A 16-Step Synthesis of the Isoryanodane Diterpene (+)-Perseanol

Arthur Han, Yujia Tao, Sarah E. Reisman*

The Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering
Division of Chemistry and Chemical Engineering, California Institute of Technology
Pasadena, California 91125
reisman@caltech.edu

Supporting Information:

Table of Contents

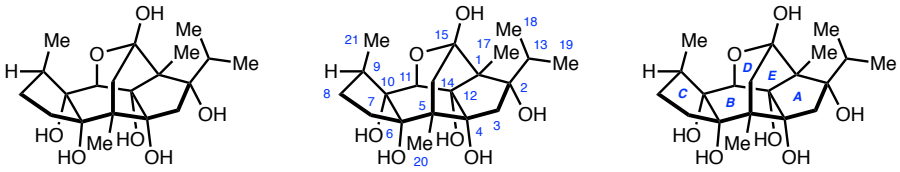
1. General Procedures

Unless otherwise stated, reactions were performed under an inert atmosphere (dry Ar) with freshly dried solvents utilizing standard Schlenk techniques. Glassware was oven-dried at 120 °C for a minimum of four hours, or flame-dried utilizing a Bunsen burner under high vacuum. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), 1,4-dioxane, and toluene (PhMe) were dried by passing through activated alumina columns. Methanol (HPLC grade) was purchased from Fisher Scientific. 1,2-dichloroethane (DCE), 2,2,6,6-tetramethylpiperidine (TMP), and diisopropylamine (*i*-Pr_2NH) were distilled from calcium hydride prior to use and stored under argon. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV (254 nm) and/or *p*-anisaldehyde or $KMnO_4$ staining. Flash column chromatography was performed using silica gel (SiliaFlash® P60, particle size 40-63 microns [230 to 400 mesh]) purchased from Silicycle. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD with Prodigy Cryoprobe (at 400 MHz and 101 MHz, respectively), Varian Inova 400 (at 400 MHz and 101 MHz, respectively), and Varian Inova 500 (at 500 MHz and 126 MHz, respectively) and are reported relative to internal $CHCl_3$ (^1H, δ = 7.26), C_6H_6 (^1H, δ = 7.16), or CD_2HOD (^1H, δ = 3.31), and $CDCl_3$ (^{13}C, δ = 77.0), C_6D_6 (^{13}C, δ = 128.0), or CD_3OD (^{13}C, δ = 49.0). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, hept = heptet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm.

Reagents were purchased from commercial vendors as follows: (*R*)-(+)-pulegone (92%) and 2-phenylnapthalene were purchased from Acros Organics. Solid potassium bis(trimethylsilyl)amide (KHMDS, 95%), tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$), and potassium fluoride (KF) were purchased from Sigma-Aldrich and stored in a nitrogen-filled glovebox. Diisobutylaluminum hydride (1.0 M in hexanes), tetrakisacetonitrile copper(I) triflate, 4,4′-dimethoxy-2,2′-bipyridine (^{MeO}bpy), 1-methylimidazole (NMI, ≥99%), 9-azabicyclo[3.3.1]nonane *N*-oxyl (ABNO), (*R*)-(+)-2-Me-CBS-oxazaborolidine, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), methylmagnesium chloride (3.0 M in THF), vanadium(V) tripropoxide ($VO(On\text{-}Pr_3)$), and TBHP (5.5 M in decane over 4 Å MS) were purchased from Sigma-Aldrich. N-formylsaccharin was purchased from TCI and stored in a nitrogen-filled glovebox. Selenium dioxide (99.999%) was purchased from Strem Chemicals and stored in a nitrogen-filled glovebox.

2. Positional Numbering

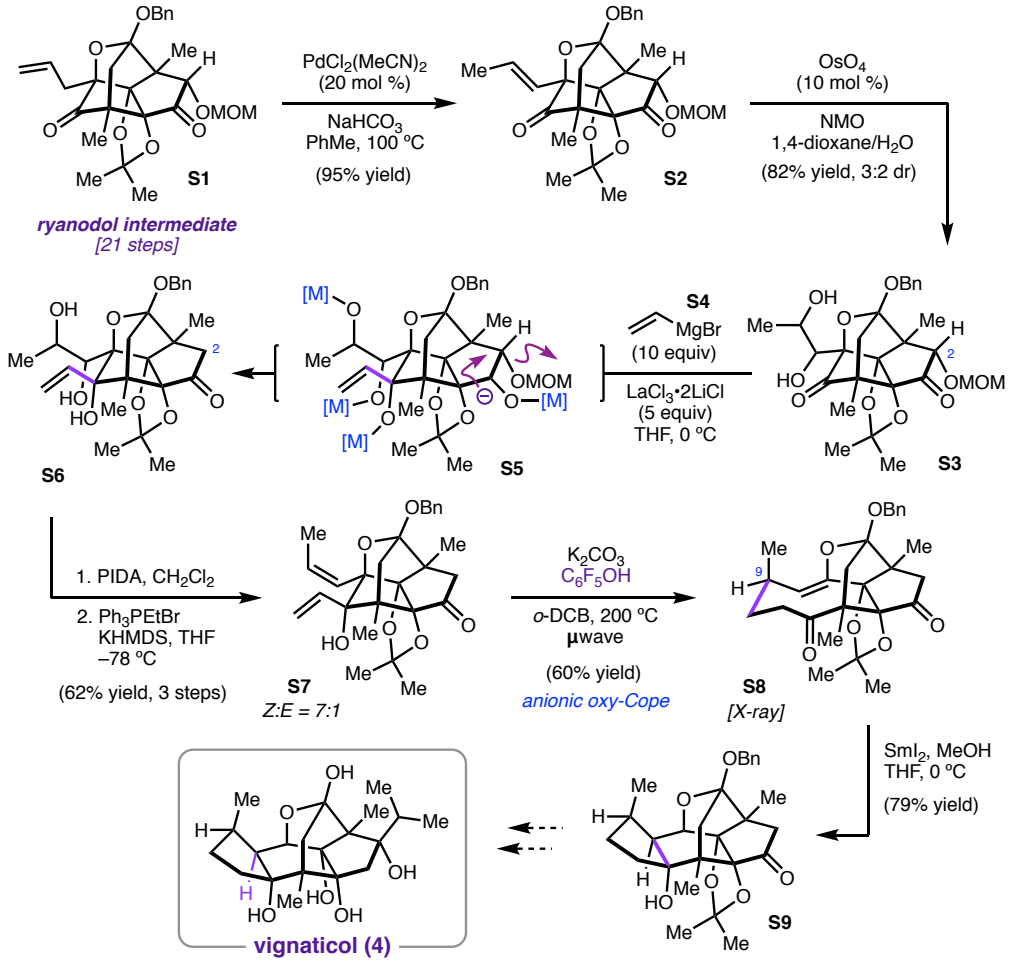
The carbon numbering system and ring assignment as outlined by Inoue and coworkers[1] are utilized throughout this Supplementary Materials file for ^{1}H and ^{13}C NMR assignments of all intermediates. Assignments were made with the aid of 2D ^{1}H-^{1}H (NOESY and COSY) and ^{1}H-^{13}C coupling experiments (HSQC and HMBC).



perseanol (3) numbering system ring assignment

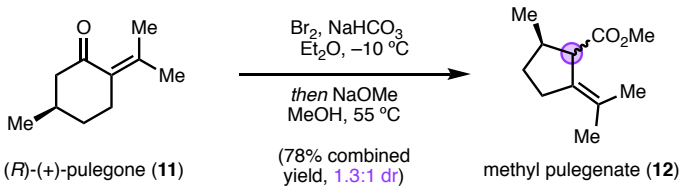
3. Synthetic Scheme of Inoue's Isoryanodane Approach

Figure S1. Inoue's conversion of a ryanodol intermediate to the isoryanodane framework.



3. Synthetic Procedures

Preparation of methyl pulegenate (12)



(*R*)-(+)-pulegone (**11**) — methyl pulegenate (**12**)

According to the one-step procedure[2] of Zhang and coworkers, an oven-dried, 250 mL round-bottomed flask was charged with distilled (*R*)-(+)-pulegone (30.0 g, 197 mmol, 1.0 equiv), anhydrous Et_2O (150 mL), and $NaHCO_3$ (4.97 g, 59.1 mmol, 0.3 equiv). The suspension was cooled to –10 ºC via an ice/acetone bath, then treated with Br_2 (11.1 mL, 217 mmol, 1.1 equiv) dropwise over 30 min via syringe pump. Upon complete addition, the reaction mixture was vigorously stirred for 2.5 h at –10 ºC and then transferred via cannula over 30 min to a freshly generated solution of NaOMe in MeOH–prepared from 9.96 g Na^0 (433 mmol, 2.2 equiv) and 200 mL anhydrous MeOH in an oven-dried, 1 L two-necked round-bottomed flask–at 0 ºC under Ar. The resulting white slurry was warmed to ambient temperature, then the flask was equipped with a reflux condenser and placed in a preheated oil bath at 55 ºC. The reaction mixture was stirred at 55 ºC for 4 h before cooling to ambient temperature, then further cooled to 0 ºC via an ice/water bath before diluting with Et_2O (100 mL) and quenching with the *careful* addition of sat. aq. NH_4Cl (450 mL). The mixture was warmed to ambient temperature, the layers were separated, and the aqueous layer was extracted with Et_2O (3 × 250 mL). The combined layers were washed with brine (500 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (2.5 to 5 to 10% Et_2O/hexanes) to afford methyl pulegenate (30.1 g, 153 mmol, 78% combined yield) as an inseparable 1.3:1 diastereomeric mixture.

Spectral data of the diastereomeric mixture of methyl pulegenates matched that previously reported.[3] Where discernable, the major *syn* diastereomer is designated by * and the minor *anti* diastereomer is designated by $^{\#}$.

TLC (10% Et_2O/hexanes): R_f 0.57 (*p*-anisaldehyde).

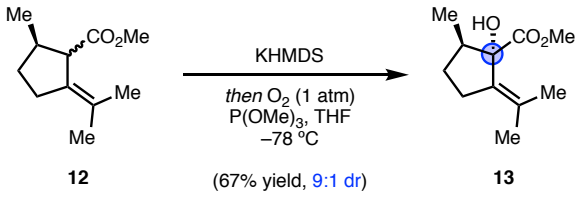
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (s, 3H)$^{\#}$, 3.65 (s, 3H)*, 3.41 (d, J = 8.0 Hz, 1H)*, 2.95 (d, J = 5.5 Hz, 1H)$^{\#}$, 2.45 (m), 2.37 (m), 2.24 (m), 1.97 (m, 1H)$^{\#}$, 1.79 (m), 1.70 (m), 1.66 (s, 3H)$^{\#}$, 1.63 (s, 3H)*, 1.61 (s, 3H)*, 1.57 (s, 3H)$^{\#}$, 1.26 (m, 1H)$^{\#}$, 1.06 (d, J = 6.8 Hz, 3H)$^{\#}$, 1.01 (d, J = 6.9 Hz, 3H)*.

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.1$^{\#}$, 174.5*, 134.9*, 134.2$^{\#}$, 125.9$^{\#}$, 125.7*, 55.6$^{\#}$, 52.7*, 51.6$^{\#}$, 51.0*, 40.8$^{\#}$, 38.9*, 33.7$^{\#}$, 32.7*, 30.4$^{\#}$, 30.2*, 21.5$^{\#}$, 21.1*, 21.0*, 20.9$^{\#}$, 19.6$^{\#}$, 15.7*.

FTIR (NaCl, thin film): 2952, 2355, 1731, 1433, 1349 cm^{-1}.

HRMS (ESI): calc'd for $[M+H]^+$ 183.1380, found 183.1375.

Preparation of α-hydroxyester 13



In a nitrogen-filled glovebox, an oven-dried, 1 L round-bottomed flask was charged with solid KHMDS (95%, 21.4 g, 102 mmol, 2.0 equiv). The flask was capped with a rubber septum, removed from the glovebox, and anhydrous THF (250 mL) was added. The resulting mixture was stirred at ambient temperature for 10-15 min to ensure complete dissolution of the solids, then cooled to –10 ºC via an ice/acetone bath and stirring continued for 15 min before adding methyl pulegenate (10.0 g, 50.9 mmol, 1.0 equiv) in anhydrous THF (150 mL) dropwise via cannula over 30 min, before another portion of THF (50 mL) was used to render the transfer quantitative. The bright-yellow reaction mixture was aged at –10 ºC an additional 20 min before it was further cooled to –78 ºC via a dry ice/acetone bath. The flask was then evacuated/refilled three times with O_2 supplied via a double-walled balloon, after which, in quick succession, $P(OMe)_3$ (12 mL, 102 mmol, 2.0 equiv) was added via syringe. The reaction was vigorously stirred (>650 rpm) under O_2 at –78 ºC until TLC analysis indicated the complete consumption of starting material (*ca.* 1 h). The reaction mixture was diluted with Et_2O (50 mL), quenched with sat. aq. NH_4Cl (200 mL) and sat. aq. $Na_2S_2O_3$ (50 mL), then warmed to ambient temperature. The layers were separated and the aqueous layer was then extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with brine (150 mL), dried over $MgSO_4$, filtered over a short, pre-equilibrated SiO_2 pad, washing with 50% EtOAc/hexanes, and concentrated *in vacuo*. ^{1}H NMR analysis of the crude product indicated that the reaction occurs with full consumption of the starting material in a 9:1 diastereomeric ratio. Purification by SiO_2 flash chromatography (5 to 10 to 20% EtOAc/hexanes) afforded α-hydroxyester **13** as a clear oil (6.77 g, 34.1 mmol, 67% yield).

TLC (20% EtOAc/hexanes): R_f 0.44 (*p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.77 (s, 3H), 2.48 – 2.37 (m, 2H), 2.20 (dt, *J* = 13.3, 6.8 Hz, 1H), 1.81 (dtd, *J* = 13.0, 6.6, 2.6 Hz, 1H), 1.65 (s, 3H), 1.63 (t, *J* = 2.1 Hz, 3H), 1.57 – 1.46 (m, 1H), 0.89 (d, *J* = 6.9 Hz, 3H).

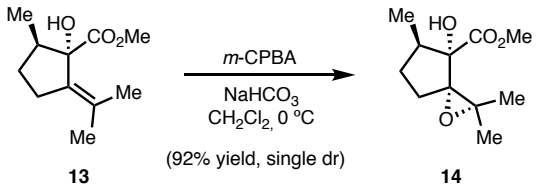
^{13}C NMR (101 MHz, $CDCl_3$): δ 176.7, 135.9, 129.5, 83.9, 52.5, 48.4, 30.0, 29.8, 22.4, 19.5, 13.4.

FTIR (NaCl, thin film): 3516, 2953, 2874, 1719, 1459, 1437, 1371, 1313, 1236, 1178, 1146, 1117, 1063 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M-OH]^+$ 181.1223, found 181.1221.

$[\alpha]_D^{25}$ = +9° (*c* = 0.905, $CHCl_3$).

Preparation of epoxide 14



An oven dried, 500 mL round-bottomed flask was charged with alkene **13** (7.28 g, 36.7 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (180 mL). The solution was cooled to 0 ºC via an ice/water bath and then treated with $NaHCO_3$ (12.3 g, 147 mmol, 4.0 equiv) and *m*-CPBA (77% w/w, 12.3 g, 55.1 mmol, 1.5 equiv) [Note: *m*-CPBA was dried *in vacuo* for >12 h prior to use to remove H_2O]. The suspension was vigorously stirred at 0 ºC for 1 h before an additional portion of *m*-CPBA (77% w/w, 4.11 g, 18.4 mmol, 0.5 equiv) was added. Stirring was continued for an additional 1 h after which TLC analysis indicated the complete consumption of starting material. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and quenched with the addition of sat. aq. $NaHCO_3$ (100 mL) and sat. aq. $Na_2S_2O_3$ (100 mL). The resulting mixture was warmed to room temperature and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL) and the combined organic layers were washed with sat. aq. $NaHCO_3$ (200 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (15 to 25 to 35% EtOAc/hexanes) to afford epoxide **14** (7.24 g, 13.9 mmol, 92% yield) as a colorless oil.

TLC (20% EtOAc/hexanes): R_f 0.23 (*p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.76 (s, 3H), 2.94 (br s, 1H), 2.31 – 2.22 (m, 1H), 2.23 – 2.16 (m, 1H), 1.91 – 1.78 (m, 2H), 1.56 – 1.44 (m, 1H), 1.32 (s, 3H), 1.21 (s, 3H), 1.00 (d, J = 6.8 Hz, 3H).

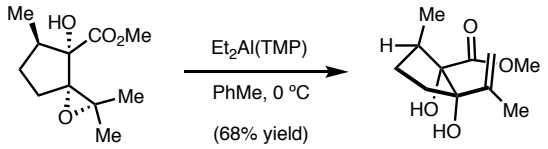
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.1, 81.6, 74.1, 63.1, 51.8, 47.7, 28.9, 27.2, 22.5, 19.2, 14.1.

FTIR (NaCl, thin film): 3480, 2957, 2876, 1756, 1723, 1463, 1436, 1377, 1238, 1187, 1142, 1068, 1005 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 215.1278, found 215.1281.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = −2° (c = 0.770, $CHCl_3$).

Preparation of diol 15



14 **15**

An oven-dried, 500 mL round-bottomed flask was charged with 2,2,6,6-tetramethylpiperidine (16 mL, 93.3 mmol, 2.5 equiv) and anhydrous PhMe (45 mL). The solution was cooled to 0 ºC via an ice/water bath and then *n*-BuLi (2.5 M in hexanes, 36 mL, 89.6 mmol, 2.4 equiv) was added dropwise via syringe. After 30 mins of continued stirring at 0 ºC, the solution of LiTMP was treated with Et_2AlCl (1.0 M in hexanes, 90 mL, 89.6 mmol, 2.4 equiv) dropwise via syringe and stirring was continued for another 30 mins at 0 ºC affording a cloudy pale-yellow solution. Epoxide **14** (8.00 g, 37.3 mmol, 1.0 equiv) in anhydrous PhMe (45 mL) was next added dropwise via cannula over 15 min to the freshly generated slurry of $Et_2Al(TMP)$, before another portion of PhMe (15 mL) was used to render the transfer quantitative. Upon complete addition, the reaction mixture was allowed 1.5 h at 0 ºC at which time TLC analysis indicated the consumption of starting material. The reaction was quenched with the *careful* addition of sat. aq. Rochelle's salt (180 mL), diluted with EtOAc (50 mL) and warmed to ambient temperature. The mixture was next vigorously stirred until two clear layers were observed, then the layers were separated, and the aqueous layer was extracted with Et_2O (3 × 180 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (20 to 30% EtOAc/hexanes) to afford diol **15** (5.44 g, 25.4 mmol, 68% yield) as a yellow oil.

TLC (20% EtOAc/hexanes): R_f 0.25 (*p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.89 (d, *J* = 1.0 Hz, 1H), 4.84 (s, 1H), 3.77 (d, *J* = 2.4 Hz, 3H), 3.09 (dd, *J* = 2.2, 0.6 Hz, 1H), 2.64 – 2.57 (m, 1H), 2.45 – 2.36 (m, 1H), 2.11 – 2.01 (m, 1H), 1.90 (ddd, *J* = 14.3, 10.1, 4.2 Hz, 1H), 1.76 (dd, *J* = 1.5, 0.7 Hz, 3H), 1.54 – 1.43 (m, 1H), 0.91 (d, *J* = 7.0 Hz, 3H).

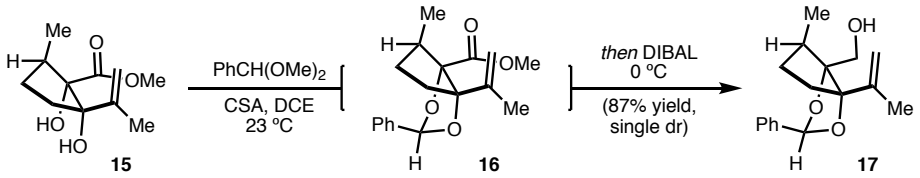
^{13}C NMR (101 MHz, $CDCl_3$): δ 174.8, 146.5, 111.9, 89.5, 84.3, 52.7, 41.9, 32.9, 27.2, 19.9, 14.2.

FTIR (NaCl, thin film): 3500, 2955, 2876, 1732, 1722, 1717, 1456, 1436, 1242, 1204, 1124, 1051 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 215.1278, found 215.1279.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}} = -11°$ (*c* = 0.560, $CHCl_3$).

Preparation of alcohol 17



An oven-dried, 500 mL round-bottomed flask was charged with diol **15** (1.00 g, 4.7 mmol, 1.0 equiv) and anhydrous DCE (47 ml). The solution was treated with (±)-10-camphorsulfonic acid (1.09 g, 4.7 mmol, 1.0 equiv) and benzaldehyde dimethyl acetal (3.5 mL, 23.4 mmol, 5.0 equiv). The resulting solution was stirred for 1.5 h at room temperature, at which point TLC analysis indicated complete conversion of starting material. ^{1}H NMR analysis of a reaction aliquot confirms that the reaction proceeds with the generation of a single dr of the benzylidene acetal. The reaction mixture was thereafter cooled to 0 °C via an ice/water bath, and then DIBAL (1.0 M in hexanes, 42 mL, 42.1 mmol, 9.0 equiv) was added dropwise via syringe. After 1 h of continued stirring at 0 °C, TLC analysis showed complete consumption of intermediate protected diol **16**. The reaction mixture was next *carefully* treated with EtOAc (30 mL) followed by sat. aq. Rochelle's salt (85 mL). The cooling bath was removed and the mixture was vigorously stirred overnight at ambient temperature. The resulting two layers were separated and the aqueous layer extracted with EtOAc (3 × 80 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by SiO_2 flash chromatography (10 to 15 to 20 % EtOAc/hexanes) to afford alcohol **17** (1.12 g, 4.1 mmol, 87% yield) as a thick, colorless oil.

benzylidene acetal 16:

TLC (20% EtOAc/hexanes): R_f 0.70 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 – 7.52 (m, 2H), 7.39 (dt, *J* = 5.2, 1.7 Hz, 3H), 6.12 (d, *J* = 1.3 Hz, 1H), 5.14 (s, 1H), 5.04 (d, *J* = 1.4 Hz, 1H), 3.75 (s, 3H), 2.59 (q, *J* = 6.9 Hz, 1H), 2.39 – 2.21 (m, 2H), 2.13 – 2.04 (m, 1H), 1.88 (s, 3H), 1.65 (td, *J* = 6.2, 5.4, 3.9 Hz, 1H), 1.08 (dd, *J* = 7.3, 1.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 143.4, 136.9, 129.5, 128.4, 126.8, 113.1, 104.9, 97.6, 96.7, 51.8, 44.9, 35.0, 31.7, 20.5, 15.1.

FTIR (NaCl, thin film): 2949, 2876, 1735, 1457, 1435, 1395, 1259, 1221, 1116, 1089, 1063, 1027 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M+H]^+$ 303.1591, found 303.1598.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = −39° (*c* = 0.590, $CHCl_3$).

alcohol 17:

TLC (20% EtOAc/hexanes): R_f 0.22 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.53 (m, 2H), 7.45 – 7.36 (m, 3H), 5.82 (d, *J* = 1.1 Hz, 1H), 5.28 – 5.19 (m, 1H), 5.08 (t, *J* = 1.5 Hz, 1H), 3.82 (dd, *J* = 12.2, 2.2 Hz, 1H), 3.76 – 3.62 (m, 1H), 2.51 (p, *J* = 7.3 Hz, 1H),

2.40 (tt, J = 12.8, 6.5 Hz, 1H), 2.18 (td, J = 13.5, 6.4 Hz, 1H), 2.01 – 1.90 (m, 2H), 1.88 (dd, J = 1.5, 0.8 Hz, 3H), 1.46 (dd, J = 12.3, 6.4 Hz, 1H), 1.07 (dd, J = 7.5, 1.1 Hz, 3H).

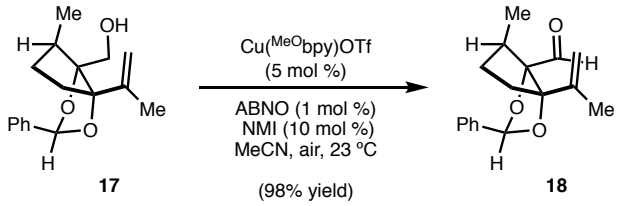
^{13}C NMR (101 MHz, $CDCl_3$): δ 143.1, 136.4, 129.8, 128.5, 126.9, 113.2, 101.4, 97.2, 94.9, 60.7, 40.8, 36.4, 29.6, 20.7, 14.5.

FTIR (thin film/NaCl): 3465, 2962, 2876, 1460, 1453, 1397, 1310, 1220, 1125, 1088, 1061, 1027 cm^{-1}.

HRMS (MM:ESI–APCI): calc'd for $[M]^+$ 274.1563, found 274.1564.

$[\alpha]_D^{25}$ = −17° (c = 0.895, $CHCl_3$).

Preparation of aldehyde 18



An oven-dried, 200 mL round-bottomed flask was charged with alcohol **17** (2.27 g, 8.27 mmol, 1.0 equiv) and anhydrous MeCN (83 mL). The solution was vigorously stirred (>700 rpm) open to air while being treated with ^{MeO}bpy (89 mg, 0.41 mmol, 0.05 equiv), $Cu(MeCN)_4OTf$ (156 mg, 0.41 mmol, 0.05 equiv), ABNO (11.6 mg, 82.7 μmol, 0.01 equiv), and then NMI (66 μL, 0.83 mmol, 0.10 equiv) via microsyringe. The resulting brick-red reaction mixture was vigorously stirred exposed to air at ambient temperature until the reaction mixture turned a blue-green (*ca.* 1.75 h), at which point TLC analysis indicated the complete consumption of starting material. The reaction mixture was diluted with Et_2O (40 mL), and filtered through a pre-equilibrated SiO_2 pad layered with Celite, washing with 50% EtOAc/hexanes. The filtrate was concentrated *in vacuo* and the crude residue was directly purified by SiO_2 flash chromatography (5 to 7.5 to 10% EtOAc/hexanes) to afford aldehyde **18** (2.21 g, 8.10 mmol, 98% yield) as a pale yellow oil.

TLC (20% EtOAc/hexanes): R_f 0.52 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.84 (s, 1H), 7.57 (m, 2H), 7.41 (m, 3H), 5.98 (s, 1H), 5.30 (t, J = 0.9 Hz, 1H), 5.11 (p, J = 1.4 Hz, 1H), 2.56 (tddd, J = 8.8, 7.5, 6.4, 1.7 Hz, 1H), 2.49 – 2.34 (m, 2H), 2.05 (m, 1H), 1.87 (dd, J = 1.5, 0.7 Hz, 3H), 1.59 (m, 1H), 1.20 (d, J = 7.6 Hz, 3H).

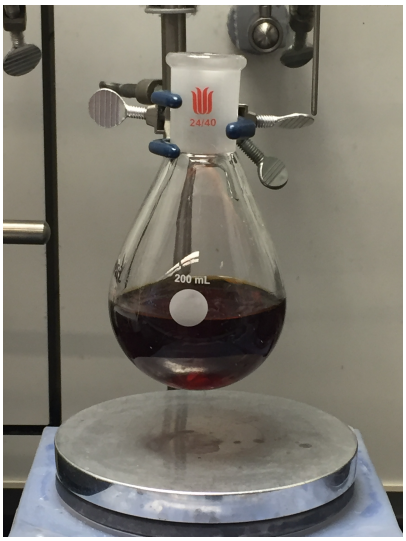
^{13}C NMR (101 MHz, $CDCl_3$): δ 200.7, 142.6, 136.2, 129.8, 128.4, 126.7, 114.5, 104.6, 97.4, 97.3, 43.5, 35.9, 31.9, 20.5, 14.5.

FTIR (NaCl, thin film): 2965, 2875, 1733, 1456, 1398, 1312, 1221, 1133, 1087, 1060, 1026 cm^{-1}.

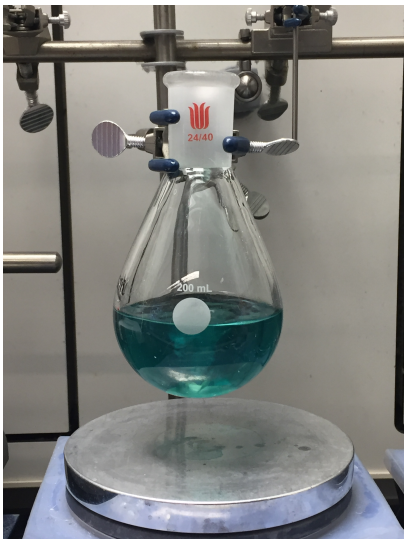
HRMS (MM:ESI–APCI): calc'd for $[M]^+$ 272.1407, found 272.1405.

$[\alpha]_D^{25}$ = −31° (c = 0.285, $CHCl_3$).

Figure S2. Progression of Stahl's Cu-catalyzed aerobic oxidation of alcohol **17**.

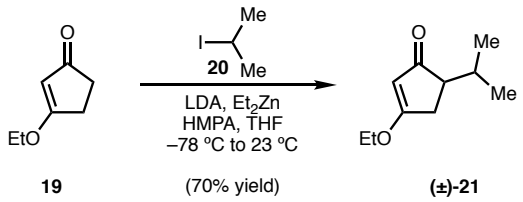


A. *t = 0 h (rxn start)*



B. *t = 1.75 h (rxn end)*

Preparation of isopropyl ester 21



An oven-dried, 500 mL round-bottomed flask was treated with freshly distilled *i*-Pr_2NH (6.4 mL, 45.6 mmol, 1.15 equiv) and anhydrous THF (45 mL). The solution was cooled to 0 ºC via an ice/water bath and stirring was continued for 15 min prior to the dropwise addition of *n*-BuLi (2.5 M in hexanes, 17 mL, 43.6 mmol, 1.1 equiv) via syringe. Upon complete addition, the reaction was continued for 30 min to produce LDA, which was then further cooled to –78 ºC via a dry ice/acetone bath. To the cooled solution was added vinylogous ester **19** (5.00 g, 39.6 mmol, 1.0 equiv) in anhydrous THF (45 mL) dropwise via cannula over 10 min at –78 ºC. The reaction was continued at –78 ºC for 45 min prior to the dropwise addition of Et_2Zn (1.0 M in hexanes, 42 mL, 41.6 mmol, 1.05 equiv) via syringe [Note: rapid generation of ethane (*g*) is observed, care should be taken to avoid overpressurization]. The reaction was continued for 5 min at –78 ºC before adding in quick succession 2-iodopropane (20 mL, 198 mmol, 5.0 equiv) and anhydrous HMPA (31 mL, 178 mmol, 4.5 equiv) via syringe. The reaction flask was immediately removed from the cooling bath and stirring continued at ambient temperature overnight (*ca*. 18-20 h) at which point TLC analysis indicated the complete consumption of starting material. The reaction was recooled to 0 ºC via an ice/water bath and *carefully* quenched with sat. aq. NH_4Cl (80 mL). The mixture was warmed to ambient temperature, diluted with Et_2O (40 mL), and the layers were separated. The

aqueous layer was extracted with Et_2O (2 × 80 mL) and the combined organic layers were washed with sat. aq. NH_4Cl (80 mL), brine (80 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (20 to 30 to 40 to 50% EtOAc/hexanes) to afford isopropyl ester **21** (4.67 g, 27.7 mmol, 70% yield) as a yellow-orange oil.

TLC (30% EtOAc/hexanes): R_f 0.42 (UV, *p*-anisaldehyde).

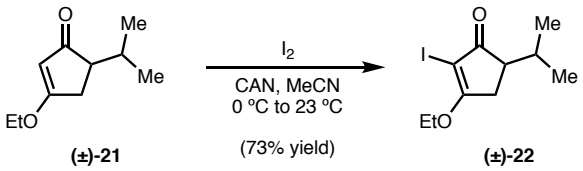
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24 (s, 1H), 4.03 (qd, *J* = 7.1, 1.1 Hz, 2H), 2.55 (ddd, *J* = 17.2, 7.3, 1.2 Hz, 1H), 2.47 (ddd, *J* = 7.2, 4.1, 2.6 Hz, 1H), 2.35 (ddd, *J* = 17.3, 2.6, 1.1 Hz, 1H), 2.27 (pd, *J* = 6.9, 4.1 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 207.9, 189.3, 104.9, 67.5, 50.8, 30.3, 28.1, 20.7, 16.5, 14.1.

FTIR (NaCl, thin film): 2958, 2873, 1693, 1594, 1466, 1338, 1029 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 191.1043, found 191.1061.

Preparation of iodoester 22



An oven-dried, 500 mL round-bottomed flask was charged with vinylogous ester **21** (4.60 g, 27.3 mmol, 1.0 equiv) and anhydrous MeCN (180 mL). The solution was cooled to 0 ºC via an ice/water bath and stirring was continued for 15 min prior to the addition of I_2 (7.29 g, 28.7 mmol, 1.05 equiv) then CAN (15.7 g, 28.7 mmol, 1.05 equiv) in quick succession. The reaction mixture was immediately removed from the ice/water bath and the reaction was continued for 0.5 h at ambient temperature, during which time CAN slowly solubilizes resulting in a deep red-black solution. After 0.5 h, TLC analysis indicated the complete consumption of starting material. The reaction mixture was recooled to 0 ºC via an ice/water bath and *carefully* quenched with the addition of sat. aq. $Na_2S_2O_3$ (60 mL) [Note: vigorous evolution of HI is observed at the initial stages of the quench]. The resulting biphasic mixture was diluted with EtOAc (60 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 80 mL) and the combined organic layers were washed with brine (80 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (20 to 35% EtOAc/hexanes) to afforded iodoester **22** (5.87 g, 20.0 mmol, 73% yield) as a yellow-orange solid.

TLC (30% EtOAc/hexanes): R_f 0.32 (UV, *p*-anisaldehyde).

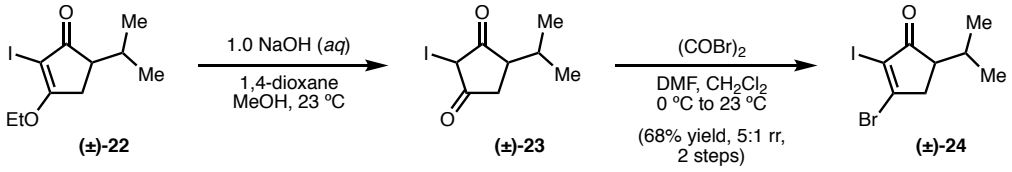
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.36 (q, *J* = 7.1 Hz, 2H), 2.80 (dd, *J* = 17.5, 7.1 Hz, 1H), 2.65 (dd, *J* = 7.0, 4.2, 2.5 Hz, 1H), 2.54 (dd, *J* = 17.4, 2.5 Hz, 1H), 2.30 (pd, *J* = 6.9, 4.1 Hz, 1H), 1.45 (t, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 201.5, 188.1, 73.9, 66.5, 49.8, 29.4, 28.6, 20.2, 16.6, 15.1.

