Total Synthesis of (–)-Securingine G

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Electronic Supplementary Information

1. General Information

All reactions were performed in oven-dried or flame-dried round-bottomed flasks. Unless otherwise noted, the flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes were used to transfer air- and moisture-sensitive liquids. Flash column chromatography was performed as described by Still et al.[1] using silica gel (60-Å pore size, 40–63 μm, 4-6% H_2O content, Merck). Analytical thin–layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light, and/or an aqueous potassium permanganate ($KMnO_4$).

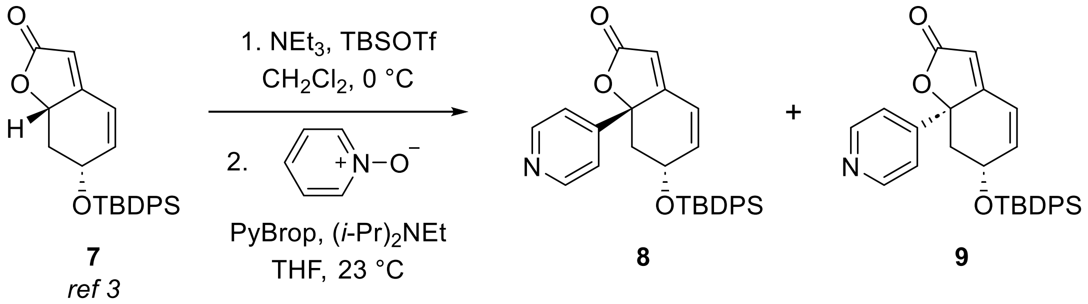
Unless otherwise stated, all commercial reagents and solvents were used without additional purification with the following exceptions as indicated below. Dichloromethane and tetrahydrofuran were purchased from Merck and Daejung Inc., respectively, and were purified by the method of Grubbs et al.[2] under positive argon pressure.

^1H and ^{13}C nuclear magnetic resonance spectra were recorded with Bruker Avance NEO (500 MHz), and calibrated by using the residual undeuterated chloroform (δ_H = 7.24 ppm) and $CDCl_3$ (δ_C = 77.23 ppm), undeuterated CD_2Cl_2 (δ_H = 5.32 ppm), and CD_2Cl_2 (δ_C = 54.00 ppm) as internal references. Data are reported in the following manners: chemical shift in ppm [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, m = multiplet, app = apparent, br = broad), coupling constant(s) in Hertz, integration]. Infrared spectra were recorded on Agilent Cary 630 FTIR spectrometer. High resolution mass spectra were obtained from KAIST Analysis Center for Research (Daejeon) by using ESI method and were obtained from Korea Basic Science Institute (Daegu) by using FAB method. Specific rotation $[\alpha]_D^T$ was obtained by JASCO P-2000 polarimeter.

All DFT calculations were conducted by Gaussian 09 package.[5] Molecular geometries were optimized using M06-2X[6] functional and 6-31G(d,p) basis set. Single point energies were calculated with M06-2X functional and 6-311+G(d,p) basis set, including solvation effect under SMD[7] solvation model with the dielectric constant of ε = 7.4257 for tetrahydrofuran. Frequency calculations were carried out at the same level of geometry optimization to confirm the stationary points as either local minima (no imaginary frequencies) or saddle points (one imaginary frequency), and to obtain thermal corrections to the Gibbs free energies at 298.15 K unless otherwise stated.

For optimized geometries by using B3LYP functional[8] and 6-31G(d,p) basis set, Gauge-invariant atomic orbital (GIAO) calculations for NMR prediction were conducted using B3LYP functional, 6-311+G(d,p) basis set and polarizable continuum model (PCM)[9] with the dielectric constant of ε = 8.93 for dichloromethane. DP4+ analyses were performed following Sarotti's[10] protocol.

2. Experimental Procedures and Physical Data for Synthesized Compounds



Compound 8 and 9

Triethylamine (0.11 mL, 0.768 mmol, 6.0 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.1 mL, 0.422 mmol, 3.3 equiv) were sequentially added to a solution of **7**[3] (50 mg, 0.128 mmol, 1.0 equiv) in dichloromethane (2.6 mL, 0.05 M) at 0 °C under argon atmosphere. After 4 h, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution (2.6 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (4 × 25 mL) and the combined organic layer was washed with brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The crude product was used for the next step without further purification.

Pyridine *N*-oxide (12.2 mg, 0.128 mmol, 1.0 equiv) and bromotripyrrolidinophosphonium hexafluorophosphate (71.6 mg, 0.154 mmol, 1.2 equiv) were dissolved in tetrahydrofuran (0.6 mL) under argon atmosphere at 23 °C and stirred for 10 min. *N*,*N*-Diisopropylethylamine (0.03 mL, 0.192 mmol, 1.5 equiv) was added at 23 °C and the resulting mixture was further stirred for 10 min. Solution of crude in tetrahydrofuran (1.0 mL) was added dropwise into the reaction mixture at 23 °C. After 23 h, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution (1.6 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 25 mL) and the combined organic layer was washed with brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 1) to afford **8** (23.9 mg, 40%) and **9** (8.7 mg, 15%) as an orange oil.

Compound 8

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 – 8.34 (m, 2H), 7.55 (ddt, J = 16.2, 6.7, 1.4 Hz, 4H), 7.51 – 7.40 (m, 2H), 7.35 (dt, J = 14.9, 7.4 Hz, 4H), 6.75 – 6.70 (m, 2H), 6.68 (dd, J = 10.1, 2.5 Hz, 1H), 6.27 (dt, J = 10.1, 1.7 Hz, 1H), 5.96 (s, 1H), 3.90 – 3.82 (m, 1H), 2.71 – 2.64 (m, 1H), 2.09 (dd, J = 11.9, 9.9 Hz, 1H), 1.03 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 170.9, 163.7, 150.3, 145.9, 144.0, 136.0, 135.8, 133.0, 132.9, 130.5, 130.4, 128.2, 128.1, 120.9, 120.5, 113.9, 85.6, 68.1, 44.0, 27.0, 19.2.

IR (KBr): 3073, 3050, 2961, 2935, 2898, 2860, 1760, 1641, 1596, 1559, 1473, 1462, 1428, 1384, 1260, 1193, 1167, 1111, 1033, 1011, 925, 876, 850, 824, 742, 705 cm^{-1}.

HRMS (ESI): Calculated for $C_{29}H_{29}NO_3Si$ $[M+H]^+$: 468.1989, found: 468.1985.

TLC (ethyl acetate : hexanes = 2 : 1) R*f*: 0.32 (UV, $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{25}}$: –71.2 (c 0.1, MeOH)

Compound 9

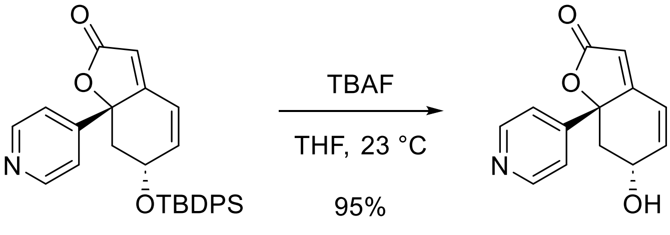
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.65 – 8.60 (m, 2H), 7.49 – 7.39 (m, 6H), 7.39 – 7.33 (m, 6H), 6.72 (d, *J* = 9.9 Hz, 1H), 5.93 (s, 1H), 5.89 (dd, *J* = 9.9, 4.6 Hz, 1H), 4.55 – 4.49 (m, 1H), 2.88 (d, *J* = 13.7 Hz, 1H), 2.19 (dd, *J* = 13.7, 5.5 Hz, 1H), 0.75 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 171.1, 163.4, 149.6, 139.3, 135.9, 135.8, 133.3, 132.7, 130.4, 130.3, 128.1, 128.0, 122.7, 121.2, 114.7, 84.7, 65.6, 42.1, 26.7, 18.9.

HRMS (ESI): Calculated for $C_{29}H_{29}NO_3Si$ $[M+H]^+$: 468.1989, found: 468.1971.

TLC (ethyl acetate : hexanes = 2 : 1) R*f*: 0.52 (UV, $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{25}}$: 115.5 (c 0.1, MeOH)



8 **10**

Compound 10

Tetrabutylammonium fluoride (1.0 M THF solution, 0.06 mL, 0.06 mmol, 1.17 equiv) was added dropwise to a solution of **8** (23.9 mg, 0.0511 mmol, 1.0 equiv) in tetrahydrofuran (1.02 mL, 0.05 M) at 23 °C under argon atmosphere. After 1 h, the reaction mixture was diluted with distilled water (1.02 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 20 mL) and the combined organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 8 cm, eluent: dichloromethane : methanol = 12 : 1) to afford **10** (11.1 mg, 95%) as a white solid.

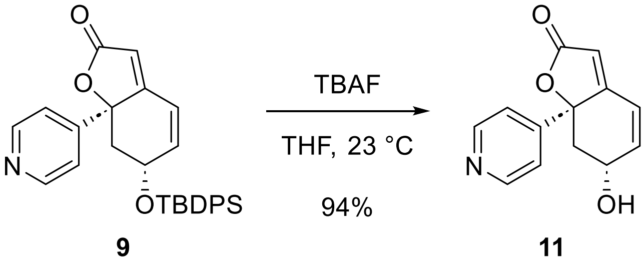
^{1}H NMR (500 MHz, CD_2Cl_2): δ 8.66 – 8.52 (m, 2H), 7.29 – 7.24 (m, 2H), 6.84 (dd, *J* = 10.0, 2.5 Hz, 1H), 6.27 (dt, *J* = 10.1, 1.8 Hz, 1H), 6.02 (s, 1H), 4.01 (dd, *J* = 10.7, 5.4 Hz, 1H), 3.14 (ddt, *J* = 11.8, 5.4, 1.1 Hz, 1H), 2.07 (dd, *J* = 11.8, 10.1 Hz, 1H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ 171.1, 163.8, 151.0, 146.8, 143.5, 121.6, 121.5, 114.7, 86.3, 66.9, 44.8.

HRMS (ESI): Calculated for $C_{13}H_{11}NO_3$ $[M+H]^+$: 230.0812, found: 230.0809.

TLC (dichloromethane : methanol = 12 : 1) R*f*: 0.30 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: –16.7 (c 0.1, MeOH)



Compound 11

Tetrabutylammonium fluoride (1.0 M THF solution, 0.02 mL, 0.02 mmol, 1.08 equiv) was added dropwise to a solution of **9** (8.7 mg, 0.0186 mmol, 1.0 equiv) in tetrahydrofuran (0.37 mL, 0.05 M) at 23 °C under argon atmosphere. After 1 h, the reaction mixture was diluted with distilled water (0.37 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 15 mL) and the combined organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 8 cm, eluent: dichloromethane : methanol = 12 : 1) to afford **11** (4.0 mg, 94%) as a colorless oil.

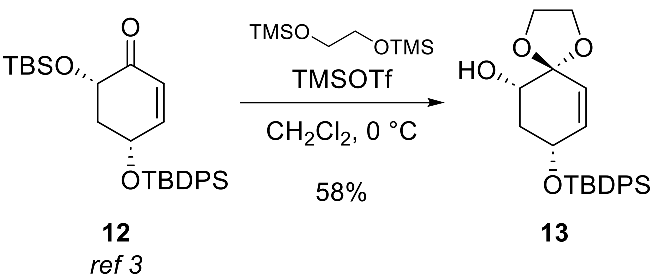
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (s, 2H), 7.37 – 7.32 (m, 2H), 6.87 (d, *J* = 9.8 Hz, 1H), 6.32 (ddd, *J* = 9.9, 4.8, 1.2 Hz, 1H), 6.02 (s, 1H), 4.60 (t, *J* = 5.1 Hz, 1H), 3.04 – 3.00 (m, 1H), 2.36 (dd, *J* = 13.9, 5.6 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 170.6, 162.6, 151.9, 147.4, 139.4, 123.5, 122.0, 115.4, 84.1, 64.3, 42.0.

HRMS (ESI): Calculated for $C_{13}H_{11}NO_3$ $[M+H]^+$: 230.0812, found: 230.0809.

TLC (dichloromethane : methanol = 12 : 1) R*f*: 0.27 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: 182.9 (c 0.1, MeOH)



Compound 13

Ethylenedioxybis(trimethylsilane) (0.38 mL, 1.535 mmol, 3.0 equiv) and trimethylsilyl trifluoromethanesulfonate (0.02 mL, 0.11 mmol, 21 mol%) were sequentially added to a solution of compound **12**[3] (246 mg, 0.512 mmol, 1.0 equiv) in dichloromethane (2.0 mL, 0.256 M) at 0 °C under argon atmosphere. After 1 h 10 min, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution (1.8 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (4 × 25 mL) and the combined organic layer was washed with brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 5 to 1 : 2) to afford **13** (121.9 mg, 58%) as a colorless oil.

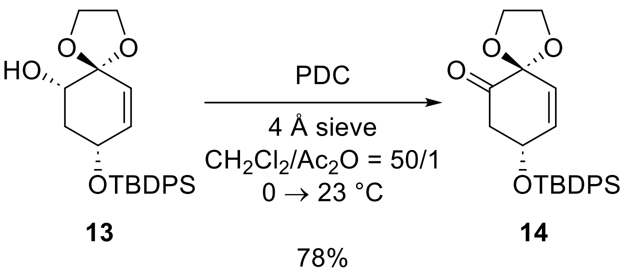
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 – 7.63 (m, 4H), 7.44 – 7.33 (m, 6H), 5.77 (ddd, *J* = 10.1, 2.6, 1.2 Hz, 1H), 5.51 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.29 – 4.24 (m, 1H), 4.07 – 3.95 (m, 4H), 3.59 (dd, *J* = 11.4, 3.3 Hz, 1H), 2.13 (dddd, *J* = 12.5, 4.9, 3.3, 1.2 Hz, 1H), 1.94 (ddd, *J* = 12.5, 11.0, 8.1 Hz, 1H), 1.03 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 136.0, 135.5, 133.8, 133.6, 130.1, 130.1, 127.9, 127.9, 126.8, 105.8, 69.8, 67.4, 66.1, 65.8, 38.7, 27.1, 19.3.

HRMS (ESI): Calculated for $C_{24}H_{30}O_4Si$ $[M+Na]^+$: 433.1806, found: 433.1814.

TLC (ethyl acetate : hexanes = 1 : 2) R*f*: 0.25 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: –3.5 (c 0.1, MeOH)



Compound 14

Acetic anhydride (0.13 mL) was added to a solution of **13** (208 mg, 0.506 mmol, 1.0 equiv), 4 Å molecular sieves (1.6 g) in dichloromethane (6.5 mL, 0.078 M) at 0 °C under argon atmosphere. After 10 min, the rubber septum was removed and pyridinium dichromate (467 mg, 1.24 mmol, 2.45 equiv) was added to a reaction mixture. The round-bottomed flask was fitted with rubber septum again and argon gas was charged by balloon. The reaction mixture was stirred at 23 °C for 7 h. Ethyl acetate was added to a reaction mixture and the insoluble salt was removed by passage through a Celite filter. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 5) to afford **14** (161.9 mg, 78%) as a white solid.

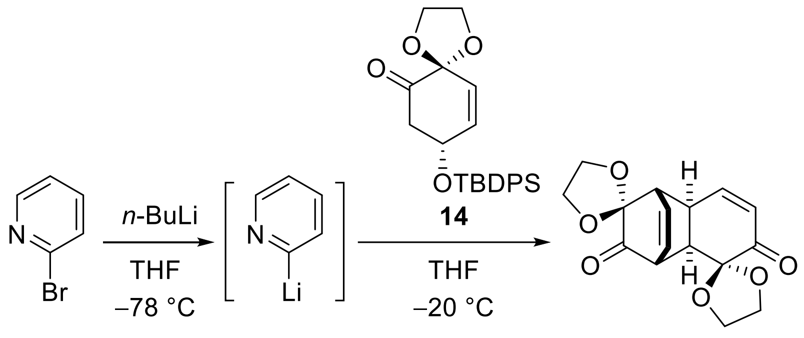
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (ddd, *J* = 7.6, 5.9, 1.5 Hz, 4H), 7.45 – 7.34 (m, 6H), 6.10 – 6.06 (m, 1H), 5.66 (dd, *J* = 10.2, 1.3 Hz, 1H), 4.52 (dddd, *J* = 7.0, 5.4, 2.8, 1.3 Hz, 1H), 4.15 – 3.99 (m, 4H), 2.91 (dd, *J* = 13.3, 7.3 Hz, 1H), 2.77 (ddd, *J* = 13.3, 5.4, 1.0 Hz, 1H), 1.04 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 201.9, 139.8, 136.0, 135.9, 133.4, 133.3, 130.3, 130.2, 128.1, 128.0, 127.2, 100.1, 68.8, 66.7, 65.8, 47.5, 27.0, 19.3.

HRMS (ESI): Calculated for $C_{24}H_{28}O_4Si$ $[M+Na]^+$: 431.1649, found: 431.1632.

TLC (ethyl acetate : hexanes = 1 : 2) R*f*: 0.73 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: –6.9 (c 0.1, MeOH)



(±)–**18**
82%

Compound (±)-18

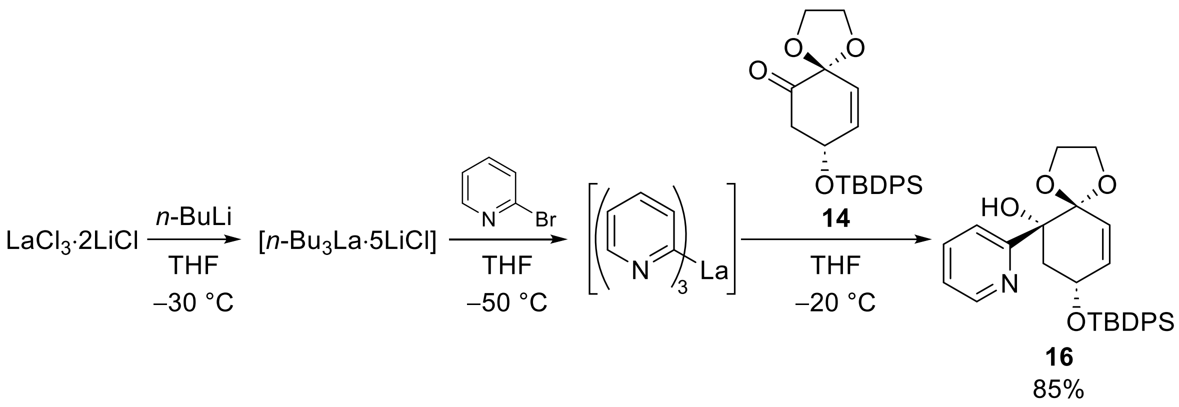
n-Butyllithium (1.6 M hexane solution, 0.1 mL, 0.16 mmol, 0.90 equiv) and 2-bromopyridine (16 μL, 0.168 mmol, 0.94 equiv) were dissolved in tetrahydrofuran (1.6 mL) under argon atmosphere at –78 °C and stirred for 1 h 20 min. Solution of **14** (73 mg, 0.179 mmol, 1.0 equiv) in tetrahydrofuran (2.0 mL) was added dropwise for 20 min into the reaction mixture at –78 °C and the reaction temperature was increased to –20 °C. After 2 h, the reaction mixture was quenched with saturated aqueous ammonium chloride solution (3.6 mL) at –20 °C and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 25 mL) and the combined organic layer was washed with saturated aqueous sodium bicarbonate solution (1 × 50 mL) and brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 3) to afford (±)-**18** (22.3 mg, 82%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.47 (dd, *J* = 10.2, 4.1 Hz, 1H), 6.41 (dddd, *J* = 8.0, 6.6, 1.4, 0.6 Hz, 1H), 6.12 (dd, *J* = 10.2, 1.7 Hz, 1H), 5.98 – 5.94 (m, 1H), 4.28 (td, *J* = 7.1, 6.1 Hz, 1H), 4.24 – 4.08 (m, 4H), 4.01 (ddt, *J* = 14.3, 7.8, 6.4 Hz, 2H), 3.85 (ddd, *J* = 7.7, 7.0, 5.6 Hz, 1H), 3.42 (dddd, *J* = 8.4, 4.1, 2.0, 0.6 Hz, 1H), 3.22 (ddd, *J* = 6.3, 2.5, 1.4 Hz, 1H), 3.18 (dt, *J* = 6.5, 1.9 Hz, 1H), 3.09 (dd, *J* = 8.5, 2.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 205.6, 192.3, 146.7, 134.1, 130.3, 128.1, 104.3, 101.3, 67.1, 66.5, 66.3, 65.0, 52.6, 43.6, 42.6, 38.6.

HRMS (ESI): Calculated for $C_{16}H_{16}O_6$ $[M+H]^+$: 305.1020, found: 305.1004.

TLC (ethyl acetate : hexanes = 1 : 2) R*f*: 0.17 (UV, $KMnO_4$).



Compound 16

Lanthanum(III) chloride bis(lithium chloride) complex (0.6 M THF solution, 0.19 mL, 0.114 mmol, 0.435 equiv) and n-Butyllithium (1.54 M hexane solution, 0.21 mL, 0.323 mmol, 1.235 equiv) were dissolved in tetrahydrofuran (0.59 mL) under argon atmosphere at –30 °C and stirred for 15 min. The reaction temperature was decreased to –50 °C. 2-Bromopyridine (25 μL, 0.262 mmol, 1.0 equiv) was added to the reaction mixture at –50 °C and stirred for 25 min. Solution of **14** (79.2 mg, 0.194 mmol, 0.74 equiv) in tetrahydrofuran (1.44 mL) was added dropwise for 15 min into the reaction mixture at –50 °C and the reaction temperature was increased to –20 °C. After 18 h, the reaction mixture was quenched with saturated aqueous ammonium chloride solution (2.25 mL) at –20 °C and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 25 mL) and the combined organic layer was washed with saturated aqueous sodium bicarbonate solution (1 × 50 mL) and brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 4) to afford **16** (80.4 mg, 85%) as a white foam.

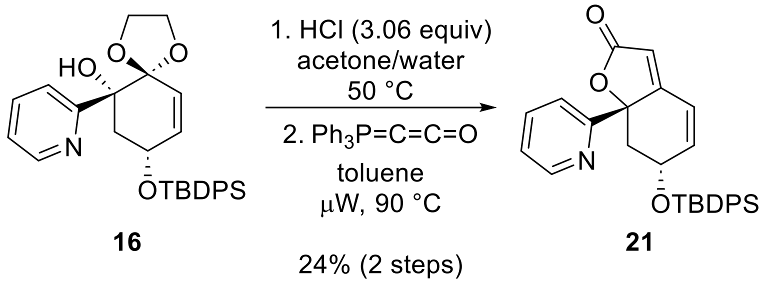
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 – 8.48 (m, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.62 (ddt, J = 15.6, 6.8, 1.4 Hz, 5H), 7.43 – 7.29 (m, 6H), 7.15 (t, J = 6.2 Hz, 1H), 5.77 (ddd, J = 10.1, 3.8, 1.0 Hz, 1H), 5.66 (dd, J = 10.1, 1.1 Hz, 1H), 5.13 (s, 1H), 4.36 – 4.30 (m, 1H), 3.94 – 3.86 (m, 1H), 3.79 – 3.70 (m, 2H), 3.03 – 2.95 (m, 1H), 2.71 (dd, J = 14.1, 4.7 Hz, 1H), 2.36 (ddd, J = 14.1, 4.6, 1.1 Hz, 1H), 1.02 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.9, 147.7, 136.1, 136.0, 133.6, 133.1, 132.4, 130.1, 130.1, 129.5, 127.9, 127.9, 122.8, 122.4, 106.8, 66.9, 66.0, 65.8, 40.5, 27.1, 19.2.

HRMS (ESI): Calculated for $C_{29}H_{33}NO_4Si$ $[M+Na]^+$: 510.2071, found: 510.2048.

TLC (ethyl acetate : hexanes = 1 : 2) R*f*: 0.15 (UV, $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{25}}$: 3.3 (c 0.1, MeOH)



Compound 21

Hydrochloric acid (3.0 M aqueous solution, 0.11 mL, 0.33 mmol, 3.06 equiv) was added to a solution of **16** (52.6 mg, 0.108 mmol, 1.0 equiv) in acetone (2.16 mL, 0.05 M) at 23 °C under argon atmosphere. The rubber septum was sealed tightly with Teflon tape and the reaction was increased to 50 °C. After 23h, the reaction flask was moved to ice bath (0 °C) and the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution (2.27 mL). The aqueous layer was extracted with ethyl acetate (5 × 20 mL) and the combined organic layer was washed with brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The crude product was used for the next step without further purification.

In a glovebox, (Triphenylphosphoranylidene)ketene (163 mg, 0.539 mmol, 5.0 equiv) was added to a solution of crude in toluene (10.8 mL, 0.01 M) at 23 °C. The microwave tube was sealed under an argon atmosphere and then heated to 90 °C for 10 h. The reaction mixture was cooled to 23 °C and quenched with saturated aqueous sodium bicarbonate solution (5.4 mL). The aqueous layer was extracted with ethyl acetate (5 × 30 mL) and the combined organic layer was washed with brine (1 × 75 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 10 cm, eluent: ethyl acetate : hexane = 1 : 1) to afford **21** (12.1 mg, 24%) as a brownish oil.

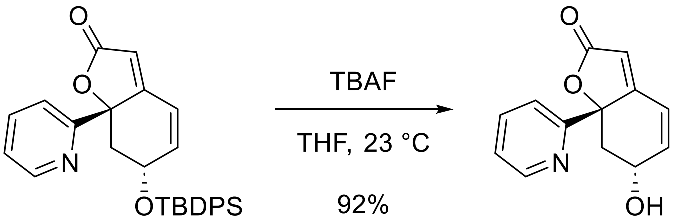
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.61 (td, *J* = 7.9, 1.4 Hz, 4H), 7.50 – 7.32 (m, 7H), 7.10 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H), 6.92 (dt, *J* = 8.0, 1.1 Hz, 1H), 6.56 (dd, *J* = 10.1, 2.4 Hz, 1H), 6.13 (dt, *J* = 10.1, 1.7 Hz, 1H), 5.92 (s, 1H), 4.36 (ddt, *J* = 9.9, 5.2, 2.4 Hz, 1H), 3.16 (ddd, *J* = 11.9, 5.6, 1.5 Hz, 1H), 2.12 (dd, *J* = 11.6, 9.5 Hz, 1H), 1.05 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.2, 165.3, 156.4, 149.0, 143.2, 137.1, 136.0, 136.0, 133.5, 133.4, 130.2, 130.1, 128.0, 128.0, 123.7, 120.9, 120.4, 112.6, 87.9, 68.3, 43.4, 27.1, 19.3.

HRMS (ESI): Calculated for $C_{29}H_{29}NO_3Si$ $[M+H]^+$: 468.1989, found: 468.1985.

TLC (ethyl acetate : hexanes = 1 : 1) R*f*: 0.60 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: –64.1 (c 0.1, MeOH)



21 securingine G (**4**)

Securingine G (4):

Tetrabutylammonium fluoride (1.0 M THF solution, 0.02 mL, 0.02 mmol, 1.316 equiv) was added dropwise to a solution of **21** (7.1 mg, 0.0152 mmol, 1.0 equiv) in tetrahydrofuran (0.3 mL, 0.05 M) at 23 °C under argon atmosphere. After 1 h, the reaction mixture was diluted with distilled water (0.3 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 15 mL) and the combined organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 8 cm, eluent: ethyl acetate : hexanes = 4 : 1) to afford securingine G (**4**) (3.2 mg, 92%) as a colorless gum.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 7.67 (td, *J* = 7.8, 1.8 Hz, 1H), 7.30 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.27 – 7.24 (m, 1H), 6.66 (dd, *J* = 10.1, 2.4 Hz, 1H), 6.21 (ddd, *J* = 10.0, 2.4, 1.3 Hz, 1H), 5.98 (s, 1H), 4.55 (ddt, *J* = 10.1, 5.3, 2.4 Hz, 1H), 3.54 (ddt, *J* = 11.6, 5.6, 1.0 Hz, 1H), 2.00 (dd, *J* = 11.6, 9.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.2, 165.1, 156.7, 149.2, 142.5, 137.5, 124.1, 121.1, 121.0, 113.0, 88.0, 66.9, 43.3.

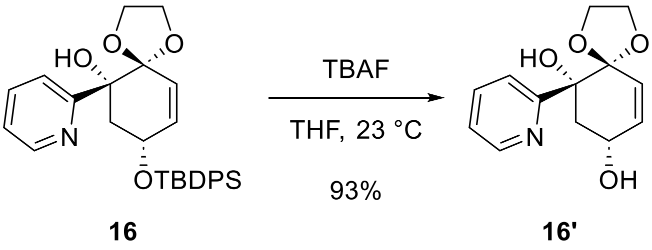
IR (KBr): 3412, 2927, 2853, 1753, 1641, 1589, 1473, 1436, 1272, 1216, 1137, 1070, 1029, 992, 925, 899, 873, 854, 805, 753, 701, 653 cm^{-1}.

HRMS (ESI): Calculated for $C_{13}H_{11}NO_3$ $[M+Na]^+$: 230.0812, found: 230.0804.

TLC (ethyl acetate : hexanes = 3 : 1) R*f*: 0.25 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: –32.1 (c 0.1, MeOH)

Reported by the Lee group: $[\alpha]_D^{25}$: –25.9 (c 0.1, MeOH)



Compound 16′

Tetrabutylammonium fluoride (1.0 M THF solution, 0.16 mL, 0.16 mmol, 1.06 equiv) was added dropwise to a solution of **16** (73.9 mg, 0.1515 mmol, 1.0 equiv) in tetrahydrofuran (1.52 mL, 0.1 M) at 23 °C under argon atmosphere. After 1 h, the reaction mixture was diluted with distilled water (1.52 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (9 × 20 mL) and the combined organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 6 cm, eluent: ethyl acetate : hexanes = 10 : 1) to afford **16′** (35.1 mg, 93%) as a white solid.

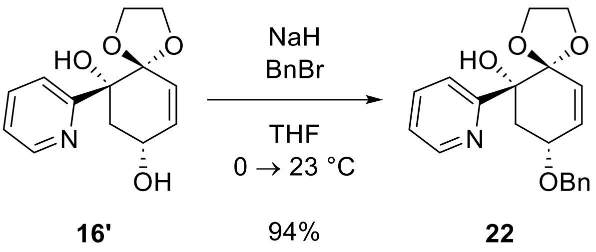
^{1}H NMR (500 MHz, $CDCl_3$): 8.57 (dt, *J* = 4.8, 1.4 Hz, 1H), 7.71 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.27 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1H), 6.28 (s, 1H), 6.20 (ddd, *J* = 10.1, 4.8, 1.7 Hz, 1H), 5.69 (dd, *J* = 10.1, 0.8 Hz, 1H), 4.32 – 4.24 (m, 1H), 3.84 – 3.75 (m, 2H), 3.72 (d, *J* = 11.3 Hz, 1H), 3.15 – 3.04 (m, 2H), 2.77 (dd, *J* = 14.2, 4.7 Hz, 1H), 2.10 (dt, *J* = 14.2, 1.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 159.0, 147.2, 136.7, 132.8, 128.3, 123.0, 122.6, 106.6, 76.0, 65.7, 65.6, 64.3, 39.0.

