Supplementary Materials

for

A 15-Step Synthesis of (+)-Ryanodol

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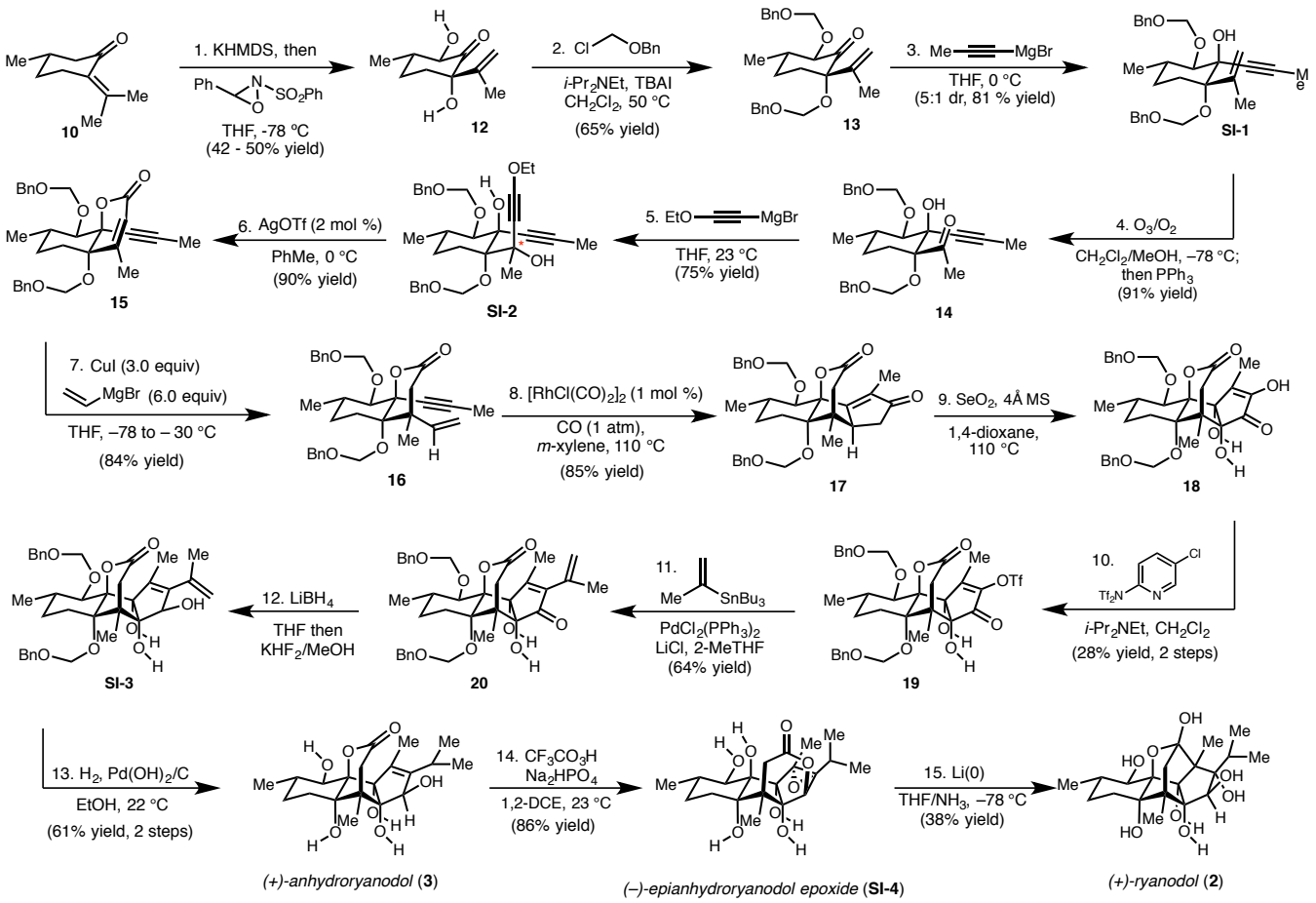
General Procedures

Unless otherwise stated, reactions were performed under an inert atmosphere (dry N_2 or 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), 1,4-dioxane, and toluene (PhMe) were dried by passing through activated alumina columns. 2-Methyltetrahydrofuran (anhydrous, >99%, inhibitor-free) and *m*-xylene (anhydrous, >99%) were purchased from Sigma-Aldrich and stored under argon. Absolute ethanol (200 Proof) was purchased from Koptec. Methanol (HPLC grade) was purchased from Fisher Scientific. 1,2-Dichloroethane was purified via distillation over calcium hydride immediately before use. Anhydrous ammonia (NH_3) was purchased from Matheson Tri-Gas and distilled over sodium metal prior to use. Triethylamine (Et_3N) and *N,N*-diisopropylethylamine (*i*-Pr_2NEt) were distilled over calcium hydride prior to use. 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), *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 Varian Inova 500 (at 500 MHz and 126 MHz, respectively) and are reported relative to internal $CHCl_3$ (^1H, δ = 7.26) or CD_2-HOD (^1H, δ = 3.31), and $CDCl_3$ (^{13}C, δ = 77.0), 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, 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 or prepared as follows: Solid potassium hexamethyldisilazide (KHMDS, 95%) was purchased from Sigma-Aldrich and stored in a nitrogen-filled glovebox. Potassium hexamethyldisilazide solution (0.5 M in PhMe) was purchased from Sigma-Aldrich and