FTIR (NaCl, thin film): 2956, 1678, 1574, 1345, 1336, 1285, 1264 1046 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 317.0009, found 317.0008.

Preparation of iodobromoenone 24



A 500 mL round-bottomed flask was treated with iodoester **22** (6.06 g, 20.6 mmol, 1.0 equiv), 1,4-dioxane (82 mL), MeOH (82 mL), and *then* 1.0 M NaOH (*aq*) (82 mL, 82.4 mmol, 10 equiv). The resulting deep brown reaction mixture was stirred at ambient temperature for 3 h, at which point TLC and LCMS indicated the complete consumption of starting material. The reaction was quenched with the addition 1.0 M HCl (*aq*) (100 mL) and diluted with 10% *i*-PrOH/$CHCl_3$ (100 mL). The layers were separated and the aqueous layer was repeatedly extracted with 10% *i*-PrOH/$CHCl_3$ (100 mL) until TLC analysis of the aqueous layer indicated that absence of the intermediate diketone. The combined organic layers were washed with brine (150 mL), filtered over Celite, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (5/1 to 10/1 to 12/1% MeOH/Et_3N/$CHCl_3$) to afford intermediate iododiketone **23** as a dark brown semi-solid [Note: iododiketone **23** is *not* stable to storage and was used immediately upon isolation].

In an oven-dried, 500 mL round-bottomed flask, the intermediate iododiketone **23** was immediately taken up in anhydrous CH_2Cl_2 (200 mL) and cooled to 0 ºC via an ice/water bath. Anhydrous DMF (4.8 mL, 61.8 mmol, 3.0 equiv) was next added and stirring continued for 15 min at 0 ºC before the dropwise addition of oxalyl bromide (2.9 mL, 30.9 mmol, 1.5 equiv) via syringe [Caution! Rapid generation of CO and CO_2. A vent needle was routinely used during this addition to prevent over-pressurization.]. Upon complete addition, the ice/water bath was removed and stirring was continued for 1 h before pouring the reaction mixture over CH_2Cl_2 (50 mL) and ice-cold H_2O (100 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 80 mL). The combined organic layers were washed with sat. aq. $Na_2S_2O_3$ (150 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (7.5 to 10 to 15% Et_2O/hexanes) to afford iodobromocyclopentenone (±)-**24** (4.60 g, 14.0 mmol, 68% yield) as a yellow oil that solidifies upon storage at –20 ºC. The regioselectivity was confirmed by HMBC analysis.

TLC (10% Et_2O/hexanes): R_f 0.36 (UV, $KMnO_4$).

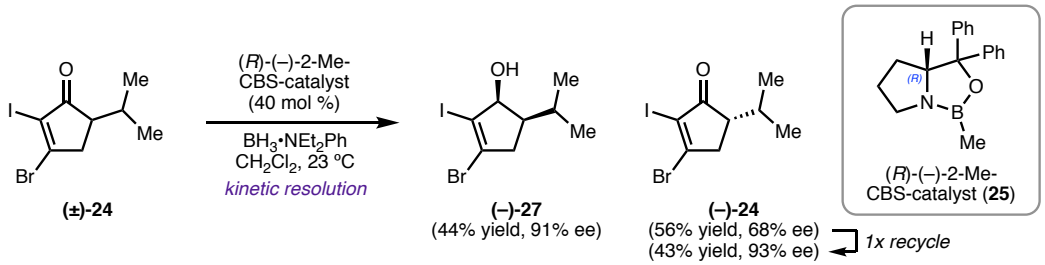
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.06 (dd, *J* = 18.6, 7.1 Hz, 1H), 2.83 (dd, *J* = 18.6, 2.6 Hz, 1H), 2.72 (ddd, *J* = 7.0, 4.4, 2.5 Hz, 1H), 2.29 (pd, *J* = 6.9, 4.4 Hz, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.0, 165.7, 108.3, 52.2, 40.5, 29.2, 20.1, 17.2.

FTIR (NaCl, thin film): 2956, 2359, 1704, 1568, 1456, 1187 cm^{-1}.

HRMS (ESI): calc'd for $[M+H]^+$ 328.9032, found 328.9024.

Preparation of enriched alcohol (–)-27



An oven-dried, 100 mL round-bottomed flask was charged with (*R*)-(+)-2-Me-CBS-oxazaborolidine (337 mg, 1.22 mmol, 0.4 equiv) and anhydrous CH_2Cl_2 (25 mL). After 15 min of continued stirring, BH_3•NEt_2Ph (373 μL, 2.13 mmol, 0.7 equiv) was added dropwise via microsyringe. The reaction mixture was stirred an additional 10 min at ambient temperature before adding cyclopentenone (±)-**24** (1 g, 3.04 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (22 mL) dropwise over 1 h via syringe pump before another portion of CH_2Cl_2 (3.0 mL) was used to render the transfer quantitative. Upon complete addition, the reaction progress was closely monitored by analytical SFC analysis. The reaction mixture was allowed to continue for an additional 3 h 20 min before it was diluted with Et_2O (20 mL) and quenched with the *careful* addition of MeOH (5 mL) followed by H_2O (20 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic layers were washed with brine (40 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (7.5 to 10 to 12.5% Et_2O/hexanes) to afford cyclopentenol (–)-**27** (442 mg, 1.34 mmol, 44% yield, 91% ee) as a white solid. The ee was determined by SFC analysis (**27:** AD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm; **24:** AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm).

Unreacted cyclopentenone (–)-**24** was recovered as a yellow oil (555 mg, 1.69 mmol, 56% yield, 68% ee) and can be further enriched to 93% ee through the following procedure (79% recovery, 43% yield over 2 steps): An oven-dried, 50 mL round-bottomed flask was charged with (*R*)-(+)-2-Me-CBS-oxazaborolidine (94 mg, 0.34 mmol, 0.2 equiv) and anhydrous CH_2Cl_2 (18 mL). After 15 min of continued stirring, BH_3•NEt_2Ph (270 μL, 1.52 mmol, 0.9 equiv) was added dropwise via microsyringe. The reaction mixture was stirred an additional 10 min at ambient temperature before adding cyclopentenone (–)-**24** (555 mg, 1.69 mmol, 68% ee, 1.0 equiv) in anhydrous

CH_2Cl_2 (7 mL) dropwise over 1 h via syringe pump before another portion of CH_2Cl_2 (3.0 mL) was used to render the transfer quantitative. Upon complete addition, the reaction progress was closely monitored by analytical SFC analysis. The reaction mixture was allowed to continue for an additional 3 h before it was diluted with Et_2O (10 mL) and quenched with the *careful* addition of MeOH (5 mL) followed by H_2O (10 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 15 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (7.5 to 10% Et_2O/hexanes) to afford cyclopentenone (–)-**24** (435 mg, 1.34 mmol, 79% recovery, 93% ee) as a yellow oil ($[\alpha]_D^{25}$ = –53° (*c* = 1.00, $CHCl_3$)).

The selectivity factor (or *S* factor) was determined in a 15 mg scale experiment run under otherwise identical conditions as above using benzyl ether as an internal standard: at 19.6% conversion, **(–)-27** was of 94.5% ee and unreacted **(–)-24** was of 23.1% ee; the *S* factor was accordingly calculated to be 44.

TLC (15% Et_2O/hexanes): R_f 0.37 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (td, *J* = 6.2, 1.7 Hz, 1H), 2.60 (dd, *J* = 16.1, 7.7 Hz, 1H), 2.52 (ddd, *J* = 16.2, 8.4, 1.7 Hz, 1H), 2.00 (dddd, *J* = 10.8, 8.4, 7.8, 6.0 Hz, 1H), 1.89 (dp, *J* = 10.8, 6.4 Hz, 1H), 1.68 (d, *J* = 6.3 Hz, 1H, OH), 1.02 (d, *J* = 6.3, 3H), 0.93 (d, *J* = 6.6 Hz, 3H).

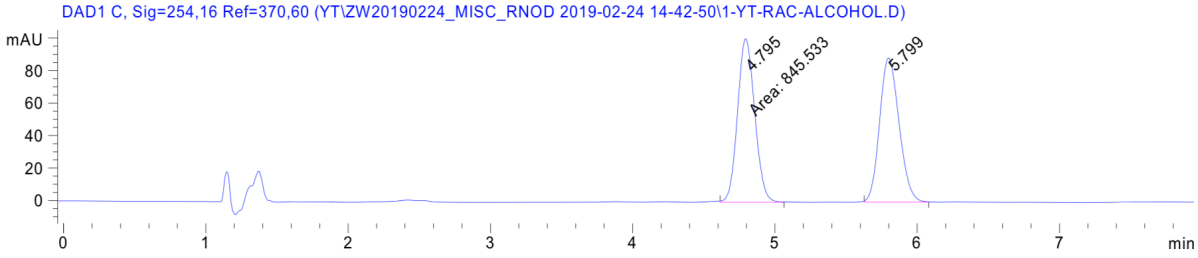
^{13}C NMR (101 MHz, $CDCl_3$): δ 136.6, 102.6, 82.1, 51.0, 42.9, 27.8, 21.4, 21.0.

FTIR (NaCl, thin film): 3330, 2956, 2869, 1598, 1241, 1096, 1065, 1011 cm^{-1}.

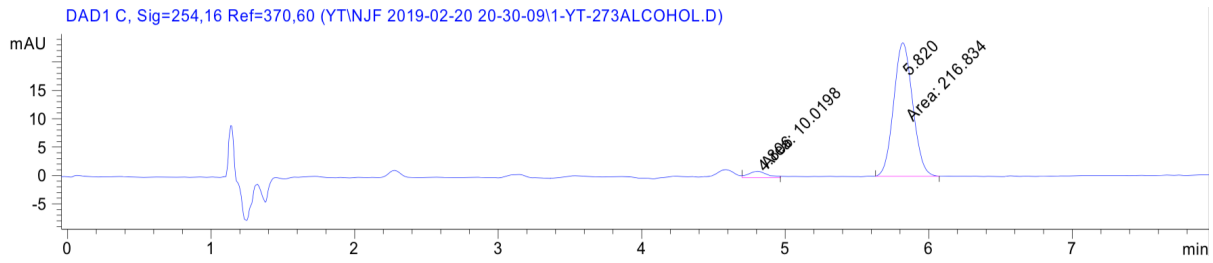
HRMS (ESI): calc'd for $[M]^+$ 329.9111, found 329.9116.

$[\alpha]_D^{25}$ = –11° (*c* = 1.19, $CHCl_3$).

Figure S3. SFC traces of racemic and enantioenriched alcohol **27**.

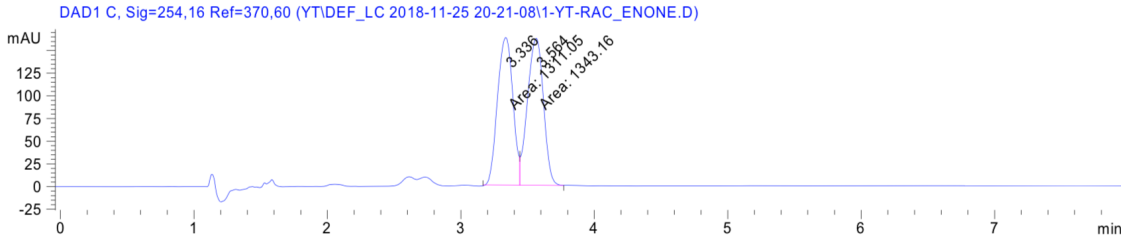


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.795	MM	0.1396	845.53265	100.94398	49.9669
2	5.799	BB	0.1475	846.65253	88.58824	50.0331

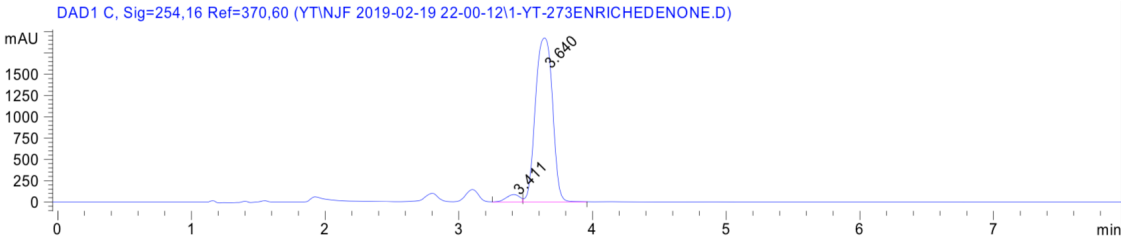


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.806	MM	0.1496	10.01976	1.11640	4.4168
2	5.820	MM	0.1533	216.83441	23.57370	95.5832

Figure S4. SFC traces of racemic and enantioenriched enone **24**.

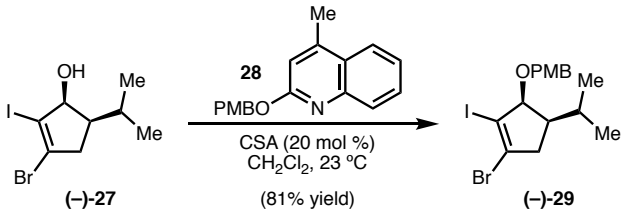


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.336	MF	0.1338	1311.04724	163.25740	49.3950
2	3.564	FM	0.1377	1343.16089	162.60211	50.6050



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.411	VV	0.1151	642.59912	90.20612	3.6092
2	3.640	VB	0.1479	1.71620e4	1927.05969	96.3908

Preparation of PMB ether 29



An oven-dried, 500 mL round-bottomed flask was charged with alcohol (–)-**27** (2.66 g, 8.03 mmol, 1.0 equiv), 2-(4-methoxybenzyloxy)-4-methylquinoline[4-5] (4.49 g, 16.1 mmol, 2.0 equiv), and anhydrous CH_2Cl_2 (80 mL). The solution was treated with (±)-10-camphorsulfonic acid (373 mg, 1.61 mmol, 0.20 equiv) and the suspension was vigorously stirred at ambient temperature under Ar for 36 h. The reaction mixture was *carefully* treated with sat. aq. $NaHCO_3$ (20 mL), diluted with Et_2O (80 mL), and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 40 mL) and the combined organic layers were washed with 1 N HCl (*aq*) (3 × 60 mL), brine (60 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* [Note: the 1 N HCl (*aq*) washes were deemed imperative for the efficient removal of the 2-lepidone byproduct]. The crude residue was purified via SiO_2 flash chromatography (2/2 to 3/3 to 4/4% Et_2O/CH_2Cl_2/hexanes) to afford PMB ether (–)-**29** (2.94 g, 6.51 mmol, 81% yield) as a thick colorless oil that solidifies to a white solid upon storage at –20 ºC. The stereochemistry was confirmed by nOe analysis.

TLC (15% Et_2O/hexanes): R_f 0.67 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (m, 2H), 6.88 (m, 2H), 4.89 (d, *J* = 10.5 Hz, 1H), 4.56 (d, *J* = 10.5 Hz, 1H), 4.38 (dd, *J* = 6.0, 1.4 Hz, 1H), 3.80 (s, 3H), 2.60 (ddd, *J* = 16.2, 8.5, 1.5 Hz, 1H), 2.54 (dd, *J* = 16.0, 7.5 Hz, 1H), 2.13 – 1.91 (m, 2H), 0.97 (d, *J* = 6.2 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H).

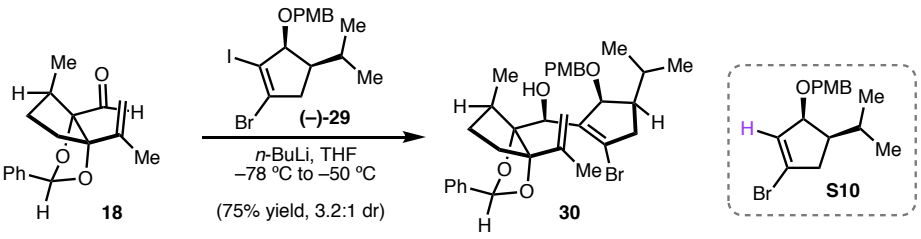
^{13}C NMR (101 MHz, $CDCl_3$): δ 159.2, 137.3, 130.4, 129.3, 113.8, 98.3, 88.0, 72.5, 55.3, 52.2, 43.2, 27.3, 21.5, 20.8.

FTIR (NaCl, thin film): 2956, 2869, 1614, 1514, 1248 cm^{-1}.

HRMS (ESI): calc'd for $[M+H_2O]^+$ 467.9792, found 467.9807.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –29° (*c* = 0.650, $CHCl_3$).

Convergent union of aldehyde 18 and iodobromocyclopentenol 29



An oven-dried, 100 mL round-bottomed flask was charged with vinyl iodide (–)-**29** (2.24 g, 4.96 mmol, 1.25 equiv) and anhydrous THF (18 mL) [Note: vinyl iodide (–)-**29** was azeotroped with PhH three times immediately prior to use]. The solution was cooled to –78 ºC via a dry ice/acetone bath and stirring continued for 15 min prior to the dropwise addition of *n*-BuLi (2.5 M in hexanes, 2.0 mL, 4.96 mmol, 1.25 equiv) via syringe. Upon complete addition, the reaction mixture was stirred an additional 15 min. Aldehyde **18** (1.08 g, 3.97 mmol, 1.0 equiv) in anhydrous THF (18 mL) was added dropwise via cannula over 15 min [Note: aldehyde **18** was azeotroped with PhH three times immediately prior to use], before another portion of THF (3 mL) was used to render the transfer quantitative. Immediately upon complete addition of aldehyde **18**, the reaction mixture was slowly warmed to –50 ºC over 15 min and the reaction was continued at –50 ºC until TLC analysis indicated the complete consumption of starting material (*ca*. 30 min). The reaction mixture was quenched with the addition of sat. aq. NH_4Cl (10 mL) and then warmed to ambient temperature and diluted with Et_2O (10 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. ^{1}H NMR analysis of the crude product indicated that the reaction occurs with full consumption of the starting material in a 3.2:1 diastereomeric ratio. Repeated purification via SiO_2 flash chromatography (5/5 to 10/5 to 15/5% Et_2O/CH_2Cl_2/hexanes) afforded a single diastereomer of alcohol **30** (1.78 g, 2.97 mmol, 75% yield) as a white foam.

TLC (10/5% Et_2O/CH_2Cl_2/hexanes): R_f 0.32 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 – 7.63 (m, 2H), 7.42 – 7.36 (m, 3H), 7.05 – 6.99 (m, 2H), 6.79 – 6.74 (m, 2H), 6.37 (s, 1H), 5.32 (d, *J* = 0.8 Hz, 1H), 5.20 (t, *J* = 1.5 Hz, 1H), 4.95 (d, *J* = 4.0 Hz, 1H), 4.65 (d, *J* = 4.6 Hz, 1H), 4.46 (d, *J* = 9.6 Hz, 1H), 4.40 (d, *J* = 9.6 Hz, 1H), 3.78 (s, 3H), 2.78 (ddd, *J* = 15.8, 9.5, 0.8 Hz, 1H), 2.44 (p, *J* = 7.0 Hz, 1H), 2.39 (dd, *J* = 15.8, 7.0 Hz, 1H), 2.27 (dq, *J* = 12.3, 6.3 Hz, 1H), 2.18 – 2.12 (m, 2H), 2.11 (d, *J* = 1.1 Hz, 3H), 1.99 (dd, *J* = 13.4, 6.3 Hz, 1H), 1.87 (tdd, *J* = 9.7, 7.0, 4.6 Hz, 1H), 1.23 (dd, *J* = 11.9, 6.0 Hz, 1H), 1.09 (d, *J* = 6.4 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7, 148.1, 142.6, 138.0, 131.2, 129.7, 129.6, 129.4, 128.4, 126.9, 113.3, 112.6, 105.0, 99.1, 96.7, 80.5, 72.4, 71.3, 55.2, 55.0, 41.8, 41.4, 38.8, 30.6, 26.0, 23.0, 21.3, 14.1.

FTIR (NaCl, thin film): 3498, 2956, 2871, 1613, 1514, 1248, 1064, 1029 cm^{-1}.

HRMS (ESI): calc'd for $[M+NH_4]^+$ 614.2476, found 614.2470.

$[\alpha]_D^{25}$ = +70° (*c* = 1.575, $CHCl_3$).

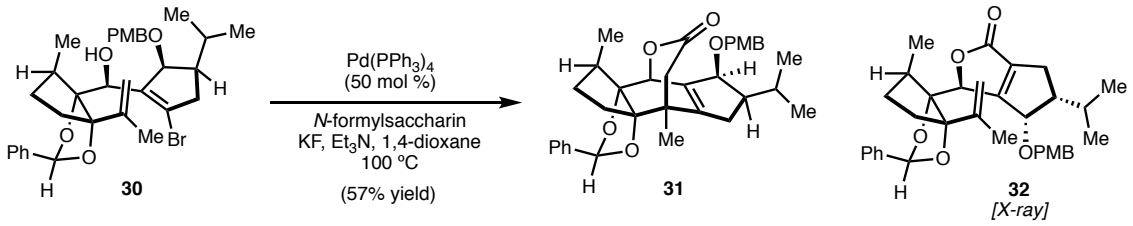
deiodination byproduct S10:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 – 7.22 (m, 2H), 6.91 – 6.76 (m, 2H), 6.19 (td, *J* = 2.5, 1.2 Hz, 1H), 4.47 (d, *J* = 11.1 Hz, 1H), 4.34 (d, *J* = 11.2 Hz, 1H), 4.23 (d, *J* = 5.9, 2.4, 1.6 Hz, 1H), 3.80 (s, 3H), 2.60 (dddd, *J* = 16.1, 8.4, 2.5, 1.6 Hz, 1H), 2.48 (ddd, *J* = 16.2, 7.4, 1.2 Hz, 1H), 2.09 – 1.79 (m, 2H), 0.97 (d, *J* = 6.0 Hz, 3H), 0.91 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 159.1, 131.5, 130.7, 129.6, 129.1, 113.7, 81.2, 70.4, 55.3, 51.9, 43.2, 27.2, 21.5, 21.3.

HRMS (ESI): calc'd for $[M+H_2O]^+$ 342.0825, found 342.0848.

Preparation of lactone 31



In a nitrogen-filled glovebox, an oven-dried, 500 mL heavy-walled pressure vessel equipped with a magnetic stirbar was charged with $Pd(PPh_3)_4$ (387 mg, 0.33 mmol, 50 mol %), *N*-formylsaccharin (170 mg, 0.80 mmol, 1.2 equiv). Vinyl bromide **30** (400 mg, 0.67 mmol, 1.0 equiv) in anhydrous 1,4-dioxane (67 mL) was carefully transferred into the reaction vessel using a glass pipette. The suspension was treated with triethylamine (0.37 mL, 2.68 mmol, 4.0 equiv) and KF (97 mg, 1.67 mmol, 2.5 equiv) before the vessel was sealed with a CAPFE O-ring lined cap, removed from the glove box, and submerged in a preheated oil bath at 100 ºC. [Note: running the reaction at 0.01 M concentration, having a reaction solvent volume to vessel volume ratio less than 1:7, and maintaining the oil bath at 100 ºC throughout the reaction are critical]. Within 15 min, the reaction mixture turned dark green. After 26 h of continued stirring at 100 ºC, the reaction mixture was cooled to ambient temperature, diluted with Et_2O (30 mL), and filtered through a pre-equilibrated SiO_2 pad layered with Celite. The orange filtrate was concentrated *in vacuo* and the crude residue was directly purified via SiO_2 flash chromatography (10 to 15 to 20% EtOAc/hexanes). The concentrated column fractions were treated with Et_2O (10 mL) and filtered through a pad of Celite. The filtrate was finally concentrated *in vacuo* to afford tetracycle **31** (207 mg, 0.38 mmol, 57% yield) as a yellow foam.

TLC (30% EtOAc/hexanes): R_f 0.71 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 – 7.34 (m, 5H), 7.32 – 7.24 (m, 2H), 6.91 – 6.82 (m, 2H), 5.65 (s, 1H), 5.06 (s, 1H), 4.64 (d, *J* = 10.5 Hz, 1H), 4.43 (d, *J* = 10.5 Hz, 1H), 4.43 (d, *J* = 6.3 Hz, 1H), 3.79 (s, 3H), 2.78 (d, *J* = 19.3 Hz, 1H), 2.68 (d, *J* = 19.3 Hz, 1H), 2.55 (dt, *J* = 13.0, 7.1 Hz, 1H), 2.49 (d, *J* = 7.9 Hz, 2H), 2.23 (m, 1H), 2.16 (dd, *J* = 13.6, 7.1 Hz, 1H), 2.10 – 1.94 (m, 2H), 1.85 (m, 1H), 1.49 (m, 1H), 1.31 (s, 3H), 1.30 (d, *J* = 7.3 Hz, 3H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.3, 159.1, 157.1, 139.9, 137.9, 130.5, 129.7, 129.5, 128.5, 126.6, 113.7, 109.5, 97.8, 95.7, 83.5, 72.3, 71.1, 55.2, 53.1, 45.1, 45.0, 40.2, 35.2, 34.8, 32.9, 27.3, 21.9, 21.4, 19.1, 13.0.

FTIR (NaCl, thin film): 2958, 1727, 1514, 1249, 1034 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 567.2717, found 567.2716.

$[\alpha]_D^{25}$ = –5° (*c* = 0.475, $CHCl_3$).

premature carbonylation side product 32:

TLC (20% EtOAc/hexanes): R_f 0.42 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7. 49 – 7.47 (m, 2H), 7.37 – 7.35 (m, 3H), 7.18 – 7.14 (m, 2H), 6.88 – 6.85 (m, 2H), 5.87 (s, 1H), 5.12 (s, 1H), 5.01 (s, 1H), 4.92 (s, 1H), 4.83 – 4.81 (m, 1H), 4.47 (d, *J* = 11.1 Hz, 1H), 4.32 (d, *J* = 11.1 Hz, 1H), 3.81 (s, 3H), 2.61 – 2.55 (m, 1H), 2.48 – 2.27 (m, 4H), 2.25 – 2.12 (m, 2H), 1.47 – 1.43 (m, 1H), 1.14 (d, *J* = 4.1 Hz, 3H), 1.09 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H).

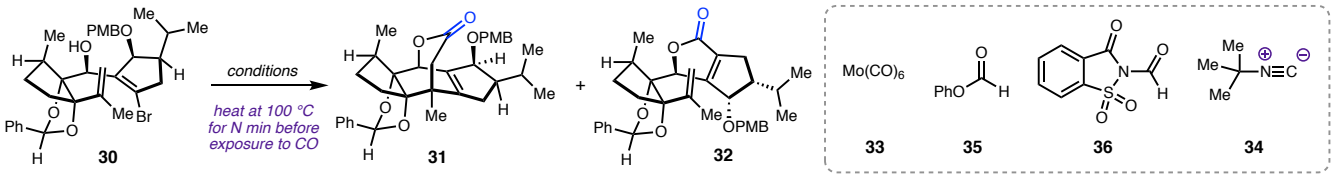
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.169.0, 159.4, 147.5, 143.5, 136.9, 130.3, 129.9, 129.1, 128.6, 127.1, 114.0, 112.7, 105.3, 96.9, 95.6, 82.4, 79.6, 70.0, 57.0, 55.4, 42.8, 40.2, 30.6, 29.4, 28.0, 22.2, 21.2, 14.2.

FTIR (NaCl, thin film): 2956, 1766, 1613, 1514, 1454 cm^{-1}.

HRMS (ESI): calc'd for $[M+NH_4]^+$ 562.3163, found 562.3160.

$[\alpha]_D^{25}$ = –76° (*c* = 0.500, $CHCl_3$).

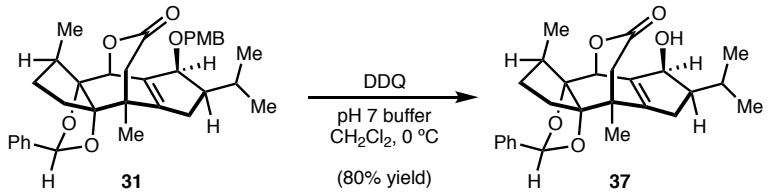
Table S1. Optimization of the Pd-catalyzed carbopalladation/carbonylation cascade.



entry	[M]	mol %	[L]	mol %	base	CO source	solvent	additive	*N* (min)	30[b] (%)	31[b] (%)	32[b] (%)
1	$Pd(P(o\text{-}Tol)_3)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	0	92	1	5
2	$Pd(P(o\text{-}Tol)_3)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	MeOH	20	67	11	15
3	$Pd(P(t\text{-}Bu)_3)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	20	65	16	2
4	$Pd(P(t\text{-}Bu)_3)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	TlOAc	20	72	18	–
5	$Pd(P(t\text{-}Bu)_3)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	MeOH	20	60	13	6
6	$Pd(P(t\text{-}Bu)_3)_2$	105	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	20	61	20	8
7	$Pd(P(t\text{-}Bu)_3)_2$	50	P(2-furyl)$_3$	100	Et_3N	CO (1 atm)	1,4 dioxane	–	5	80	7	9
8	$Pd(P(t\text{-}Bu)_3)_2$	50	$P(p\text{-F-Ph})_3$	100	Et_3N	CO (1 atm)	1,4 dioxane	–	5	75	10	5
9	$Pd(P(t\text{-}Bu)_3)_2$	50	Xantphos	100	Et_3N	CO (1 atm)	1,4 dioxane	–	5	77	4	12
10	$Pd(P(t\text{-}Bu)_3)_2$	50	$P(p\text{-F-Ph})_3$	100	Et_3N	CO (1 atm)	1,4 dioxane	–	30	60	22	6
11	$Pd(P(t\text{-}Bu)_3)_2$	50	$P(p\text{-F-Ph})_3$	100	Et_3N	CO (1 atm)	1,4 dioxane	–	60	50	34	9
12	$Pd(P(t\text{-}Bu)_3)_2$	120	$P(p\text{-F-Ph})_3$	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	–	57	6
13	$Pd(OAc)_2$	50	P(2-furyl)$_3$	100	Et_3N	CO (1 atm)	1,4 dioxane	–	80	97	0	–
14	$Pd(OAc)_2$	120	$P(p\text{-F-Ph})_3$	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	32	0	–
15	$PdCl_2$(dppf)	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	80	96	0	–
16	Pd_2dba_3	25	Xantphos	100	Et_3N	CO (1 atm)	1,4 dioxane	–	80	94	1	3
17	Pd_2dba_3	60	$P(p\text{-F-Ph})_3$	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	62	23	9
18	$Pd(P(t\text{-}Bu)_3)_2$	120	–	–	Et_3N	CO (1 atm)	DMF	–	80	35	28	20
19	$Pd(P(t\text{-}Bu)_3)_2$	120	–	–	Et_3N	CO (1 atm)	PhMe	–	80	–	0	–
20	$Pd(P(t\text{-}Bu)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	80	–	0	–
21	$Pd(P(t\text{-}Bu)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	70	–	0	–
22	$Pd(P(t\text{-}Bu)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	60	–	0	–
23	$Pd(P(t\text{-}Bu)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	40	6	0	–
24	$Pd(P(t\text{-}Bu)_3)_2$	120	$P(t\text{-Bu})_3$	240	Et_3N	CO (1 atm)	1,4 dioxane	–	60	28	11	–
25	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	DIPEA	CO (1 atm)	1,4 dioxane	–	80	–	51	–
26	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	DBU	CO (1 atm)	1,4 dioxane	–	80	–	6	–
27	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	Cs_2CO_3	CO (1 atm)	1,4 dioxane	–	80	–	0	–
28	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	DMAP	CO (1 atm)	1,4 dioxane	–	80	–	0	–
29	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	80	–	52	–
30	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	Et_3N	CO (10 atm)	1,4 dioxane	–	80	–	53	–
31	$Pd(P(o\text{-}Tol)_3)_2$	120	$P(p\text{-F-Ph})_3$	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	7	42	7
32	$Pd(P(o\text{-}Tol)_3)_2$	120	*rac*-BINAP	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	–	41	29
33	$Pd(P(o\text{-}Tol)_3)_2$	120	PEt_3	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	–	0	75
34	$Pd(P(o\text{-}Tol)_3)_2$	120	SPhos	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	–	51	–
35	$Pd(P(o\text{-}Tol)_3)_2$	120	dtbpf	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	18	7	22
36	$Pd(P(o\text{-}Tol)_3)_2$	120	dppf	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	9	13	48
37	$Pd(P(o\text{-}Tol)_3)_2$	120	dppb	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	6	18	19
38	$Pd(P(o\text{-}Tol)_3)_2$	120	dppp	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	6	21	31
39	$Pd(P(o\text{-}Tol)_3)_2$	120	dppe	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	17	17	17
40	$Pd(P(o\text{-}Tol)_3)_2$	120	dppm	240	Et_3N	CO (1 atm)	1,4 dioxane	–	80	80	0	12
41	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	MeOH	80	6	18	14
42	$Pd(P(o\text{-}Tol)_3)_2$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	*t*-BuOH	80	–	31	6
43	$Pd(PPh_3)_4$	50	–	–	Et_3N	CO (1 atm)	DMF	–	90	35	27	12
44	$Pd(PPh_3)_4$	50	–	–	Et_3N	CO (1 atm)	PhMe	–	90	35	5	–
45	$Pd(PPh_3)_4$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	90	34	31	9
46	$Pd(PPh_3)_4$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	90	23	48	13
47	$Pd(PPh_3)_4$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	TBAI	90	3	5	1
48	$Pd(PPh_3)_4$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	TBABr	90	20	15	20
49	$Pd(PPh_3)_4$	120	–	–	Et_3N	CO (1 atm)	1,4 dioxane	TBACl	90	22	12	22
50	$Ni(COD)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	30	35	0	–
51	$NiCl_2(PPh_3)_2$	50	–	–	Et_3N	CO (1 atm)	1,4 dioxane	–	30	28	0	–
52	$Pd(P(o\text{-}Tol)_3)_2$	50	–	–	Et_3N	**33**	1,4 dioxane	DBU	–	76	0	11
53	$Pd(PPh_3)_4$	50	–	–	Et_3N	**33**	1,4 dioxane	DBU	–	85	0	8
54	$Pd(PPh_3)_4$	50	–	–	Et_3N	**35**	1,4 dioxane	–	–	14	7	4
55	$Pd(P(t\text{-}Bu)_3)_2$	50	–	–	Et_3N	**35**	1,4 dioxane	–	–	4	1	–
56	$Pd(PPh_3)_4$	50	–	–	Et_3N	**34**	1,4 dioxane	–	–	90	0	–
57	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**	1,4 dioxane	KF	–	3	53	–
58	$Pd(PPh_3)_4$	30	–	–	Et_3N	**36**	1,4 dioxane	KF	–	14	32	14
59	$Pd(PPh_3)_4$	40	–	–	Et_3N	**36**	1,4 dioxane	KF	–	13	44	12
60	$Pd(PPh_3)_4$	60	–	–	Et_3N	**36**	1,4 dioxane	KF	–	0	52	–
61	$Pd(PPh_3)_4$	120	–	–	Et_3N	**36**	1,4 dioxane	KF	–	0	59	–
62	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**	1,4 dioxane	–	–	22	31	10
63	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**	1,4 dioxane	LiF	–	19	30	10
64	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**	1,4 dioxane	NaF	–	13	28	9
65	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**	1,4 dioxane	CsF	–	0	16	13
66	$Pd(PPh_3)_4$	50	–	–	–	**36**	1,4 dioxane	KF	–	0	49	12
67	$Pd(OAc)_2$	50	DPEphos	75	Et_3N	**36**	1,4 dioxane	KF	–	2	3	6
68	$Pd(OAc)_2$	50	Xantphos	100	Et_3N	**36**	1,4 dioxane	KF	–	70	0	4
69	$Pd(P(t\text{-}Bu)_3)_2$	50	$P(p\text{-F-Ph})_3$	100	Et_3N	**36**	1,4 dioxane	KF	–	31	6	–
70	$Pd(P(o\text{-}Tol)_3)_2$	50	–	–	Et_3N	**36**	1,4 dioxane	KF	–	60	0	–
71	$PdCl_2$(dppf)	50	–	–	Et_3N	**36**	1,4 dioxane	KF	–	80	0	–
72	$PdCl_2$(Xantphos)	50	–	–	Et_3N	**36**	1,4 dioxane	KF	–	55	1	4
73	$PdCl_2(PPh_3)_2$	50	–	–	Et_3N	**36**	1,4 dioxane	KF	–	11	14	4
74	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**[c]	1,4 dioxane	KF	–	0	48	13
75	$Pd(PPh_3)_4$	50	–	–	Et_3N	**36**[d]	1,4 dioxane	KF	–	12	42	13

[a]Reactions were run on 0.01 mmol scale of **30** at 100 °C. [b]Yields determined by ^{1}H NMR of the crude product using pyrazine as the internal standard.
[c]**36** was added via syringe pump over 30 min. [d]**36** was added via syringe pump over 1 h.