HRMS (ESI): Calculated for $C_{13}H_{15}NO_4$ $[M+Na]^+$: 272.0893, found: 272.0898.

TLC (ethyl acetate : hexanes = 8 : 1) R*f*: 0.29 (UV, $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$: 33.1 (c 0.1, MeOH)



Compound 22

Sodium hydride (60% dispersion in mineral oil, 43.4 mg, 1.085 mmol, 4.8 equiv) and benzyl bromide (34 μL, 0.286 mmol, 1.266 equiv) were sequentially added to a solution of **16′** (56.3 mg, 0.226 mmol, 1.0 equiv) in tetrahydrofuran (4.51 mL, 0.05 M) at 0 °C and stirred for 20 min. The reaction temperature was increased to 23 °C. After 2 h, the reaction mixture was quenched with saturated aqueous ammonium chloride solution (4.51 mL) at 23 °C and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 25 mL) and the combined organic layer was washed with saturated aqueous sodium bicarbonate solution (1 × 50 mL) and brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 6 cm, eluent: ethyl acetate : hexane = 10 : 1) to afford **22** (72.1 mg, 94%) as a white solid.

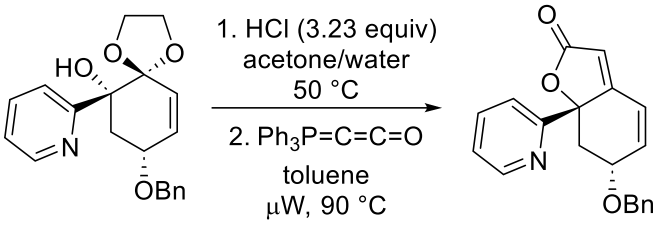
^{1}H NMR (500 MHz, $CDCl_3$): 8.57 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.32 – 7.24 (m, 5H), 7.20 (ddd, J = 7.2, 4.8, 1.4 Hz, 1H), 6.14 (ddd, J = 10.2, 3.7, 1.0 Hz, 1H), 5.82 (dd, J = 10.2, 1.3 Hz, 1H), 5.09 (s, 1H), 4.62 (d, J = 11.9 Hz, 1H), 4.55 (d, J = 11.9 Hz, 1H), 4.20 – 4.12 (m, 1H), 3.91 (dt, J = 7.6, 6.5 Hz, 1H), 3.79 (ddd, J = 7.5, 6.3, 5.2 Hz, 1H), 3.68 (ddd, J = 7.5, 6.2, 5.2 Hz, 1H), 3.13 (dt, J = 7.5, 6.3 Hz, 1H), 2.81 (dd, J = 14.2, 5.3 Hz, 1H), 2.38 (ddd, J = 14.2, 4.4, 1.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.6, 147.8, 138.3, 136.2, 131.0, 130.4, 128.6, 127.9, 122.7, 122.6, 106.8, 76.5, 71.3, 70.9, 66.0, 65.9, 37.5.

HRMS (ESI): Calculated for $C_{20}H_{21}NO_4$ $[M+H]^+$: 340.1543, found: 340.1538.

TLC (ethyl acetate : hexanes = 8 : 1) R*f*: 0.43 (UV, $KMnO_4$).

$[\boldsymbol{\alpha}]_D^{25}$: 4.8 (c 0.1, MeOH)



22 **23**

57% (2 steps)

Compound 23

Hydrochloric acid (3.0 M aqueous solution, 0.11 mL, 0.33 mmol, 3.23 equiv) was added to a solution of **22** (34.7 mg, 0.102 mmol, 1.0 equiv) in acetone (2.0 mL, 0.05 M) at 23 °C under argon atmosphere. The rubber septum was sealed tightly with Teflon tape and the reaction was increased to 50 °C. After 21h 30min, the reaction flask was moved to ice bath (0 °C) and the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution (2.11 mL). The aqueous layer was extracted with ethyl acetate (5 × 20 mL) and the combined organic layer was washed with brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The crude product was used for the next step without further purification.

In a glovebox, (Triphenylphosphoranylidene)ketene (154.5 mg, 0.511 mmol, 5.0 equiv) was added to a solution of crude in toluene (10.2 mL, 0.01 M) at 23 °C. The microwave tube was sealed under an argon atmosphere and then heated to 90 °C for 10 h. The reaction mixture was cooled to 23 °C and quenched with saturated aqueous sodium bicarbonate solution (5.1 mL). The aqueous layer was extracted with ethyl acetate (5 × 30 mL) and the combined organic layer was washed with brine (1 × 75 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 10 cm, eluent: ethyl acetate : hexane = 1 : 1) to afford **23** (18.5 mg, 57%) as a brownish oil.

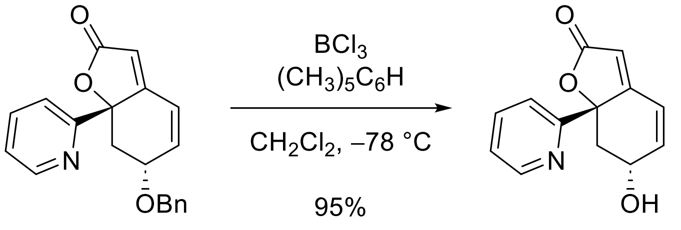
^{1}H NMR (500 MHz, CD_2Cl_2): δ 8.54 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 7.69 (td, *J* = 7.8, 1.8 Hz, 1H), 7.34 (d, *J* = 4.1 Hz, 4H), 7.32 – 7.26 (m, 2H), 7.25 (dt, *J* = 8.0, 1.1 Hz, 1H), 6.68 (dd, *J* = 10.1, 2.4 Hz, 1H), 6.25 (dt, *J* = 10.1, 1.8 Hz, 1H), 5.97 (s, 1H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.31 – 4.24 (m, 1H), 3.66 (ddt, *J* = 11.5, 5.6, 1.0 Hz, 1H), 2.04 (dd, *J* = 11.4, 9.5 Hz, 1H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ 172.3, 165.5, 156.9, 149.6, 141.0, 138.7, 137.7, 128.9, 128.4, 128.3, 124.4, 121.5, 121.3, 113.2, 88.3, 73.7, 71.6, 40.4.

HRMS (ESI): Calculated for $C_{20}H_{17}NO_3$ $[M+Na]^+$: 342.1101, found: 342.1110.

TLC (ethyl acetate : hexanes = 1 : 1) R*f*: 0.41 (UV, $KMnO_4$).

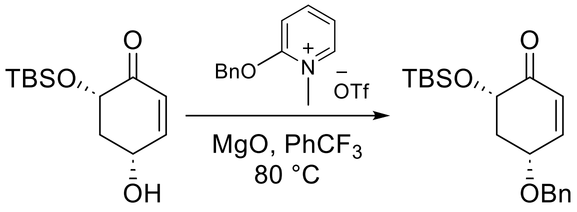
$[\boldsymbol{\alpha}]_D^{25}$: –12.5 (c 0.1, MeOH)



23 securingine G (**4**)

Securingine G (4)

Boron trichloride (1.0 M dichloromethane solution, 0.17 mL, 0.17 mmol, 3.16 equiv) was added to a solution of **23** (17.2 mg, 0.054 mmol, 1.0 equiv), pentamethylbenzene (36 mg, 0.242 mmol, 4.5 equiv) in dichloromethane (1.79 mL, 0.03 M) at –78 °C under argon atmosphere. After 1 h, the reaction was quenched with methanol (0.9 mL) at –78 °C and the reaction mixture was concentrated under reduced pressure. The crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 8 cm, eluent: ethyl acetate : hexane = 4 : 1) to afford securingine G (**4**) (11.7 mg, 95%) as a colorless gum. See above for characterization data



24
ref 3

59%
brsm 96%

25

Compound 25

A mixture of 2-benzyloxy-1-methylpyridinium triflate (450.3 mg, 1.289 mmol, 1.91 equiv), magnesium oxide (52 mg, 1.290 mmol, 1.91 equiv), and compound **24**[3] (163.4 mg, 0.674 mmol, 1.0 equiv) in α,α,α-trifluorotoluene (6.74 mL, 0.1 M) was heated at 80 °C under argon atmosphere. After 48 h, ethyl acetate was added to a reaction mixture and the insoluble salt was removed by passage through a Celite filter. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 8 to 1 : 1) to afford **25** (133.1 mg, 59%) as a colorless oil and recovered starting material **24** (60.6 mg, 37%).

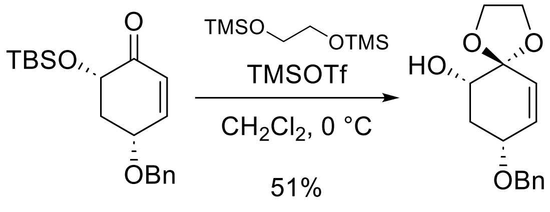
^{1}H NMR (500 MHz, CDCl$_3$): δ 7.36 (d, J = 4.0 Hz, 4H), 7.33 – 7.28 (m, 1H), 6.91 (dt, J = 10.3, 2.0 Hz, 1H), 5.99 (dd, J = 10.3, 2.4 Hz, 1H), 4.67 (d, J = 11.7 Hz, 1H), 4.62 (d, J = 11.7 Hz, 1H), 4.36 (ddt, J = 10.6, 4.8, 2.2 Hz, 1H), 4.10 (dd, J = 13.4, 5.0 Hz, 1H), 2.60 (dtd, J = 12.1, 5.0, 2.2 Hz, 1H), 2.08 (ddd, J = 13.3, 11.9, 10.5 Hz, 1H), 0.90 (s, 9H), 0.16 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 198.3, 150.5, 137.8, 128.8, 128.3, 128.2, 128.0, 73.5, 72.8, 71.1, 40.2, 26.0, 18.7.

HRMS (FAB): Calculated for $C_{19}H_{28}O_3Si$ [M+H]$^+$: 333.1880, found: 333.1884.

TLC (ethyl acetate : hexanes = 1 : 8) R*f*: 0.33 (UV, $KMnO_4$).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$: 37.7 (c 1.0, MeOH)



25   26

Compound 26

Ethylenedioxybis(trimethylsilane) (0.25 mL, 1.02 mmol, 5.13 equiv) and trimethylsilyl trifluoromethanesulfonate (0.01 mL, 0.055 mmol, 28 mol%) were sequentially added to a solution of compound **25** (66.2 mg, 0.199 mmol, 1.0 equiv) in dichloromethane (1.0 mL, 0.199 M) at 0 °C under argon atmosphere. After 5 h 10 min, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution (1.0 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (4 × 25 mL) and the combined organic layer was washed with brine (1 × 50 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 1) to afford **26** (26.4 mg, 51%) as a white solid.

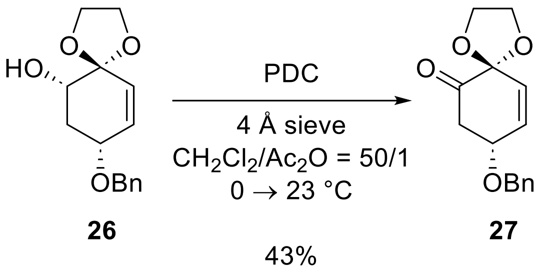
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (d, *J* = 4.4 Hz, 4H), 7.29 – 7.25 (m, 1H), 6.00 (ddd, *J* = 10.2, 2.6, 1.2 Hz, 1H), 5.65 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.12 – 3.98 (m, 5H), 3.73 (d, *J* = 11.3 Hz, 1H), 2.42 – 2.31 (m, 2H), 1.92 (ddd, *J* = 12.5, 11.1, 8.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 138.3, 132.8, 128.7, 128.2, 128.0, 127.9, 105.8, 72.3, 70.6, 69.9, 66.2, 65.9, 35.4.

HRMS (FAB): Calculated for $C_{15}H_{18}O_4$ $[M+H]^+$: 263.1278, found: 263.1285.

TLC (ethyl acetate : hexanes = 1 : 1) R*f*: 0.27 (UV, $KMnO_4$).

$[\alpha]_D^{25}$: 14.9 (c 0.2, MeOH)



Compound 27

Acetic anhydride (0.03 mL) was added to a solution of **26** (33.9 mg, 0.129 mmol, 1.0 equiv), 4 Å molecular sieves (0.4 g) in dichloromethane (1.5 mL, 0.086 M) at 0 °C under argon atmosphere. After 10 min, the rubber septum was removed and pyridinium dichromate (119.2 mg, 0.317 mmol, 2.46 equiv) was added to a reaction mixture. The round-bottomed flask was fitted with rubber septum again and argon gas was charged by balloon. The reaction mixture was stirred at 23 °C for 12 h. Ethyl acetate was added to a reaction mixture and the insoluble salt was removed by passage through a Celite filter. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 4 cm, ht: 12 cm, eluent: ethyl acetate : hexane = 1 : 2) to afford **27** (14.3 mg, 43%) as a colorless oil.

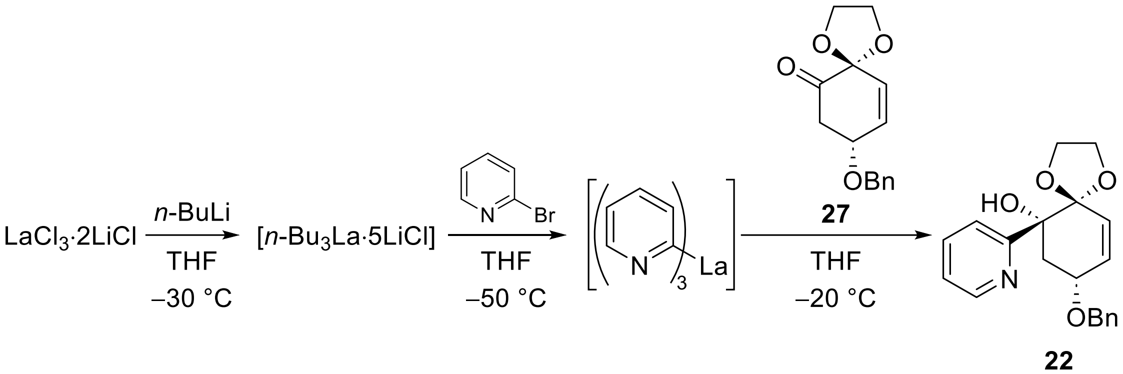
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 – 7.26 (m, 5H), 6.30 (ddd, J = 10.3, 2.8, 1.0 Hz, 1H), 5.82 (dd, J = 10.2, 1.4 Hz, 1H), 4.59 (d, J = 11.8 Hz, 1H), 4.54 (d, J = 11.8 Hz, 1H), 4.35 (dddd, J = 7.1, 5.5, 2.8, 1.5 Hz, 1H), 4.19 – 4.01 (m, 4H), 3.00 (ddd, J = 13.3, 5.5, 1.0 Hz, 1H), 2.93 (dd, J = 13.3, 7.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 201.8, 137.8, 137.1, 128.8, 128.8, 128.2, 127.9, 100.2, 73.7, 70.9, 66.8, 65.9, 44.4.

HRMS (FAB): Calculated for $C_{15}H_{16}O_4$ $[M+H]^+$: 261.1121, found: 261.1131.

TLC (ethyl acetate : hexanes = 1 : 1) R*f*: 0.69 ($KMnO_4$).

$[\alpha]_D^{25}$: 7.4 (c 0.1, MeOH)

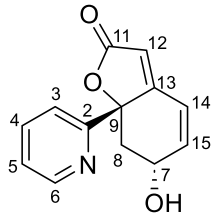


22
54%

Compound 22

Lanthanum(III) chloride bis(lithium chloride) complex (0.6 M THF solution, 0.08 mL, 0.048 mmol, 0.458 equiv) and n-Butyllithium (1.54 M hexane solution, 0.08 mL, 0.123 mmol, 1.175 equiv) were dissolved in tetrahydrofuran (0.21 mL) under argon atmosphere at –30 °C and stirred for 15 min. The reaction temperature was decreased to –50 °C. 2-Bromopyridine (0.01 mL, 0.105 mmol, 1.0 equiv) was added to the reaction mixture at –50 °C and stirred for 20 min. Solution of **27** (18.3 mg, 0.07 mmol, 0.67 equiv) in tetrahydrofuran (0.5 mL) was added dropwise for 6 min into the reaction mixture at –50 °C and the reaction temperature was increased to –20 °C. After 23 h 30 min, the reaction mixture was quenched with saturated aqueous ammonium chloride solution (0.68 mL) at –20 °C and the layers were separated. The aqueous layer was extracted with ethyl acetate (4 × 20 mL) and the combined organic layer was washed with saturated aqueous sodium bicarbonate solution (1 × 40 mL) and brine (1 × 40 mL). The washed organic layer was dried over anhydrous sodium sulfate. The resulting filtrate was concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (silica gel: diam: 2 cm, ht: 6 cm, eluent: ethyl acetate : hexane = 8 : 1) to afford **22** (12.9 mg, 54%) as a white solid. See above for characterization data.

3. Spectroscopic Data Comparison Between Synthetic and Isolated securingine G (4)



securingine G (**4**)

position	Isolation report (ppm ; multi, *J* in Hz)[4, a]	This work (ppm ; multi, *J* in Hz)[b]	Difference (ppm)
3	7.35 (d, 8.0)	7.30 (dt, 8.0, 1.0)	0.05
4	7.72 (td, 8.0, 1.8)	7.67 (td, 7.8, 1.8)	0.05
5	7.30 (overlap)	7.25 (m)	0.05
6	8.57 (m)	8.53 (ddd, 4.8, 1.8, 0.9)	0.04
7	4.61 (brs)	4.55 (ddt, 10.1, 5.3, 2.4)	0.06
8	a 3.59 (dd, 11.6, 5.6)	a 3.54 (ddt, 11.6, 5.6, 1.0)	0.05
	b 2.05 (dd, 11.6, 9.6)	b 2.00 (dd, 11.6, 9.5)	0.05
12	6.02 (s)	5.98 (s)	0.04
14	6.70 (dd, 10.0, 2.3)	6.66 (dd, 10.1, 2.4)	0.04
15	6.25 (brd, 10.0)	6.21 (ddd, 10.0, 2.4, 1.3)	0.04

[a] Reference: residual chloroform δ = 7.28 ppm.

[b] Reference: residual chloroform δ = 7.24 ppm.

Table S1. Comparison of ^{1}H NMR spectroscopic data between synthetic and isolated securingine G (**4**).

position	Isolation report (ppm) [4, a]	This work (ppm)[b]	Difference (ppm)
2	156.7	156.7	-
3	121.1	121.1	-
4	137.4	137.5	-0.1
5	124.1	124.1	-
6	149.1	149.2	-0.1
7	66.9	66.9	-
8	43.3	43.3	-
9	88.0	88.0	-
11	172.1	172.2	-0.1
12	112.9	113.0	-0.1
13	165.0	165.1	-0.1
14	121.0	121.0	-
15	142.4	142.5	-0.1

[a] Reference: $CDCl_3$ $\delta = 77.23$ ppm

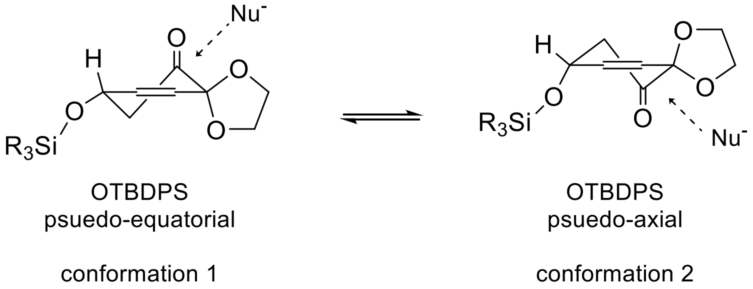
[b] Reference: $CDCl_3$ $\delta = 77.23$ ppm

Table S2. Comparison of ^{13}C NMR spectroscopic data between synthetic and isolated securingine G (**4**).

4. Computational Studies

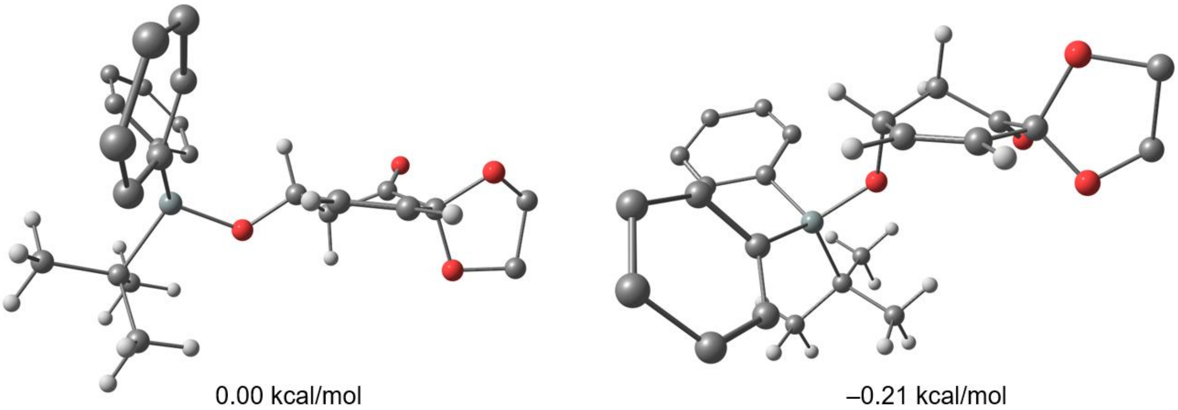
4.1 The facial selectivity of compound **16**

Compound **14** can adopt two distinct conformations: one with the bulky OTBDPS group in the pseudo-equatorial position (conformation 1), and the other with the group in the pseudo-axial position (conformation 2). Conformation 1 seems much more stable due to smaller steric hindrance, suggesting that the pseudo-axial oxygen in the dioxolane moiety would impede nucleophilic attacks from the bottom face of the carbonyls.

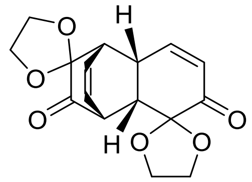


To gain further insight, DFT calculations were conducted. Surprisingly, the pseudo-axial conformation (conformation 2) was found to be stable with 0.21 kcal/mol. This suggests that both conformations coexist in roughly equal proportions. However, despite conformation 2 being more stable than conformation 1, the facial selectivity remains unaffected.

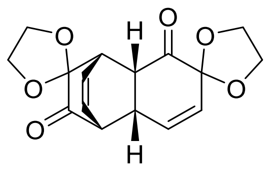
When considering a nucleophilic attack in this context, conformation 1 presents no steric hindrance on the top face, while the bottom face is obstructed by the oxygen of the dioxolane moiety. In contrast, conformation 2 places the OTBDPS group on the bottom face, and places the oxygen and hydrogen on the top face, hindering nucleophilic access in the axial direction. Consequently, nucleophiles are more likely to approach from the top face only in conformation 1, resulting in the formation of the *trans* product.



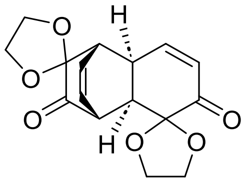
4.2 Energy profile of possible structures of compound (±)-**18**



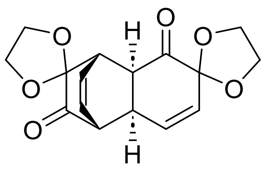
isomer 1



isomer 2



isomer 3



isomer 4

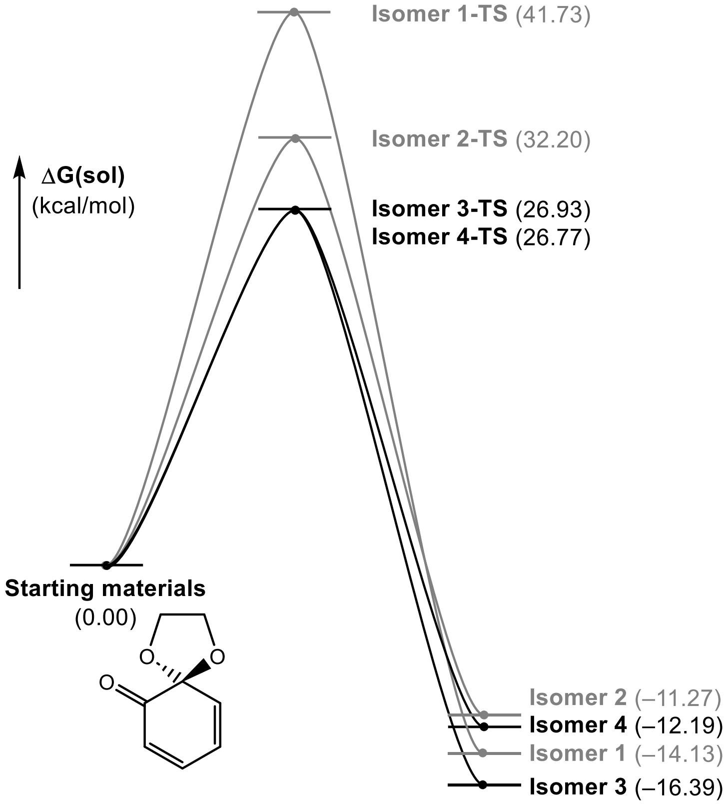
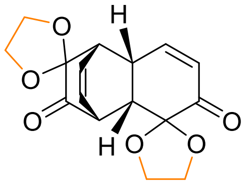


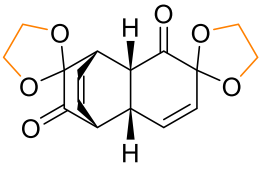
Figure S1. Energy diagram of possible isomers.

4.3 DP4+ analysis of Possible structure of compound (±)-**18**

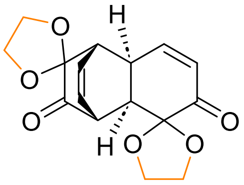
Protons and carbons not used for DP4+ analysis are indicated in orange.



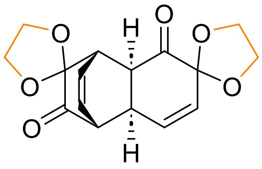
isomer 1



isomer 2



isomer 3

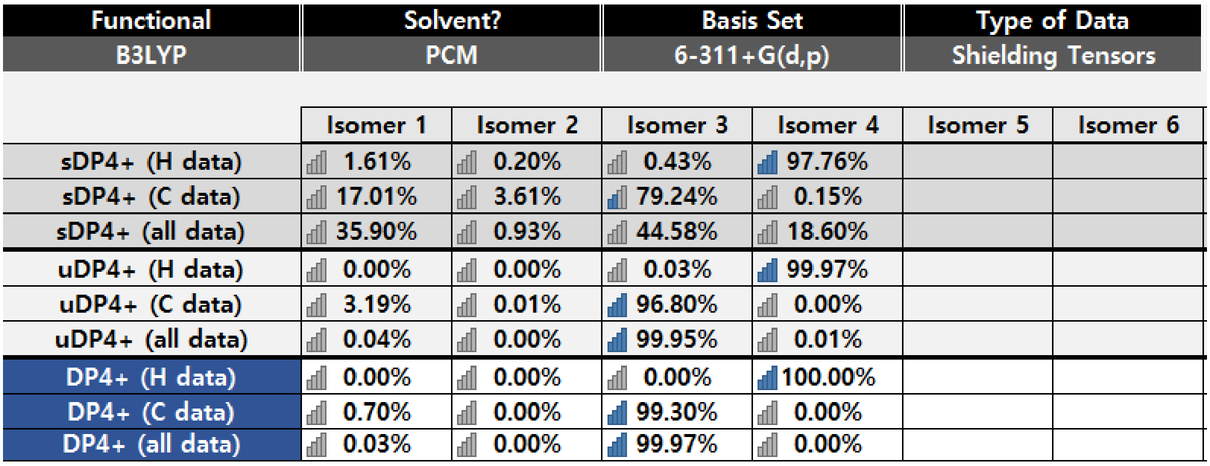


isomer 4

Functional	Solvent?	Basis Set	Type of Data
B3LYP	PCM	6-311+G(d,p)	Shielding Tensors

		DP4+	0.03%	0.00%	99.97%	0.00%	
Nuclei	**sp2?**	**Experimental**	**Isomer 1**	**Isomer 2**	**Isomer 3**	**Isomer 4**	**Isomer 5**
C	x	205.64	-34.4960	-35.3930	-34.6940	-36.1280	
C	x	192.32	-19.4670	-34.1730	-18.6760	-38.8840	
C	x	146.75	18.1250	36.6320	20.5900	36.3000	
C	x	134.06	45.6650	36.6250	47.3570	38.8960	
C	x	130.32	51.0080	48.3230	46.3120	48.1800	
C	x	128.10	35.9120	44.5770	38.3180	45.9770	
C		104.31	73.8360	79.2160	73.9340	80.8580	
C		101.26	76.2870	77.3170	77.0600	76.9740	
C		52.60	130.5380	121.9730	130.0340	122.5800	
C		43.58	129.1290	130.5940	126.3850	128.6050	
C		42.56	135.2740	132.7220	132.6030	132.0380	
C		38.65	138.1250	139.3720	139.0180	138.1640	
H	x	6.47	24.4920	25.4970	24.7930	25.4580	
H	x	6.41	25.3640	24.9000	25.5250	25.1280	
H	x	6.12	25.6380	25.8460	25.6080	25.8890	
H	x	5.96	24.9150	25.3100	25.3820	25.5170	
H		3.42	28.9900	28.8600	28.1130	28.5550	
H		3.22	28.9370	28.6520	28.8910	28.6990	
H		3.18	28.6620	28.3850	28.3230	28.6330	
H		3.09	29.3230	29.2230	29.1220	28.5160	

Table S3. Shielding tensor values of possible isomers for DP4+ analysis.



Functional	Solvent?	Basis Set	Type of Data
B3LYP	PCM	6-311+G(d,p)	Shielding Tensors

	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5	Isomer 6
sDP4+ (H data)	1.61%	0.20%	0.43%	97.76%		
sDP4+ (C data)	17.01%	3.61%	79.24%	0.15%		
sDP4+ (all data)	35.90%	0.93%	44.58%	18.60%		
uDP4+ (H data)	0.00%	0.00%	0.03%	99.97%		
uDP4+ (C data)	3.19%	0.01%	96.80%	0.00%		
uDP4+ (all data)	0.04%	0.00%	99.95%	0.01%		
DP4+ (H data)	0.00%	0.00%	0.00%	100.00%		
DP4+ (C data)	0.70%	0.00%	99.30%	0.00%		
DP4+ (all data)	0.03%	0.00%	99.97%	0.00%		

Table S4. Detailed results for possible isomers.

