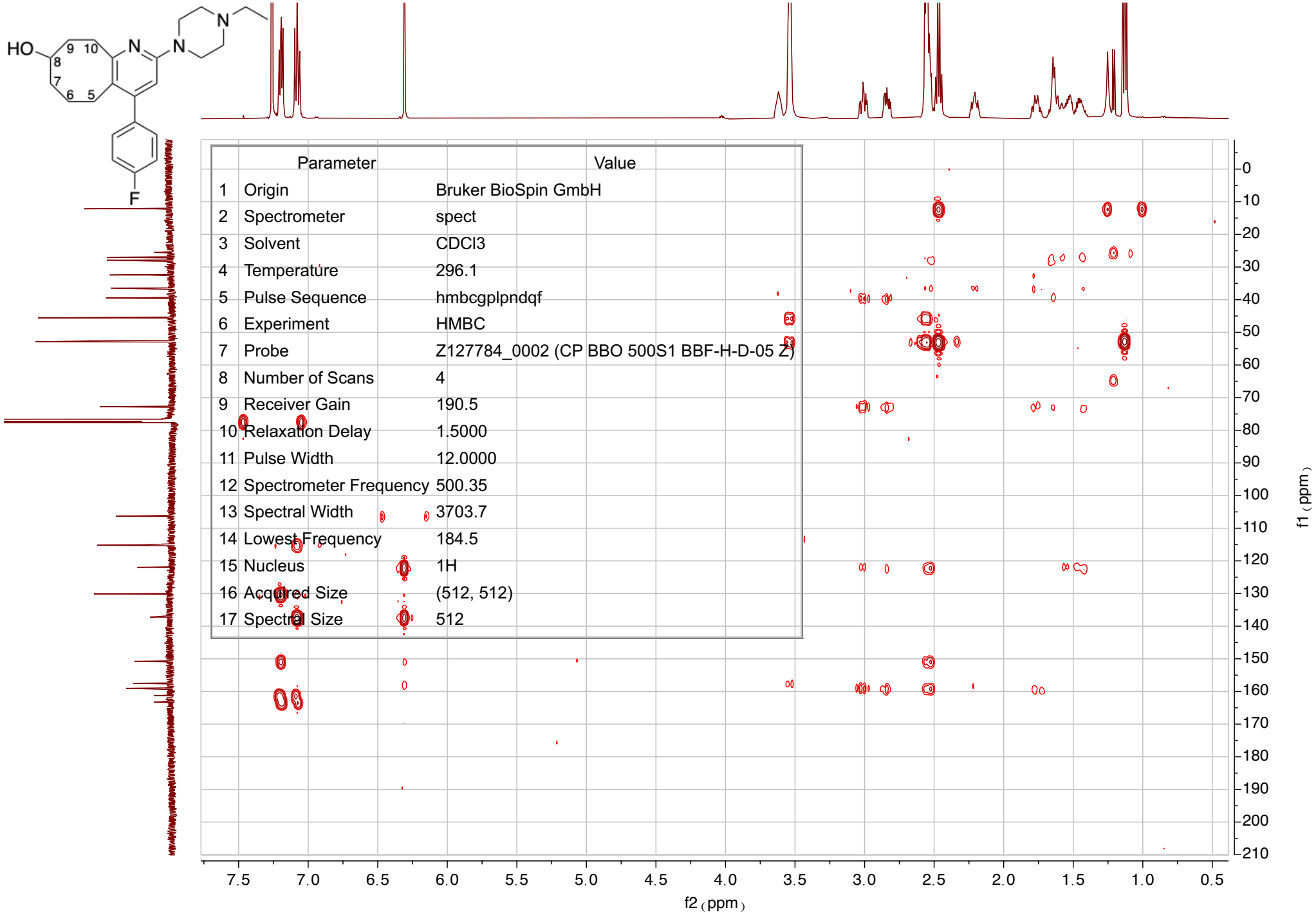
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1898.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

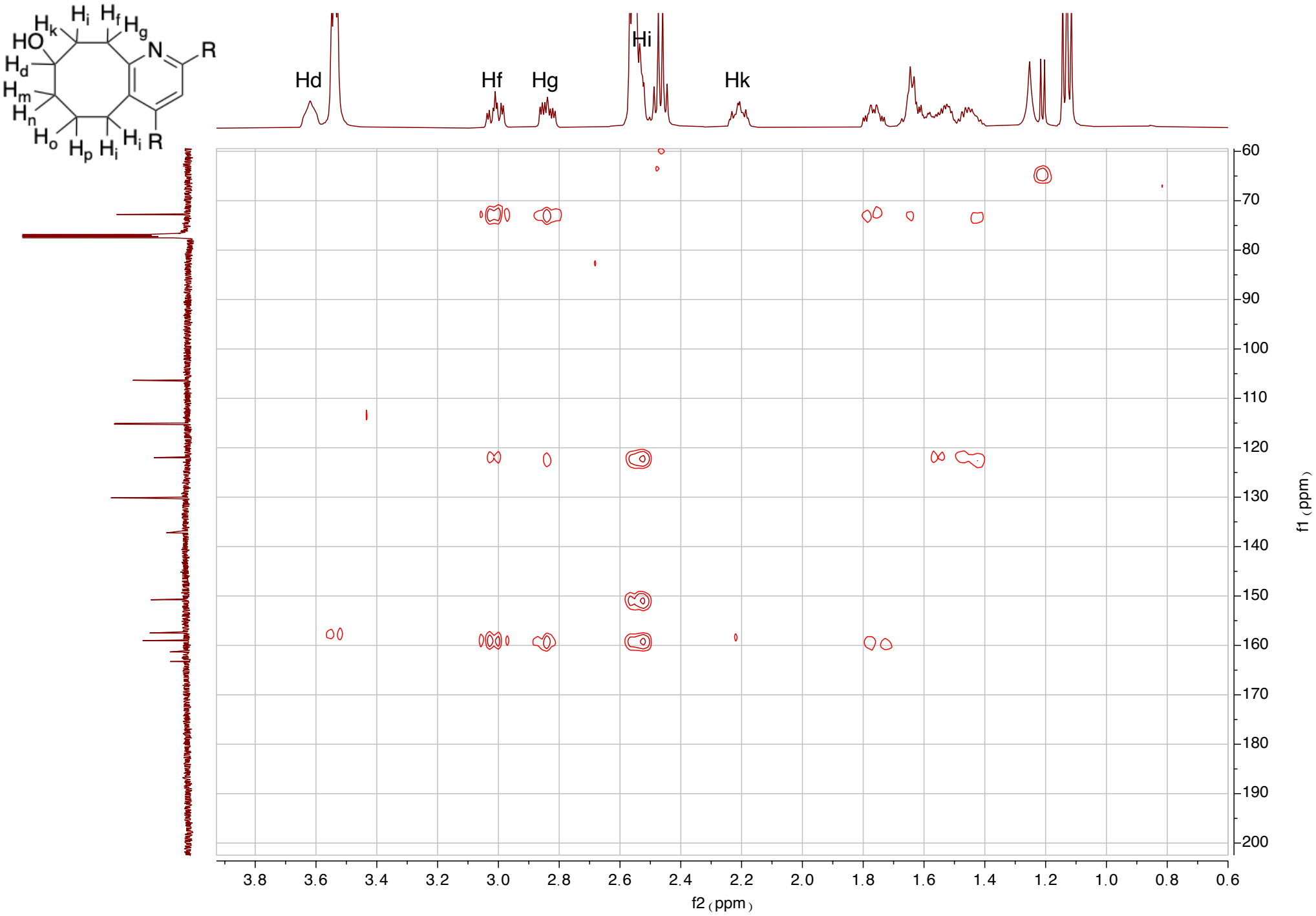
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

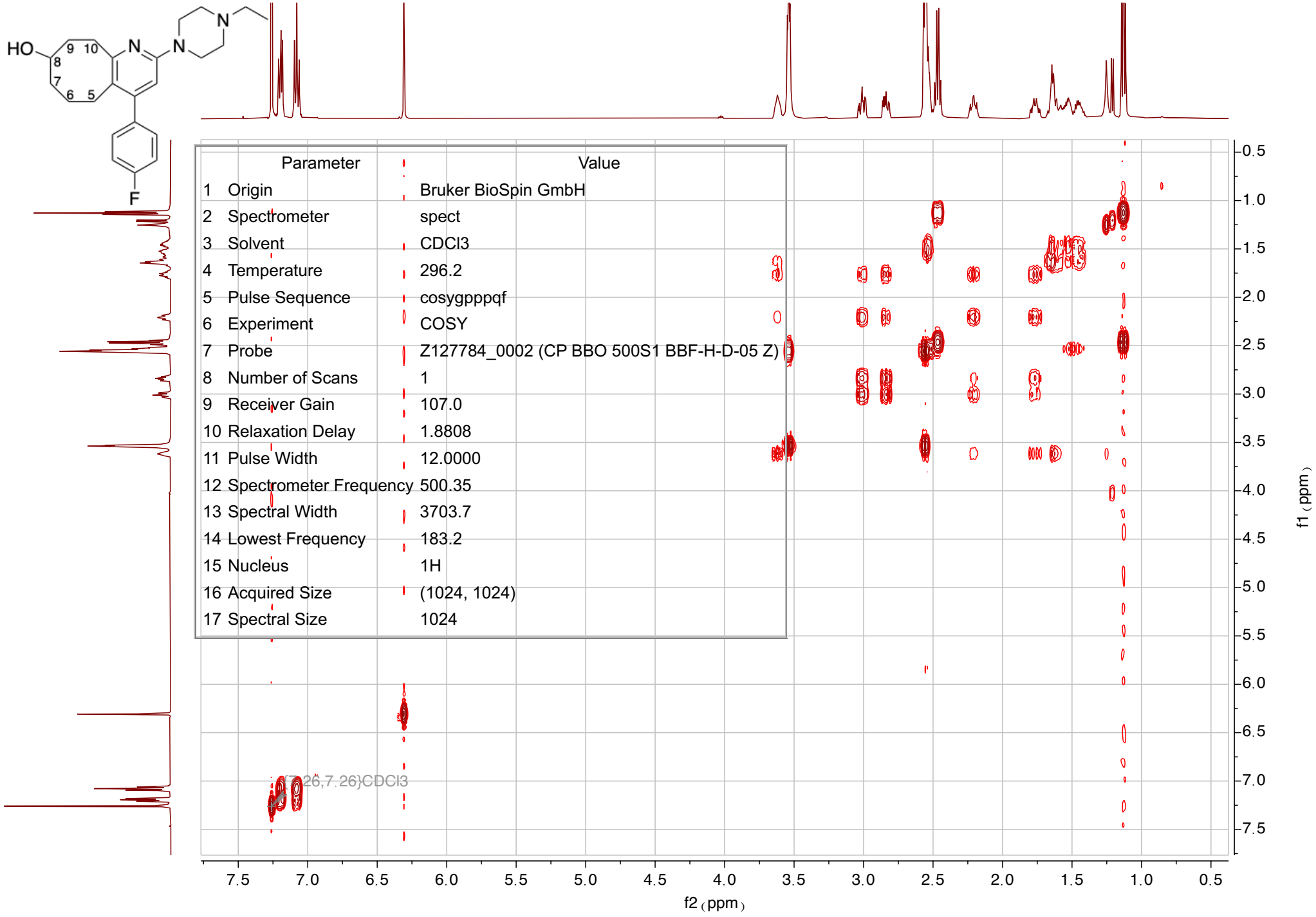


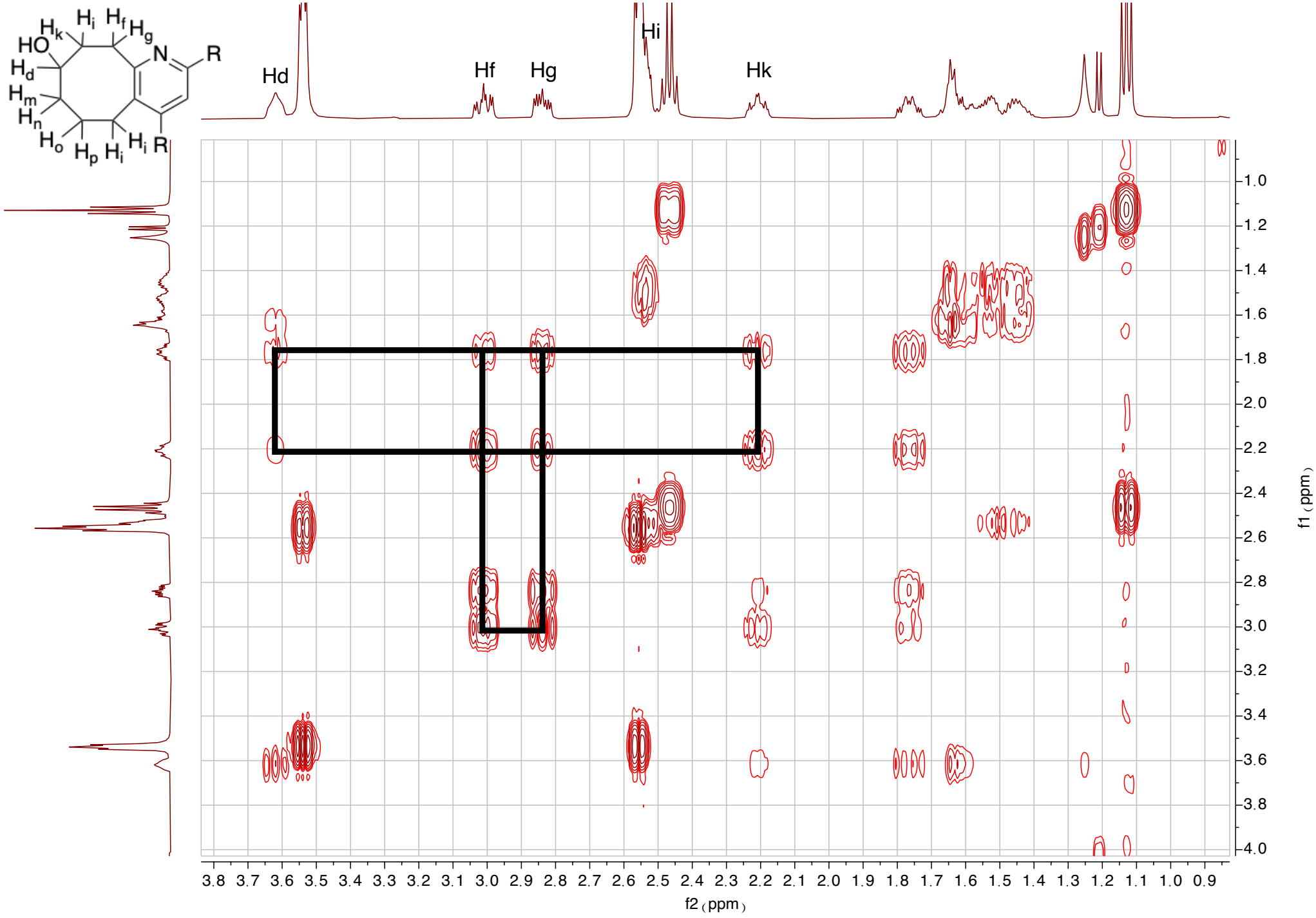


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	hsqcedetgp
6	Experiment	HSQC-EDITED
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	2
9	Receiver Gain	190.5
10	Relaxation Delay	1.5000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	3703.7
14	Lowest Frequency	186.4
15	Nucleus	1H
16	Acquired Size	(512, 512)
17	Spectral Size	512

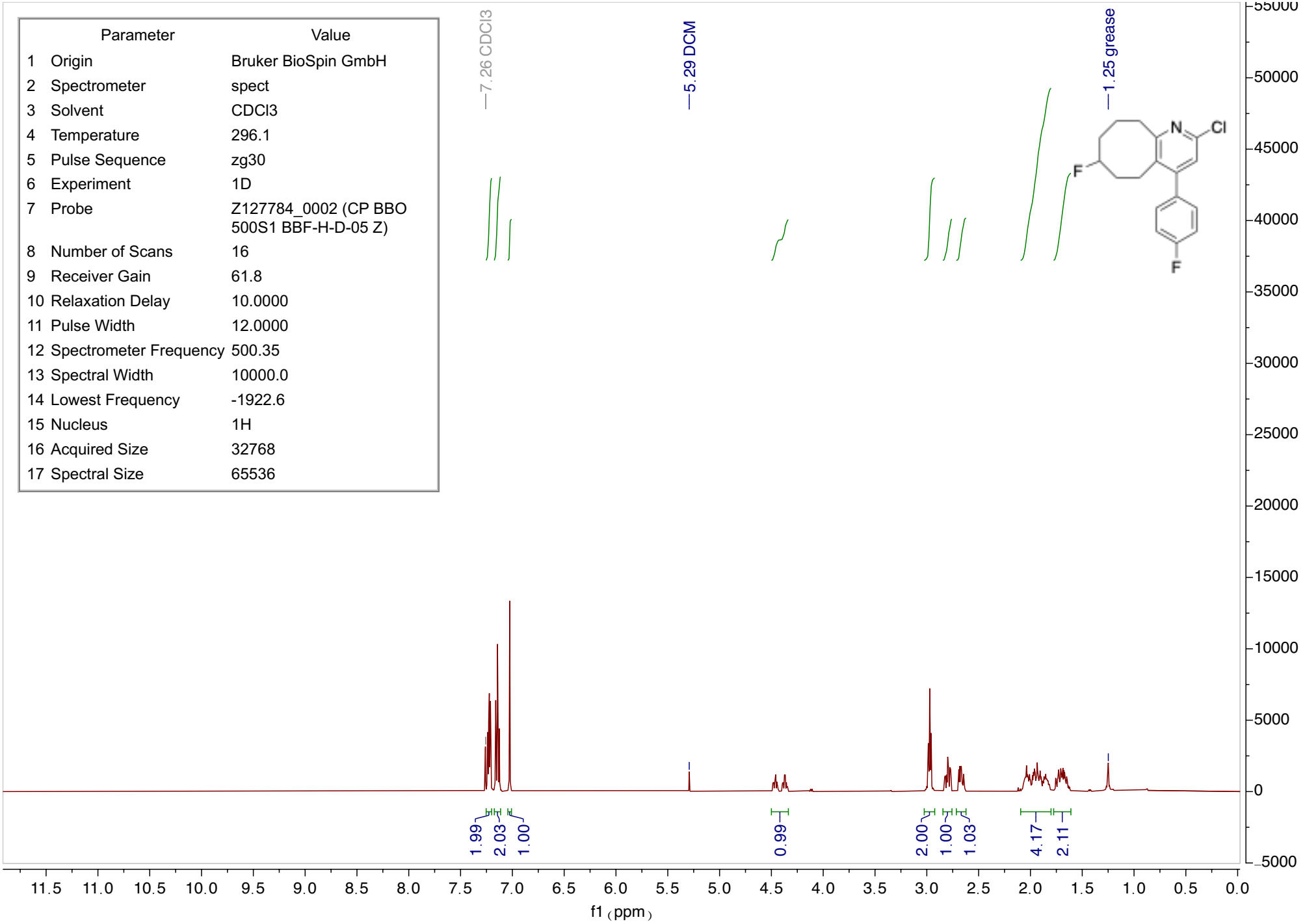

HO
9
10
8
7
6
5
N
N
N
F
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 3703.7
14 Lowest Frequency 184.5
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
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
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
f1 (ppm)

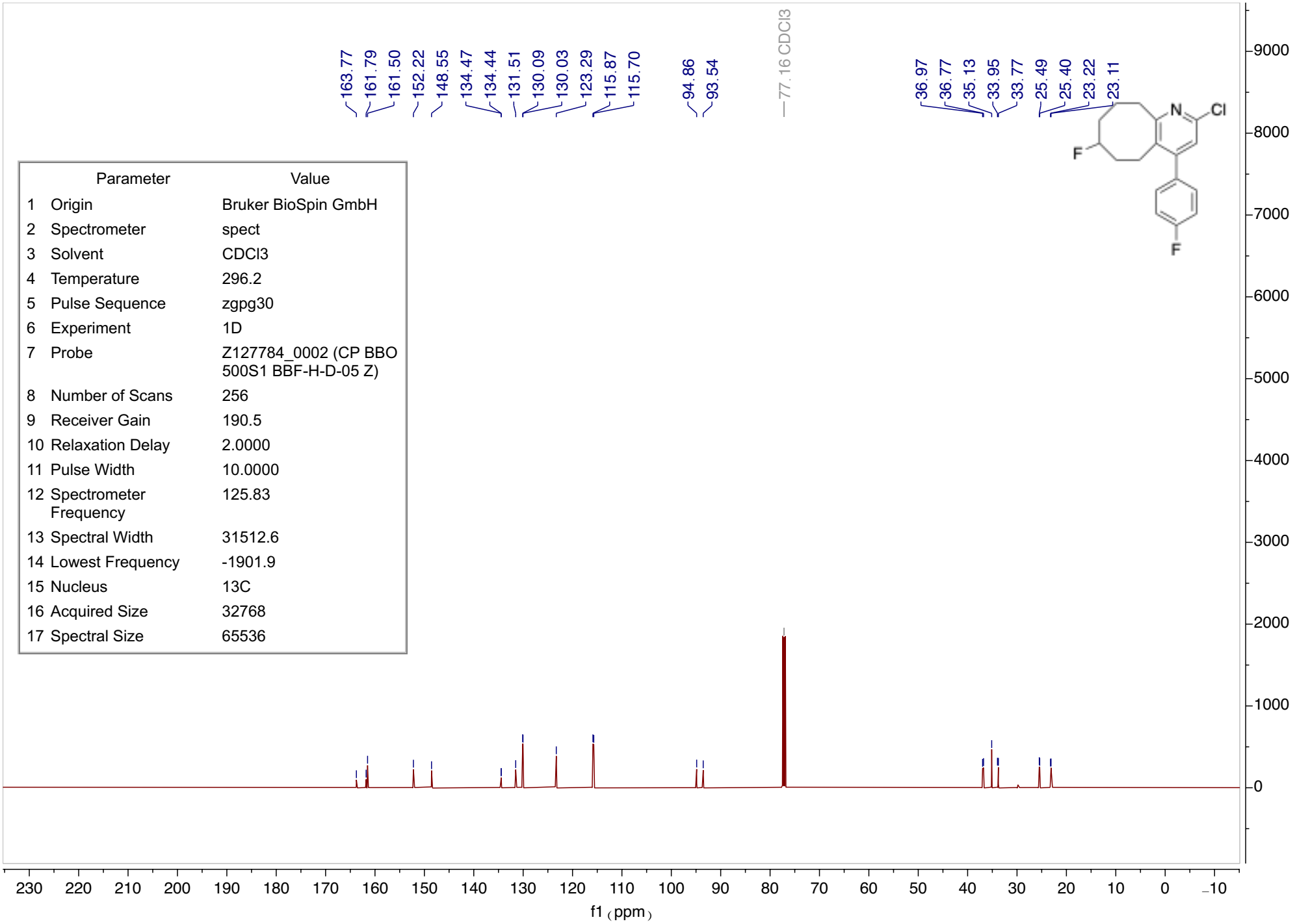

Hd
Hf
Hg
Hi
Hk
f2 (ppm)
f1 (ppm)
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200


HO
9 10
8
7
6 5
N
N
N
F
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 1
9 Receiver Gain 107.0
10 Relaxation Delay 1.8808
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 3703.7
14 Lowest Frequency 183.2
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
7.26,7.26)CDCl3
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
f2 (ppm)
0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5
f1 (ppm)


Hd
Hf
Hg
Hi
Hk
f2 (ppm)
f1 (ppm)

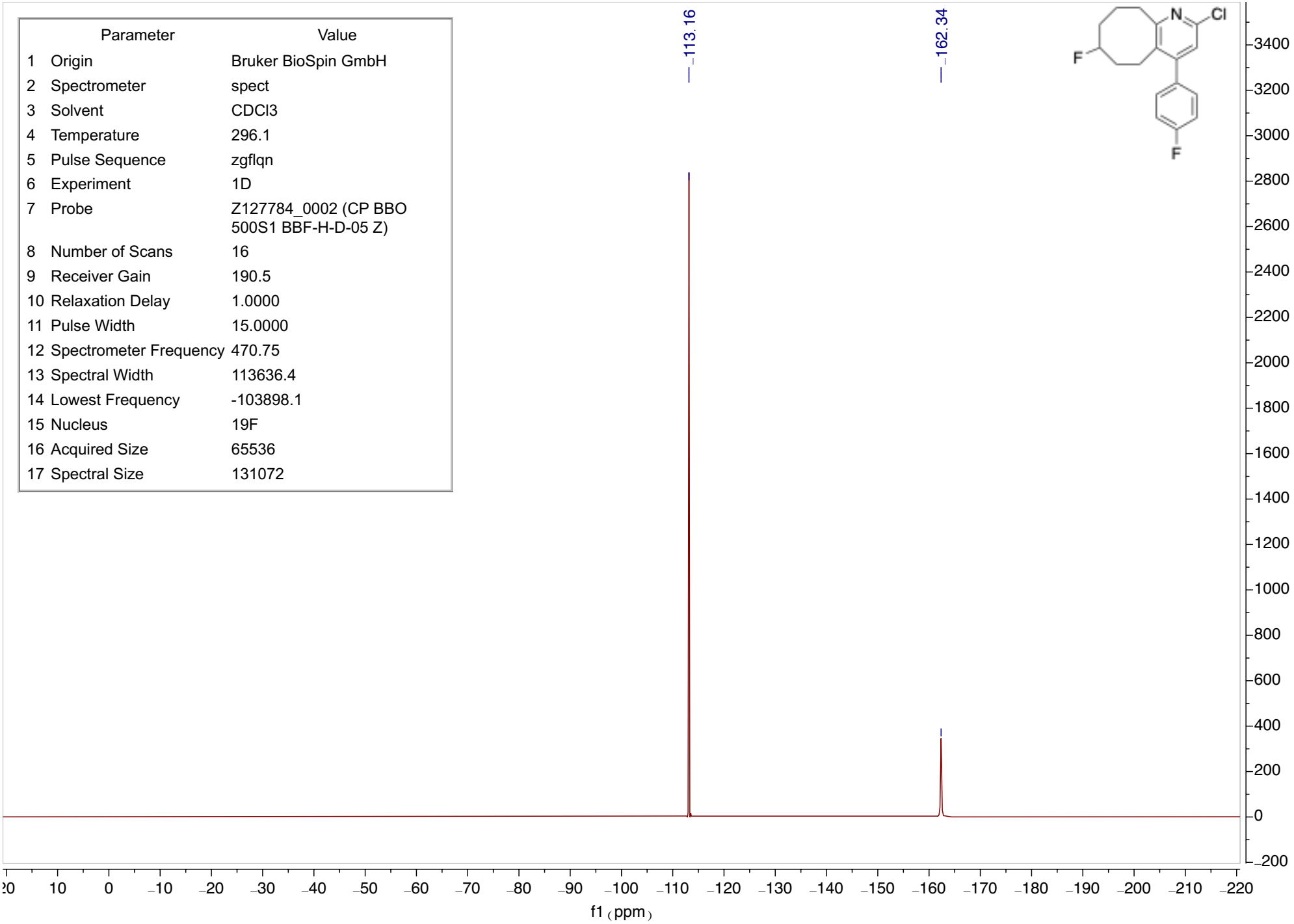
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



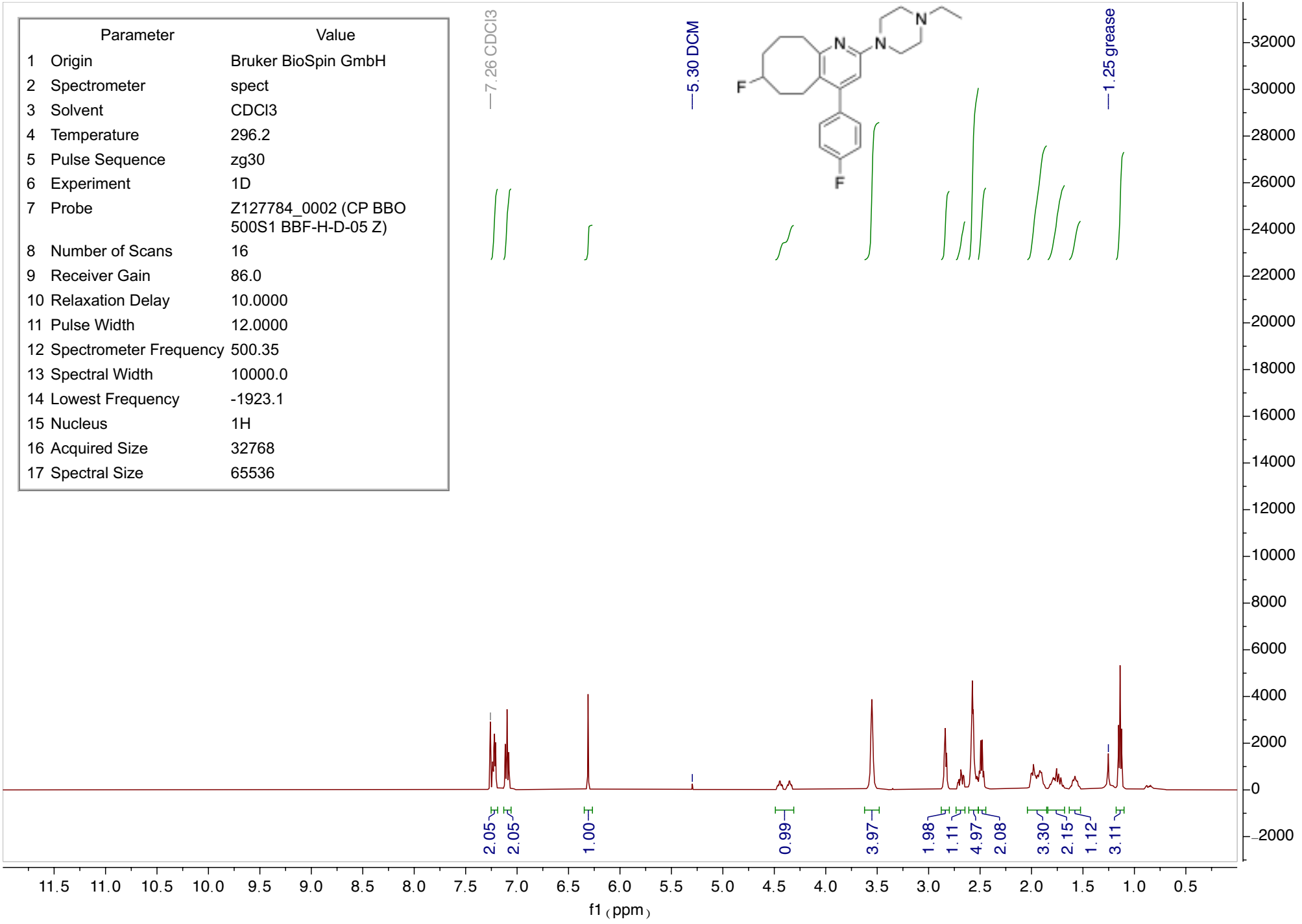


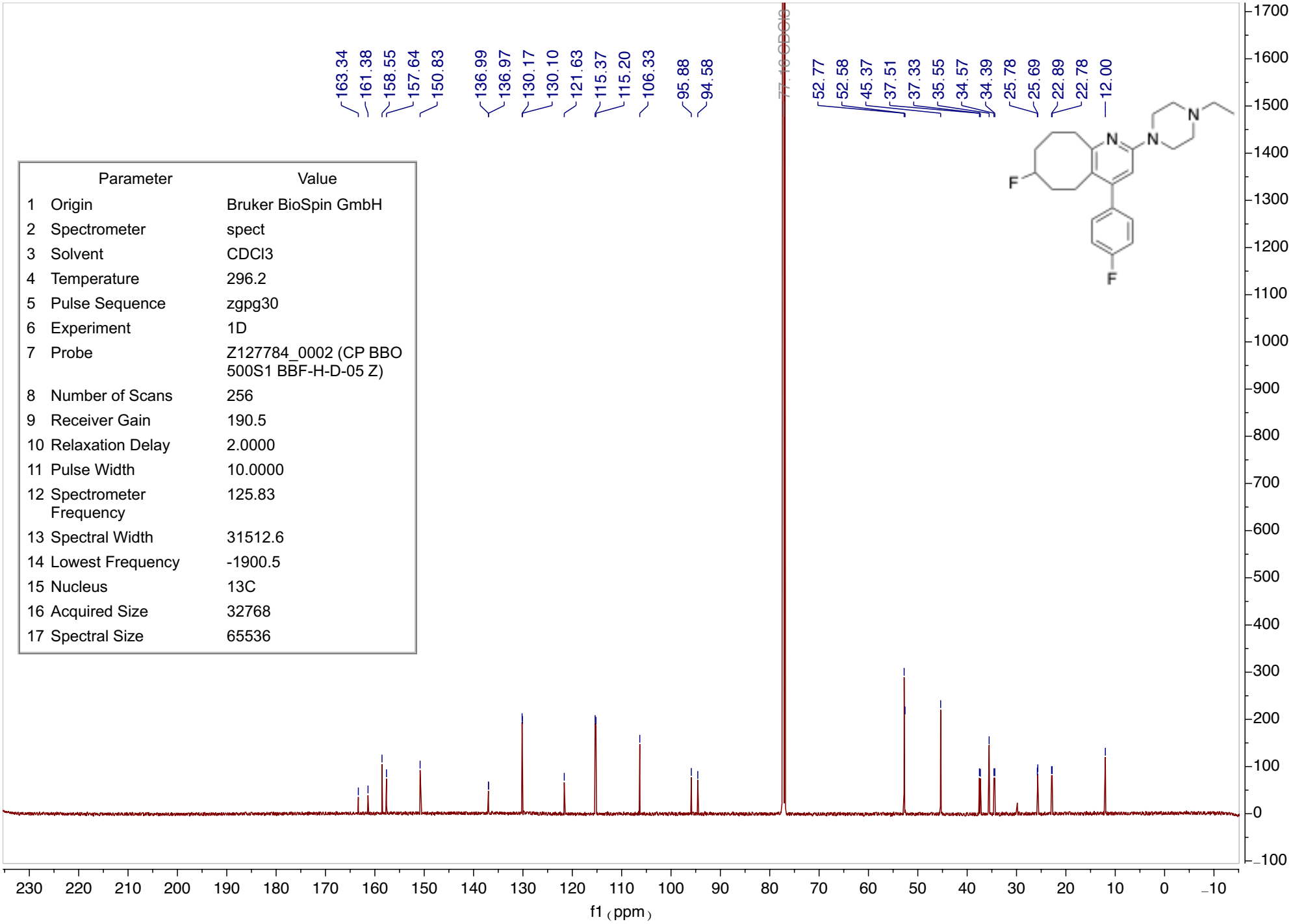
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



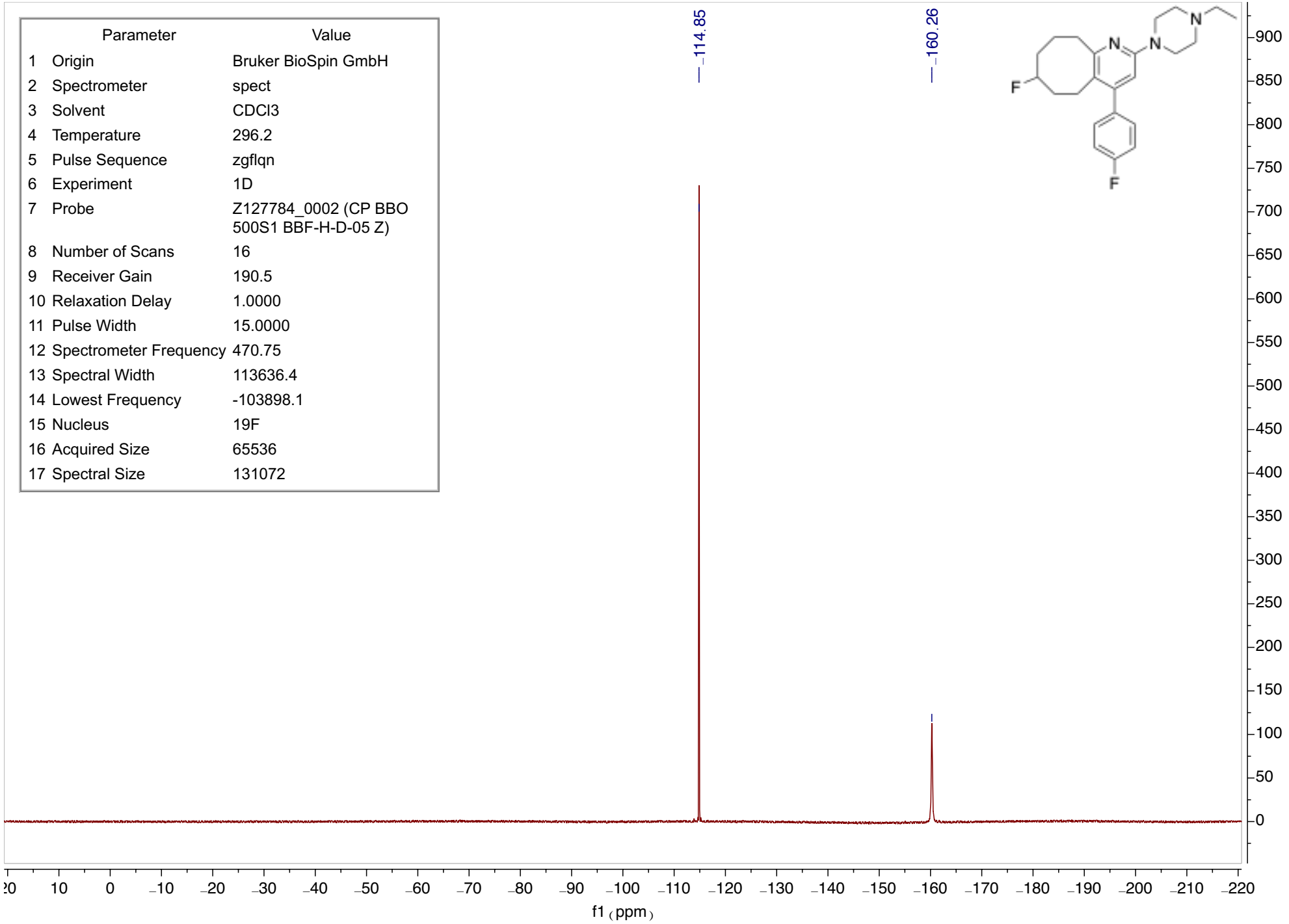
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	86.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