Preparation of alcohol 37



An oven-dried, 100 mL round-bottomed flask was charged with PMB ether **31** (1.11 g, 2.04 mmol, 1.0 equiv), CH_2Cl_2 (55 mL), and pH 7 buffer (11 mL). The mixture was cooled to 0 ºC via an ice/water bath and stirring was continued for 15 min prior to the addition of DDQ (555 mg, 2.45 mmol, 1.2 equiv) as a single portion. The reaction mixture quickly becomes a deep green suspension and vigorous stirring (≥800 rpm) is continued for 40 min prior to the addition of another portion of DDQ (278 mg, 1.22 mmol, 0.6 equiv). The reaction was continued at 0 ºC until TLC analysis indicated the complete consumption of the starting material (*ca*. 1.5 h). Sat. aq. $NaHCO_3$ (20 mL) was added and the mixture was diluted with $CHCl_3$ (10 mL) before the layers were separated [Note: the use of $CHCl_3$ over CH_2Cl_2 proved advantageous in obtaining clear partitioning of the two layers]. The aqueous layer was extracted with $CHCl_3$ (3 × 20 mL) and the combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (20 to 35 to 45% EtOAc/hexanes) to afford alcohol **37** (692 mg, 1.63 mmol, 80% yield) as a white foam.

TLC (30% EtOAc/hexanes): R_f 0.24 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.33 (m, 5H), 5.65 (s, 1H), 5.13 (s, 1H), 4.72 (t, *J* = 6.1 Hz, 1H), 2.78 (d, *J* = 19.3 Hz, 1H), 2.67 (d, *J* = 19.3 Hz, 1H), 2.55 (dd, *J* = 16.8, 7.1 Hz, 1H), 2.53 (m, 1H), 2.41 (ddd, *J* = 17.1, 8.0, 1.9 Hz, 1H), 2.28 – 2.10 (m, 2H), 2.01 (m, 1H), 1.93 – 1.76 (m, 2H), 1.43 (qd, *J* = 13.2, 7.4 Hz, 1H), 1.32 (s, 3H), 1.28 (s, 3H), 1.09 (d, *J* = 6.2 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H).

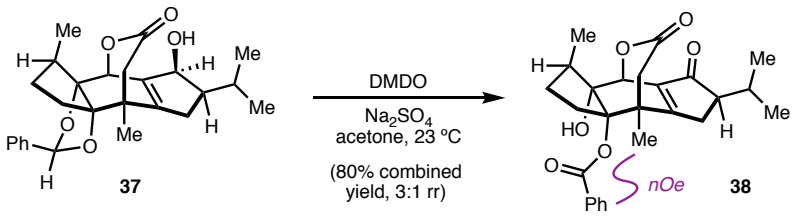
^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 155.7, 140.8, 137.9, 129.5, 128.5, 126.6, 109.5, 97.9, 95.7, 77.5, 71.9, 52.2, 44.9, 44.8, 40.2, 35.3, 34.4, 33.0, 27.6, 22.0, 21.5, 19.1, 13.0.

FTIR (NaCl, thin film): 3434, 2958, 1702, 1381, 1217, 1101, 1063, 1023 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 447.2142, found 447.2144.

$[\alpha]_D^{25}$ = +51° (*c* = 0.165, $CHCl_3$).

Preparation of enone 38



An oven-dried, 200 mL round-bottomed flask was charged with alcohol **37** (738 mg, 1.74 mmol, 1.0 equiv) and Na_2SO_4 (1.48 g, 0.39 mmol, 200% w/w) before adding freshly generated DMDO[6] (0.08 M in acetone, 43 mL, 3.48 mmol, 2.0 equiv) at ambient temperature. The reaction was continued for 1 h with vigorous stirring (800 rpm) before an additional portion of DMDO (0.08 M in acetone, 22 mL, 1.74 mmol, 1.0 equiv) was added. After LCMS analysis indicated the complete consumption of starting material (*ca.* 2 h), the reaction mixture was diluted with CH_2Cl_2 (20 mL) and filtered through a short pad of Celite. The filtrate was concentrated *in vacuo* and directly purified via SiO_2 flash chromatography (35 to 45 to 55% EtOAc/hexanes) to afford an inseparable regioisomeric mixture of hydroxybenzoate **38** (610 mg, 1.39 mmol, 80% combined yield, 3:1 rr) as a white foam [Note: attempts to purify the regioisomeric mixture by preparative HPLC and SFC were both unsuccessful] that was used in the next step without further purification. The regioselectivity of the major regioisomer (drawn) was confirmed by nOe analysis.

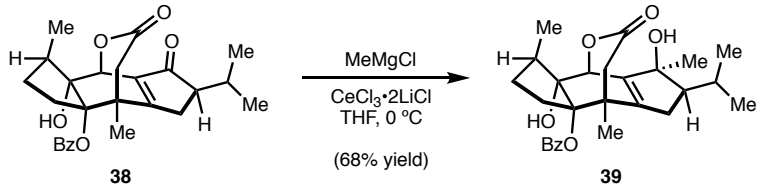
TLC (40% EtOAc/hexanes): R_f 0.37 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 5.09 (s, 1H), 3.02 (d, *J* = 19.4 Hz, 1H), 2.85 – 2.72 (m, 3H), 2.65 – 2.58 (m, 3H), 2.61 (d, *J* = 19.7 Hz, 1H), 2.32 (td, *J* = 7.0, 4.6 Hz, 1H), 2.22 (dd, *J* = 14.3, 7.7 Hz, 1H), 2.08 (m, 1H), 1.52 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 3H), 1.20 (m, 1H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 6.7 Hz, 3H).

FTIR (NaCl, thin film): 3453, 2960, 1728, 1704, 1694, 1276, 1114 cm^{-1}.

HRMS (ESI): calc'd for $[M+NH_4]^+$ 456.2381, found 456.2377.

Preparation of alcohol 39



An oven-dried, 10 mL round-bottomed flask was charged with $CeCl_3$•2LiCl[7] (0.3 M in THF, 4.0 mL) [Note: the use of $LaCl_3$•2LiCl provided lower yields of 1,2-addition product **39**] via syringe and the solution was immediately cooled to 0 ºC via an ice/water bath. After 15 min of continued stirring at 0 ºC, MeMgCl (3.0 M in THF, 0.4 mL) was added dropwise via syringe. Upon complete addition, the resulting dark-yellow reaction mixture was stirred for an additional 20 min at 0 ºC affording a 0.27 M stock solution of nucleophile that was used immediately.

A separate oven-dried, 100 mL round-bottomed flask was charged with a 3:1 regioisomeric mixture of enone **38** (399 mg, 0.91 mmol, 1.0 equiv) and anhydrous THF (18 mL). The resulting solution was cooled to 0 ºC via an ice/water bath and after 15 min of continued stirring, the freshly prepared stock solution of nucleophile (0.27 M in THF, 6.7 mL, 1.82 mmol, 2.0 equiv) was added dropwise via syringe. Upon complete addition, the reaction was continued at 0 ºC for 20 min at which point TLC and LCMS analysis indicated the complete consumption of starting material. The reaction was quenched with the addition of pH 7 buffer (3.6 mL) at 0 ºC and then warmed to ambient temperature. The mixture was diluted with Et_2O (10 mL) and filtered through a pre-equilibrated SiO_2 pad layered with Celite, washing with 80/1% EtOAc/Et_3N/hexanes. The filtrate was then concentrated *in vacuo* and directly purified via SiO_2 flash chromatography (25/1 to 35/1 to 45/1% EtOAc/Et_3N/hexanes) to afford alcohol **39** (281 mg, 0.62 mmol, 68% yield, single dr) as a white foam. The diastereoselectivity was confirmed by nOe analysis.

TLC (40% EtOAc/hexanes): R_f 0.34 (UV, *p*-anisaldehyde).

^{1}H NMR (500 MHz, C_6D_6): δ 7.96 (d, *J* = 6.9 Hz, 2H), 7.10 – 6.99 (m, 3H), 4.85 (s, 1H), 2.75 (td, *J* = 14.6, 14.2, 7.7 Hz, 1H), 2.62 (s, 1H, OH), 2.49 (d, *J* = 19.3 Hz, 1H), 2.35 (m, 1H), 2.22 (d, *J* = 19.3 Hz, 1H), 1.73 (s, 1H, OH), 1.69 – 1.51 (m, 3H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.17 (s, 3H), 1.09 (m, 1H), 1.04 (d, *J* = 6.3 Hz, 3H), 0.94 (s, 3H), 0.82 (d, *J* = 6.4 Hz, 3H).

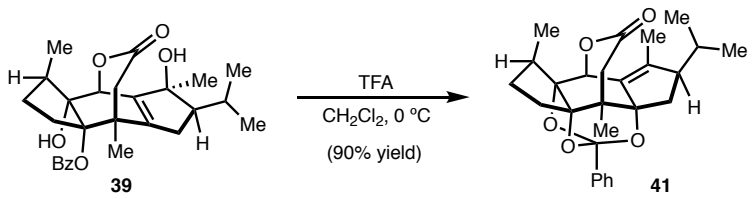
^{13}C NMR (101 MHz, C_6D_6): δ 168.4, 167.4, 148.6, 145.0 133.1, 131.9, 129.6, 128.6, 96.8, 85.5, 82.7, 71.9, 60.4, 45.0, 44.4, 41.7, 33.5, 30.0, 28.5, 22.4, 21.9, 20.3, 19.8, 12.4.

FTIR (NaCl, thin film): 3460, 2960, 2884, 1724, 1274, 1115, 1023 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 477.2248, found 477.2229.

$[\alpha]_D^{25}$ = +10° (*c* = 0.125, CH_2Cl_2).

Preparation of orthobenzoate 41



An oven-dried, 50 mL round-bottomed flask was treated with hydroxybenzoate **39** (281 mg, 0.62 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (20 mL). The resulting solution was cooled to 0 ºC via an ice/water bath and stirring was continued at this temperature for 15 min prior to the addition of TFA (0.24 mL, 3.09 mmol, 5.0 equiv) *as a single portion* via syringe. The reaction was allowed 5 min at 0 ºC, during which time the colorless reaction mixture becomes bright pink, diluted with CH_2Cl_2 (10 mL) and treated with sat. aq. $NaHCO_3$ (10 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue could be used directly in the next step after azeotroping with anhydrous PhMe three times immediately prior to use. The crude residue was purified via SiO_2 flash chromatography (10 to 20% EtOAc/hexanes) for characterization purposes to afford orthobenzoate **41** (243 mg, 0.56 mmol, 90% yield) as a white foam.

TLC (10% EtOAc/hexanes): R_f 0.24 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.53 (m, 2H), 7.43 – 7.31 (m, 3H), 5.37 (s, 1H), 3.06 (t, *J* = 9.2 Hz, 1H), 2.71 (d, *J* = 19.0 Hz, 1H), 2.62 (d, *J* = 19.0 Hz, 1H), 2.54 (dt, *J* = 12.5, 7.2 Hz, 1H), 2.23 – 2.09 (m, 2H), 2.07 – 1.93 (m, 2H), 1.89 (dd, *J* = 14.2, 6.9 Hz, 1H), 1.83 (d, *J* = 1.3 Hz, 3H), 1.69 (dd, *J* = 14.2, 8.2 Hz, 1H), 1.65 (m, 1H), 1.27 (d, *J* = 7.1 Hz, 3H), 1.25 (s, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H).

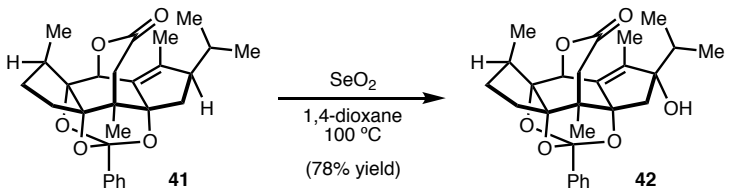
^{13}C NMR (101 MHz, $CDCl_3$): δ 171.0, 150.2, 135.0, 134.2, 129.6, 128.1, 126.0, 120.9, 94.5, 91.0, 91.0, 69.5, 51.9, 42.1, 41.7, 40.1, 34.1, 30.5, 28.5, 27.3, 21.1, 17.4, 15.7, 13.0, 12.6.

FTIR (NaCl, thin film): 2958, 2878, 1731, 1351, 1190 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 459.2142, found 459.2154.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$ = –201° (*c* = 0.175, $CHCl_3$).

Preparation of allylic alcohol 42



An oven-dried 48 mL pressure flask was charged with orthobenzoate **41** (242 mg, 0.55 mmol, 1.0 equiv), anhydrous 1,4-dioxane (18 mL), and SeO_2 (308 mg, 2.77 mmol, 5.0 equiv) [Note: SeO_2 was stored in a nitrogen-filled glove box to maintain the integrity of the reagent]. The flask was immediately capped with a CAPFE O-ring lined cap and submerged in a preheated oil bath at 100 ºC. The reaction mixture was vigorously stirred for 1 h at this temperature, at which point TLC and LCMS analysis indicated the complete consumption of starting material. The pressure flask was removed from the oil bath and cooled to ambient temperature, and the reaction mixture was diluted with Et_2O (10 mL) and filtered over a pre-equilibrated SiO_2 pad layered with Celite, washing with 80% EtOAc/hexanes. The filtrate was concentrated *in vacuo* and the crude residue was directly purified via SiO_2 flash chromatography (5 to 10 to 20 to 30% EtOAc/hexanes) to afford alcohol **42** (196 mg, 0.43 mmol, 78% yield) as a yellow foam.

TLC (15% EtOAc/hexanes): R_f 0.14 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, C_6D_6): δ 7.83 – 7.65 (m, 2H), 7.14 – 7.01 (m, 3H), 5.35 (s, 1H), 2.49 (d, *J* = 18.9 Hz, 1H), 2.40 (dq, *J* = 11.7, 7.1 Hz, 1H), 2.29 (d, *J* = 18.9 Hz, 1H), 2.01 (s, 1H), 1.91 (hept, *J* = 6.8 Hz, 1H), 1.81 (m, 1H), 1.80 (d, *J* = 14.6 Hz, 1H), 1.73 – 1.63 (m, 3H), 1.67 (d, *J* = 14.7 Hz, 1H), 1.52 (s, 3H), 1.18 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.97 (s, 3H), 0.46 (d, *J* = 6.7 Hz, 3H).

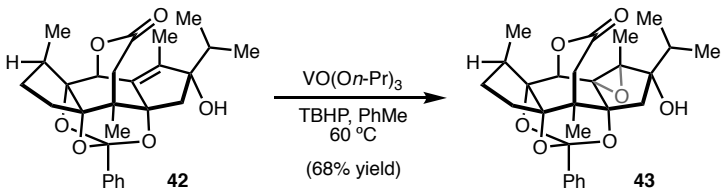
^{13}C NMR (101 MHz, C_6D_6): δ 168.8, 150.7, 137.1, 135.7, 129.8, 126.4, 121.6, 94.6, 91.3, 90.0, 87.9, 69.0, 42.0, 41.9, 39.1, 37.8, 34.3, 32.3, 28.6, 18.1, 17.6, 16.7, 13.0, 9.4.

FTIR (NaCl, thin film): 3540, 2960, 2879, 1732, 1352, 1078, 1038 cm^{-1}.

HRMS (ESI): calc'd for $[M+H]^+$ 453.2272, found 453.2271.

$[\alpha]_D^{25}$ = –161° (*c* = 0.115, CH_2Cl_2).

Preparation of epoxide 43



An oven-dried, 20 mL scintillation vial was treated with alkene **42** (104 mg, 230 μmol, 1.0 equiv) and anhydrous PhMe (7.7 mL). The resulting solution was treated with VO(O*n*-Pr)$_3$ (26 μL, 115 μmol, 0.5 equiv) via microsyringe prior to the addition of TBHP (5.5 M in decanes, 125 μL, 689 μmol, 3.0 equiv) via microsyringe. The vial was capped with a Teflon-lined cap under Ar and immediately placed in a preheated heating block at 60 ºC. The reaction was left to stir at this temperature for 14 h prior to adding an additional portion of VO(O*n*-Pr)$_3$ (26 μL, 115 μmol, 0.5 equiv) and TBHP (5.5 M in decanes, 125 μL, 689 μmol, 3.0 equiv) via syringe at ambient temperature. The reaction was continued at 60 ºC for an additional 14 h at which point LCMS analysis indicated complete consumption of the starting material [Note: the starting material and product epoxide are indistinguishable by TLC and thus requires the use of LCMS for reaction monitoring]. The reaction was cooled to ambient temperature and quenched with the addition of pH 7 buffer (6 mL) and sat. aq. $Na_2S_2O_3$ (3 mL). EtOAc (10 mL) was added and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered over Celite, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (1 to 2 to 3% acetone/CH_2Cl_2) to afford epoxide **43** (73.2 mg, 156 μmol, 68% yield) as a white foam. The stereochemistry was confirmed by nOe analysis.

TLC (4% acetone/CH_2Cl_2): R_f 0.43 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, C_6D_6): δ 7.89 (m, 2H), 7.14 (m, 3H), 4.66 (s, 1H), 3.07 (s, 1H, OH), 2.70 (d, *J* = 19.6 Hz, 1H), 2.52 (d, *J* = 19.6 Hz, 1H), 2.30 (m, 1H), 2.14 (d, *J* = 16.4 Hz, 1H), 1.82 (p, *J* = 6.8 Hz, 1H), 1.72 (m, 1H), 1.66 – 1.54 (m, 2H), 1.57 (d, *J* = 16.4 Hz, 1H), 1.44 (m, 1H), 1.35 (s, 3H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 7.1 Hz, 3H), 0.89 (s, 3H), 0.74 (d, *J* = 6.8 Hz, 3H).

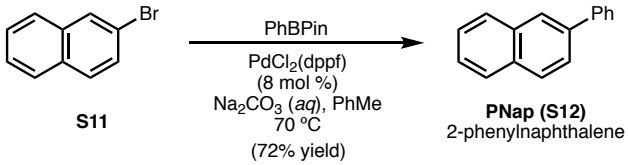
^{13}C NMR (101 MHz, C_6D_6): δ 167.8, 135.5, 129.8, 128.2, 126.5, 121.7, 93.9, 91.9, 85.0, 81.7, 76.5, 76.1, 74.8, 42.5, 41.6, 40.4, 39.6, 34.1, 33.8, 28.5, 19.6, 17.9, 17.4, 13.0, 12.9.

FTIR (NaCl, thin film): 3506, 2964, 2880, 1737, 1360, 1199 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 491.2040, found 491.2030.

$[\alpha]_D^{25}$ = –136° (*c* = 0.185, $CHCl_3$).

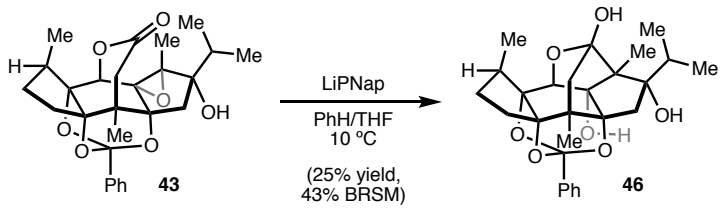
Preparation of 2-phenylnaphthalene (S12)

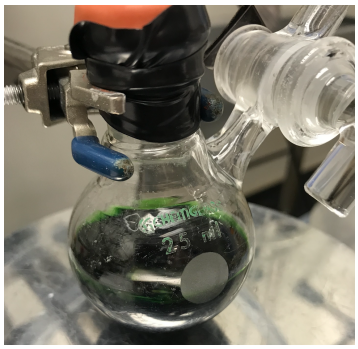


An oven-dried, 250 mL round-bottomed flask was charged with 2-bromonaphthalene (3.11 g, 15.0 mmol, 1.0 equiv), phenylboronic acid pinacol ester (6.12 g, 30.0 mmol, 2.0 equiv), and $PdCl_2(dppf)•CH_2Cl_2$ (980 mg, 1.20 mmol, 8 mol %). The flask was equipped with a rubber septum and evacuated/refilled three times with Ar. Anhydrous PhMe (100 mL) and freshly degassed 2.0 M Na_2CO_3 (*aq*) (37.5 mL, 75.0 mmol, 5.0 equiv) were subsequently added via syringe [Note: 2.0 M Na_2CO_3 (*aq*) was degassed by sparging with Ar for ≥15 min]. The biphasic mixture was immediately placed in a preheated oil bath at 70 ºC equipped with a double-walled Ar balloon and the reaction was continued at 70 ºC with vigorous stirring (≥700 rpm) until TLC analysis indicated the complete consumption of starting material (*ca*. 2 h). The reaction mixture was cooled to ambient temperature, diluted with EtOAc (40 mL), and treated with sat. aq. NH_4Cl (60 mL). The layers were separated and the aqueous layer was extracted with EtOAc (1 × 100 mL). The combined layers were washed with brine (50 mL), dried over Na_2SO_4, filtered over Celite, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (5% CH_2Cl_2/hexanes) to afford 2-phenylnaphthalene (2.25 g, 11.0 mmol, 72% yield) as a white solid [Note: the impure fractions can be pooled and repurified to improve the isolated yield if desired].

Spectral data of synthetic 2-phenylnaphthalene (**S12**) matched that obtained on an authentic sample purchased from Acros Organics.

Preparation of pentacycle 46





LiPNap was prepared according to the following procedure: An oven-dried, 25 mL Schlenk flask containing a borosilicate glass-coated magnetic stirbar was charged with 2-phenylnaphthalene (409 mg, 2.0 mmol) and freshly cut lithium wire (14.0 mg, 2.0 mmol) [Note: Immediately prior to use, lithium wire was washed with hexanes, hammered out into a foil, and cut into several small strips]. The Schlenk flask was evacuated and refilled with Ar three times before anhydrous THF (12.5 mL) was added and the resulting reaction mixture was vigorously stirred (900-1000 rpm) at ambient temperature for 10 min, at which point the solution becomes a deep-green. After the reaction mixture was stirred at ambient temperature for approximately 4 h, the LiPNap solution (~0.16 M) was cooled to 0 ºC via an ice/water bath and immediately used.

An oven-dried, 2 dram vial was charged with epoxide **43** (20.4 mg, 43.5 μmol, 1.0 equiv) and anhydrous PhH (1.4 mL) [Note: epoxide **43** was azeotroped with PhH three times prior to use]. The solution was cooled to +10 ºC via a dry ice/1,4-dioxane bath and stirring was continued for 15 min at this temperature prior to the dropwise addition of freshly generated LiPNap (0.16 M in THF, 1.2 mL, 196 μmol, 4.5 equiv). Upon complete addition, the resulting dark-orange reaction mixture was stirred for 5 min before adding sat. aq. $NaHCO_3$ (1 mL). The mixture was warmed to ambient temperature, diluted with $CHCl_3$ (1 mL), and the layers were separated. The aqueous layer was extracted with $CHCl_3$ (5 × 1 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified via preparative TLC (3% MeOH/CH_2Cl_2) to afford pentacycle **46** (5.1 mg, 10.8 μmol, 25% yield) as an off-white foam. A second round of purification of the less polar fraction via SiO_2 flash chromatography (0 to 2 to 4% acetone/CH_2Cl_2) affords recovered **43** (8.8 mg, 43% BRSM).

TLC (7% MeOH/CH_2Cl_2): R_f 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 – 7.59 (m, 2H), 7.47 – 7.33 (m, 3H), 4.25 (s, 1H), 3.19 (s, 1H, OH), 3.09 (d, *J* = 1.9 Hz, 1H, OH), 2.81 (s, 1H, OH), 2.56 (d, *J* = 15.5 Hz, 1H), 2.31 (dt, *J* = 10.5, 7.1 Hz, 1H), 2.14 – 2.04 (m, 2H), 2.11 (d, *J* = 15.6 Hz, 1H), 2.08 (d, *J* = 14.7 Hz, 1H), 1.97 (m, 1H), 1.96 (d, *J* = 14.7 Hz, 1H), 1.88 (m, 1H),

1.72 (m, 1H), 1.40 (s, 3H), 1.29 (s, 3H), 1.14 (d, J = 7.1 Hz, 3H), 1.06 (d, J = 6.7 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H).

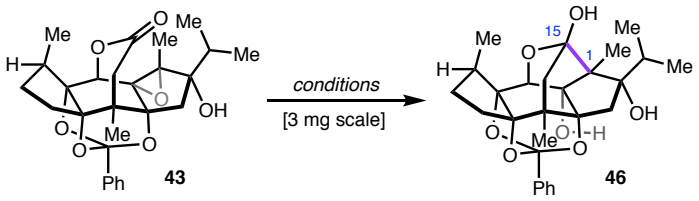
^{13}C NMR (101 MHz, $CDCl_3$): δ 134.6, 129.9, 128.2, 126.0, 120.4, 104.8, 96.0, 92.6, 88.6, 85.7, 81.0, 74.2, 60.1, 47.8, 42.1, 41.4, 39.1, 34.1, 33.3, 28.6, 20.1, 18.8, 18.6, 14.0, 9.7.

FTIR (NaCl, thin film): 3451, 2957, 2924, 1853, 1725, 1462, 1350, 1033 cm^{-1}.

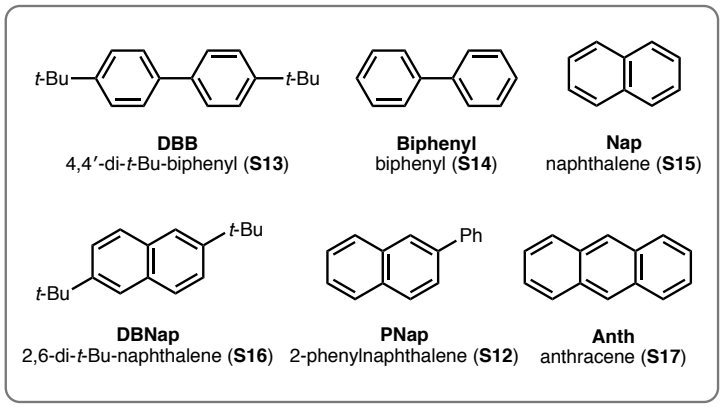
HRMS (ESI): calc'd for $[M+H]^+$ 471.2377, found 471.2385.

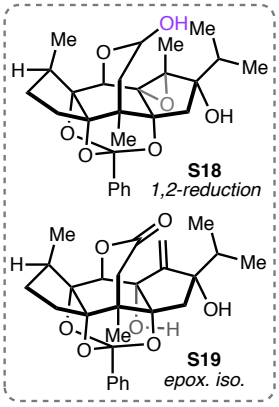
$[\alpha]_D^{25}$ = –52° (c = 0.090, $CHCl_3$).

Table S2. Optimization of reductive cyclization to convert epoxide **43** to pentacycle **46**.

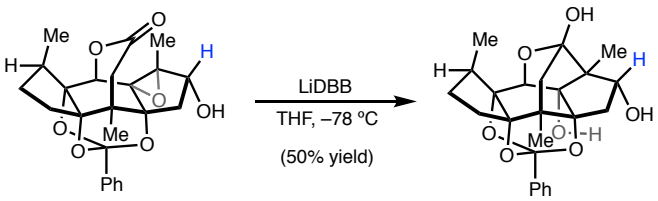


entry	reagent	temperature	solvent	additive	ratio	yield
1	LiDBB	–78 °C	THF	–	messy	–
2	LiDBB	–20 °C	THF	–	messy	–
3	LiBiphenyl	–20 °C	THF	–	3:1 **43**:**46**	–
4	LiDBNap	–20 °C	THF	–	3:1 **43**:**46**	–
5	LiNap	–40 °C	THF	–	2:1 **43**:**46**	10% yield
6	LiNap	–20 °C	THF	–	2:1 **43**:**46**	17% yield
7	LiNap	–20 °C	THF	BMEA	6:1 **43**:**46**	–
8	NaNap	–20 °C	THF	–	>10:1 **43**:**46**	–
9	LiAnth	23 °C	THF	–	full conversion	**S19** only
10	LiPNap	–20 °C	2-MeTHF	–	3:1 **43**:**46**	14% yield
11	LiPNap	10 °C	THF	–	2:1 **43**:**46**	14% yield
12	LiPNap	10 °C	PhH	–	2:1 **43**:**46**	23% yield
13	LiPNap	23 °C	PhH	–	3:1 **43**:**46**	13% yield
14	LiPNap	10 °C	$PhCF_3$	–	no reaction	–
15	LiPNap	–20 °C	PhMe	–	2.5:1 **43**:**46**	20% yield
16	SmI_2	0 °C	THF	H_2O+Et_3N	70% conversion	**S18** only
17	SmI_2	23 °C	THF	H_2O+Et_3N	85% conversion	**S18** only





Reductive cyclization of epoxylactone S20



S20 **S21** *[X-ray]*

An oven-dried, 25 mL round-bottomed flask containing a borosilicate glass-coated magnetic stirbar was charged with epoxide **S20** (55.8 mg, 0.13 mmol, 1.0 equiv) and anhydrous THF (9.8 mL) [Note: epoxide **S20** was azeoptroped with PhH three times prior to use]. The solution was cooled to –78 ºC via a dry ice/acetone bath and stirring was continued for 15 min at this temperature prior to the dropwise addition of freshly generated LiDBB[8] (0.16 M in THF, 3.3 mL, 0.52 mmol, 4.0 equiv). Upon complete addition, the resulting dark-orange reaction mixture was stirred for 5 min before adding sat. aq. NH_4Cl (10 mL). The mixture was warmed to ambient temperature, diluted with $CHCl_3$ (10 mL), and the layers were separated. The aqueous layer was extracted with $CHCl_3$ (5 × 10 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified via SiO_2 flash chromatography (4 to 6 to 8% MeOH/$CHCl_3$) to afford pentacycle **S21** (28.0 mg, 65.4 μmol, 50% yield) as an off-white foam.

TLC (8% MeOH/CH_2Cl_2): R_f 0.33 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CD_3OD): δ 7.63 (m, 2H), 7.37 (m, 3H), 4.21 (s, 1H), 3.88 (dd, *J* = 7.5, 6.4 Hz, 1H), 2.62 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.31 (dp, *J* = 10.0, 7.0 Hz, 1H), 2.14 (m, 1H), 2.06 (m, 1H), 2.06 (dd, *J* = 13.7, 6.4 Hz, 1H), 2.00 (d, *J* = 14.8 Hz, 1H), 1.87 – 1.71 (m, 2H), 1.63 (d, *J* = 14.8 Hz, 1H), 1.26 (s, 3H), 1.16 (s, 3H), 1.13 (d, *J* = 7.1 Hz, 3H).

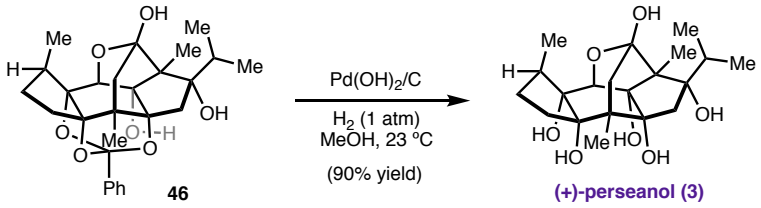
^{13}C NMR (101 MHz, CD_3OD): δ 136.8, 130.5, 128.8, 127.3, 121.8, 106.4, 96.9, 93.7, 87.3, 87.0, 76.4, 70.0, 58.4, 43.1, 42.8, 42.4, 39.7, 34.7, 29.8, 20.1, 14.1, 8.7.

FTIR (NaCl, thin film): 3418, 2938, 1462, 1453, 1350, 1026 cm^{-1}.

HRMS (ESI): calc'd for $[M+Na]^+$ 451.1727, found 451.1726.

$[\alpha]_D^{25}$ = –80° (*c* = 0.065, $CHCl_3$).

Preparation of (+)-perseanol (3)



An oven-dried, 2 dram vial was charged with pentacycle **46** (6.7 mg, 14.2 μmol, 1.0 equiv), $Pd(OH)_2/C$ (20 wt %, 14 mg), and MeOH (2.9 mL). The vial was capped with a rubber septum and the reaction mixture was vigorously stirred (1000 rpm) while flushing the headspace with H_2 for 5 minutes via a double-walled balloon. The suspension was vigorously stirred under H_2 until LCMS indicated complete consumption of the starting material (*ca.* 1.5 h) then immediately diluted with CH_2Cl_2 (2 mL), filtered through a short pad of Celite, and concentrated *in vacuo*. Purification of the crude residue by SiO_2 flash chromatography (4 to 8 to 10% MeOH/$CHCl_3$) afforded (+)-perseanol (4.9 mg, 12.8 μmol, 90% yield) as a white solid.