stored under Argon. *Rac*-3-phenyl-2-(phenylsulfonyl)-1,2-oxaziridine (Davis Oxaziridine) was prepared according to literature procedures (*36*). Chloromethyl benzyl ether ($BnOCH_2Cl$) was prepared from paraformaldehyde, benzyl alcohol, and gaseous hydrogen chloride according literature procedures (*46*). Propynylmagnesium bromide (0.5 M in THF) was purchased from Alfa Aesar or freshly prepared via direct deprotonation of propyne with ethylmagnesium bromide (1 M in THF). Ethoxyacetylene (50 wt % in hexanes) was purchased from GFS Chemicals and used as received. Silver triflate (AgOTf, 99%), selenium dioxide (SeO_2, 99.8%), and chlorodicarbonyl rhodium (I) dimer ($[RhCl(CO)_2]_2$) were purchased from Strem Chemicals and stored in a nitrogen-filled glovebox. *N*-(5-Chloro-2-pyridyl)bis(trifluoromethanesulfonimide) (Comins Reagent) was purchased from Oakwood Chemicals. Copper(I) iodide (CuI) and palladium hydroxide on Carbon (Pearlman's Catalyst, 20 wt % on C) were purchased from Alfa Aesar. $LiBH_4$ (>95%) and lithium (wire stored in mineral oil, 99.9% trace metal basis) were purchased from Sigma-Aldrich.



Scheme S1: Complete synthetic scheme for the synthesis of (+)-ryanodol from (*S*)-pulegone.

Positional Numbering System. The carbon numbering system and ring assignment as outlined by Deslongchamps (*24–28*) is utilized through the Supplementary Materials file for ^{1}H and ^{13}C NMR assignments. Assignments were performed with the aid of 2D ^{1}H-^{1}H (NOESY2D, gCOSY) and ^{1}H-^{13}C coupling experiments (gHSQC and gHMBC).

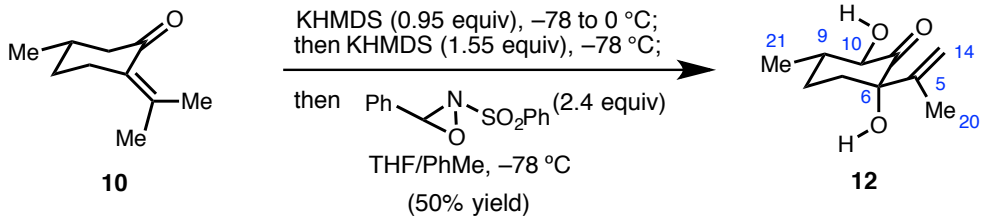
Scheme S2: Carbon numbering and ring assignment.

Synthetic Procedures

Notes on the preparation of Diol 12: Both the selectivity and yields obtained for the α,α'-bishydroxylation of pulegone were finely dependent on the quality of KHMDS utilized in the reaction, as well as precise temperature control. Improved selectivities and yields were more readily obtained on smaller scale (50% yield, 10 mmol scale) for the preparation of diol **12** via pre-equilibration of the potassium enolate at 0 °C to the thermodynamically-preferred, conjugated dienolate, as well as utilizing KHMDS (0.5 M) in PhMe solution. However, in order to improve material throughput on scale, a simplified protocol was established for larger scale (42% yield, 120 mmol scale) at the slight cost of reaction efficiency.

Additionally, separation of the diastereomeric products was improved via use of wet silica gel, prepared as follows: Silica gel (SiliaFlash® P60, particle size 40-63 microns [230 to 400 mesh], purchased from Silicycle, 950 g) was slowly mixed with deionizied water (50 mL) in a 1-liter media bottle. The silica was then vigorously shaken for five minutes, and then allowed to equilibrate for 12 h before use as normal for silica gel purification. The product obtained by this method was typically 97% pure by ^{1}H NMR analysis, containing some minor oxaziridine-derived products.