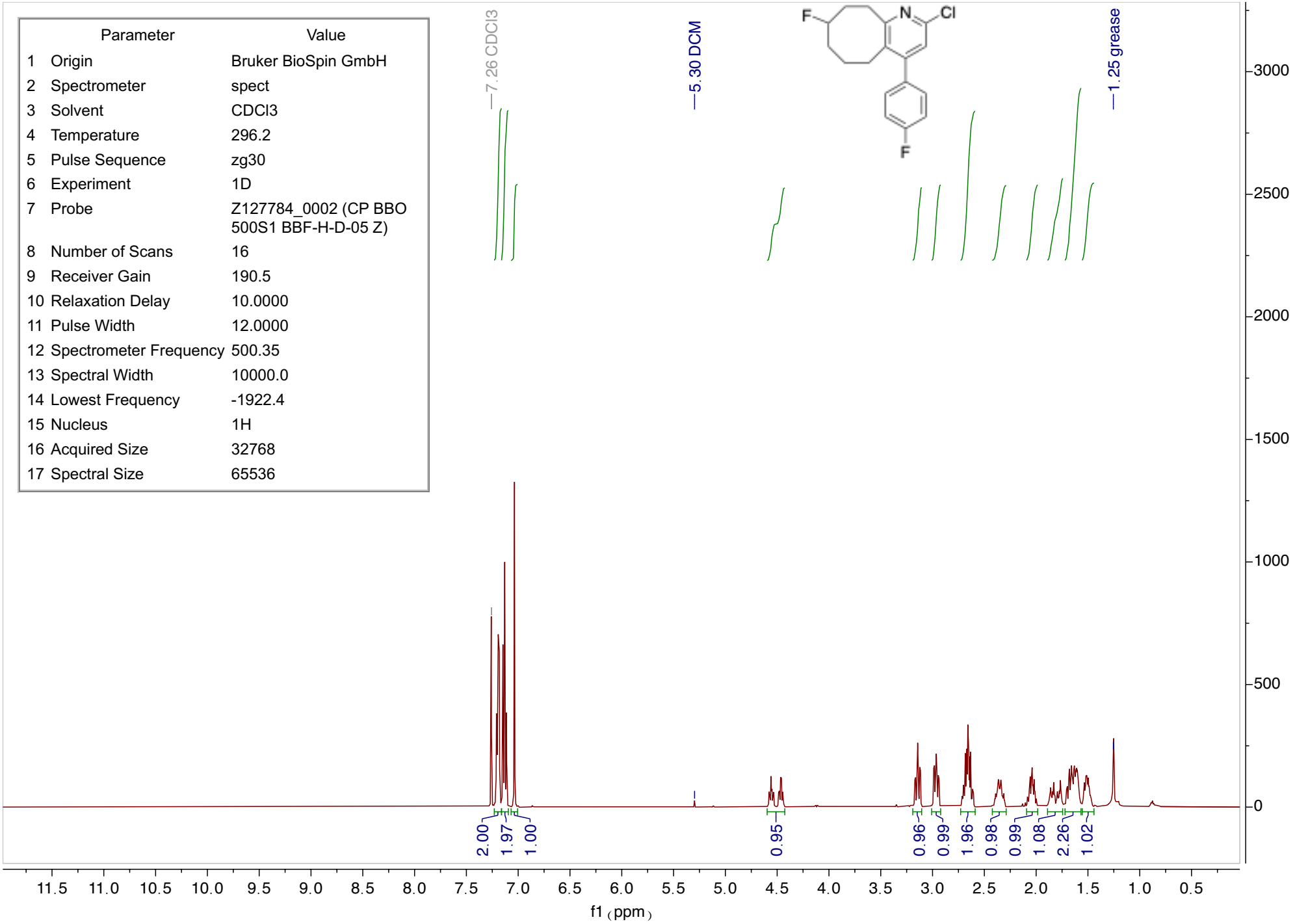


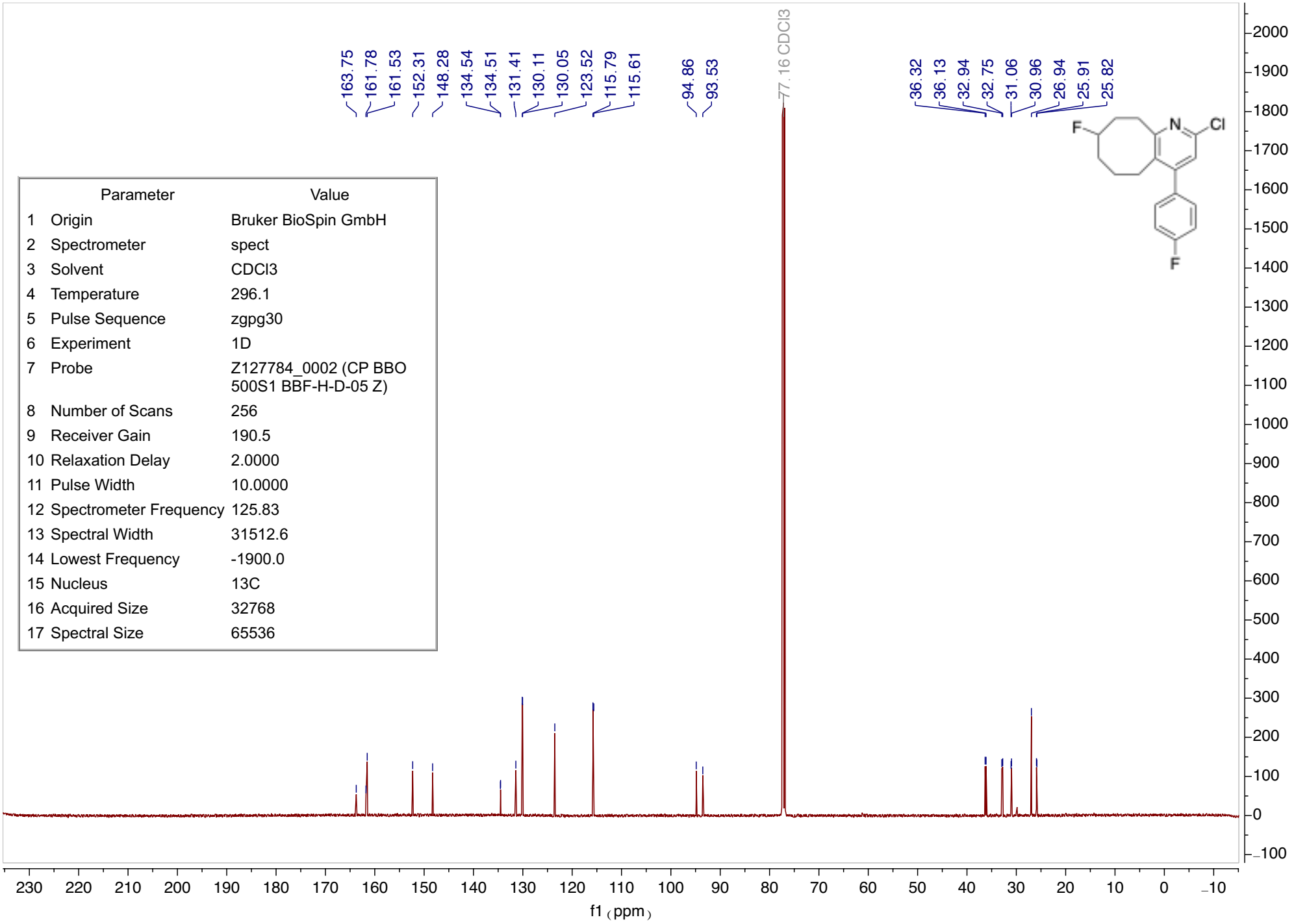
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



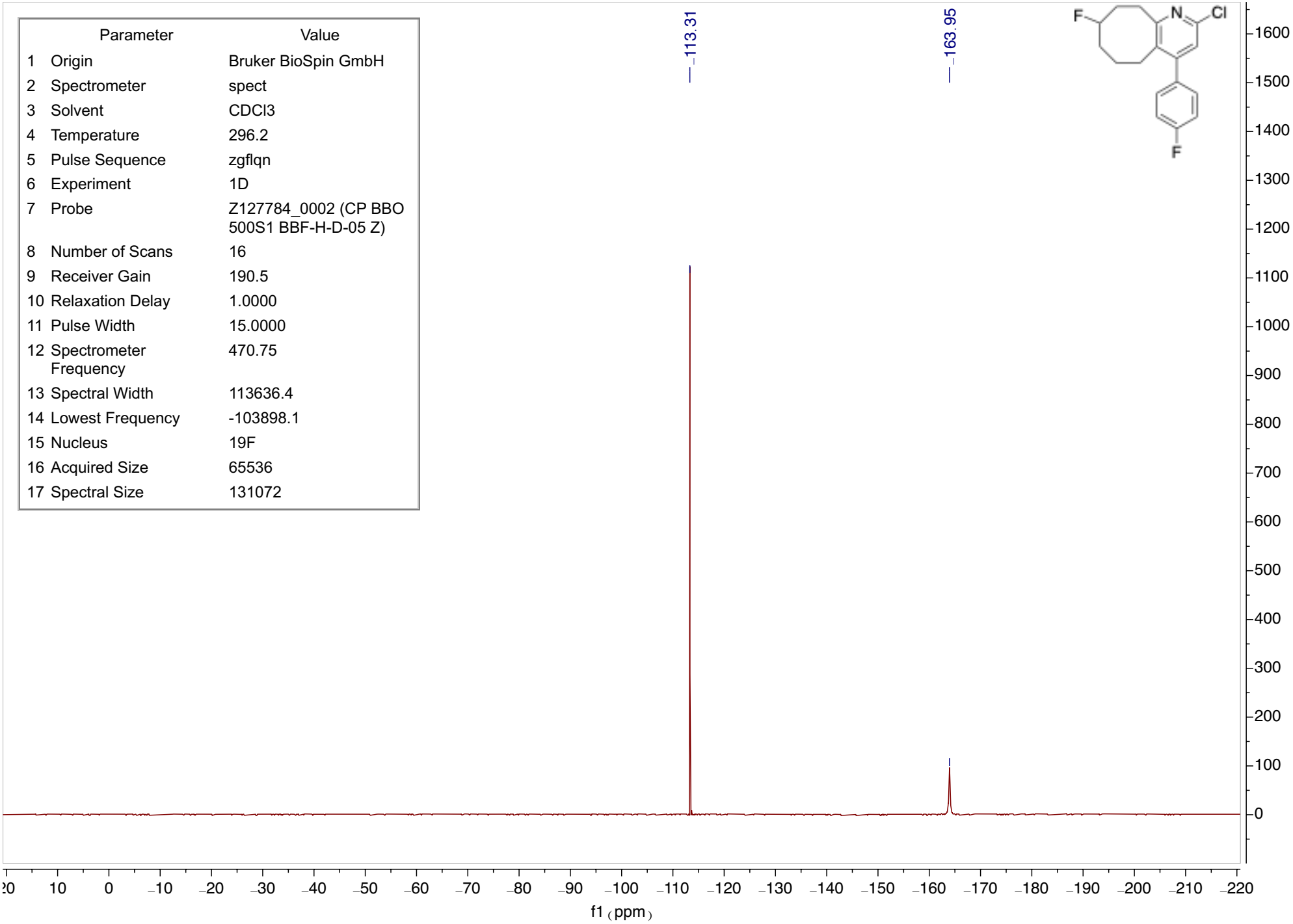
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



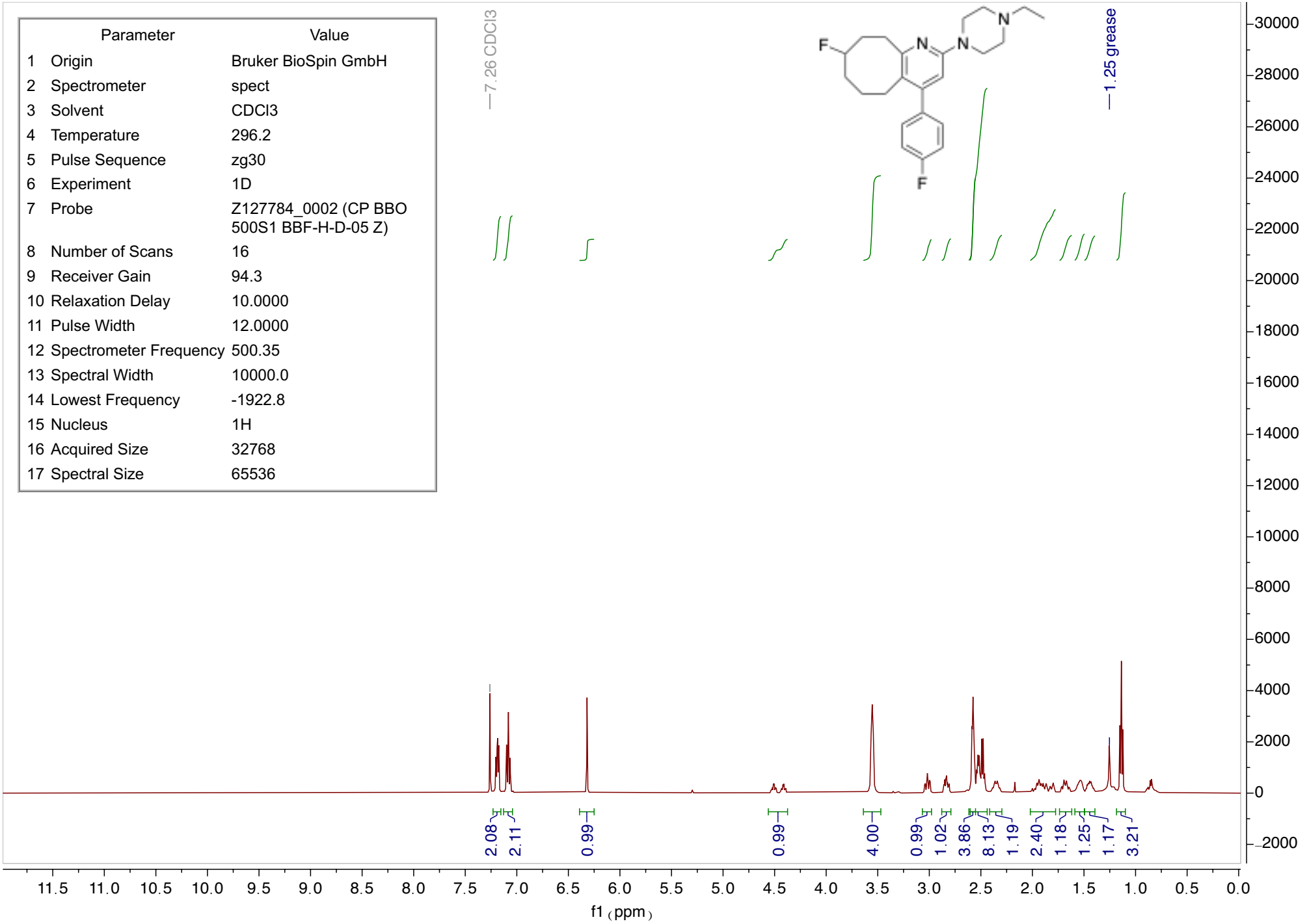


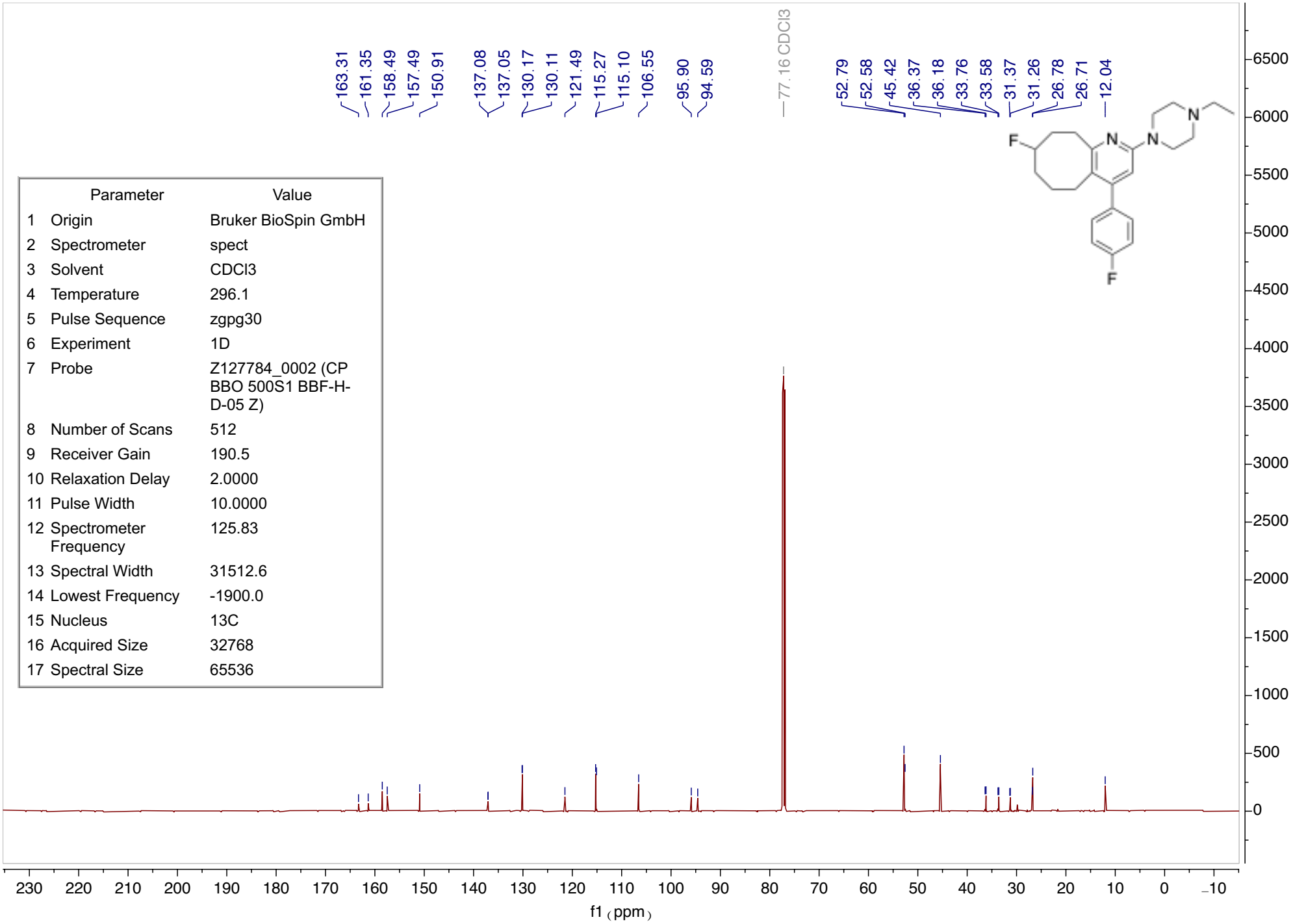
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



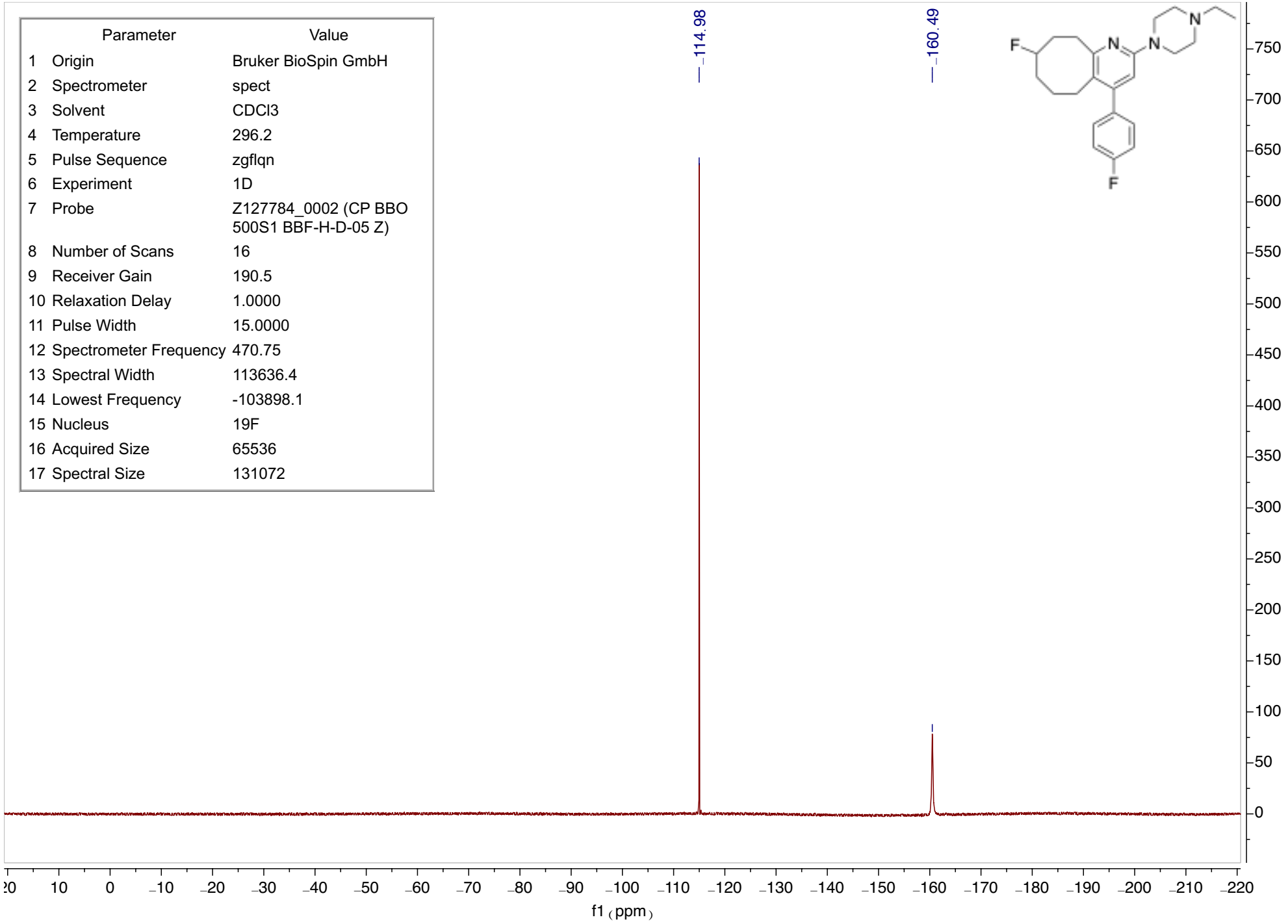
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	94.3
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



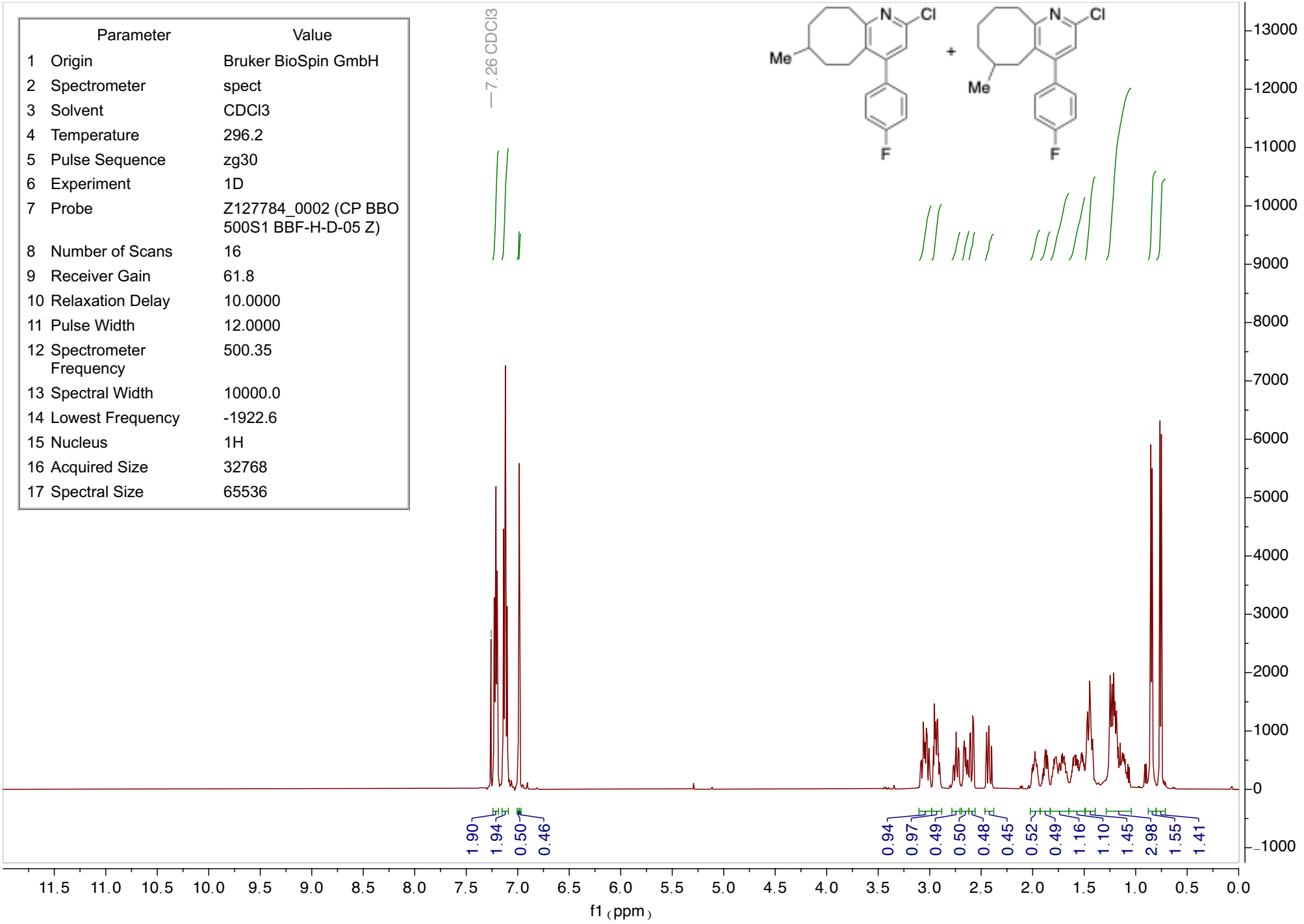


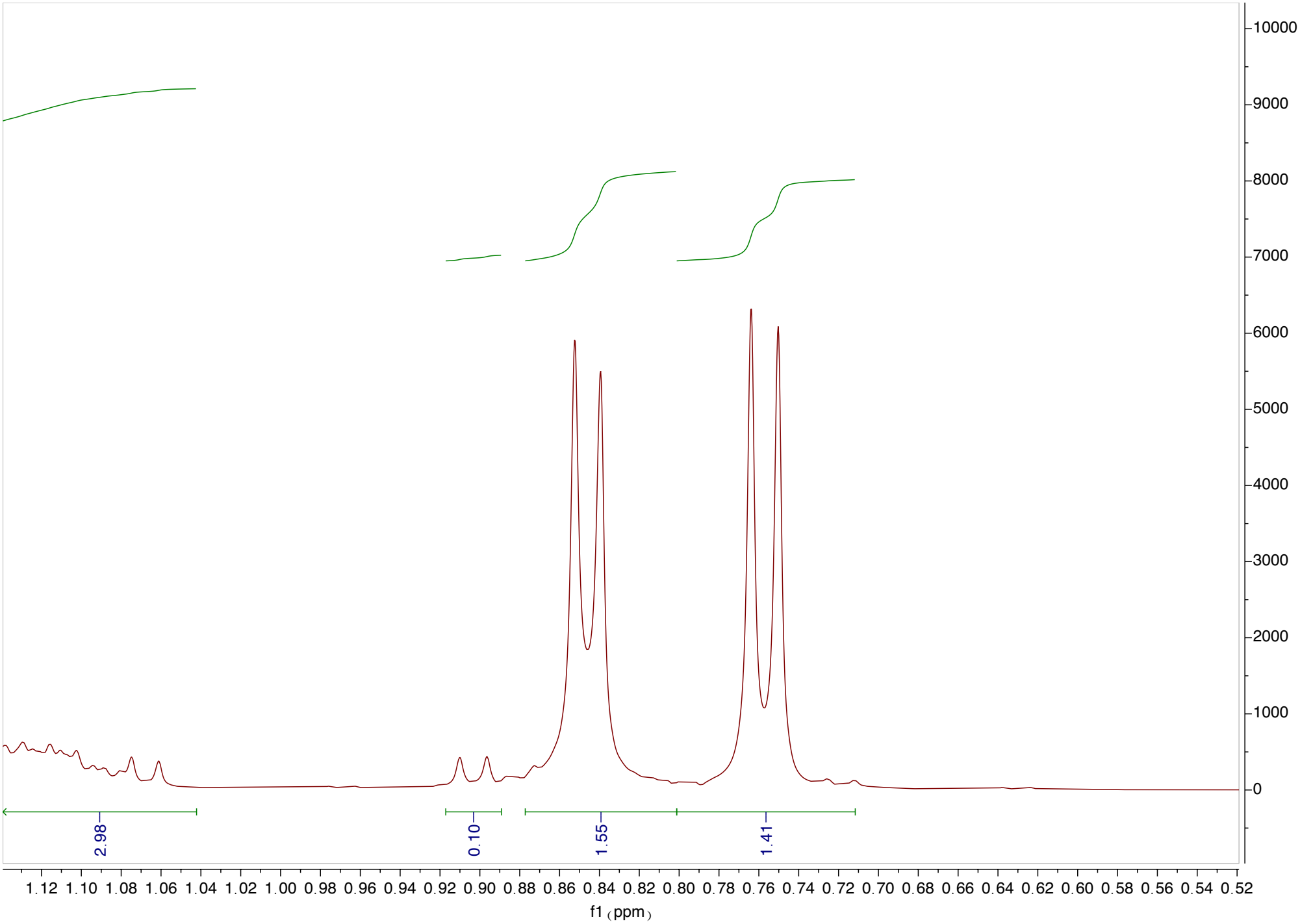
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

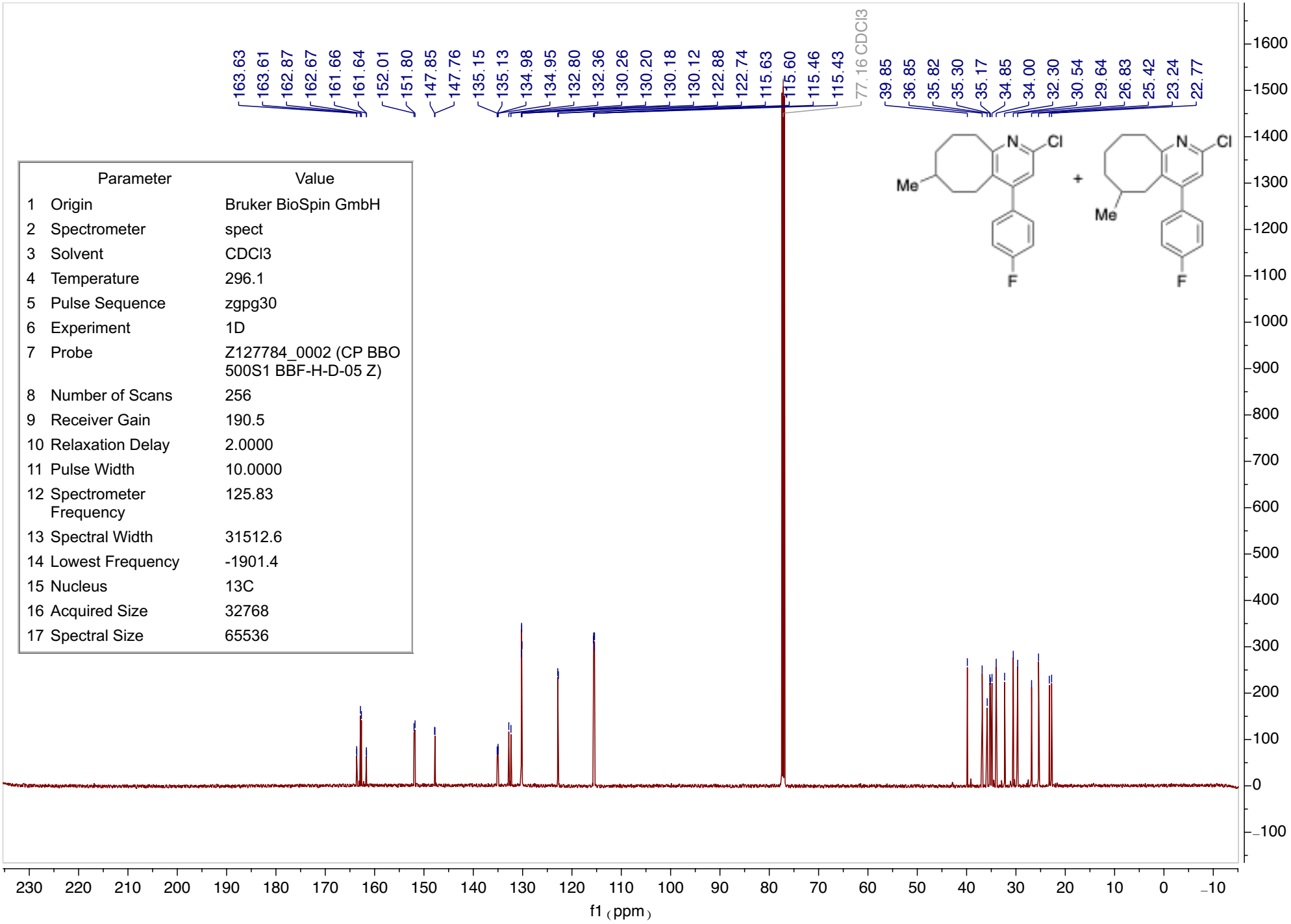
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	61.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

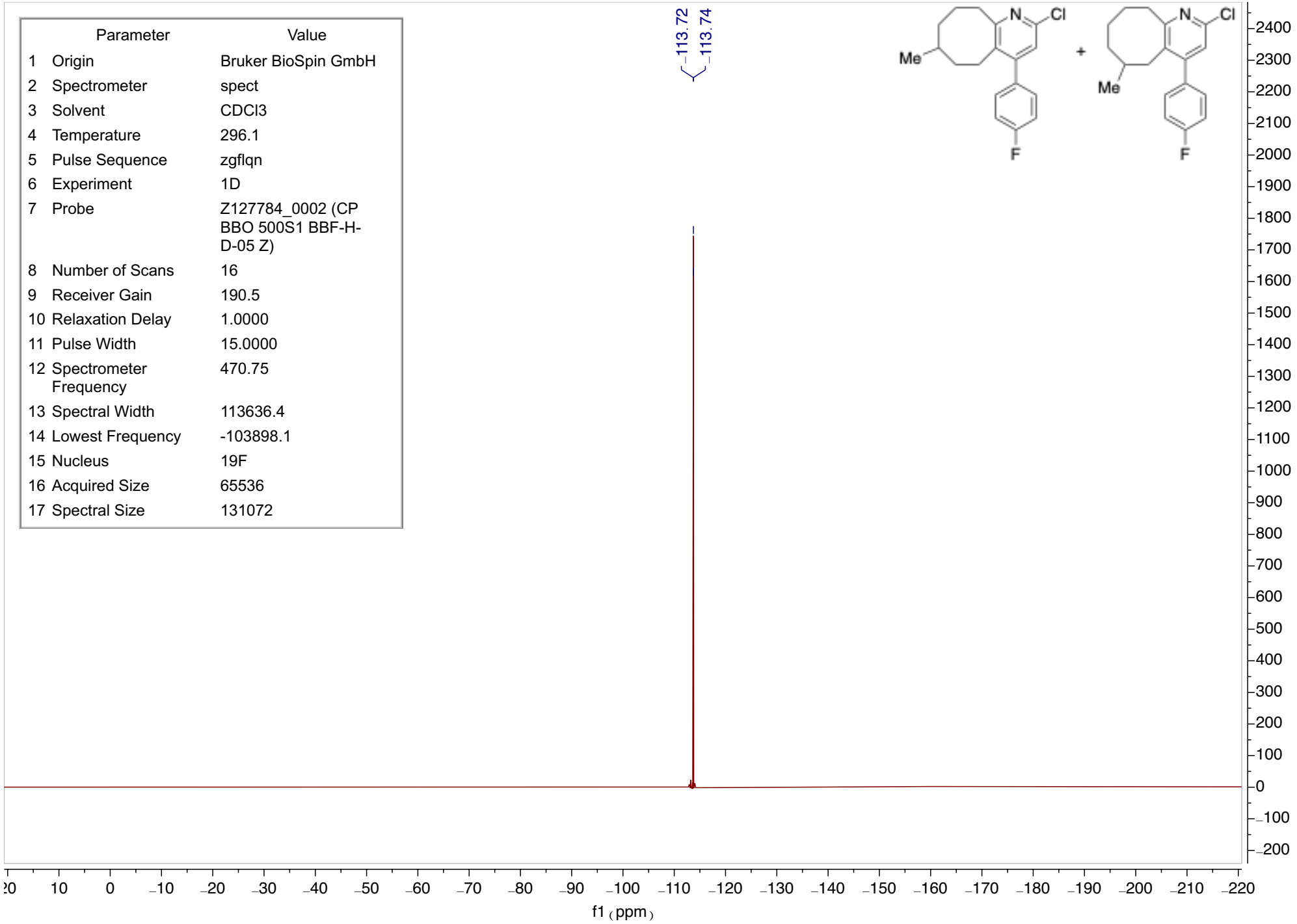


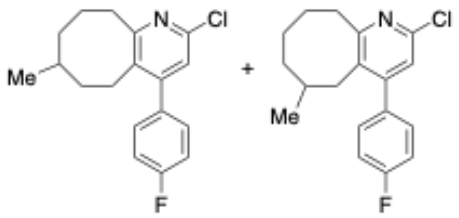

10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2.98
0.10
1.55
1.41
1.12 1.10 1.08 1.06 1.04 1.02 1.00 0.98 0.96 0.94 0.92 0.90 0.88 0.86 0.84 0.82 0.80 0.78 0.76 0.74 0.72 0.70 0.68 0.66 0.64 0.62 0.60 0.58 0.56 0.54 0.52
f1 (ppm)