4.4 Cartesian Coordinates of the Optimized Geometries

Conformation 1

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1521.66979048 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p), 253 K]: 0.42910200 Hartree

C	0.485959000	2.423080000	-2.192216000
C	-0.295294000	1.171610000	-1.876556000
C	0.182034000	0.564379000	-0.553774000
C	1.689876000	0.518767000	-0.482943000
C	2.498332000	1.245271000	-1.252042000
C	2.004671000	2.191585000	-2.306770000
O	-0.011455000	3.508063000	-2.374281000
O	2.726538000	3.382436000	-2.253130000
C	2.735384000	3.900044000	-3.576646000
C	2.847845000	2.625195000	-4.414176000
O	2.211190000	1.637540000	-3.611382000
O	-0.356536000	-0.743002000	-0.447158000
H	-1.362762000	1.397400000	-1.855502000
H	-0.087844000	0.433612000	-2.660399000
H	-0.190837000	1.190028000	0.275196000
H	2.104580000	-0.155300000	0.263246000
H	3.578893000	1.187361000	-1.159069000
H	1.807565000	4.442810000	-3.777452000
H	3.593286000	4.566419000	-3.676518000
H	3.893322000	2.340889000	-4.577366000
H	2.336286000	2.697332000	-5.377111000
C	0.565031000	-1.245054000	2.279697000
Si	-0.824355000	-1.408962000	1.018916000
C	-2.284499000	-0.414433000	1.653360000
C	1.541724000	-2.232389000	2.480883000
C	2.614103000	-2.026588000	3.345074000
C	2.736830000	-0.818575000	4.026741000
C	1.780507000	0.176971000	3.846288000
C	0.707285000	-0.038508000	2.985660000
C	-2.644044000	-0.404412000	3.009103000
C	-3.768503000	0.289062000	3.449726000
C	-4.551545000	0.993703000	2.538379000
C	-4.211038000	0.999624000	1.187821000
C	-3.089880000	0.297854000	0.752892000
C	-1.338031000	-3.174373000	0.585664000
C	-1.607402000	-3.973401000	1.868113000
C	-0.272113000	-3.871968000	-0.272916000
C	-2.635143000	-3.092228000	-0.238097000
H	1.470821000	-3.180955000	1.957319000
H	3.354138000	-2.808188000	3.485117000

H	3.574083000	-0.654679000	4.697824000
H	1.868841000	1.119928000	4.376465000
H	-0.037400000	0.745671000	2.866868000
H	-2.029174000	-0.935784000	3.733132000
H	-4.031123000	0.284766000	4.502966000
H	-5.425128000	1.539524000	2.880754000
H	-4.818045000	1.550080000	0.475984000
H	-2.833770000	0.296852000	-0.304597000
H	-2.375850000	-3.491687000	2.484093000
H	-1.968950000	-4.978493000	1.616282000
H	-0.707124000	-4.085488000	2.481196000
H	-0.060545000	-3.298222000	-1.179557000
H	-0.631813000	-4.864989000	-0.572078000
H	0.672756000	-4.016725000	0.258937000
H	-3.452188000	-2.641248000	0.333408000
H	-2.491374000	-2.503685000	-1.150731000
H	-2.947118000	-4.101520000	-0.535639000

Conformation 2

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1521.66877687 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p), 253 K]: 0.42775400 Hartree

C	-0.953041000	0.208842000	0.353512000
C	-0.423135000	-0.997766000	1.088755000
C	0.929427000	-1.390543000	0.489549000
C	1.861845000	-0.198746000	0.410250000
C	1.428014000	1.058331000	0.364026000
C	-0.023769000	1.436174000	0.438031000
O	-2.017154000	0.252784000	-0.213379000
Si	1.660866000	-3.017301000	-1.580179000
H	-0.284653000	-0.718807000	2.139676000
H	-1.137856000	-1.818868000	1.010643000
H	1.386546000	-2.173469000	1.113876000
O	0.680473000	-1.896081000	-0.816007000
H	2.926580000	-0.409555000	0.346027000
H	2.111178000	1.899169000	0.281179000
O	-0.304265000	2.036549000	1.708583000
O	-0.314599000	2.391002000	-0.533650000
C	-1.019970000	3.244901000	1.477273000
H	-1.899598000	3.278423000	2.124991000
C	-1.373513000	3.181761000	-0.010294000
H	-0.369671000	4.097463000	1.702240000
H	-1.349005000	4.153492000	-0.505672000
H	-2.334454000	2.690479000	-0.183632000

C	3.470579000	-2.536542000	-1.380452000
C	4.170625000	-2.951926000	-0.235410000
C	4.130555000	-1.671403000	-2.266282000
C	5.467337000	-2.512597000	0.021207000
C	5.429244000	-1.234229000	-2.020398000
C	6.098332000	-1.650746000	-0.872168000
H	3.695253000	-3.631801000	0.468244000
H	3.625421000	-1.324681000	-3.162579000
H	5.985421000	-2.844790000	0.915417000
H	5.917669000	-0.565776000	-2.722370000
H	7.109145000	-1.307093000	-0.676034000
C	1.415076000	-4.664773000	-0.713041000
C	0.254359000	-4.891879000	0.039905000
C	2.333737000	-5.717122000	-0.842070000
C	0.018086000	-6.123473000	0.645683000
C	2.100570000	-6.952967000	-0.244331000
C	0.941808000	-7.155857000	0.501916000
H	-0.474799000	-4.091059000	0.145062000
H	3.251126000	-5.564924000	-1.407945000
H	-0.885194000	-6.279192000	1.227274000
H	2.822693000	-7.755709000	-0.356224000
H	0.759691000	-8.117427000	0.971608000
C	1.008007000	-3.073353000	-3.351054000
C	-0.374310000	-3.748638000	-3.314303000
H	-0.800143000	-3.769774000	-4.325616000
H	-0.314277000	-4.779517000	-2.951645000
H	-1.069464000	-3.198893000	-2.670523000
C	1.951524000	-3.899387000	-4.235369000
H	2.073751000	-4.917764000	-3.847742000
H	1.541631000	-3.980452000	-5.250137000
H	2.945669000	-3.446063000	-4.310894000
C	0.831842000	-1.658153000	-3.922742000
H	0.369736000	-1.718784000	-4.916576000
H	0.186566000	-1.050210000	-3.282432000
H	1.781880000	-1.128765000	-4.040708000

Starting material

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -535.22726470 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.11554400 Hartree

C	-1.232503000	2.163896000	-0.301105000
C	-1.436450000	0.848094000	-0.214558000
C	-0.312421000	-0.114373000	0.035347000
C	1.086811000	0.539723000	0.174526000
C	1.200101000	2.003237000	0.065027000
C	0.106755000	2.749656000	-0.158015000
O	2.049674000	-0.176543000	0.371571000
O	-0.273311000	-1.053015000	-1.010845000
C	0.233182000	-2.268479000	-0.466866000
C	0.020272000	-2.123562000	1.055283000
O	-0.588664000	-0.844359000	1.205442000
H	-2.064162000	2.837085000	-0.481659000
H	-2.416842000	0.394603000	-0.317015000
H	2.192835000	2.426813000	0.171123000
H	0.195767000	3.829299000	-0.239161000
H	-0.343782000	-3.087134000	-0.903392000
H	1.291655000	-2.386596000	-0.710517000
H	0.969612000	-2.163079000	1.594726000
H	-0.671528000	-2.864267000	1.463087000

Relative energies were calculated from 2 equivalences of the starting material.

Isomer 1

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.51165337 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.26570000 Hartree

C	-1.436905000	0.403824000	-0.787204000
C	-2.147213000	0.109057000	0.530328000
C	-0.476931000	-0.781009000	-1.090219000
C	-0.392164000	-1.762651000	0.076559000
C	-1.824926000	-2.246181000	0.198121000
C	-2.725878000	-1.283839000	0.411320000
C	-0.015855000	-0.997983000	1.372707000
C	-1.104107000	0.068054000	1.684580000
C	1.409918000	-0.455574000	1.265562000
C	1.735233000	0.636244000	2.303121000
C	0.685925000	1.658055000	2.461493000
C	-0.578051000	1.411155000	2.103053000
O	2.819376000	0.686751000	2.842008000
O	1.641578000	0.187556000	0.014467000
C	2.733204000	-0.465775000	-0.629027000
C	3.401904000	-1.219741000	0.517188000
O	2.288579000	-1.537564000	1.342689000
O	0.020672000	-0.947511000	-2.179210000
O	-0.753758000	1.621716000	-0.724133000
C	-0.544069000	2.003275000	-2.076715000
C	-1.744057000	1.368070000	-2.817983000
O	-2.358262000	0.534127000	-1.838467000
H	-2.900689000	0.881057000	0.703444000
H	0.327527000	-2.552538000	-0.141038000
H	-2.072906000	-3.294430000	0.075827000
H	-3.791089000	-1.463694000	0.499317000
H	0.016711000	-1.724797000	2.190099000
H	-1.674511000	-0.288554000	2.552607000
H	0.991277000	2.613983000	2.874219000
H	-1.326249000	2.195697000	2.203258000
H	3.373123000	0.290839000	-1.087560000
H	2.342497000	-1.140175000	-1.400217000
H	3.877563000	-2.152763000	0.211841000
H	4.109202000	-0.590642000	1.065309000
H	-0.531508000	3.093634000	-2.118725000
H	0.407768000	1.603495000	-2.440071000
H	-1.417794000	0.773447000	-3.674498000
H	-2.482137000	2.108385000	-3.137051000

Isomer 2

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.50567469 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.26428100 Hartree

C	-0.318375000	0.872303000	1.350985000
C	0.306610000	1.844246000	0.350285000
C	0.808626000	0.262115000	2.218251000
C	2.185558000	0.652793000	1.702511000
C	2.195747000	2.162904000	1.792589000
C	1.217742000	2.770840000	1.116198000
C	2.246179000	0.205650000	0.203002000
C	1.193656000	1.000354000	-0.615445000
C	2.112508000	-1.290958000	0.127743000
C	1.303235000	-1.963898000	-0.682862000
C	0.431152000	-1.318580000	-1.709034000
C	0.294112000	0.208273000	-1.561650000
O	-0.497136000	0.796686000	-2.264537000
O	-0.833838000	-1.921696000	-1.714533000
C	-1.337846000	-1.866661000	-3.043317000
C	-0.099154000	-1.557165000	-3.911302000
O	0.983582000	-1.565340000	-2.989540000
O	0.582195000	-0.442020000	3.172654000
O	-0.958169000	-0.172480000	0.665380000
C	-1.924641000	-0.709592000	1.558970000
C	-2.207757000	0.458429000	2.533695000
O	-1.294689000	1.481588000	2.140452000
H	-0.482627000	2.347181000	-0.209554000
H	2.961441000	0.166141000	2.295766000
H	2.930058000	2.681895000	2.398285000
H	1.078662000	3.845606000	1.092895000
H	3.247712000	0.472606000	-0.154019000
H	1.705302000	1.717786000	-1.263811000
H	2.744331000	-1.847019000	0.818725000
H	1.267127000	-3.049017000	-0.679506000
H	-1.782185000	-2.839344000	-3.270408000
H	-2.092723000	-1.081905000	-3.133456000
H	0.102285000	-2.323060000	-4.663627000
H	-0.189423000	-0.578865000	-4.392297000
H	-1.516122000	-1.577580000	2.083985000
H	-2.790473000	-1.006268000	0.965258000
H	-3.218387000	0.860196000	2.431806000
H	-2.026274000	0.164852000	3.570462000

Isomer 3

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.51288165 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.26332200 Hartree

C	2.369153000	0.086807000	1.909779000
C	2.046909000	-1.302355000	1.534232000
C	1.466151000	-1.450736000	0.114504000
C	0.359419000	-0.450467000	-0.206989000
C	0.667058000	0.991597000	0.284552000
C	1.775090000	1.110726000	1.290245000
C	-1.023768000	-0.924358000	0.336579000
C	-2.048318000	-0.025724000	-0.336862000
C	-1.758345000	1.471974000	-0.079598000
C	-0.629358000	1.576565000	0.942585000
C	-0.992311000	0.693232000	2.112010000
C	-1.160834000	-0.596342000	1.807353000
O	-2.901998000	2.144550000	0.359133000
C	-3.641565000	2.502965000	-0.803915000
C	-2.610930000	2.411228000	-1.953561000
O	-1.392306000	2.070245000	-1.299803000
O	-2.979372000	-0.391446000	-1.013888000
O	2.309460000	-2.267133000	2.218733000
O	1.020250000	-2.747291000	-0.133896000
C	2.156501000	-3.483839000	-0.566034000
C	2.898403000	-2.441310000	-1.399358000
O	2.582513000	-1.216483000	-0.747172000
H	3.097766000	0.229673000	2.701404000
H	0.300390000	-0.443379000	-1.301183000
H	0.904820000	1.622931000	-0.576935000
H	2.035348000	2.130180000	1.573010000
H	-1.206825000	-1.968336000	0.089302000
H	-0.495346000	2.626824000	1.210667000
H	-1.066298000	1.087936000	3.118547000
H	-1.408677000	-1.365294000	2.529972000
H	-4.471964000	1.809859000	-0.958476000
H	-4.023880000	3.515324000	-0.654932000
H	-2.455074000	3.360029000	-2.470715000
H	-2.888931000	1.636182000	-2.673187000
H	2.742506000	-3.813717000	0.296580000
H	1.808412000	-4.342592000	-1.141274000
H	2.527773000	-2.417291000	-2.430749000
H	3.982178000	-2.576737000	-1.403659000

Isomer 4

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.50611767 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.26324500 Hartree

C	2.670829000	-0.089586000	-0.300665000
C	2.518743000	-1.499810000	-0.764901000
C	1.349204000	-2.035785000	-1.101396000
C	0.018495000	-1.345024000	-1.045370000
C	0.080130000	0.191898000	-0.863342000
C	1.451979000	0.800107000	-0.613279000
C	-0.838418000	-1.977991000	0.110331000
C	-2.241754000	-1.415281000	-0.033235000
C	-2.250879000	0.131136000	0.003399000
C	-0.839489000	0.617676000	0.319936000
C	-0.363028000	-0.117694000	1.550737000
C	-0.343183000	-1.448048000	1.436645000
O	-3.171549000	0.608813000	0.939629000
C	-4.440920000	0.632201000	0.294718000
C	-4.102543000	0.598335000	-1.213923000
O	-2.678851000	0.601685000	-1.250859000
O	-3.251548000	-2.062444000	-0.179604000
O	3.828537000	0.468557000	-0.858155000
C	4.356131000	1.411624000	0.067660000
C	3.584172000	1.135212000	1.374753000
O	2.861266000	-0.058737000	1.102250000
O	1.585534000	2.004151000	-0.590203000
H	3.441489000	-2.070647000	-0.800588000
H	1.319466000	-3.077796000	-1.414850000
H	-0.510934000	-1.558762000	-1.981914000
H	-0.297309000	0.684612000	-1.764308000
H	-0.861540000	-3.066736000	0.043097000
H	-0.842093000	1.703421000	0.420984000
H	-0.027667000	0.414579000	2.432922000
H	-0.006951000	-2.118243000	2.218899000
H	-4.949047000	1.550641000	0.596801000
H	-5.035902000	-0.236281000	0.587994000
H	-4.495310000	-0.305647000	-1.687513000
H	-4.449482000	1.481733000	-1.753557000
H	5.428375000	1.221152000	0.164019000
H	4.188915000	2.429981000	-0.289900000
H	2.899387000	1.956830000	1.609570000
H	4.233746000	0.940168000	2.230216000

Isomer1-TS

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.41545798 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.25851200 Hartree

C	-1.530120000	0.340208000	-0.861001000
C	-2.492341000	-0.001205000	0.243610000
C	-0.583065000	-0.838304000	-1.186171000
C	-0.670312000	-2.011782000	-0.285484000
C	-1.948830000	-2.341229000	0.142006000
C	-2.877895000	-1.316962000	0.398876000
C	0.069771000	-0.914019000	1.586011000
C	-0.925800000	-0.023579000	1.967104000
C	1.454626000	-0.377907000	1.280932000
C	1.790530000	0.896068000	2.101327000
C	0.666180000	1.830217000	2.302140000
C	-0.598576000	1.394728000	2.199680000
O	2.928726000	1.128504000	2.443267000
O	1.626604000	0.093248000	-0.054133000
C	2.703613000	-0.626992000	-0.643873000
C	3.443015000	-1.192600000	0.564821000
O	2.376094000	-1.404513000	1.482611000
O	0.081053000	-0.838850000	-2.201838000
O	-0.825943000	1.512892000	-0.582750000
C	-0.414022000	2.029115000	-1.840260000
C	-1.511066000	1.530441000	-2.807024000
O	-2.281630000	0.618886000	-2.026298000
H	-3.146055000	0.817333000	0.533266000
H	0.088373000	-2.775970000	-0.430171000
H	-2.177543000	-3.360068000	0.439408000
H	-3.803945000	-1.555307000	0.912771000
H	0.082209000	-1.915893000	1.995207000
H	-1.752230000	-0.399965000	2.557161000
H	0.912322000	2.847209000	2.586592000
H	-1.425162000	2.075893000	2.384484000
H	3.302582000	0.066202000	-1.238131000
H	2.299424000	-1.411760000	-1.293632000
H	3.923106000	-2.153918000	0.375343000
H	4.160656000	-0.479377000	0.978548000
H	-0.371269000	3.116301000	-1.752100000
H	0.570488000	1.633941000	-2.105728000
H	-1.082060000	1.020967000	-3.672954000
H	-2.178510000	2.331046000	-3.136619000

Isomer2-TS

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.43147628 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.25934800 Hartree

C	-0.258322000	0.856117000	1.334295000
C	0.227432000	2.014405000	0.497089000
C	0.876257000	0.213036000	2.154050000
C	2.103798000	0.996454000	2.266915000
C	2.099470000	2.349543000	1.960221000
C	1.144003000	2.882040000	1.089843000
C	2.327629000	0.133813000	-0.077265000
C	1.425938000	0.922065000	-0.807684000
C	2.102210000	-1.299568000	0.099863000
C	1.156168000	-1.961926000	-0.572540000
C	0.338789000	-1.311150000	-1.648761000
C	0.375836000	0.234177000	-1.633359000
O	-0.344849000	0.858870000	-2.381855000
O	-0.978494000	-1.784230000	-1.628878000
C	-1.466128000	-1.771058000	-2.965391000
C	-0.195364000	-1.664464000	-3.835189000
O	0.873161000	-1.714484000	-2.897785000
O	0.701177000	-0.868140000	2.689019000
O	-0.886187000	-0.094683000	0.530483000
C	-1.885687000	-0.745046000	1.306310000
C	-2.056186000	0.181876000	2.531012000
O	-1.245226000	1.316122000	2.230140000
H	-0.502411000	2.381027000	-0.220822000
H	2.903198000	0.549753000	2.850808000
H	2.923046000	2.973263000	2.295682000
H	1.243961000	3.900370000	0.730030000
H	3.323612000	0.511603000	0.117578000
H	1.789067000	1.826143000	-1.282584000
H	2.724523000	-1.822423000	0.819608000
H	0.995442000	-3.027871000	-0.450298000
H	-2.014330000	-2.702895000	-3.126691000
H	-2.128721000	-0.916624000	-3.122084000
H	-0.070539000	-2.504703000	-4.521782000
H	-0.176543000	-0.723557000	-4.392697000
H	-1.546643000	-1.741772000	1.595125000
H	-2.783058000	-0.817620000	0.688642000
H	-3.079109000	0.539008000	2.664241000
H	-1.708921000	-0.306477000	3.445708000

Isomer3-TS

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.43899506 Hartree

Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.25846800 Hartree

C	2.246817000	0.061974000	1.800612000
C	2.001007000	-1.299602000	1.318753000
C	1.476637000	-1.409310000	-0.127539000
C	0.598551000	-0.245362000	-0.527092000
C	0.948894000	1.024101000	-0.052636000
C	1.823903000	1.134226000	1.091551000
C	-1.150927000	-0.884168000	0.482413000
C	-1.942282000	0.053346000	-0.352129000
C	-1.876301000	1.539731000	0.041263000
C	-0.994468000	1.774207000	1.232320000
C	-0.869331000	0.799930000	2.193422000
C	-0.939144000	-0.554516000	1.823626000
O	-3.175656000	1.980792000	0.367336000
C	-3.816070000	2.323206000	-0.856801000
C	-2.649509000	2.586058000	-1.833670000
O	-1.480509000	2.309529000	-1.067446000
O	-2.608183000	-0.297926000	-1.303265000
O	2.312053000	-2.305729000	1.929965000
O	0.864075000	-2.645916000	-0.354610000
C	1.878673000	-3.585939000	-0.692456000
C	3.128472000	-2.717574000	-0.944664000
O	2.618814000	-1.390485000	-0.965613000
H	2.823357000	0.163082000	2.714228000
H	0.200962000	-0.333898000	-1.535730000
H	0.735407000	1.900245000	-0.651359000
H	2.080983000	2.134753000	1.431098000
H	-1.189801000	-1.920944000	0.168500000
H	-0.821029000	2.822076000	1.461761000
H	-0.519910000	1.061308000	3.186685000
H	-0.696310000	-1.333349000	2.539318000
H	-4.446227000	1.500955000	-1.205056000
H	-4.427525000	3.208807000	-0.670677000
H	-2.590672000	3.627218000	-2.159205000
H	-2.700587000	1.925708000	-2.702518000
H	2.032689000	-4.285059000	0.131944000
H	1.551617000	-4.123306000	-1.586327000
H	3.603957000	-2.905302000	-1.908688000
H	3.861572000	-2.838869000	-0.140312000

Isomer4-TS

E [M06-2X/6-311+G(d,p), SMD (tetrahydrofuran)]: -1070.43927158 Hartree
Thermal Correction to Gibbs free energy [M06-2X/6-31G(d,p)]: 0.25848600 Hartree

C	2.571556000	-0.013940000	-0.106411000
C	2.385346000	-1.491095000	-0.246278000
C	1.375547000	-2.035103000	-0.945276000
C	0.256032000	-1.260373000	-1.442708000
C	0.195420000	0.116484000	-1.180223000
C	1.431688000	0.817704000	-0.734076000
C	-1.262270000	-2.287305000	0.282145000
C	-2.229294000	-1.421568000	-0.392964000
C	-2.180346000	0.060941000	0.016804000
C	-0.825497000	0.433456000	0.574258000
C	-0.266689000	-0.451235000	1.503082000
C	-0.509019000	-1.820923000	1.345033000
O	-3.145817000	0.256897000	1.028529000
C	-4.384725000	0.410821000	0.345681000
C	-3.980646000	1.004113000	-1.020241000
O	-2.560550000	0.892393000	-1.042283000
O	-3.077750000	-1.813847000	-1.174752000
O	3.789765000	0.339765000	-0.713305000
C	4.302337000	1.480479000	-0.034468000
C	3.506018000	1.529088000	1.286277000
O	2.703460000	0.353087000	1.252038000
O	1.559983000	2.020425000	-0.830275000
H	3.195573000	-2.091736000	0.154771000
H	1.354979000	-3.109513000	-1.104490000
H	-0.409181000	-1.698659000	-2.178092000
H	-0.466970000	0.737942000	-1.775497000
H	-1.340739000	-3.348304000	0.064155000
H	-0.667399000	1.504657000	0.676308000
H	0.473599000	-0.104291000	2.213273000
H	0.030901000	-2.528541000	1.966584000
H	-5.009623000	1.076648000	0.943099000
H	-4.881434000	-0.556560000	0.223278000
H	-4.414915000	0.440446000	-1.848381000
H	-4.233069000	2.063480000	-1.111955000
H	5.372093000	1.319813000	0.121058000
H	4.143054000	2.382855000	-0.629226000
H	2.877812000	2.422747000	1.337188000
H	4.138769000	1.468751000	2.174335000

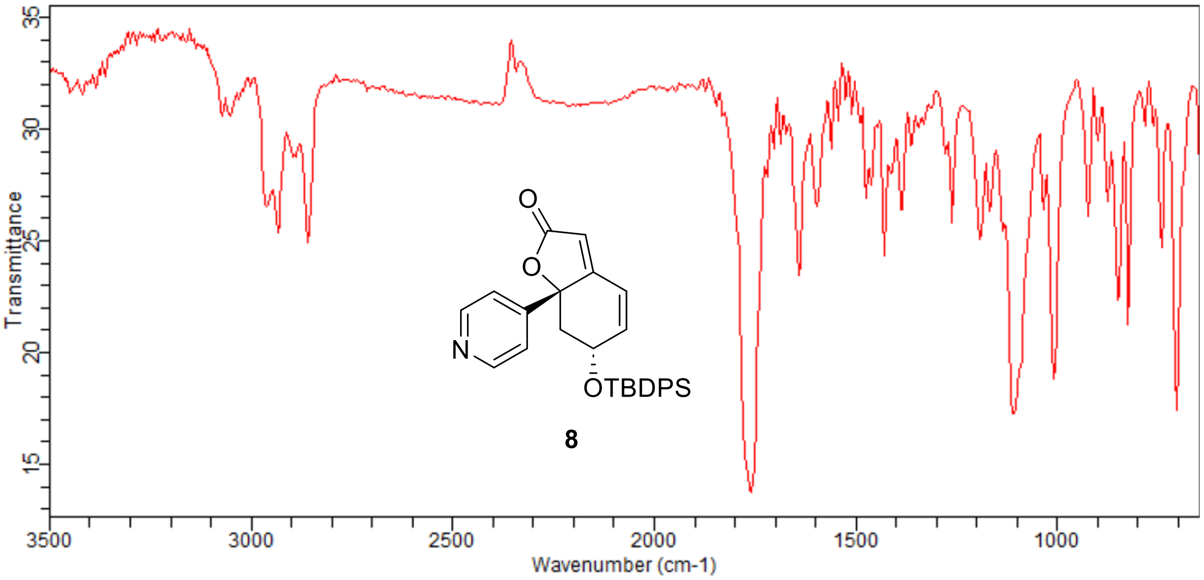
5. References

1. W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
2. A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen and F. J. Timmers, *Organometallics*, 1996, **15**, 1518.
3. S. Park, G. Kang, C. Kim, D. Kim and S. Han, *Nat. Commun.*, 2022, **13**, 5149.

~~4.~~ K. J. Park, C. S. Kim, Z. Khan, J. Oh, S. Y. Kim, S. U. Choi and K. R. Lee, *J. Nat. Prod.*, 2019, **82**, 1345.

5. Gaussian 09, Revision D.01, M. J. Frisch, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.
6. Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215.
7. A. V. Marenich, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem. B*, 2009, **113**, 6378.
8. (a) A. D. Becke, *Phys. Rev. A*, 1988, **38**, 3098. (b) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785.
9. B. Mennucci, E. Cancens and J. Tomasi, *J. Phys. Chem. B*, 1997, **101**, 10506.
10. M. M. Zanardi and A. M. Sarotti. *J. Org. Chem.*, 2021, **86**, 8544.