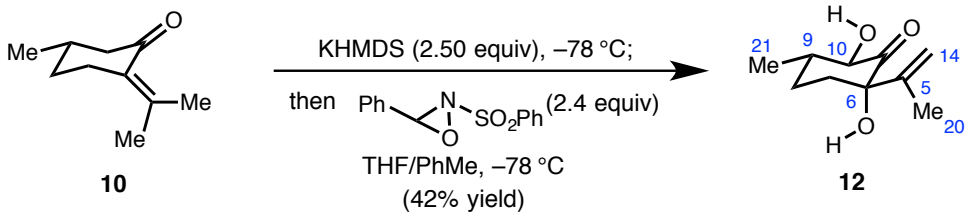
Preparation of Diol 10 (10 mmol scale):



To a flame-dried, 250-mL, round-bottomed flask equipped with a magnetic stirbar was added (*S*)-pulegone (1.52 g, 10.0 mmol, 1.0 equiv) and THF (50 mL). The solution was cooled to –78 °C in a dry ice/acetone bath and KHMDS (19.0 mL, 0.5 M solution in PhMe, 9.50 mmol, 0.95 equiv) was added dropwise by cannula transfer over 10 minutes. After completion of the transfer, the dry ice/acetone bath was replaced with an ice/water bath, and the flask was stirred at 0 °C for 1 h. The solution was then recooled to –78 °C in a dry ice/acetone bath, and additional KHMDS solution (31.0 mL, 0.5 M solution PhMe, 15.5 mmol, 1.55 equiv) was added rapidly via cannula transfer and the flask stirred for 15 minutes to ensure complete cooling of the solution. A solution of *rac*-3-phenyl-2-(phenylsulfonyl)-1,2-oxaziridine (6.31 g, 24.0 mmol, 2.4 equiv) in THF (400 mL) was then added dropwise by cannula transfer over the course of 1 h, producing a deep orange-red solution that was stirred for 15 minutes. It is critical that the enolate solution is efficiently stirred during the addition to maintain a consistent internal temperature. Sat. aq. NH_4Cl (90 mL) was then added and the flask allowed to warm to ambient temperature and stirred for 1 h, until TLC-analysis indicated complete hydrolysis of the imine

byproduct (*N*-benzylidenebenzenesulfonamide). The resulting mixture was extracted with EtOAc (150 mL), washed with sat. aq. NH_4Cl (2 x 150 mL), and the combined aqueous layers extracted with EtOAc (200 mL). The combined organic layers were washed with brine (200 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel chromatography (20 to 30 to 40% EtOAc in hexanes) on wet silica gel (see above) affords diol **12** as a white solid (923 mg, 5.01 mmol, 50% yield).

Preparation of Diol 12 (120 mmol scale):



To a 1-liter, flame-dried flask equipped with a large magnetic stirbar was added solid KHMDS (95% KHMDS, 63.0 g, 300 mmol, 2.5 equiv) in a nitrogen-filled glovebox. The flask was capped with a rubber septum, removed from the glovebox, and anhydrous THF (300 mL) was charged to the flask and the resulting mixture stirred at 22 °C for 10 minutes to ensure complete dissolution of the solid. The resulting solution was then cooled to –78 °C in a dry ice/acetone bath (Note: Adequate cooling of the reaction mixture is critical for this reaction. A large capacity Pope brand cryogenic dewar was utilized for this procedure). After stirring for 20 minutes at –78 °C, a solution of (*S*)-pulegone (18.3 g, 120 mmol, 1.0 equiv) in THF (50 mL) was added dropwise by cannula transfer over 30 minutes, resulting in a homogenous yellow solution that was stirred for an additional 20 minutes. A solution of *rac*-3-phenyl-2-(phenylsulfonyl)-1,2-oxaziridine (72.1 g, 276 mmol, 2.3 equiv) in THF (400 mL) was then added dropwise by cannula transfer over the course of 1 h, producing a deep orange-red solution that was stirred for an additional 15 minutes. The reaction was then quenched by the addition of sat. aq. NH_4Cl solution (250 mL) and the cold bath replaced with a water bath at ambient temperature. Once the temperature of the mixture had reached 23 °C, the biphasic mixture was then stirred rapidly for 1 h to allow for hydrolysis of the imine byproduct (*N*-benzylidenebenzenesulfonamide). The mixture was subsequently poured into a separatory funnel, diluted with EtOAc (500 mL), and washed with sat. aq. NH_4Cl (3 x 250 mL). The combined aqueous washings were then extracted with EtOAc (2 x 300 mL), and the combined organic layers washed with brine (500 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting thick slurry was then redissolved in EtOAc (100 mL) and treated with hexanes (400 mL), resulting in the precipitation of benzenesulfonamide, and the solids removed by filtration over Celite, rinsing with 4:1 hexanes/EtOAc (200 mL) to fully elute off the products. Concentration *in vacuo* affords an orange oil. Repeated purification by silica gel

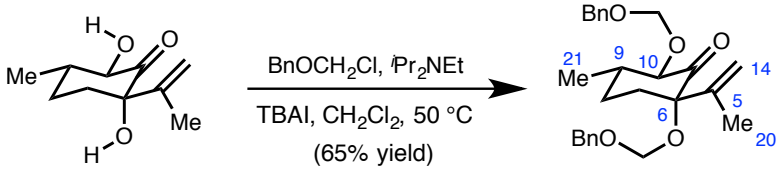
chromatography (500 g wet silica, 20 to 30 to 40% EtOAc in hexanes) affords a thick, slightly yellow oil that was determined to be 97% pure by ^{1}H NMR (9.19 g, 49.9 mmol, 42% yield).