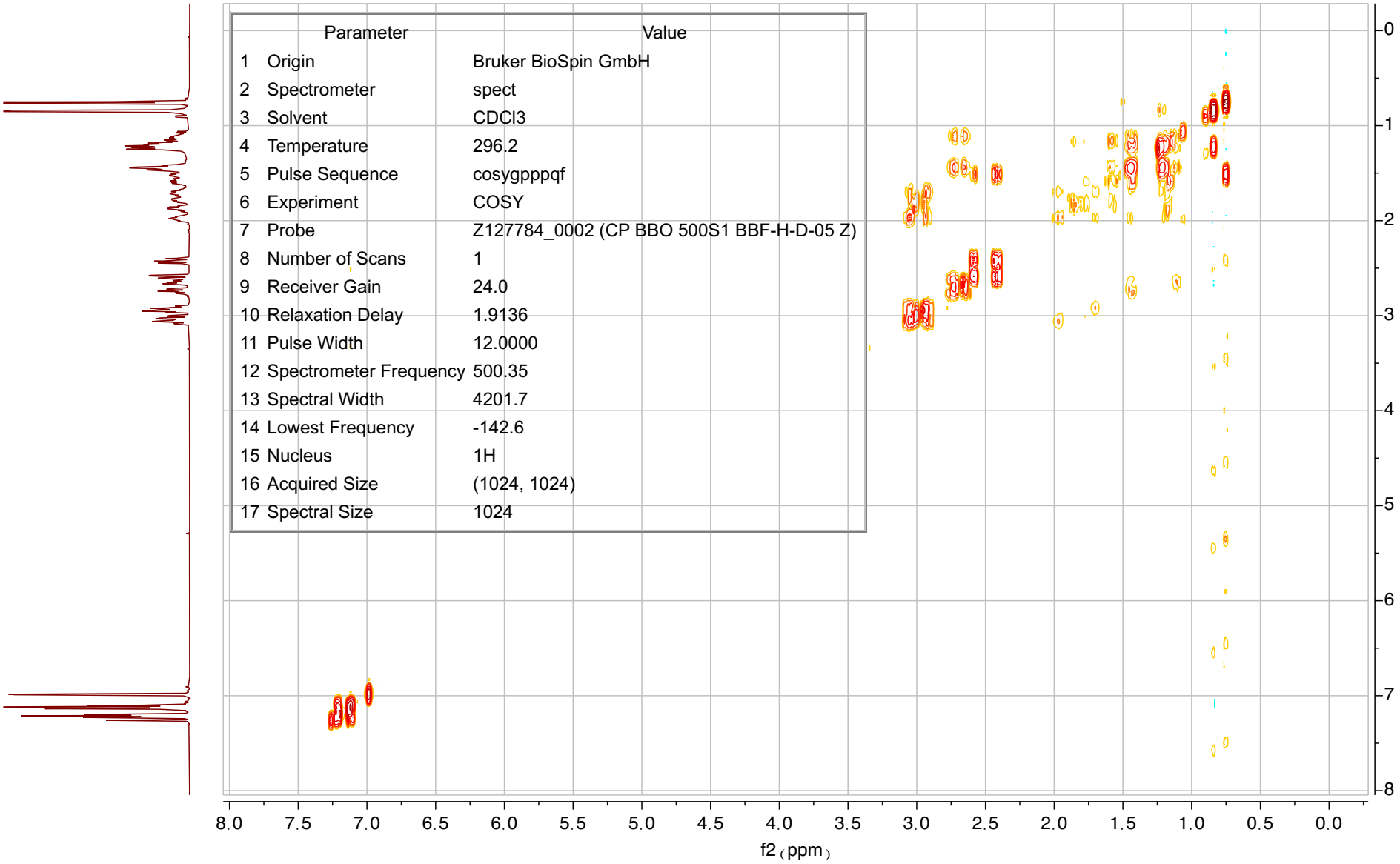
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1901.4
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

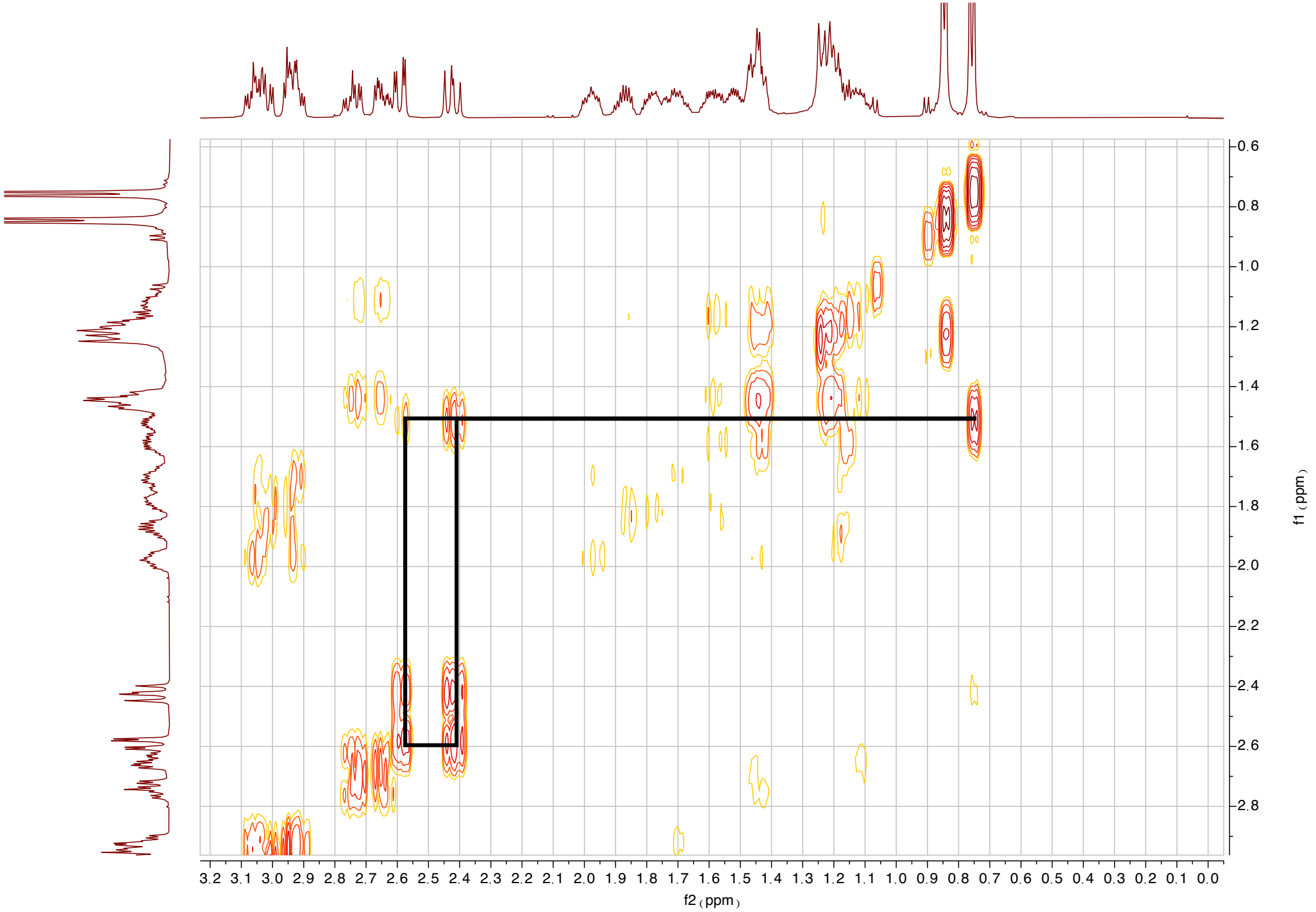
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

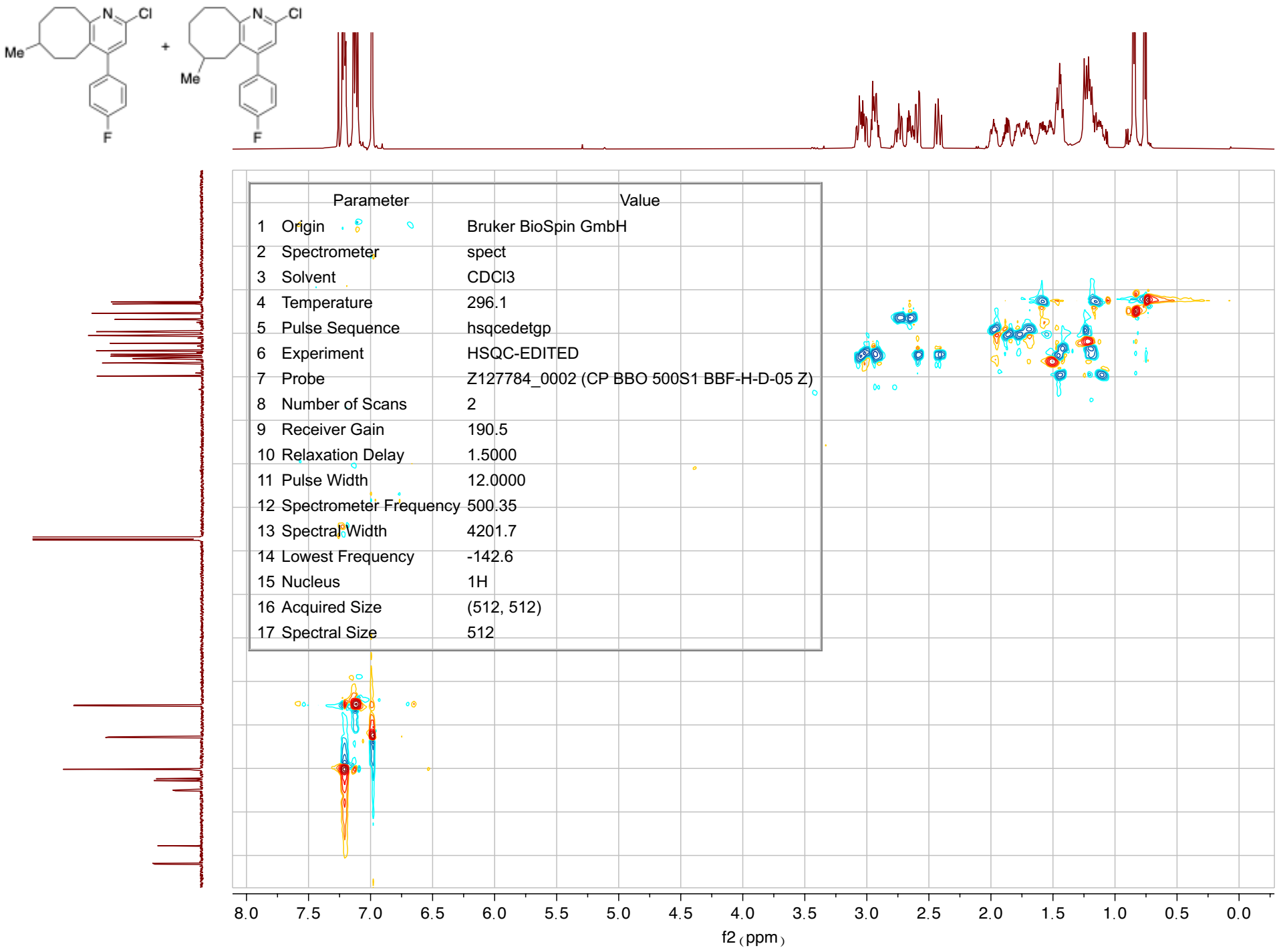


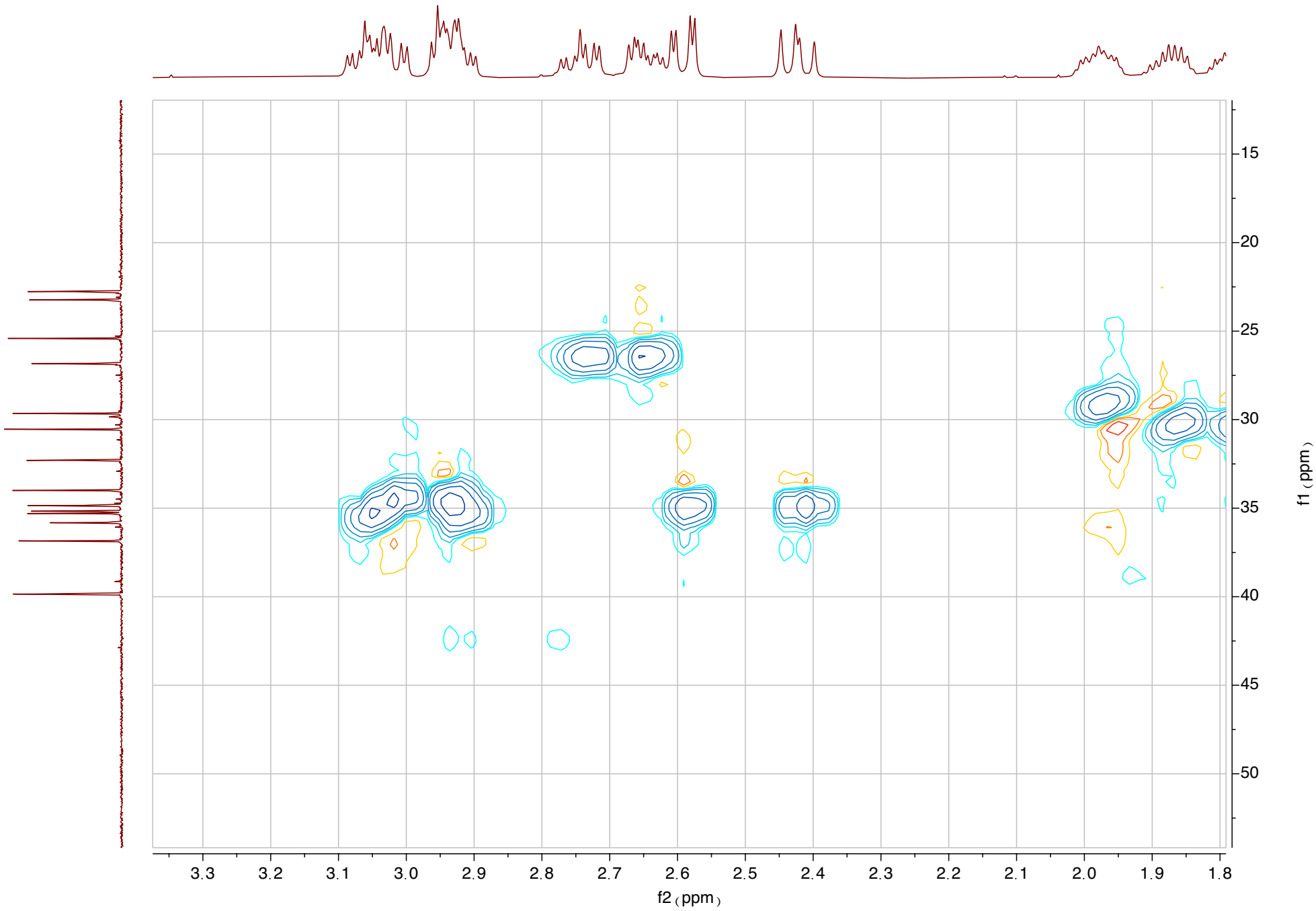


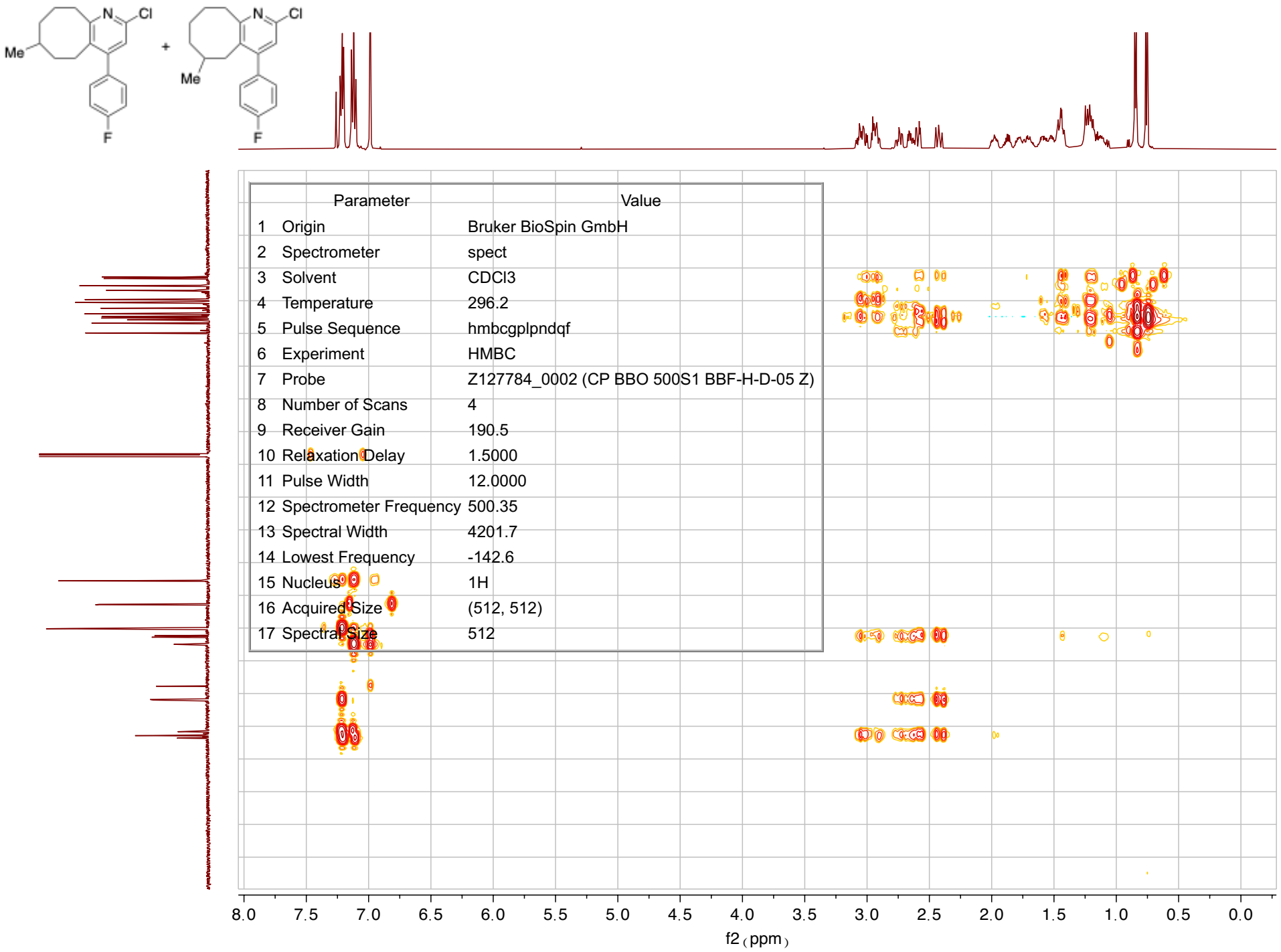
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	24.0
10	Relaxation Delay	1.9136
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4201.7
14	Lowest Frequency	-142.6
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024



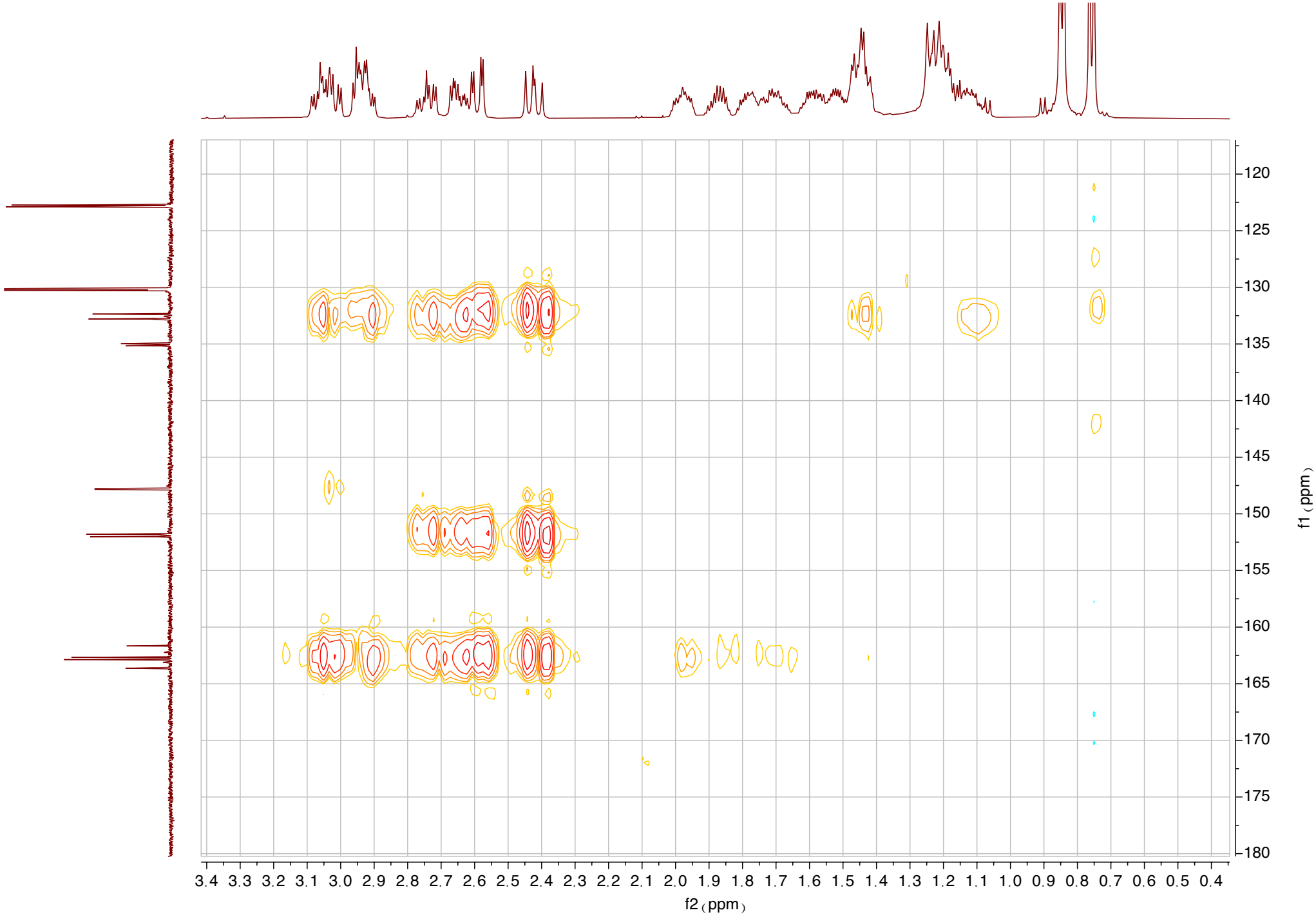

3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1 0.0
f2 (ppm)
0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8
f1 (ppm)


Me
N
Cl
F
+
Me
N
Cl
F
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence hsqcedetgp
6 Experiment HSQC-EDITED
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 2
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4201.7
14 Lowest Frequency -142.6
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)

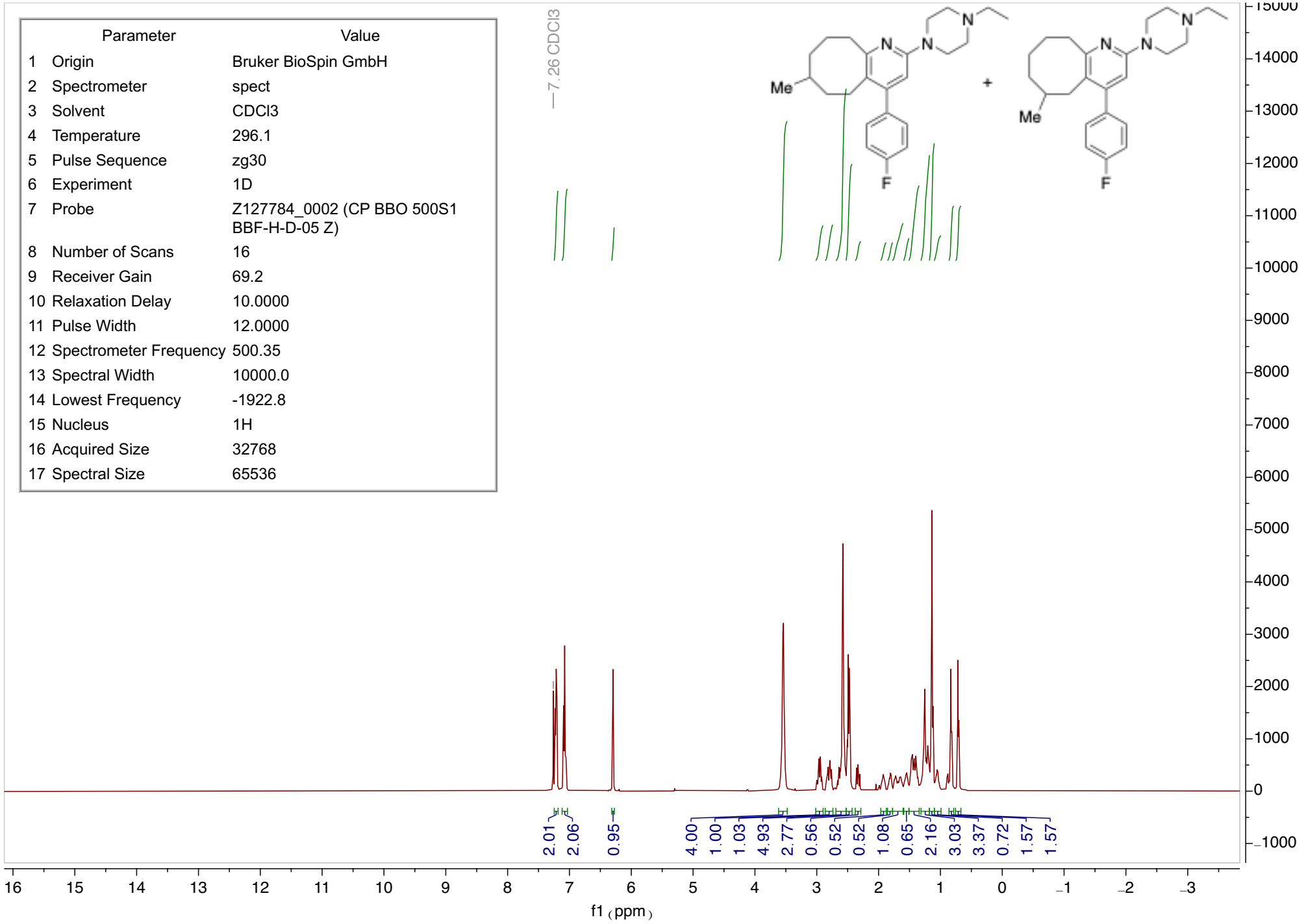

3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
f2 (ppm)
15
20
25
30
35
40
45
50
f1 (ppm)

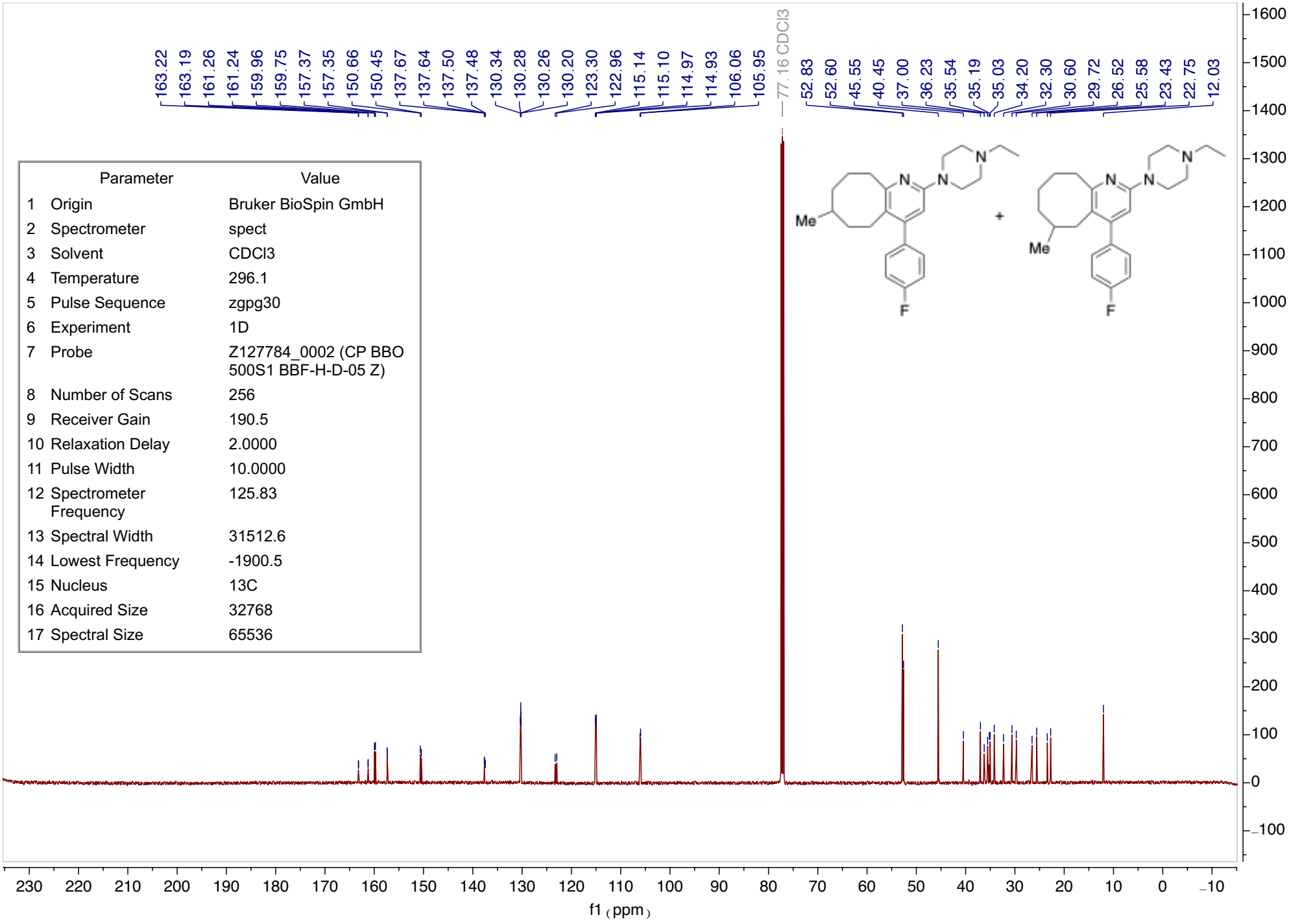

Me
N
Cl
F
+
Me
N
Cl
F
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4201.7
14 Lowest Frequency -142.6
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
f1 (ppm)

800


120
125
130
135
140
145
150
155
160
165
170
175
180
f1 (ppm)
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5 0.4
f2 (ppm)

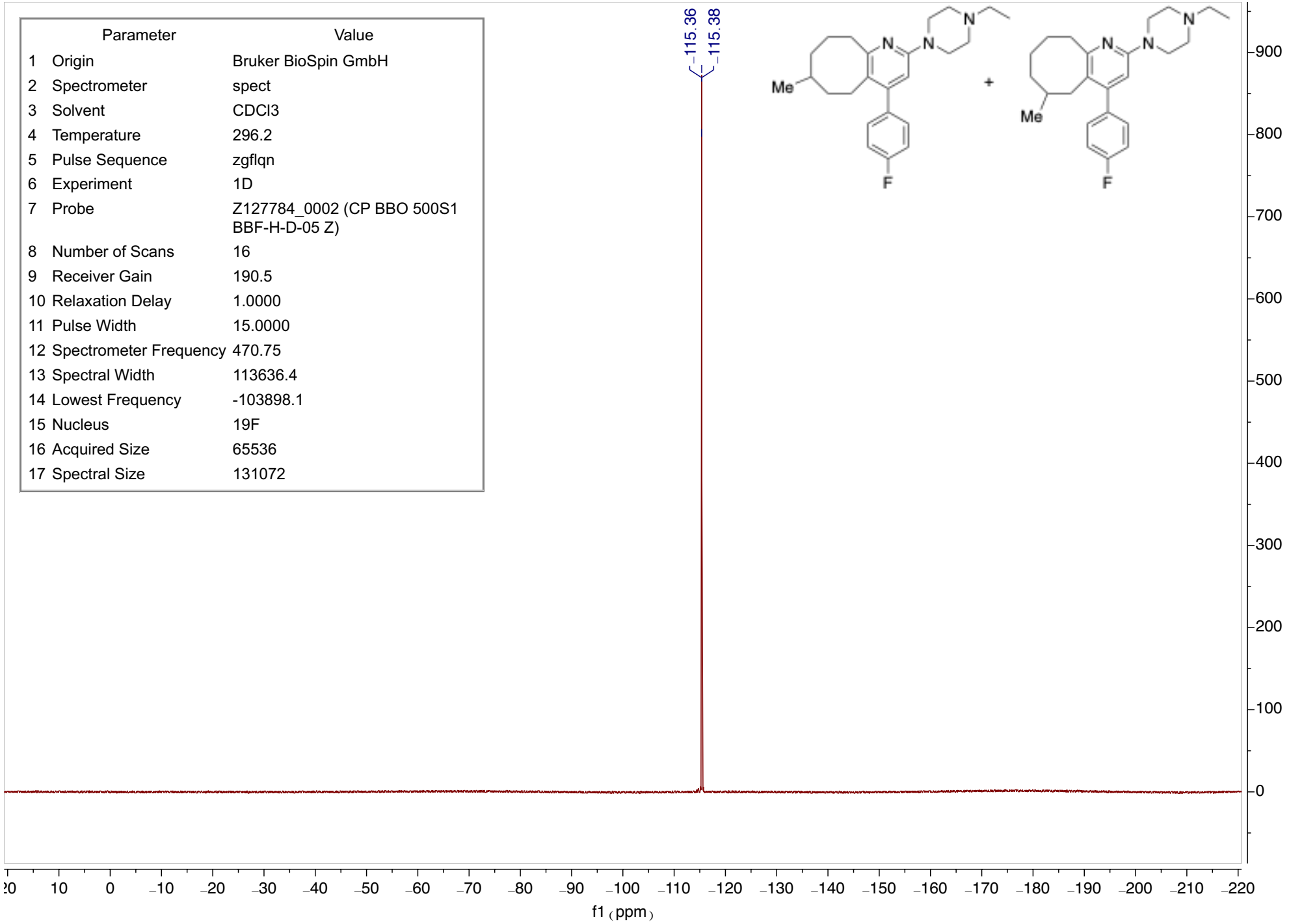
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	69.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