6. Copies of IR Spectra of Representatively Synthesized Compounds



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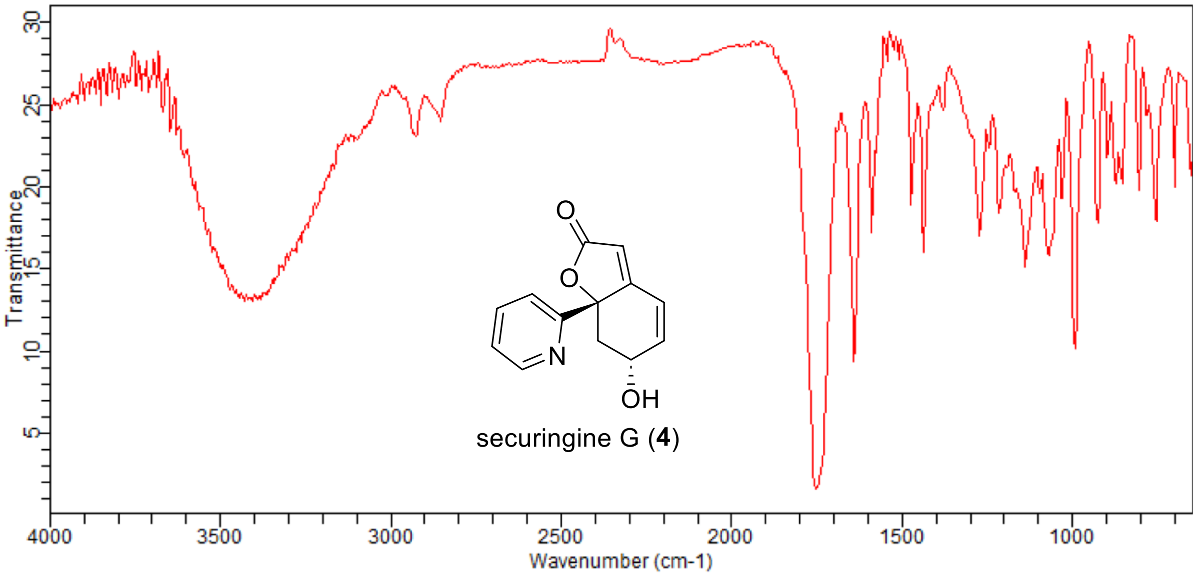
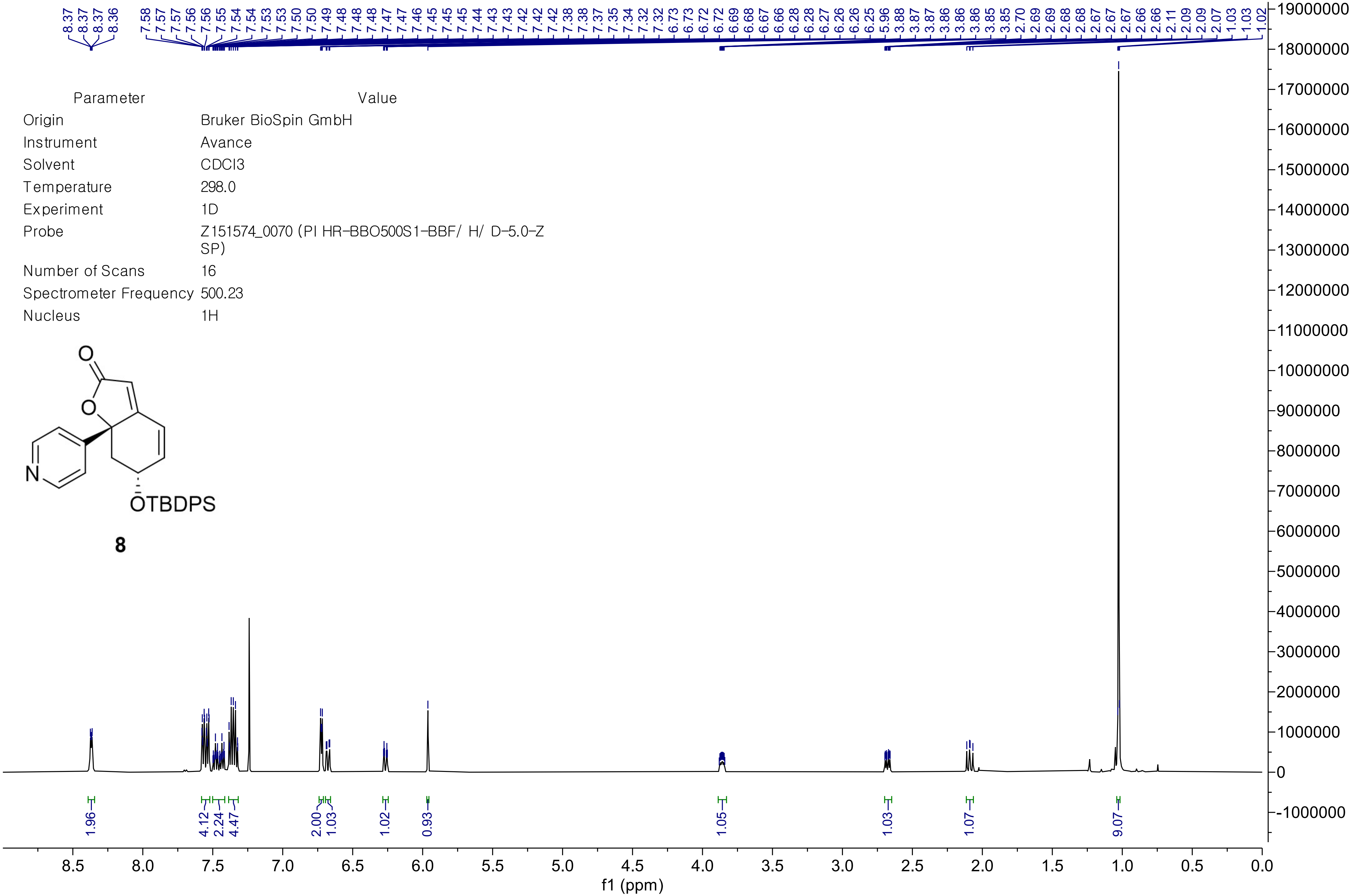


securingine G (**4**)

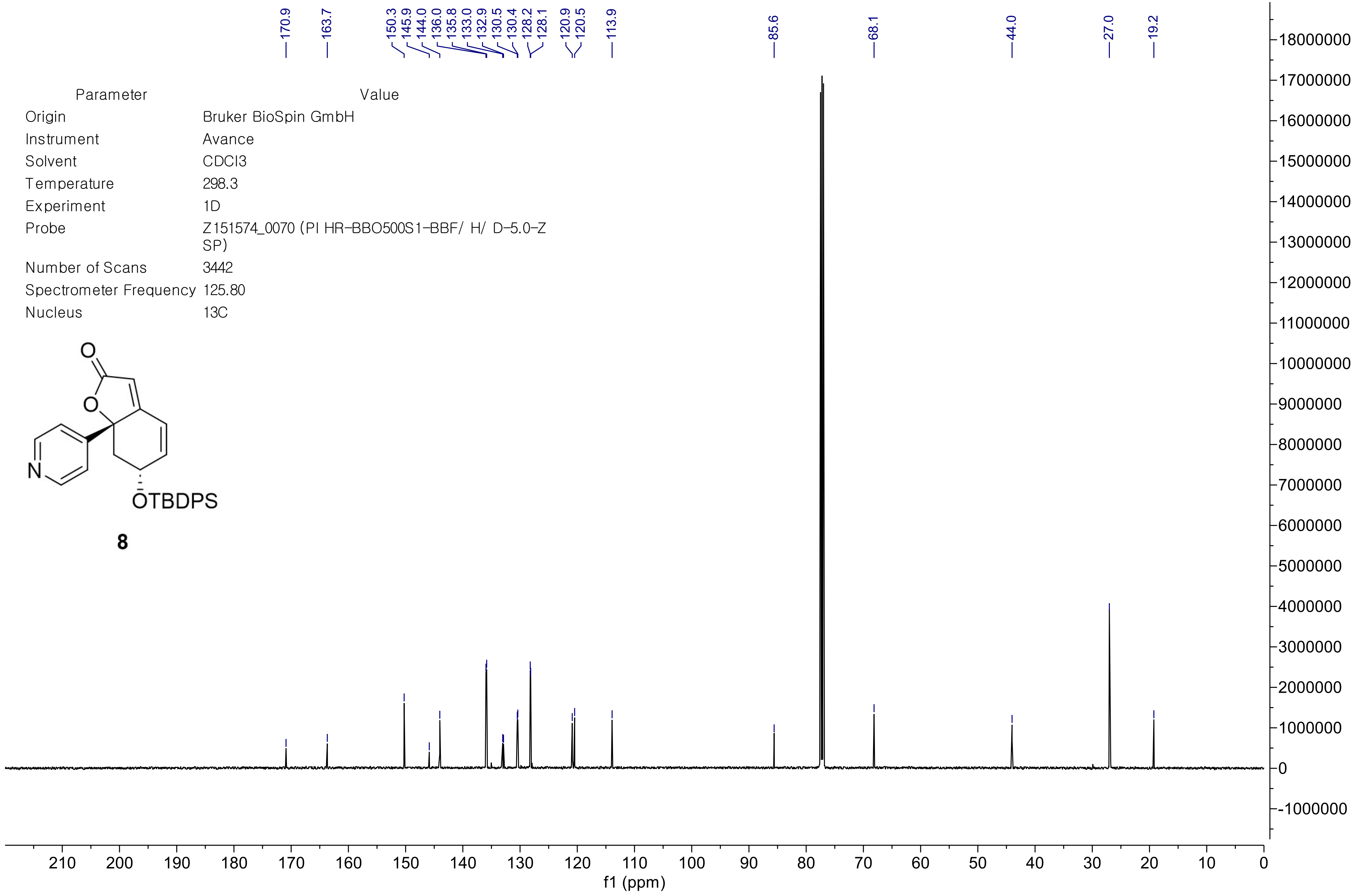
7. Copies of NMR Spectra of Newly Synthesized Compounds

Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

8



Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.3
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	3442
Spectrometer Frequency	125.80
Nucleus	13C



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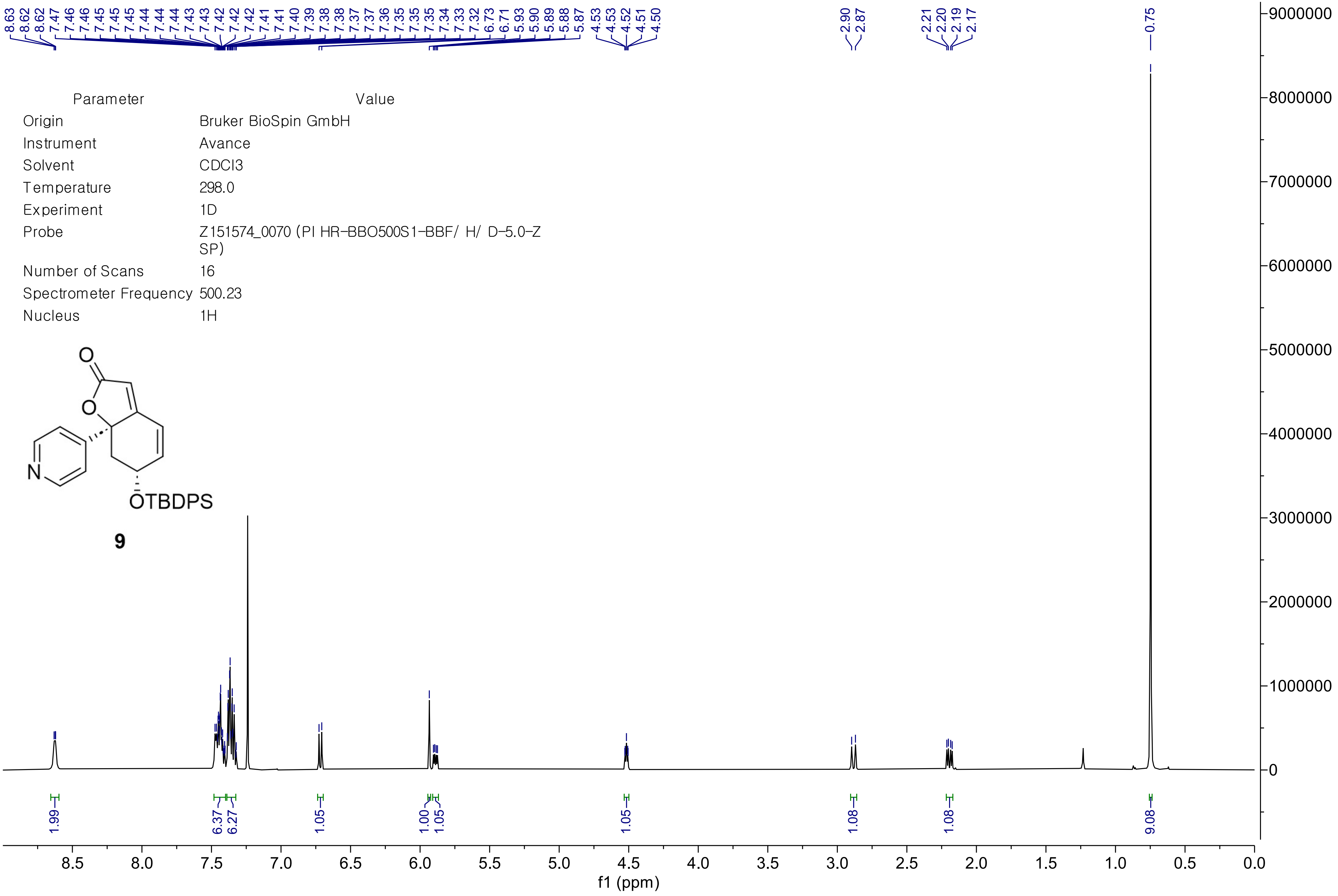
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



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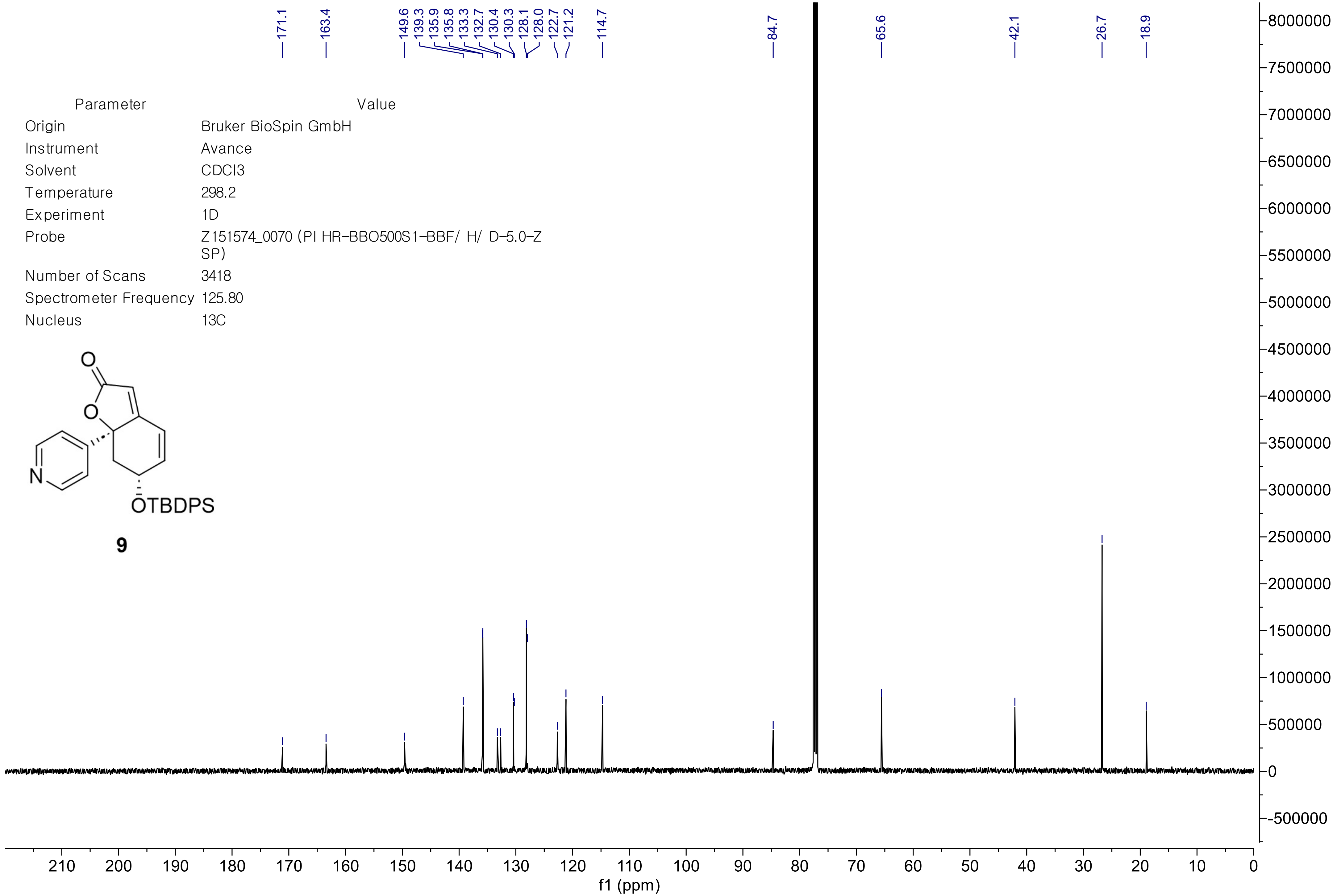
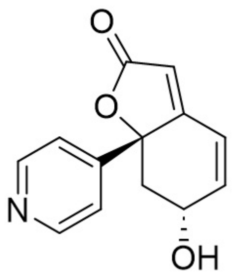


Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.2
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	3418
Spectrometer Frequency	125.80
Nucleus	13C

9

Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CD2Cl2
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



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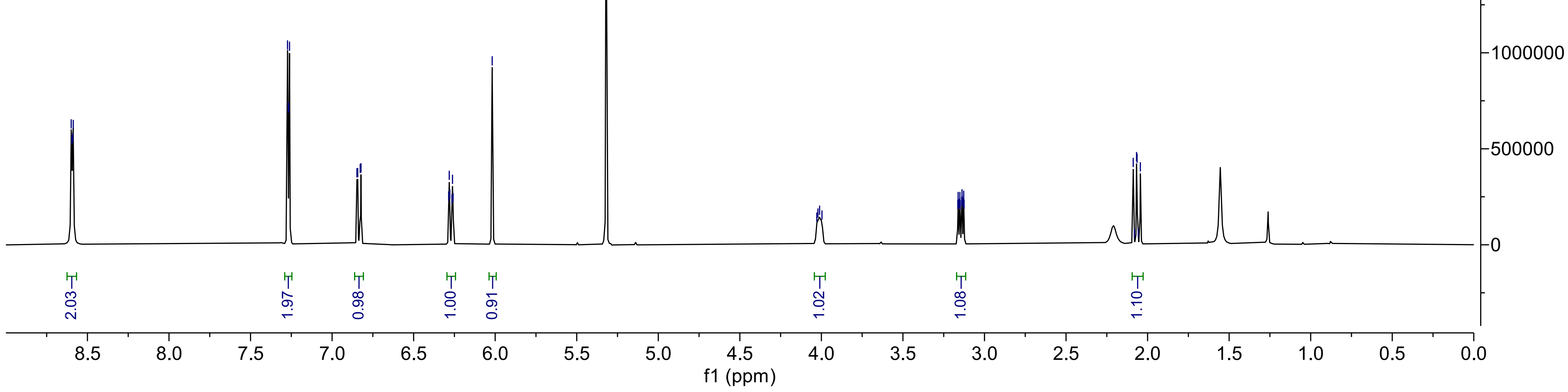
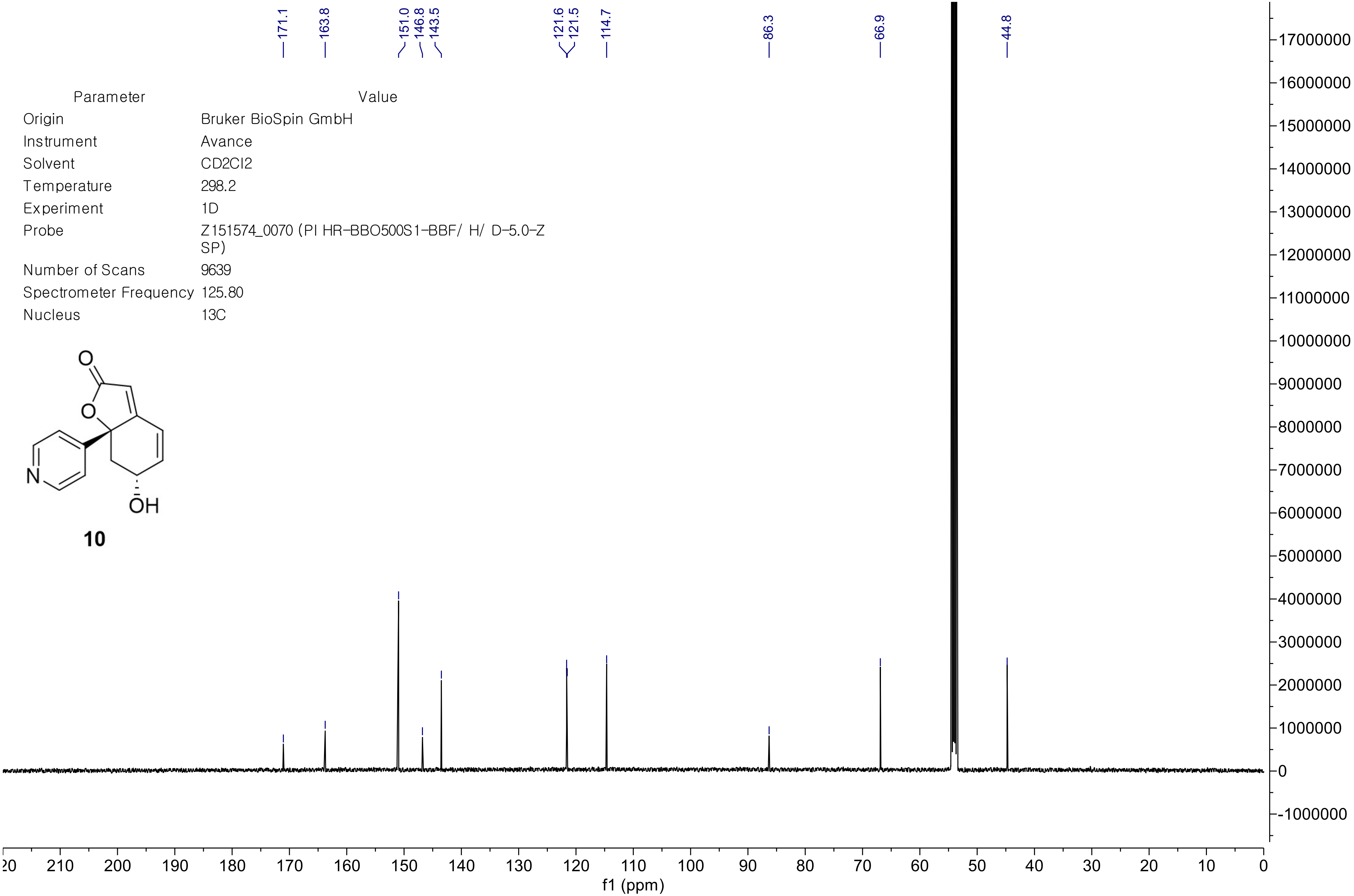
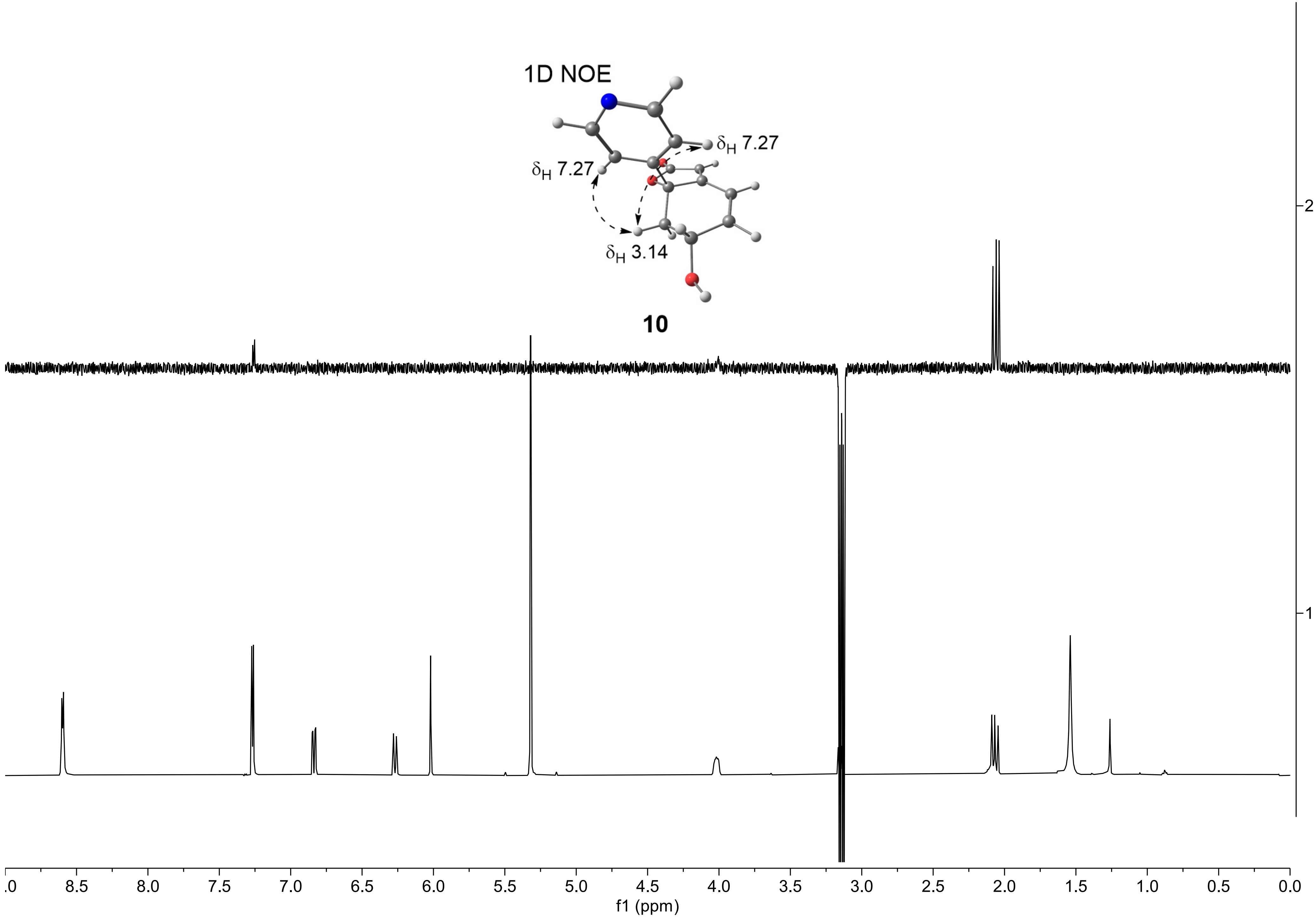




Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CD2Cl2
Temperature	298.2
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	9639
Spectrometer Frequency	125.80
Nucleus	13C

10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6.5
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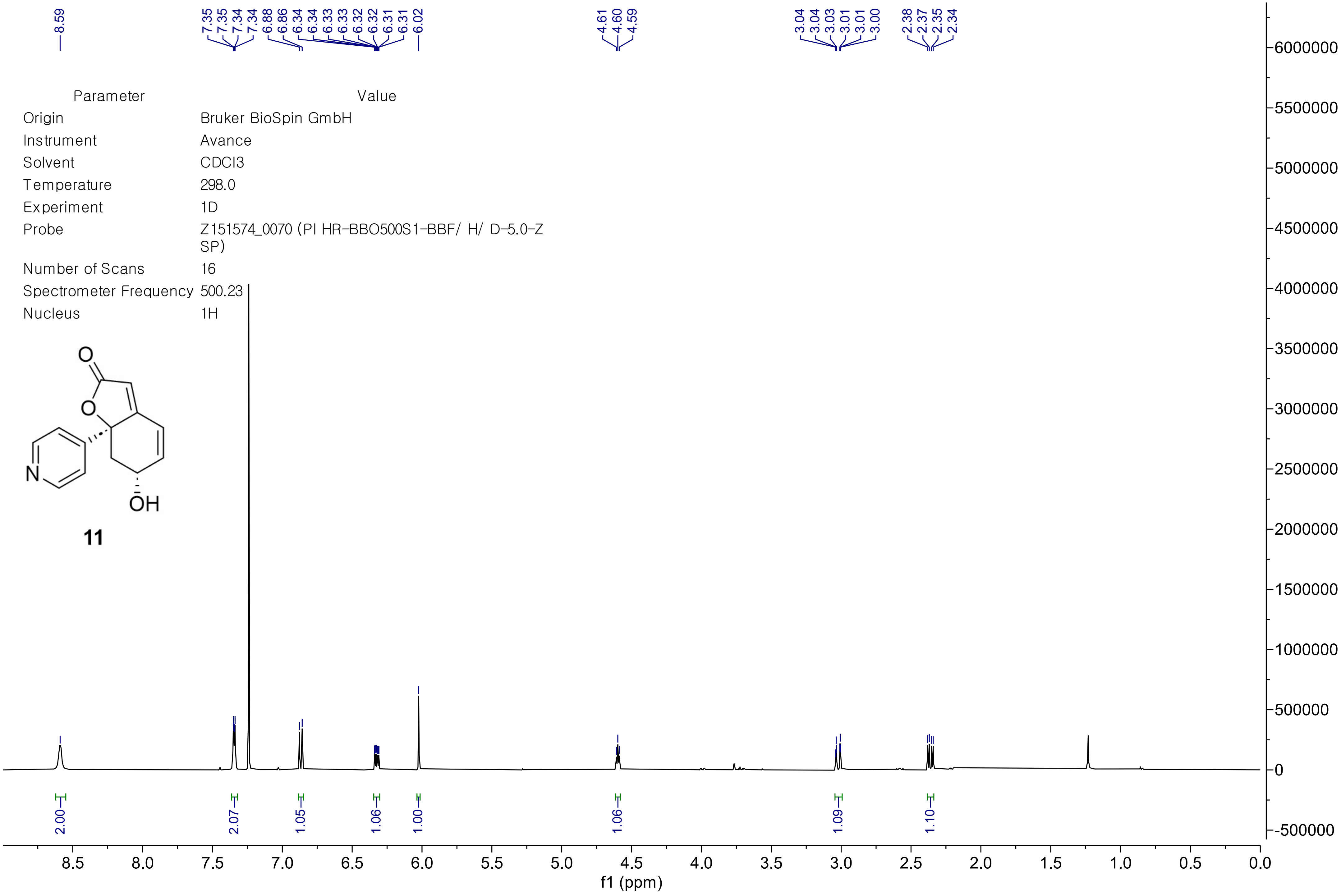
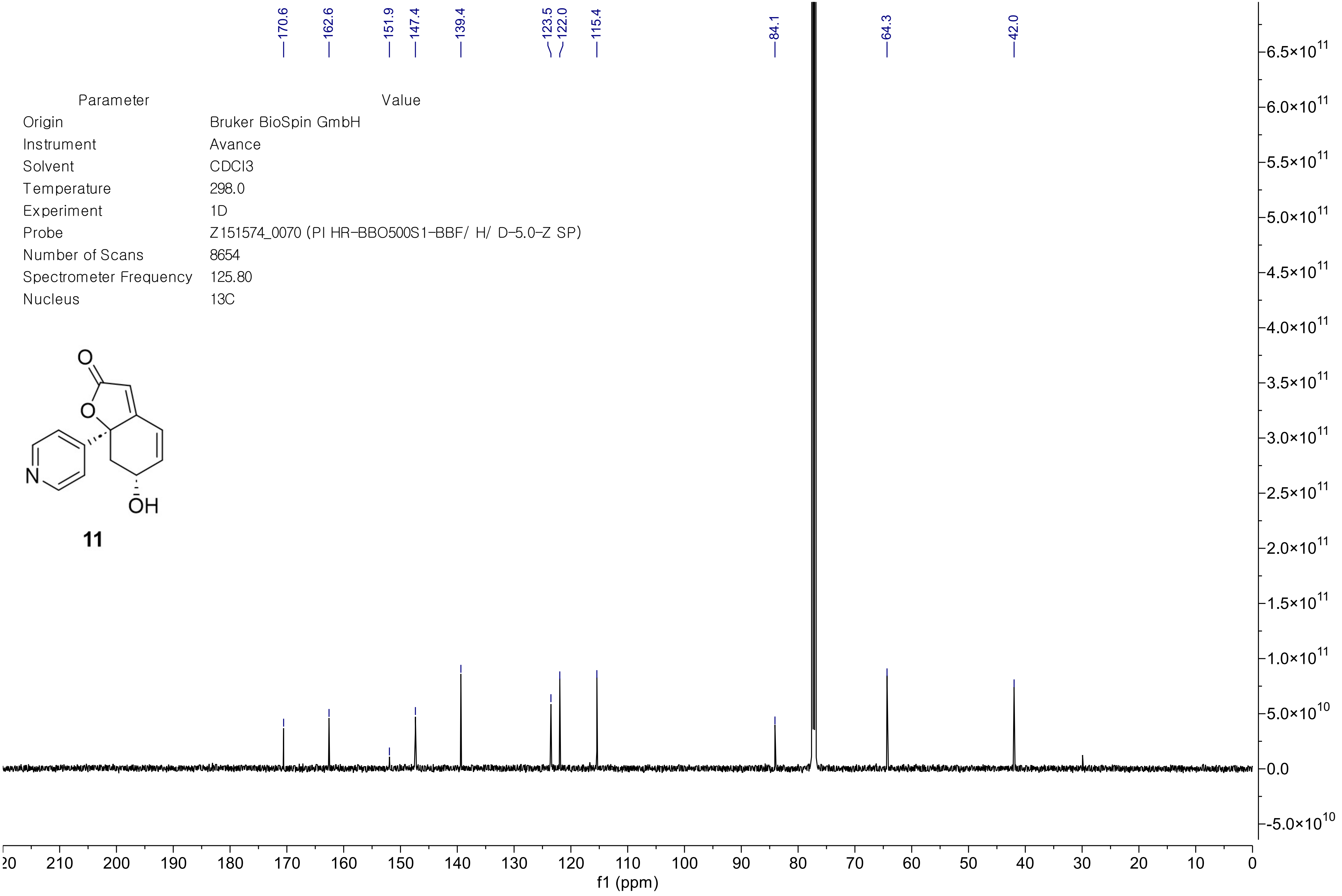