Notes: Residual imine byproduct, *N*-benzylidenebenzenesulfonamide, has a slightly higher R_f than the product that can be challenging to remove by chromatography. In cases where the imine is not fully hydrolyzed, the product can be redissolved in EtOAc (200 mL) and stirred with sat. aq. NH_4Cl (200 mL) for 12 h. The resulting benzaldehyde and benzenesulfonamide products are then readily removed by silica gel chromatography.

A ^{1}H NMR spectrum is included of the material obtained through the above procedures (97% purity). A sample was further purified by silica gel chromatography for characterization purposes.

TLC (40% EtOAc/Hexanes), R_f: 0.43 (*p*-anisaldehyde); **^{1}H NMR ($CDCl_3$, 500 MHz):** δ 5.06 (m, 2H, C=C***H***$_2$), 4.34 (dd, *J* = 10.9, 4.7 Hz, 1H, ***H***C$_{10}$), 3.37 (d, *J* = 4.7 Hz, 1H, O***H***), 2.48 (s, 1H, O***H***), 2.03 – 1.82 (m, 3H, ***H***$_2$C$_7$, ***H***$_A$C$_8$), 1.81 (app. s, 3H, ***H***$_3$C$_{20}$), 1.68 – 1.52 (m, 2H, ***H***$_B$C$_8$, ***H***C$_9$), 1.19 (d, *J* = 6.3 Hz, C$_{21}$***H***$_3$); **^{13}C NMR ($CDCl_3$, 126 MHz):** δ 209.7 (**C$_{11}$**=O), 145.4 (**C$_5$**), 112.5 (**C$_{14}$**H$_2$), 80.1 (**C$_6$**), 77.8 (**C$_{10}$**H), 43.6 (**C$_9$**H), 37.1 (**C$_7$**H$_2$), 26.7 (**C$_8$**H$_2$), 19.7 (**C$_{20}$**H$_3$), 19.0 (**C$_{21}$**H$_3$); **FTIR (NaCl, thin film):** 3421, 2955, 2929, 1720, 1456, 1376 cm^{-1}; **LRMS:** calc'd for $[M+H]^+$: 185.1, found: 185.1; **$[\alpha]_D^{25}$:** –38 (*c* = 1.0 $CHCl_3$).

Preparation of Ketone 13:



12 **13**

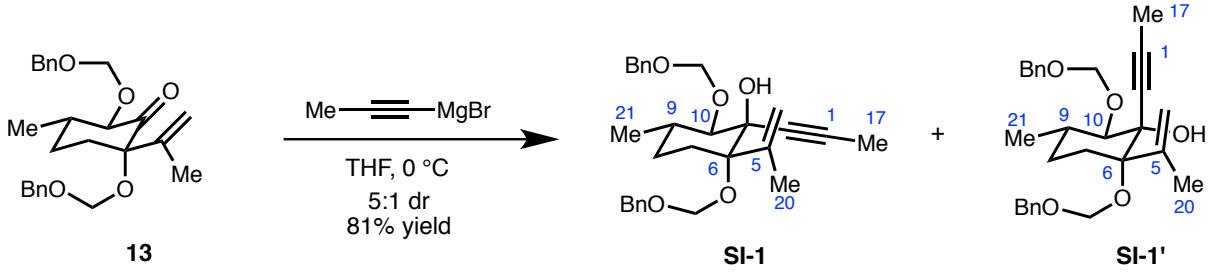
To a 500-mL, flame-dried flask was added diol **12** (9.14 g, 49.6 mmol, 1.0 equiv), tetrabutylammonium iodide (36.6 g, 99.2 mmol, 2.0 equiv), and anhydrous CH_2Cl_2 (200 mL). The solution was cooled to 0 °C in an ice/water bath and ^{i}Pr$_2$NEt (69 mL, 400 mmol, 8.0 equiv) was added rapidly via syringe. After 10 minutes, chloromethyl benzyl ether (34.4 mL, 248 mmol, 5.0 equiv) was added dropwise via syringe. The cold bath was subsequently removed and the solution was allowed to warm to 20 °C over 45 minutes. The flask was equipped with an oven-dried reflux condenser and then submerged into a preheated oil bath at 55 °C (internal temp. 50 °C), resulting in gentle reflux of the pale yellow solution. As the reaction proceeds, the color of the solution changes to a deep red. After 40 h, the solution was cooled to ambient temperature, poured into a 1-liter separatory funnel, diluted with additional CH_2Cl_2 (250 mL), and washed sequentially with sat. aq. $NaHCO_3$ (250 mL) and sat. aq. NH_4Cl (3 x 200 mL). The combined aqueous washings were then extracted with CH_2Cl_2 (2 x 100 mL), then the