TLC (10% MeOH/CH_2Cl_2): R_f 0.21 (*p*-anisaldehyde).

^{1}H NMR (500 MHz, CD_3OD): δ 3.82 (s, 1H, C_{11}), 2.59 (d, J = 15.8 Hz, 1H, C_3), 2.23 (m, 1H, C_7), 1.98 (dt, J = 12.7, 6.8 Hz, 1H, C_9), 1.92 (d, J = 14.7 Hz, 1H, C_{14}), 1.90 (d, J = 15.8 Hz, 1H, C_3), 1.86 (p, J = 6.7 Hz, 1H, C_{13}), 1.64 – 1.53 (m, 2H, C_8), 1.64 (d, J = 14.7 Hz, 1H, C_{14}), 1.57 (m, 1H, C_7), 1.29 (s, 3H, C_{17}), 1.13 (s, 3H, C_{20}), 1.11 (d, J = 6.9 Hz, 3H, C_{21}), 1.02 (d, J = 6.6 Hz, 3H, C_{19}), 0.97 (d, J = 6.8 Hz, 3H, C_{18}).

^{13}C NMR (101 MHz, CD_3OD): δ 104.3 (C_{15}), 89.2 (C_{12}), 85.1 (C_4), 83.1 (C_6), 82.1 (C_2), 81.6 (C_{10}), 77.7 (C_{11}), 63.0 (C_1), 52.6 (C_3), 46.9 (C_9), 45.5 (C_{14}), 44.7 (C_5), 37.5 (C_7), 35.3 (C_{13}), 30.1 (C_8), 18.9 (C_{18}), 18.9 (C_{19}), 18.5 (C_{21}), 12.8 (C_{20}), 10.7 (C_{17}).

FTIR (NaCl, thin film): 3383, 2925, 2855, 1728, 1463, 1384, 1287, 1106, 1029 cm^{-1}.

HRMS (ESI:NES): calc'd for $[M–H]^-$ 383.2075, found 383.2075.

HRMS (ESI:PES): calc'd for $[M+Na]^+$ 407.2040, found 407.2039.

$[\alpha]_D^{25}$ = +3° (*c* = 0.085, MeOH).

4. ^{1}H and ^{13}C NMR Comparison Tables for Perseanol

Table S3. Comparison of ^{1}H NMR data for Perseanol.

Proton No.	Zhang and coworkers Natural Perseanol ^{1}H NMR, 400 MHz, CD_3OD ^{1}H [δ, multi., *J* (Hz)]	This Work, Synthetic Perseanol ^{1}H NMR, 500 MHz, CD_3OD ^{1}H [δ, multi., *J* (Hz)]
1		
2		
3a	1.90 (d, *J* = 15.8 Hz)	1.90 (d, *J* = 15.8 Hz)
3b	2.59 (d, *J* = 15.8 Hz)	2.59 (d, *J* = 15.8 Hz)
4		
5		
6		
7a	2.22 (m)	2.23 (m)
7b	1.57 (m)	1.57 (m)
8	1.63 – 1.52 (m)	1.64 – 1.53 (m)
9	1.98 (dt, *J* = 12.9, 7.0 Hz)	1.98 (dt, *J* = 12.7, 6.9 Hz)
10		
11	3.82 (s)	3.82 (s)
12		
13	1.87 (p, *J* = 6.6 Hz)	1.86 (p, *J* = 6.7 Hz)
14a	1.64 (d, *J* = 14.6 Hz)	1.64 (d, *J* = 14.7 Hz)
14b	1.92 (d, *J* = 14.7 Hz)	1.92 (d, *J* = 14.7 Hz)
15		
17	1.30 (s)	1.29 (s)
18	0.97 (d, *J* = 6.8 Hz)	0.97 (d, *J* = 6.8 Hz)
19	1.02 (d, *J* = 6.6 Hz)	1.02 (d, *J* = 6.6 Hz)
20	1.13 (s)	1.13 (s)
21	1.11 (d, *J* = 7.0 Hz)	1.11 (d, *J* = 6.9 Hz)

Table S4. Comparison of ^{13}C NMR data for Perseanol.

Carbon No.	Zhang and coworkers Natural Perseanol ^{13}C NMR, 101 MHz, CD_3OD ^{13}C (δ) ppm	This Work, Synthetic Perseanol ^{13}C NMR, 101 MHz, CD_3OD ^{13}C (δ) ppm	Chemical Shift Difference, Δδ
1	63.0	63.0	0
2	82.1	82.1	0
3	52.6	52.6	0
4	85.1	85.1	0
5	44.7	44.7	0
6	83.1	83.1	0
7	37.5	37.5	0
8	30.1	30.1	0
9	46.9	46.9	0
10	81.7	81.6	0.1
11	77.6	77.7	0.1
12	89.2	89.2	0
13	35.2	35.3	0.1
14	45.5	45.5	0
15	104.3	104.3	0
17	10.7	10.7	0
18	18.9	18.9	0
19	18.9	18.9	0
20	12.8	12.8	0
21	18.5	18.5	0

5. Single Crystal X-ray Diffraction Data

Low-temperature diffraction data (φ- and ω-scans) was collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Cu-K_α radiation (λ = 1.54178 Å) from a $I_\mu S$ HB micro-focus sealed X-ray tube. All diffractometer manipulations, including data collection, integration, and scaling were carried out using the Bruker APEXII software.[9] Absorption corrections were applied using SADABS.[10] The structure was solved by intrinsic phasing using SHELXT[11] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[11] using established refinement techniques.[12] All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups and hydroxyl groups). Absolute configuration was determined by anomalous dispersion.[13] Crystallographic data for **32** and **S21** can be obtained free of charge from The Cambridge Crystallographic Data Center (CCDC) via www.ccdc.cam.ac.uk/data_request/cif under CCDC deposition number 1909375 and 1914686, respectively. Graphical representation of **32** and **S21** with 50% probability thermal ellipsoids was generated using Mercury visualization software.

Table S5. Crystal data and structure refinement for **32**.

Identification code	v18645_a	
Empirical formula	$C_{34}H_{40}O_6$	
Formula weight	544.66	
Temperature	100.03 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P12_11$	
Unit cell dimensions	a = 11.6776(5) Å	α= 90°.
	b = 8.9076(4) Å	β= 108.474(2)°.
	c = 14.9231(7) Å	γ = 90°.
Volume	1472.30(12) $Å^3$	
Z	2	
Density (calculated)	1.229 Mg/m^3	
Absorption coefficient	0.667 mm^{-1}	
F(000)	584	
Crystal size	0.34 x 0.1 x 0.02 mm^3	
Theta range for data collection	3.122 to 80.960°.	
Index ranges	-12<=h<=14, -11<=k<=11, -19<=l<=17	
Reflections collected	27822	
Independent reflections	5545 [R(int) = 0.0500]	
Completeness to theta = 67.679°	94.4%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7543 and 0.5508	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5545 / 1 / 367	
Goodness-of-fit on F^2	1.061	
Final R indices [I>2sigma(I)]	R1 = 0.0353, wR2 = 0.0879	
R indices (all data)	R1 = 0.0373, wR2 = 0.0895	
Absolute structure parameter	0.21(6)	
Extinction coefficient	0.0078(7)	
Largest diff. peak and hole	0.256 and -0.282 e.$Å^{-3}$	

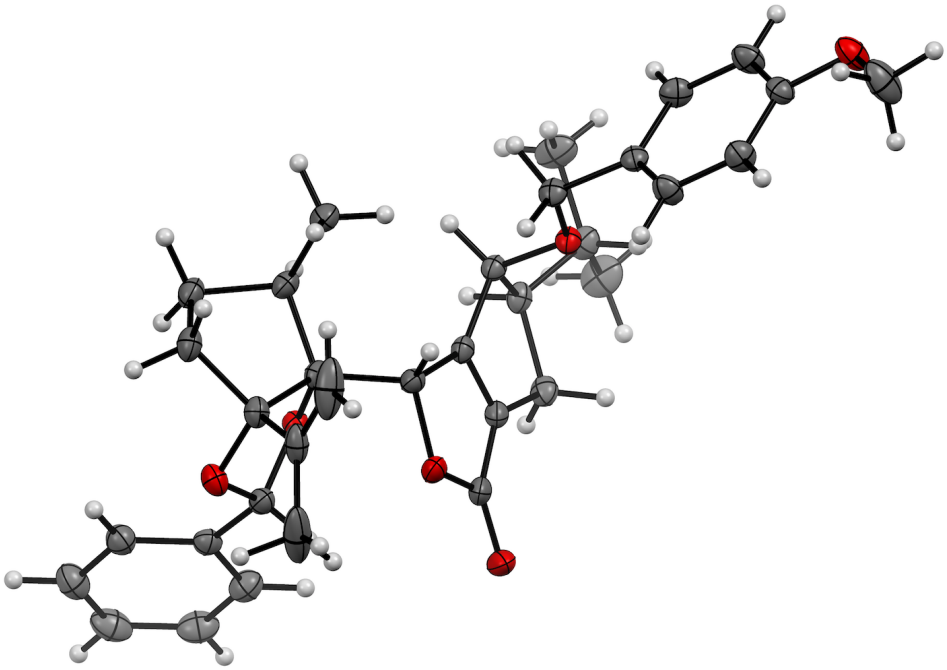


Figure S5. Structure of **32** with 50% probability anisotropic displacement ellipsoids.

Special Refinement Details for 32

Compound **32** crystallizes in the monoclinic space group $P2_1$ with one molecule in the asymmetric unit. The Flack parameter was determined to be 0.21(6); abs(x) is too high for valid absolute structure assignment by anomalous dispersion.[13] Absolute configuration was determined by synthesis with respect to an unchanging chiral center on the molecule.[2]

Table S6. Crystal data and structure refinement for **S21**.

Identification code	v18190_h	
Empirical formula	$2(C_{24}H_{28}O_7)$, H_2O	
Formula weight	874.94	
Temperature	100.0 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P12_11$	
Unit cell dimensions	a = 12.4227(7) Å	α= 90°.
	b = 10.3715(6) Å	β= 93.088(3)°.
	c = 15.5943(9) Å	γ = 90°.
Volume	2006.3(2) $Å^3$	
Z	2	
Density (calculated)	1.448 Mg/m^3	
Absorption coefficient	0.889 mm^{-1}	
F(000)	932	
Crystal size	0.09 x 0.07 x 0.06 mm^3	
Theta range for data collection	2.838 to 79.031°.	
Index ranges	-15<=h<=15, -12<=k<=13, -19<=l<=19	
Reflections collected	43703	
Independent reflections	8046 [R(int) = 0.0580]	
Completeness to theta = 67.679°	98.5%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7437 and 0.6601	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8046 / 1 / 580	
Goodness-of-fit on F^2	1.064	
Final R indices [I>2sigma(I)]	R1 = 0.0611, wR2 = 0.1539	
R indices (all data)	R1 = 0.0665, wR2 = 0.1597	
Absolute structure parameter	-0.02(6)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.828 and -0.464 e.$Å^{-3}$	

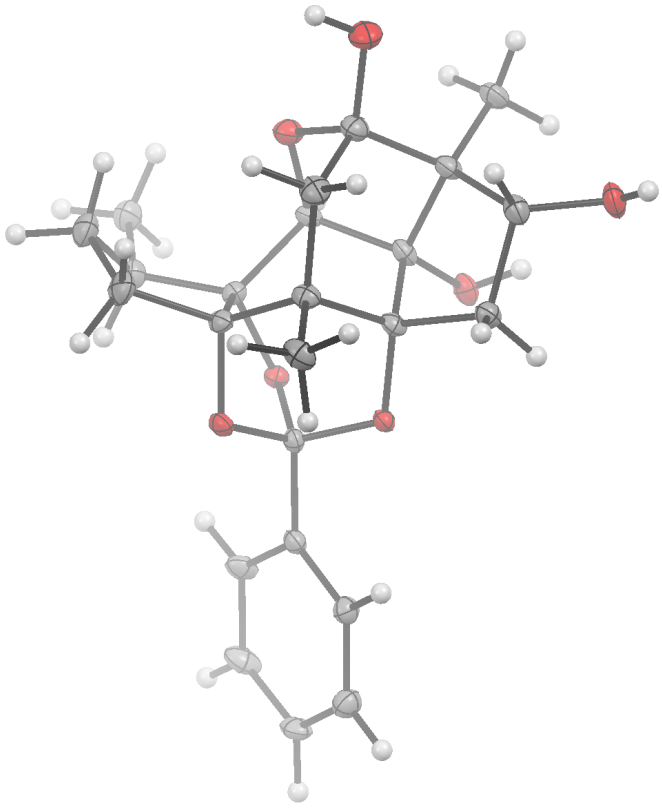


Figure S6. Structure of **S21** with 50% probability anisotropic displacement ellipsoids. Co-crystallized water and the second molecule of **S21** are omitted for clarity.

Special Refinement Details for S21

Compound **S21** crystallizes in the monoclinic space group $P12_11$ with two molecules in the asymmetric unit along with one molecule of water. The hydrogen atoms for all hydroxyl groups and the water molecule were not located in the difference Fourier synthesis and were included into the model at geometrically calculated positions and refined using a riding model. No hydrogen bond acceptor was found for H6A and H8A. Absolute configuration was determined by anomalous dispersion (Flack = -0.01(6)).[13]

6. References

1. Koshimizu, M.; Nagatomo, M.; Inoue, M. Construction of a pentacyclic ring system of isoryanodane diterpenoids by SmI_2-mediated transannular cyclization. *Tetrahedron* **2018**, *74*, 3384.

2. Shen, Y.; Li, L. B.; Pan, Z. S.; Wang, Y. L.; Li, J. D.; Wang, K. Y.; Wang, X. C.; Zhang, Y. Y.; Hu, T. H.; Zhang, Y. D. Protecting-group-free total synthesis of (–)-Jiadifenolide: development of a [4+1] annulation toward multisubstituted tetrahydrofurans. *Org. Lett.* **2015**, *17*, 5480.

3. Niwa, H.; Kunitani, K.; Nagoya, T.; Yamada, K. Enantioselective synthesis of the macrocyclic pyrrolizidine alkaloid yamataimine. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3094.

4. Nwoye, E. O.; Dudley, G. B. Synthesis of *para*-methoxybenzyl (PMB) ethers under neutral conditions. *Chem. Commun.* **2007**, 1436.

5. Stewart, C. A.; Peng, X. W.; Paquette, L. A. An efficient means for generating *p*-methoxybenzyl (PMB) ethers under mildly acidic conditions. *Synthesis* **2008**, 433.

6. Murray, R. W.; Singh, M. Synthesis of epoxides using dimethyldioxirane: *trans*-stilbene oxide. *Org. Synth.* **1997**, *74*, 91.

7. Krasovskiy, A.; Kopp, F.; Knochel, P. Soluble lanthanide salts $LnCl_3$•2LiCl for the improved addition of organomagnesium reagents to carbonyl compounds. *Angew. Chem. Int. Ed.* **2006**, *45*, 497.

8. Xu, C.; Han, A.; Virgil, S. C.; Reisman, S. E. Chemical synthesis of (+)-Ryanodine and (+)-20-Deoxyspiganthine. *ACS. Cent. Sci.* **2017**, *3*, 278.

9. APEX2, Version 2 User Manual, M86-E01078. Bruker Analytical X-ray Systems: Madison, WI.

10. Sheldrick, G. M. SADABS (version 2008/1): Program for Absorption Correction for Data from Area Detector Frames. University of Göttingen, 2008.

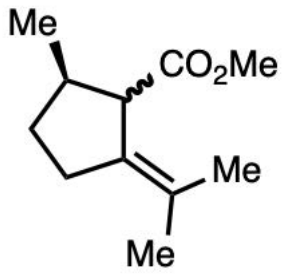
11. Sheldrick, G. M. A short history of SHELX. *Acta Cryst.* **2008**, *64*, 112.

12. Müller, P. Practical suggestions for better crystal structures. *Crystallogr. Rev.* **2009**, *15*, 57.

13. Parsons, S.; Flack, H. D.; Wagner, T. Use of intensity quotients and differences in absolute structure refinement. *Acta Cryst.* **2013**, *69*, 249.

7. ^{1}H and ^{13}C NMR Spectral Data

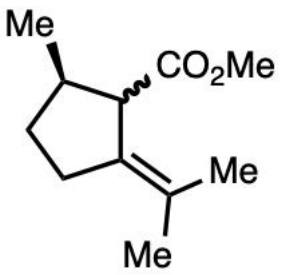
Data File Name	/ Volumes/ nmrdata-1/ ytao/ nmr/ 2-YT-203P/ 1/ fid
Title	2-YT-203P.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.0
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	101.0
Relaxation Delay	1.0000
Pulse Width	9.7500
Acquisition Time	3.9977
Acquisition Date	2019-05-07T18:00:20
Spectrometer Frequency	400.15
Spectral Width	8196.7
Lowest Frequency	-1637.1
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



methyl pulegenate (**12**)

1.3:1 dr

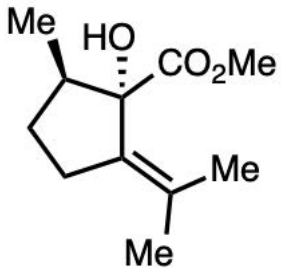
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ ytao/ nmr/ 2-YT-203/ 2/ fid
Title	2-YT-203.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.0
Pulse Sequence	zgpg30
Number of Scans	128
Receiver Gain	54.3
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3763
Acquisition Date	2019-05-07T17:31:50
Spectrometer Frequency	100.63
Spectral Width	23809.5
Lowest Frequency	-1845.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



methyl pulegenate (**12**)

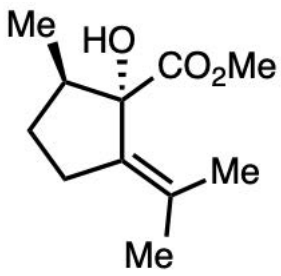
1.3:1 dr

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-044-CH/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	34
Relaxation Delay	1.0000
Pulse Width	4.2500
Acquisition Time	2.5559
Acquisition Date	2015-03-14T14:02:38
Spectrometer Frequency	399.80
Spectral Width	6410.3
Lowest Frequency	-806.8
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



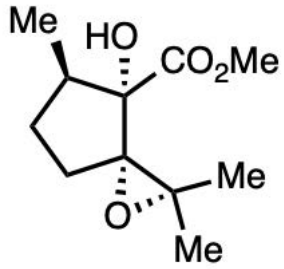
13

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-044-CH/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	1000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	3.4500
Acquisition Time	1.3107
Acquisition Date	2015-03-14T14:03:19
Spectrometer Frequency	100.54
Spectral Width	25000.0
Lowest Frequency	-1442.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

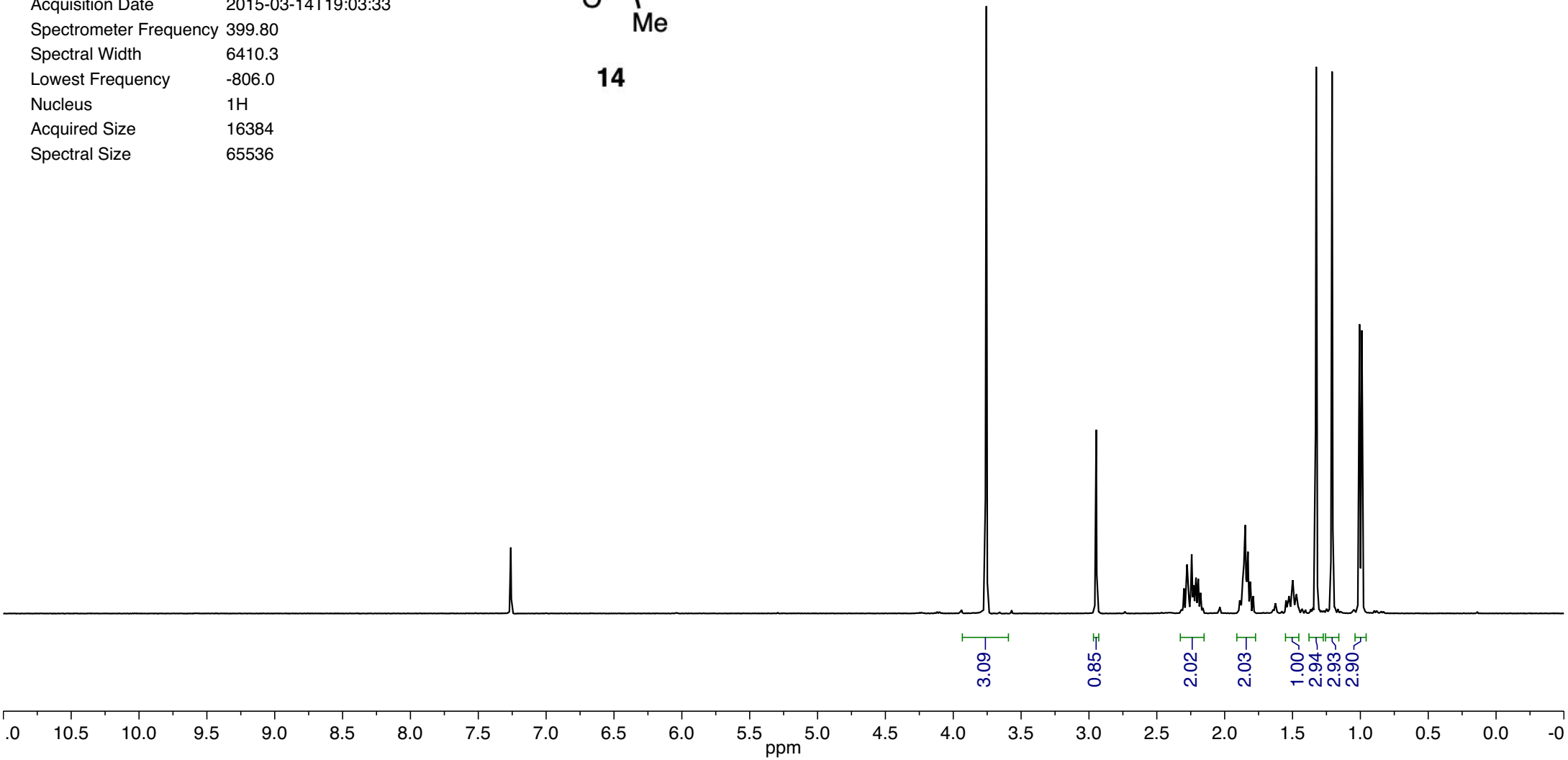


13

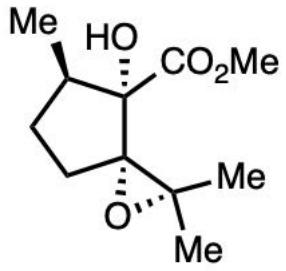
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-045-CH/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	34
Relaxation Delay	1.0000
Pulse Width	4.2500
Acquisition Time	2.5559
Acquisition Date	2015-03-14T19:03:33
Spectrometer Frequency	399.80
Spectral Width	6410.3
Lowest Frequency	-806.0
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



14

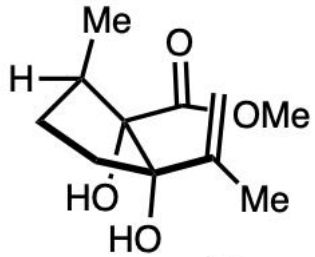


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-045-CH/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	1000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	3.4500
Acquisition Time	1.3107
Acquisition Date	2015-03-14T19:04:21
Spectrometer Frequency	100.54
Spectral Width	25000.0
Lowest Frequency	-1443.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



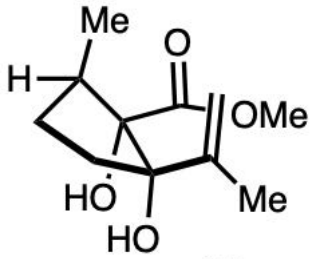
14

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ ahan/ nmr/ 3-AH-046-CH/ 1/ fid
Title	3-AH-046-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.2
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	156.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2015-03-15T16:16:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



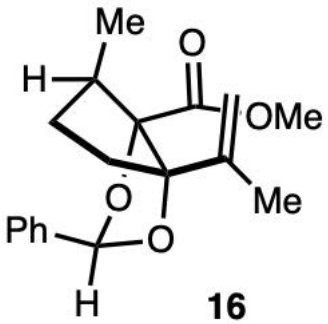
15

Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ ahan/ nmr/ 3-AH-046-CH/ 2/ fid
Title	3-AH-046-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.2
Pulse Sequence	zgpg30
Number of Scans	768
Receiver Gain	72.0
Relaxation Delay	2.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2015-03-15T15:38:00
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1959.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

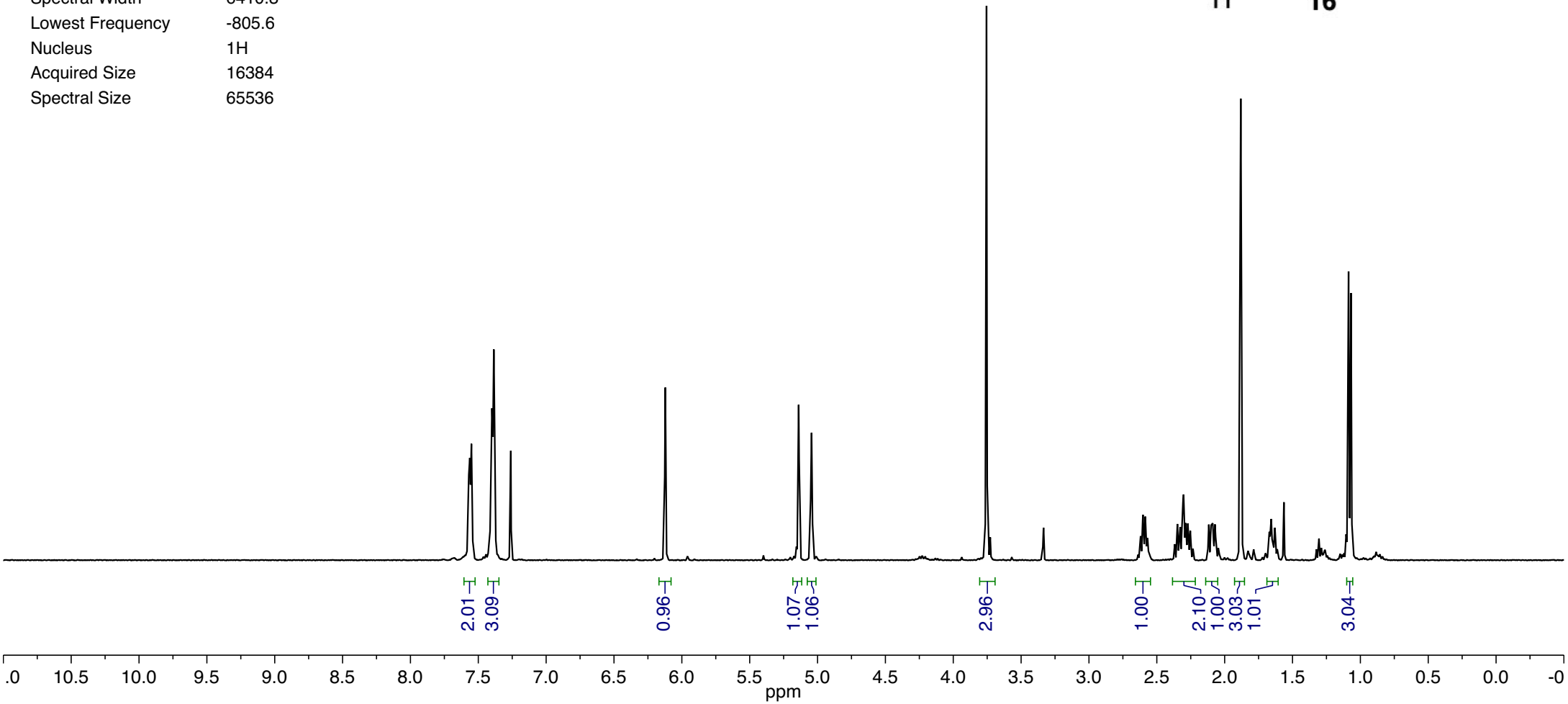


15

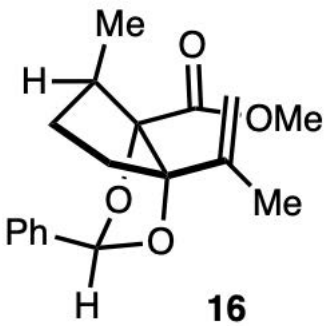
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-012-CH/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	38
Relaxation Delay	1.0000
Pulse Width	4.2500
Acquisition Time	2.5559
Acquisition Date	2015-03-18T12:25:58
Spectrometer Frequency	399.80
Spectral Width	6410.3
Lowest Frequency	-805.6
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



16

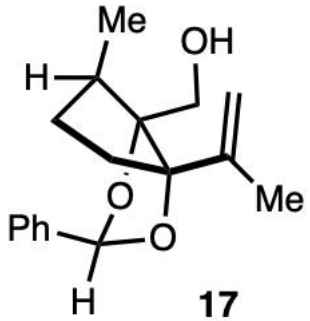


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-012-CH/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	1000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	3.4500
Acquisition Time	1.3107
Acquisition Date	2015-03-18T12:26:46
Spectrometer Frequency	100.54
Spectral Width	25000.0
Lowest Frequency	-1442.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

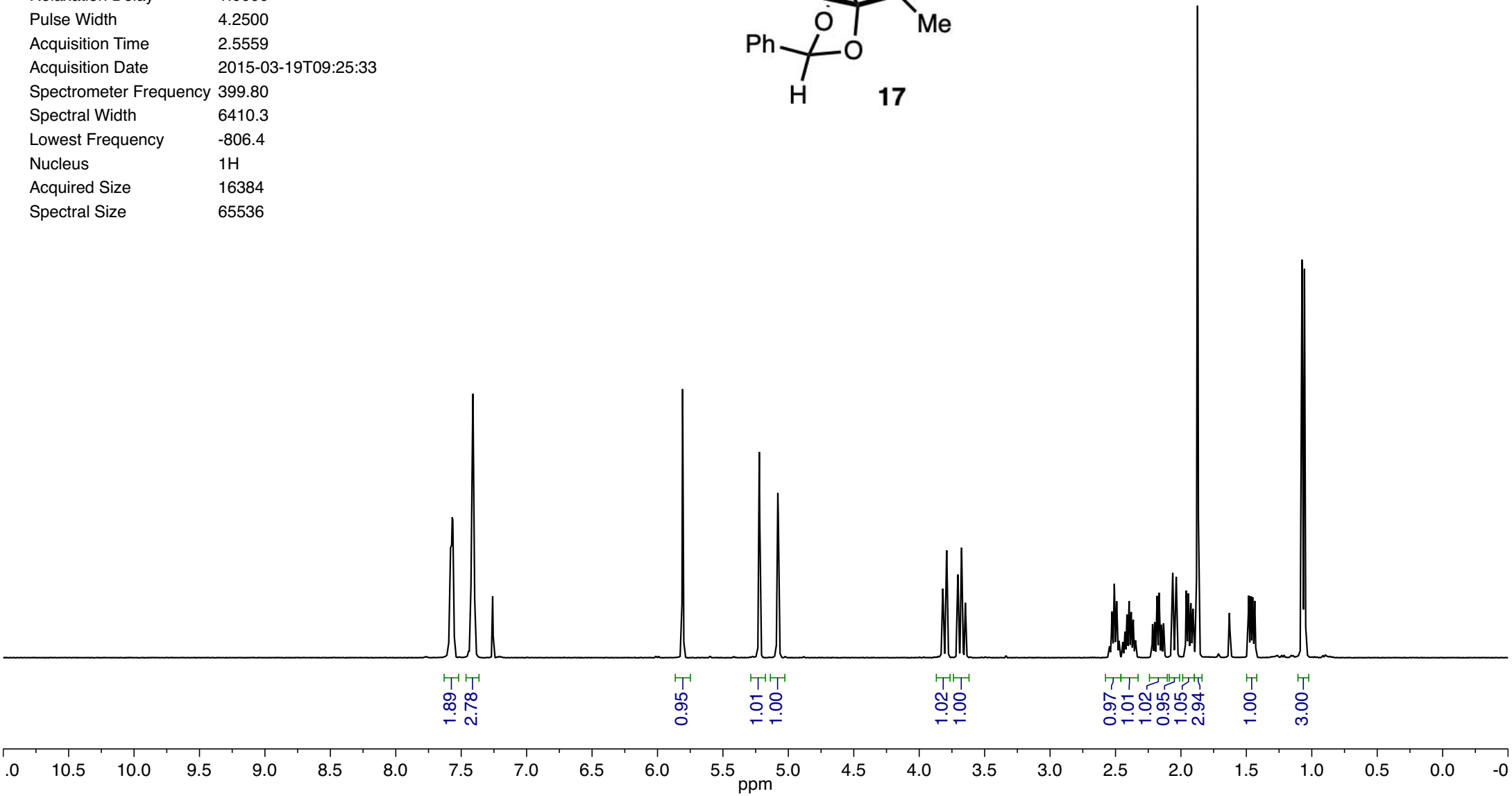


16

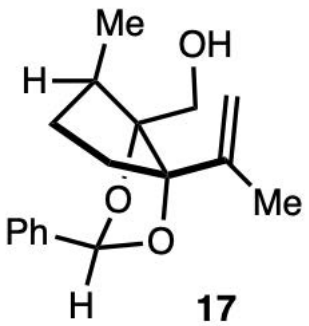
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-026-CH/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	4.2500
Acquisition Time	2.5559
Acquisition Date	2015-03-19T09:25:33
Spectrometer Frequency	399.80
Spectral Width	6410.3
Lowest Frequency	-806.4
Nucleus	1H
Acquired Size	16384
Spectral Size	65536



17

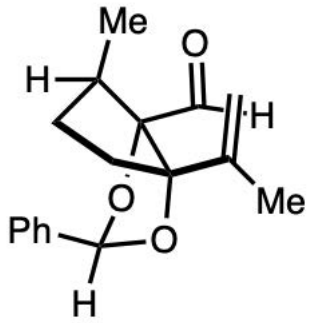


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 3-AH-026-CH/ CARBON01.fid/ fid
Title	CARBON01
Origin	Varian
Solvent	CDCl3
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	1000
Receiver Gain	30
Relaxation Delay	1.0000
Pulse Width	3.4500
Acquisition Time	1.3107
Acquisition Date	2015-03-19T09:26:14
Spectrometer Frequency	100.54
Spectral Width	25000.0
Lowest Frequency	-1444.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