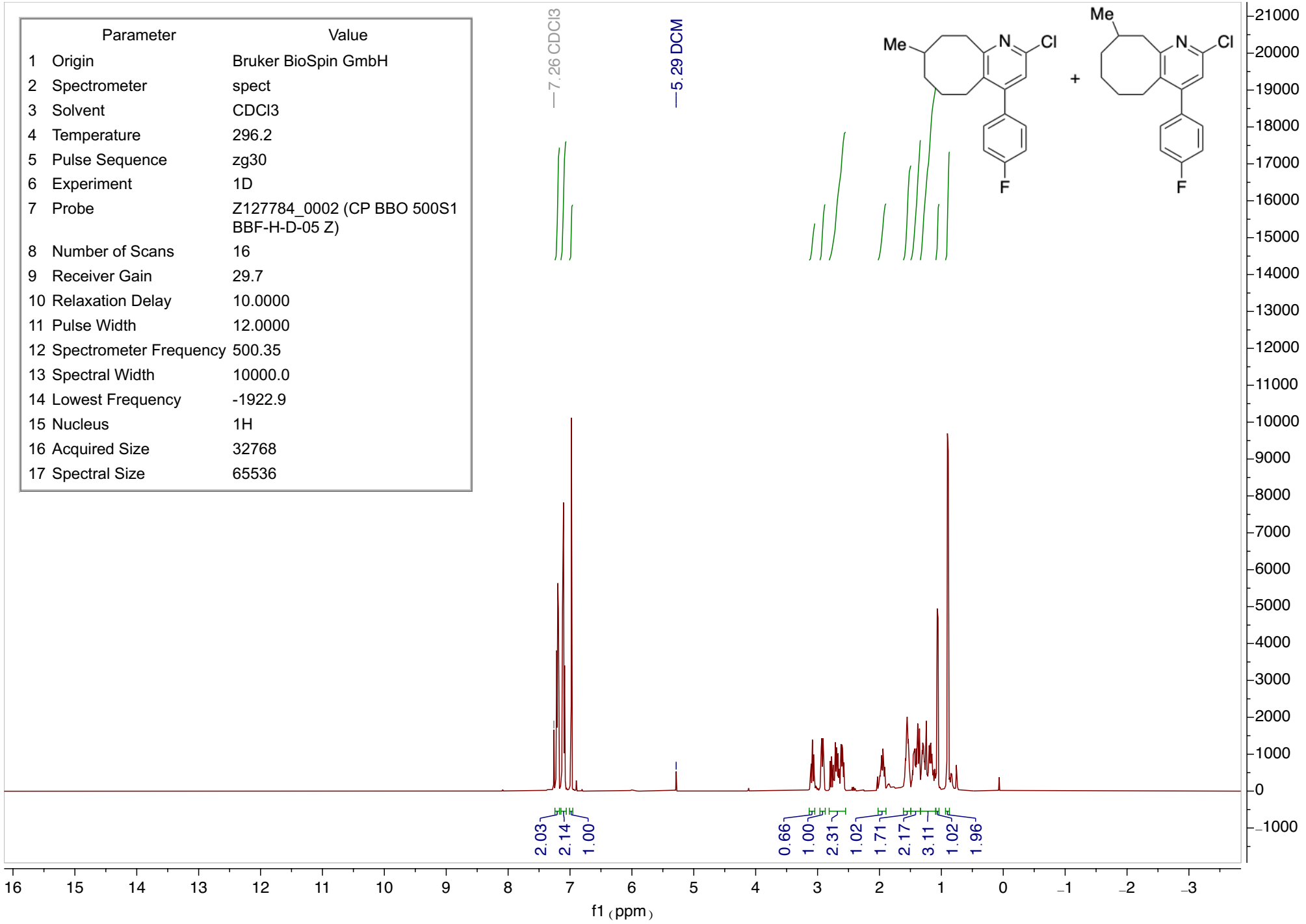


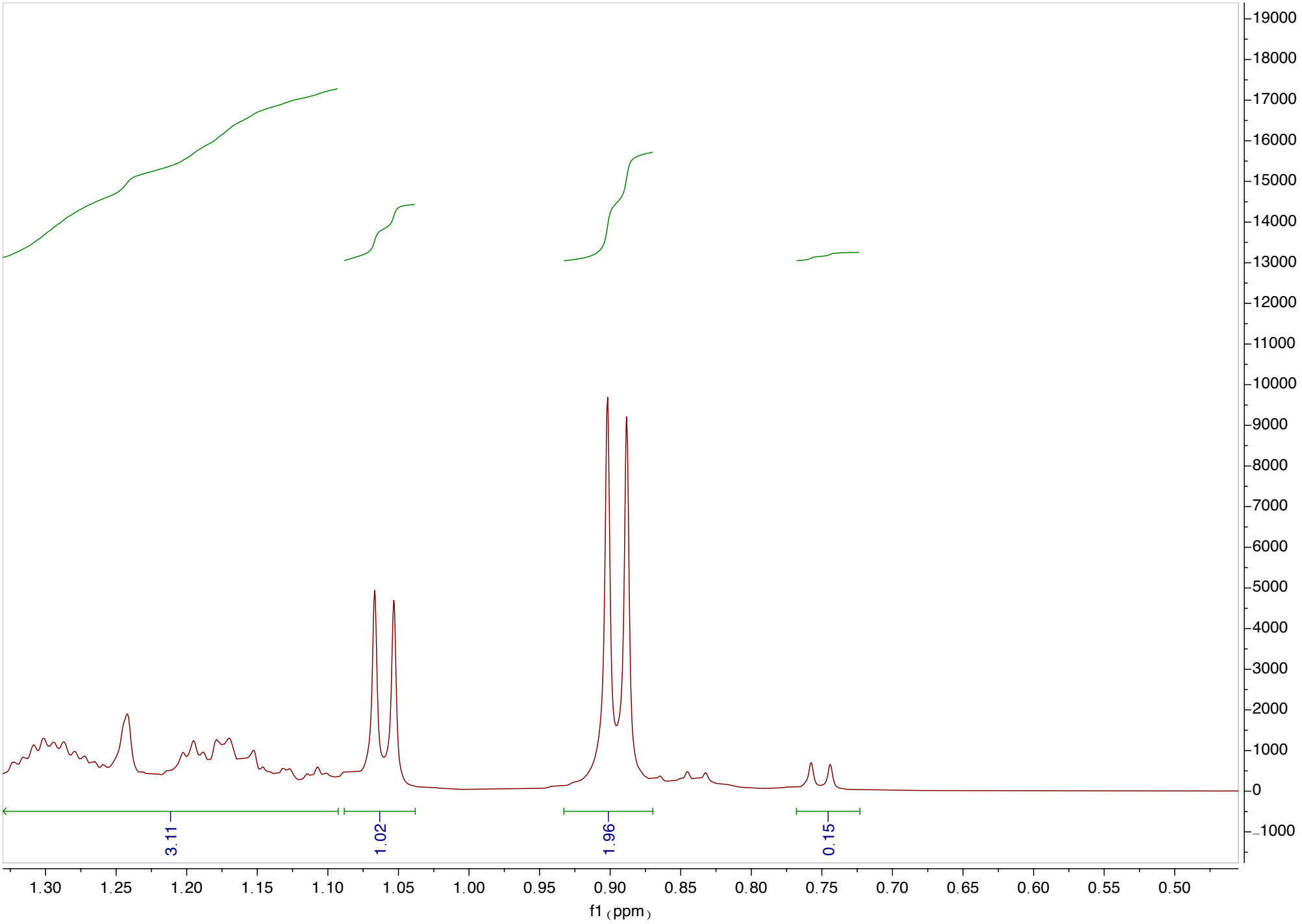
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.5
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

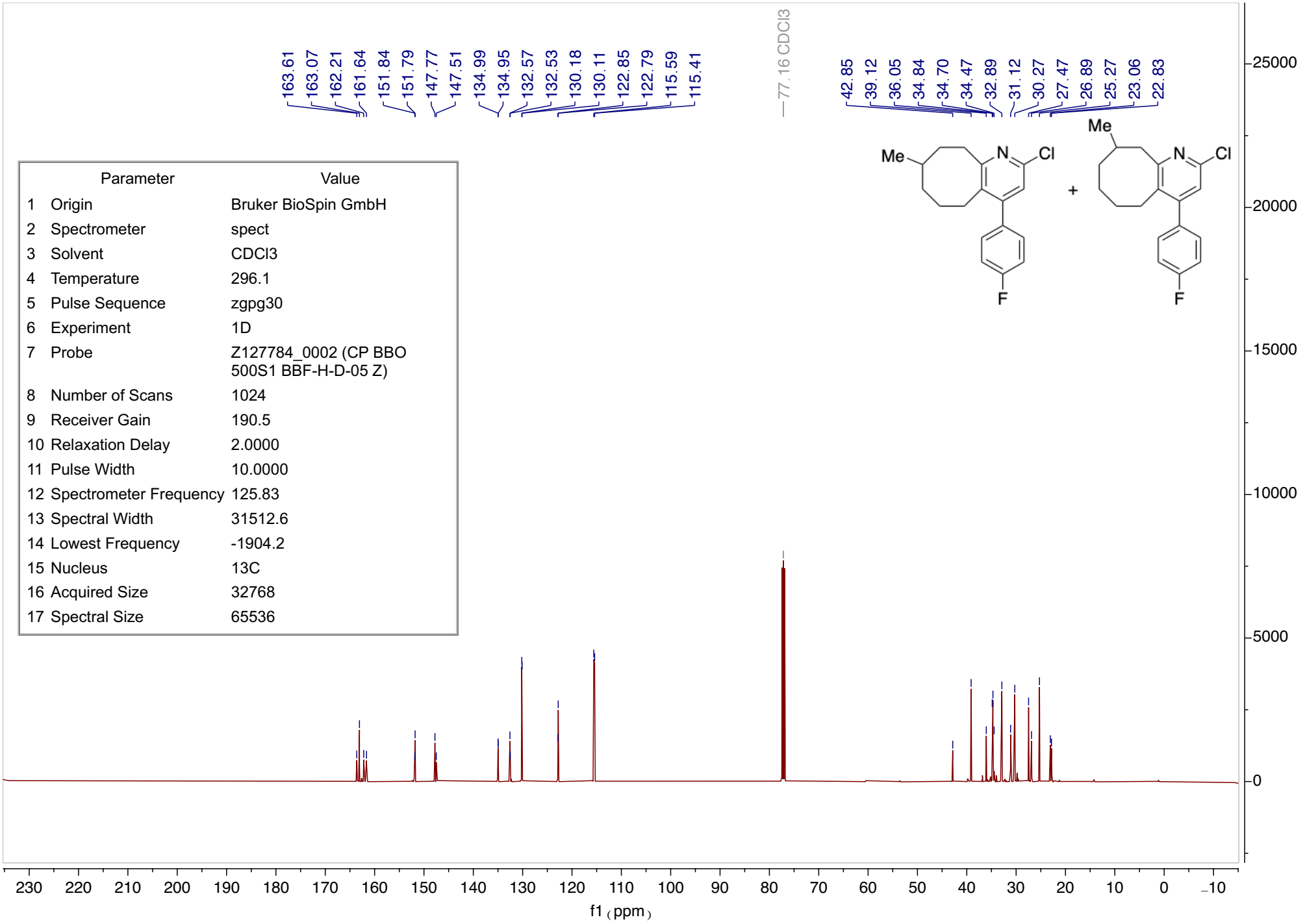
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

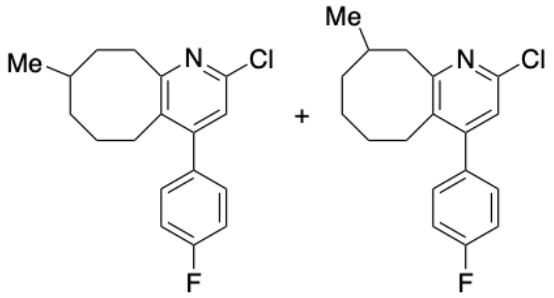



19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
3.11
1.02
1.96
0.15
1.30
1.25
1.20
1.15
1.10
1.05
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
f1 (ppm)

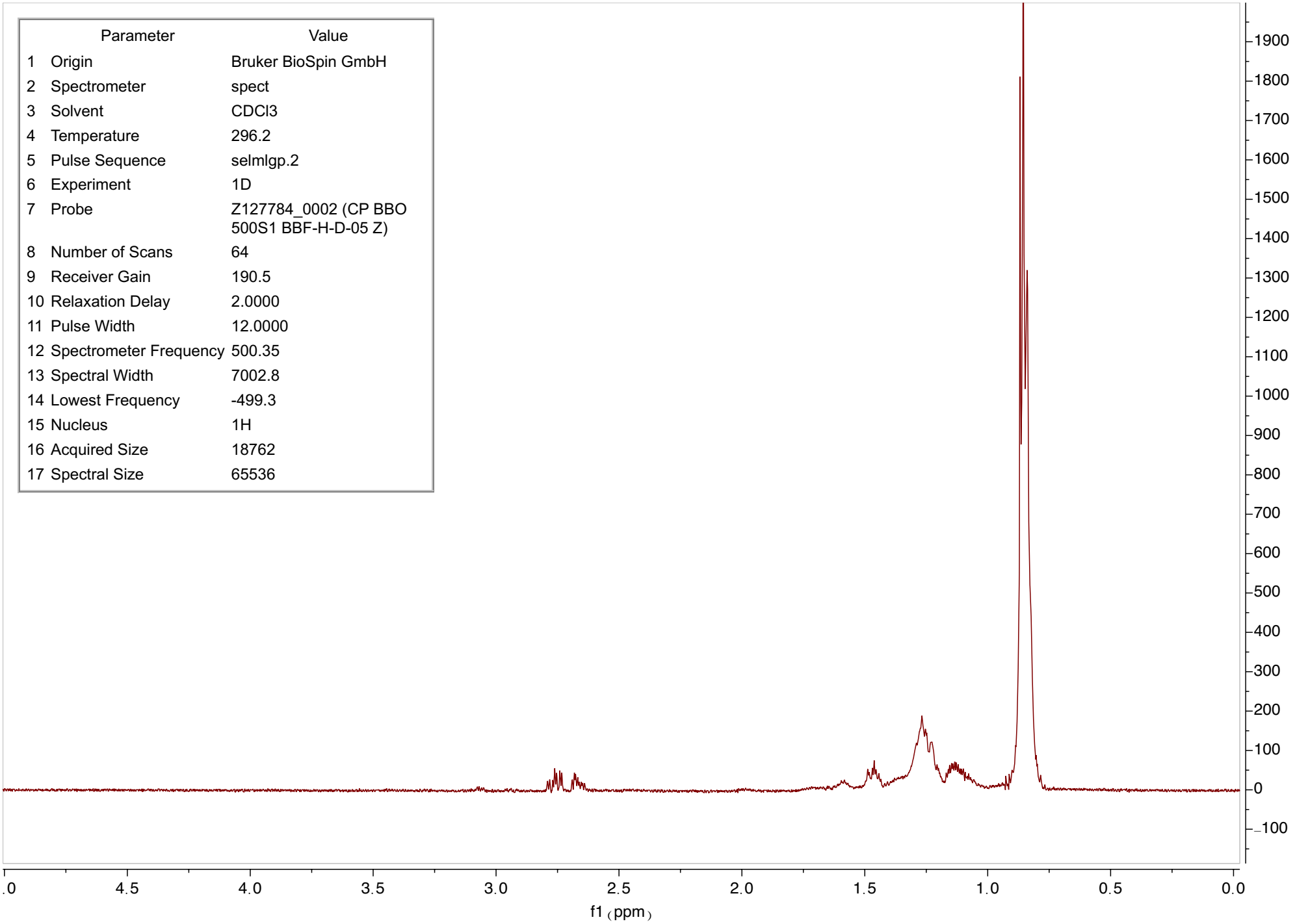


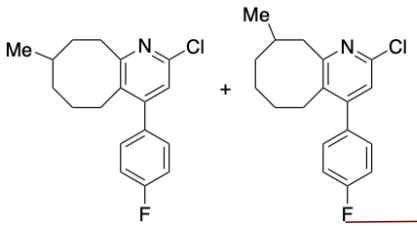
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1904.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



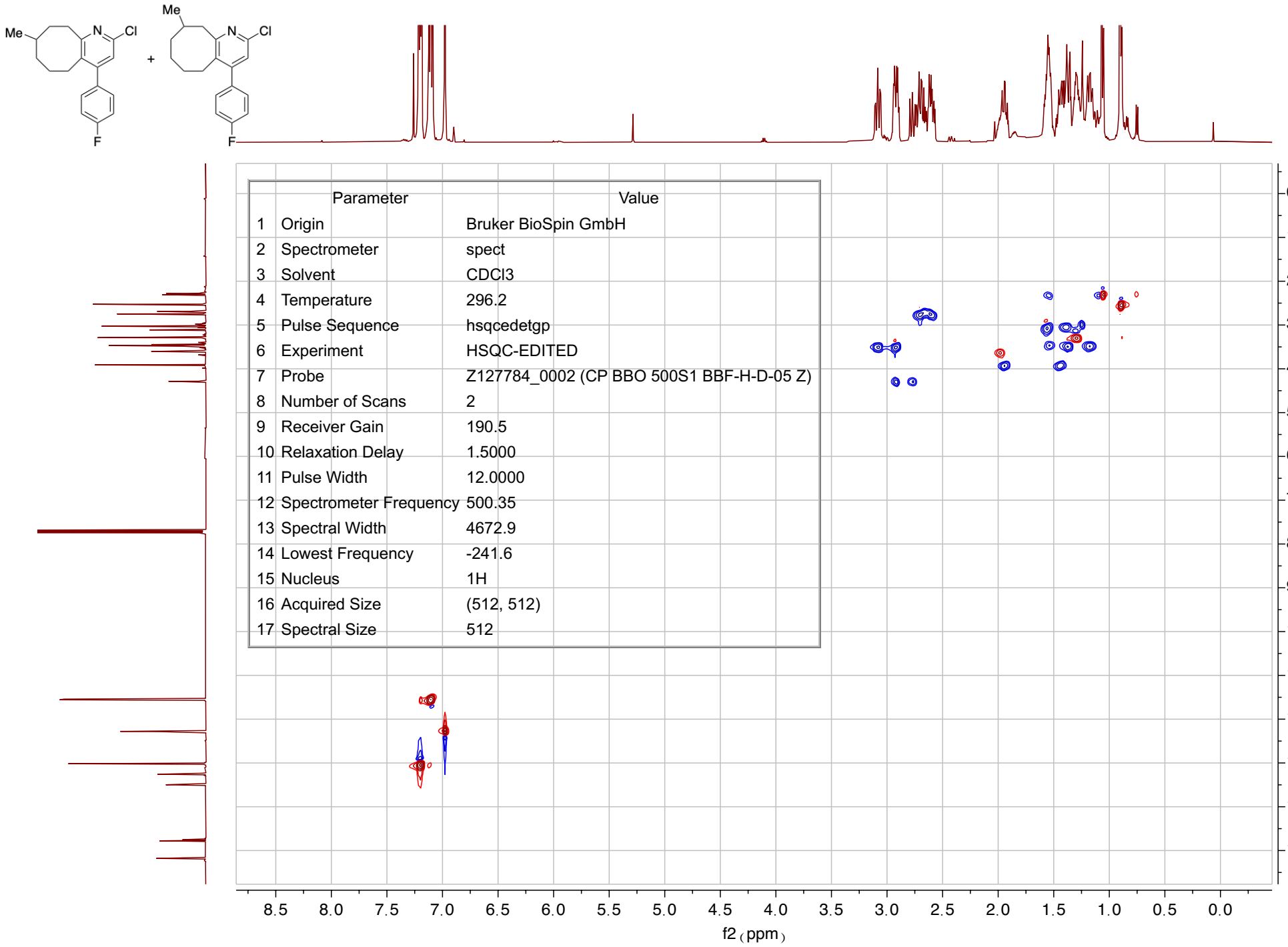
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	selmlgp.2
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	64
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	7002.8
14	Lowest Frequency	-499.3
15	Nucleus	1H
16	Acquired Size	18762
17	Spectral Size	65536

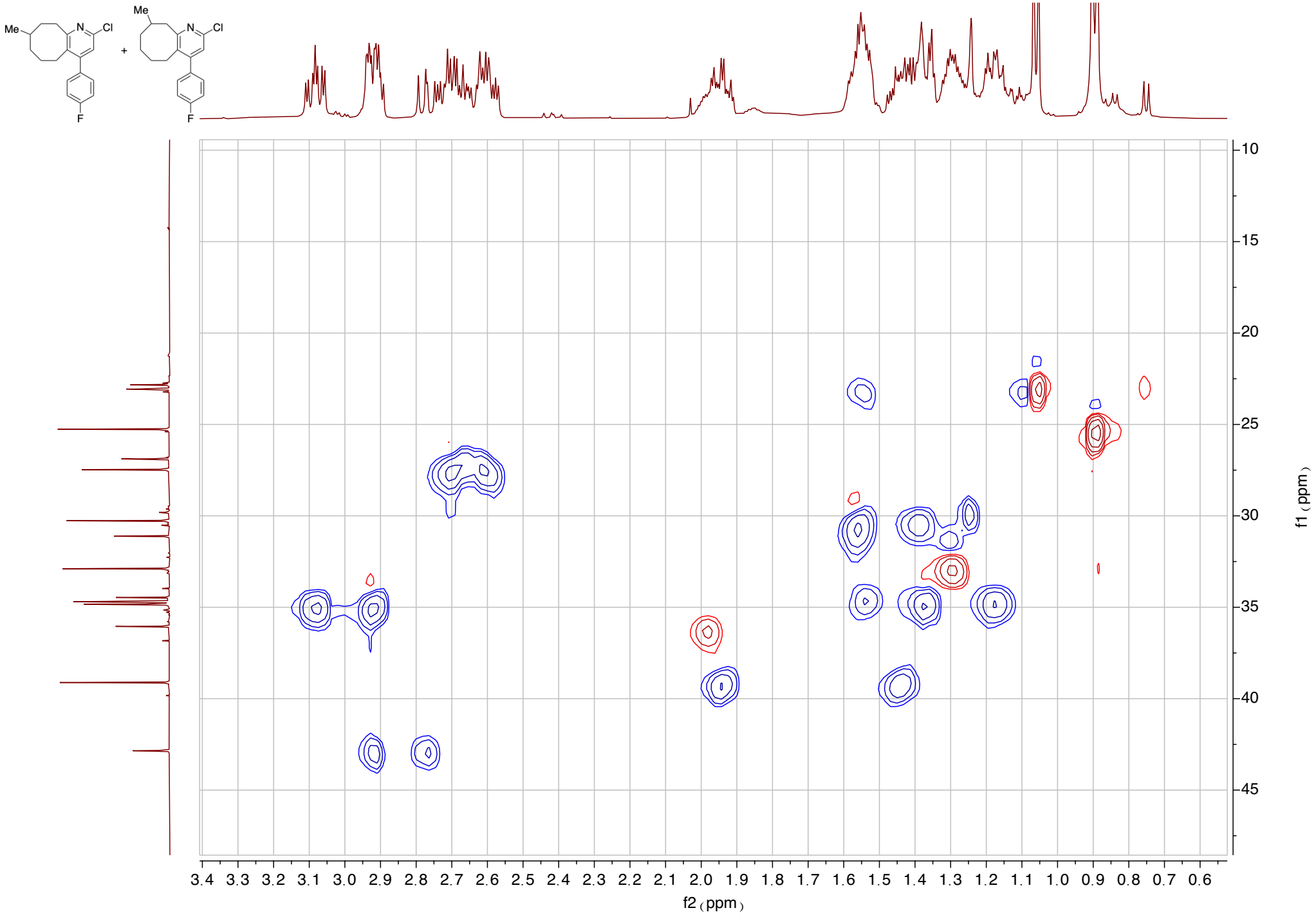


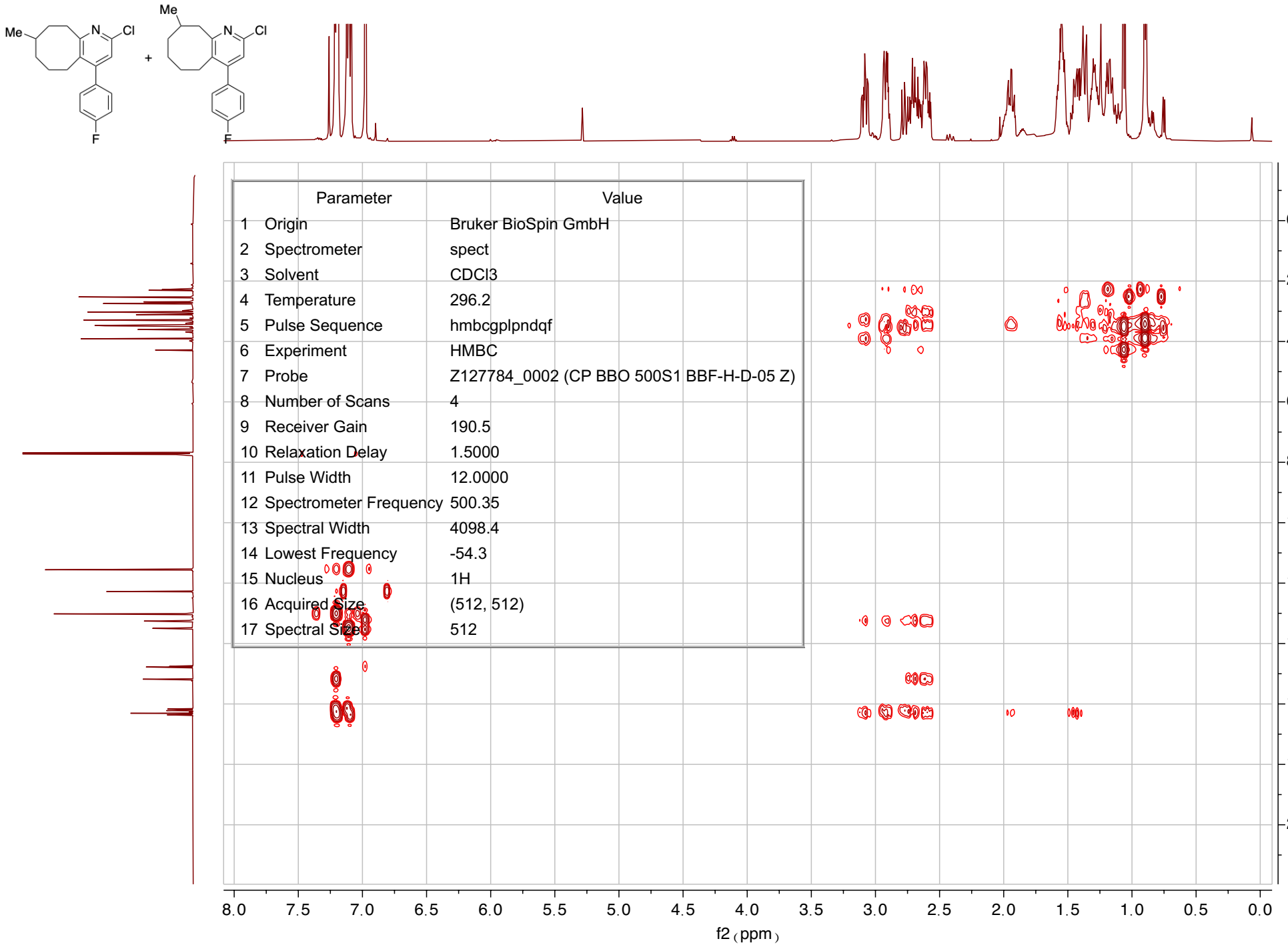


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	cosygpppqf
6	Experiment	COSY
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1
9	Receiver Gain	13.7
10	Relaxation Delay	1.9074
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	4098.4
14	Lowest Frequency	-56.2
15	Nucleus	1H
16	Acquired Size	(1024, 1024)
17	Spectral Size	1024

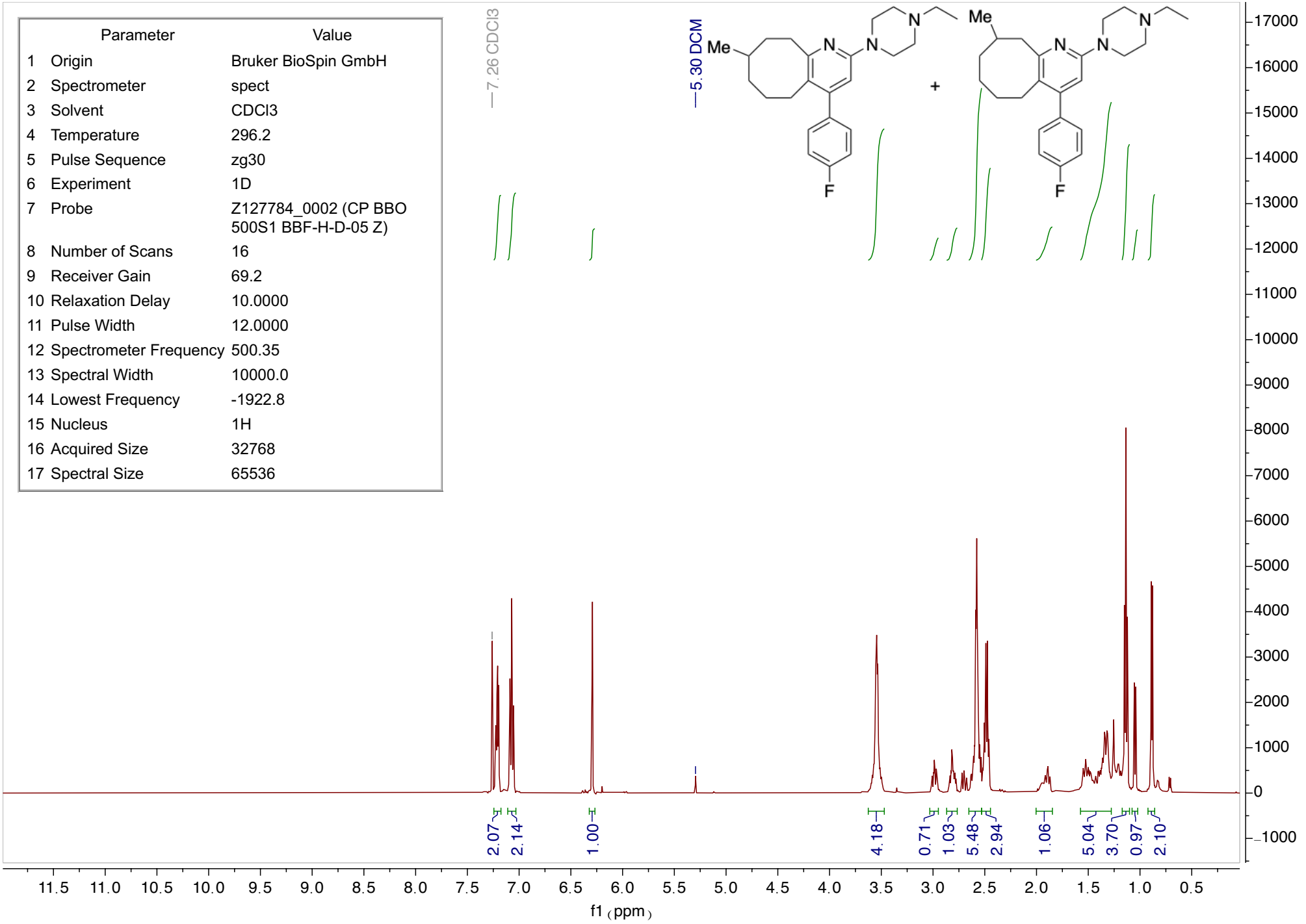

Me
N
Cl
F
+
Me
N
Cl
F
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
f1 (ppm)
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6 0.5
f2 (ppm)

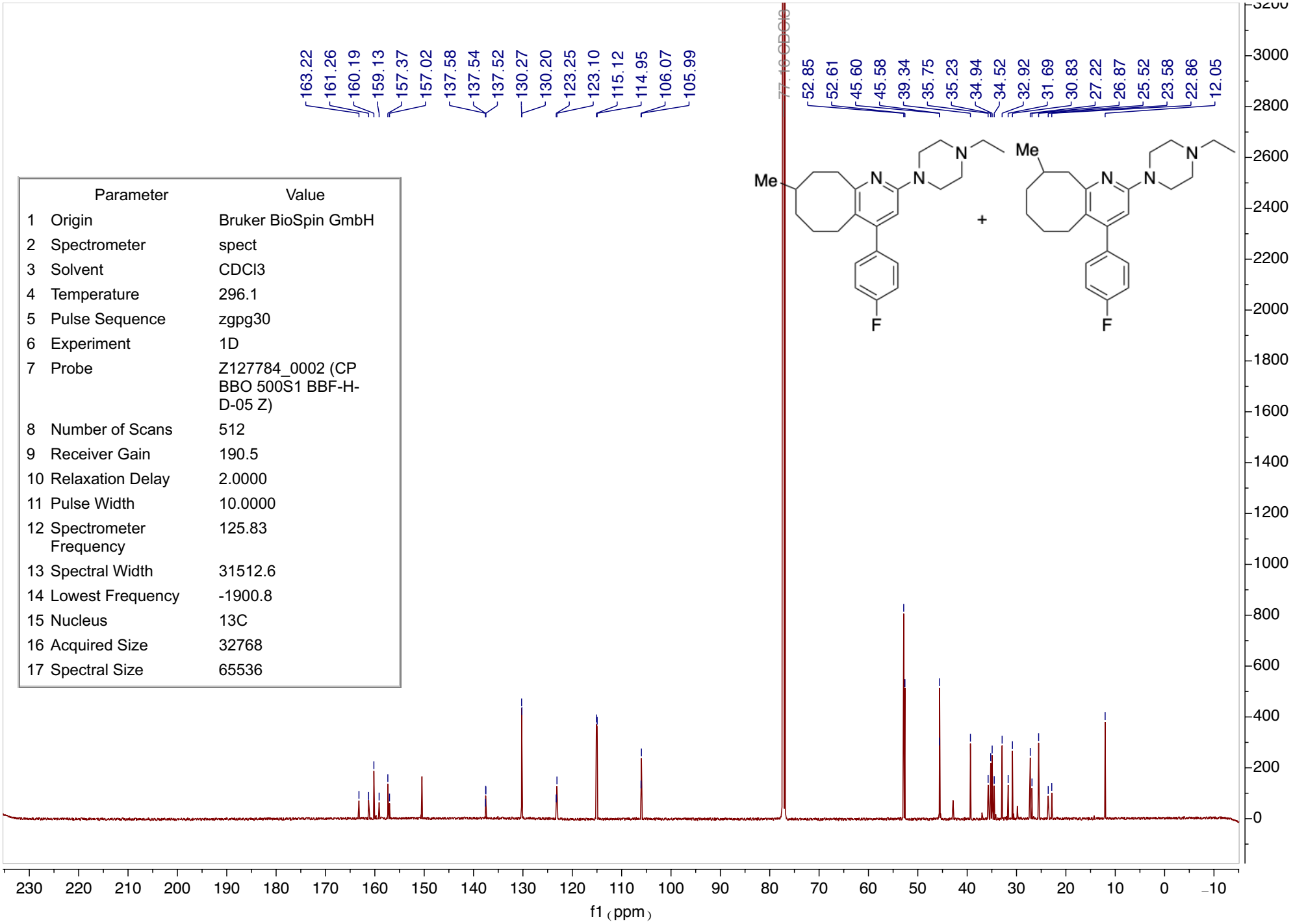

Me
N
Cl
F
+
Me
N
Cl
F
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hsqcedetgp
6 Experiment HSQC-EDITED
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 2
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4672.9
14 Lowest Frequency -241.6
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)


Me
N
Cl
F
+
Me
N
Cl
F
10
15
20
25
30
35
40
45
f1 (ppm)
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6
f2 (ppm)


Me
N
Cl
F
+
Me
N
Cl
F
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer spect
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hmbcgplpndqf
6 Experiment HMBC
7 Probe Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8 Number of Scans 4
9 Receiver Gain 190.5
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 500.35
13 Spectral Width 4098.4
14 Lowest Frequency -54.3
15 Nucleus 1H
16 Acquired Size (512, 512)
17 Spectral Size 512
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
f2 (ppm)
0 20 40 60 80 100 120 140 160 180 200
f1 (ppm)

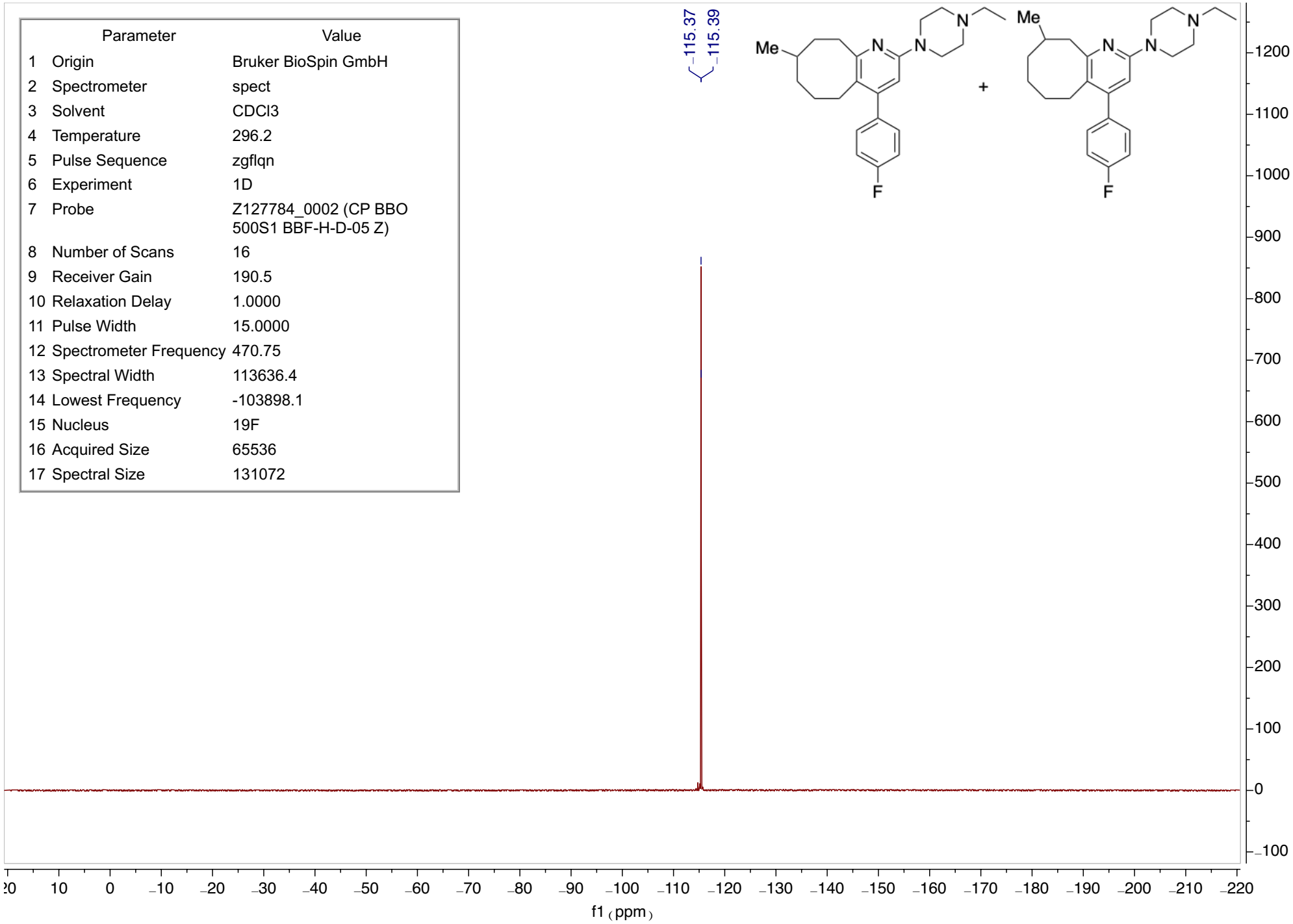
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	69.2
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