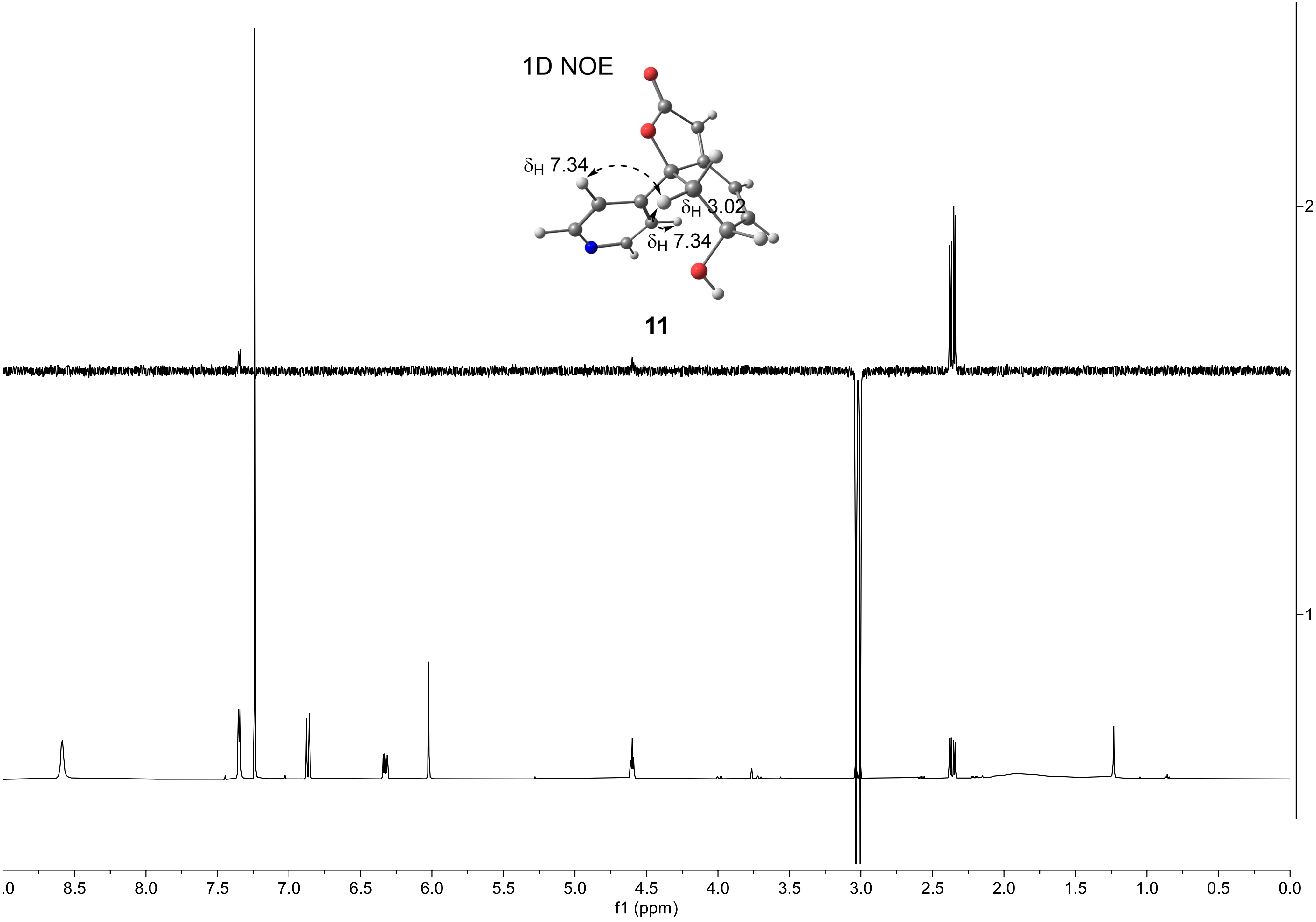
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

11

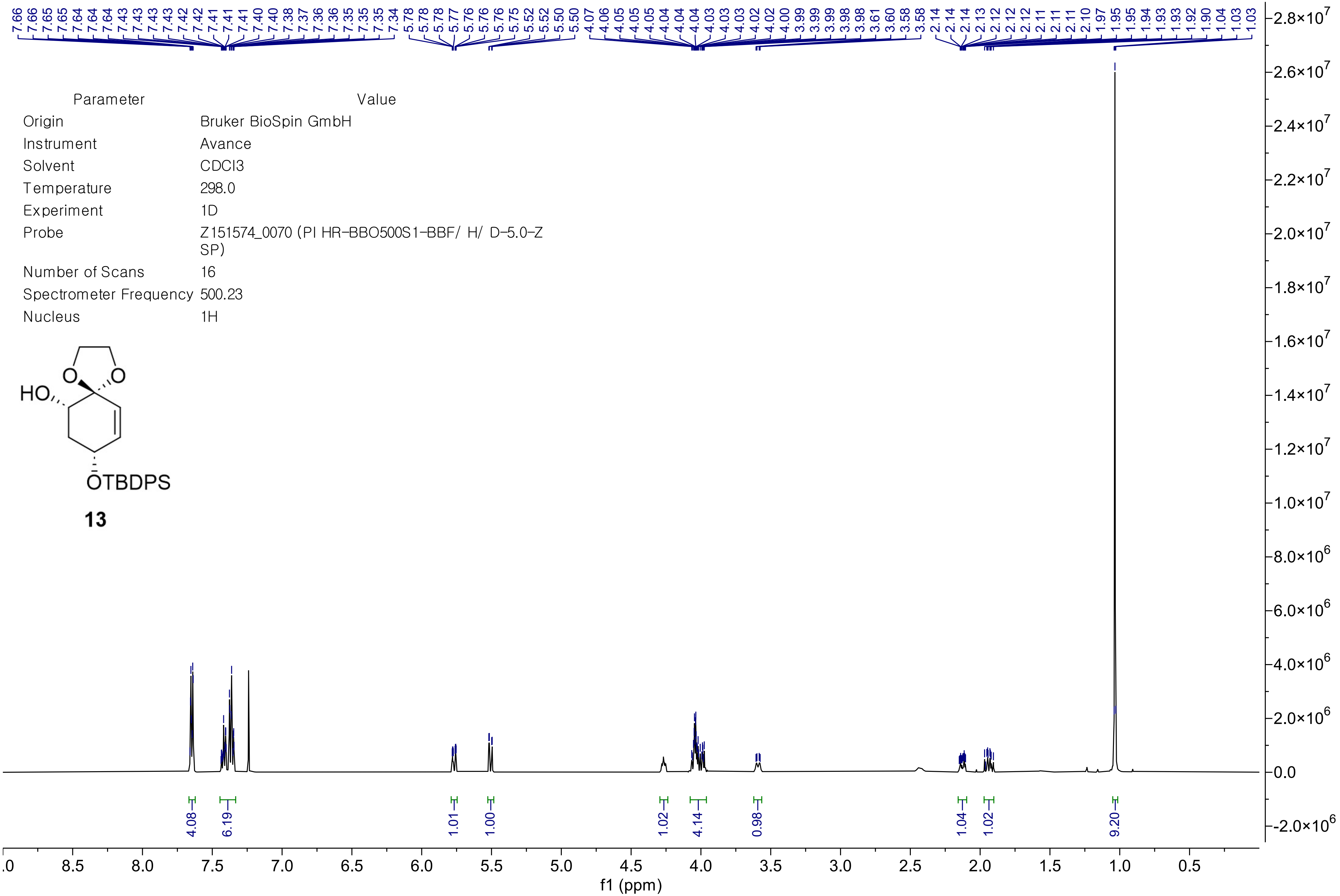


Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	8654
Spectrometer Frequency	125.80
Nucleus	13C

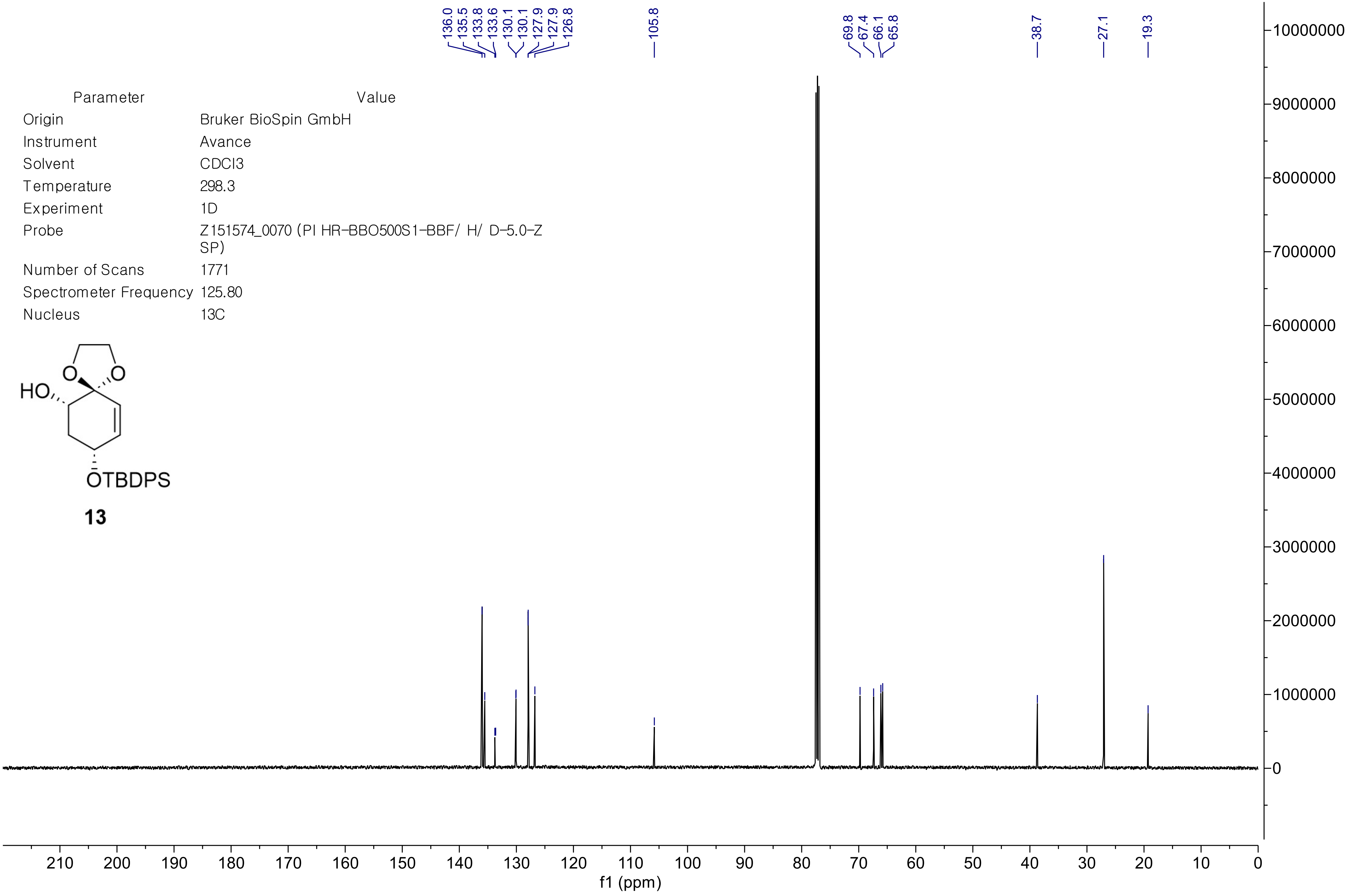
11


1D NOE
δ_H 7.34
δ_H 3.02
δ_H 7.34
11
2
1
.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
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



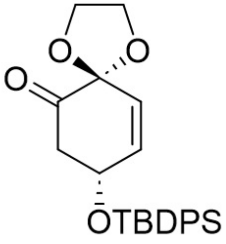
13



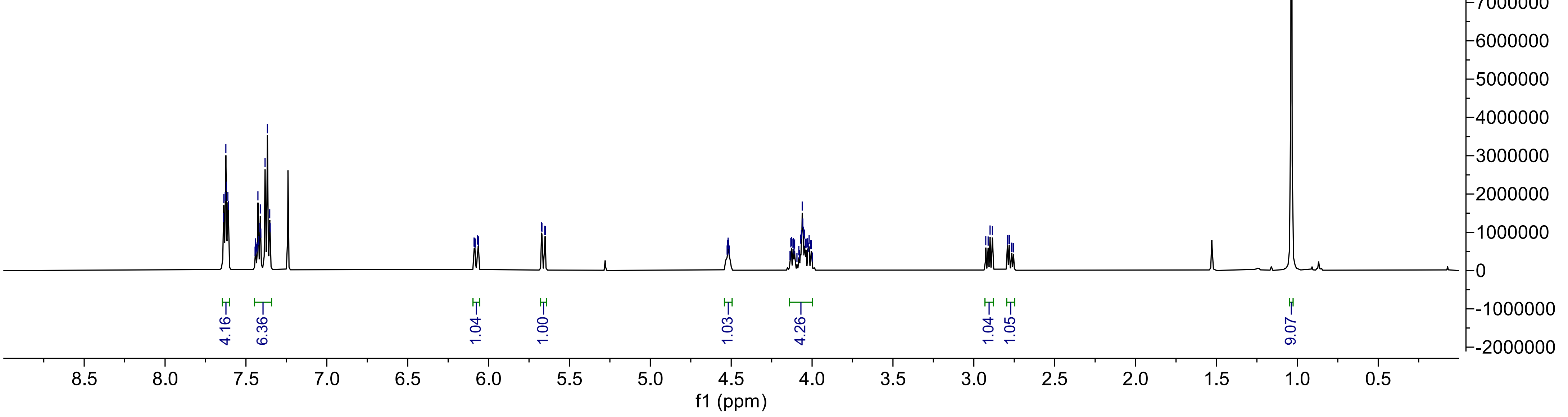
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.3
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	1771
Spectrometer Frequency	125.80
Nucleus	13C

13

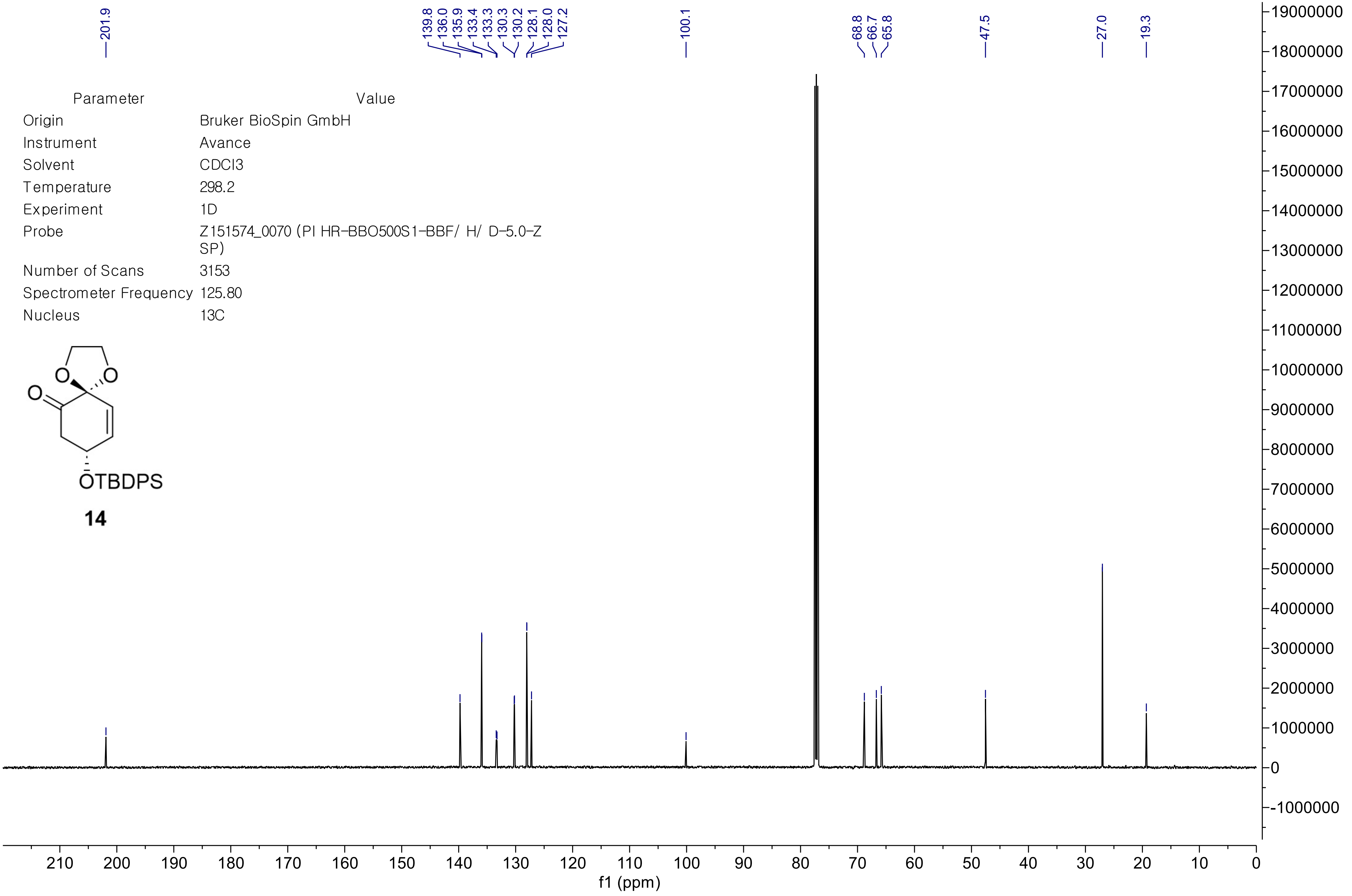
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



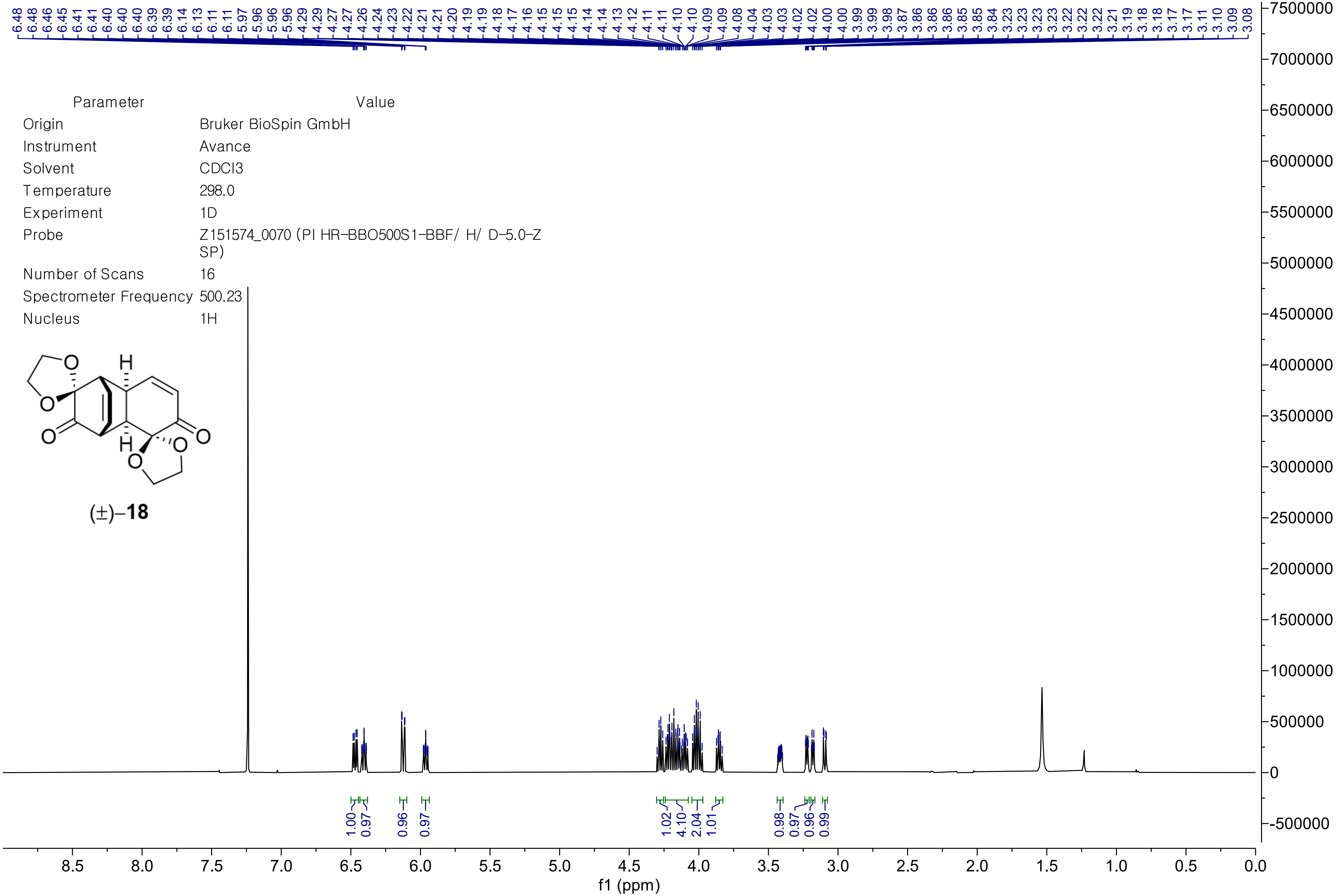
14



Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.2
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	3153
Spectrometer Frequency	125.80
Nucleus	13C



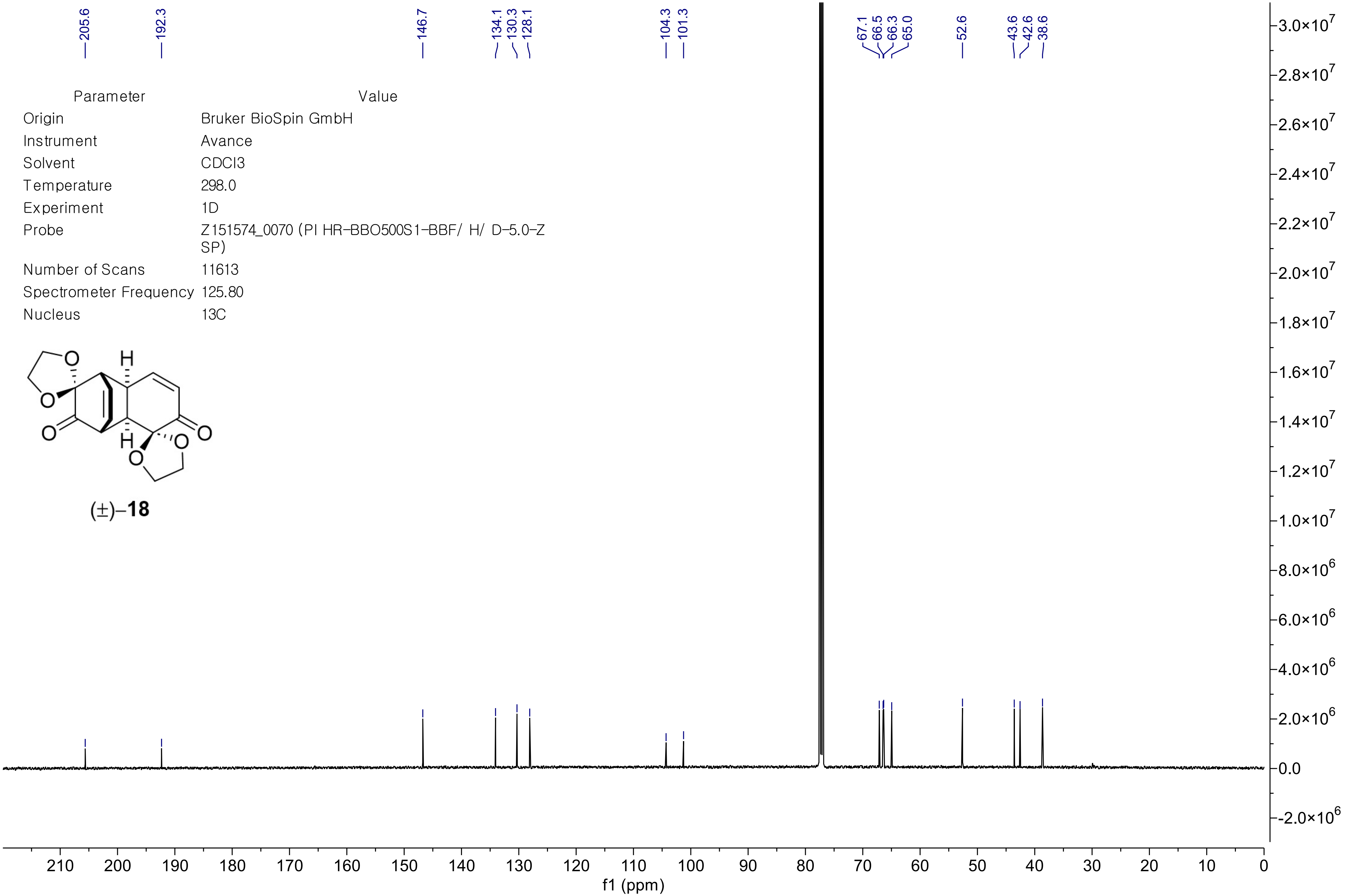
14



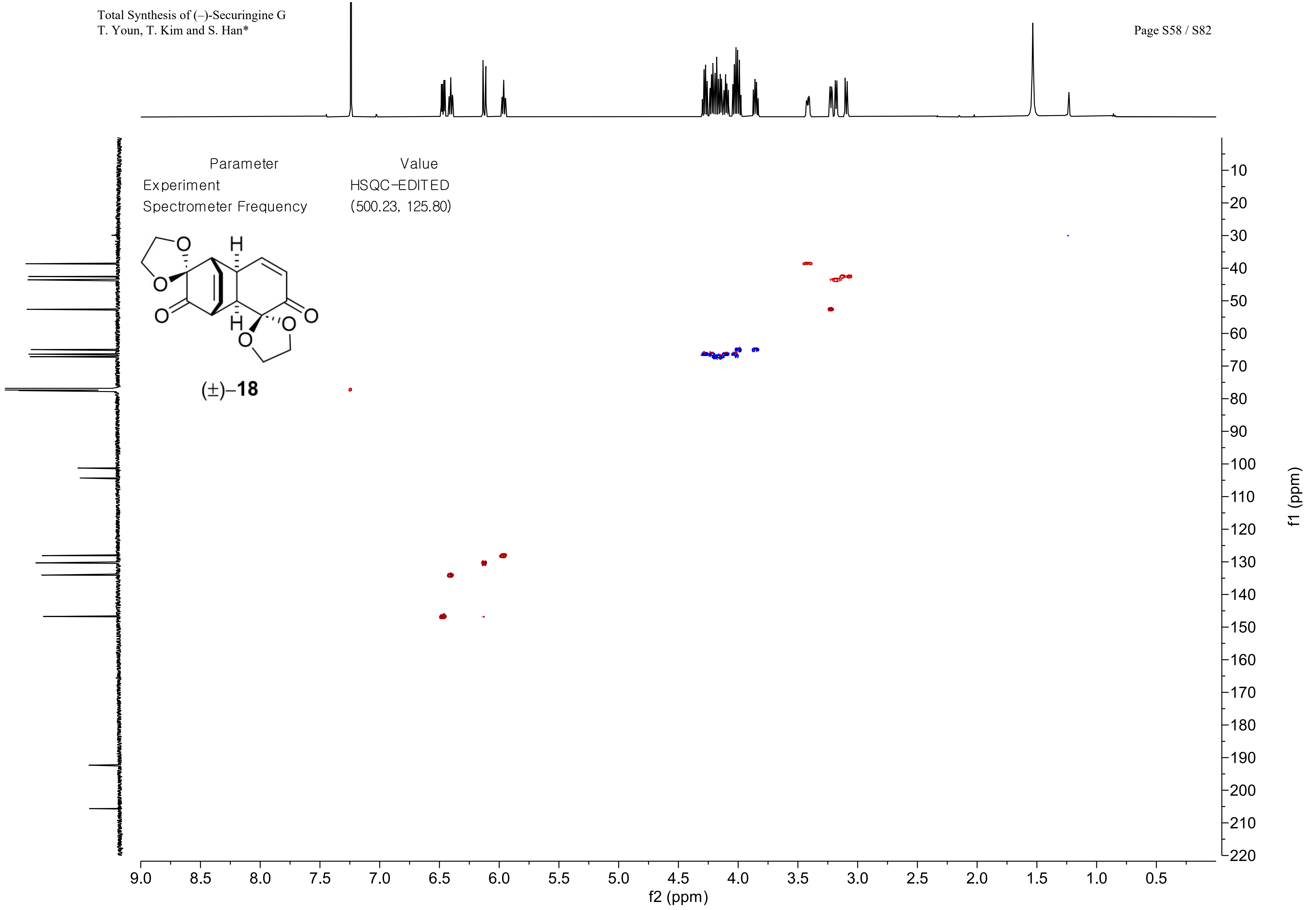
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