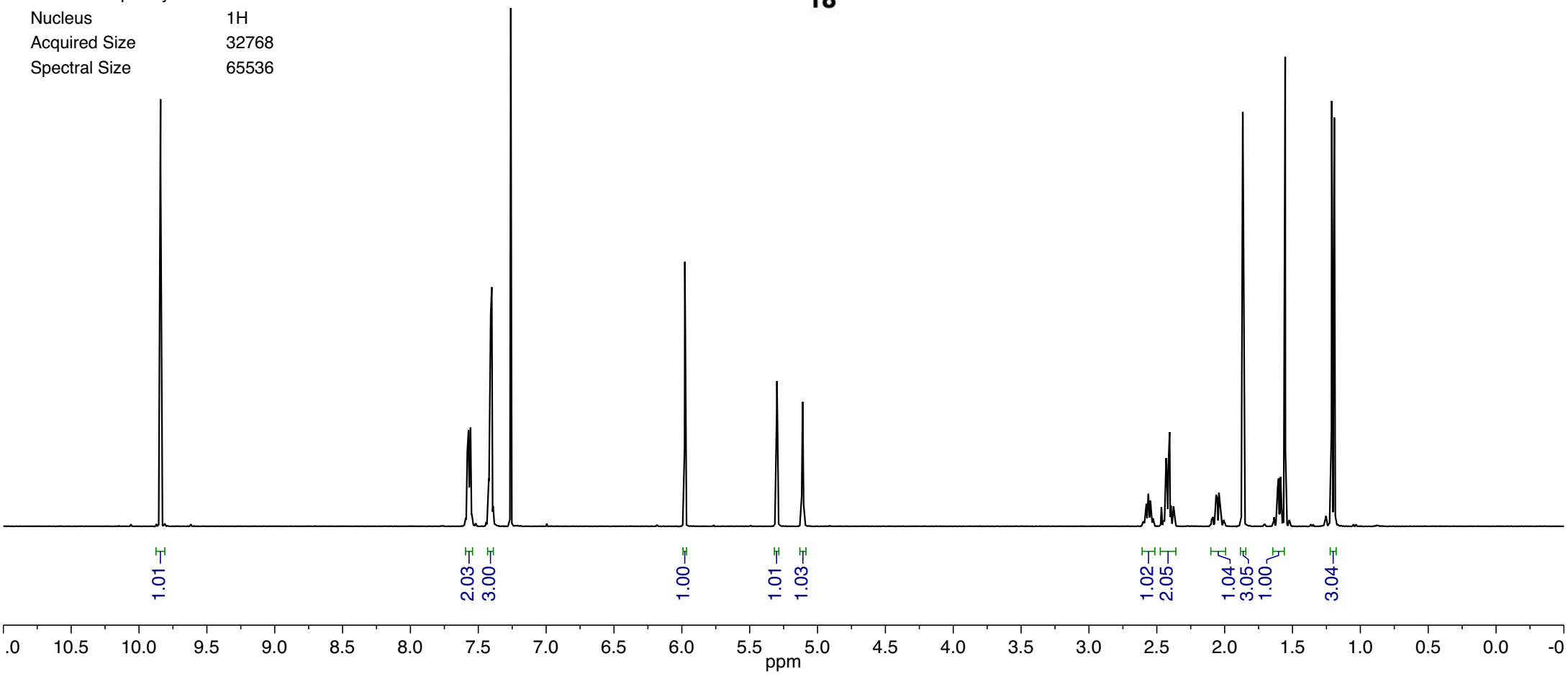


17

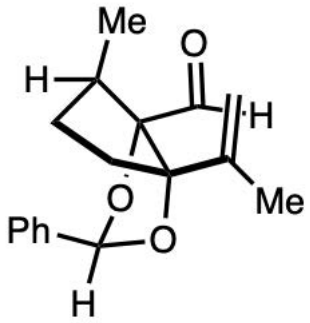
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-041-CH/ 1/ fid
Title	9-AH-041-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-07-16T09:10:17
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



18

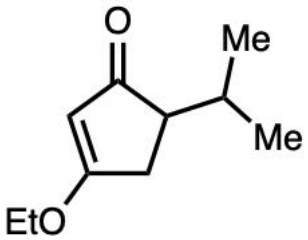


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-041-CH/ 2/ fid
Title	9-AH-041-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	750
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-07-16T09:41:07
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

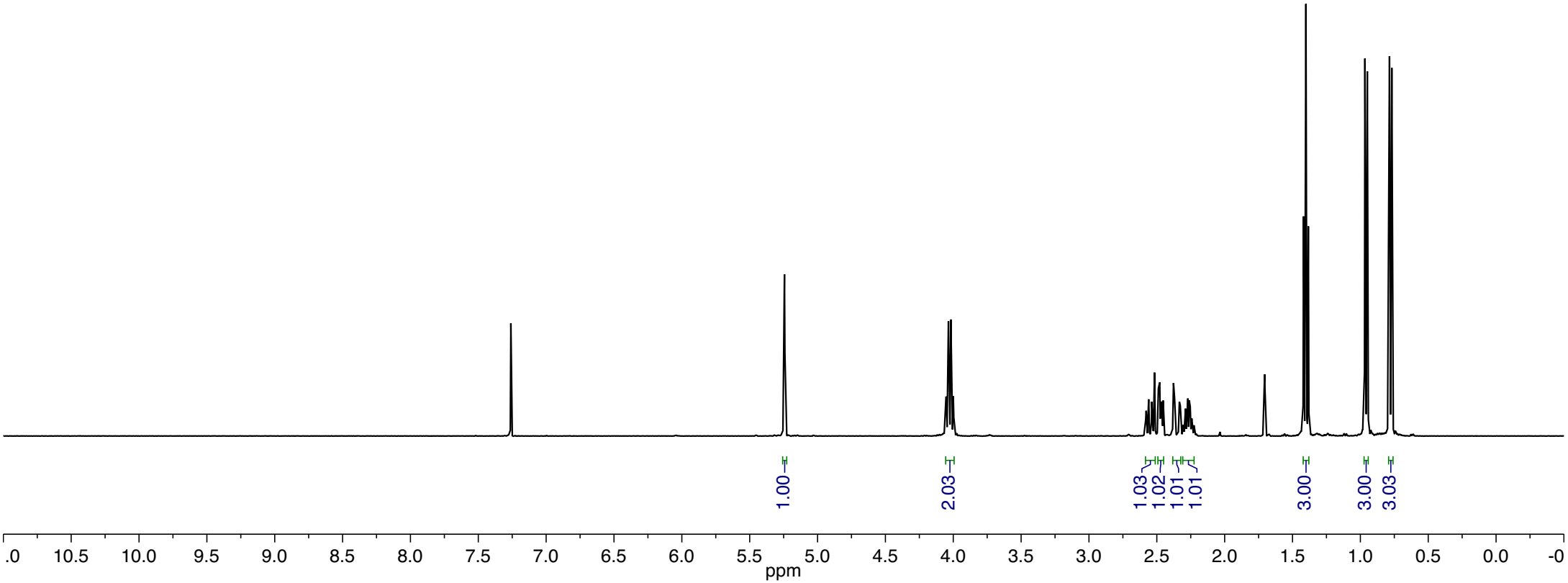


18

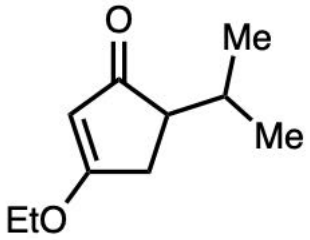
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-054-CH/ 1/ fid
Title	9-AH-054-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.1
Pulse Sequence	zg30
Number of Scans	2
Receiver Gain	100.0
Relaxation Delay	5.0000
Pulse Width	10.0000
Acquisition Time	3.9977
Acquisition Date	2018-08-01T09:05:57
Spectrometer Frequency	400.15
Spectral Width	8196.7
Lowest Frequency	-1639.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



(±)-21

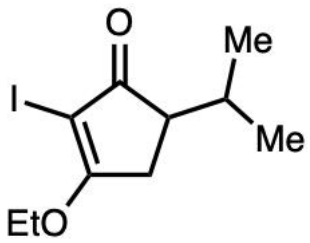


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-054-CH/ 2/ fid
Title	9-AH-054-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.1
Pulse Sequence	zgpg30
Number of Scans	1000
Receiver Gain	15.3
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3763
Acquisition Date	2018-08-01T09:49:08
Spectrometer Frequency	100.63
Spectral Width	23809.5
Lowest Frequency	-1846.1
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

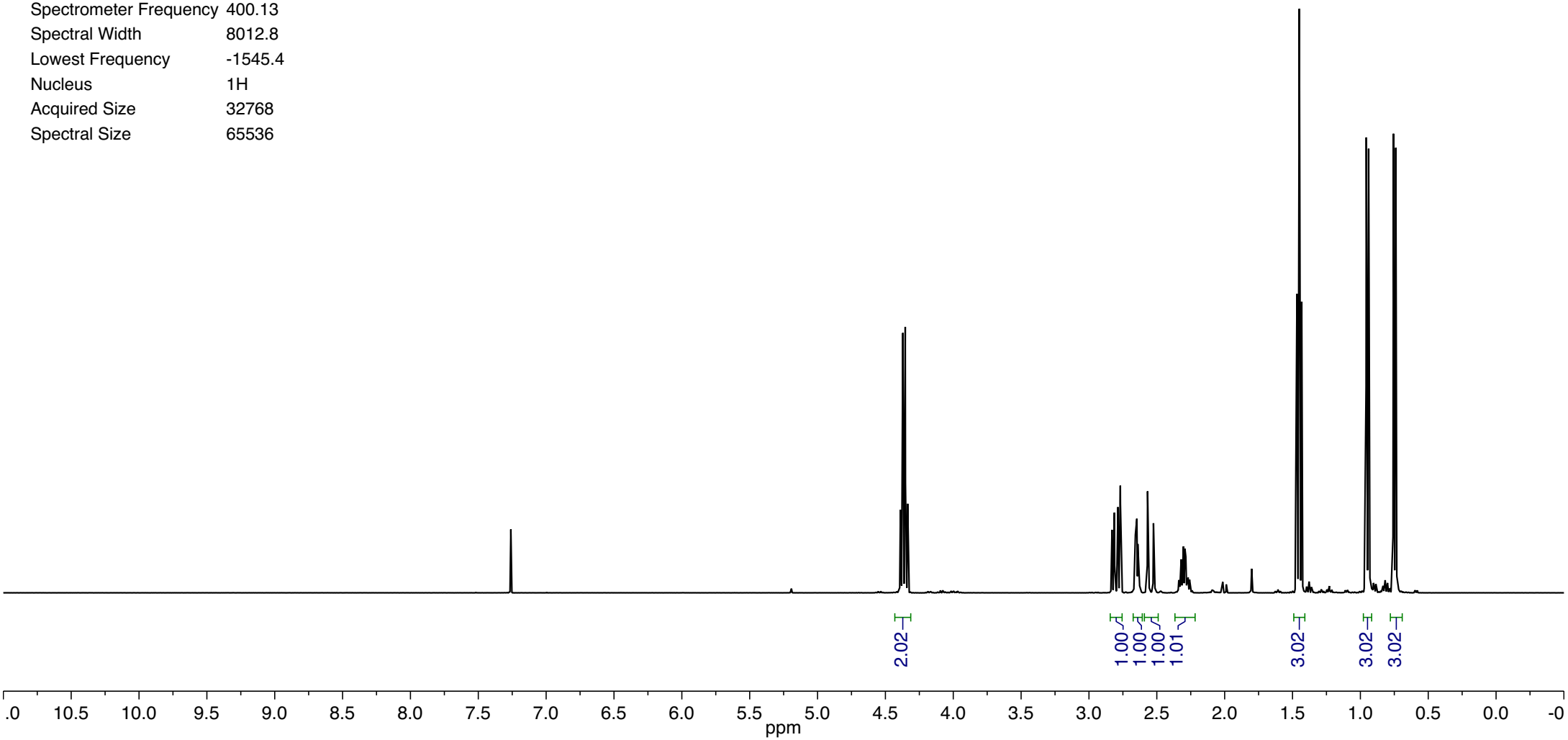


(±)-21

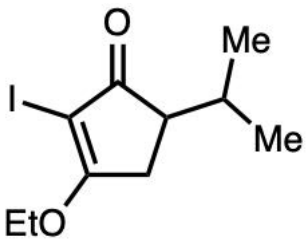
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-054-CH/ 1/ fid
Title	9-AH-054-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	1
Receiver Gain	30.3
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-08-04T13:35:43
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



(±)-22

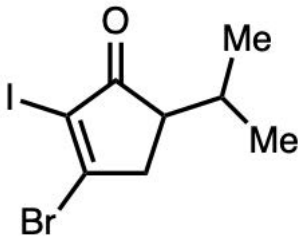


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-054-CH/ 2/ fid
Title	9-AH-054-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	26
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-08-04T13:37:49
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1968.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

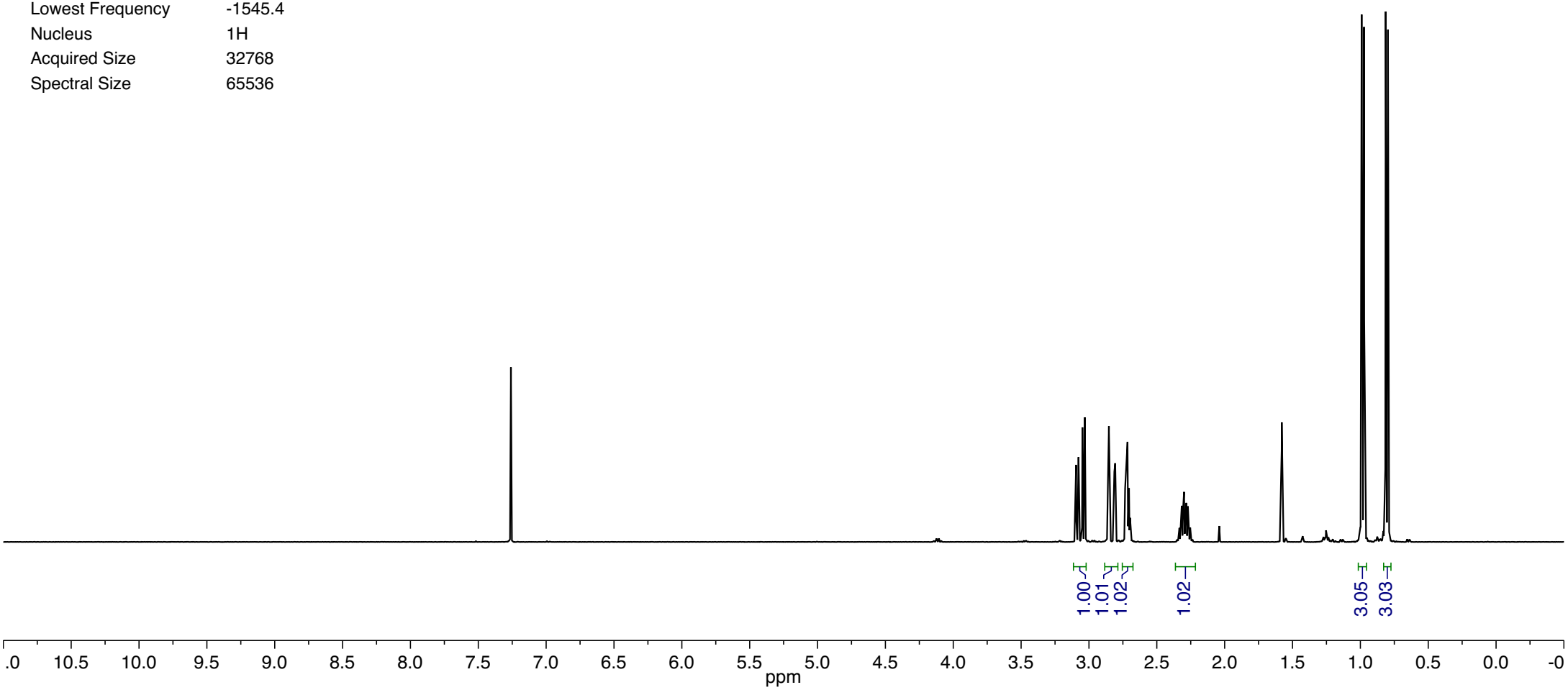


(±)-22

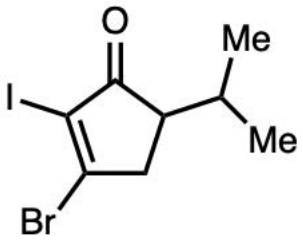
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 8-AH-169-CH/ 1/ fid
Title	8-AH-169-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	1
Receiver Gain	142.8
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-22T06:52:52
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



(±)-24

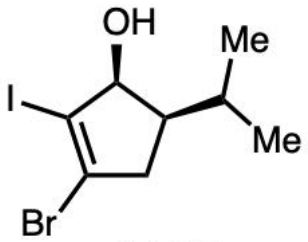


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 8-AH-169-CH/ 4/ fid
Title	8-AH-169-CH.4.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	700
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-22T07:57:44
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1962.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

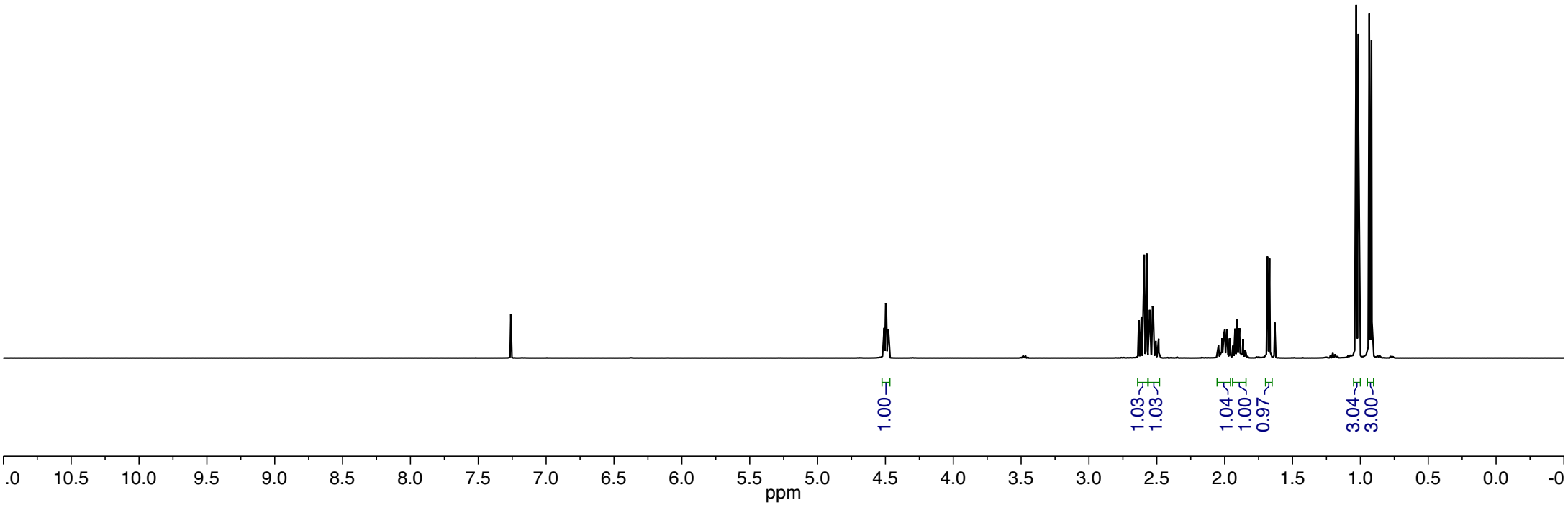


(±)-24

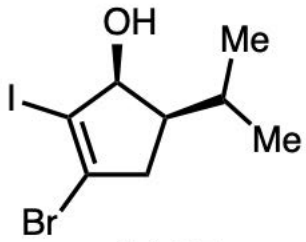
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-075-CH/ 1/ fid
Title	9-AH-075-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	2
Receiver Gain	72.0
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-08-27T10:54:41
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



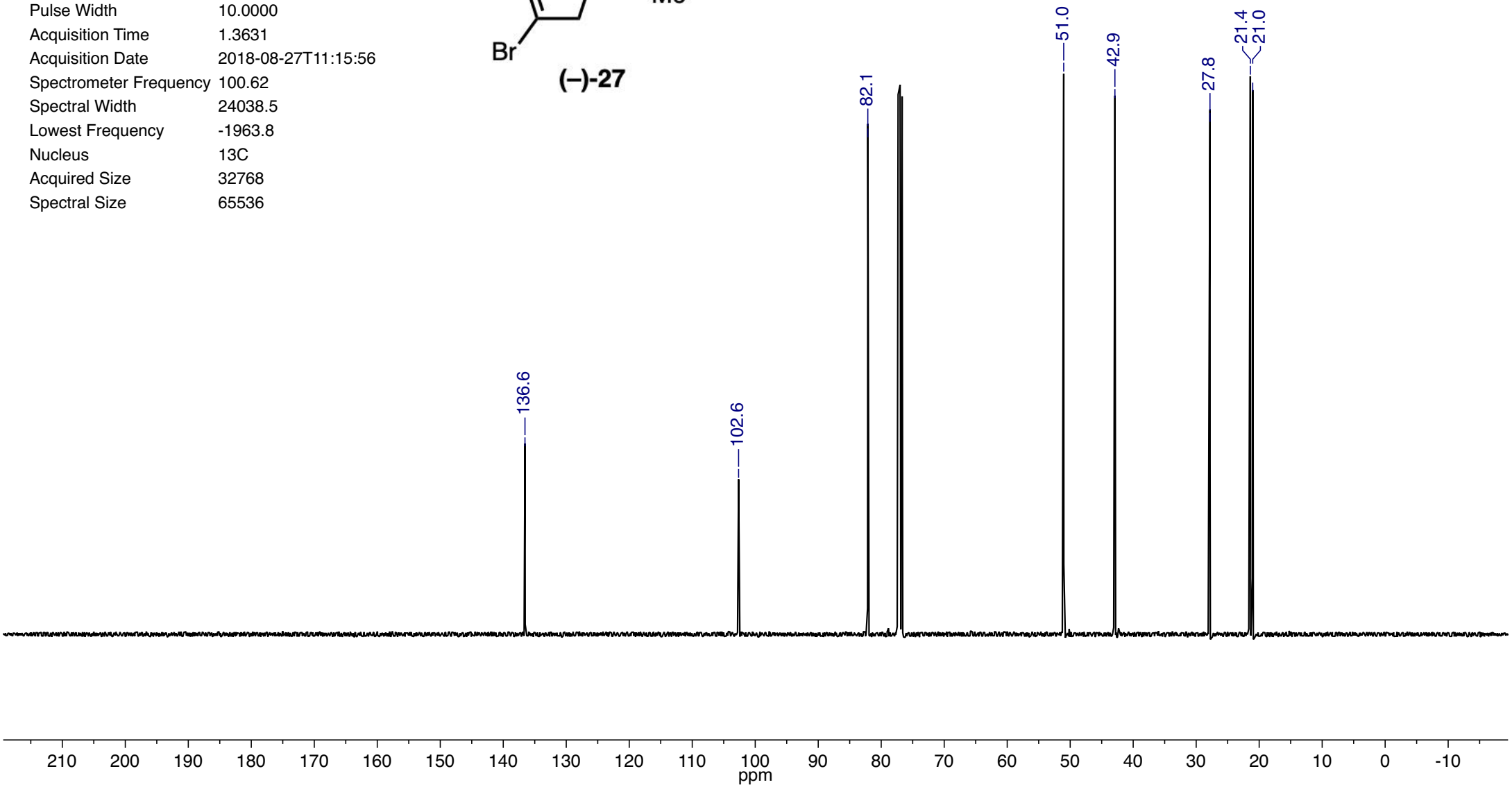
(–)-27



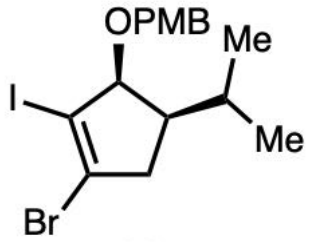
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-075-CH/ 2/ fid
Title	9-AH-075-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	512
Receiver Gain	50.3
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-08-27T11:15:56
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1963.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



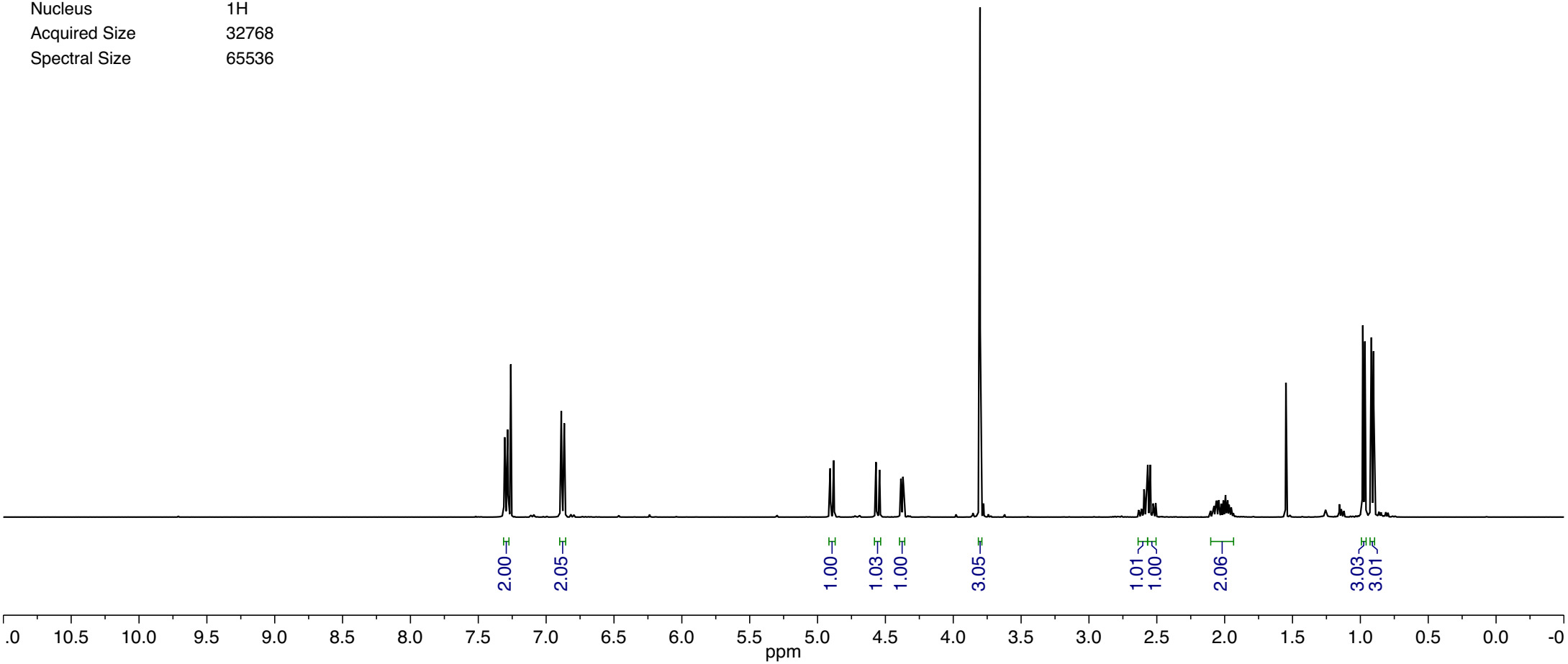
(–)-27



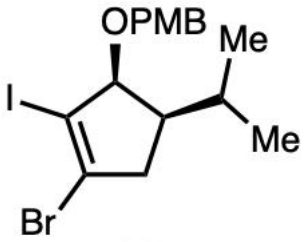
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 8-AH-198-CH/ 1/ fid
Title	8-AH-198-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.2
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	176.8
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-18T17:48:08
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



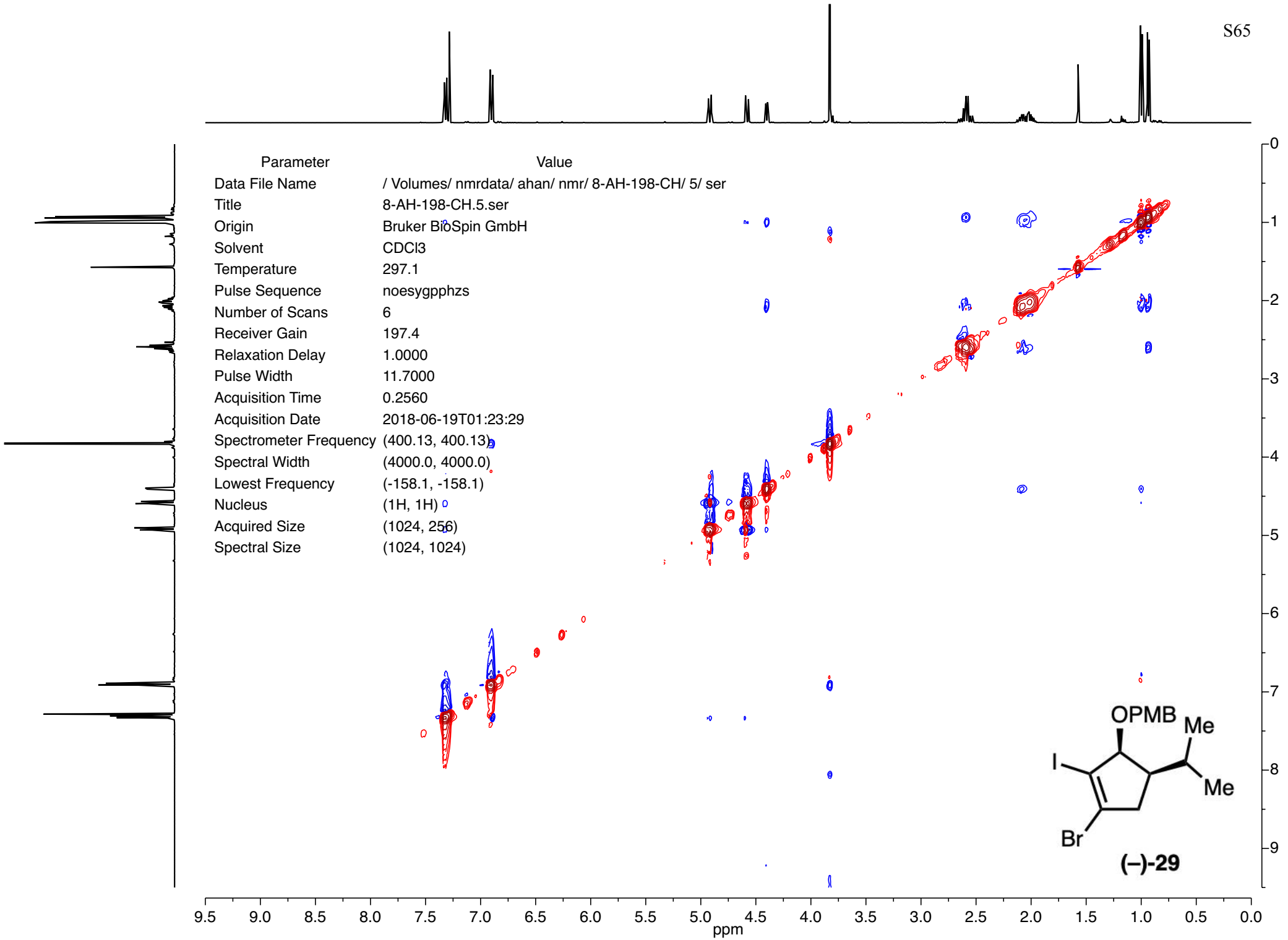
(–)-29



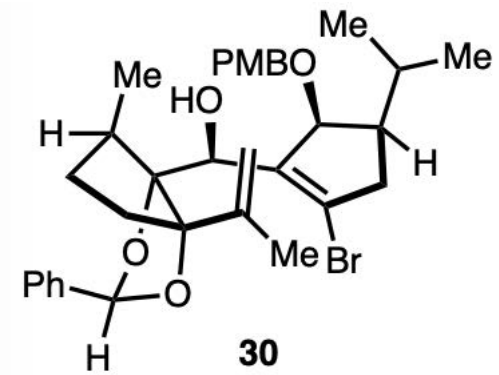
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 8-AH-198-CH/ 6/ fid
Title	8-AH-198-CH.6.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zgpg30
Number of Scans	800
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-19T02:41:45
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1960.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



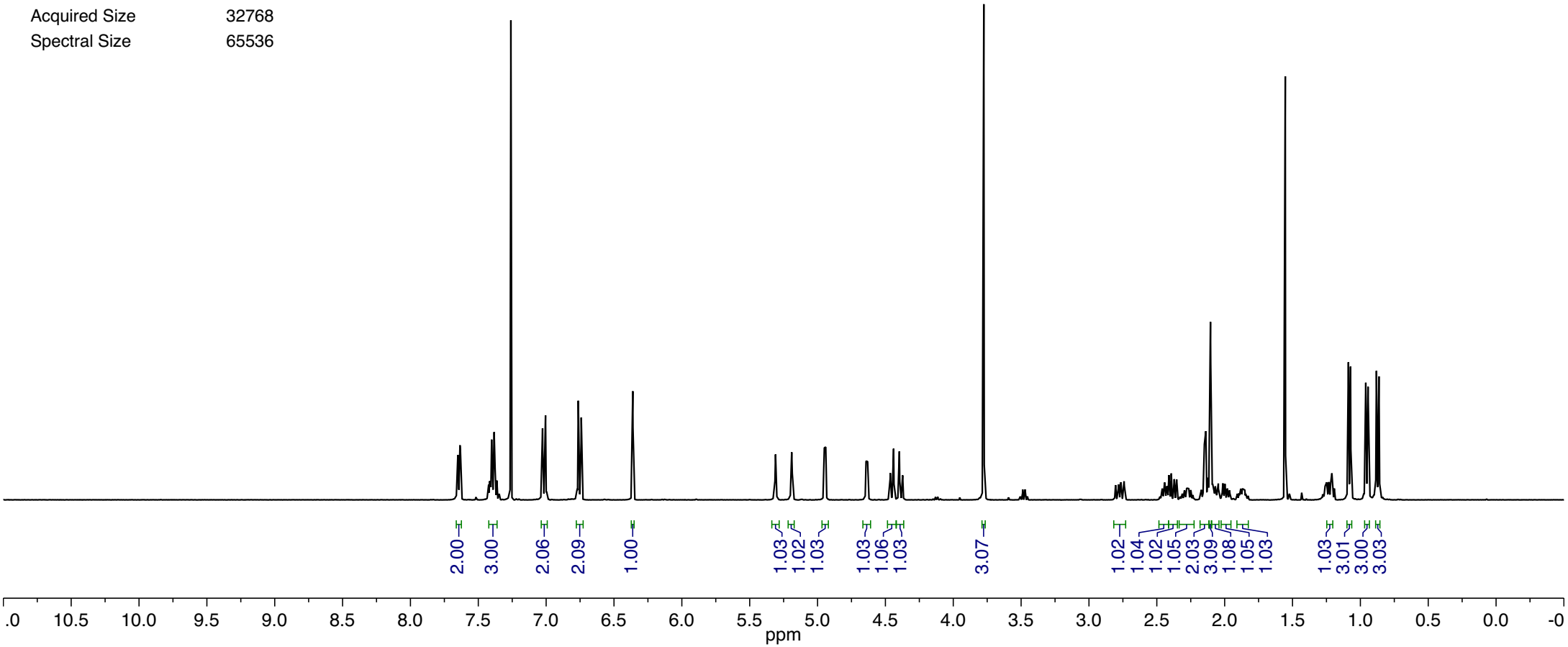
(–)-29


Parameter Value
Data File Name / Volumes/ nmrdata/ ahan/ nmr/ 8-AH-198-CH/ 5/ ser
Title 8-AH-198-CH.5.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 297.1
Pulse Sequence noesygpphzs
Number of Scans 6
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-06-19T01:23:29
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Lowest Frequency (-158.1, -158.1)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OPMB
Me
I
Me
Br
(–)-29
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
ppm
0 1 2 3 4 5 6 7 8 9