combined organic layers were washed with 0.2 N NaOH (300 mL) and brine (300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a thick red slurry. EtOAc (100 mL) was added and the suspension vigorously agitated to ensure suspension of the solids. The suspension was then treated with hexanes (400 mL) resulting in the additional precipitation of ammonium salts, and the solids removed via filtration over Celite, rinsing with hexanes/EtOAc (4:1, 200 mL). Concentration *in vacuo* resulted in isolation of a homogeneous red oil. Purification by silica gel chromatography (7 to 9 to 12% EtOAc in hexanes) afforded ketone **13** as a thick, colorless oil (13.6 g, 32.1 mmol, 65% yield).

Notes: A similar yield was obtained albeit at longer reaction times in the absence of Bu_4NI.

TLC (10% EtOAc/Hexanes), R_f: 0.23 (UV, *p*-anisaldehyde). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38 – 7.26 (m, 10H, **H**-Ar), 5.20 (app. p, *J* = 1.4 Hz, 1H, $\boldsymbol{H_A}C_{14}$), 5.05 (app. t, *J* = 1.0 Hz, 1H, $\boldsymbol{H_B}C_{14}$), 4.84 (d, *J* = 7.1 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.80 (d, *J* = 11.9 Hz, 1H, PhC$\boldsymbol{H}_2$O), 4.78 (d, *J* = 7.1 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.78 (d, *J* = 7.1 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.74 (d, *J* = 11.7 Hz, 1H, PhC$\boldsymbol{H}_2$O), 4.72 (d, *J* = 7.1 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.66 (d, *J* = 11.7 Hz, 1H, PhC$\boldsymbol{H}_2$O), 4.65 (d, *J* = 10.9 Hz, 1H, $\boldsymbol{H}C_{10}$), 4.64 (d, *J* = 11.9 Hz, 1H, PhC$\boldsymbol{H}_2$O), 2.29 (dt, *J* = 14.4, 2.9 Hz, 1H, $\boldsymbol{H}_A C_7$), 1.96 – 1.77 (m, 3H, $\boldsymbol{H_A}C_8$, $\boldsymbol{H_B}C_7$, $\boldsymbol{H}C_9$), 1.74 – 1.67 (m, 1H, $\boldsymbol{H_B}C_8$), 1.71 (app. q, *J* = 0.7 Hz, 3H, $\boldsymbol{H_3}C_{20}$), 1.20 (d, *J* = 6.1 Hz, 3H, $\boldsymbol{H_3}C_{21}$). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 206.3 ($\mathbf{C_{11}}$=O), 142.8 ($\mathbf{C_5}$), 137.8 ($\mathbf{C_{Ar\text{-}\textit{ipso}}}$), 137.5 ($\mathbf{C_{Ar\text{-}\textit{ipso}}}$), 128.5 ($\mathbf{C_{Ar}}$H), 128.4 ($\mathbf{C_{Ar}}$H), 127.9 ($\mathbf{C_{Ar}}$H), 127.8 ($\mathbf{C_{Ar}}$H), 127.8 ($\mathbf{C_{Ar}}$H), 127.6 ($\mathbf{C_{Ar}}$H), 116.4 ($\mathbf{C_{14}}H_2$), 94.3 (BnO**C**$H_2$O), 90.4 (BnO**C**$H_2$O), 87.8 ($\mathbf{C_6}$), 83.0 ($\mathbf{C_{10}}$H), 71.1 (Ph**C**$H_2$O), 69.9 (Ph**C**$H_2$O), 41.8 ($\mathbf{C_9}$H), 34.2 ($\mathbf{C_7}H_2$), 27.6 ($\mathbf{C_8}H_2$), 19.7 ($\mathbf{C_{20}}H_3$), 19.5 ($\mathbf{C_{21}}H_3$). **FTIR (NaCl, thin film):** 2890, 1734, 1454, 1379, 1157, 1057, 1015 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 447.2142, found: 447.2126. **$[\alpha]_D^{25}$:** +58 (*c* = 1.0, $CHCl_3$).