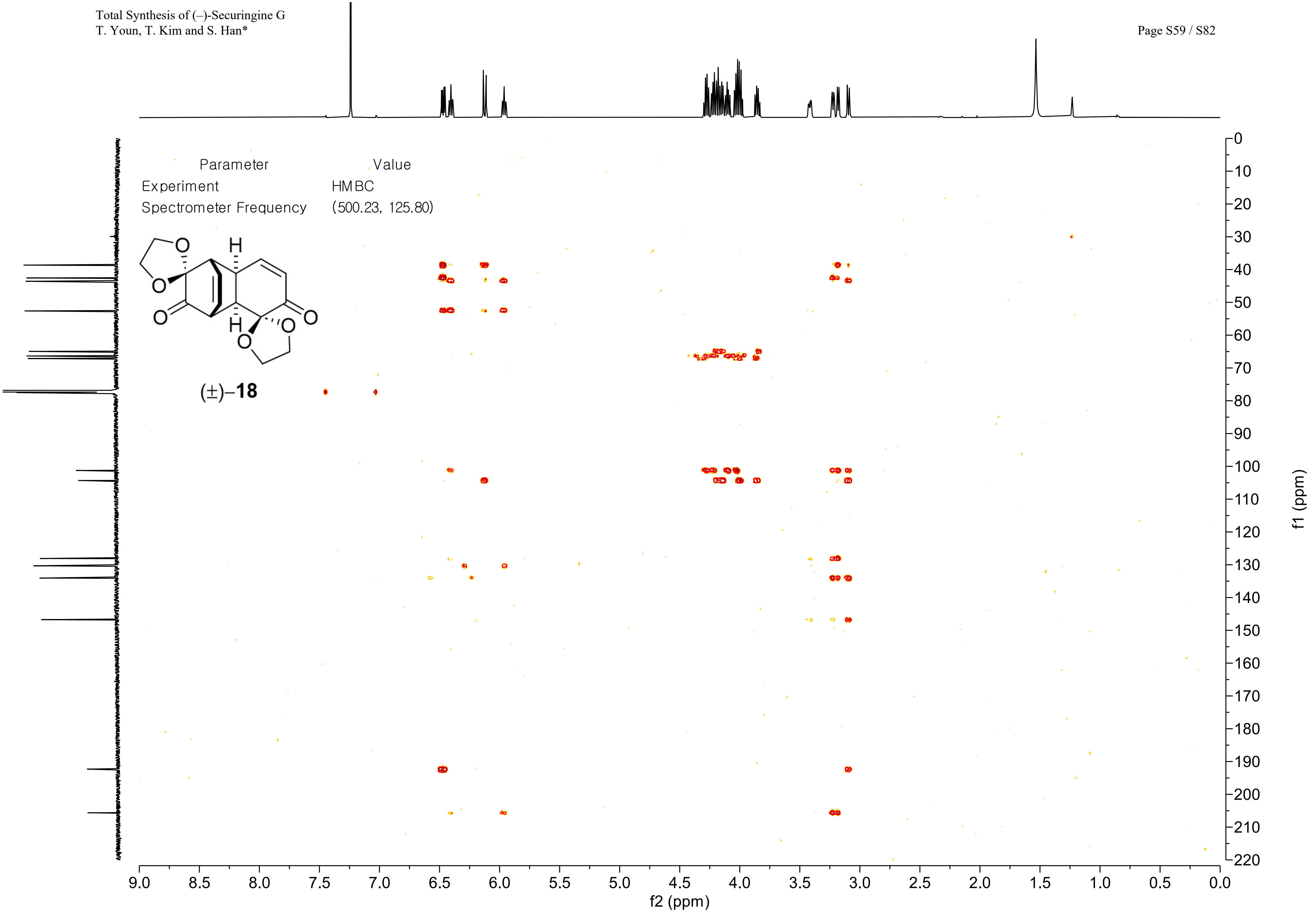
(±)-**18**

Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	11613
Spectrometer Frequency	125.80
Nucleus	13C



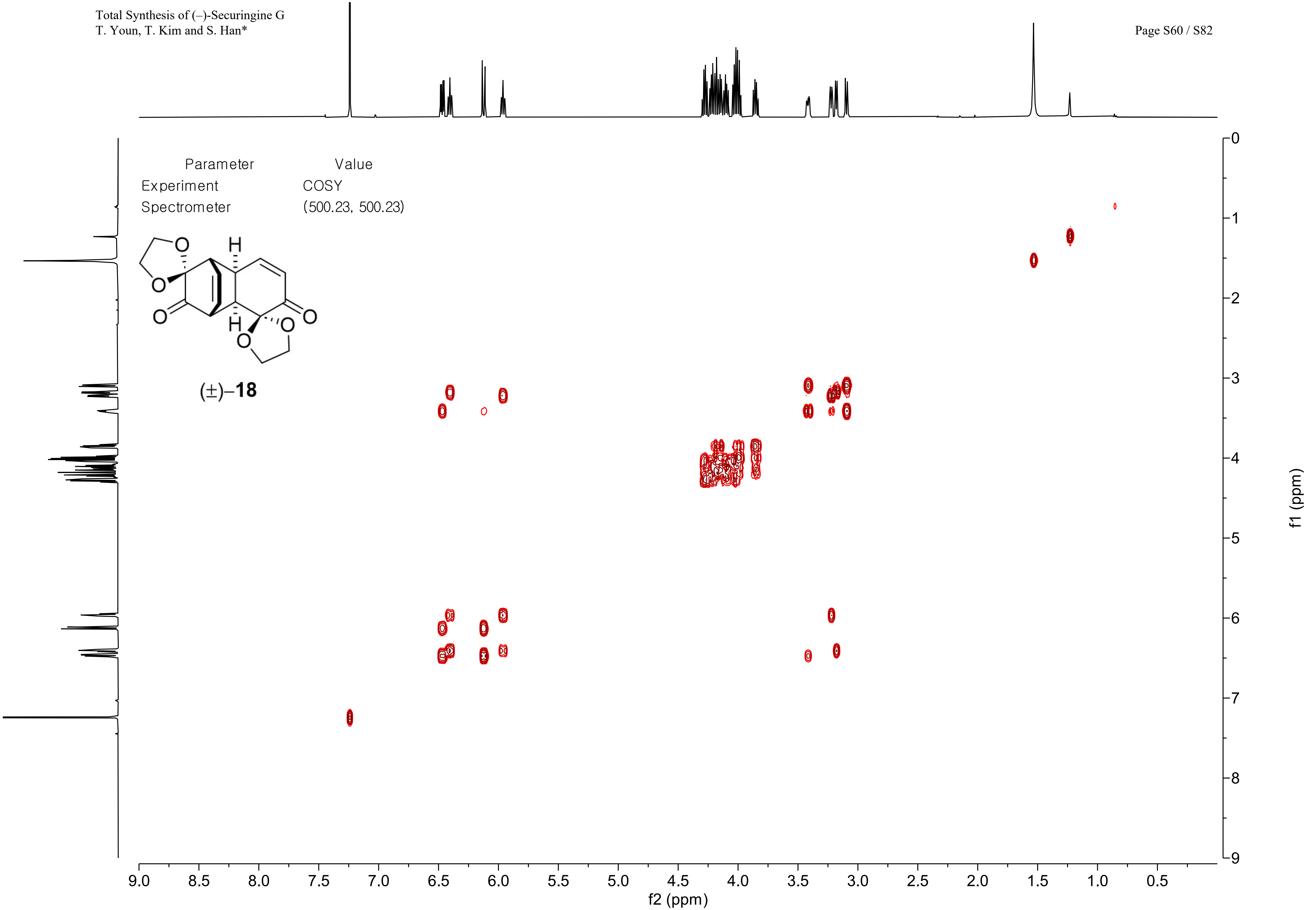
(±)-**18**


Parameter
Value
Experiment
HSQC-EDITED
Spectrometer Frequency
(500.23, 125.80)
(±)–18
f1 (ppm)
f2 (ppm)
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
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220



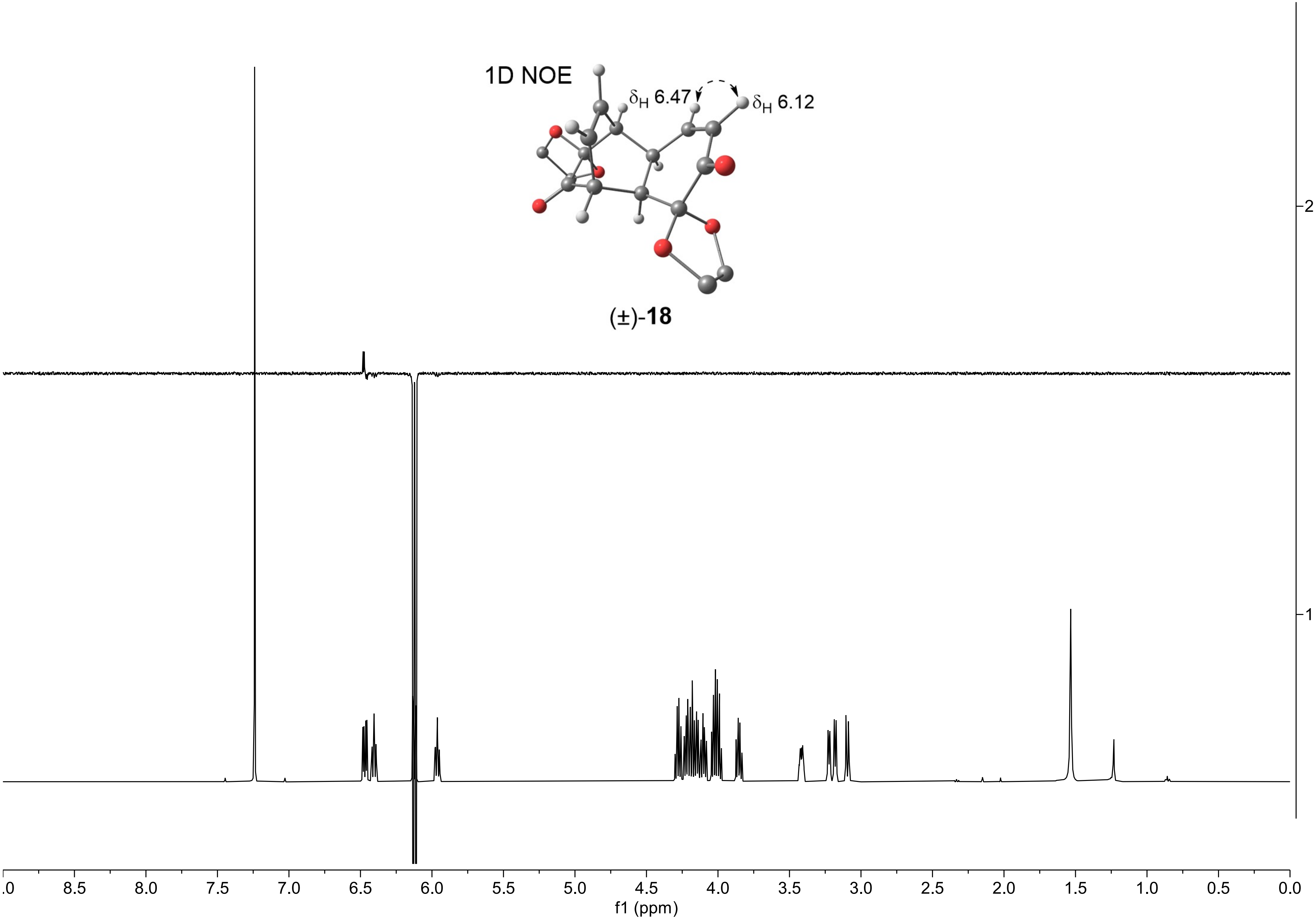
Parameter	Value
Experiment	HMBC
Spectrometer Frequency	(500.23, 125.80)

(±)–**18**



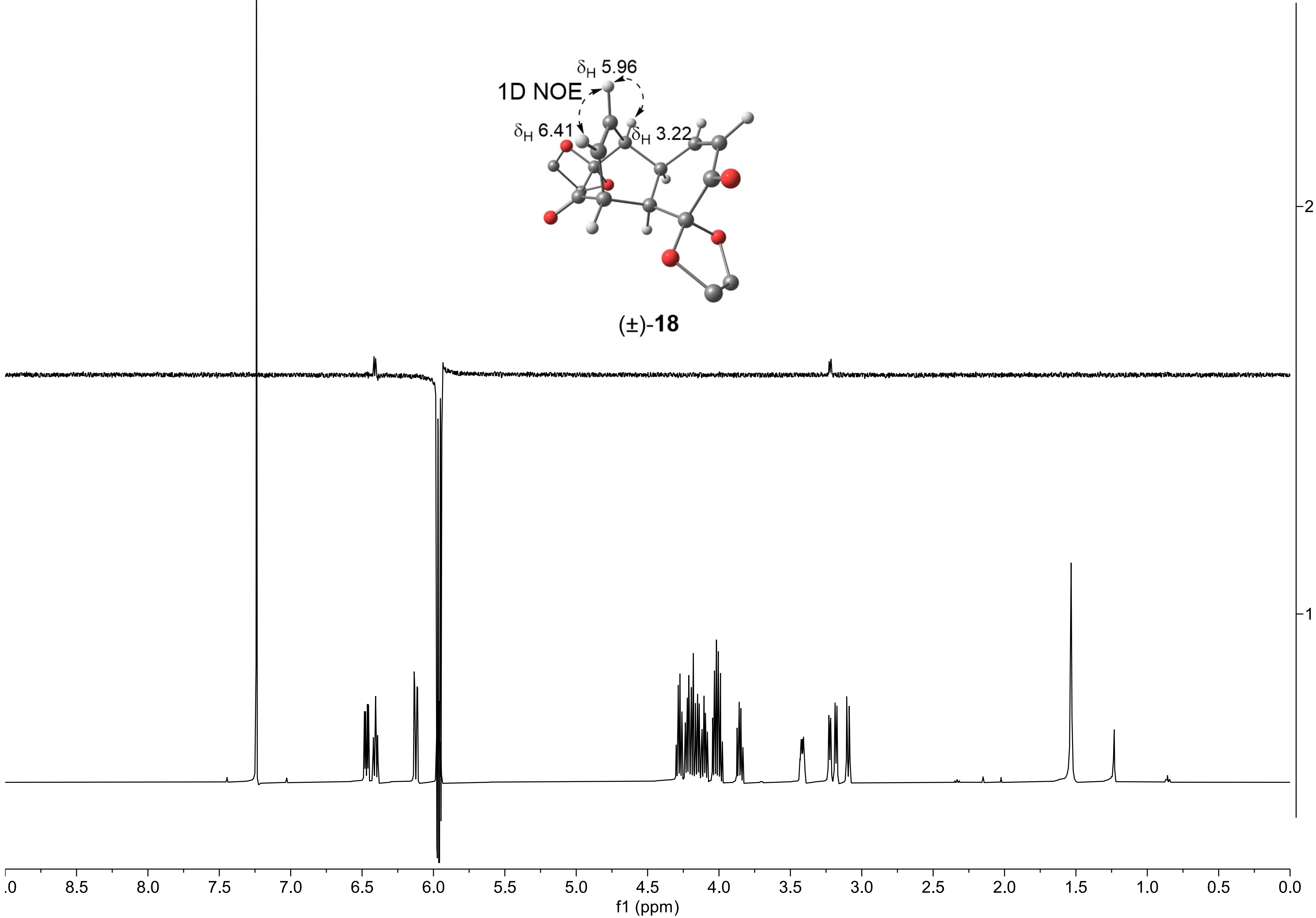
Parameter	Value
Experiment	COSY
Spectrometer	(500.23, 500.23)

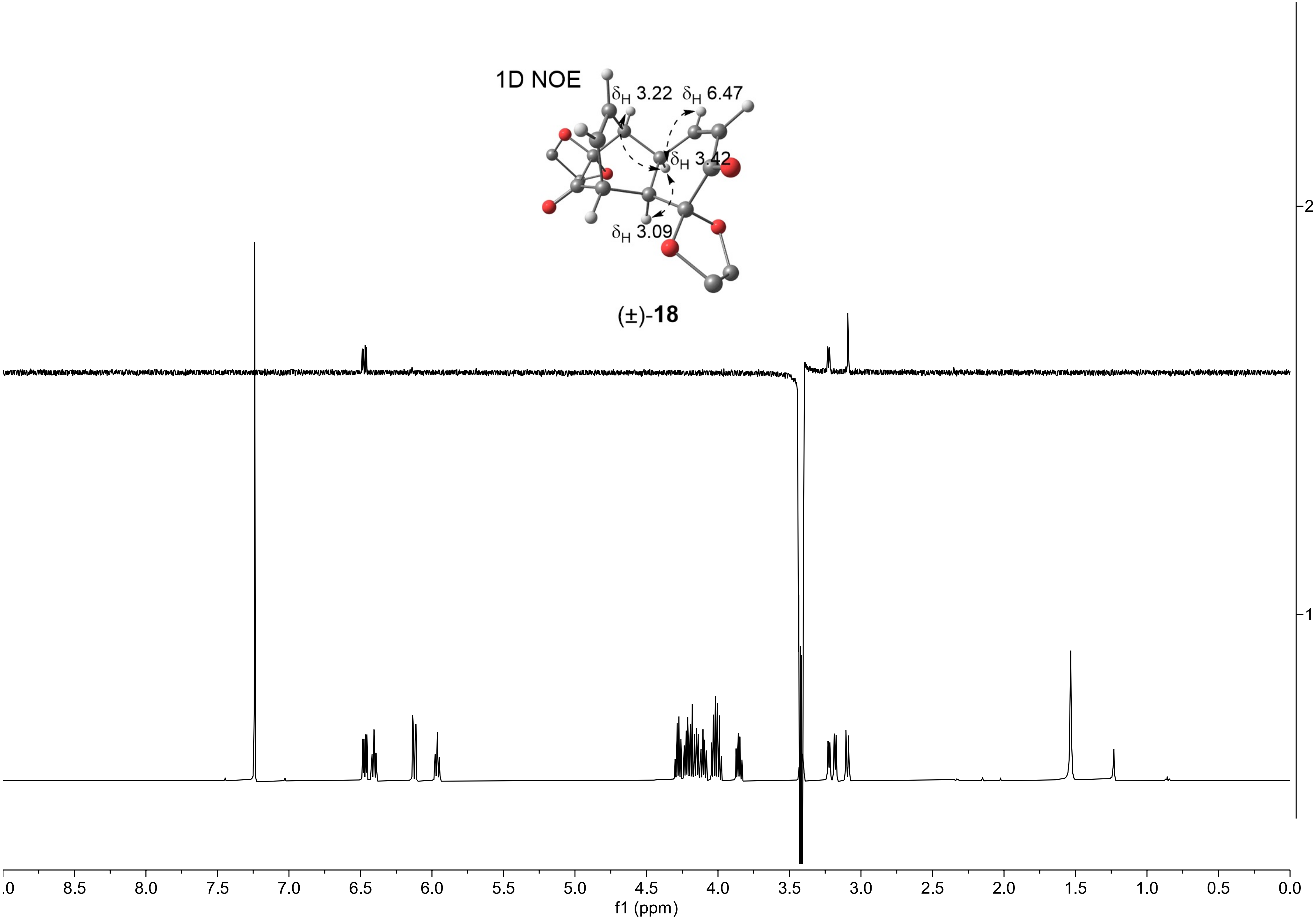
(±)–**18**

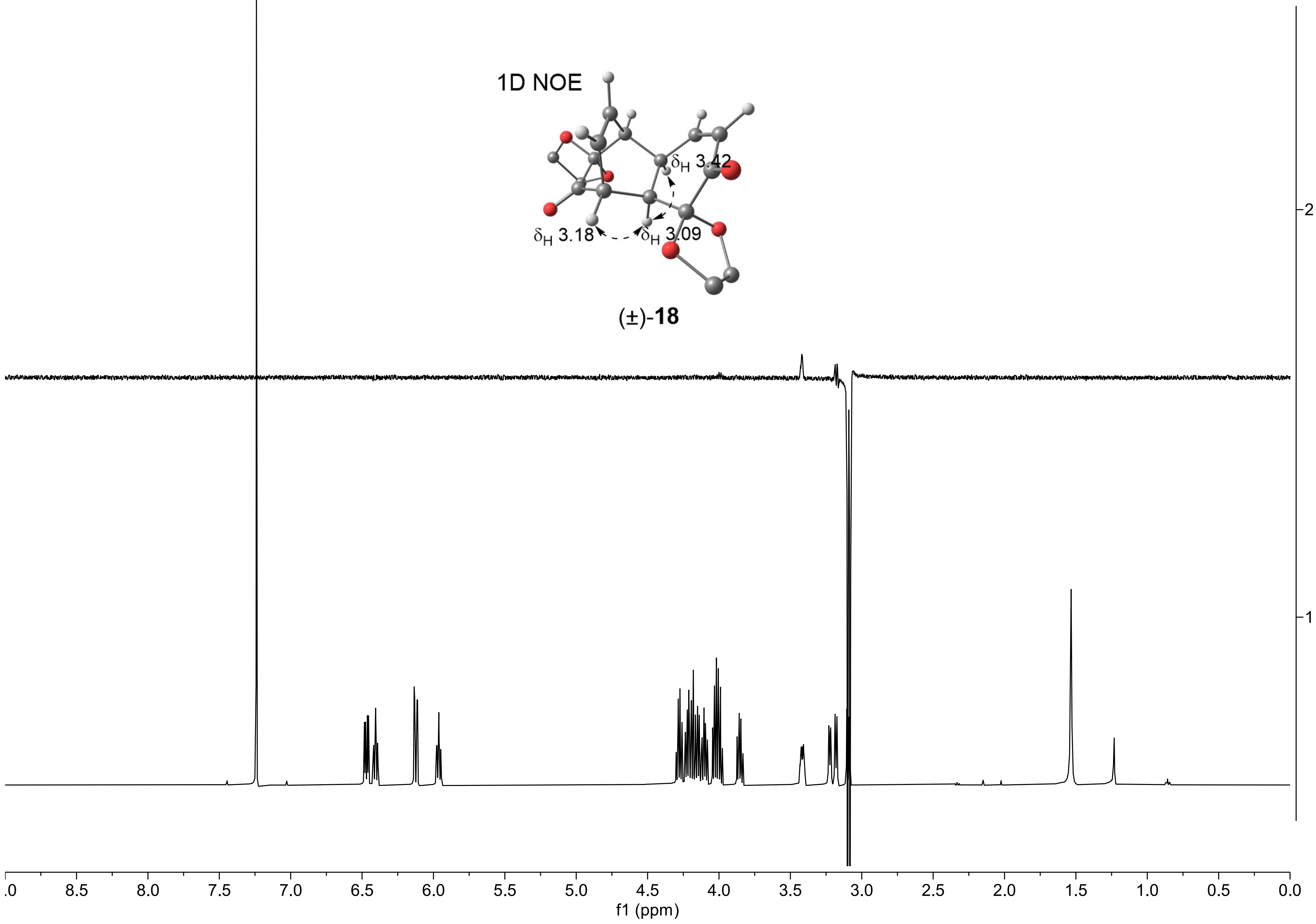

1D NOE
δH 6.47
δH 6.12
(±)-18
2
1
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

1D NOE
δ_H 5.96
δ_H 6.41
δ_H 3.22

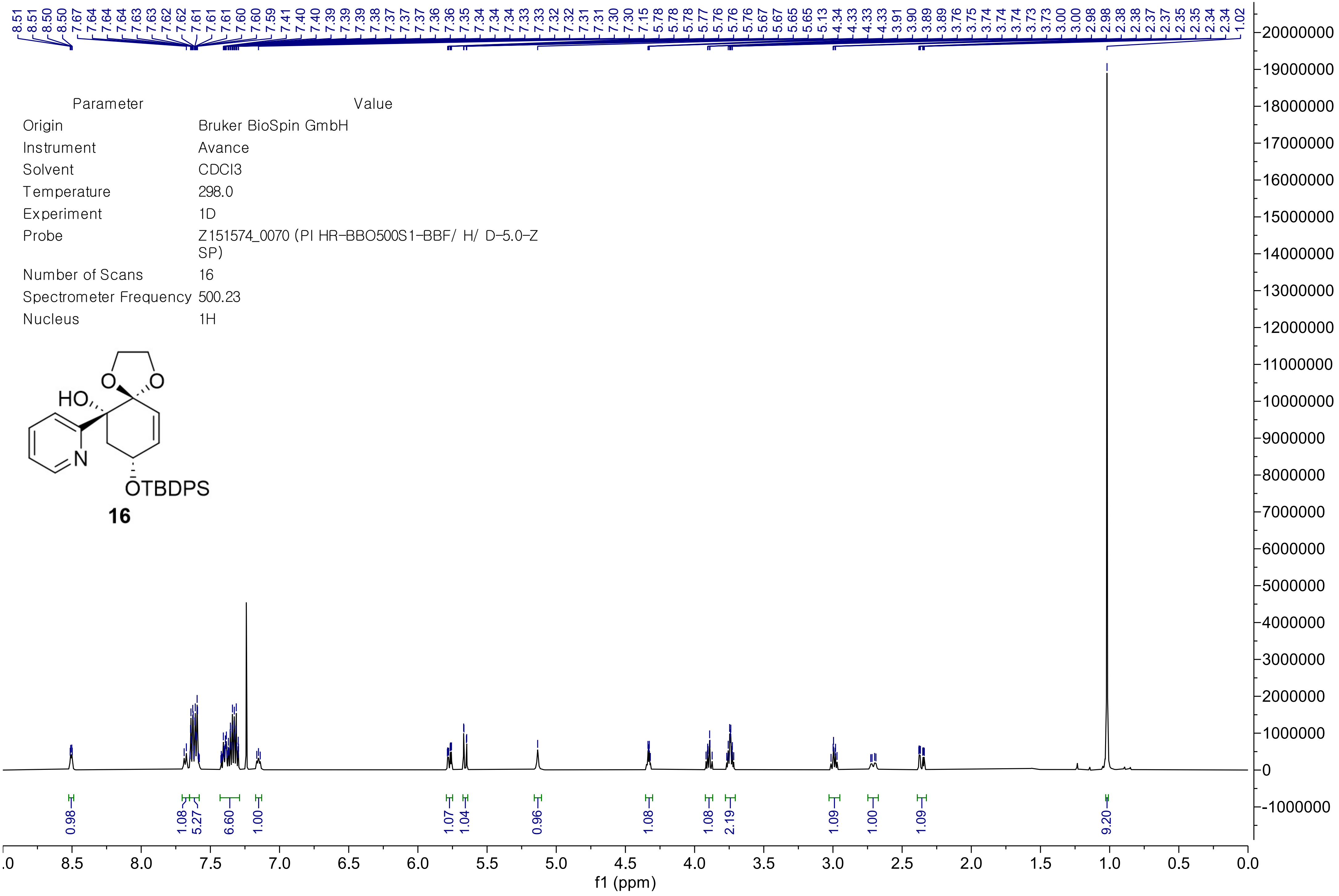
(±)-**18**


2
1
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)


1D NOE
δ_H 3.22
δ_H 6.47
δ_H 3.42
δ_H 3.09
(±)-**18**
2
1
.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)


1D NOE
δH 3.42
δH 3.18
δH 3.09
2
1
.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)

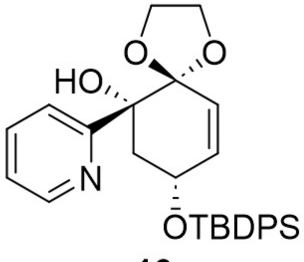
(±)-**18**



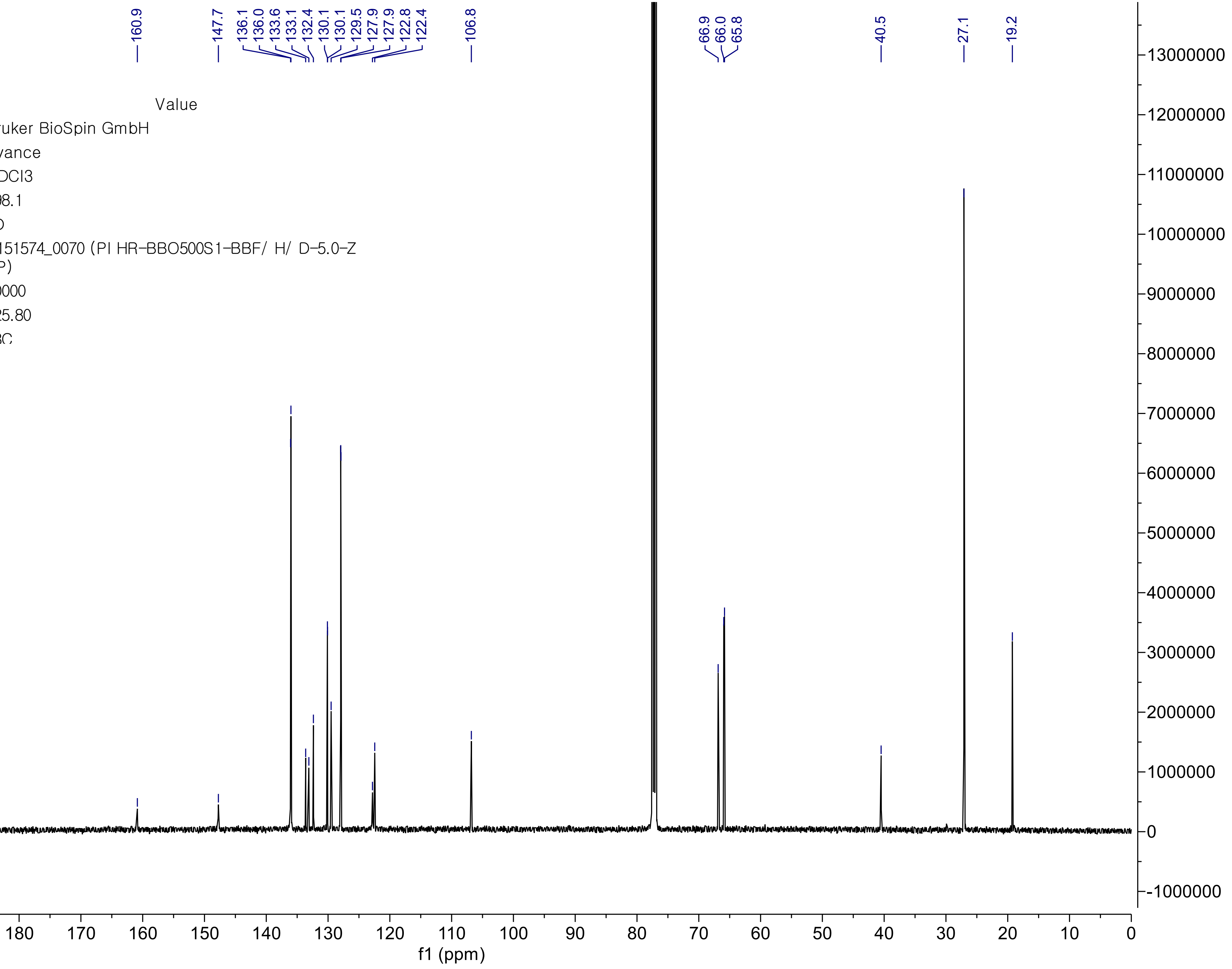
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