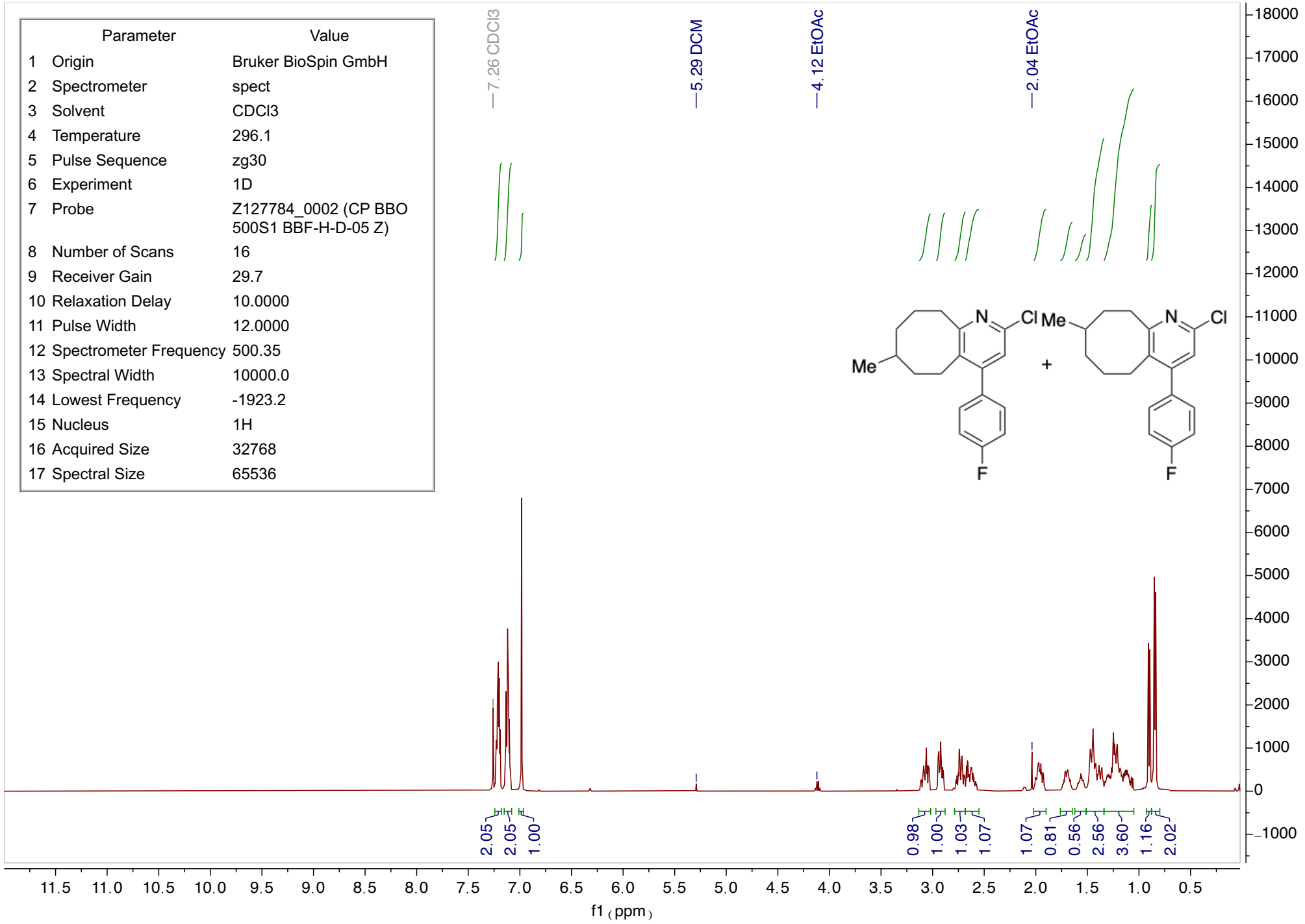


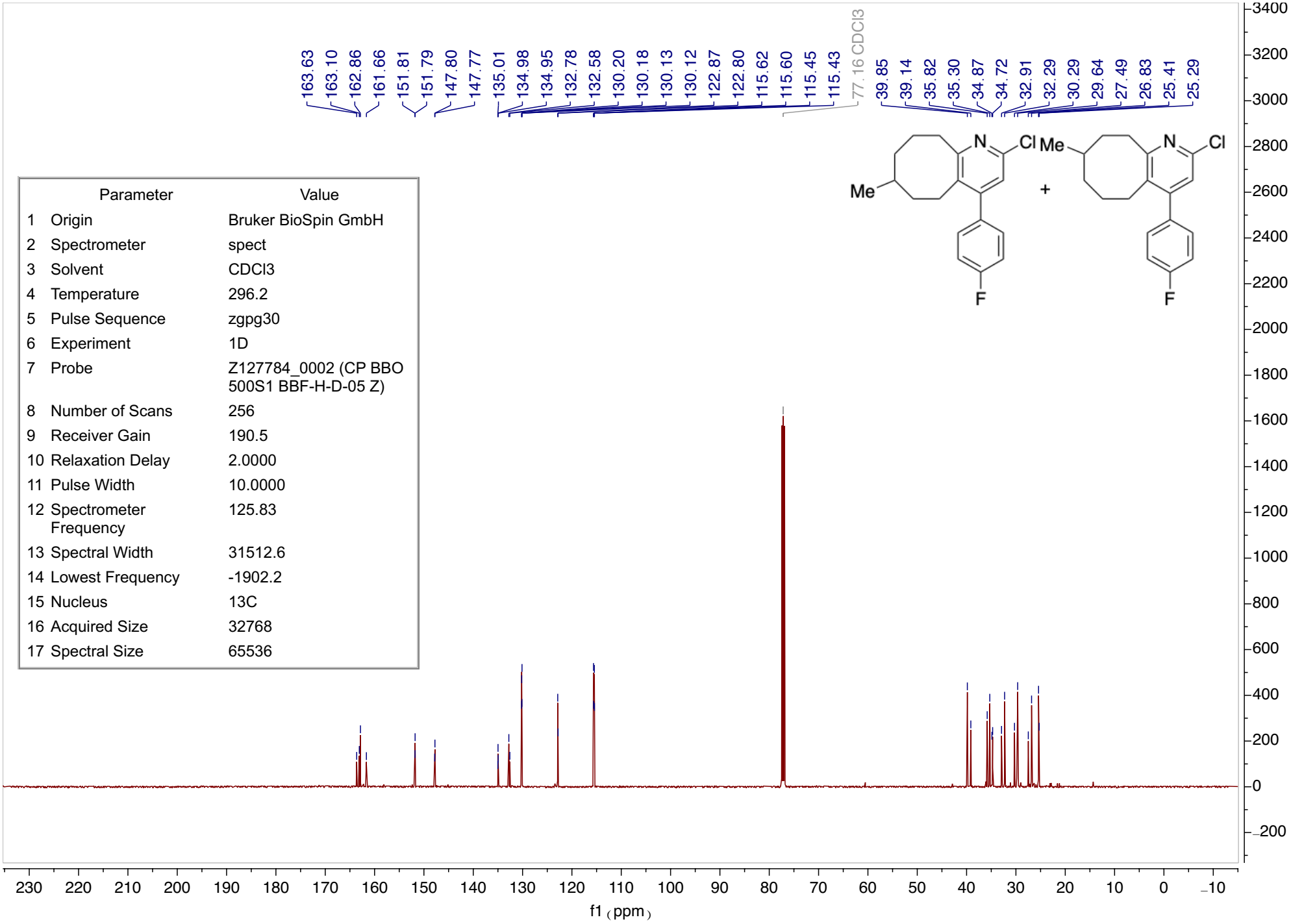
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.8
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



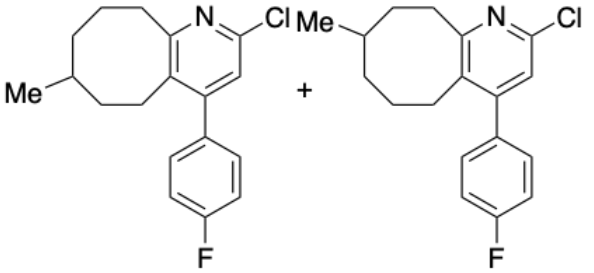
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.2
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

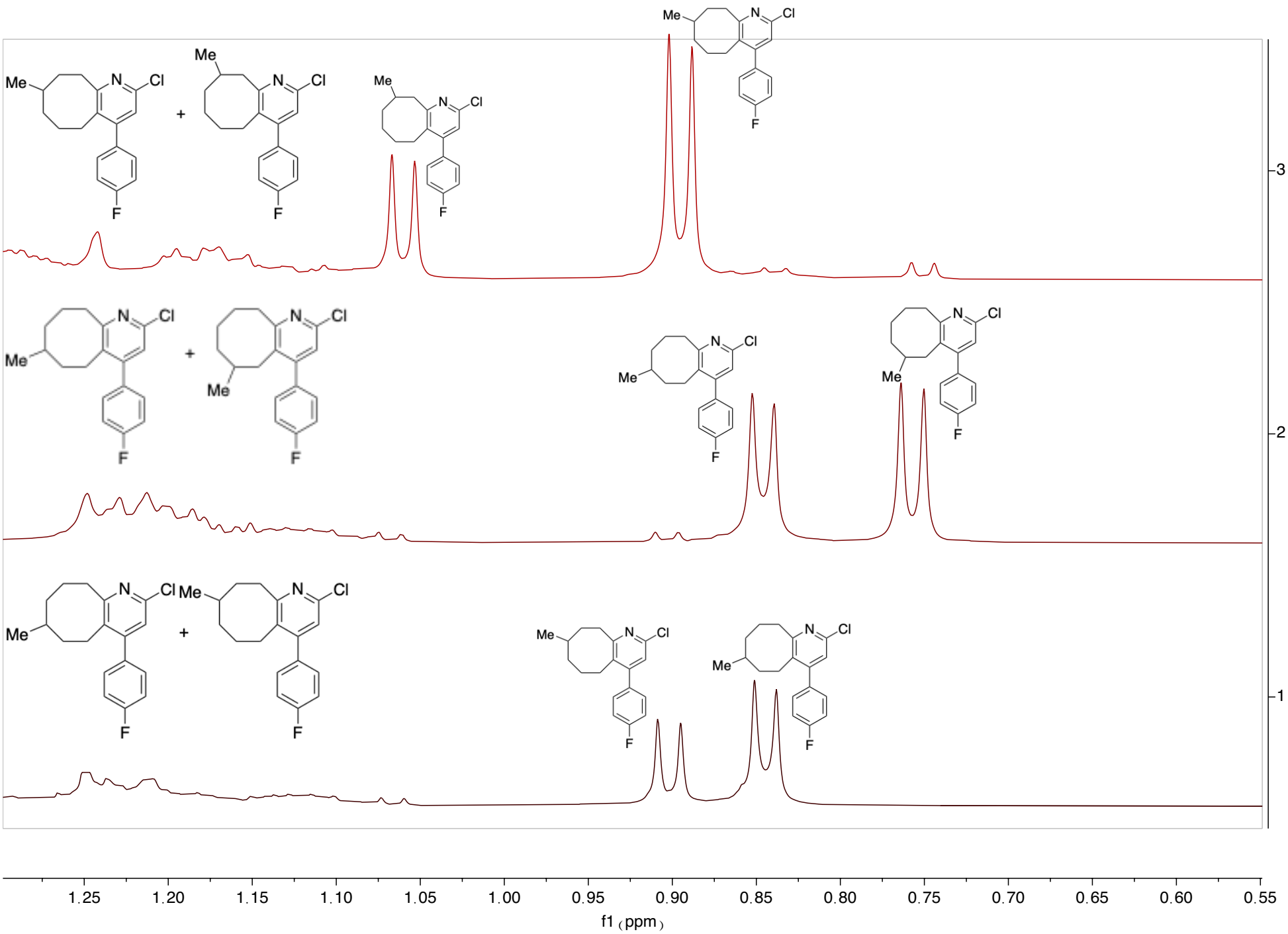




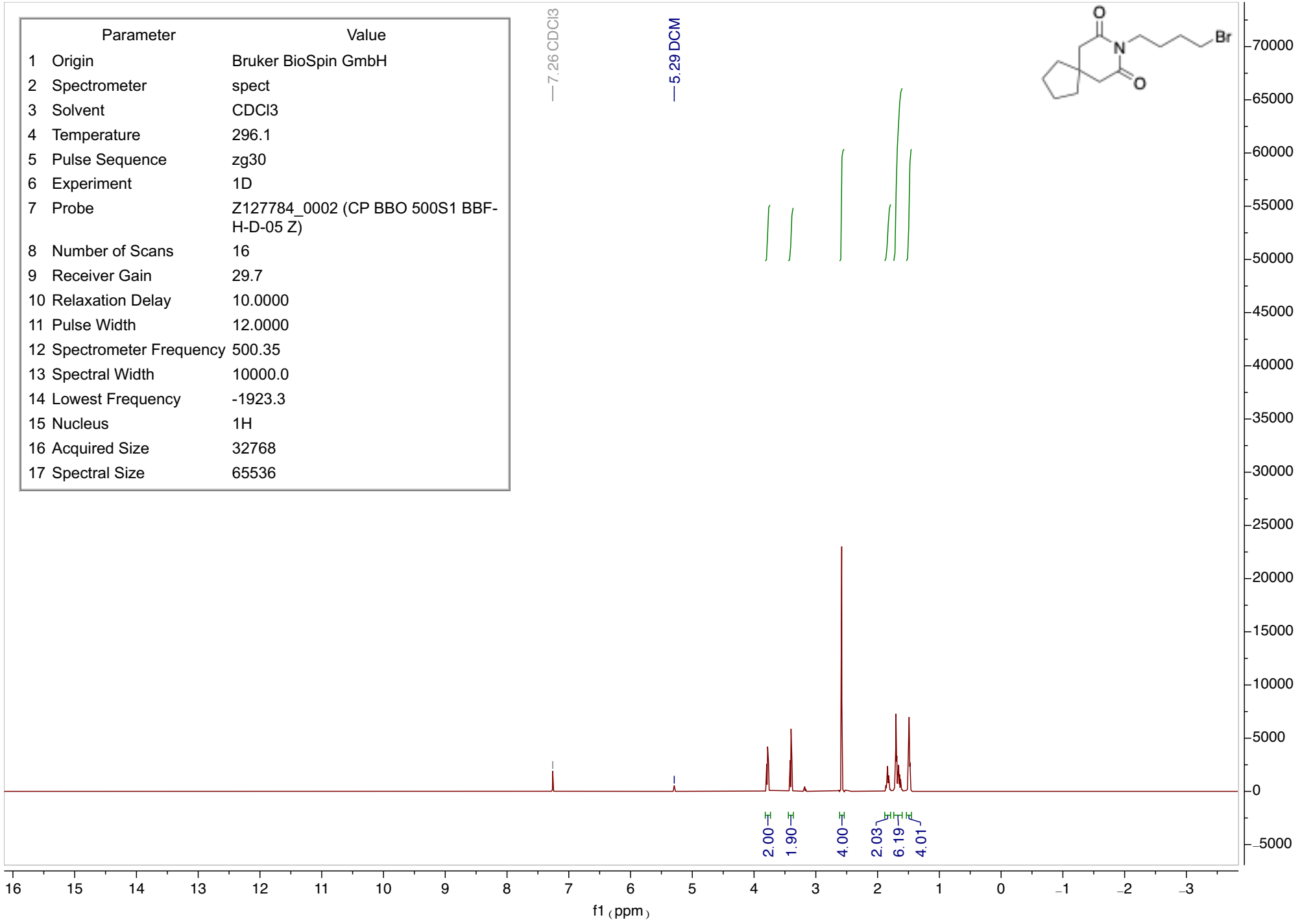
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

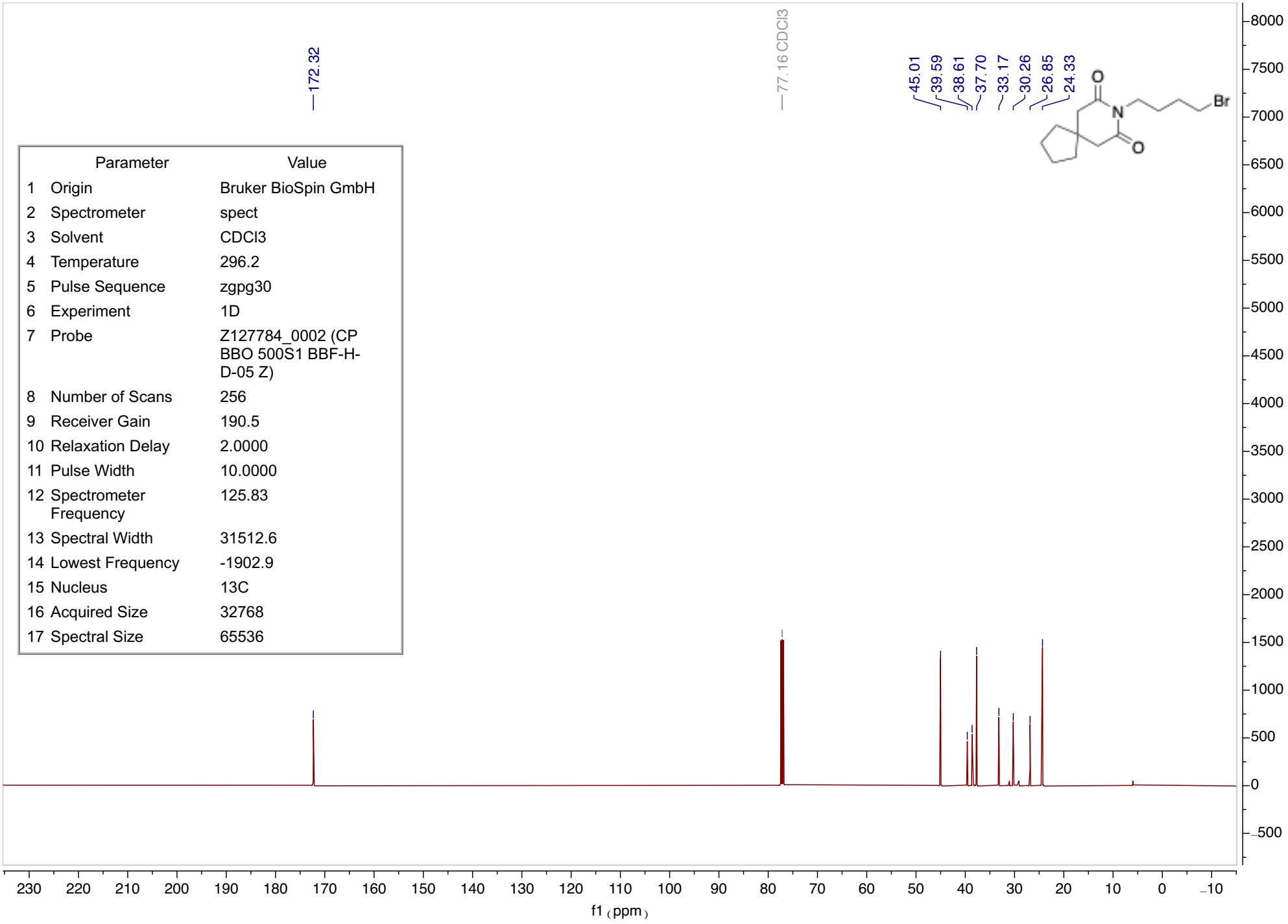
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



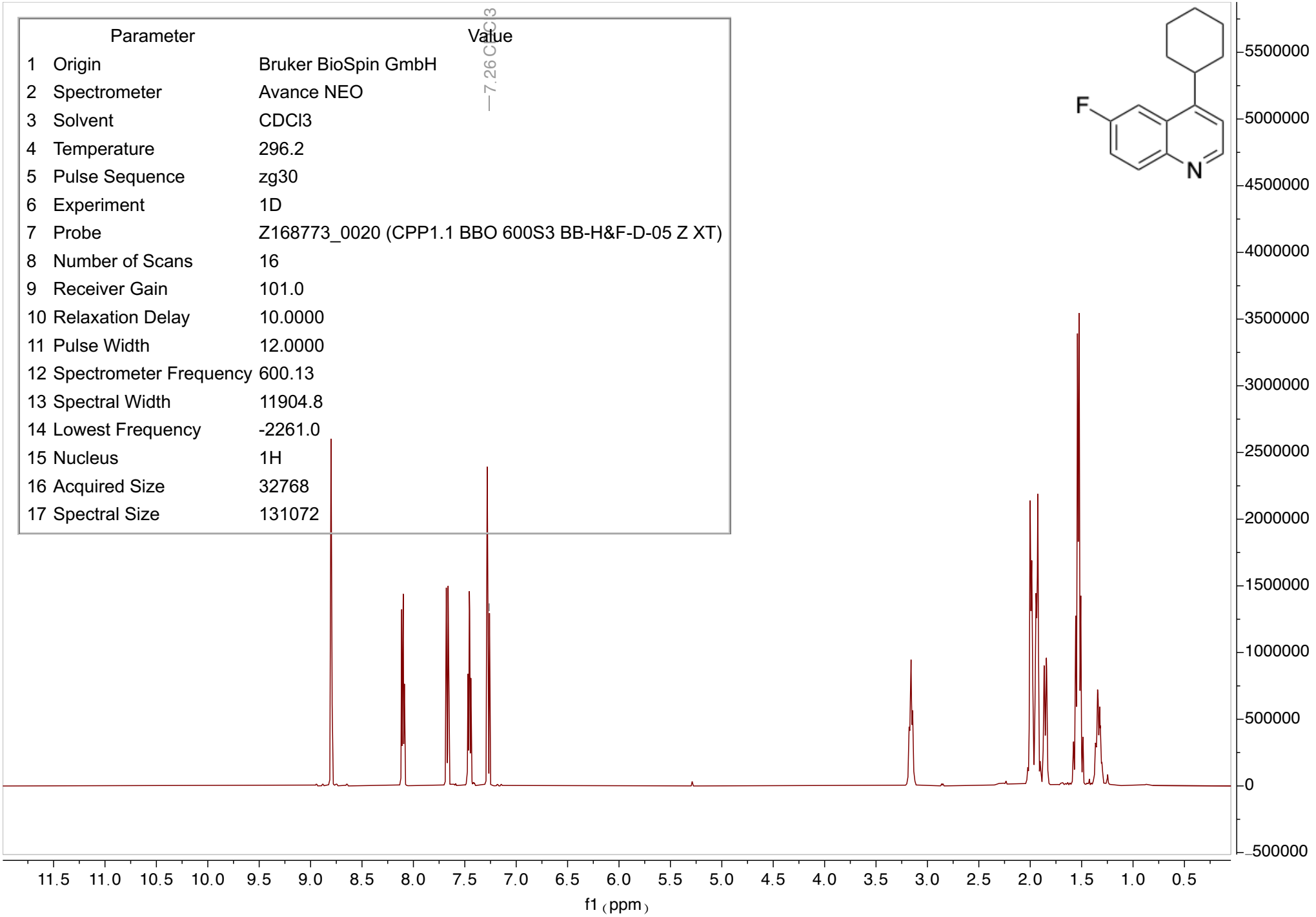

Me
N
Cl
F
+
3
2
1
1.25
1.20
1.15
1.10
1.05
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
f1 (ppm)

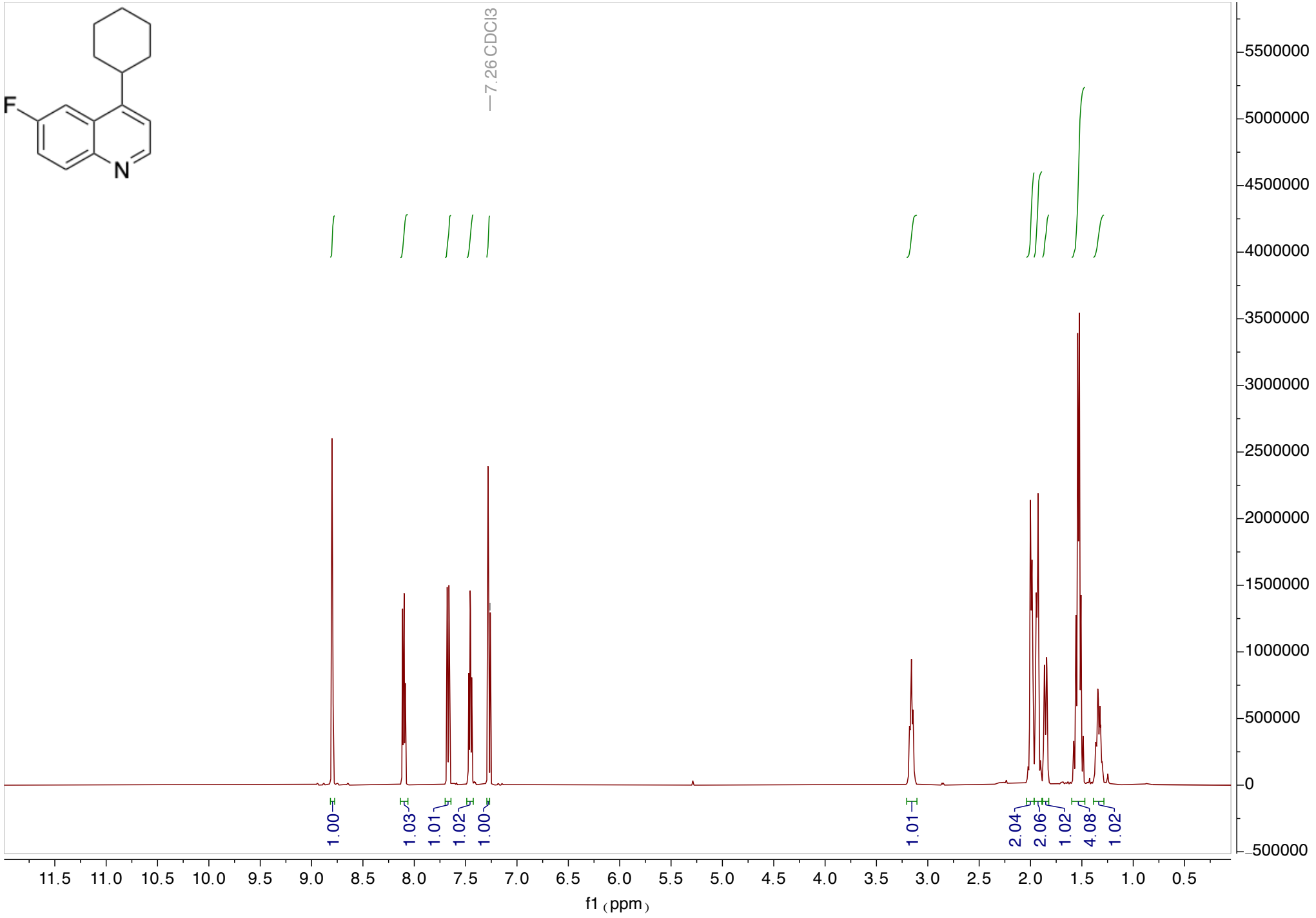
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.3
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

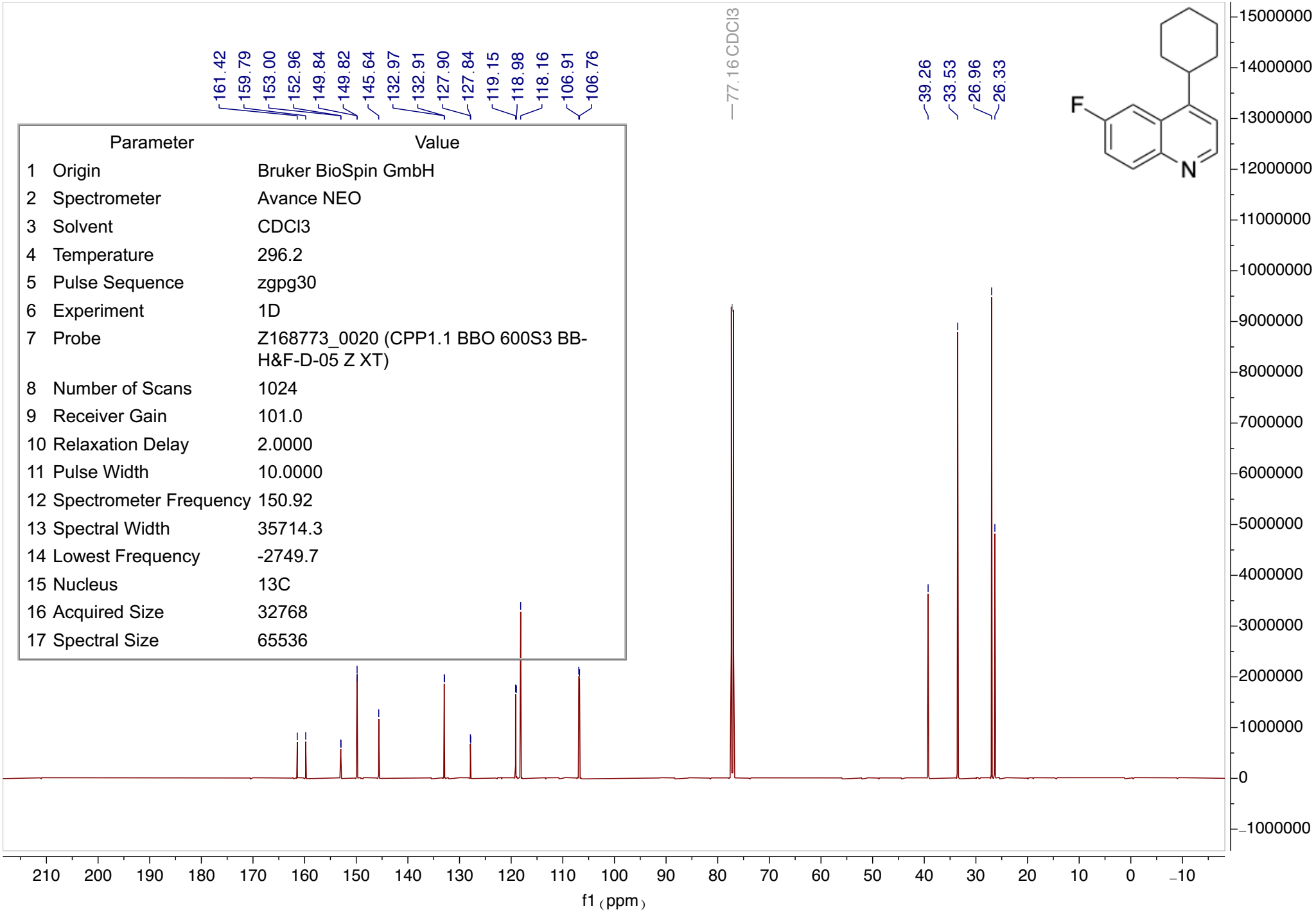




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1902.9
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

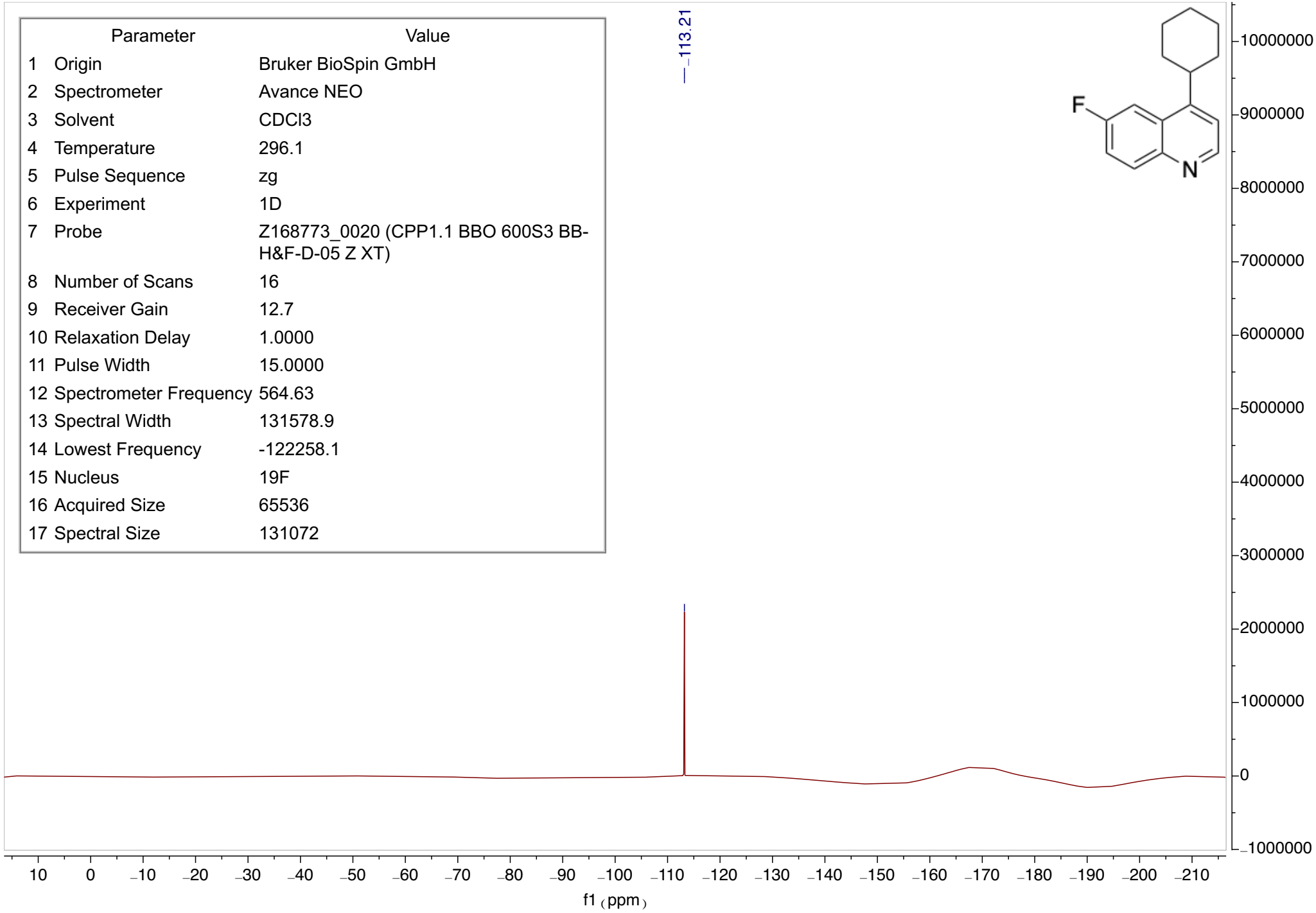

Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 101.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2261.0
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
7.26 CDCl3
F
N
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
11.5 11.0 10.5 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
f1 (ppm)


F
N
7.26 CDCl3
1.00
1.03
1.01
1.02
1.00
1.01
2.04
2.06
1.02
4.08
1.02
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
11.5 11.0 10.5 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
f1 (ppm)

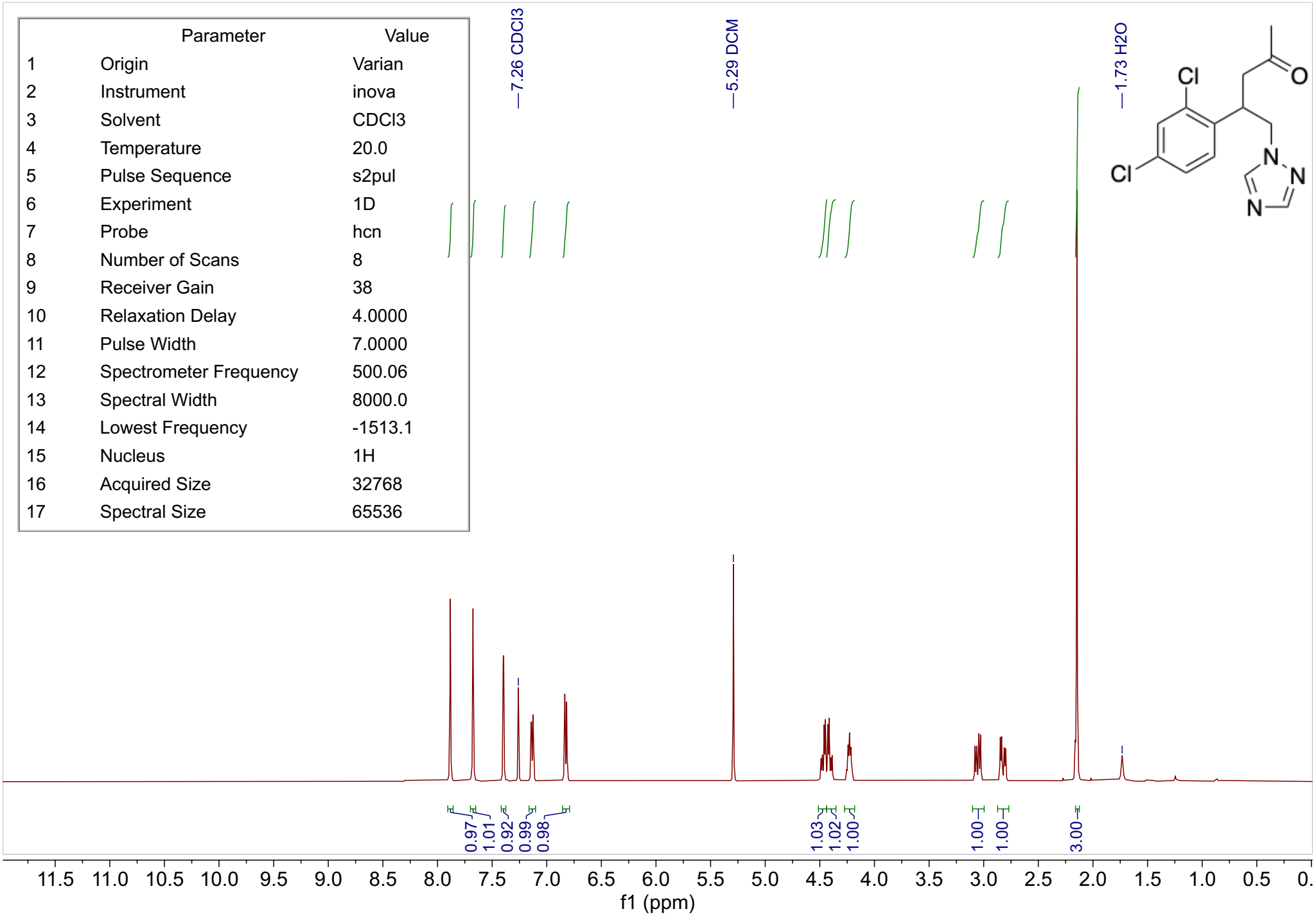


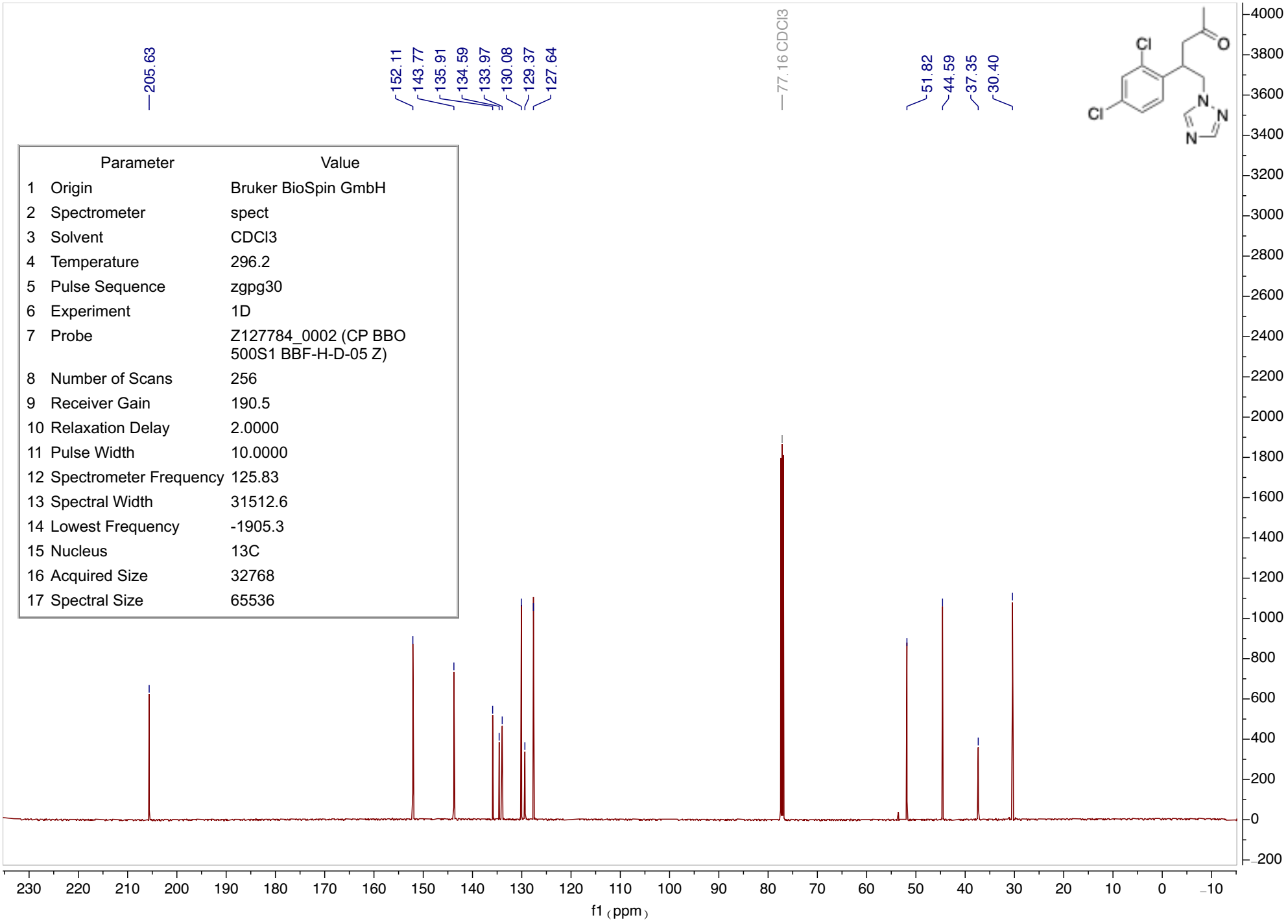
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2749.7
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	12.7
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072