Preparation of Enyne SI-1:



To a 1-liter, flame-dried round-bottomed flask was charged ketone **13** (13.3 g, 31.3 mmol, 1.0 equiv) and THF (310 mL). The solution was placed in an ice/water bath at 0 °C and stirred for 25 minutes for adequate cooling, then a solution of propynylmagnesium bromide (0.5 M solution, 125 mL, 62.5 mmol, 2.0 equiv) was added dropwise by cannula transfer over 45 min. The reaction was stirred for an additional 30 min and then carefully quenched by the addition of sat. aq. NH_4Cl (300 mL). The mixture was diluted with Et_2O (300 mL) and washed with sat. aq. NH_4Cl (2 x 100 mL), then the combined aqueous layers extracted with Et_2O (200 mL). The

combined organic layers were then washed with brine (300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a thick, light yellow oil. ^{1}H NMR analysis of the crude product indicated that the reaction occurs with complete consumption of starting material in a 5:1 diastereomeric ratio. Purification by silica gel chromatography (15 to 20 EtOAc in hexanes) afforded enyne **SI-1** as a viscous oil that slowly solidifies into colorless, semicrystalline needles (11.8 g, 25.4 mmol, 81% yield) in addition to minor diastereomer **SI-1'** (1.75 g, 3.76 mmol, 12% yield).

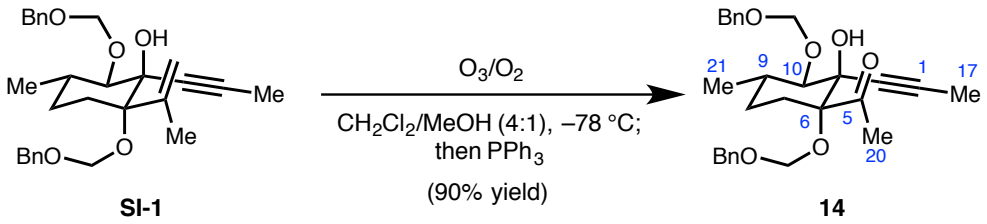
Major Diastereomer (SI-1):

TLC (20% EtOAc/Hexanes), R_f: 0.38 (*p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.33 (m, 8H, **H-**Ar), 7.32 – 7.27 (m, 2H, **H-**Ar), 5.24 (p, *J* = 1.5 Hz, 1H, $\boldsymbol{H_A}C_{14}$), 5.20 (d, *J* = 6.9 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 5.20 (dd, *J* = 1.8, 0.8 Hz, 1H, $\boldsymbol{H_B}C_{14}$), 4.96 (d, *J* = 6.8 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.89 (d, *J* = 12.0 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.82 (d, *J* = 11.8 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.77 (d, *J* = 6.8 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.74 (d, *J* = 6.8 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.63 (d, *J* = 12.0 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.58 (d, *J* = 11.8 Hz, 1H, PhC$\boldsymbol{H_2}$O), 3.64 (d, *J* = 10.6 Hz, 1H, $\boldsymbol{H}C_{10}$), 2.72 (s, 1H, O***H***), 2.17 – 2.08 (m, 1H, $\boldsymbol{H_A}C_7$), 1.96 – 1.92 (m, 1H, $\boldsymbol{H}C_9$), 1.81 (s, 3H, $\boldsymbol{H_3}C_{17}$), 1.74 (dt, *J* = 14.4, 3.1 Hz, 1H, $\boldsymbol{H_B}C_7$), 1.55 – 1.48 (m, 2H, $\boldsymbol{H_2}C_8$), 1.09 (d, *J* = 6.5 Hz, 3H, $\boldsymbol{H_3}C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 144.7 (**C_5**), 138.0 (**$C_{Ar\text{-}ipso}$**), 137.9 (**$C_{Ar\text{-}ipso}$**), 128.4 (**C_{Ar}**H), 128.4 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.7 (**C_{Ar}**H), 127.6 (**C_{Ar}**H), 117.0 (**$C_{14}H_2$**), 96.7 (BnO***C***H_2O), 90.3 (BnO***C***H_2O), 86.4 (**C_{10}**H), 85.3 (**C_{12}**), 82.0 (**C**), 80.9 (**C**), 75.3 (**C_1**), 70.7 (Ph**C**H_2O), 70.5 (Ph**C**H_2O), 31.8 (**C_9**H), 27.6 (**C_8H_2**), 27.1 (**C_7H_2**), 22.0 (**$C_{20}H_3$**), 19.0 (**$C_{21}H_3$**), 3.8 (**$C_{17}H_3$**); **FTIR (NaCl, thin film):** 3401, 2952, 2927, 2240, 1497, 1453, 1379, 1022 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 487.2445, found: 487.2438; **$[\alpha]_D^{25}$:** +84 (*c* = 1.1, $CHCl_3$).