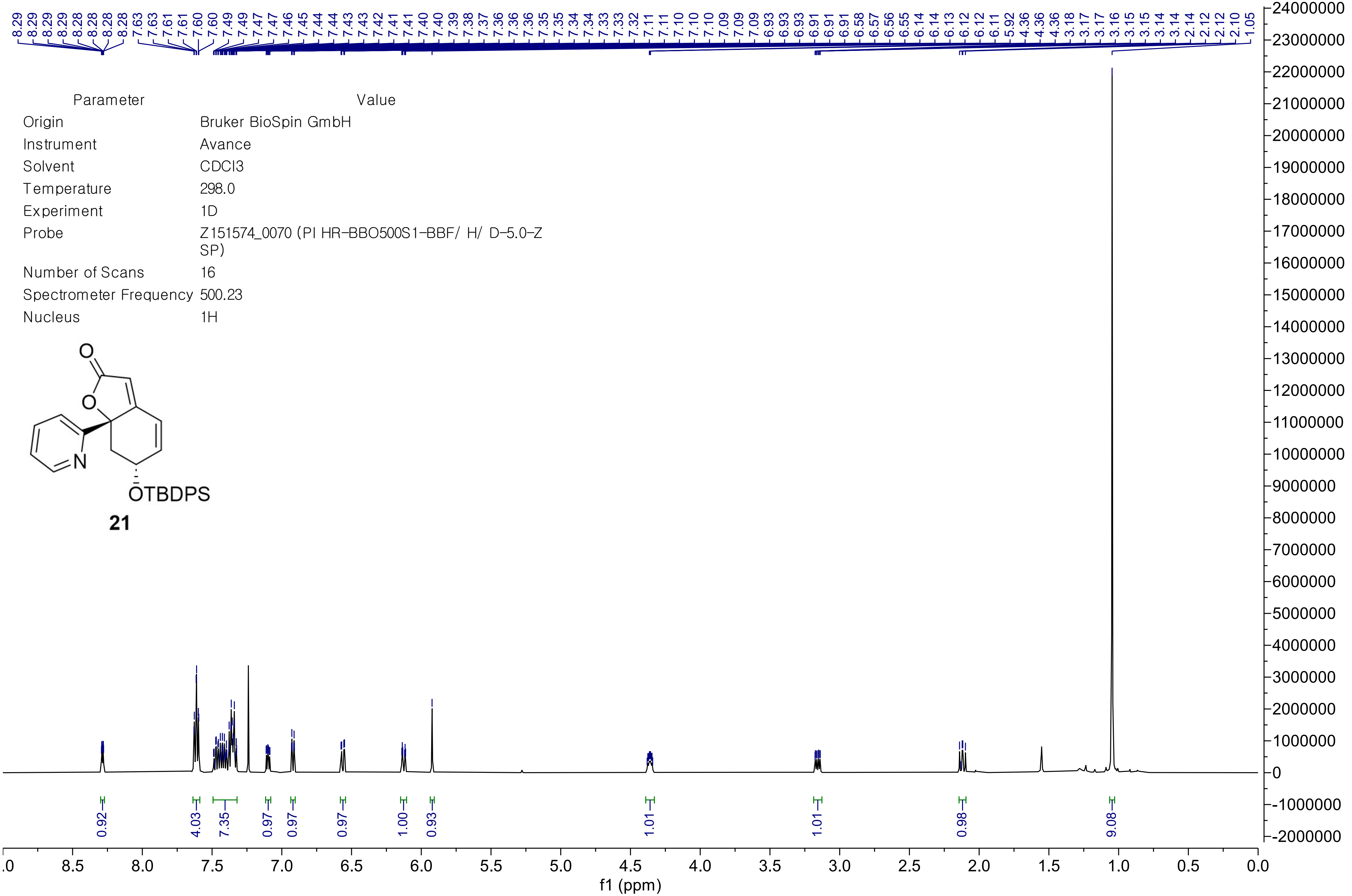
16

Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.1
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	10000
Spectrometer Frequency	125.80
Nucleus	13C



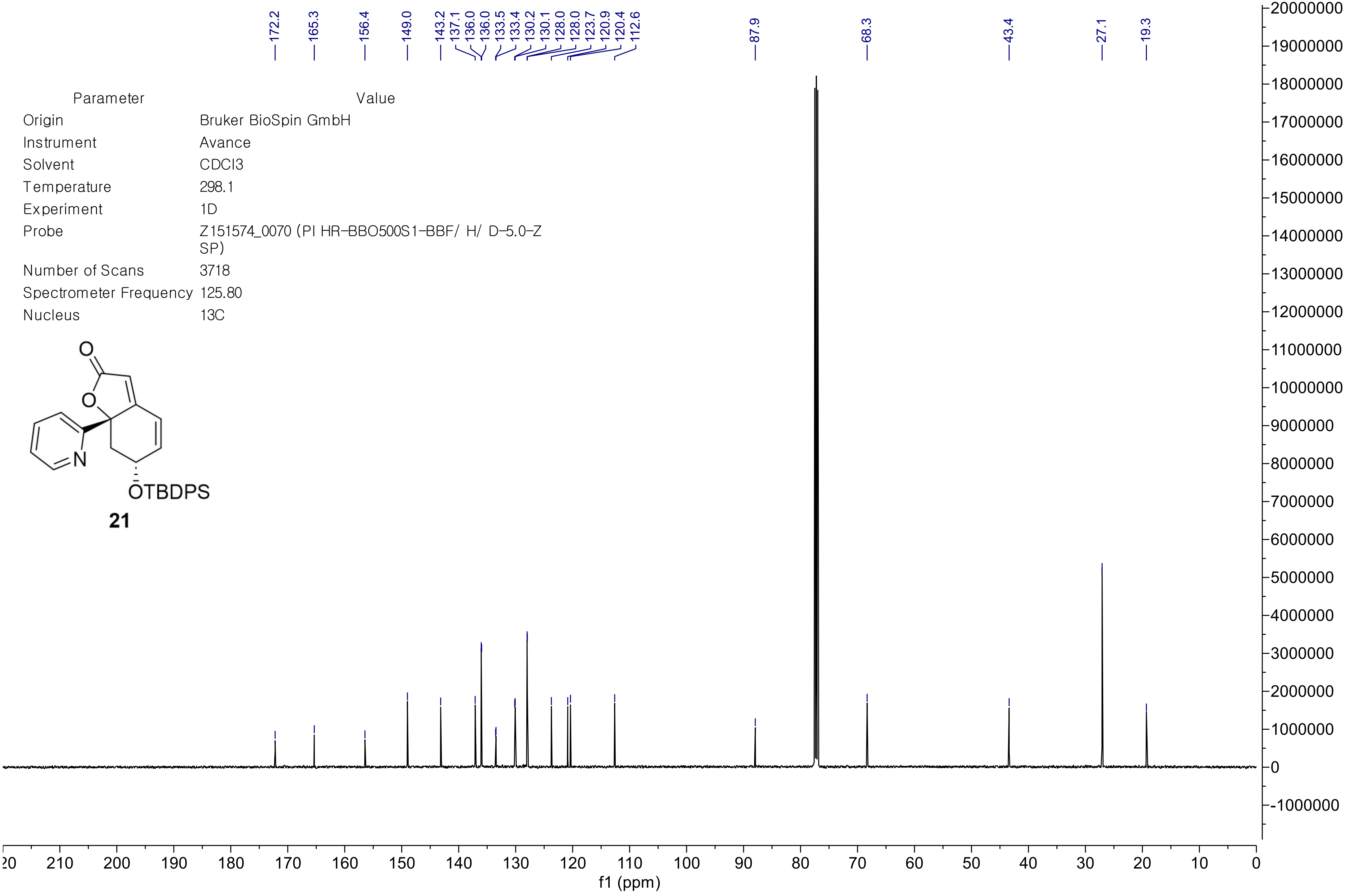
16





Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

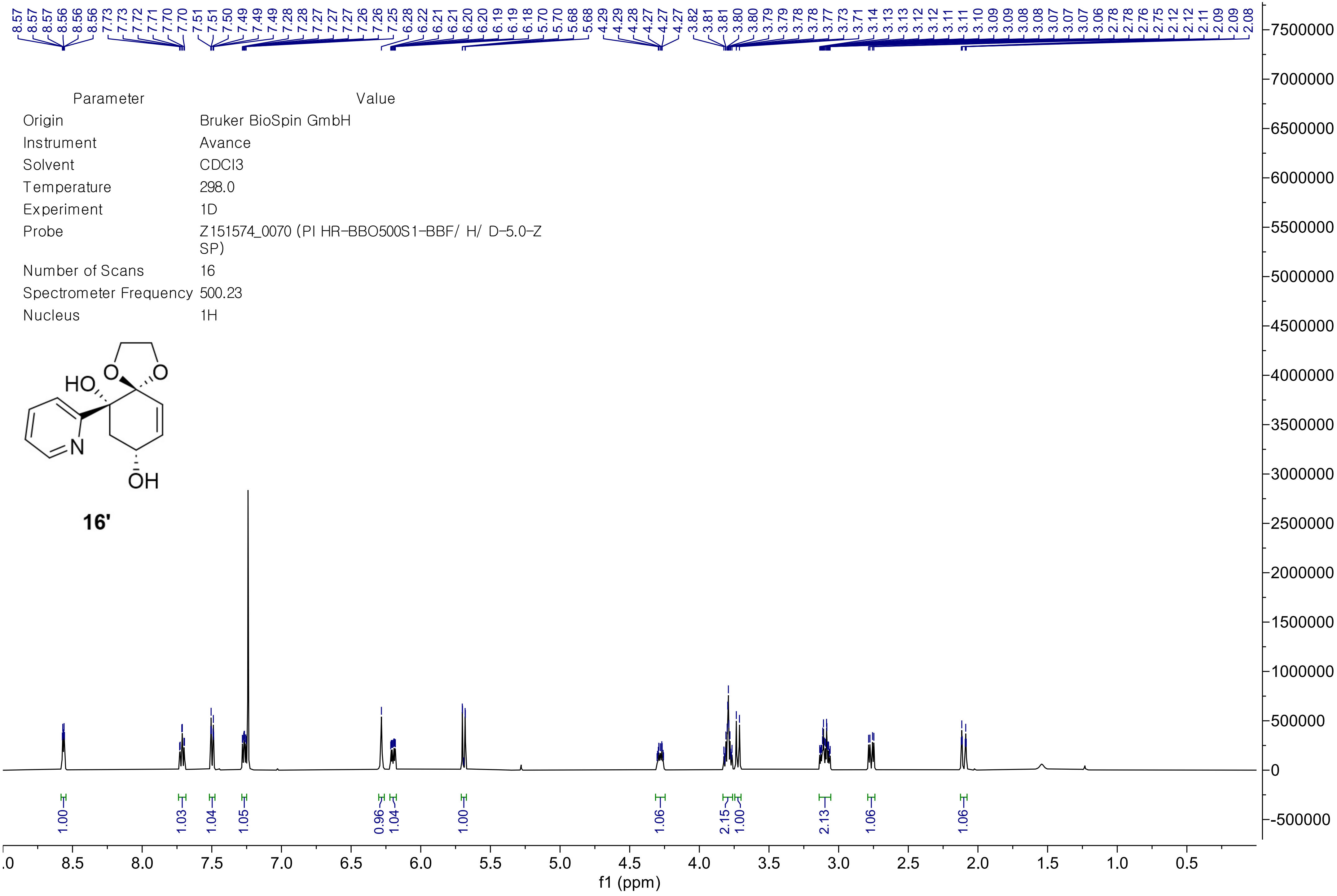
21



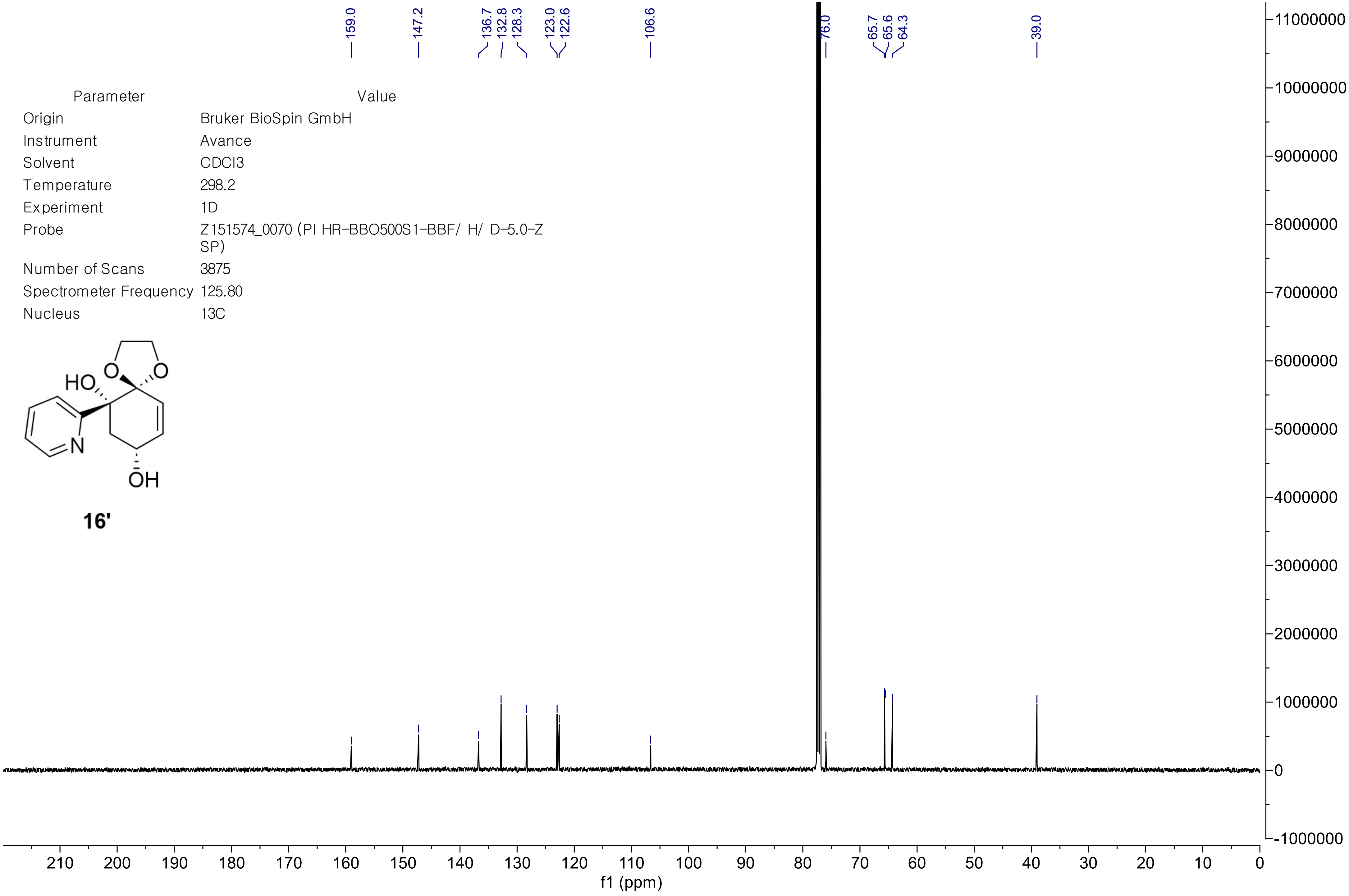
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.1
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	3718
Spectrometer Frequency	125.80
Nucleus	13C

21

Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



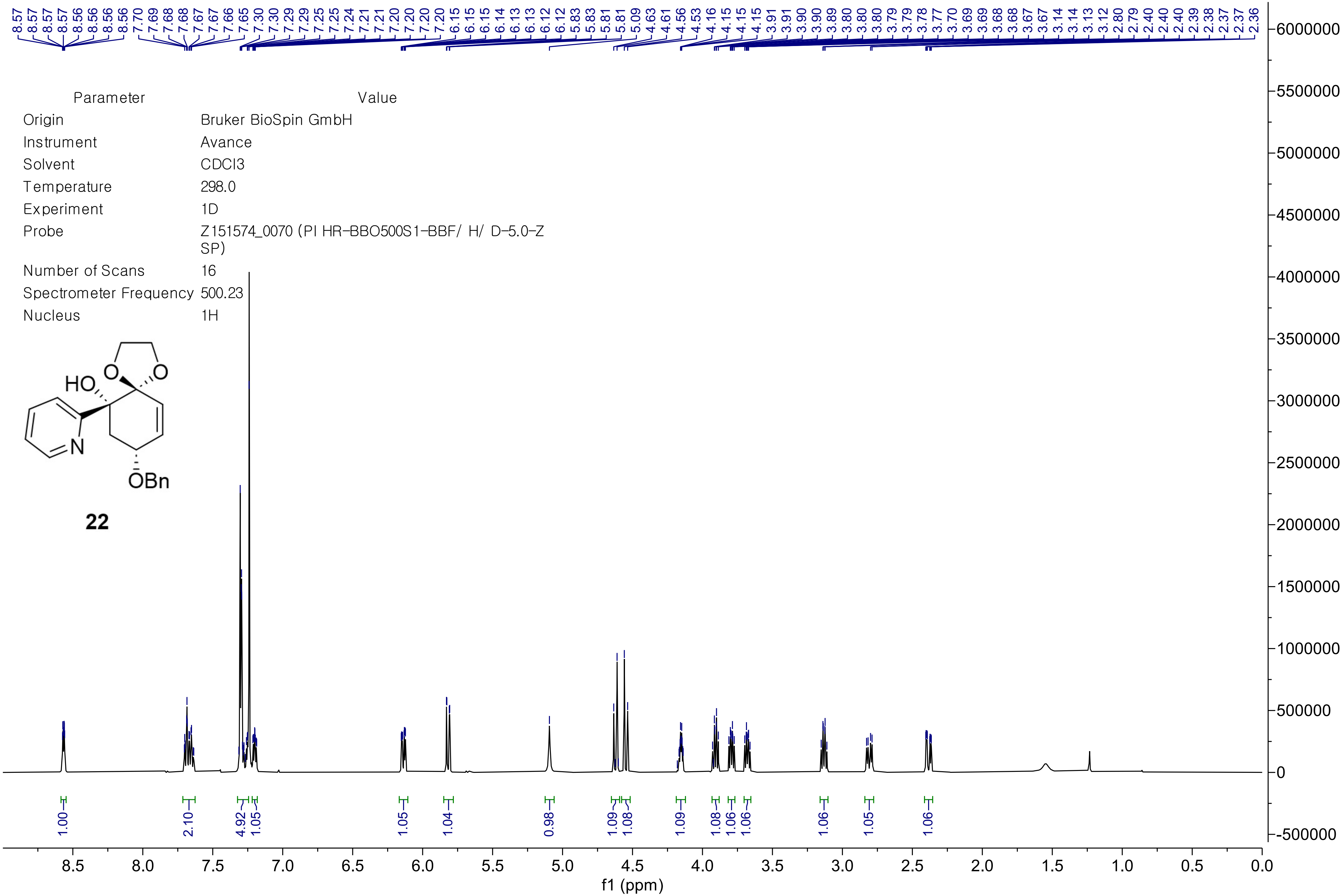
16'



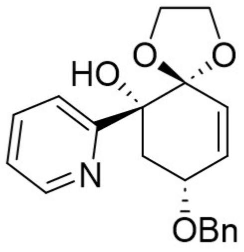
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.2
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	3875
Spectrometer Frequency	125.80
Nucleus	13C

16'

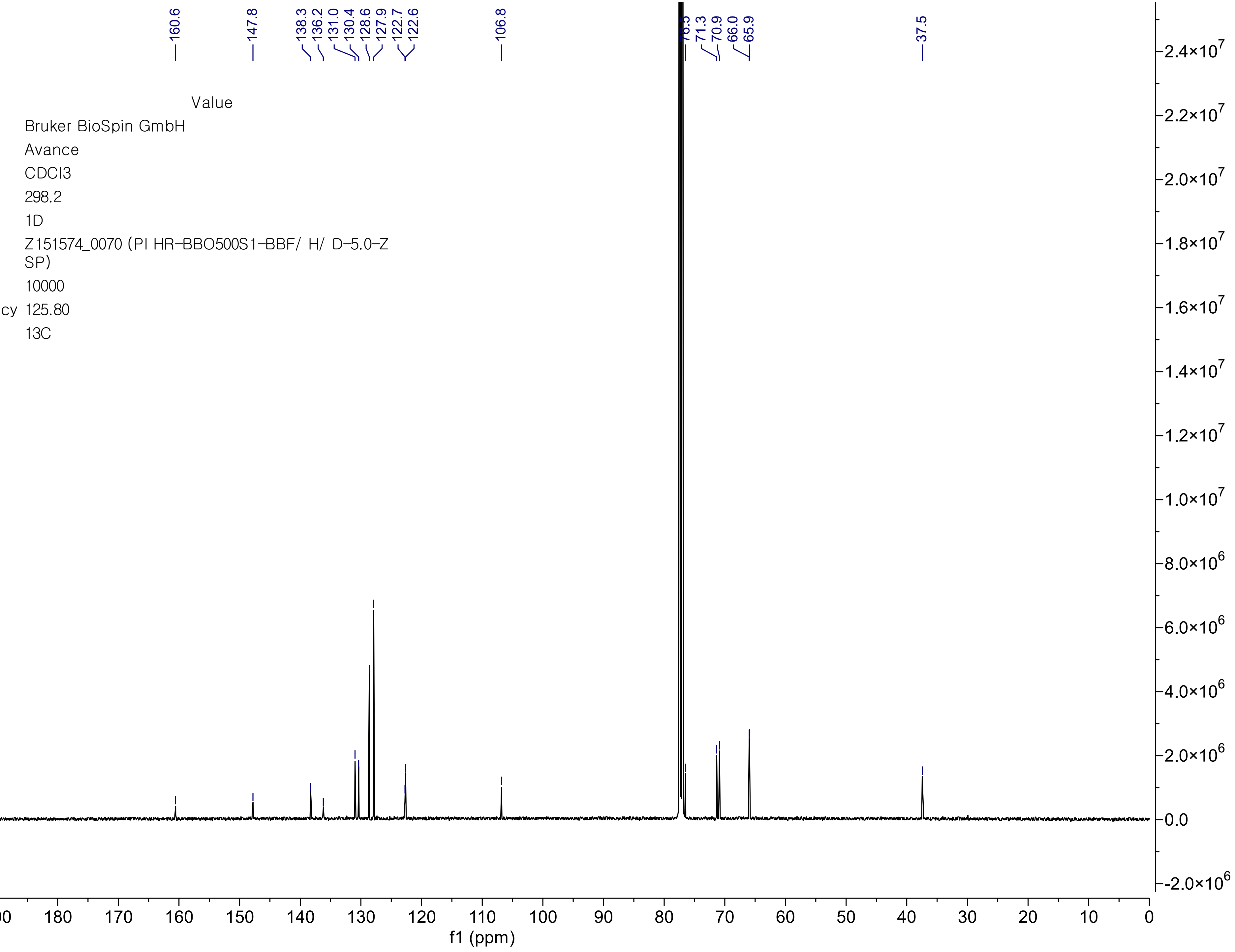
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

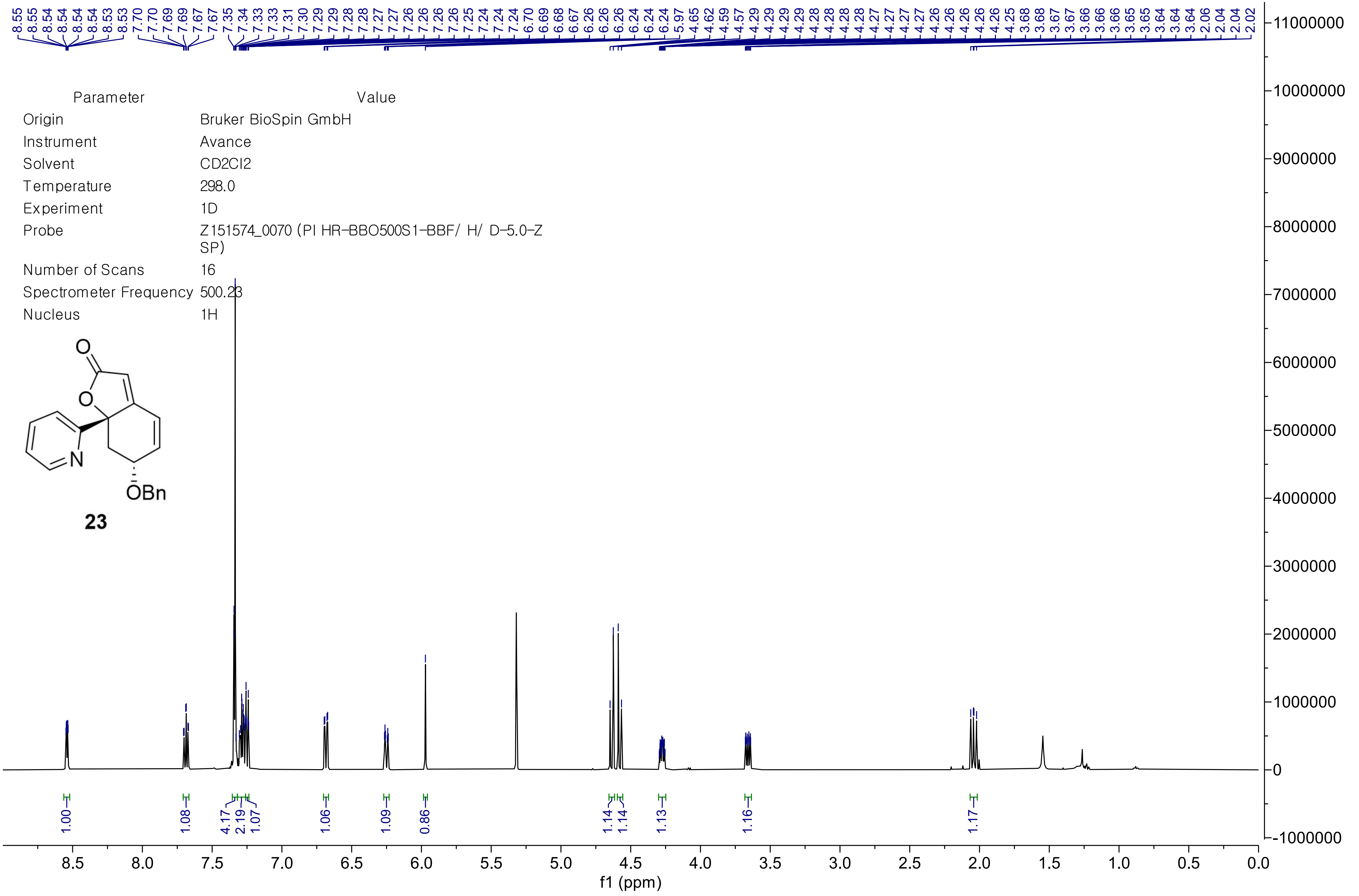


Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.2
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	10000
Spectrometer Frequency	125.80
Nucleus	13C

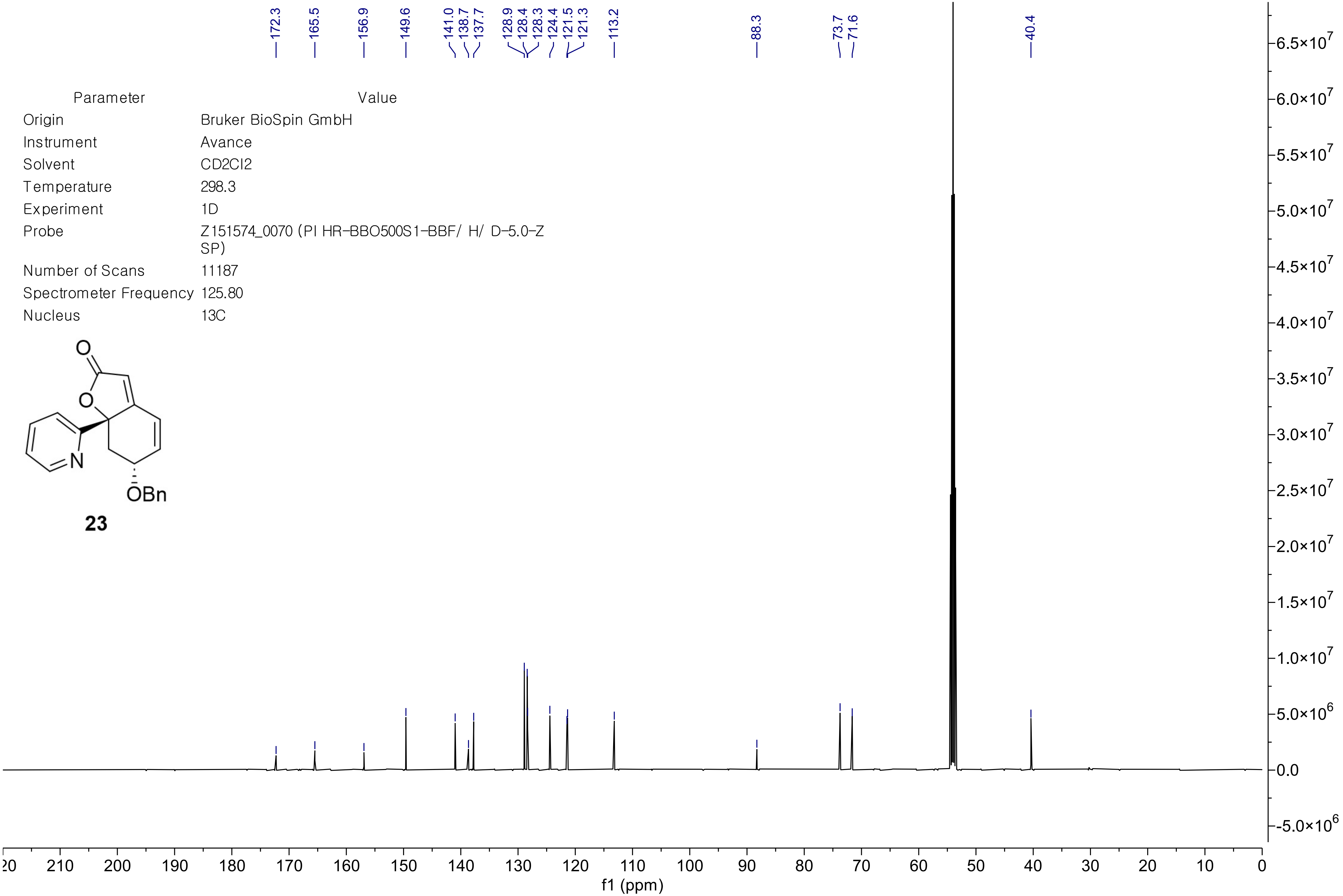


22



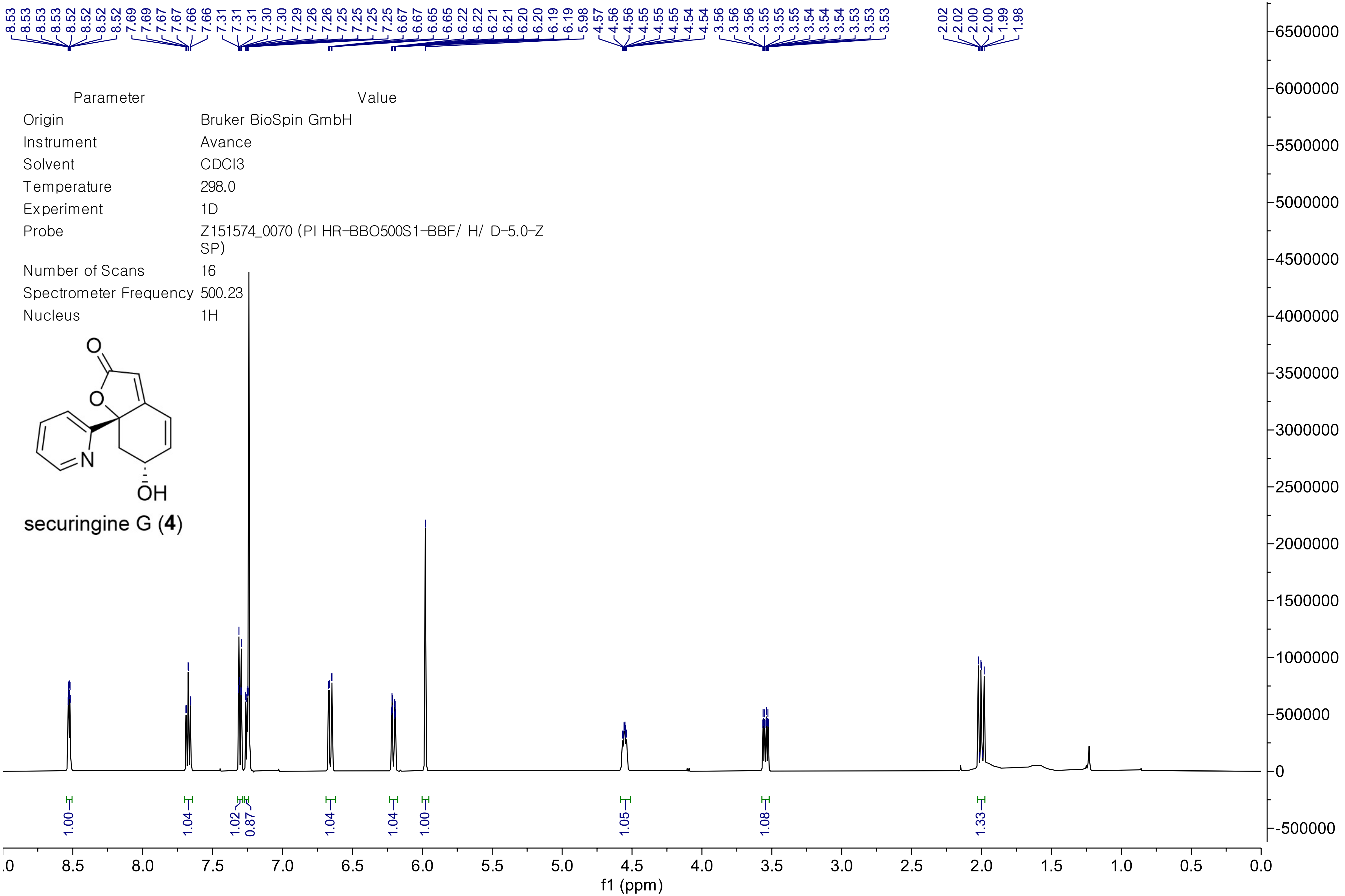


Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CD2Cl2
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