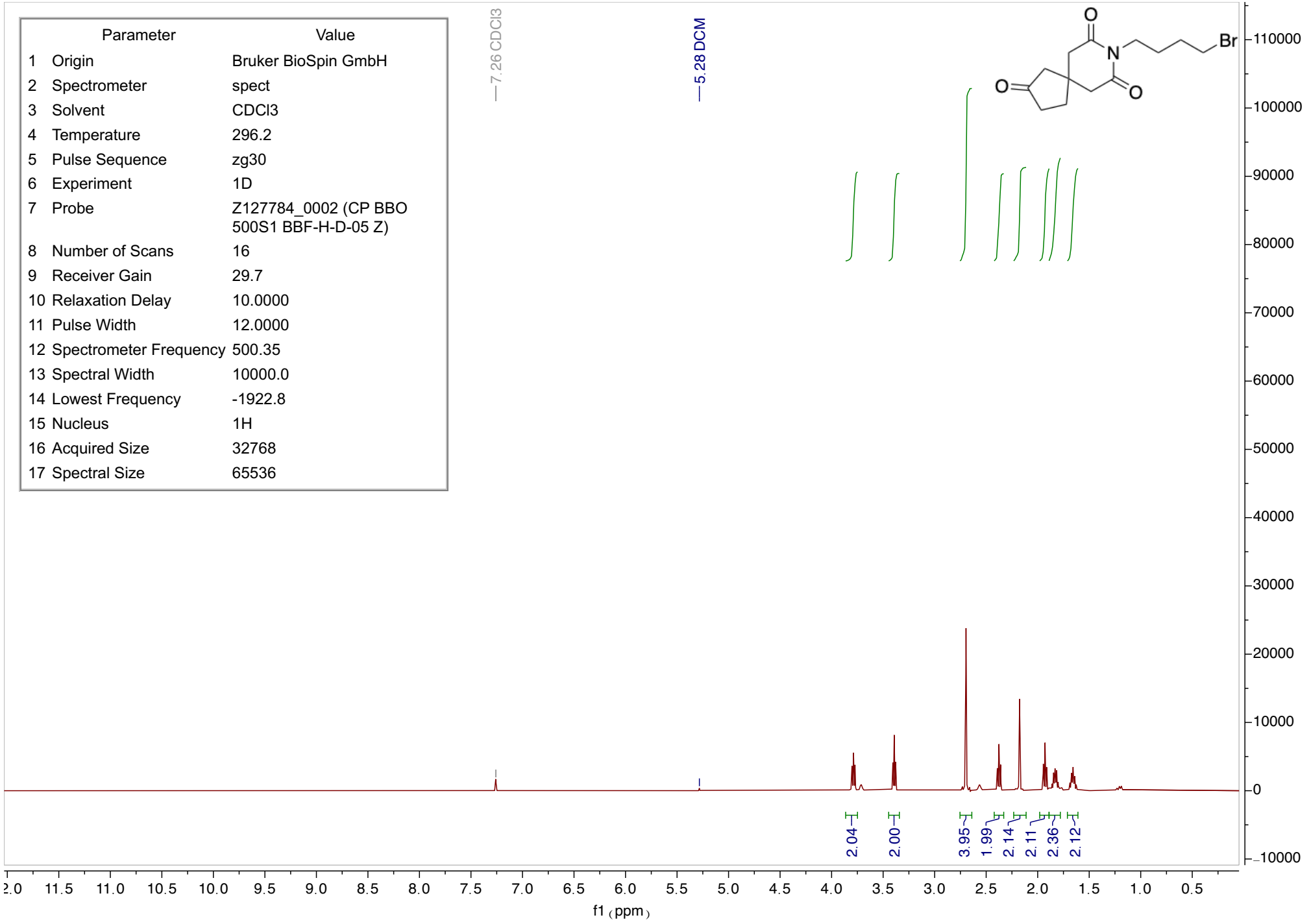
	Parameter	Value
1	Origin	Varian
2	Instrument	inova
3	Solvent	CDCl3
4	Temperature	20.0
5	Pulse Sequence	s2pul
6	Experiment	1D
7	Probe	hcn
8	Number of Scans	8
9	Receiver Gain	38
10	Relaxation Delay	4.0000
11	Pulse Width	7.0000
12	Spectrometer Frequency	500.06
13	Spectral Width	8000.0
14	Lowest Frequency	-1513.1
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

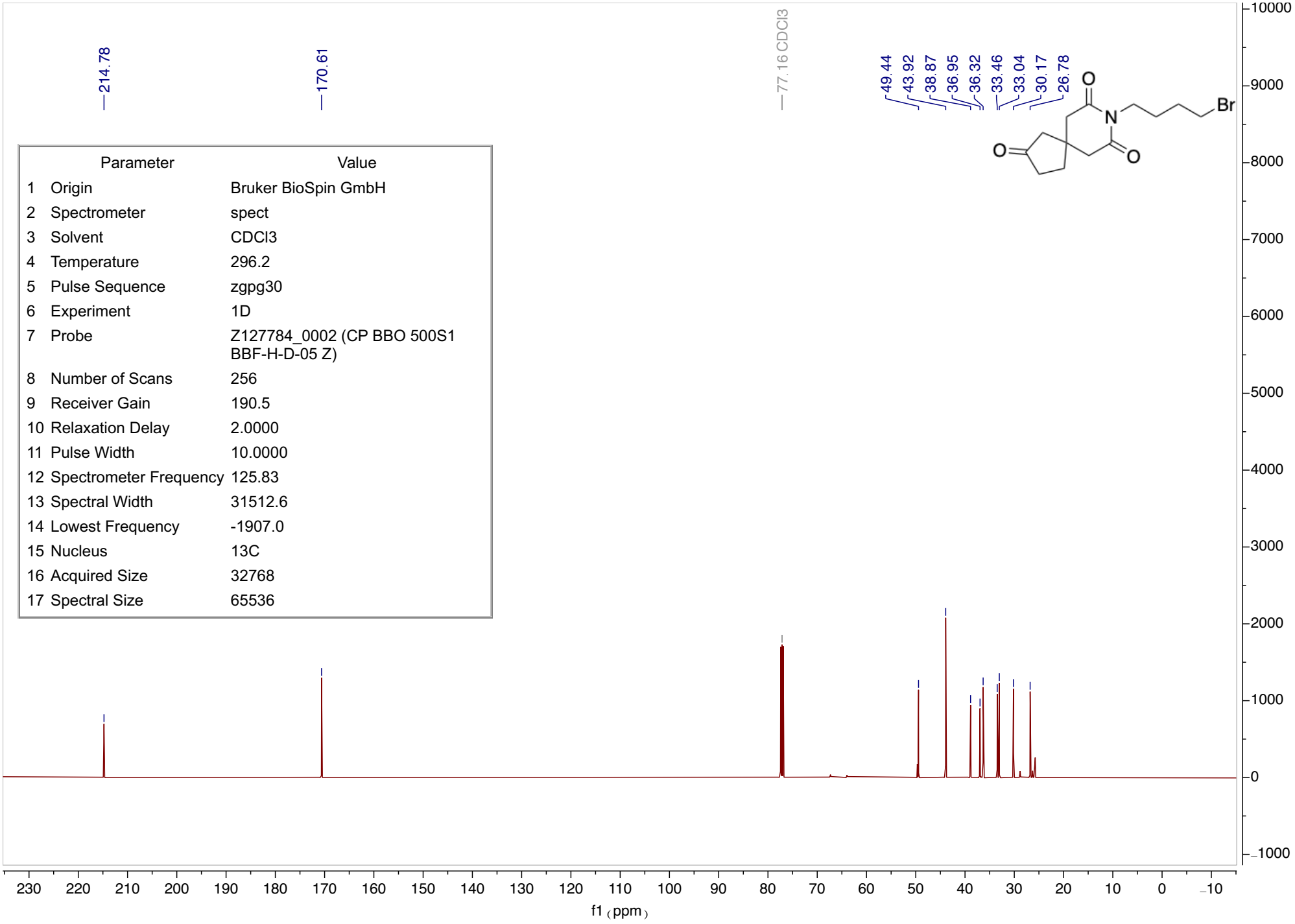




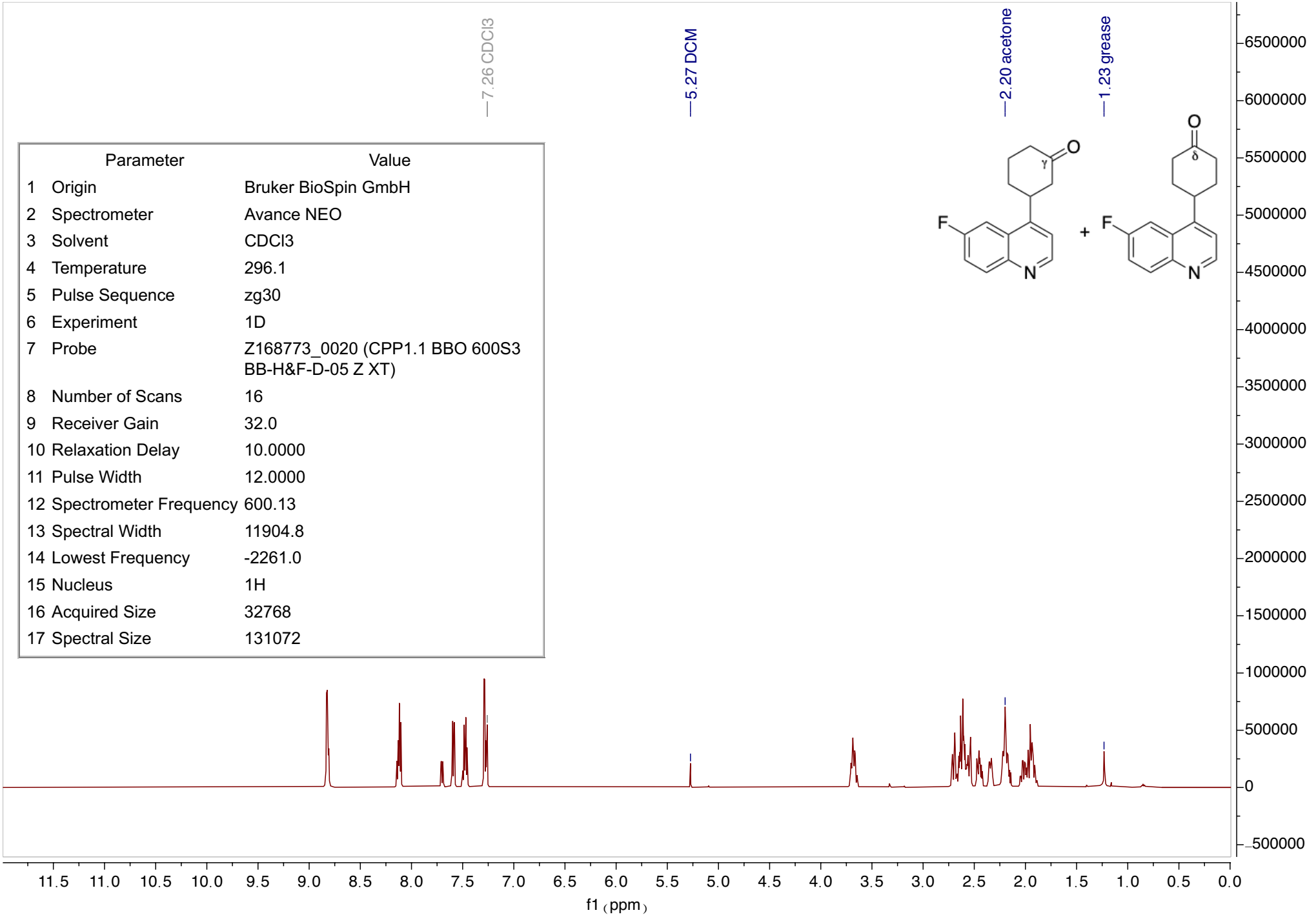
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1905.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

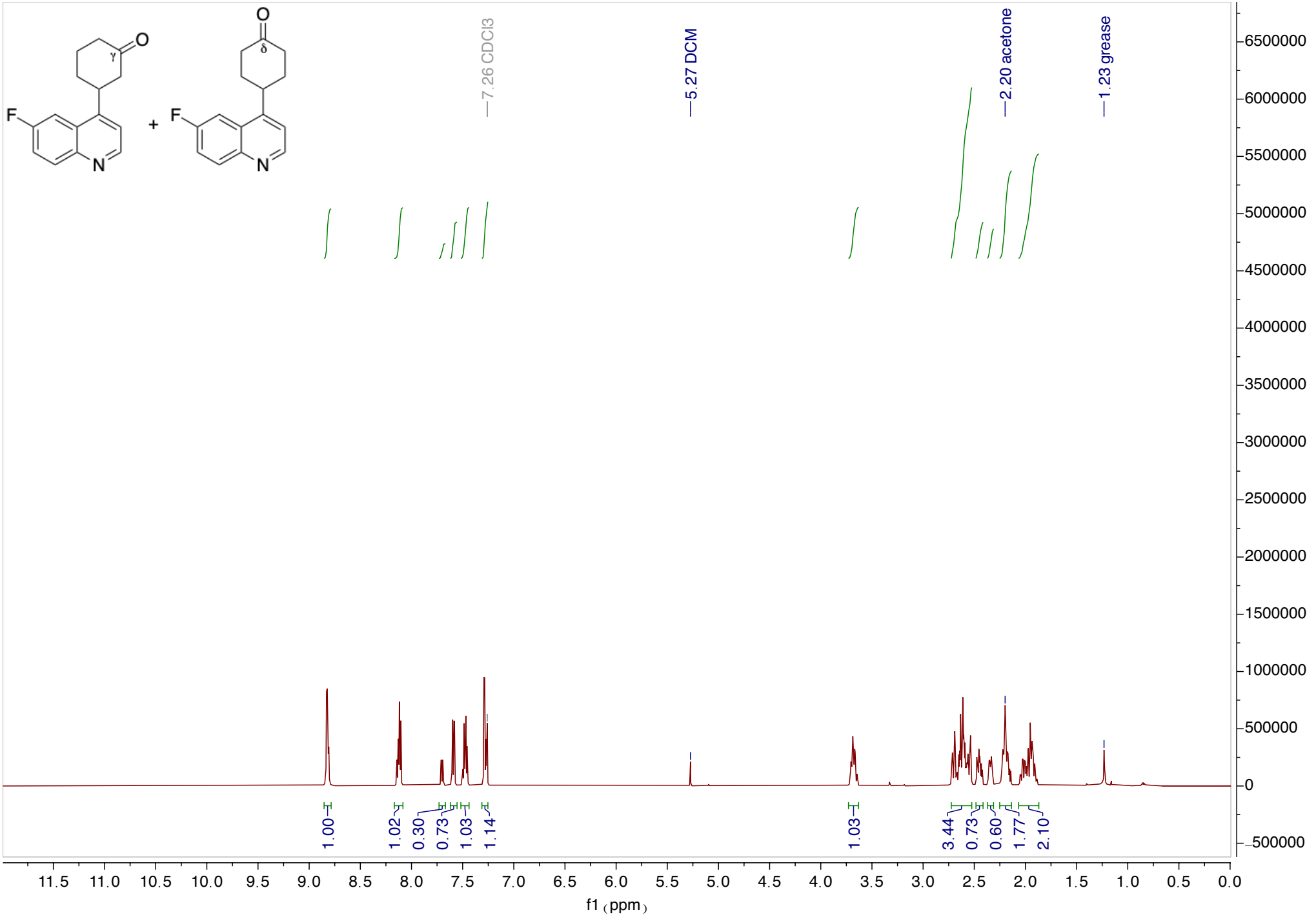
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.8
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

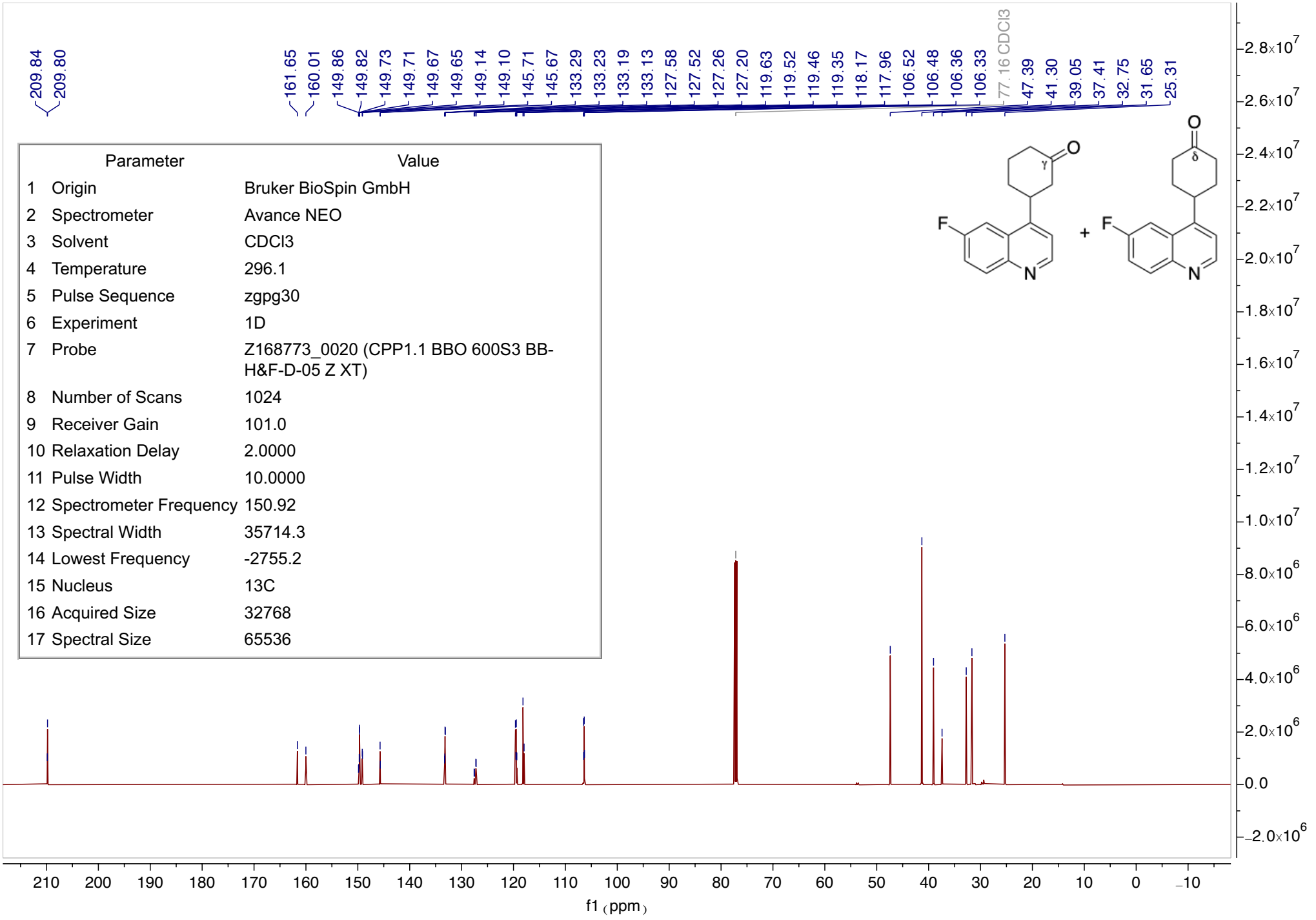




	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	256
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1907.0
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

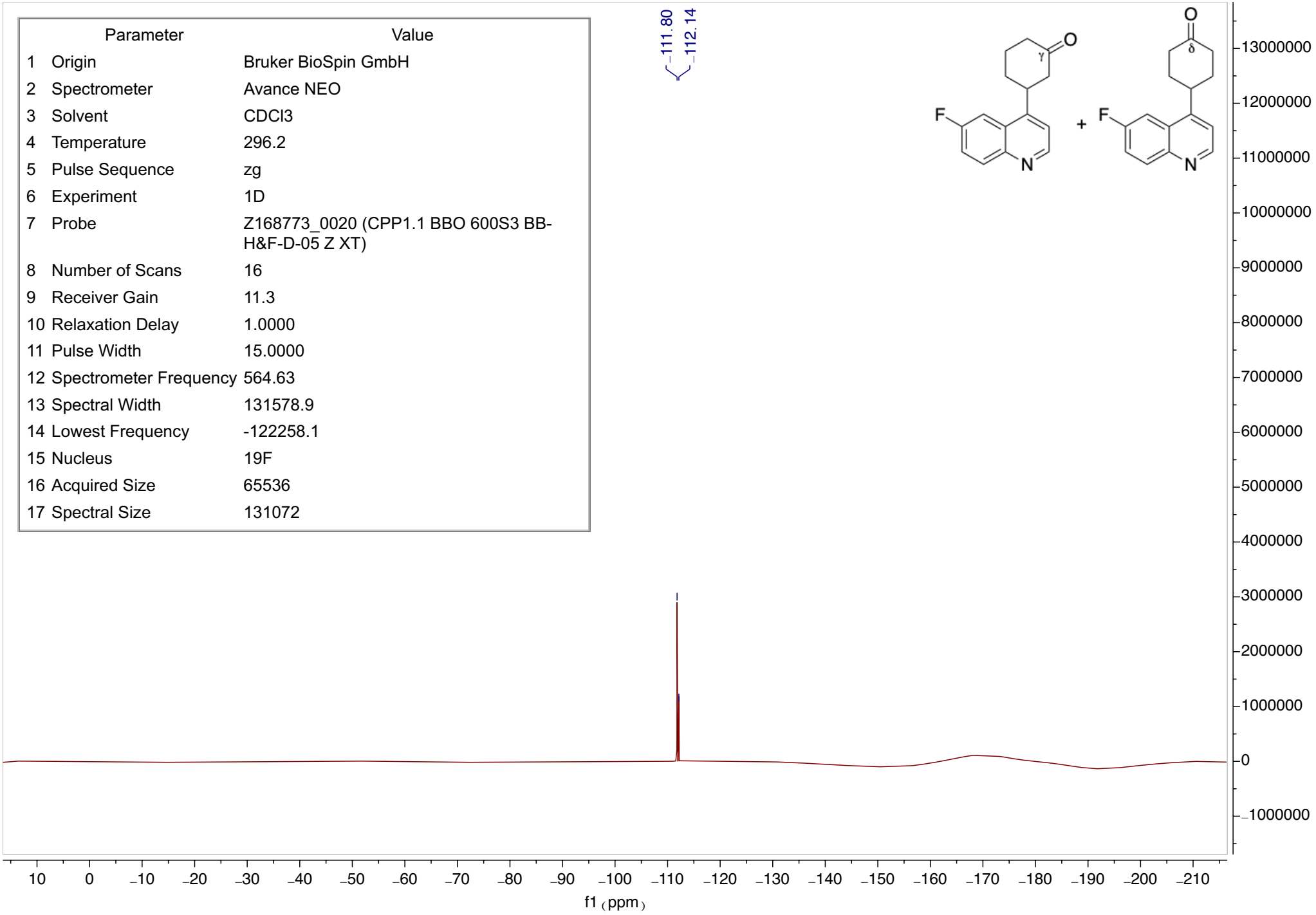

7.26 CDCl3
5.27 DCM
2.20 acetone
1.23 grease
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence zg30
6 Experiment 1D
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 16
9 Receiver Gain 32.0
10 Relaxation Delay 10.0000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 11904.8
14 Lowest Frequency -2261.0
15 Nucleus 1H
16 Acquired Size 32768
17 Spectral Size 131072
F
O
γ
N
+
F
O
δ
N
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
−500000
11.5 11.0 10.5 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)

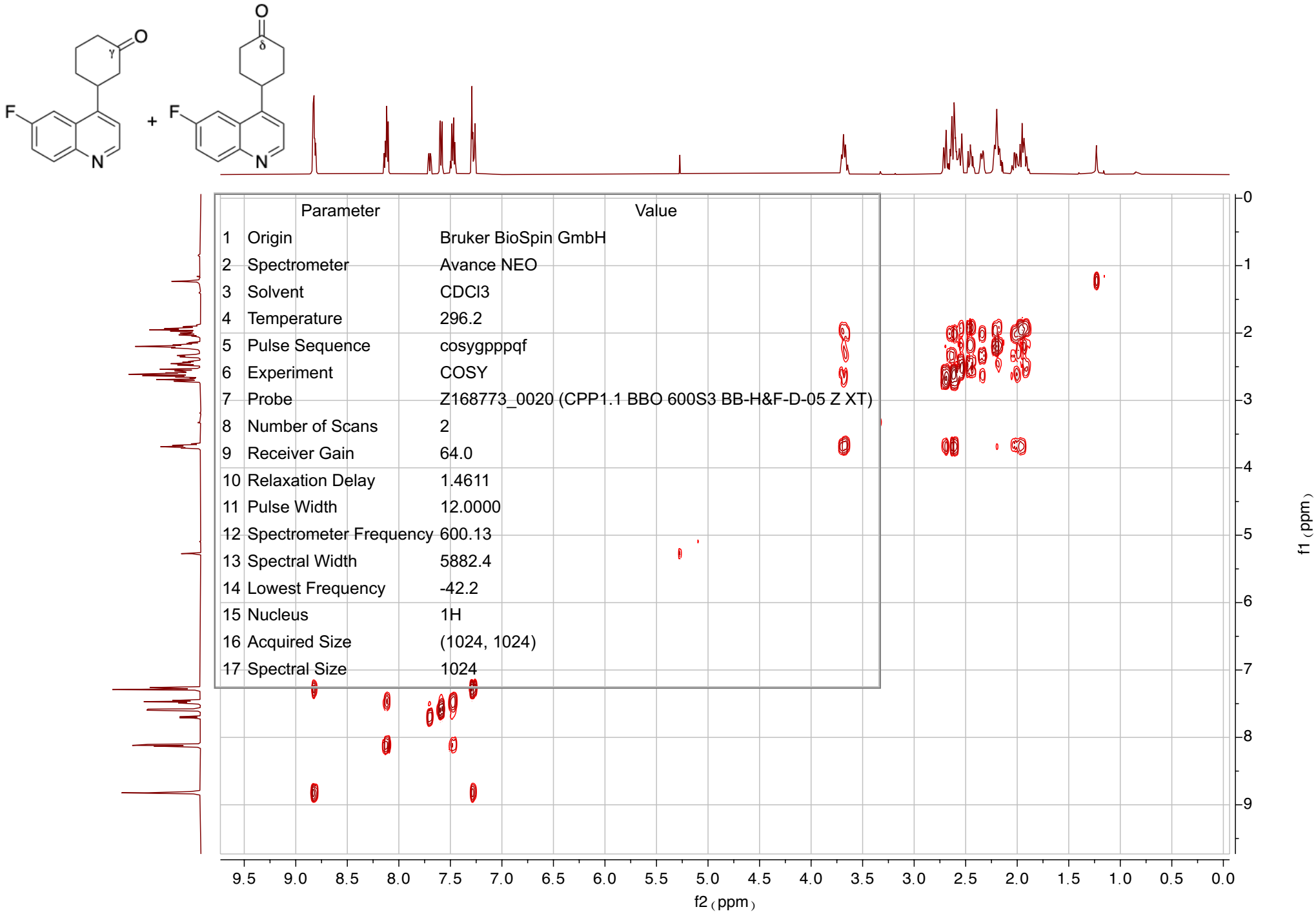

7.26 CDCl3
5.27 DCM
2.20 acetone
1.23 grease
1.00
1.02
0.30
0.73
1.03
1.14
1.03
3.44
0.73
0.60
1.77
2.10
f1 (ppm)

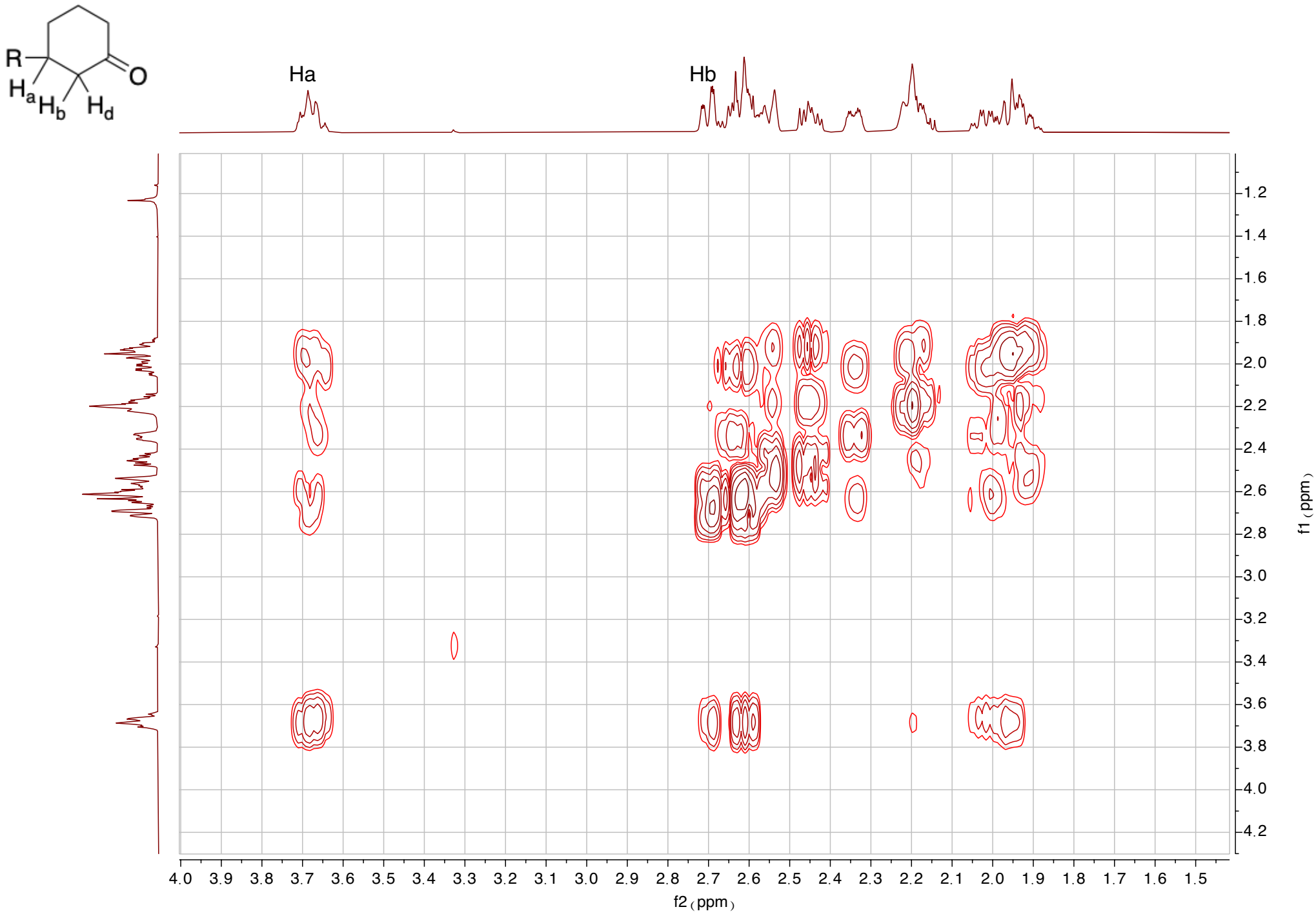


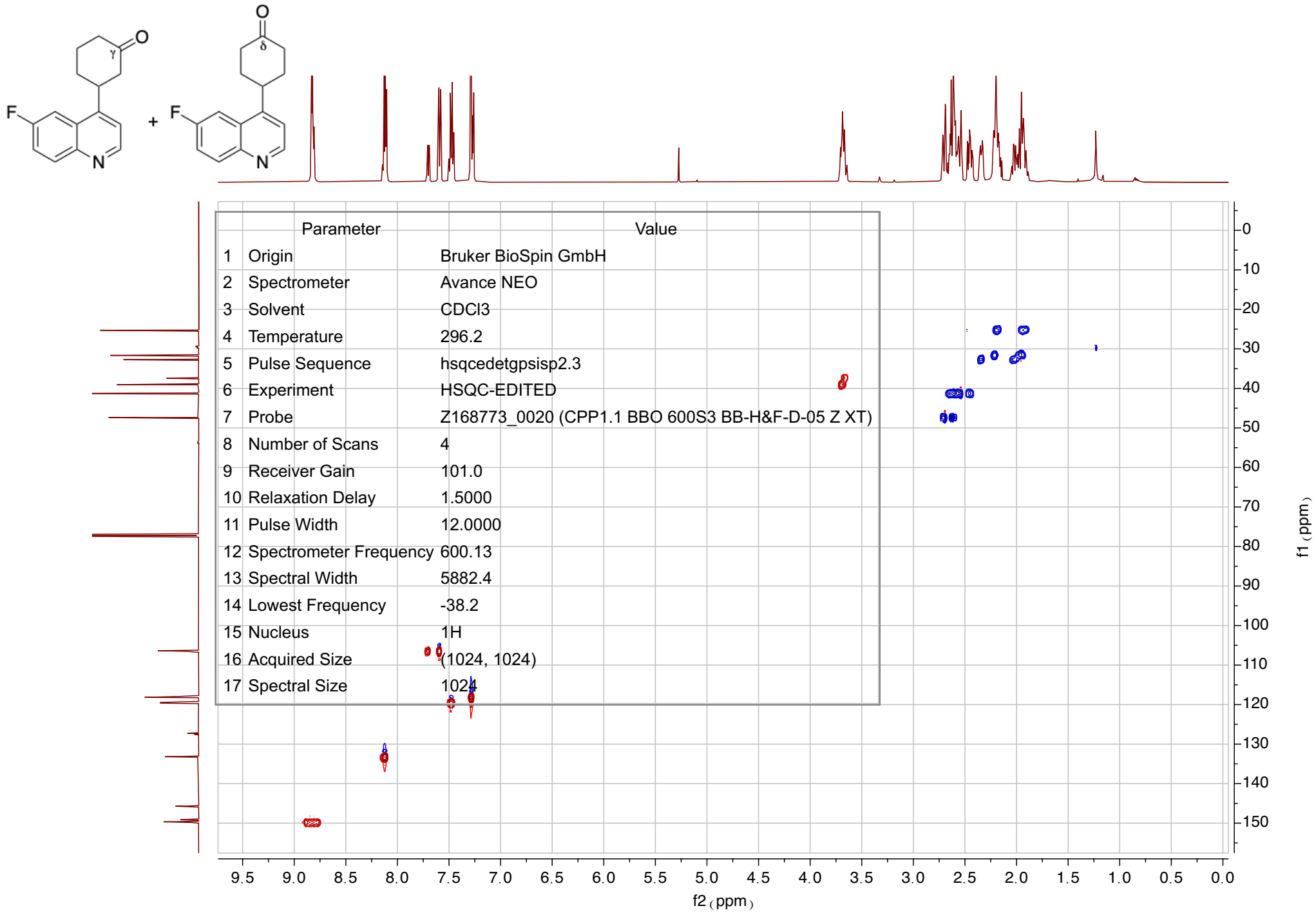
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	1024
9	Receiver Gain	101.0
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	150.92
13	Spectral Width	35714.3
14	Lowest Frequency	-2755.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