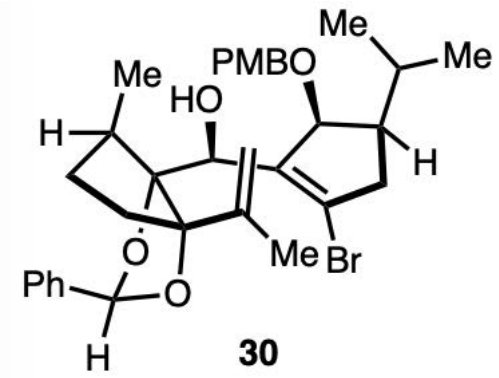
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-1-CH/ 1/ fid
Title	9-AH-079-1-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-13T18:51:25
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



30



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-1-CH/ 2/ fid
Title	9-AH-079-1-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	1000
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-13T19:32:54
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.2
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

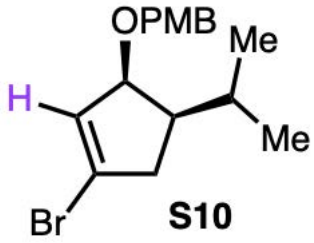


30

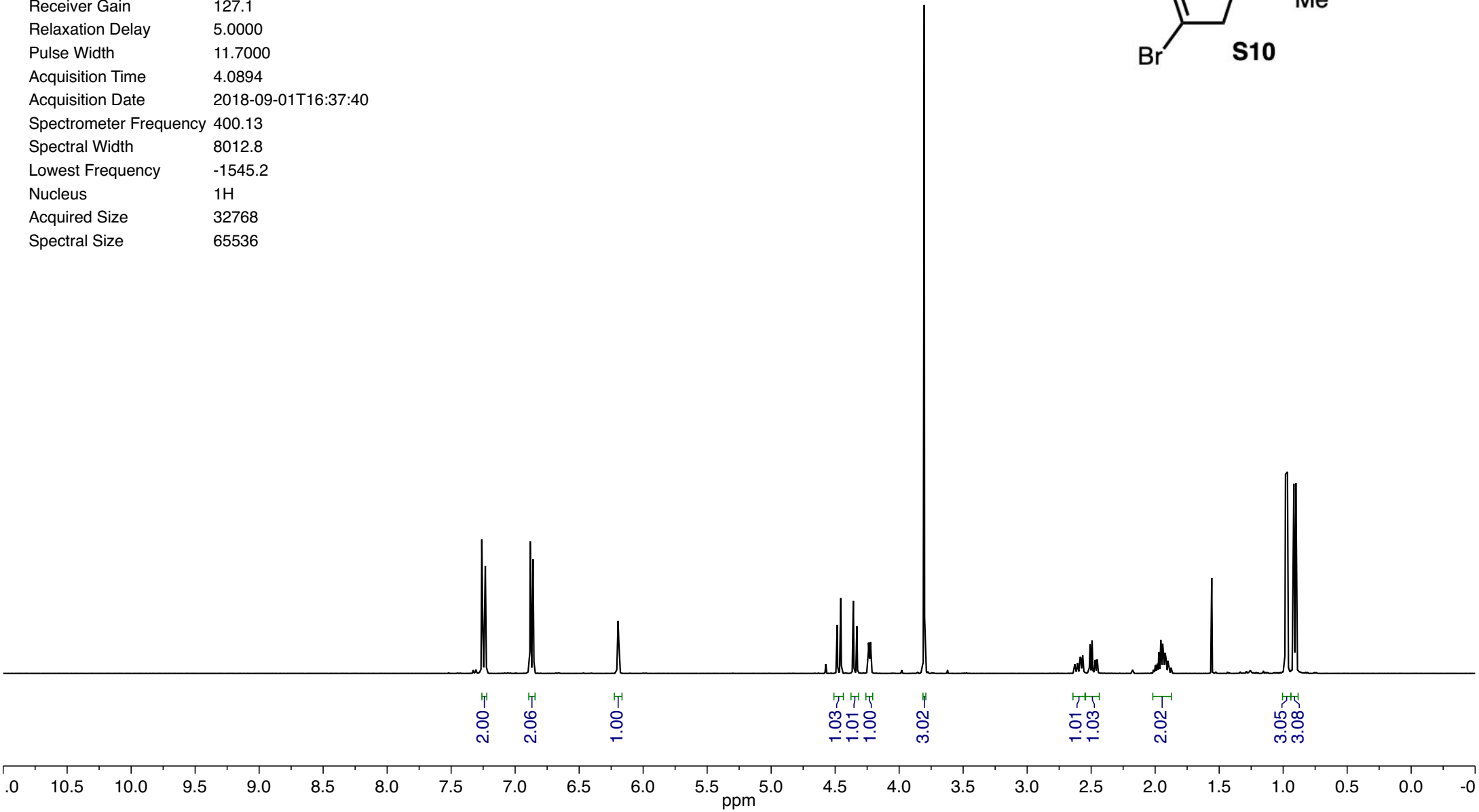
131.2
129.7
129.6
129.4
128.4
126.9
113.3
112.6
158.7
148.1
142.6
138.0
105.0
99.1
96.7
80.5
72.4
71.3
55.2
55.0
41.8
41.4
38.8
30.6
26.0
23.0
21.3
14.1

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

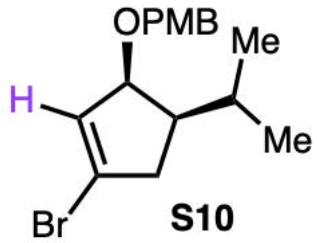
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-P/ 1/ fid
Title	9-AH-079-P.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	4
Receiver Gain	127.1
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-01T16:37:40
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



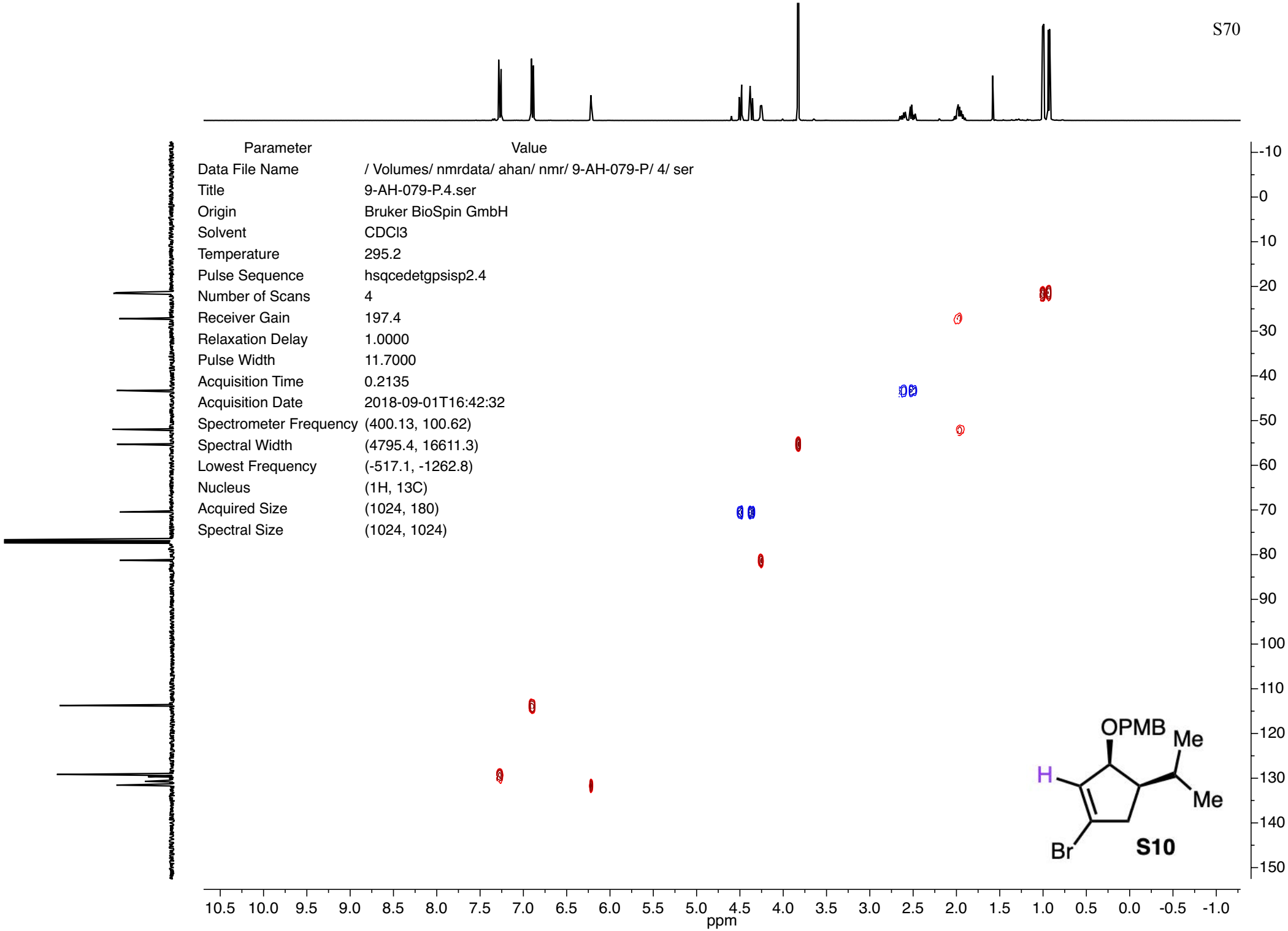
S10

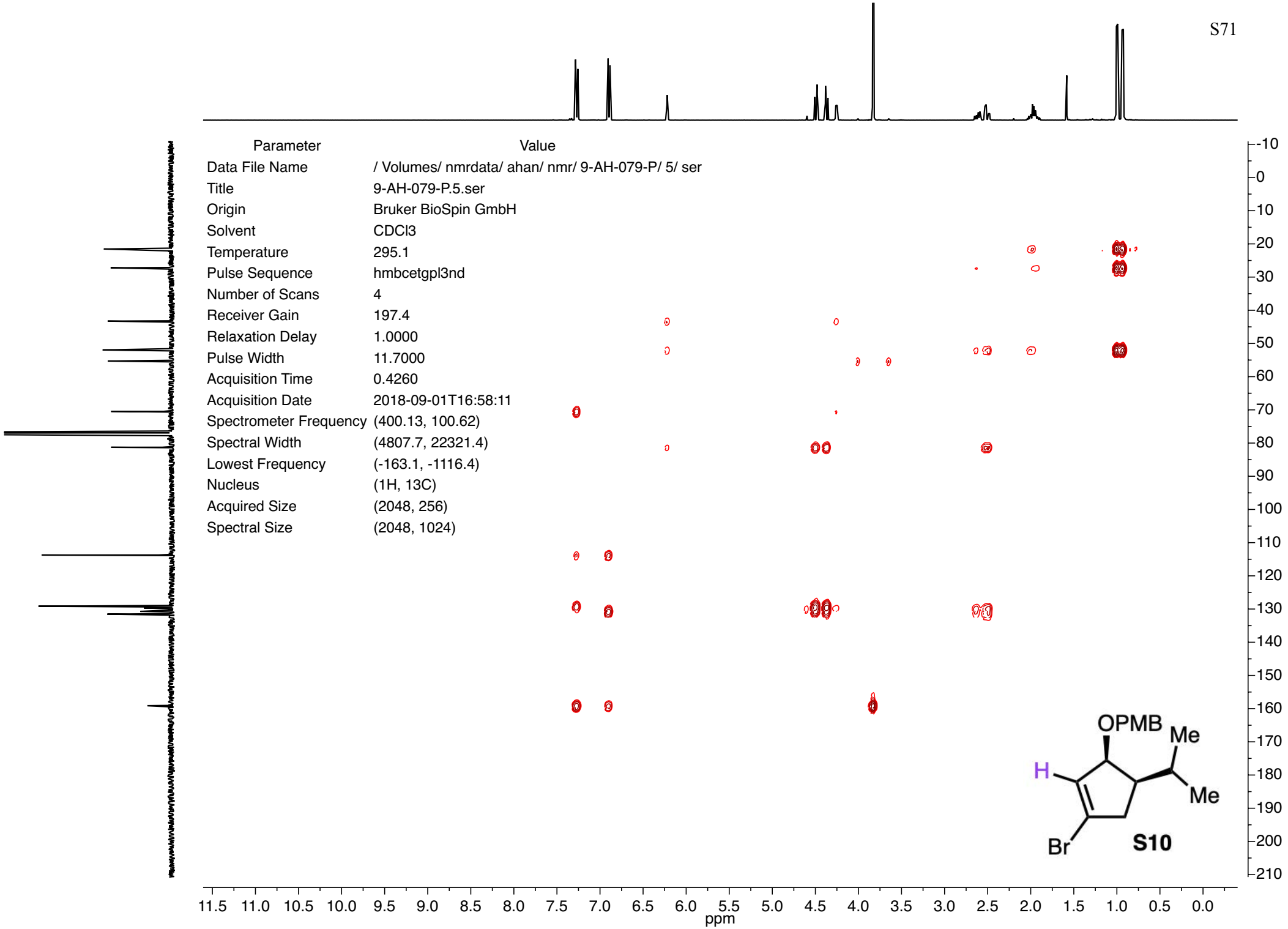


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-P/ 7/ fid
Title	9-AH-079-P.7.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	59
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-01T16:40:35
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



S10

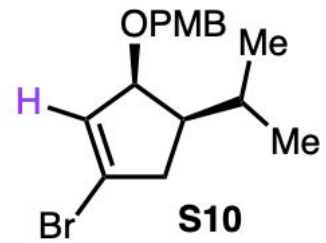

Parameter Value
Data File Name / Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-P/ 4/ ser
Title 9-AH-079-P.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-09-01T16:42:32
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Lowest Frequency (-517.1, -1262.8)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
OPMB
Me
H
Me
Br
S10
ppm



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-P/ 5/ ser
Title	9-AH-079-P.5.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	hmbcetgpl3nd
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-01T16:58:11
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1116.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-079-P/ 6/ ser
Title	9-AH-079-P.6.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	noesygpphzs
Number of Scans	5
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2560
Acquisition Date	2018-09-01T17:25:09
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(4000.0, 4000.0)
Lowest Frequency	(-158.1, -158.1)
Nucleus	(1H, 1H)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)

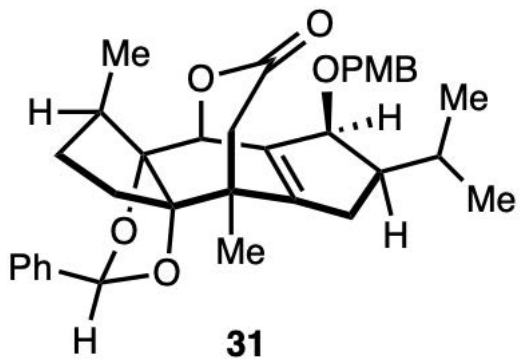
0.00



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
ppm

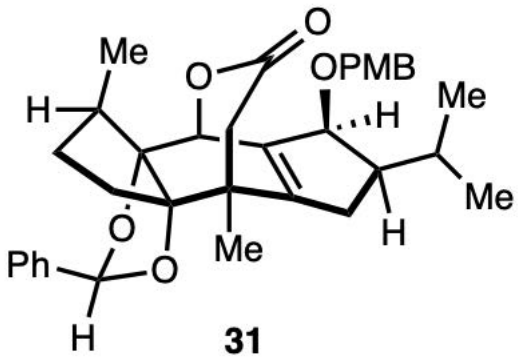
0 1 2 3 4 5 6 7 8 9

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-083-CH/ 1/ fid
Title	9-AH-083-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	1
Receiver Gain	142.8
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-04T06:31:21
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

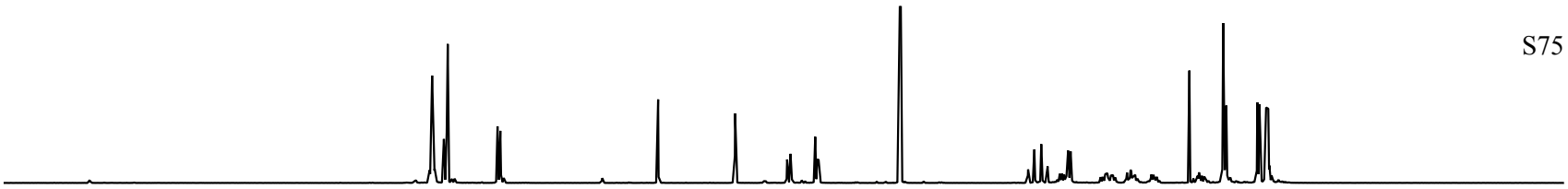


31

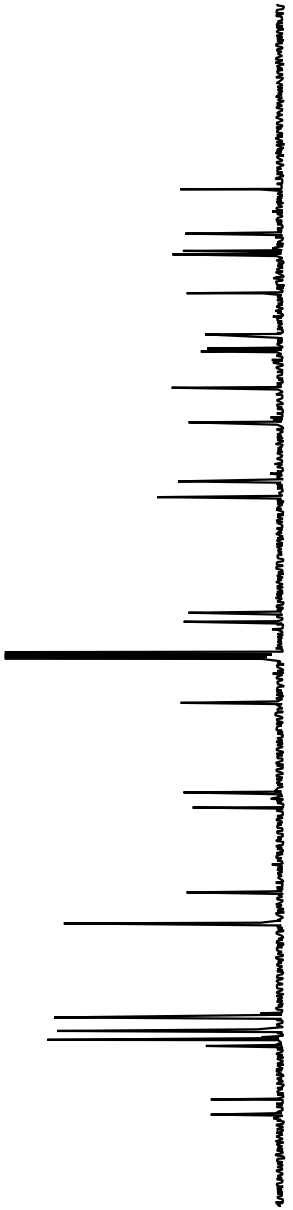
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-083-CH/ 2/ fid
Title	9-AH-083-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	750
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-04T07:02:56
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.8
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

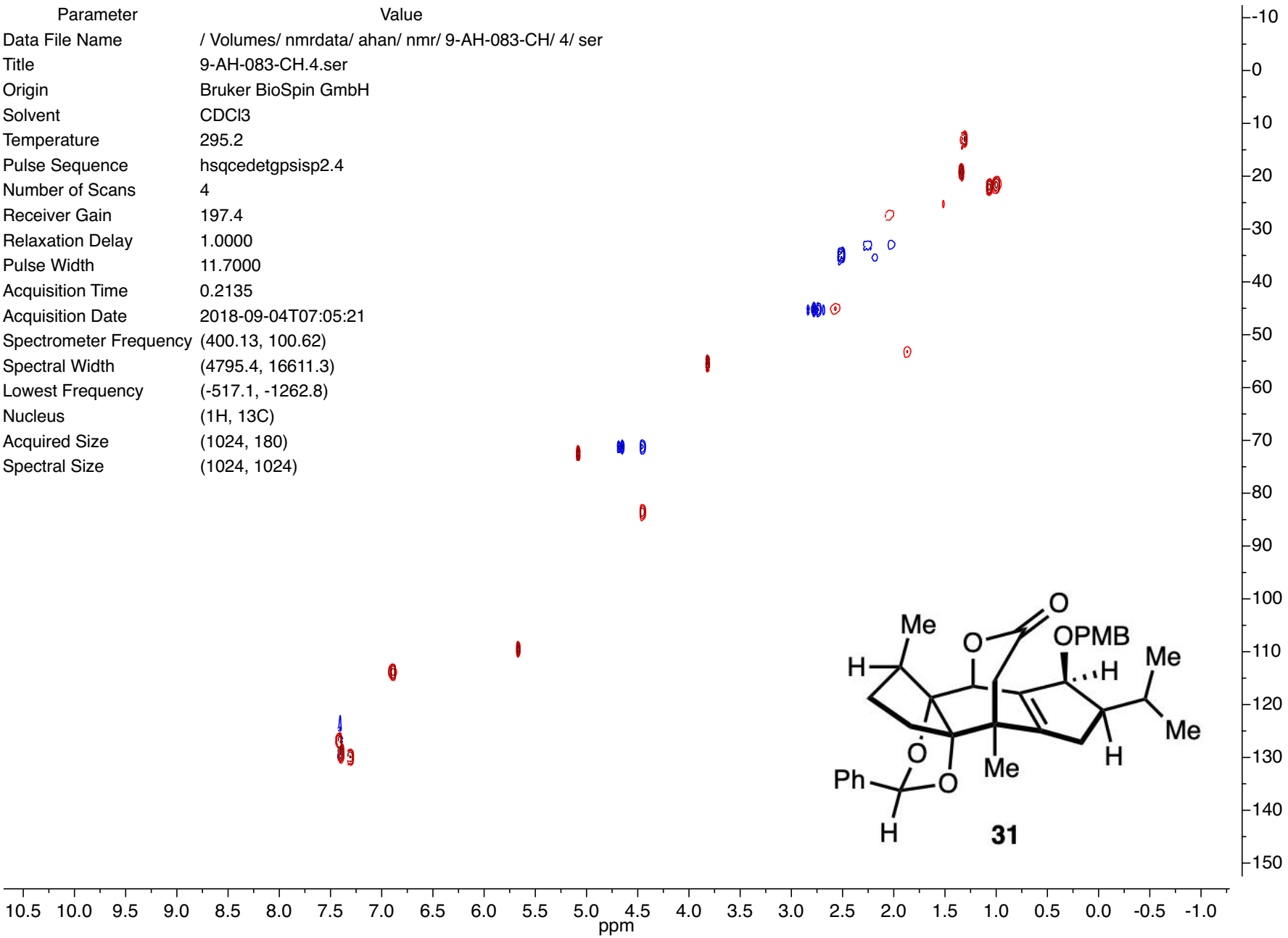


31

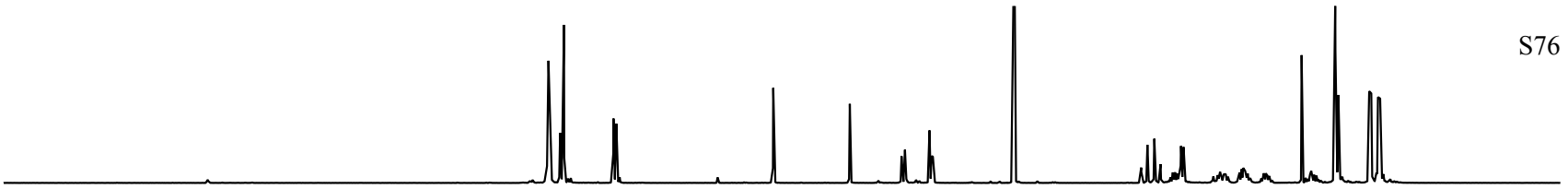


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-083-CH/ 4/ ser
Title	9-AH-083-CH.4.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hsqcedetgpsisp2.4
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2018-09-04T07:05:21
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-517.1, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

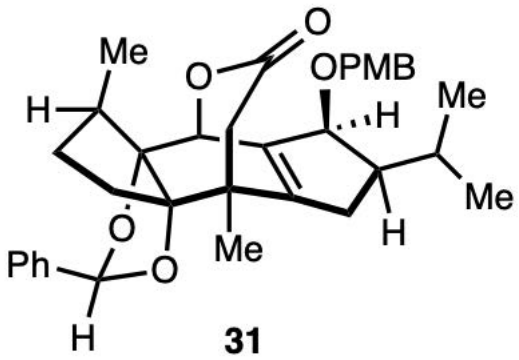




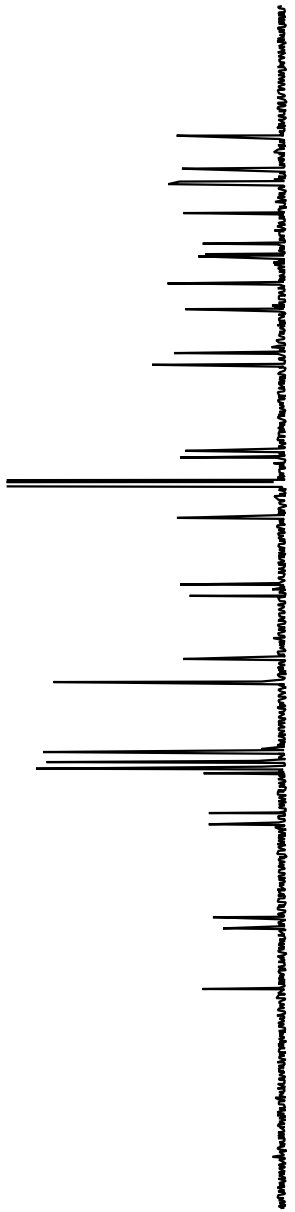
31



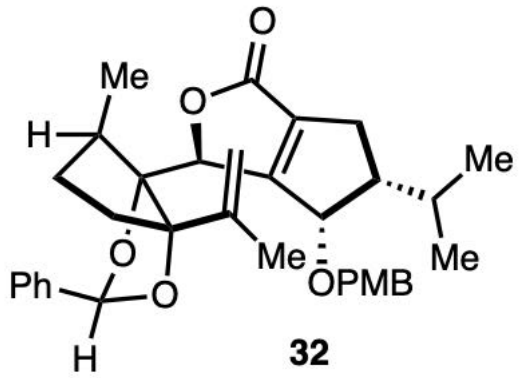
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-083-CH/ 5/ ser
Title	9-AH-083-CH.5.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	hmbcetgpl3nd
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-04T07:20:59
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1116.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 247)
Spectral Size	(2048, 1024)



31

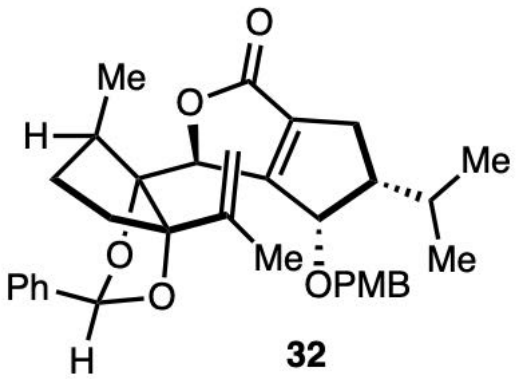


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ytao/ nmr/ 1-YT-168CHAR3/ 1/ fid
Title	1-YT-168CHAR3.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	16
Receiver Gain	142.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-12-07T20:47:49
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

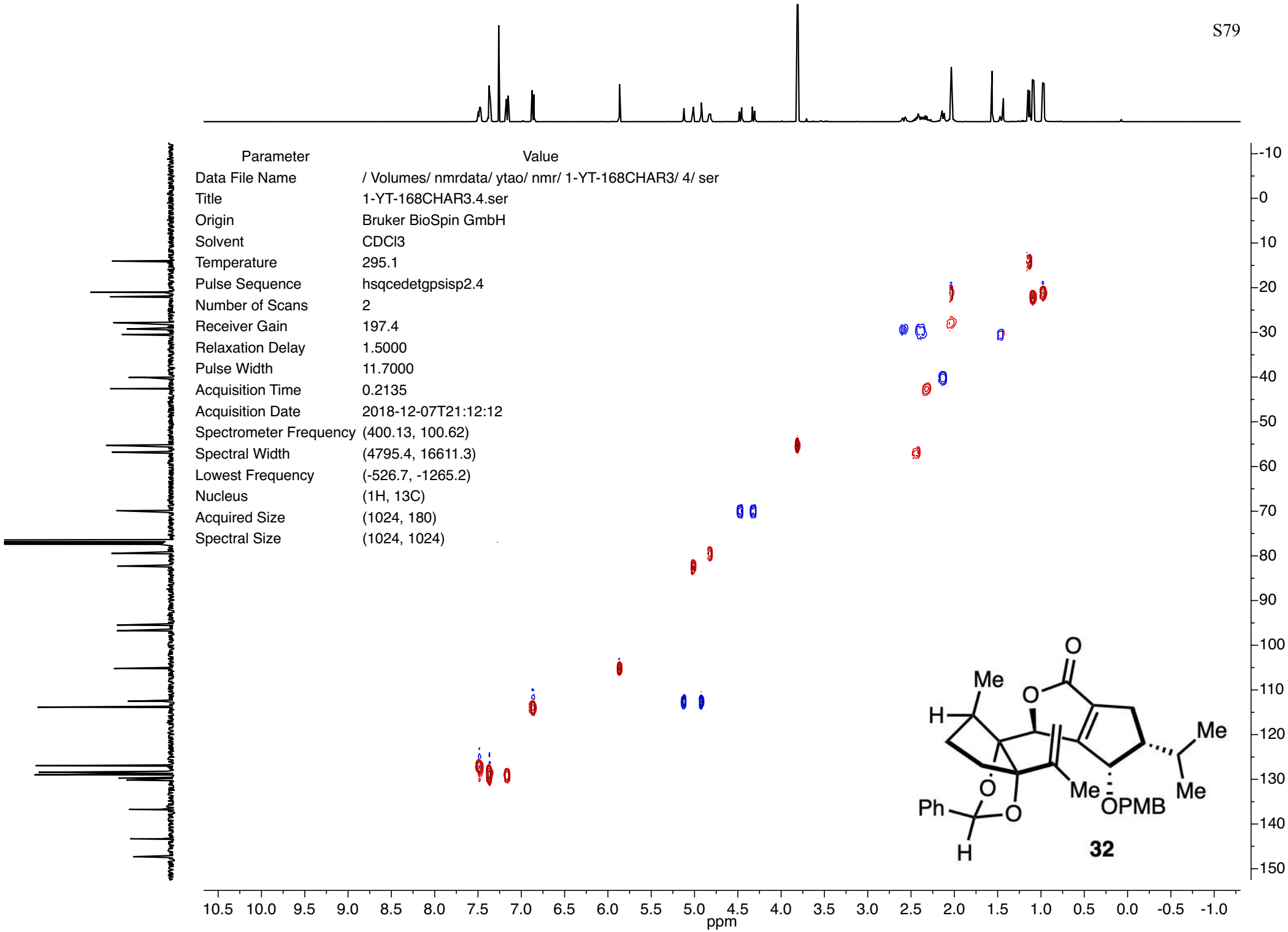


32

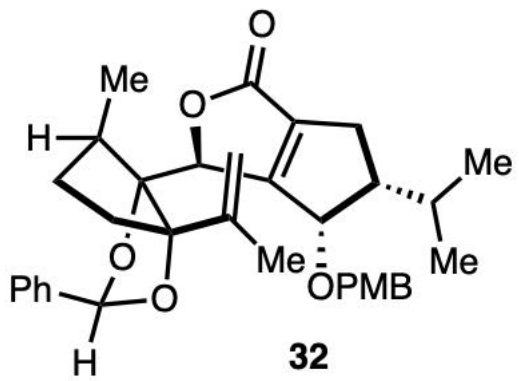
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ytao/ nmr/ 1-YT-168CHAR3/ 2/ fid
Title	1-YT-168CHAR3.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	512
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-12-07T21:09:02
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.7
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



32


Parameter Value
Data File Name / Volumes/ nmrdata/ ytao/ nmr/ 1-YT-168CHAR3/ 4/ ser
Title 1-YT-168CHAR3.4.ser
Origin Bruker BioSpin GmbH
Solvent CDCl3
Temperature 295.1
Pulse Sequence hsqcedetgpsisp2.4
Number of Scans 2
Receiver Gain 197.4
Relaxation Delay 1.5000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-12-07T21:12:12
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Lowest Frequency (-526.7, -1265.2)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
Me
H
O
O
Me
Me
Me
OPMB
Ph
O
O
H
32
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 -0.5 -1.0
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150

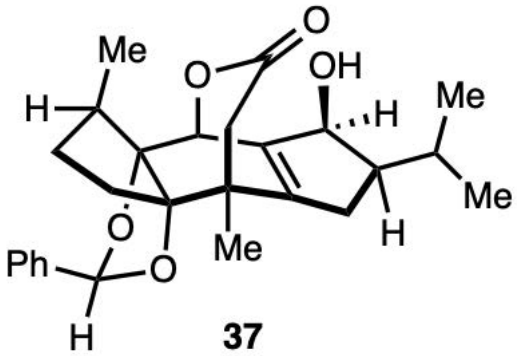
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ytao/ nmr/ 1-YT-168CHAR3/ 5/ ser
Title	1-YT-168CHAR3.5.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	hmbcetgpl3nd
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	2.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-12-07T21:23:44
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-172.7, -1118.8)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)