Minor Diastereomer (SI-1'):

TLC (20% EtOAc/Hexanes), R_f: 0.31 (*p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.31 (m, 8H, **H-**Ar), 7.31 – 7.26 (m, 2H, **H-**Ar), 5.24 (p, *J* = 1.4 Hz, 1H, $\boldsymbol{H_A}C_{14}$), 5.16 (dd, *J* = 1.6, 0.8 Hz, 1H, $\boldsymbol{H_B}C_{14}$), 5.10 (d, *J* = 7.0 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.86 (d, *J* = 7.0 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.85 (d, *J* = 12.0 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.81 (d, *J* = 11.8 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.81 (d, *J* = 7.2 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.77 (d, *J* = 7.2 Hz, 1H, BnOC$\boldsymbol{H_2}$O), 4.70 (d, *J* = 12.0 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.55 (d, *J* = 11.9 Hz, 1H, PhC$\boldsymbol{H_2}$O), 4.05 (s, 1H, O***H***), 3.58 (d, *J* = 10.5 Hz, 1H, $\boldsymbol{H}C_{10}$), 2.19 – 2.11 (m, 1H, $\boldsymbol{H_A}C_7$), 1.96 (q, *J* = 0.7 Hz, 3H, $\boldsymbol{H_3}C_{20}$), 1.95 – 1.87 (m, 2H, $\boldsymbol{H_B}C_7$, $\boldsymbol{H}C_9$), 1.87 (s, 3H, $\boldsymbol{H_3}C_{17}$), 1.59 – 1.54 (m, 2H, $\boldsymbol{H_2}C_8$), 1.06 (d, *J* = 6.5 Hz, 3H, $\boldsymbol{H_3}C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 144.5 (**C_5**), 137.8 (**$C_{Ar\text{-}ipso}$**), 137.5 (**$C_{Ar\text{-}ipso}$**), 128.4 (**C_{Ar}**H), 128.4 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.7 (**C_{Ar}**H), 127.7 (**C_{Ar}**H), 117.5 (**$C_{14}H_2$**), 97.0 (BnO***C***H_2O), 91.1 (BnO***C***H_2O), 89.2 (**C_{10}**H), 86.4 (**C_{12}**), 83.2 (**C_6**), 78.3 (**C_{11}**), 77.5 (**C_1**), 71.1 (Ph**C**H_2O), 70.2 (Ph**C**H_2O), 35.3 (**C_9**H), 29.9 (**C_7H_2**), 27.9 (**C_8H_2**), 22.4 (**$C_{20}H_3$**), 18.6 (**$C_{21}H_3$**), 3.9 (**$C_{17}H_3$**); **FTIR (NaCl, thin film):** 2952, 2927, 2240, 1454, 1380, 1023 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 487.2445, found: 487.2456; **$[\alpha]_D^{25}$:** +61 (*c* = 0.90, $CHCl_3$).

Preparation of Methyl Ketone 14:



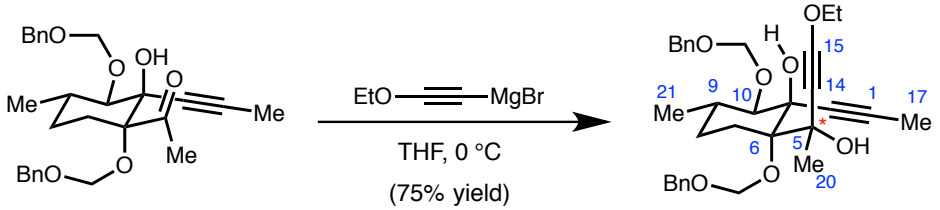
To a 1-liter, round-bottomed flask was charged enyne **SI-1** (11.7 g, 25.2 mmol, 1.0 equiv), followed by CH_2Cl_2 (400 mL) and MeOH (100 mL). The solution was purged with O_2 by means of a gas dispersion tube while cooling to –78 °C in a dry ice/acetone bath. A mixture of O_3/O_2 [Caution! Ozone is an extremely hazardous chemical! Proper training and use in a well-ventilated fume hood are necessary] was then passed through the solution and the reaction carefully monitored by TLC to track disappearance of the starting material. After 4.5 h, the solution slowly changed from a colorless solution to a very slight, pale blue color. O_2 (g) was sparged through the solution at an increased rate to purge out excess ozone, followed by N_2 (g) for 10 minutes. Triphenylphosphine (6.61 g, 25.2 mmol, 1.0 equiv) was then added in a single portion to the mixture at –78 °C. The mixture was allowed to warm to 23 °C with efficient stirring under N_2 over the course of 1 h, then concentrated *in vacuo* to afford a thick oil. Purification by silica gel chromatography (20 to 30 to 35% EtOAc in hexanes, sample loaded in 10 mL of CH_2Cl_2) afforded methyl ketone **14** as a white amorphous solid (10.6 g, 22.7 mmol, 90% yield).

Notes: The product readily precipitates from hexanes/EtOAc solutions. To ensure quantitative transfer and prevent streaking, complete dissolution in CH_2Cl_2 (10 mL) is necessary for loading the silica gel column. Furthermore, although triphenylphosphine oxide could be removed by careful trituration from the reaction mixture, purification in this manner was undesirable due to the risk of product loss.