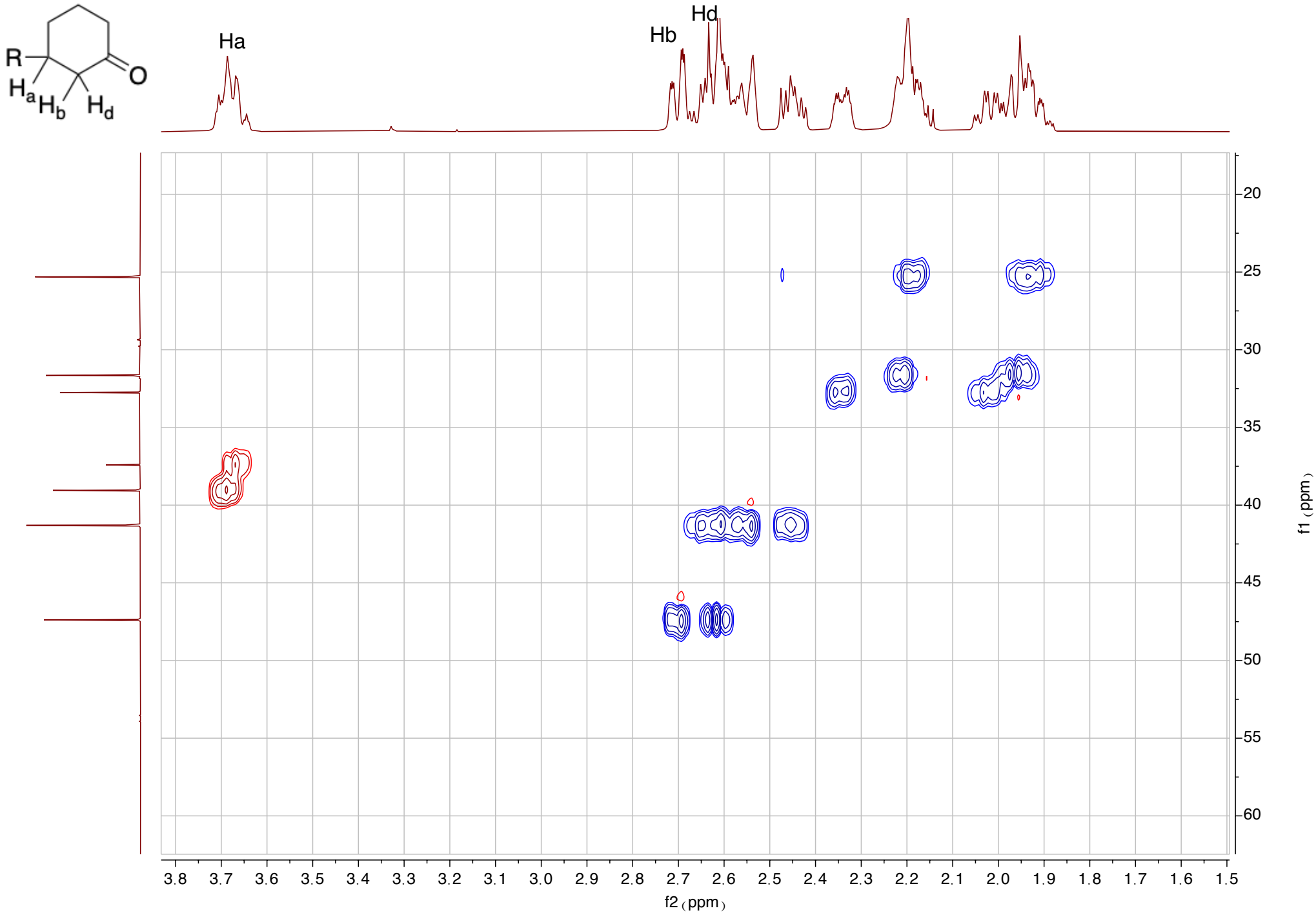
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	Avance NEO
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg
6	Experiment	1D
7	Probe	Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8	Number of Scans	16
9	Receiver Gain	11.3
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	564.63
13	Spectral Width	131578.9
14	Lowest Frequency	-122258.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

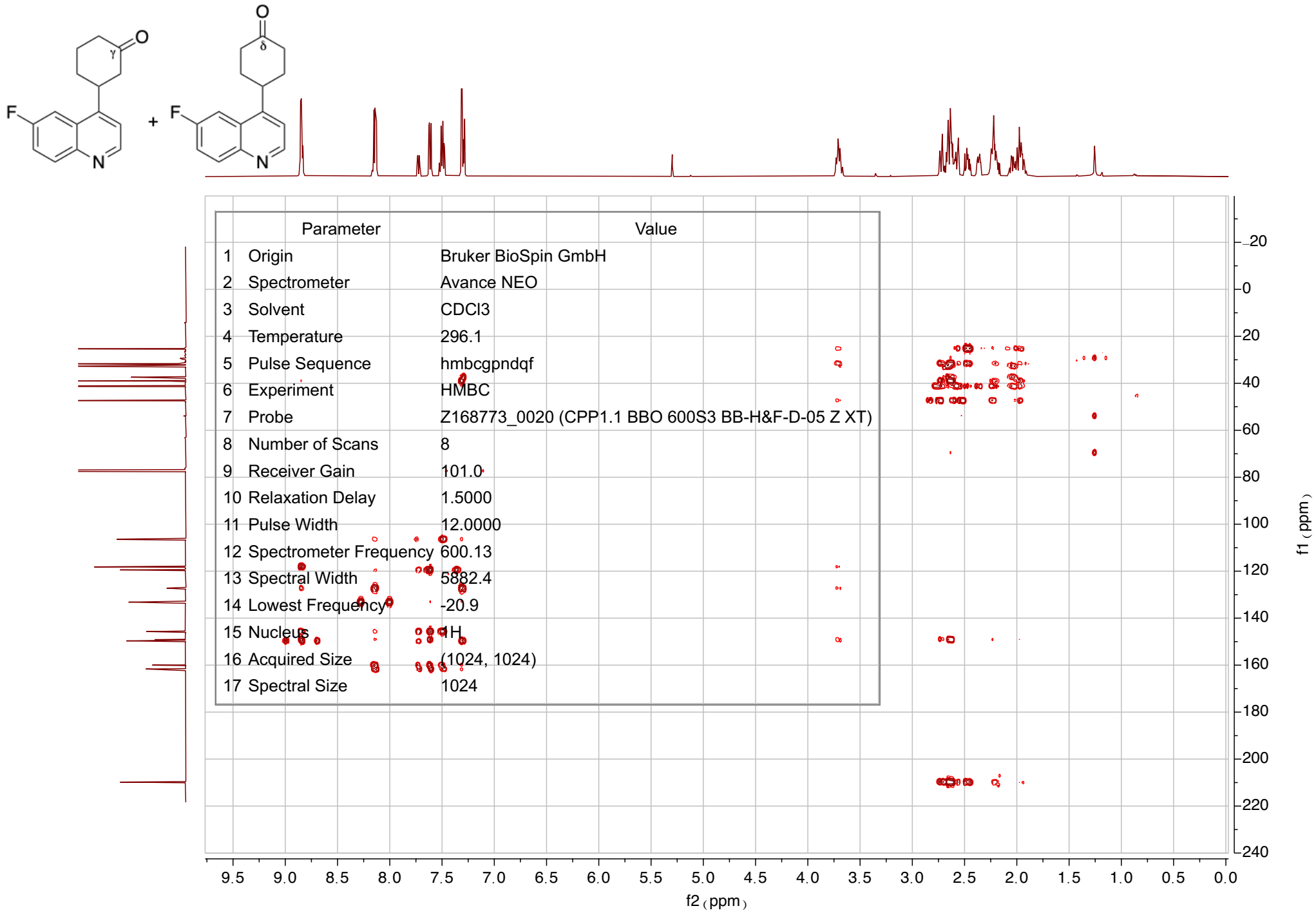


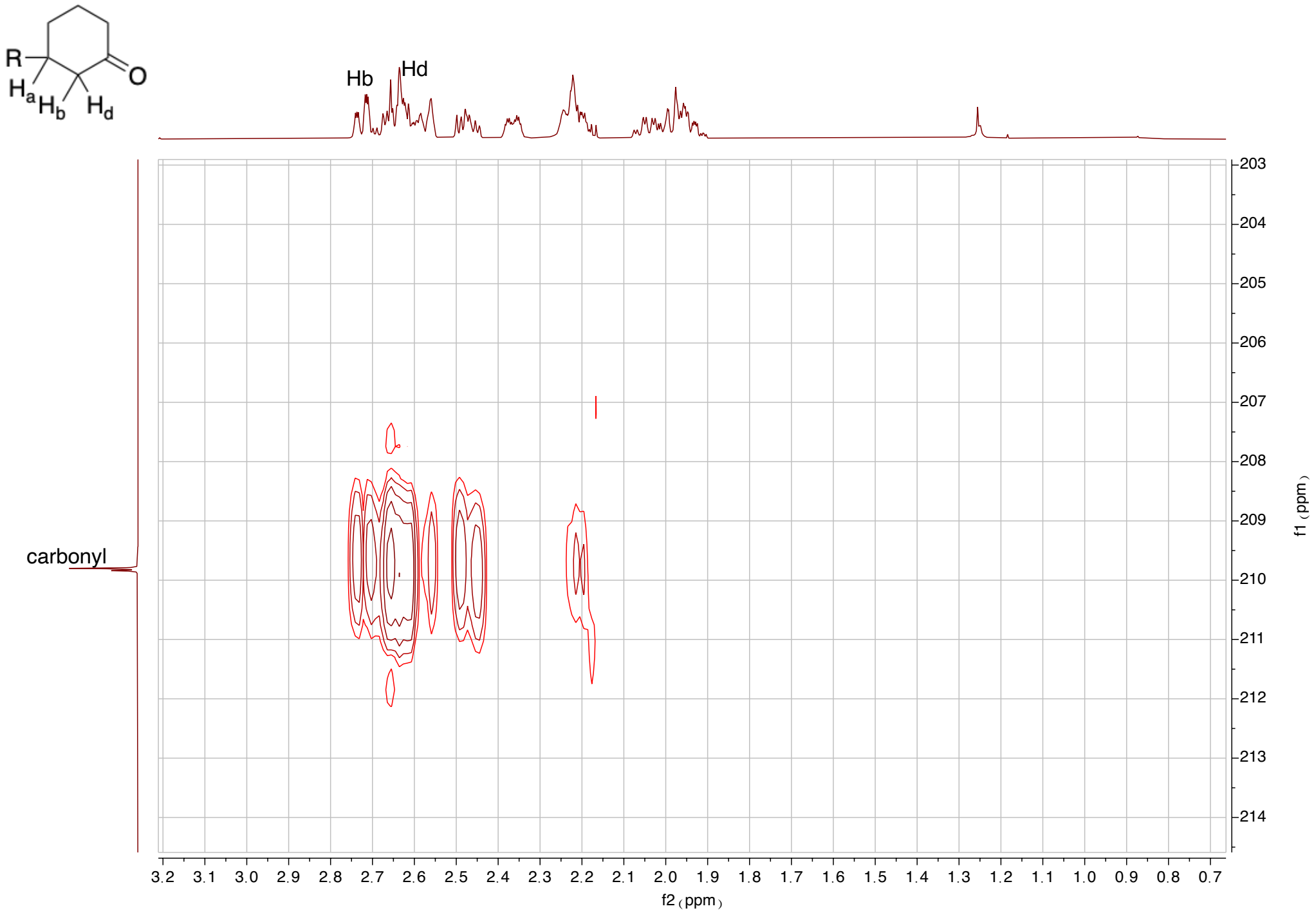

O
γ
F
N
+
O
δ
F
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence cosygpppqf
6 Experiment COSY
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 2
9 Receiver Gain 64.0
10 Relaxation Delay 1.4611
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5882.4
14 Lowest Frequency -42.2
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 1 2 3 4 5 6 7 8 9
f1 (ppm)


R
O
Ha
Hb
Hd
Ha
Hb
4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5
f2 (ppm)
1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8 4.0 4.2
f1 (ppm)

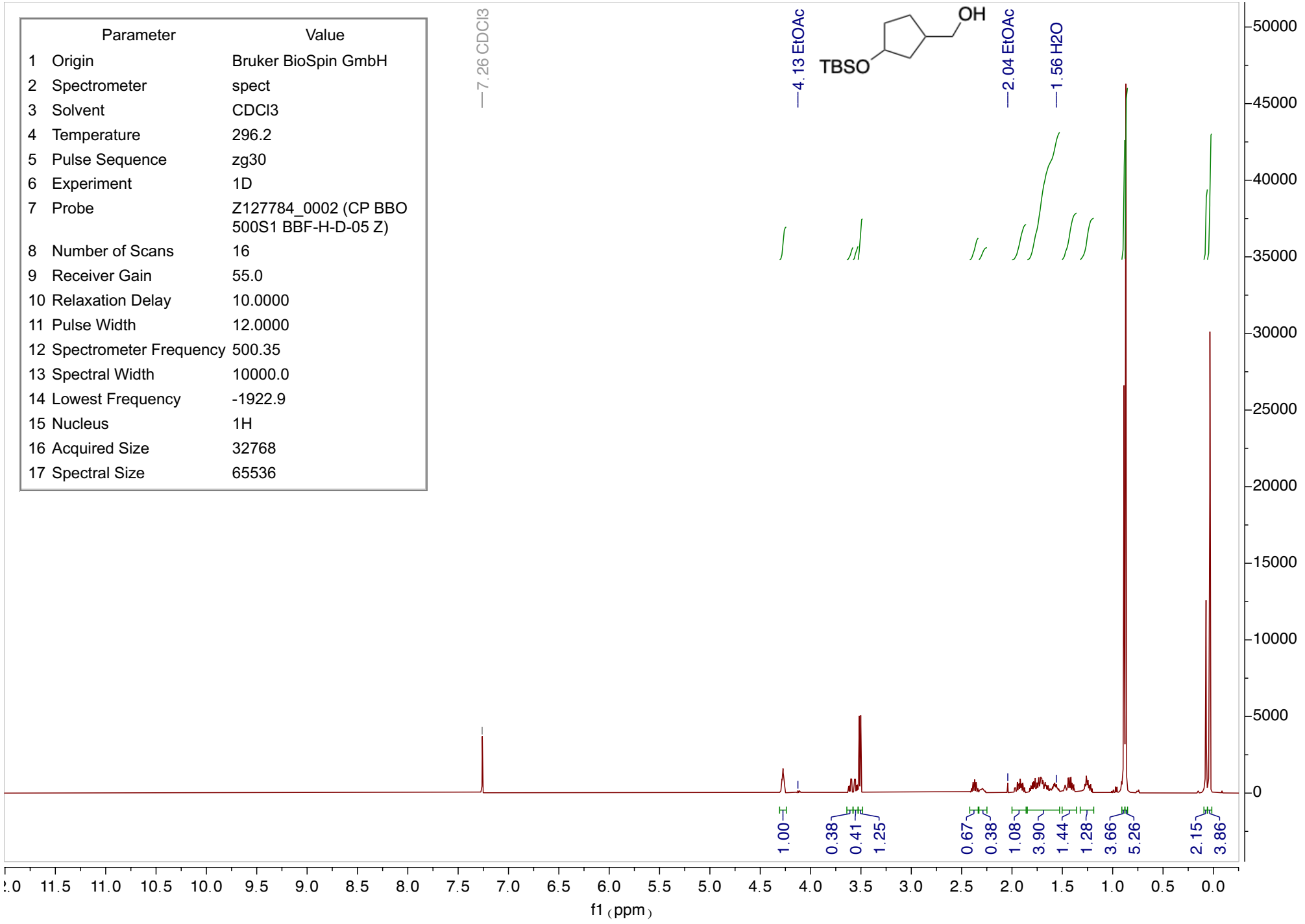

O
γ
F
N
+
O
δ
F
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.2
5 Pulse Sequence hsqcedetgpsisp2.3
6 Experiment HSQC-EDITED
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 4
9 Receiver Gain 101.0
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5882.4
14 Lowest Frequency -38.2
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
f1 (ppm)


R
O
Ha
Hb
Hd
Ha
Hb
Hd
3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5
f2 (ppm)
20 25 30 35 40 45 50 55 60
f1 (ppm)

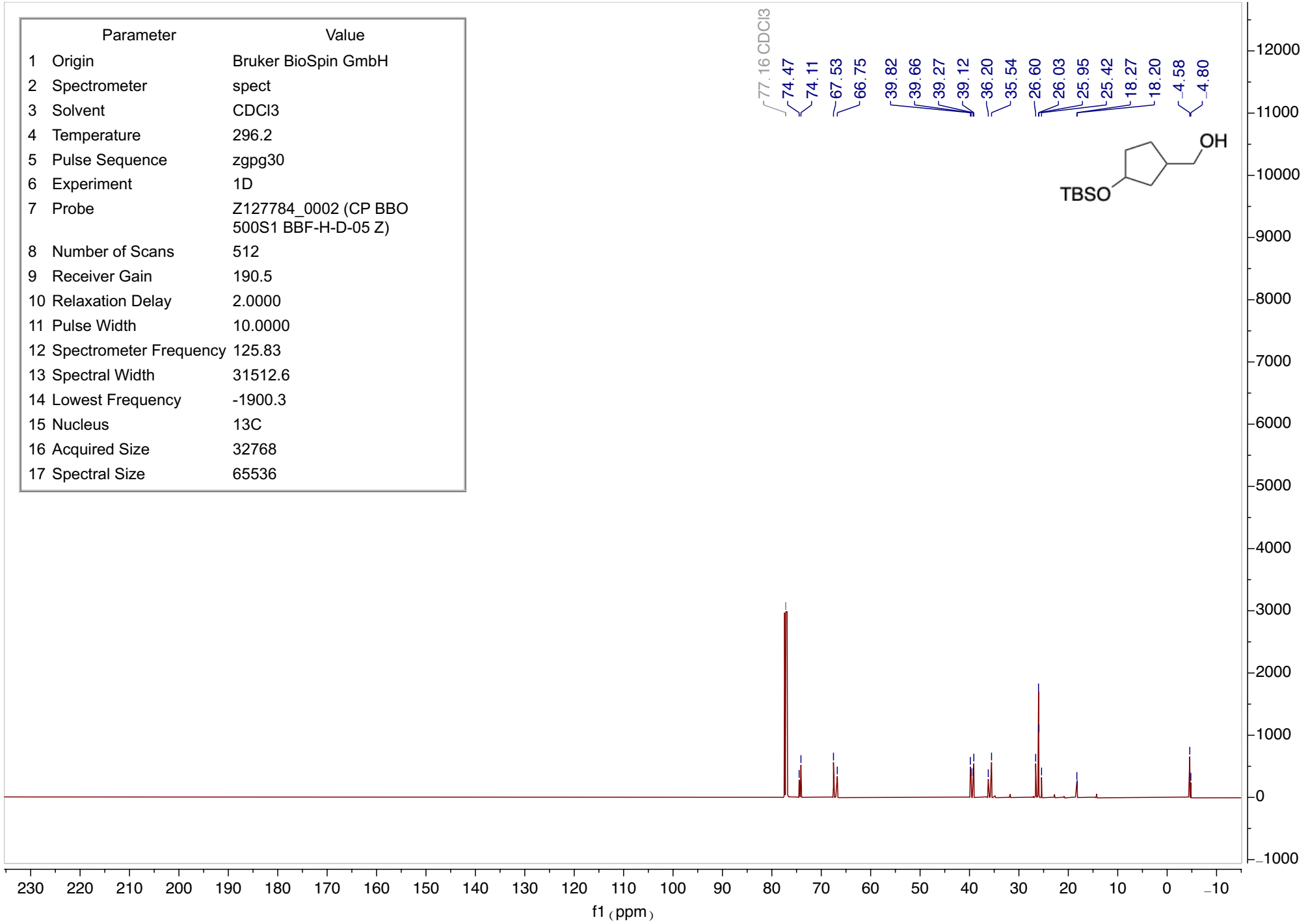

O
γ
F
N
+
O
δ
F
N
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Spectrometer Avance NEO
3 Solvent CDCl3
4 Temperature 296.1
5 Pulse Sequence hmbcgpndqf
6 Experiment HMBC
7 Probe Z168773_0020 (CPP1.1 BBO 600S3 BB-H&F-D-05 Z XT)
8 Number of Scans 8
9 Receiver Gain 101.0
10 Relaxation Delay 1.5000
11 Pulse Width 12.0000
12 Spectrometer Frequency 600.13
13 Spectral Width 5882.4
14 Lowest Frequency -20.9
15 Nucleus 1H
16 Acquired Size (1024, 1024)
17 Spectral Size 1024
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
f2 (ppm)
-20 0 20 40 60 80 100 120 140 160 180 200 220 240
f1 (ppm)


R
O
Ha
Hb
Hd
Hb
Hd
carbonyl
203
204
205
206
207
208
209
210
211
212
213
214
f1 (ppm)
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
f2 (ppm)

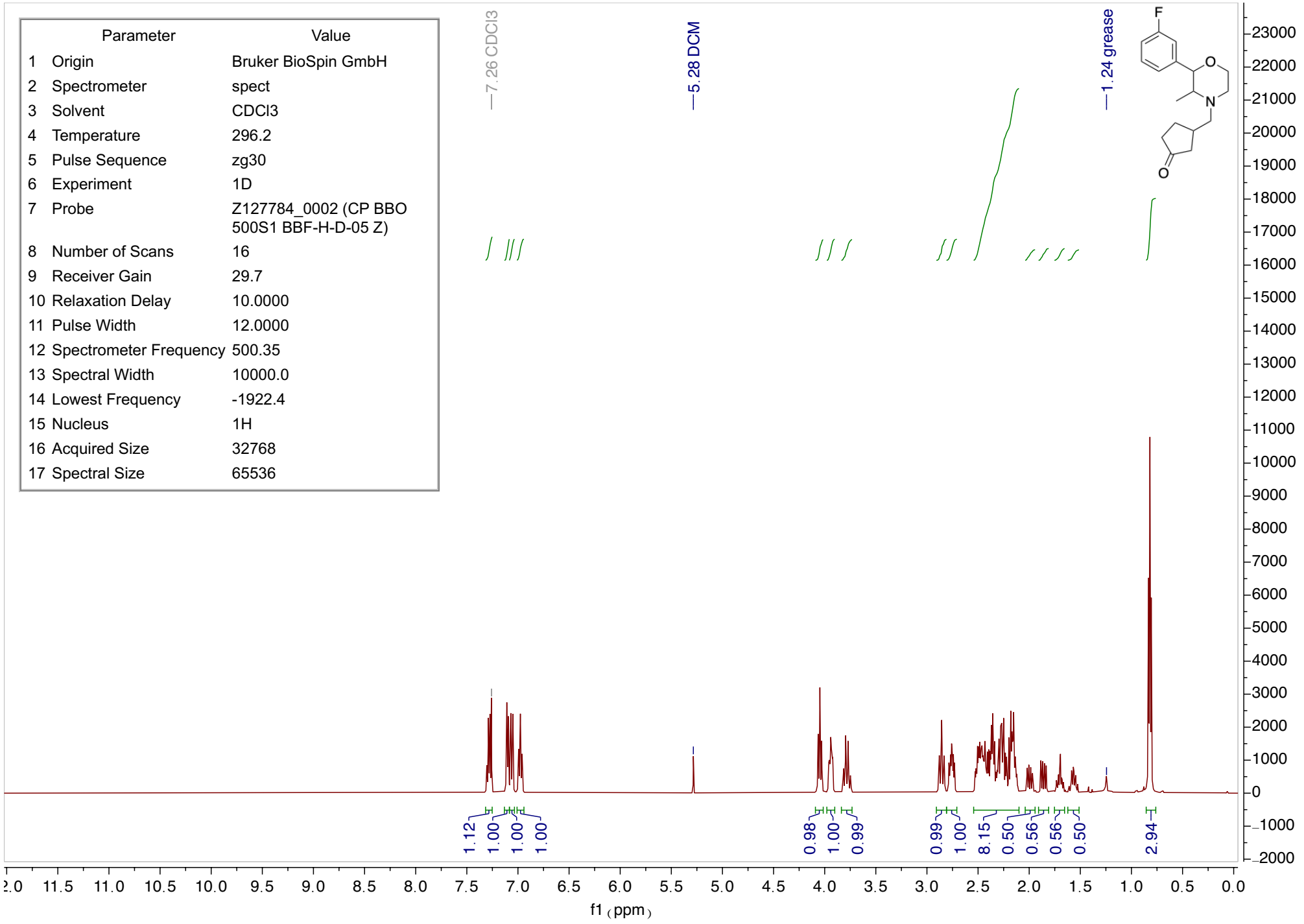
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	55.0
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.9
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

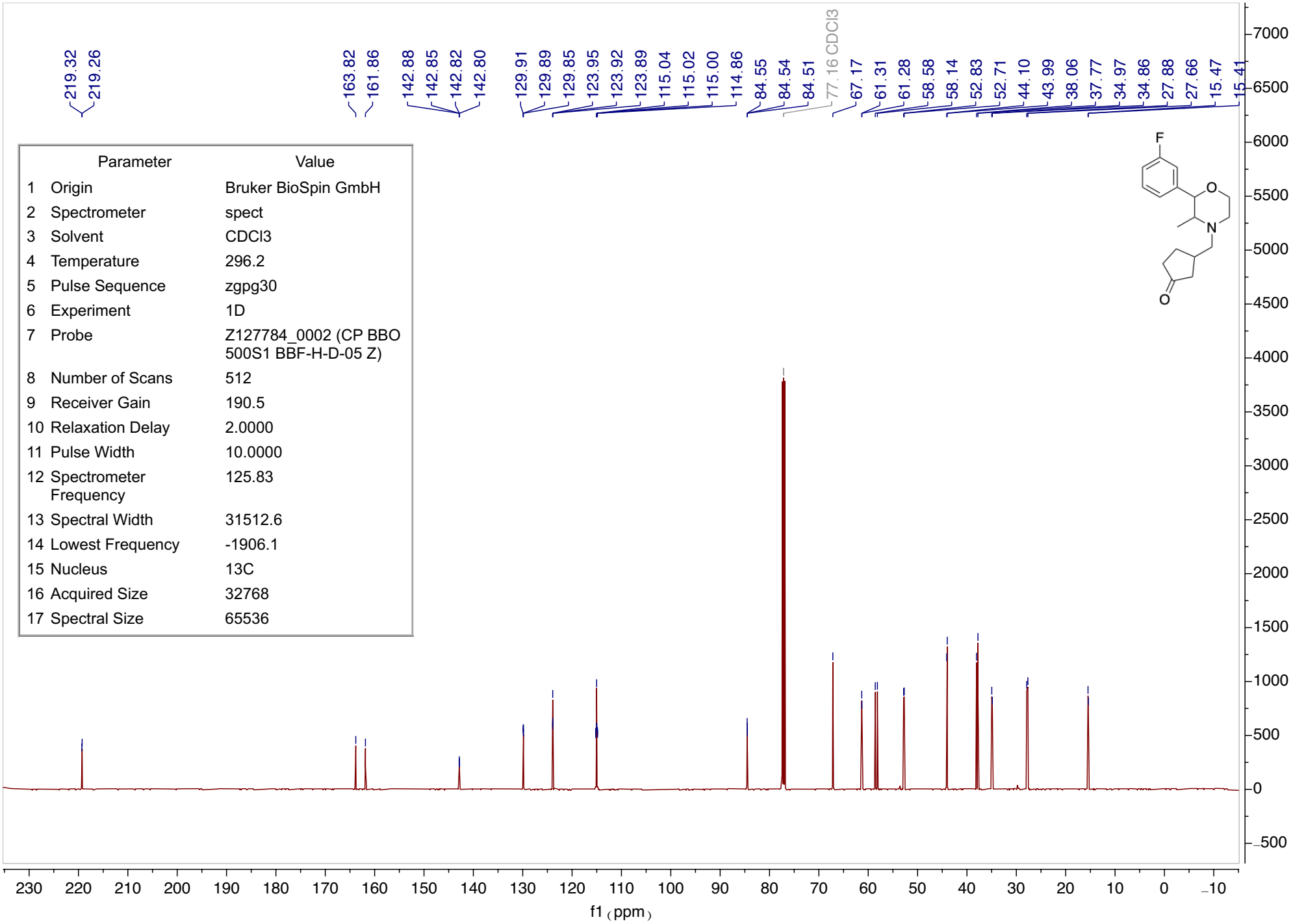


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1900.3
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536



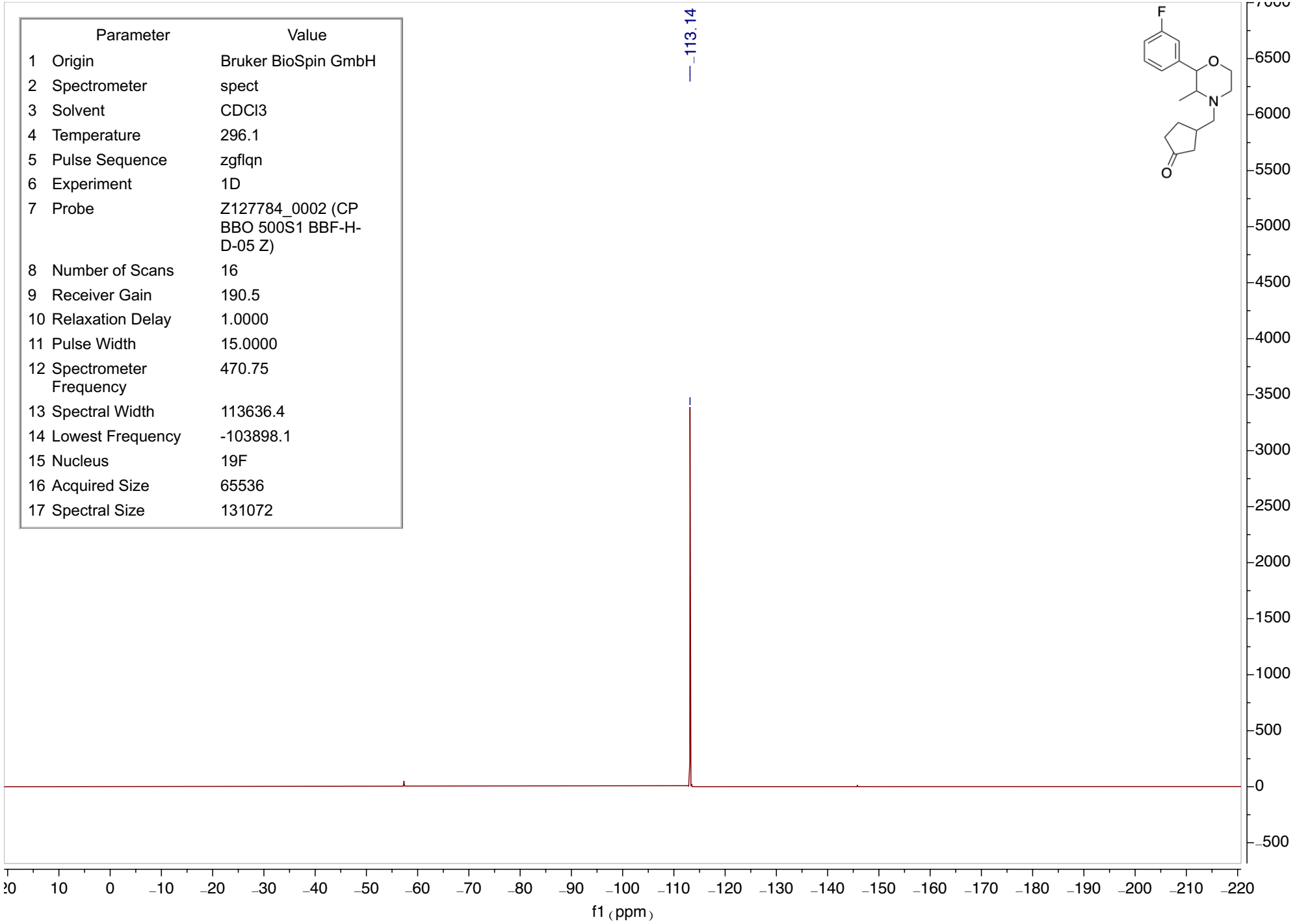
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1922.4
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

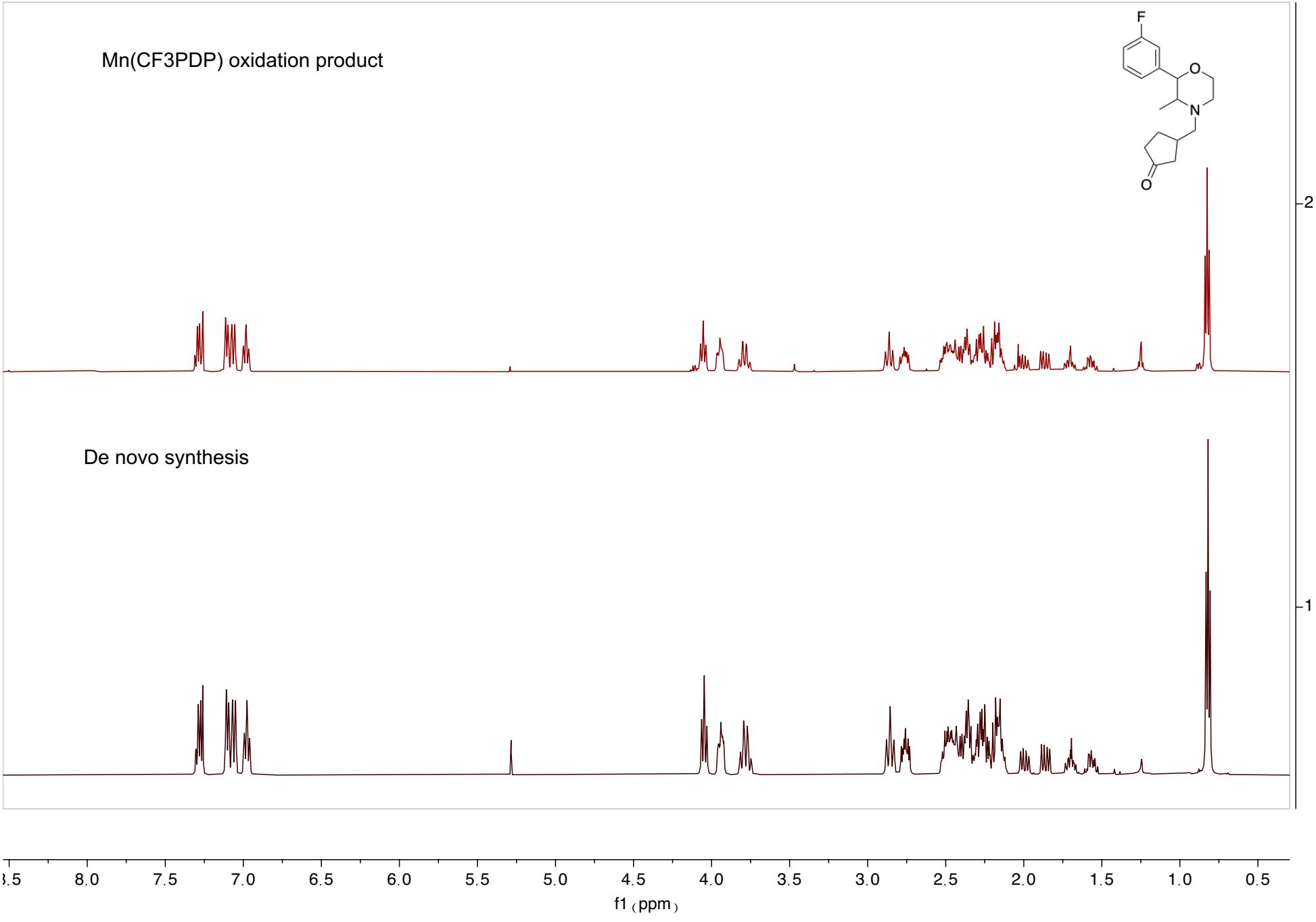


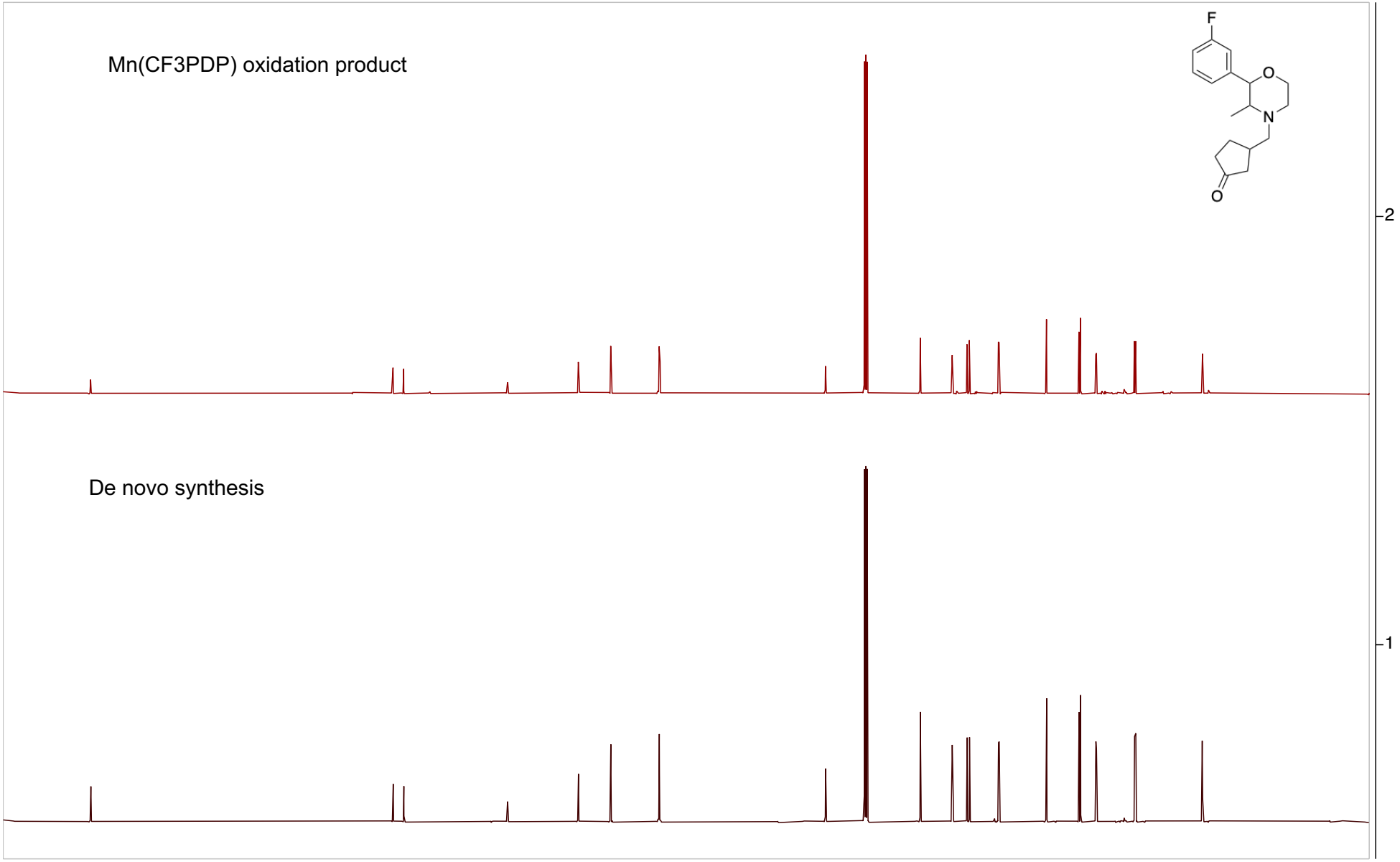


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1906.1
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