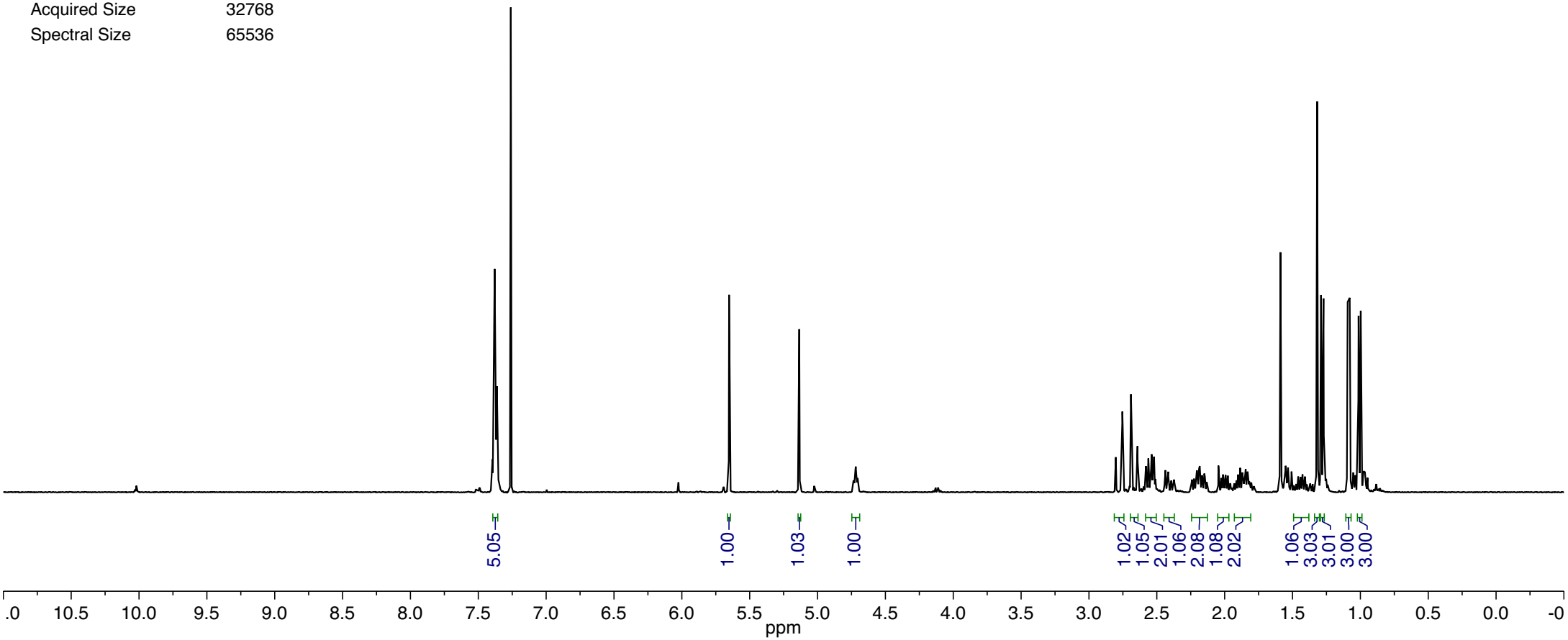
32

ppm

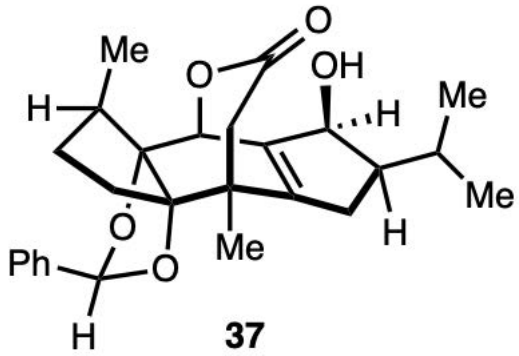
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-084-CH/ 1/ fid
Title	9-AH-084-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	1
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-04T12:06:09
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.2
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



37

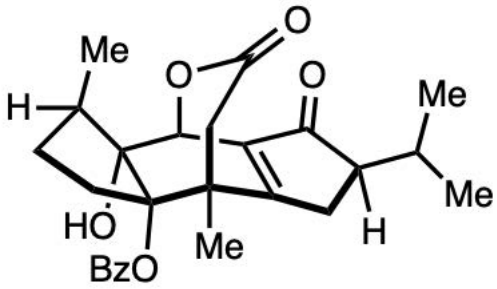


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-084-CH/ 2/ fid
Title	9-AH-084-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	750
Receiver Gain	87.8
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-04T12:36:58
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.4
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



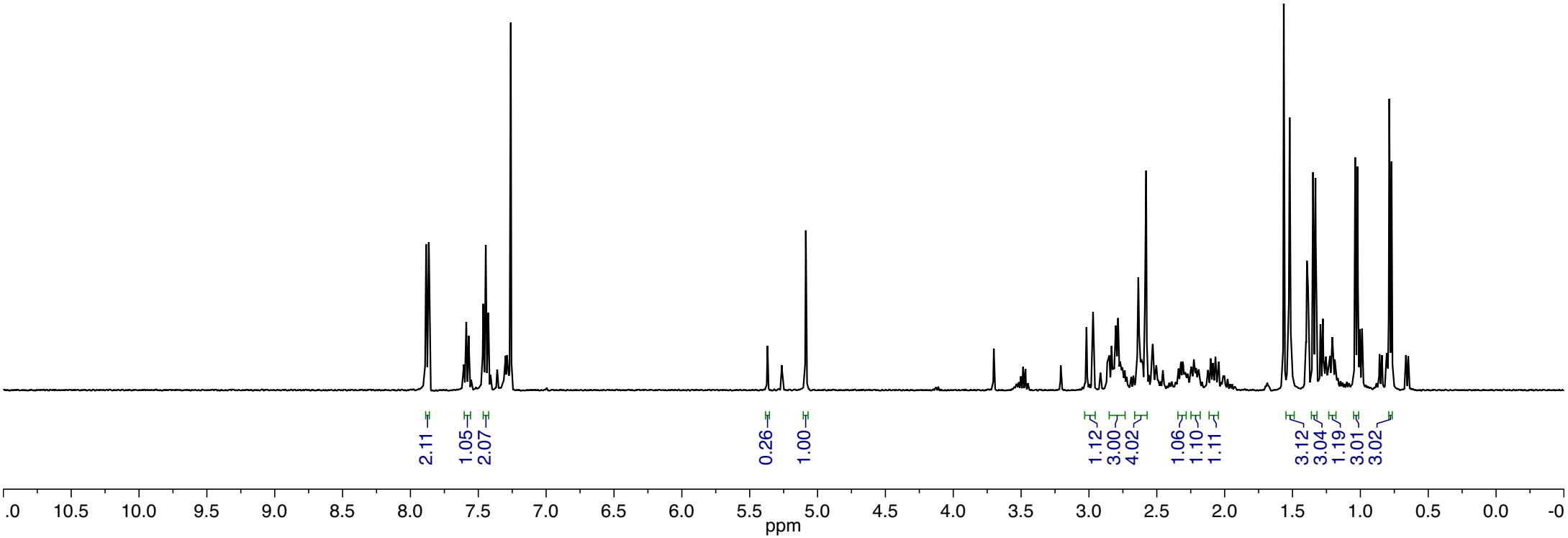
37

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-085-CH/ 1/ fid
Title	9-AH-085-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	298.1
Pulse Sequence	zg30
Number of Scans	3
Receiver Gain	101.0
Relaxation Delay	5.0000
Pulse Width	10.0000
Acquisition Time	3.9977
Acquisition Date	2018-09-05T07:20:37
Spectrometer Frequency	400.15
Spectral Width	8196.7
Lowest Frequency	-1637.0
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

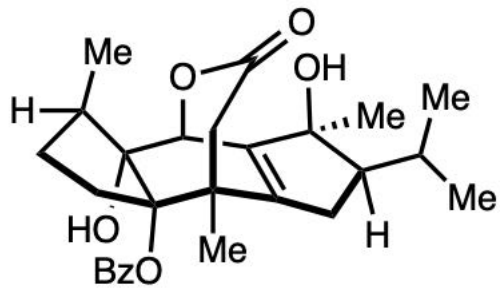


38

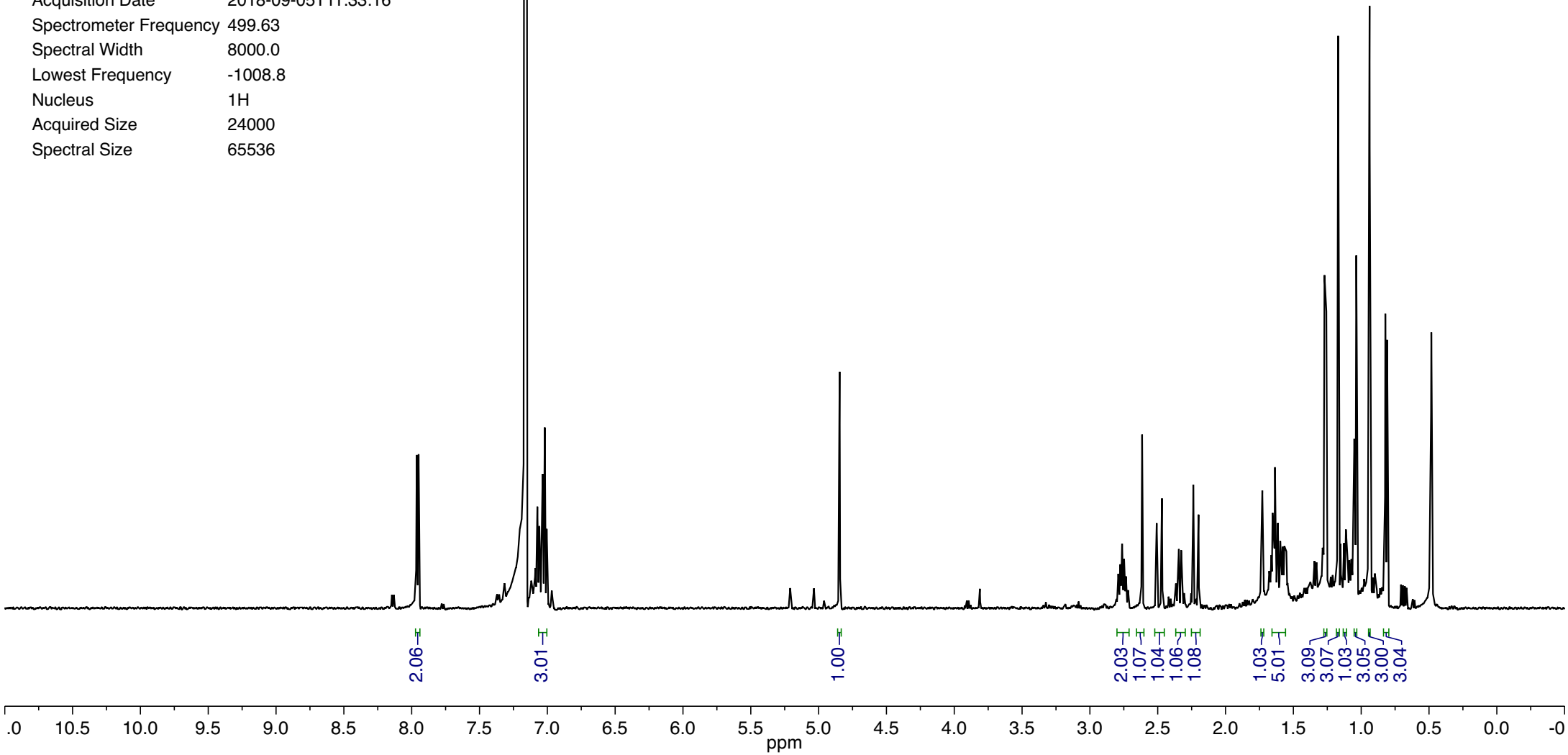
3:1 rr



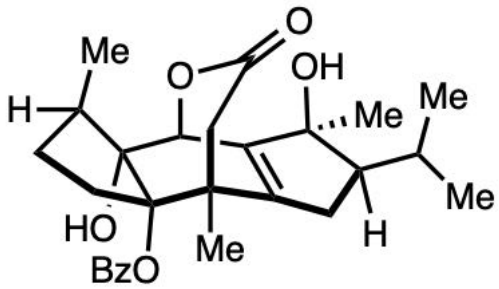
Parameter	Value
Data File Name	/ Volumes/ nmrdata-1/ ahan/ vnmrsys/ data/ 9-AH-086-P/ PROTON02.fid/ fid
Title	PROTON02
Origin	Varian
Solvent	c6d6
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	8
Receiver Gain	42
Relaxation Delay	5.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2018-09-05T11:33:16
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1008.8
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



39

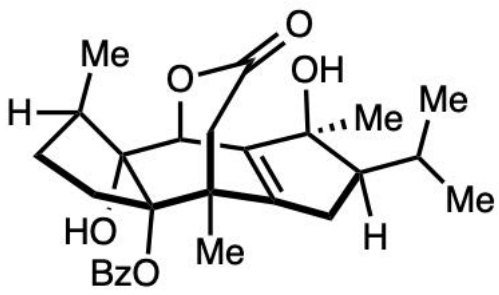


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-086-CH/ 2/ fid
Title	9-AH-086-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	800
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-05T14:01:42
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1927.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

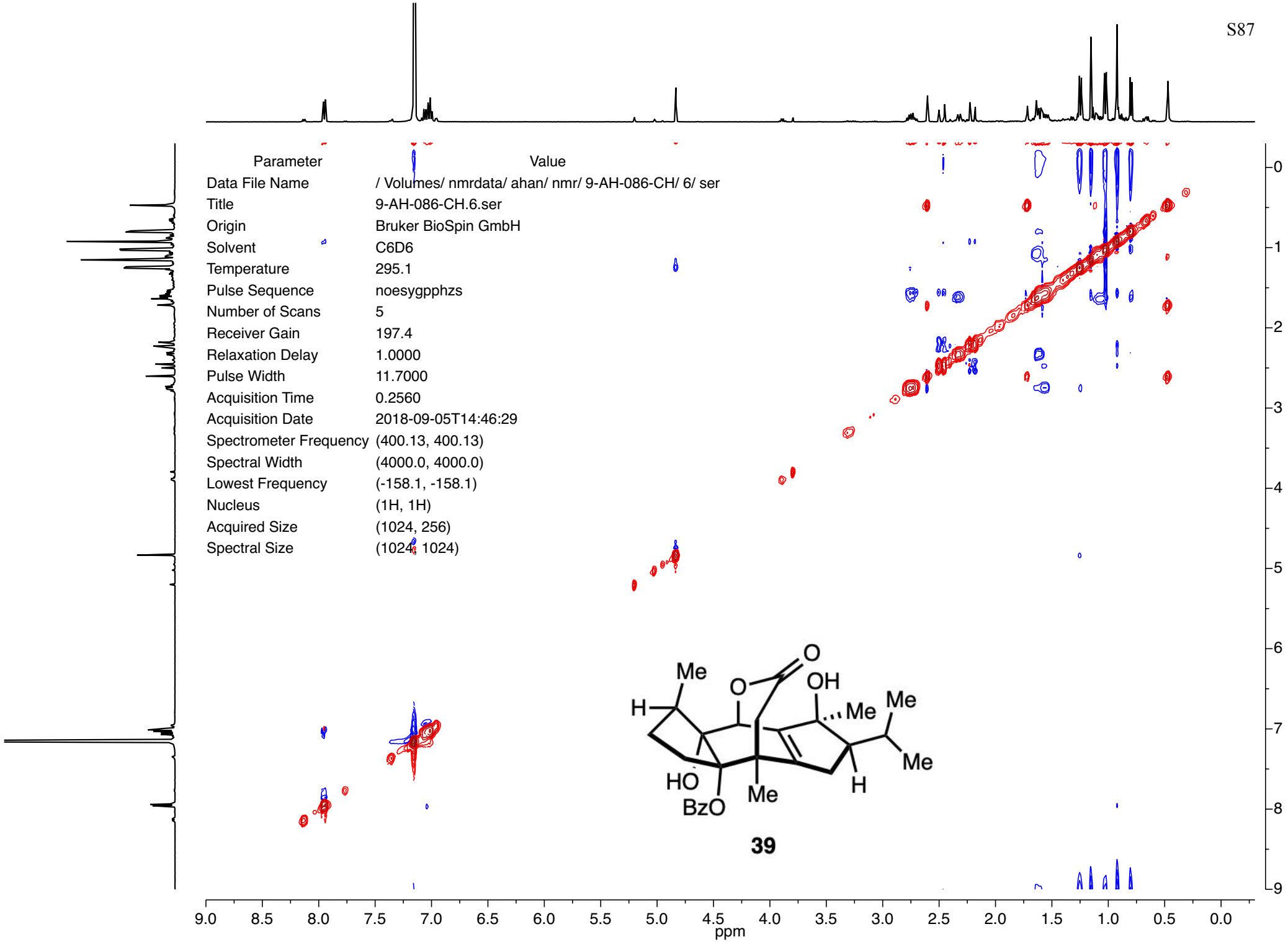


39

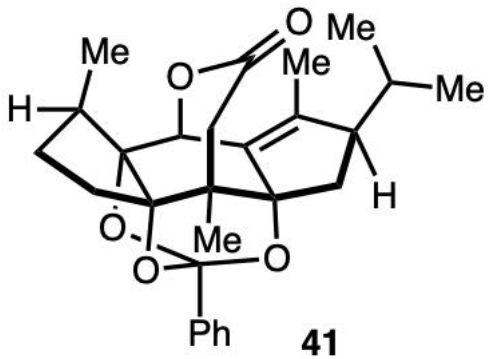
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-086-CH/ 5/ ser
Title	9-AH-086-CH.5.ser
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.1
Pulse Sequence	hmbcetgpl3nd
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-05T14:19:27
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1115.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 140)
Spectral Size	(2048, 1024)



39

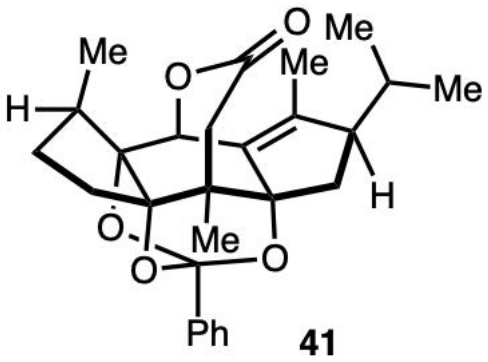

Parameter Value
Data File Name / Volumes/ nmrdata/ ahan/ nmr/ 9-AH-086-CH/ 6/ ser
Title 9-AH-086-CH.6.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.1
Pulse Sequence noesygpphzs
Number of Scans 5
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-09-05T14:46:29
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Lowest Frequency (-158.1, -158.1)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
Me
O
OH
H
Me
Me
Me
HO
BzO
Me
H
39
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
ppm
0 1 2 3 4 5 6 7 8 9

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-087-CH/ 1/ fid
Title	9-AH-087-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	1
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-06T06:39:57
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



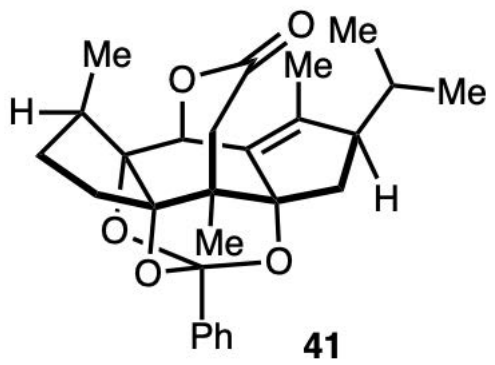
41

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-087-CH/ 2/ fid
Title	9-AH-087-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	1000
Receiver Gain	72.0
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-06T07:20:53
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1961.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



41

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-087-CH/ 5/ ser
Title	9-AH-087-CH.5.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hsqcedetgpsisp2.4
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2018-09-06T08:09:47
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-517.1, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)

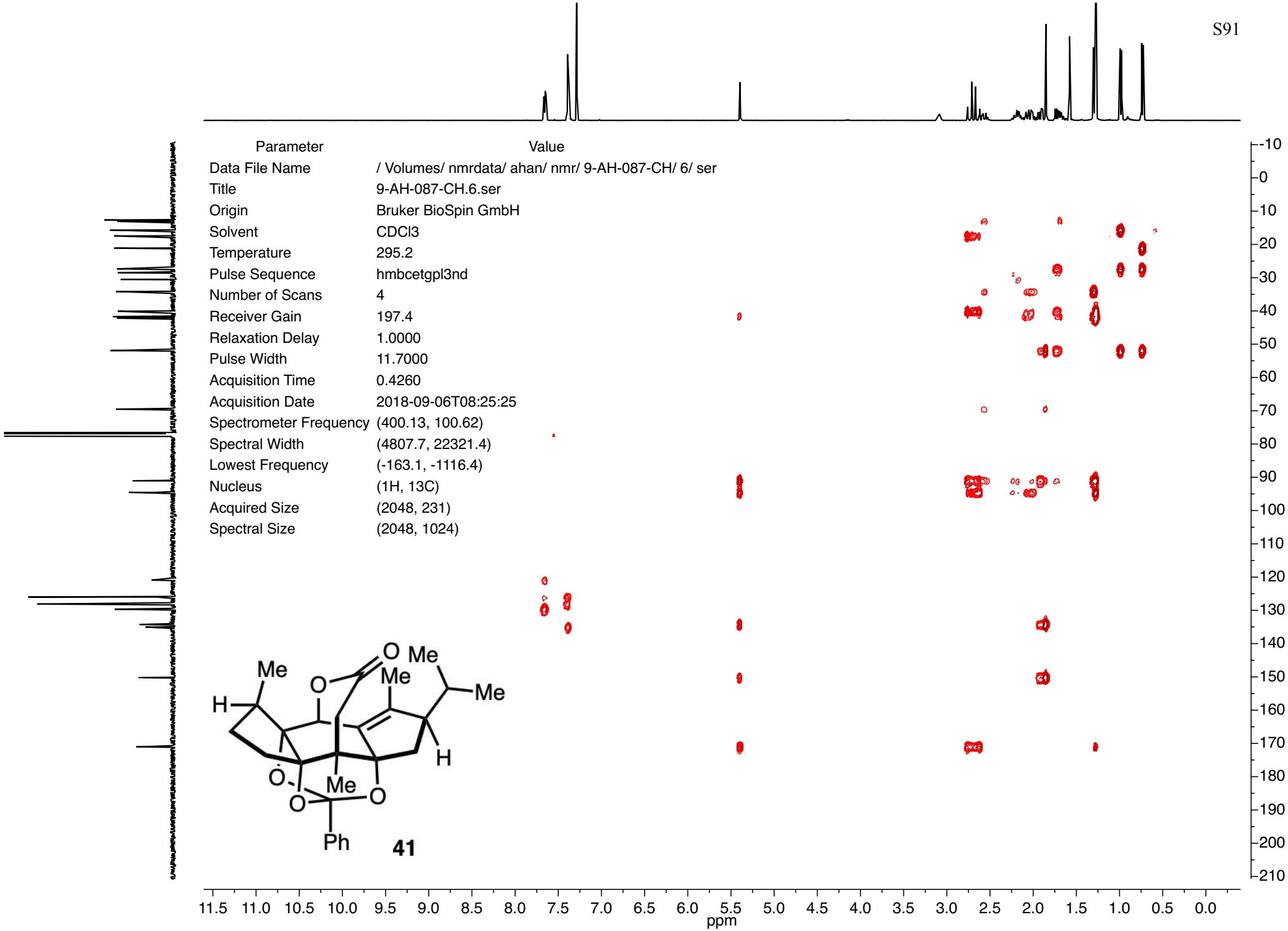


41

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 -0.5 -1.0

ppm

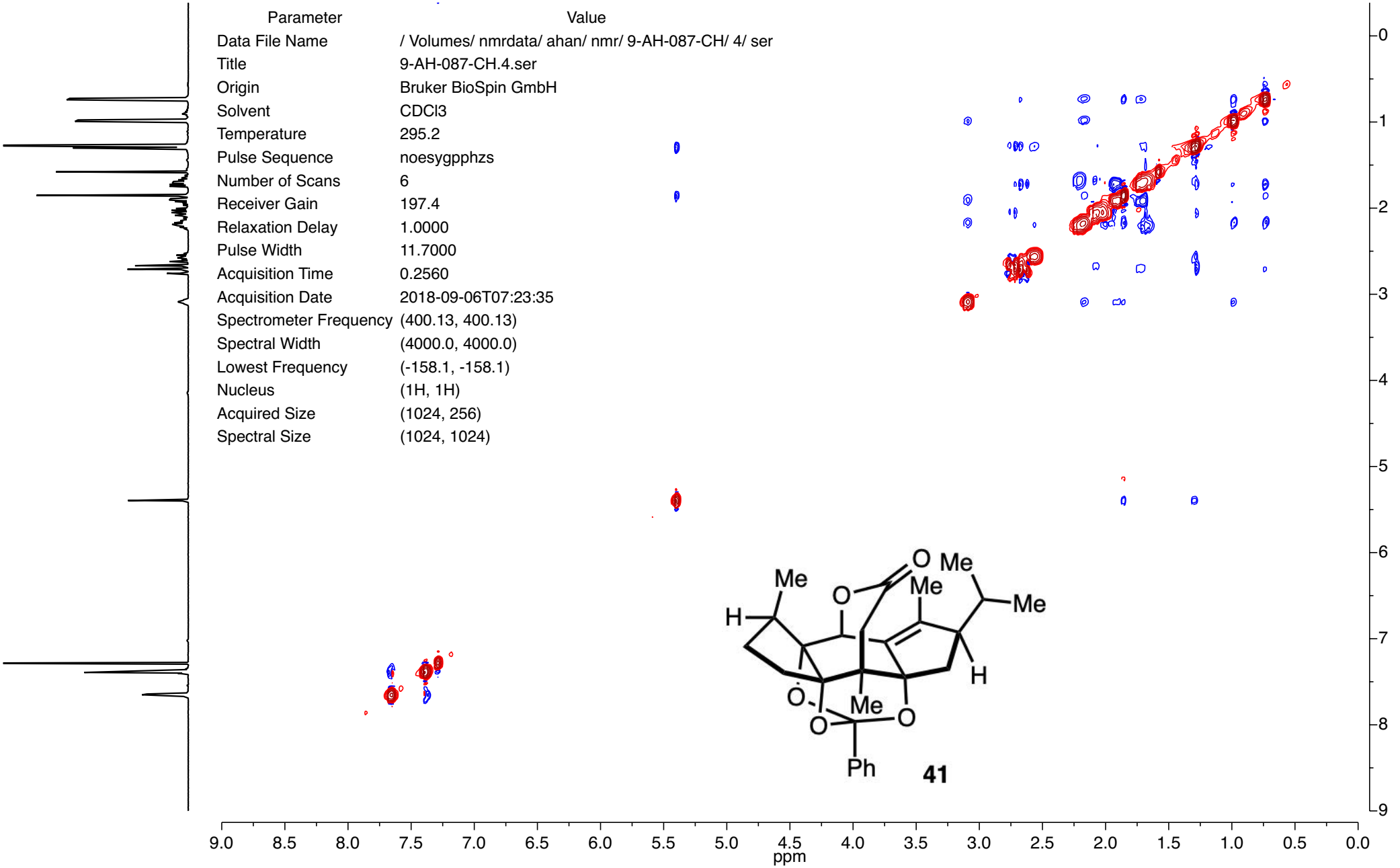
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150



Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-087-CH/ 6/ ser
Title	9-AH-087-CH.6.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hmbcetgpl3nd
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-06T08:25:25
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1116.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 231)
Spectral Size	(2048, 1024)

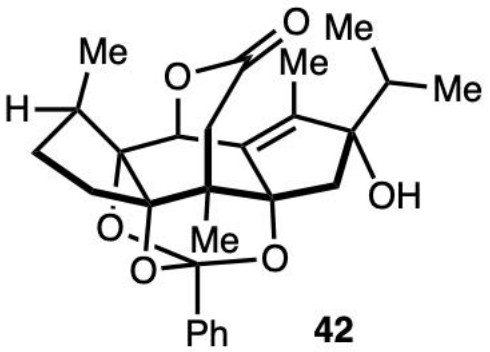
41

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-087-CH/ 4/ ser
Title	9-AH-087-CH.4.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	noesygpphzs
Number of Scans	6
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2560
Acquisition Date	2018-09-06T07:23:35
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(4000.0, 4000.0)
Lowest Frequency	(-158.1, -158.1)
Nucleus	(1H, 1H)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)



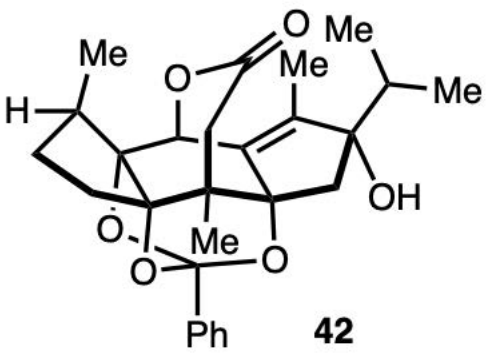
41

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-088-CH/ 1/ fid
Title	9-AH-088-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	1
Receiver Gain	176.8
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-06T12:12:19
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1532.8
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



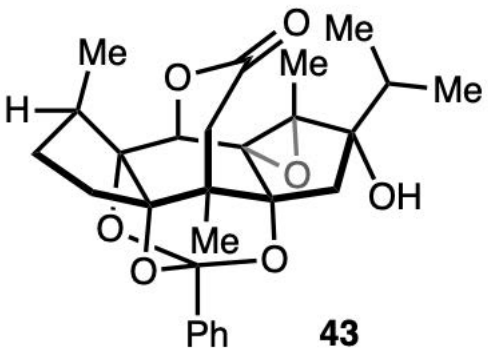
42

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-088-CH/ 2/ fid
Title	9-AH-088-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	1000
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-06T12:53:53
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1927.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536

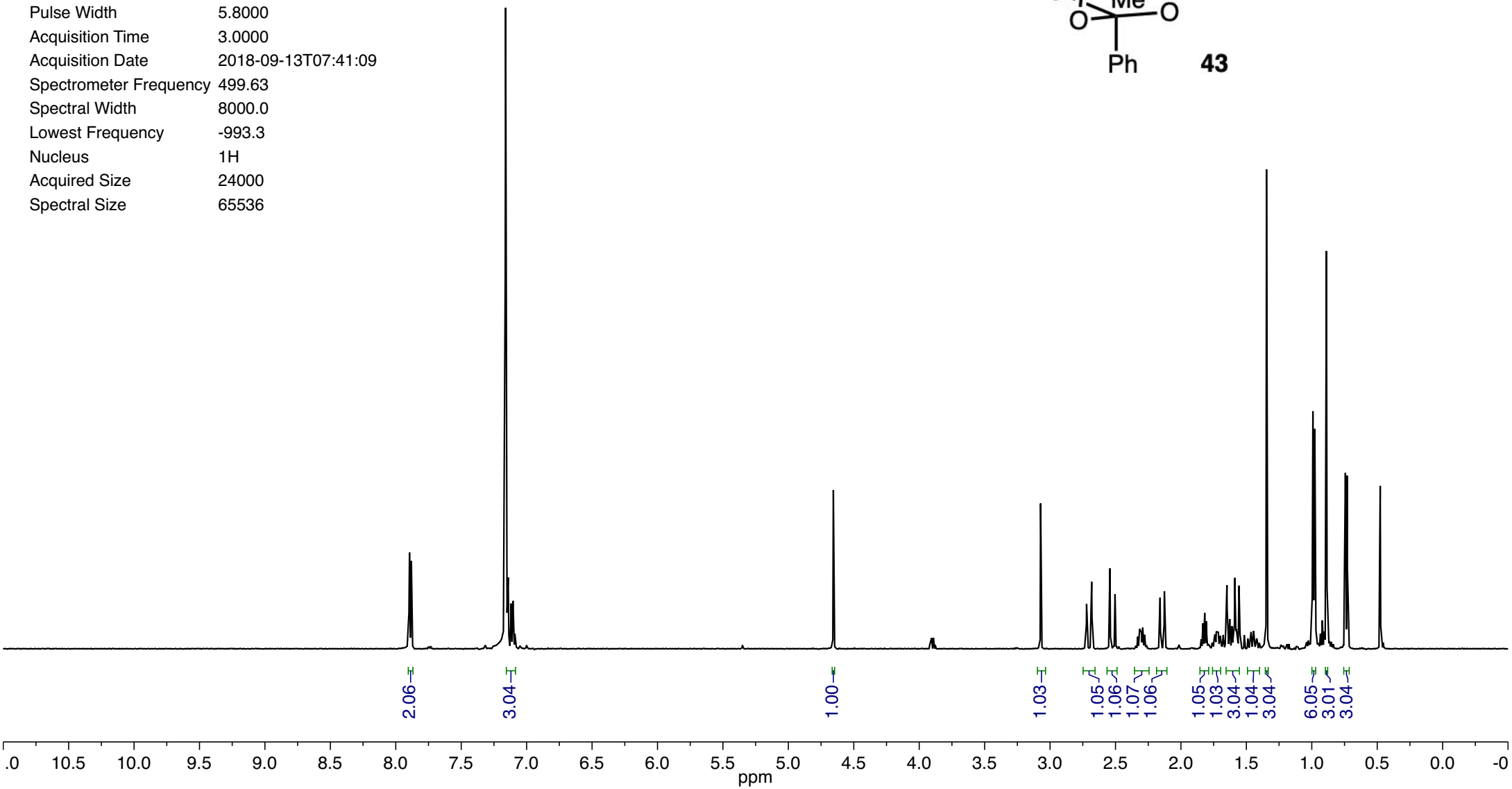


42

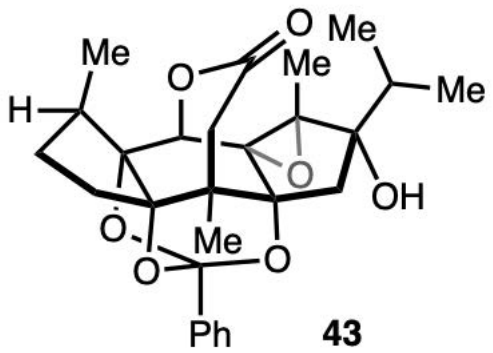
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 9-AH-089-CH/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Solvent	c6d6
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	4
Receiver Gain	36
Relaxation Delay	5.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2018-09-13T07:41:09
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-993.3
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