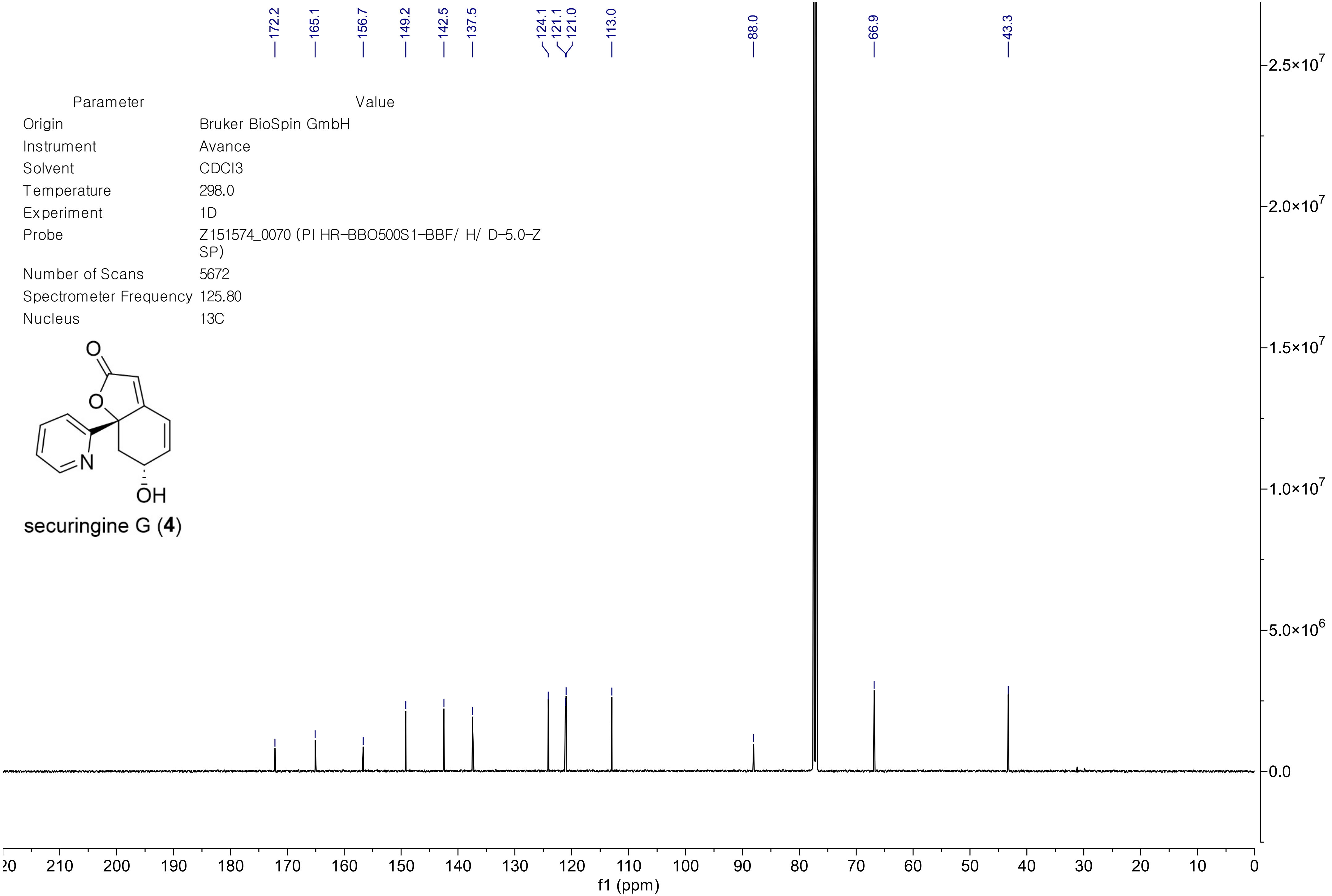
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CD2Cl2
Temperature	298.3
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	11187
Spectrometer Frequency	125.80
Nucleus	13C

23



Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

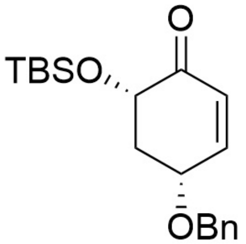
securingine G (**4**)



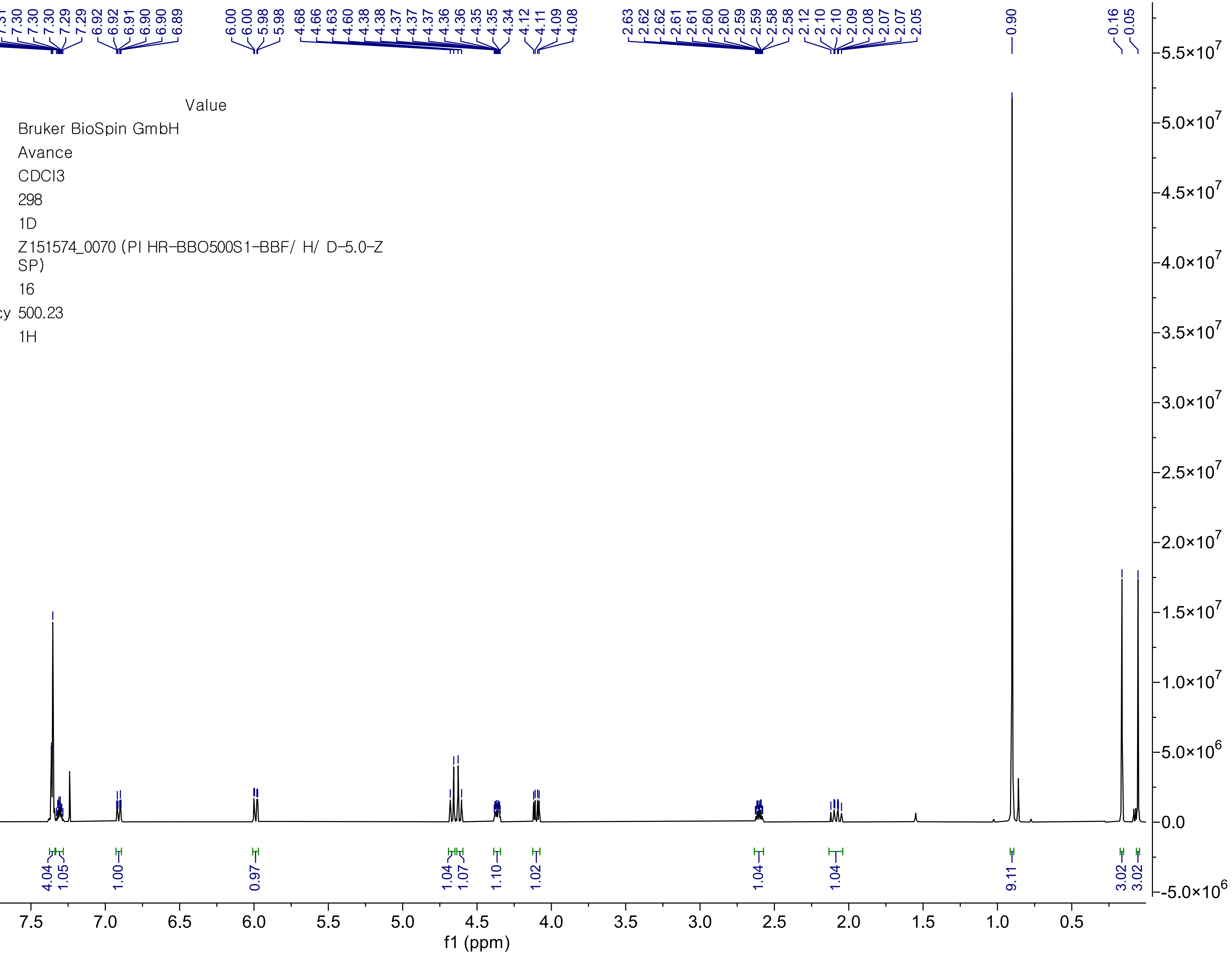
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298.0
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	5672
Spectrometer Frequency	125.80
Nucleus	13C

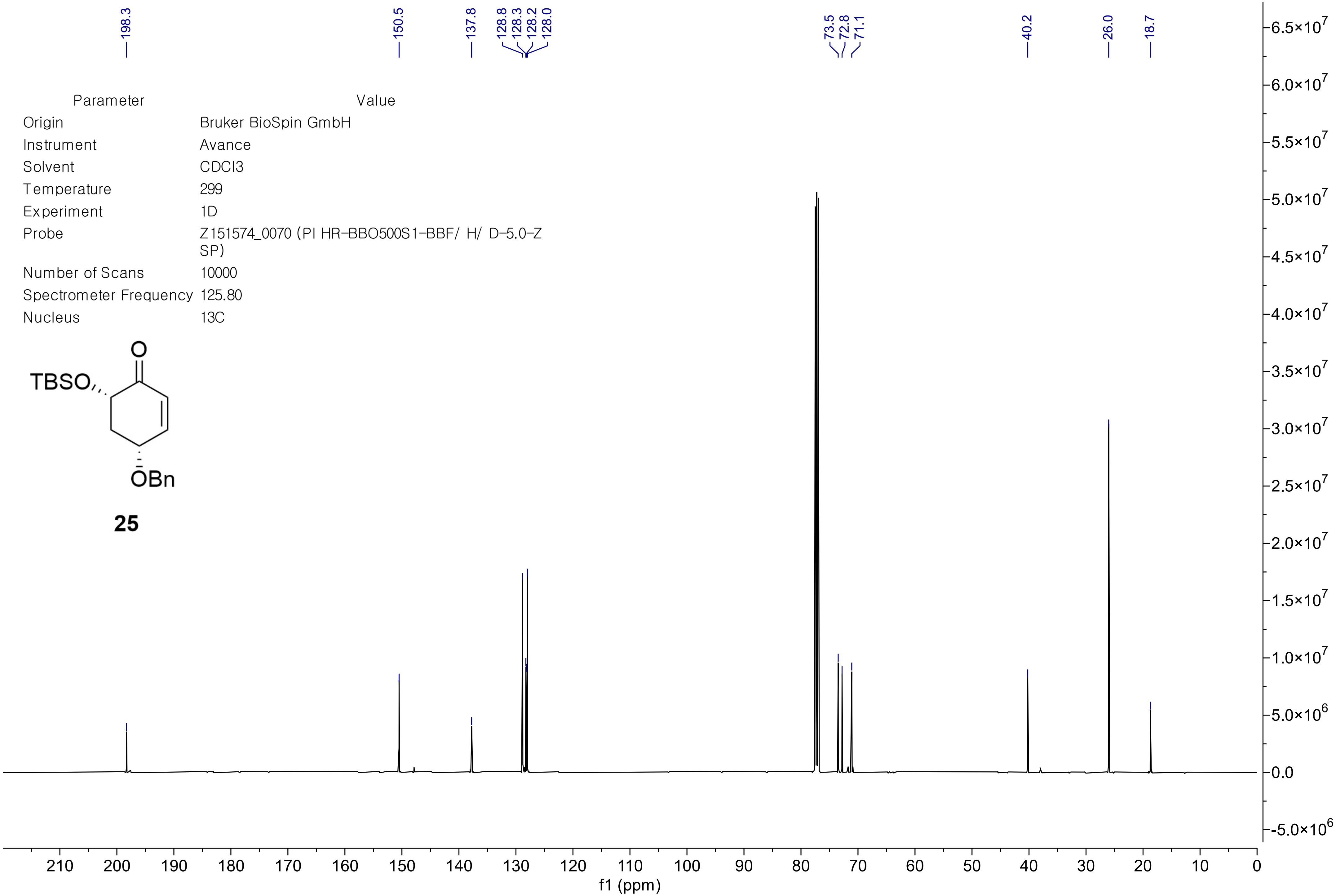
securingine G (**4**)

Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H



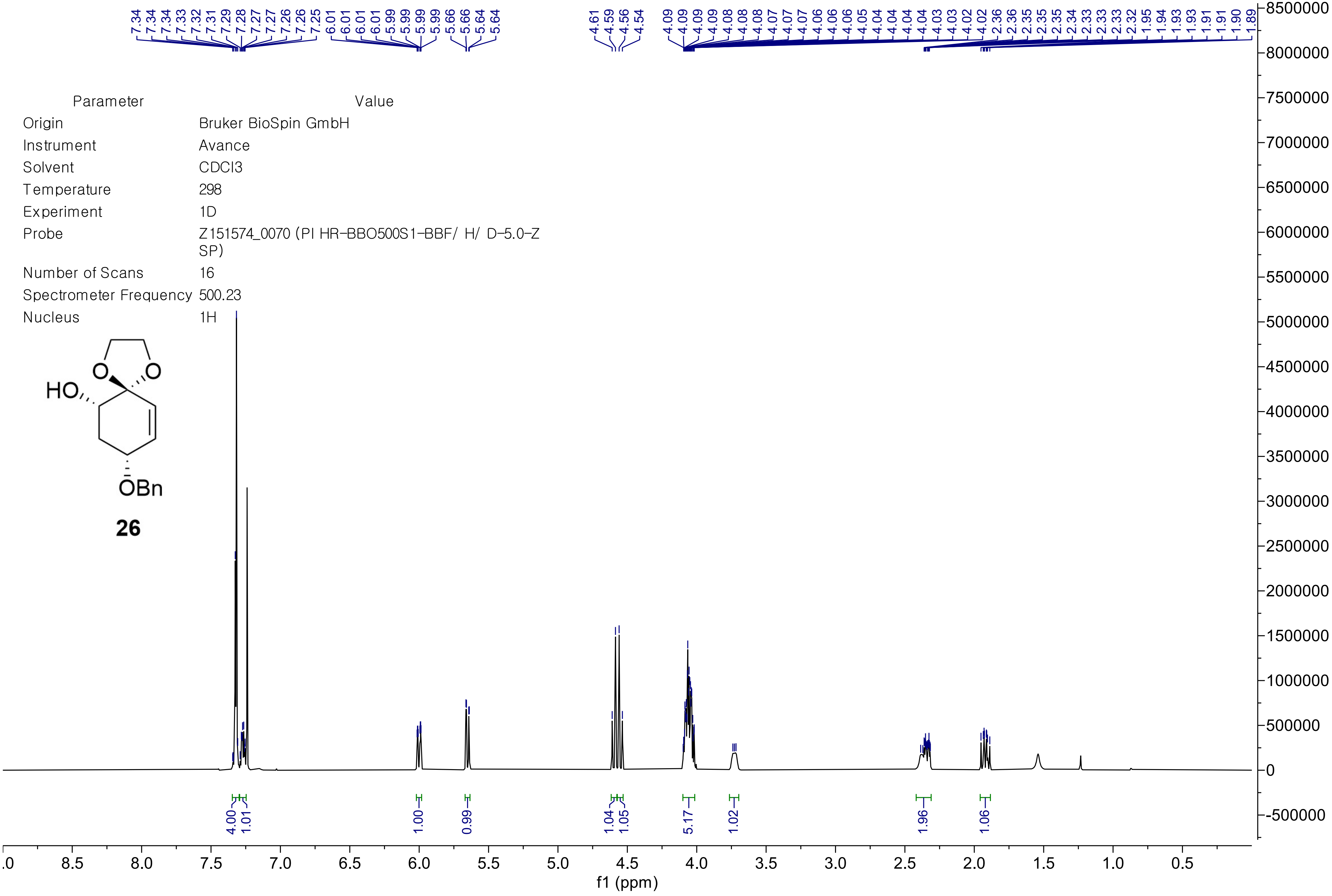
25





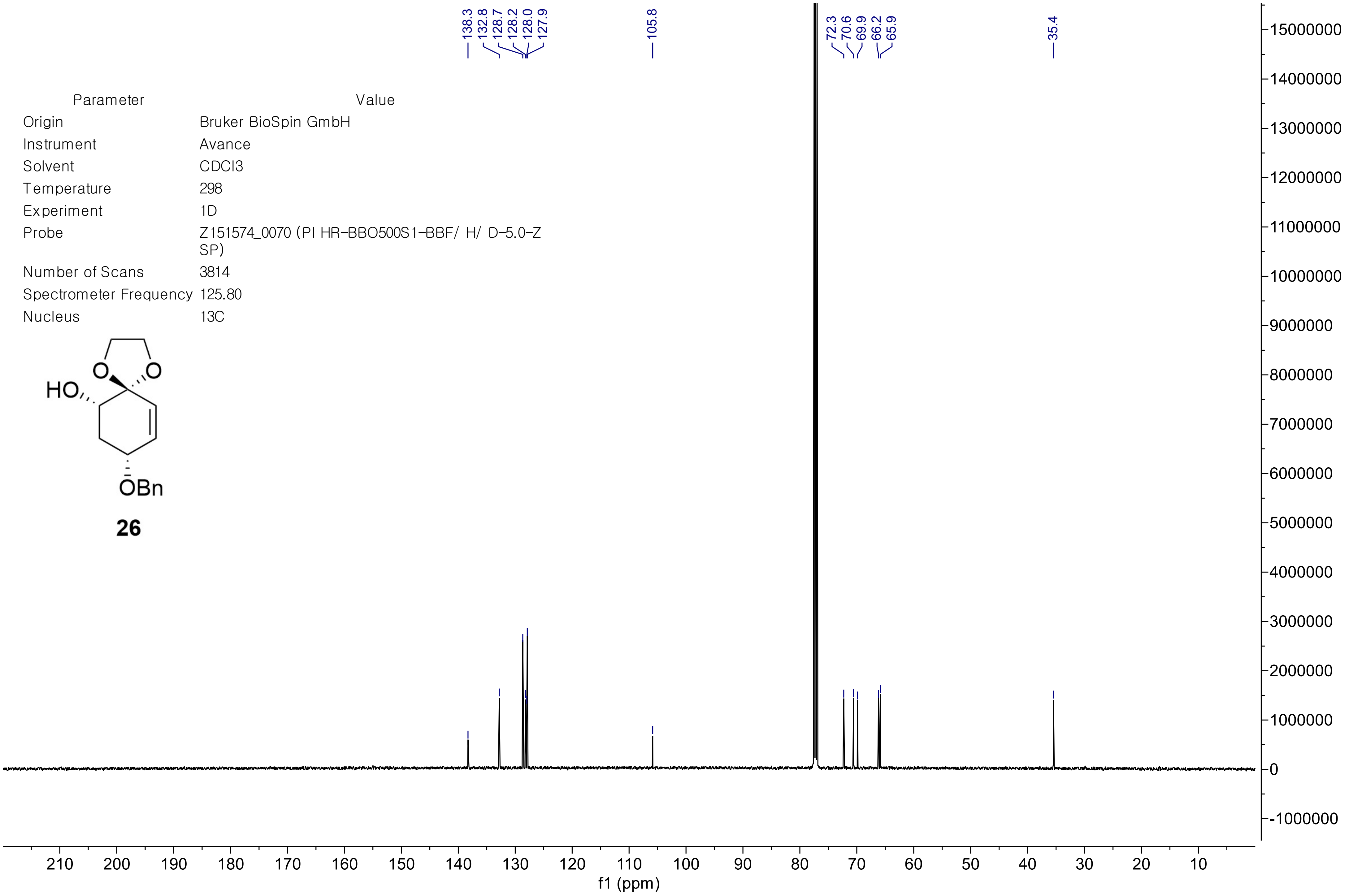
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	299
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	10000
Spectrometer Frequency	125.80
Nucleus	13C

25



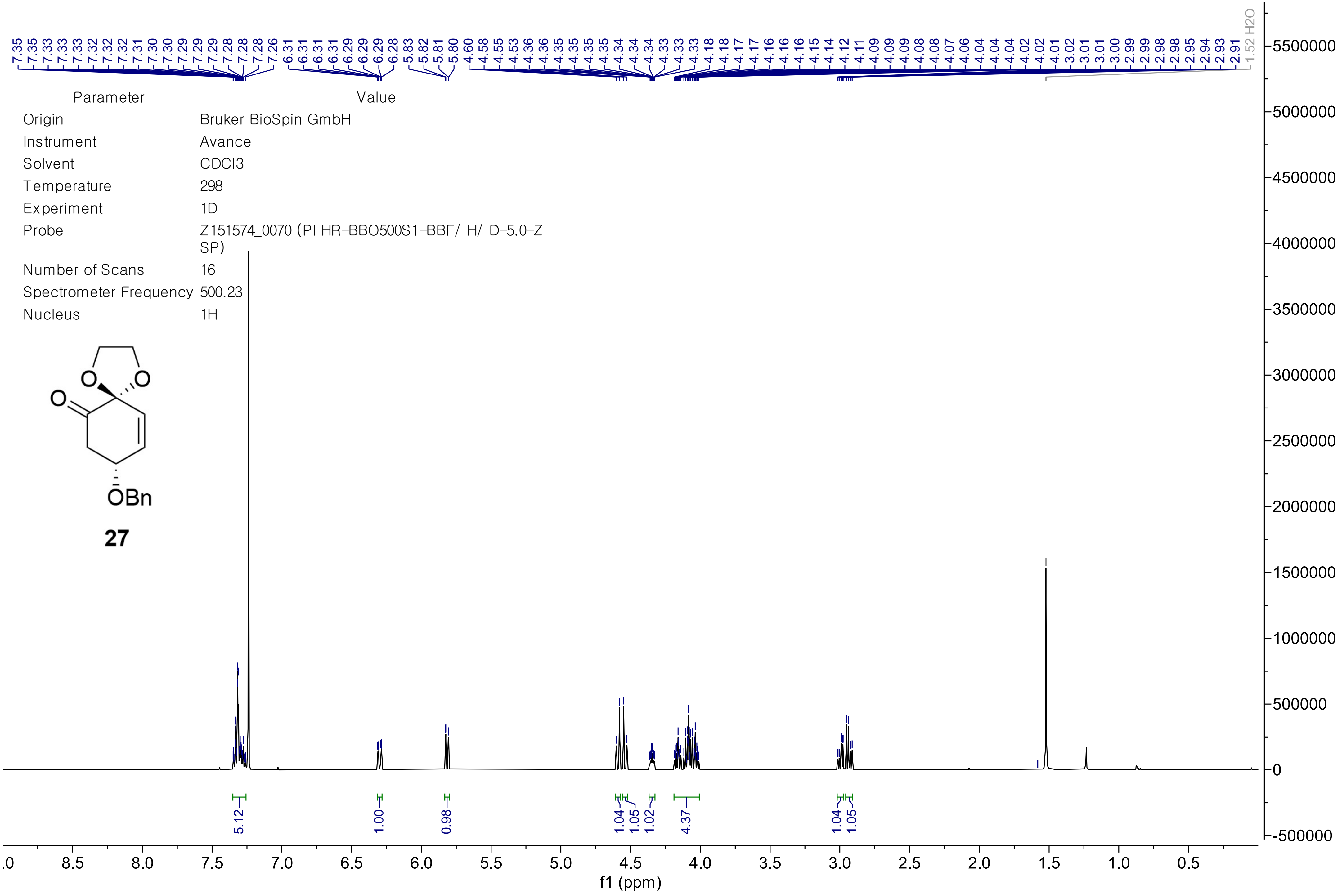
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

26



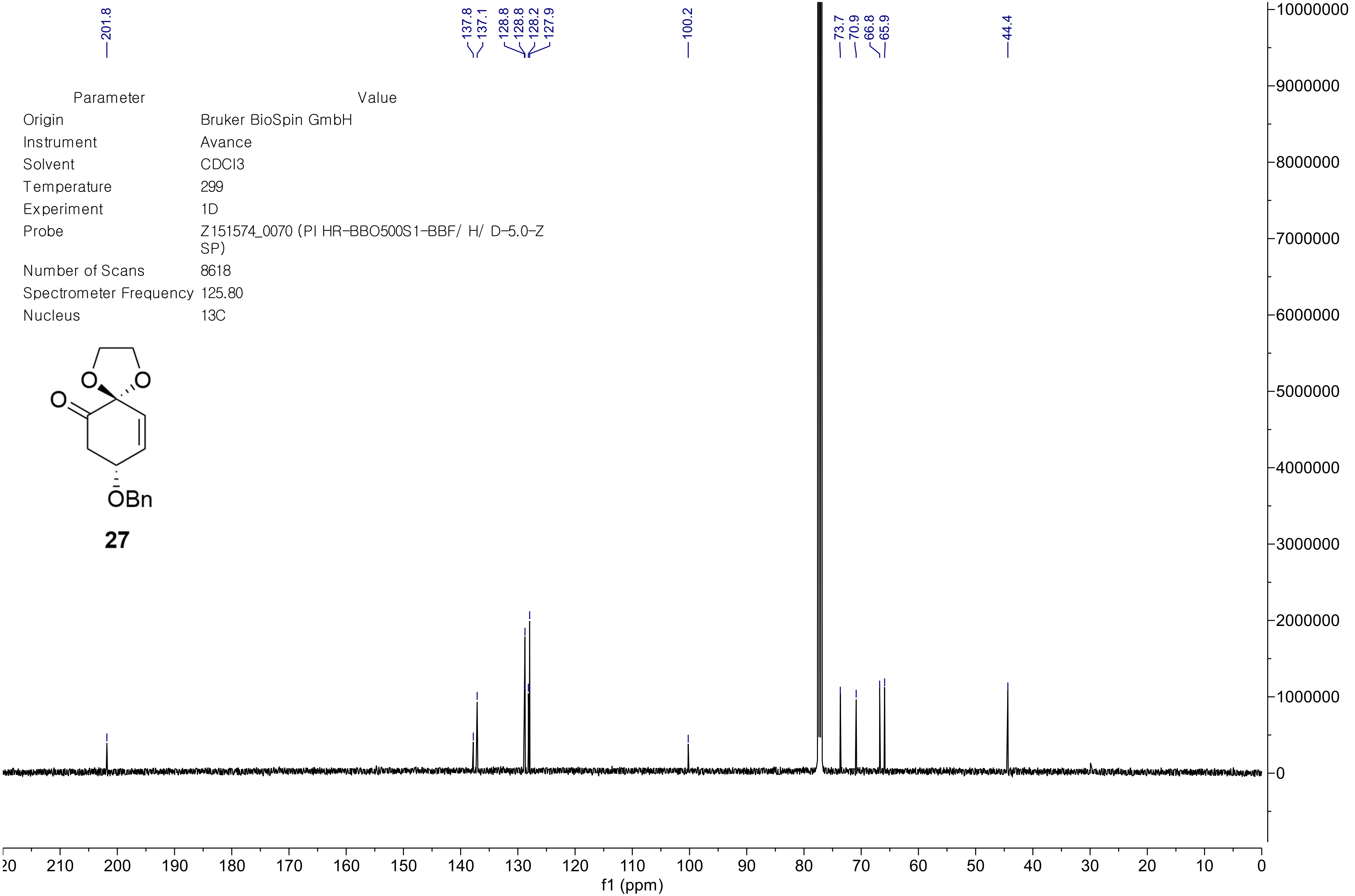
Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	3814
Spectrometer Frequency	125.80
Nucleus	13C

26



Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	298
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	16
Spectrometer Frequency	500.23
Nucleus	1H

27



Parameter	Value
Origin	Bruker BioSpin GmbH
Instrument	Avance
Solvent	CDCl3
Temperature	299
Experiment	1D
Probe	Z151574_0070 (PI HR-BBO500S1-BBF/ H/ D-5.0-Z SP)
Number of Scans	8618
Spectrometer Frequency	125.80
Nucleus	13C

27