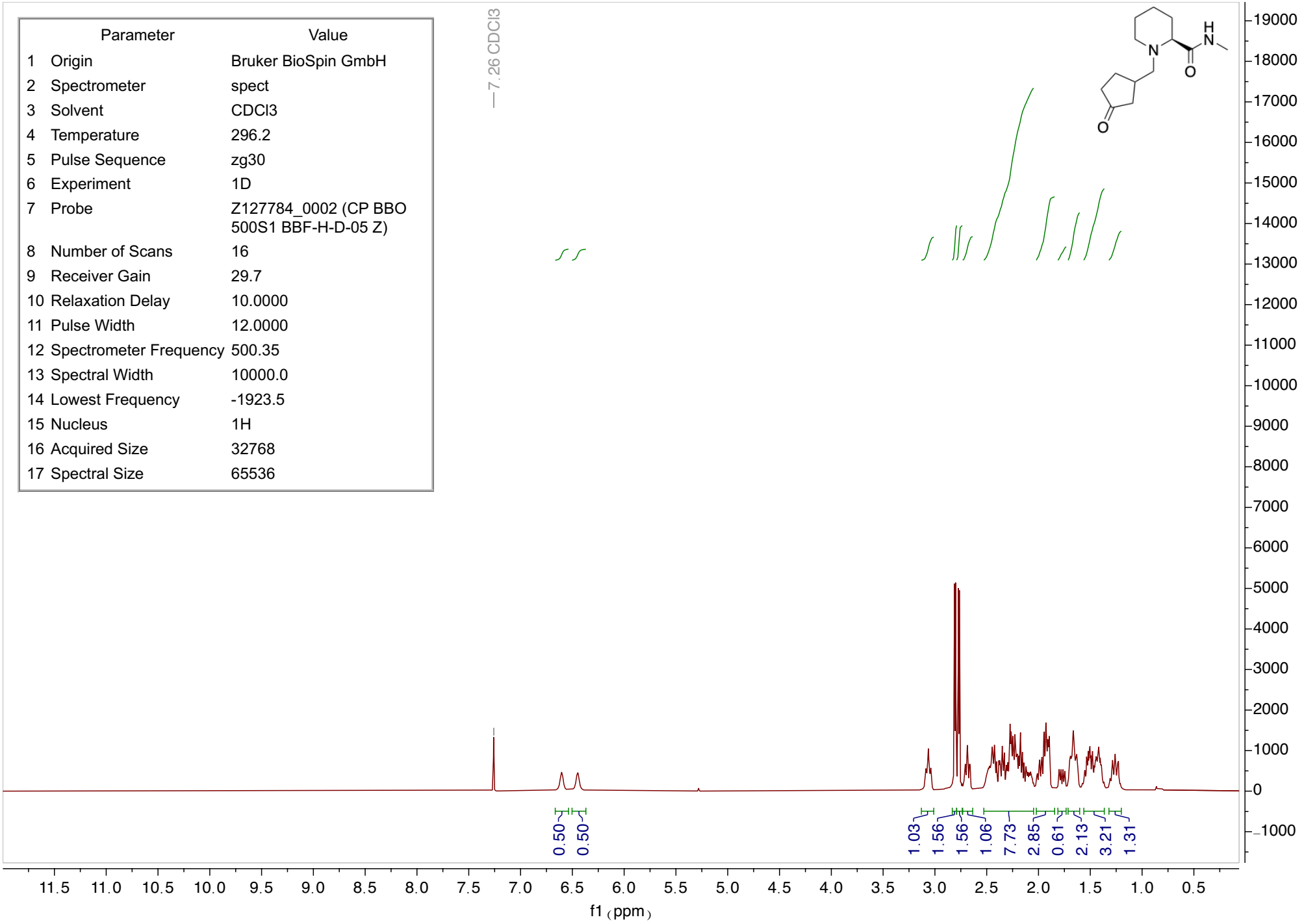
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072

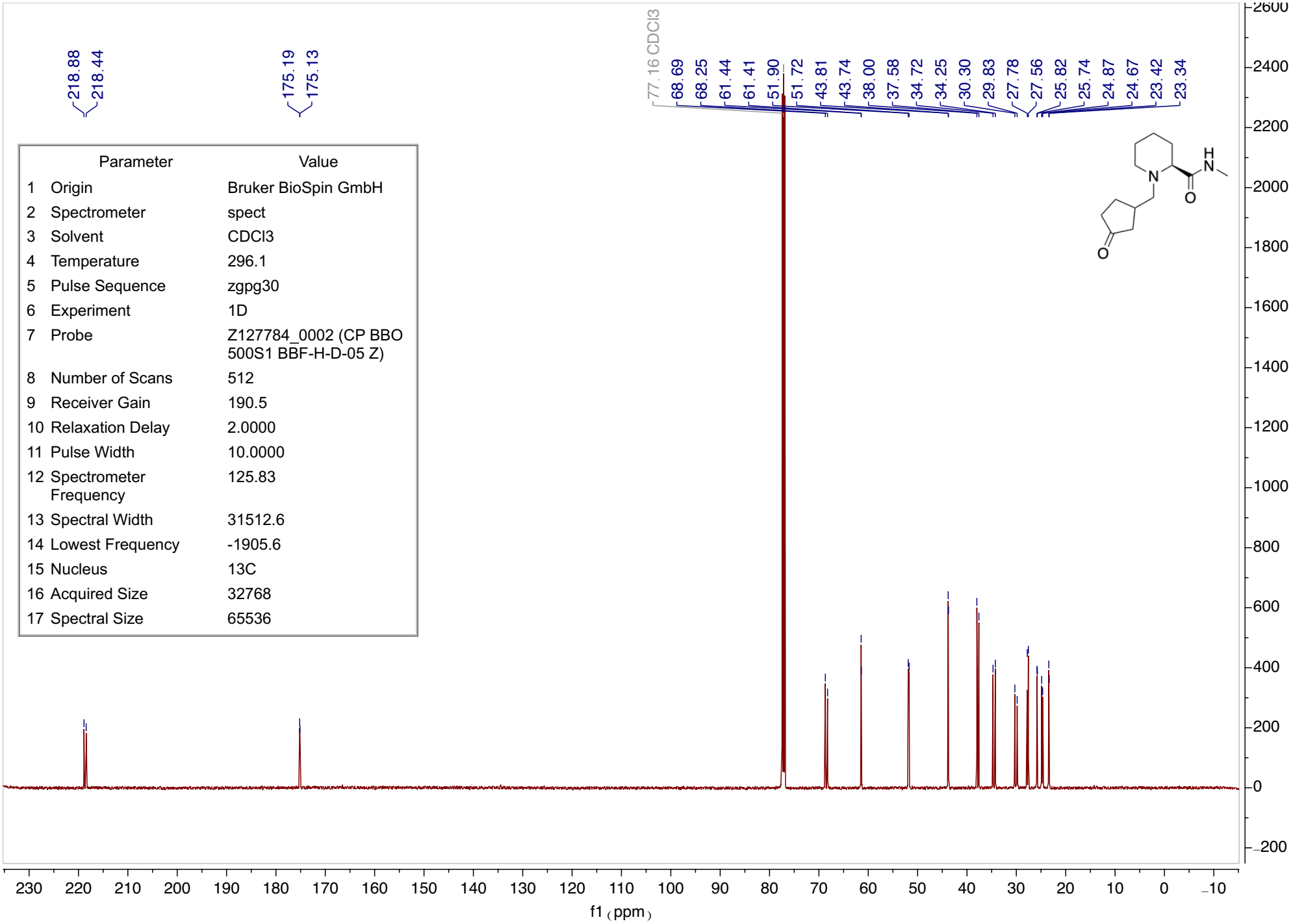



Mn(CF3PDP) oxidation product
F
O
N
O
2
De novo synthesis
1
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

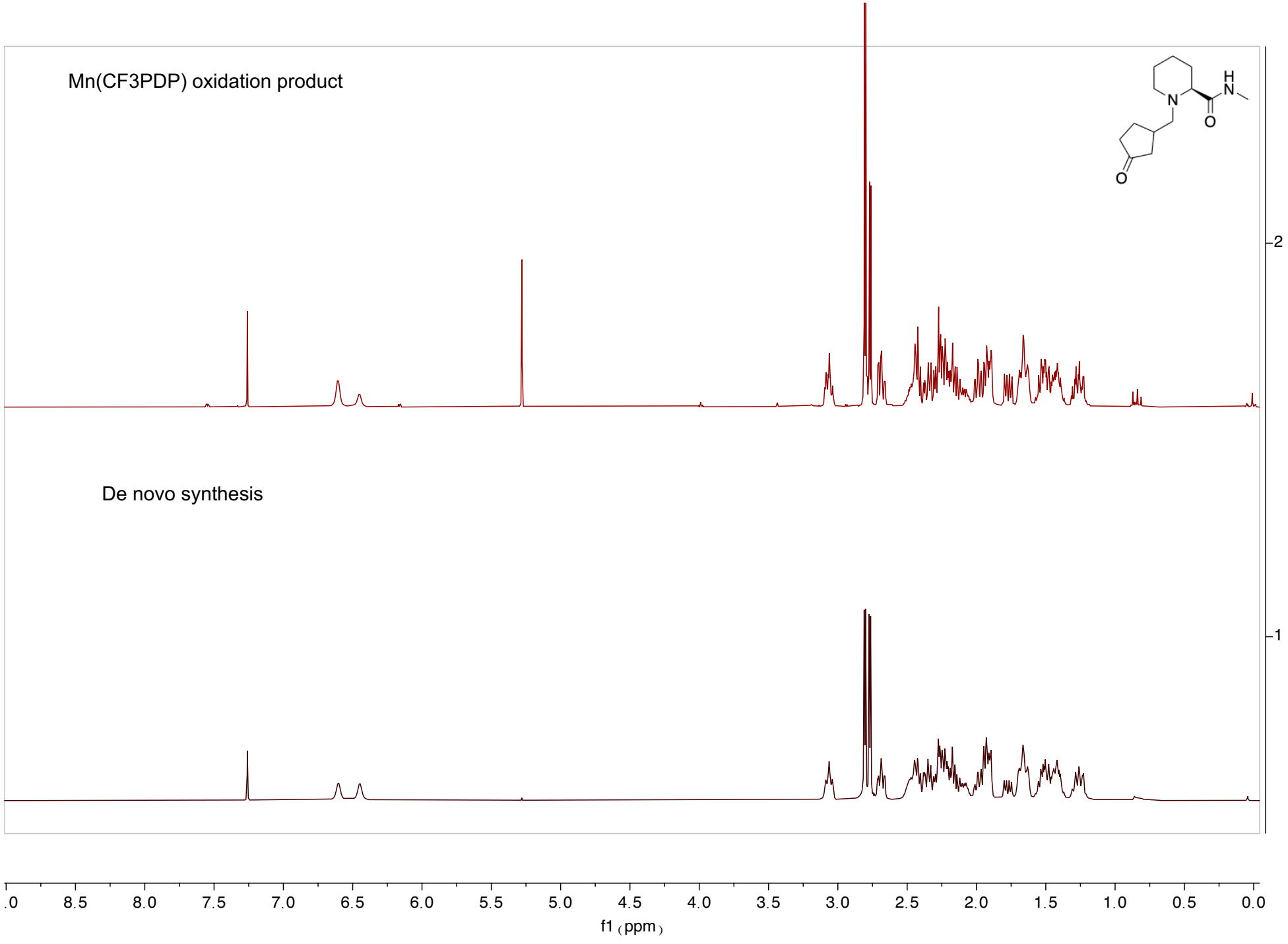

Mn(CF3PDP) oxidation product
De novo synthesis
F
O
N
O
2
1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

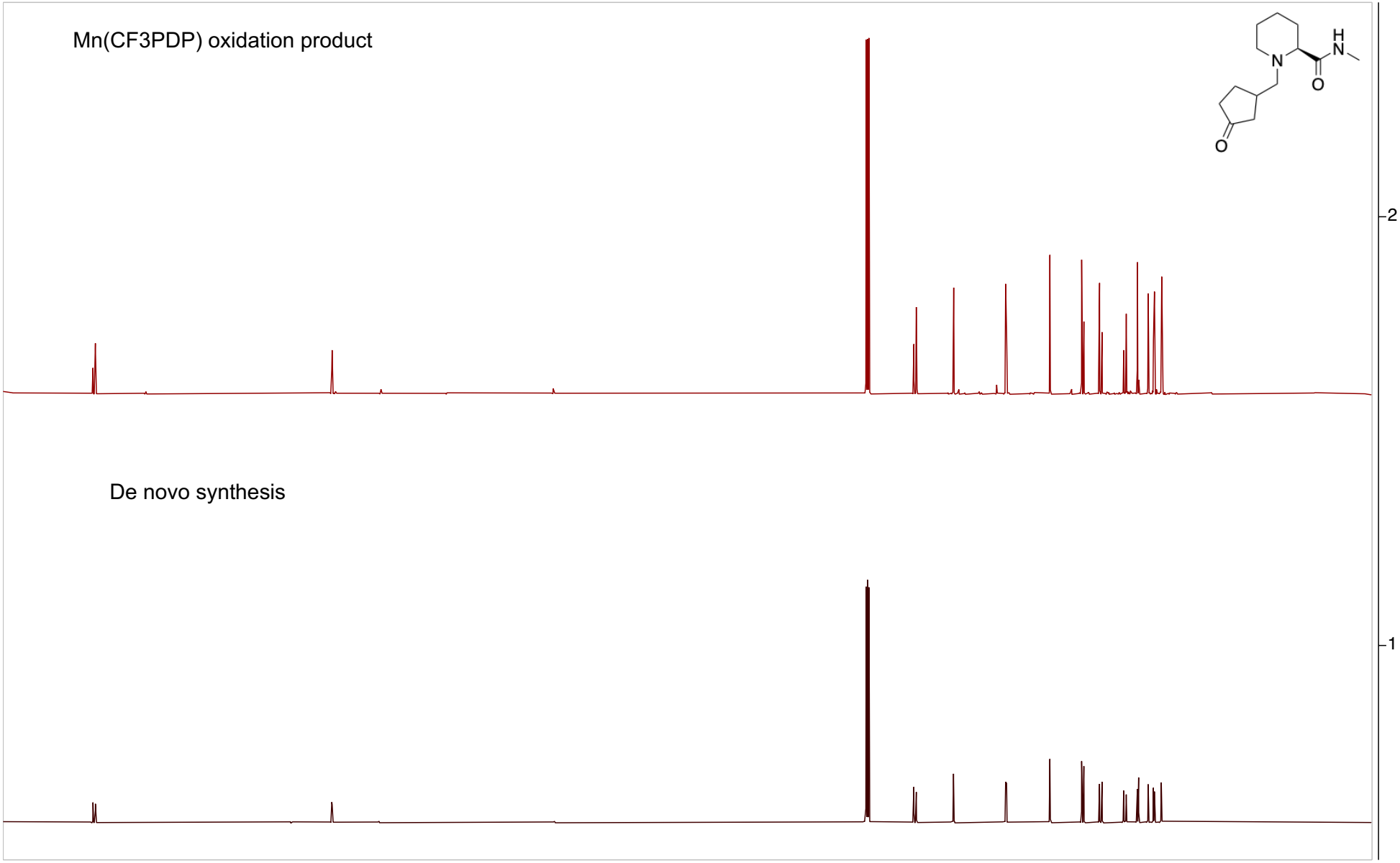
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	29.7
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.5
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536



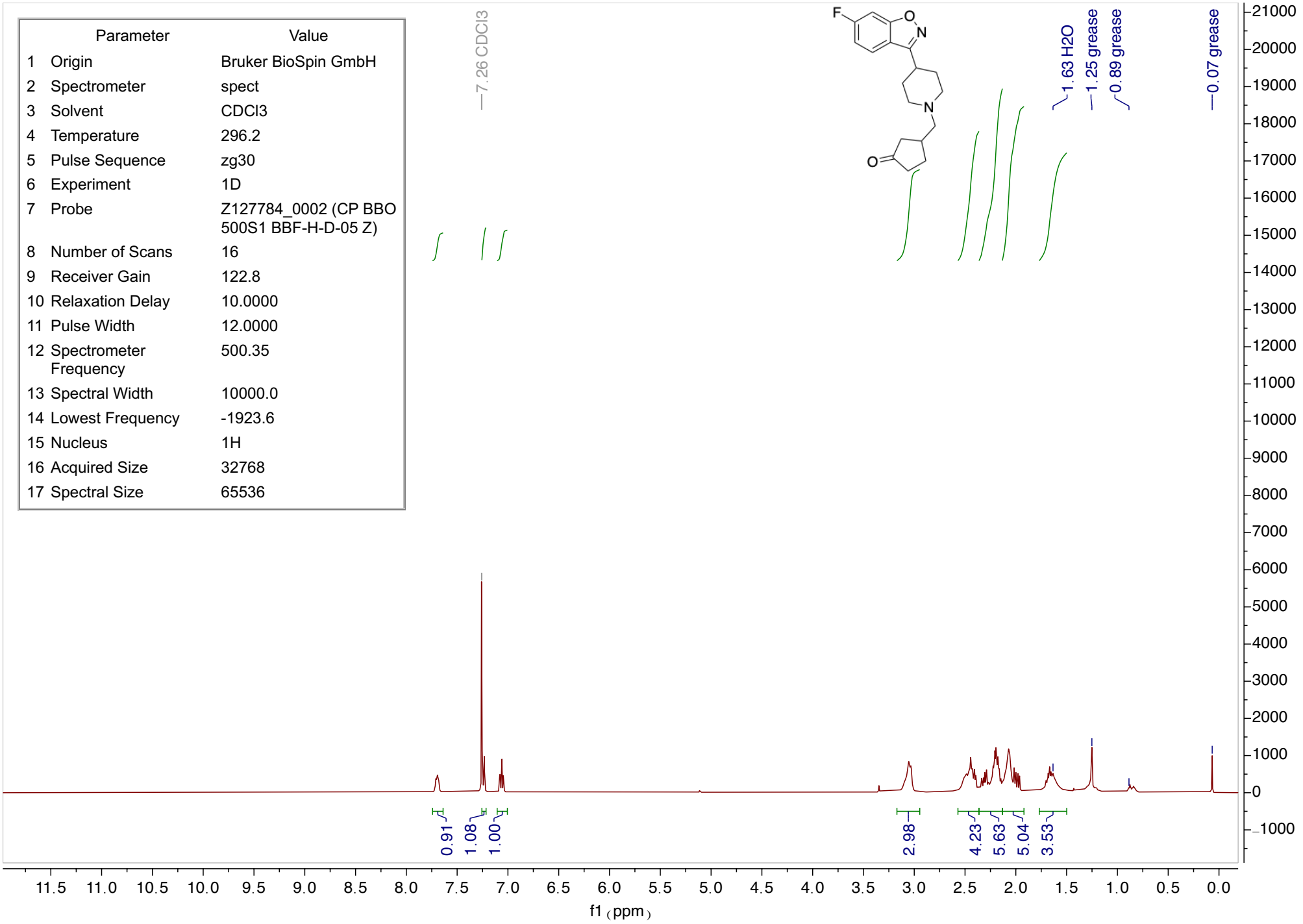


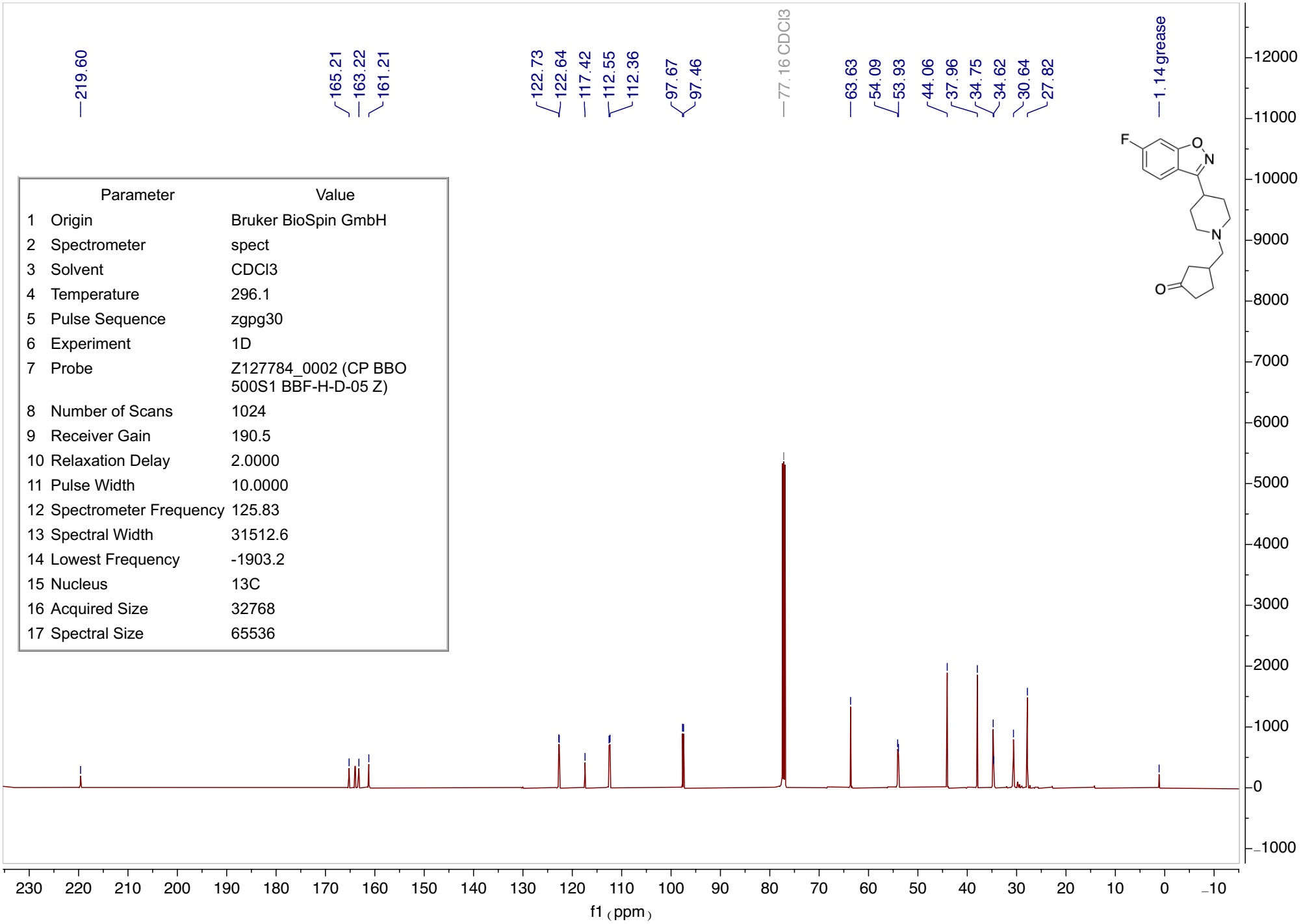
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	512
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1905.6
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536


Mn(CF3PDP) oxidation product
De novo synthesis
2
1
f1 (ppm)


Mn(CF3PDP) oxidation product
De novo synthesis
H
N
N
O
O
2
1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

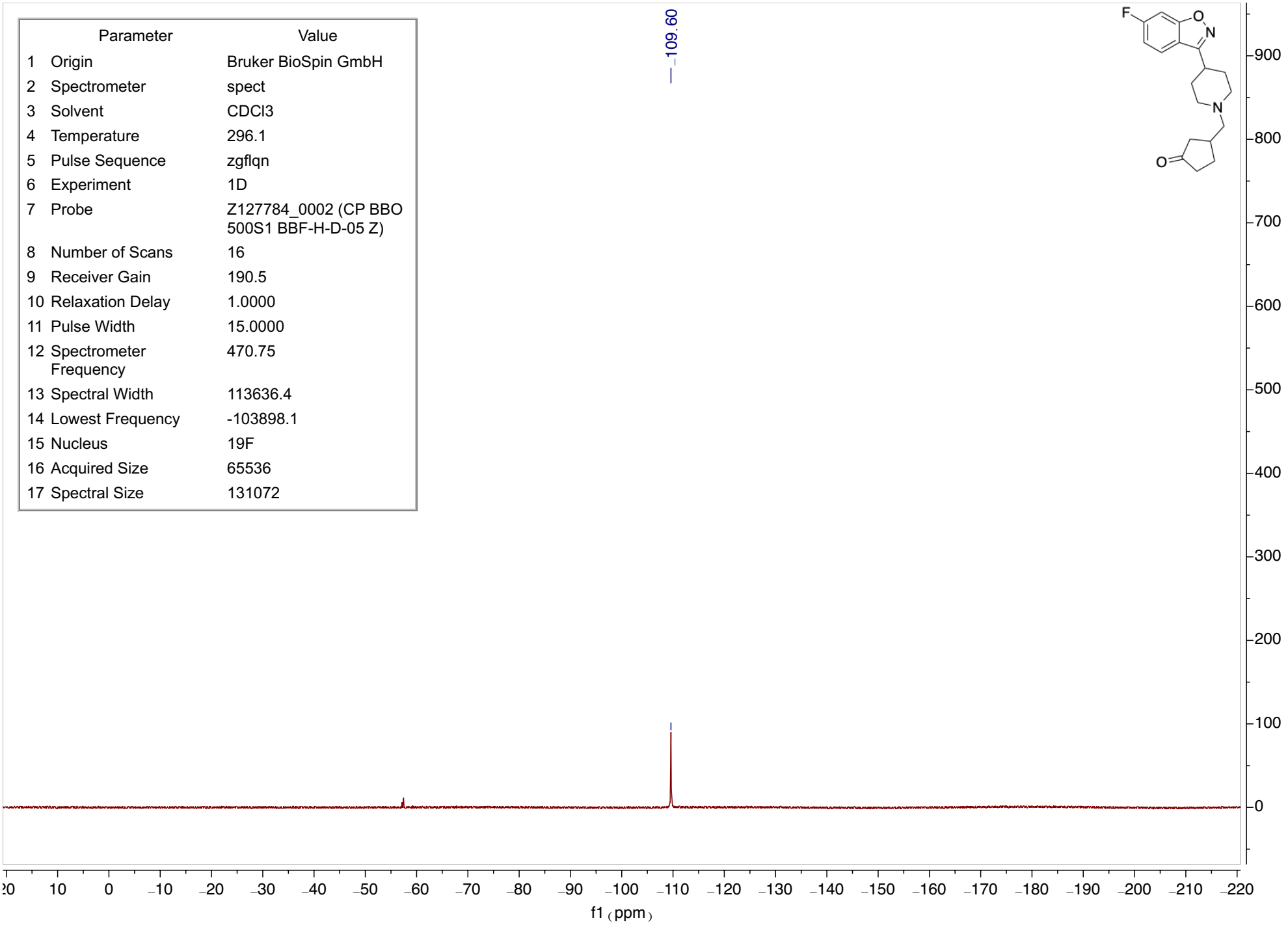
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.2
5	Pulse Sequence	zg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	122.8
10	Relaxation Delay	10.0000
11	Pulse Width	12.0000
12	Spectrometer Frequency	500.35
13	Spectral Width	10000.0
14	Lowest Frequency	-1923.6
15	Nucleus	1H
16	Acquired Size	32768
17	Spectral Size	65536

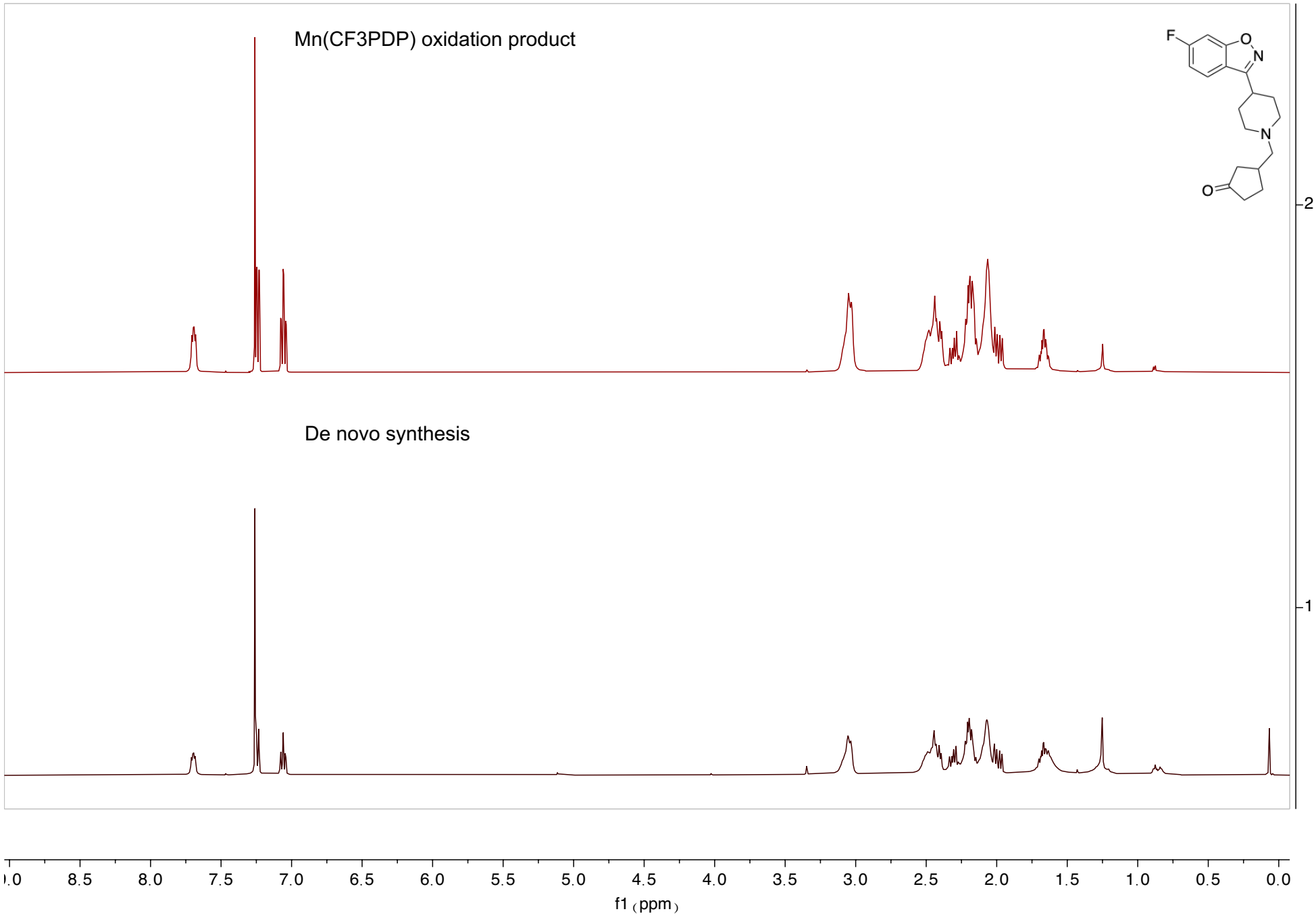


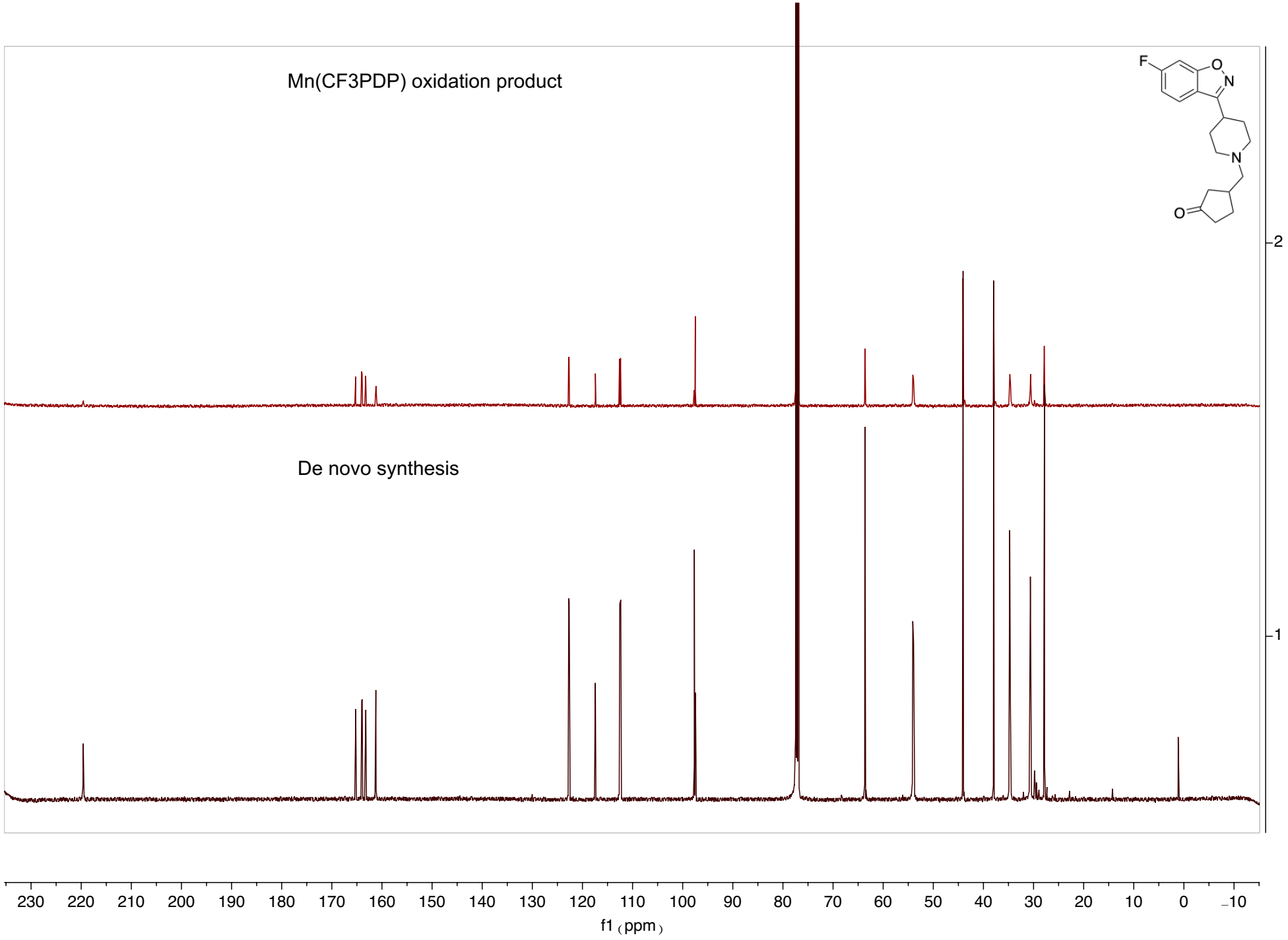


	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgpg30
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	1024
9	Receiver Gain	190.5
10	Relaxation Delay	2.0000
11	Pulse Width	10.0000
12	Spectrometer Frequency	125.83
13	Spectral Width	31512.6
14	Lowest Frequency	-1903.2
15	Nucleus	13C
16	Acquired Size	32768
17	Spectral Size	65536

	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Spectrometer	spect
3	Solvent	CDCl3
4	Temperature	296.1
5	Pulse Sequence	zgflqn
6	Experiment	1D
7	Probe	Z127784_0002 (CP BBO 500S1 BBF-H-D-05 Z)
8	Number of Scans	16
9	Receiver Gain	190.5
10	Relaxation Delay	1.0000
11	Pulse Width	15.0000
12	Spectrometer Frequency	470.75
13	Spectral Width	113636.4
14	Lowest Frequency	-103898.1
15	Nucleus	19F
16	Acquired Size	65536
17	Spectral Size	131072




Mn(CF3PDP) oxidation product
F
O
N
N
O
2
De novo synthesis
1
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)


Mn(CF3PDP) oxidation product
De novo synthesis
F
O
N
N
O
2
1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)