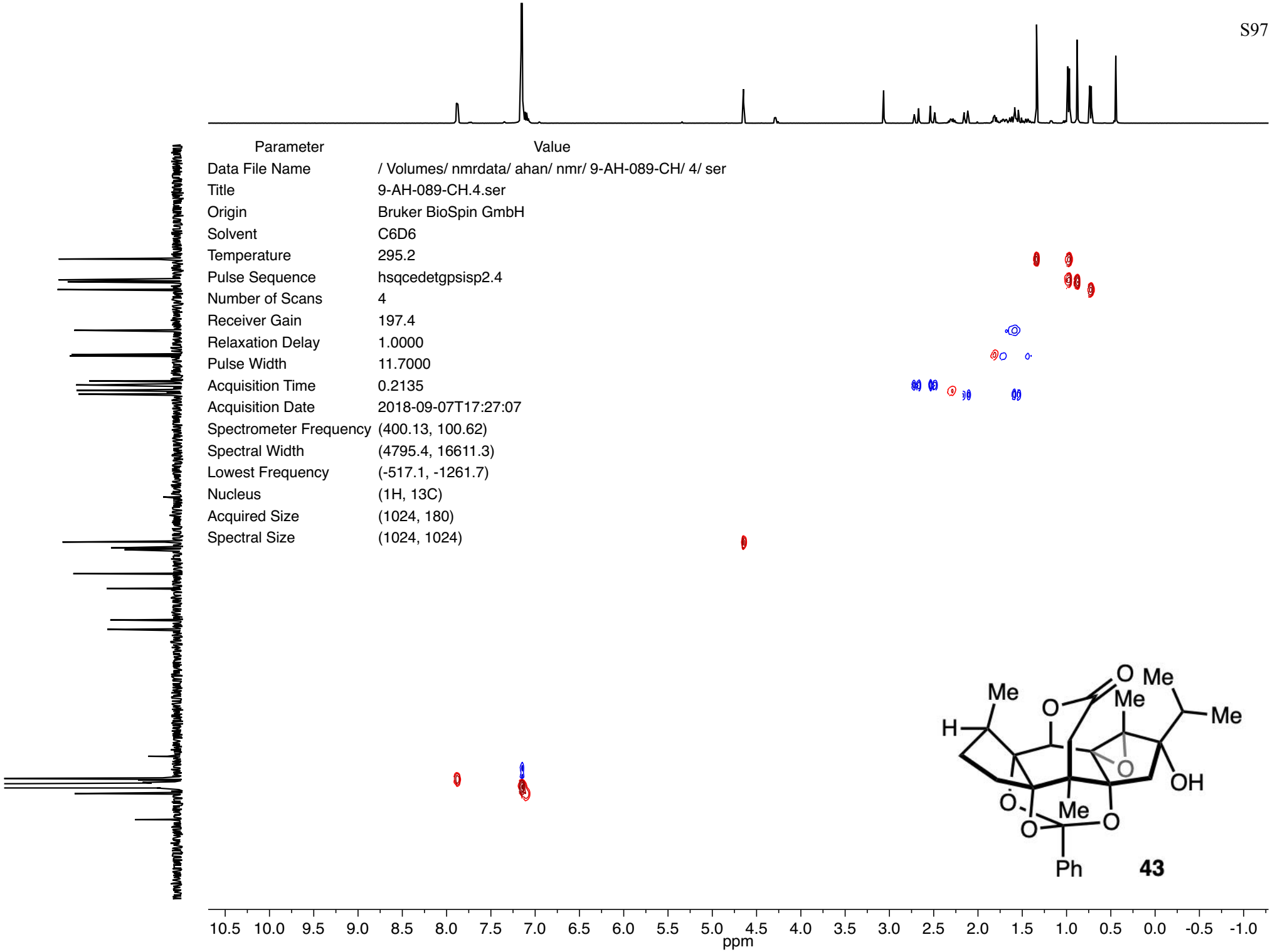
43



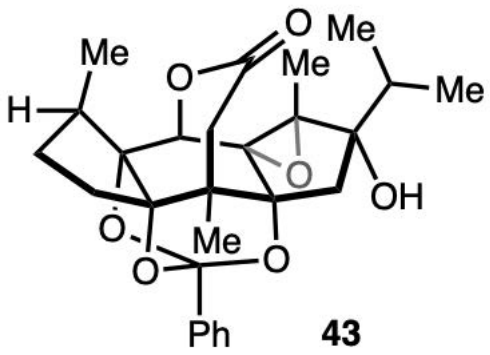
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-089-CH/ 1/ fid
Title	9-AH-089-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	1000
Receiver Gain	55.5
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-07T16:45:46
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1927.3
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



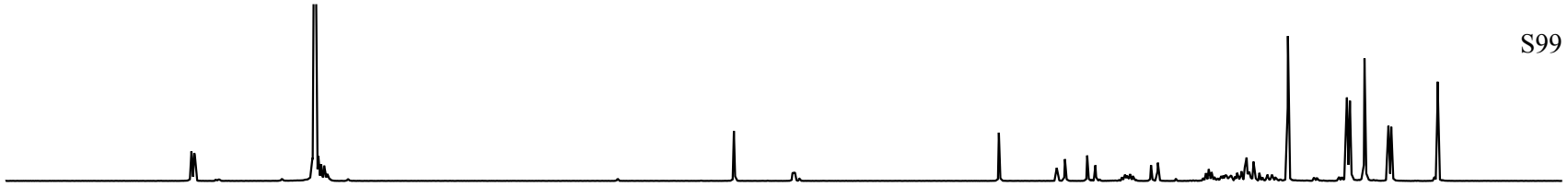
43


Parameter Value
Data File Name / Volumes/ nmrdata/ ahan/ nmr/ 9-AH-089-CH/ 4/ ser
Title 9-AH-089-CH.4.ser
Origin Bruker BioSpin GmbH
Solvent C6D6
Temperature 295.2
Pulse Sequence hsqcedetgpsisp2.4
Number of Scans 4
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2135
Acquisition Date 2018-09-07T17:27:07
Spectrometer Frequency (400.13, 100.62)
Spectral Width (4795.4, 16611.3)
Lowest Frequency (-517.1, -1261.7)
Nucleus (1H, 13C)
Acquired Size (1024, 180)
Spectral Size (1024, 1024)
Me
O
Me
Me
H
Me
O
OH
O
Me
O
O
Ph
43
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 -0.5 -1.0
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150

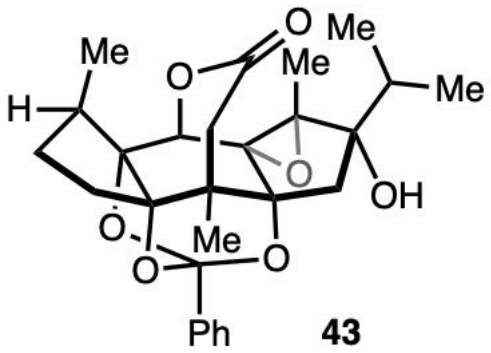
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-089-CH/ 5/ ser
Title	9-AH-089-CH.5.ser
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.2
Pulse Sequence	hmbcetgpl3nd
Number of Scans	4
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-07T17:42:45
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1115.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 150)
Spectral Size	(2048, 1024)



43

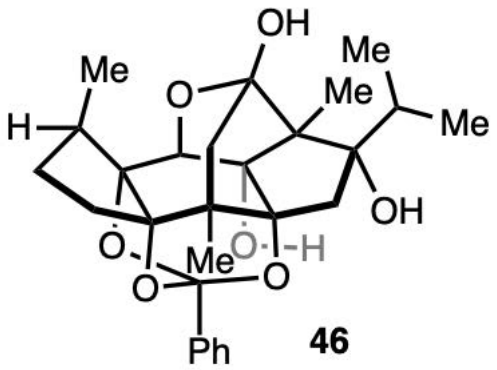


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-089-CH/ 3/ ser
Title	9-AH-089-CH.3.ser
Origin	Bruker BioSpin GmbH
Solvent	C6D6
Temperature	295.1
Pulse Sequence	noesygpphzs
Number of Scans	5
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2560
Acquisition Date	2018-09-07T16:48:27
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(4000.0, 4000.0)
Lowest Frequency	(-158.1, -158.1)
Nucleus	(1H, 1H)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)



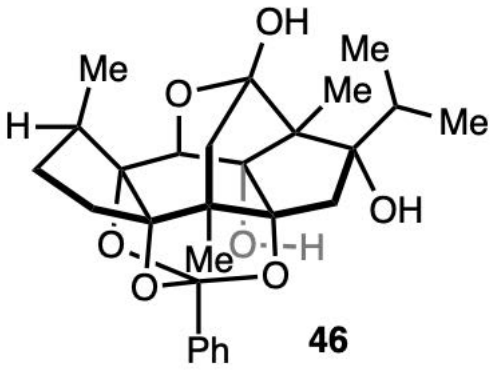
43

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-092-CH/ 1/ fid
Title	9-AH-092-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-11T14:54:04
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



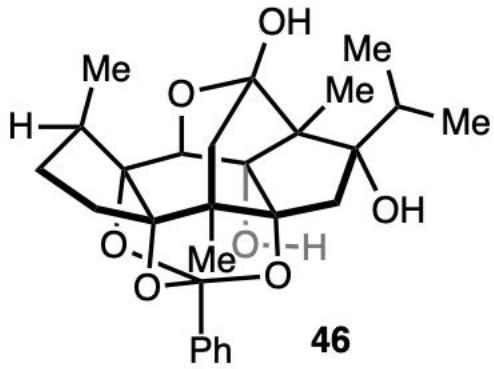
46

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-092-CH/ 2/ fid
Title	9-AH-092-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	zgpg30
Number of Scans	1105
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-11T15:40:00
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1960.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



46

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-092-CH/ 4/ ser
Title	9-AH-092-CH.4.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.1
Pulse Sequence	hsqcedetgpsisp2.4
Number of Scans	6
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2018-09-11T15:42:27
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-517.1, -1262.8)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)



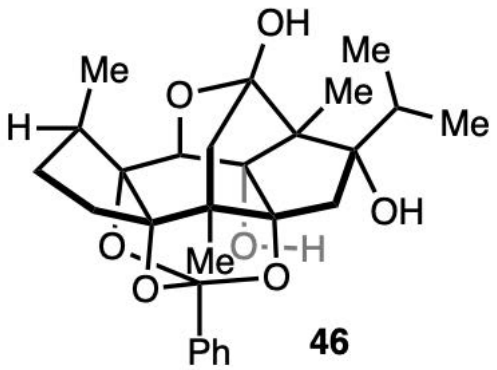
46

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 -0.5 -1.0

ppm

-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150

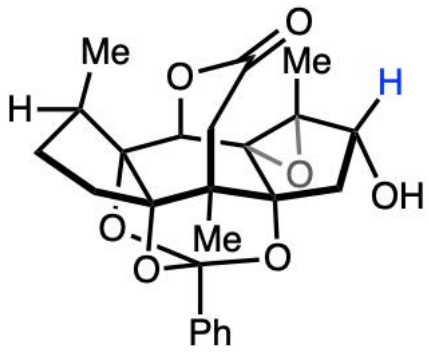
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-092-CH/ 5/ ser
Title	9-AH-092-CH.5.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	295.2
Pulse Sequence	hmbcetgpl3nd
Number of Scans	6
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-11T16:05:36
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1116.4)
Nucleus	(1H, 13C)
Acquired Size	(2048, 178)
Spectral Size	(2048, 1024)



46

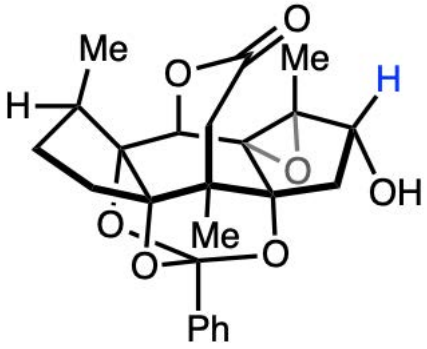
ppm

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-011-CH/ 1/ fid
Title	9-AH-011-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-14T21:20:49
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1545.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536

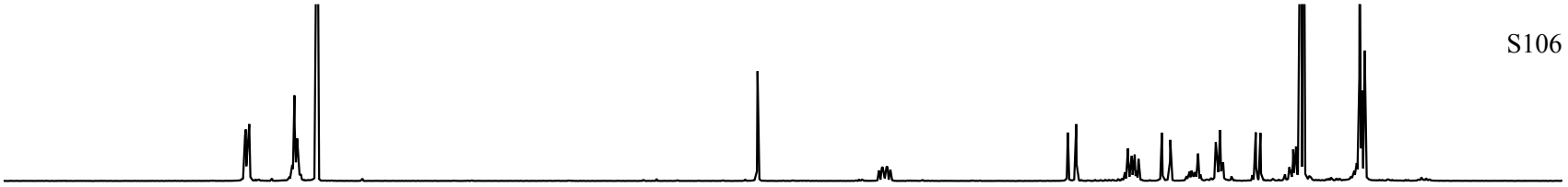


S20

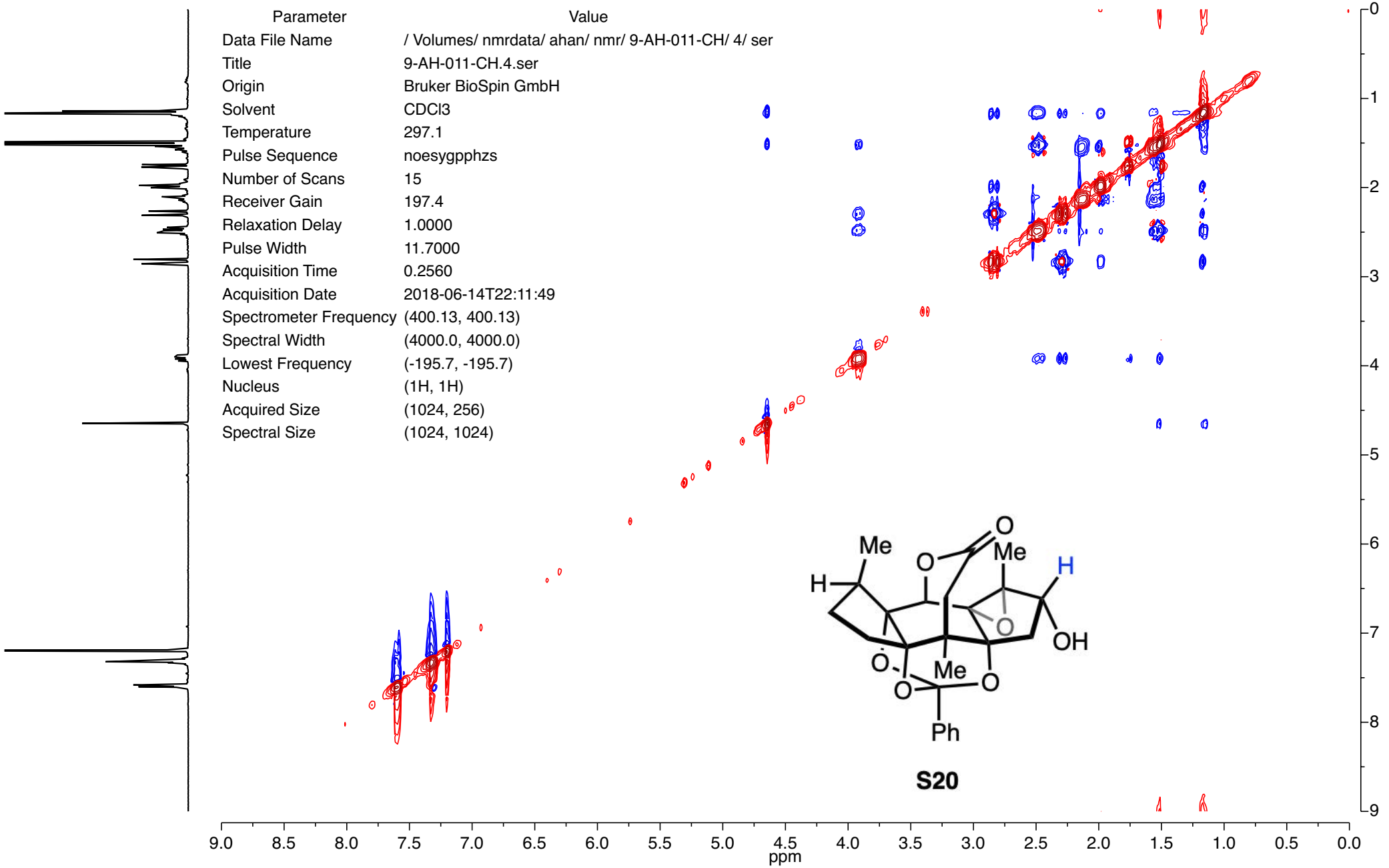
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-011-CH/ 6/ fid
Title	9-AH-011-CH.6.fid
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	zgpg30
Number of Scans	4500
Receiver Gain	78.7
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-15T03:29:29
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1960.6
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



S20

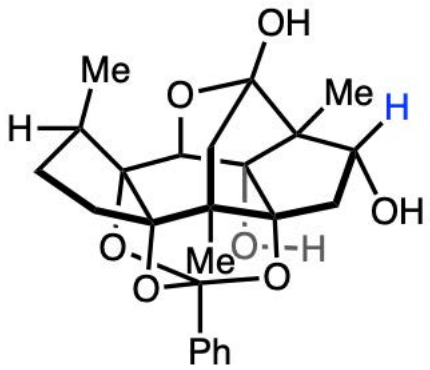


Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-011-CH/ 4/ ser
Title	9-AH-011-CH.4.ser
Origin	Bruker BioSpin GmbH
Solvent	CDCl3
Temperature	297.1
Pulse Sequence	noesygpphzs
Number of Scans	15
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2560
Acquisition Date	2018-06-14T22:11:49
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(4000.0, 4000.0)
Lowest Frequency	(-195.7, -195.7)
Nucleus	(1H, 1H)
Acquired Size	(1024, 256)
Spectral Size	(1024, 1024)



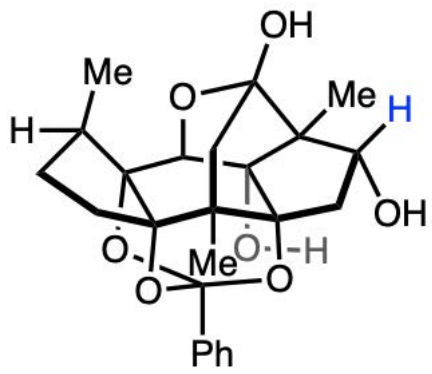
S20

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-012-CH/ 1/ fid
Title	9-AH-012-CH.1.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	297.1
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-06-15T10:47:00
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1543.4
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



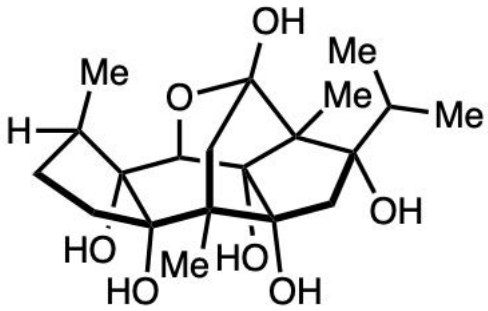
S21

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-012-CH/ 4/ fid
Title	9-AH-012-CH.4.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	297.2
Pulse Sequence	zgpg30
Number of Scans	1100
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-06-15T12:36:20
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1816.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



S21

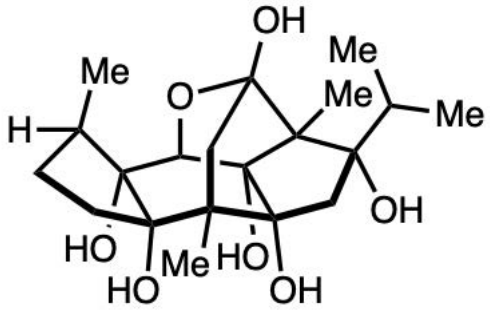
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-094-CH/ 9/ fid
Title	9-AH-094-CH.9.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.1
Pulse Sequence	zg30
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	5.0000
Pulse Width	11.7000
Acquisition Time	4.0894
Acquisition Date	2018-09-13T12:00:33
Spectrometer Frequency	400.13
Spectral Width	8012.8
Lowest Frequency	-1543.6
Nucleus	1H
Acquired Size	32768
Spectral Size	65536



(+)-perseanol (3)

^{1}H NMR (400 MHz, CD_3OD)

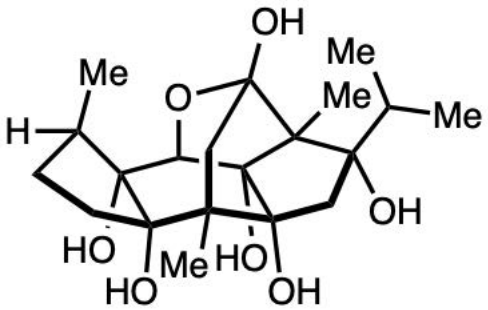
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ vnmrsys/ data/ 9-AH-094-CH/ PROTON01.fid/ fid
Title	PROTON01
Origin	Varian
Solvent	cd3od
Temperature	25.0
Pulse Sequence	s2pul
Number of Scans	16
Receiver Gain	38
Relaxation Delay	5.0000
Pulse Width	5.8000
Acquisition Time	3.0000
Acquisition Date	2018-09-13T06:00:59
Spectrometer Frequency	499.63
Spectral Width	8000.0
Lowest Frequency	-1011.7
Nucleus	1H
Acquired Size	24000
Spectral Size	65536



(+)-perseanol (3)

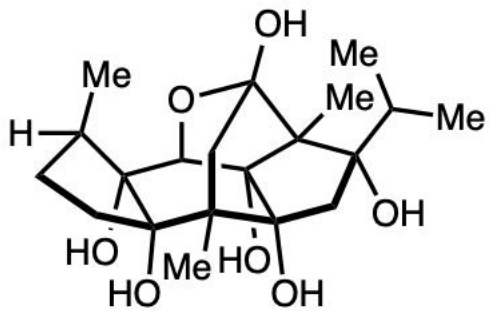
^{1}H NMR (500 MHz, CD_3OD)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-094-CH/ 2/ fid
Title	9-AH-094-CH.2.fid
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.1
Pulse Sequence	zgpg30
Number of Scans	3000
Receiver Gain	64.2
Relaxation Delay	1.0000
Pulse Width	10.0000
Acquisition Time	1.3631
Acquisition Date	2018-09-12T23:31:17
Spectrometer Frequency	100.62
Spectral Width	24038.5
Lowest Frequency	-1816.9
Nucleus	13C
Acquired Size	32768
Spectral Size	65536



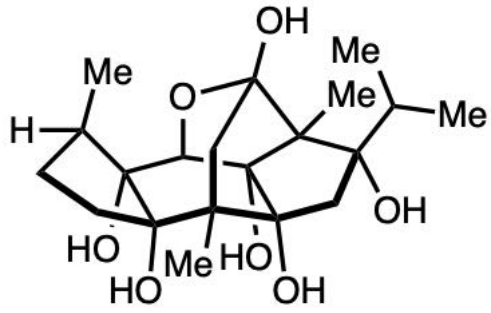
(+)-perseanol (3)

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-094-CH/ 7/ ser
Title	9-AH-094-CH.7.ser
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.2
Pulse Sequence	cosygpppqf
Number of Scans	10
Receiver Gain	142.8
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.1970
Acquisition Date	2018-09-13T02:58:21
Spectrometer Frequency	(400.13, 400.13)
Spectral Width	(5197.5, 5197.5)
Lowest Frequency	(-198.0, -198.0)
Nucleus	(1H, 1H)
Acquired Size	(1024, 128)
Spectral Size	(1024, 1024)



(+)-perseanol (3)

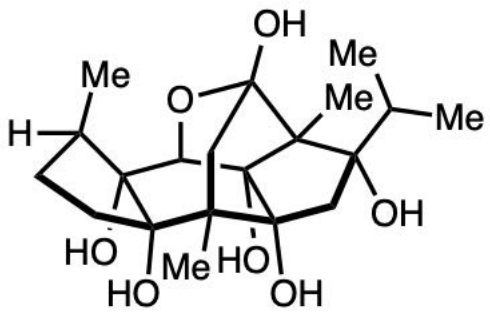
Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-094-CH/ 4/ ser
Title	9-AH-094-CH.4.ser
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.2
Pulse Sequence	hsqcedetgpsisp2.4
Number of Scans	8
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.2135
Acquisition Date	2018-09-12T23:34:23
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4795.4, 16611.3)
Lowest Frequency	(-517.1, -1335.2)
Nucleus	(1H, 13C)
Acquired Size	(1024, 180)
Spectral Size	(1024, 1024)



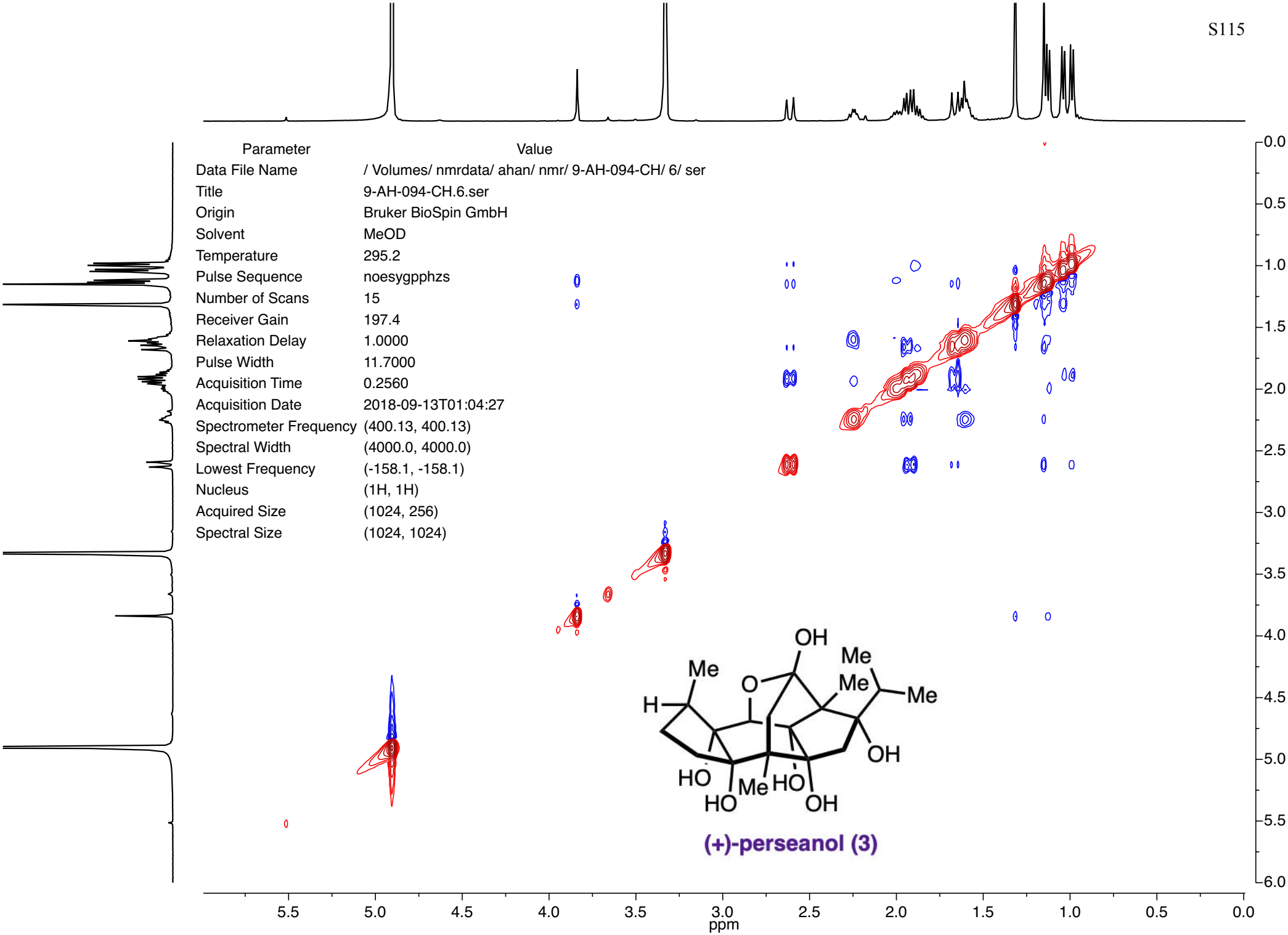
(+)-perseanol (3)

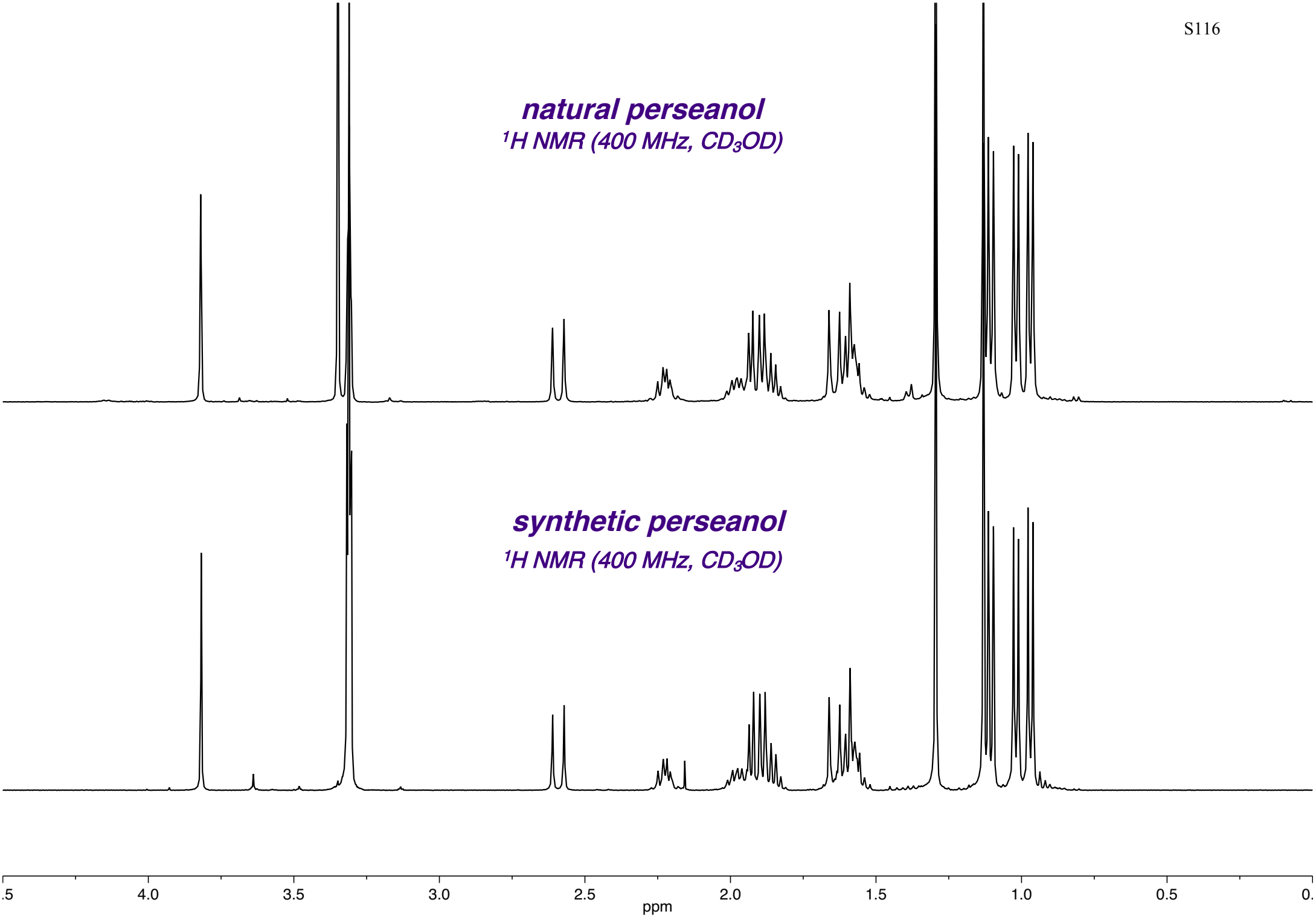
ppm

Parameter	Value
Data File Name	/ Volumes/ nmrdata/ ahan/ nmr/ 9-AH-094-CH/ 5/ ser
Title	9-AH-094-CH.5.ser
Origin	Bruker BioSpin GmbH
Solvent	MeOD
Temperature	295.2
Pulse Sequence	hmbcetgpl3nd
Number of Scans	9
Receiver Gain	197.4
Relaxation Delay	1.0000
Pulse Width	11.7000
Acquisition Time	0.4260
Acquisition Date	2018-09-13T00:05:03
Spectrometer Frequency	(400.13, 100.62)
Spectral Width	(4807.7, 22321.4)
Lowest Frequency	(-163.1, -1188.8)
Nucleus	(1H, 13C)
Acquired Size	(2048, 256)
Spectral Size	(2048, 1024)



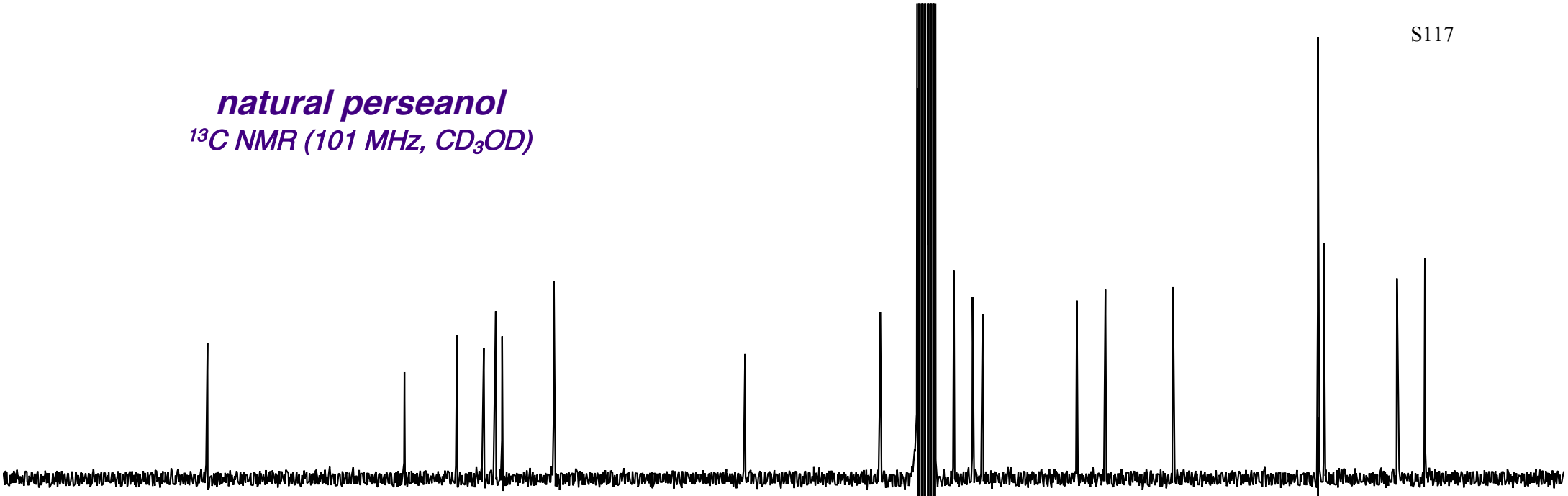
(+)-perseanol (3)


Parameter Value
Data File Name / Volumes/ nmrdata/ ahan/ nmr/ 9-AH-094-CH/ 6/ ser
Title 9-AH-094-CH.6.ser
Origin Bruker BioSpin GmbH
Solvent MeOD
Temperature 295.2
Pulse Sequence noesygpphzs
Number of Scans 15
Receiver Gain 197.4
Relaxation Delay 1.0000
Pulse Width 11.7000
Acquisition Time 0.2560
Acquisition Date 2018-09-13T01:04:27
Spectrometer Frequency (400.13, 400.13)
Spectral Width (4000.0, 4000.0)
Lowest Frequency (-158.1, -158.1)
Nucleus (1H, 1H)
Acquired Size (1024, 256)
Spectral Size (1024, 1024)
OH
Me
Me
Me
Me
O
H
OH
HO
Me
HO
HO
OH
(+)-perseanol (3)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
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
ppm


natural perseanol
¹H NMR (400 MHz, CD3OD)
synthetic perseanol
¹H NMR (400 MHz, CD3OD)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

natural perseanol

^{13}C NMR (101 MHz, CD_3OD)



synthetic perseanol

^{13}C NMR (101 MHz, CD_3OD)