TLC (40% EtOAc/Hexanes), R_f: 0.50 (UV, *p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38 – 7.33 (m, 8H, **H**-Ar), 7.33 – 7.27 (m, 2H, **H**-Ar), 5.17 (d, *J* = 7.0 Hz, 1H, BnOC***H***$_2$O), 4.93 (d, *J* = 7.0 Hz, 1H, BnOC***H***$_2$O), 4.89 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.88 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.77 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.76 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.64 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.62 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 3.57 (d, *J* = 10.6 Hz, 1H, ***H***C$_{10}$), 3.08 (s, 1H, O***H***), 2.40 (s, 3H, ***H***$_3$C$_{20}$), 2.26 (ddd, *J* = 15.0, 13.8, 4.3 Hz, 1H, ***H***$_A$C$_7$), 1.96 – 1.85 (m, 1H, ***H***C$_9$), 1.83 (s, 3H, ***H***$_3$C$_{17}$), 1.77 (dt, *J* = 15.0, 3.2 Hz, 1H, ***H***$_B$C$_7$), 1.57 (dtd, *J* = 13.6, 4.3, 2.9 Hz, 1H, ***H***$_A$C$_8$), 1.36 (tdd, *J* = 13.7, 12.5, 3.5 Hz, 1H, ***H***$_B$C$_8$), 1.06 (d, *J* = 6.5 Hz, 3H, ***H***$_3$C$_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 209.4 (**C**$_5$=O), 137.8 (**C**$_{Ar\text{-}ipso}$), 137.4 (**C**$_{Ar\text{-}ipso}$), 128.4 (**C**$_{Ar}$H), 128.4 (**C**$_{Ar}$H), 127.8 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 96.5 (BnO**C**H$_2$O), 91.1 (BnO**C**H$_2$O), 88.1 (**C**), 85.7 (**C**$_{10}$H), 82.9 (**C**), 80.1 (**C**), 72.5 (**C**$_1$), 70.8 (Ph**C**H$_2$O), 70.6 (Ph**C**H$_2$O), 31.5 (**C**$_9$H), 28.1 (**C**$_{20}$H$_3$), 27.1 (**C**H$_2$), 24.6 (**C**H$_2$), 18.7

(**$C_{21}H_3$**), 3.8 (**$C_{17}H_3$**); **FTIR (NaCl, thin film):** 3402, 2951, 2927, 2235, 1713, 1453, 1020 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 489.2248, found: 489.2246; **$[\alpha]_D^{25}$:** +97 (*c* = 1.0, $CHCl_3$).

Preparation of Diyne SI-2:



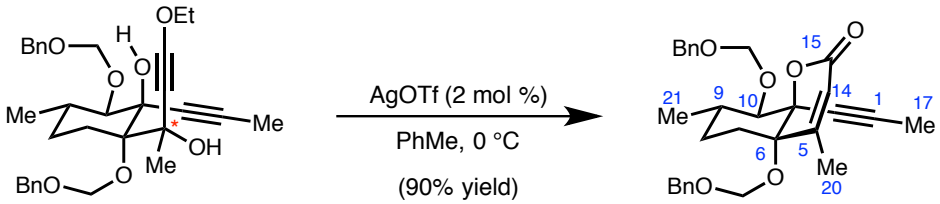
To a 1-liter, oven-dried, round-bottomed flask was added ethylmagnesium bromide (1.0 M in THF, 114 mL, 114 mmol, 5.0 equiv) and THF (114 mL). The solution was cooled to 0 °C in an ice/water bath and ethoxyacetylene (50 wt % in hexanes, 23.8 mL, 6.0 equiv) added dropwise by syringe. The resulting brown solution was stirred at 0 °C for 15 minutes, then removed from the ice bath and allowed to warm to room temperature over 30 minutes. The dark brown solution was then recooled to 0 °C in an ice/water bath, and a solution of ketone **14** (10.6 g, 22.7 mmol, 1.0 equiv) in THF (100 mL) was added via cannula transfer over 30 minutes. Upon completion of the addition, the dark brown solution was stirred for an additional 20 minutes, then quenched by the addition of sat. aq. NH_4Cl (300 mL), diluted with EtOAc (300 mL), and washed with additional sat. aq. NH_4Cl (2 x 200 mL). The combined organic layers were extracted with additional EtOAc (250 mL), and the combined organic layers were washed with brine (300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. ^{1}H NMR analysis of the mixture reveals approximately 85% conversion. Purification of the resulting brown oil, twice, by silica gel chromatography (30 to 35% EtOAc in hexanes) afforded diyne **SI-2** (9.13 g, 17.0 mmol, 75% yield) as a light yellow oil that very slowly solidified to a slightly yellow amorphous solid under high vacuum, along with a mixture of recovered starting material and product (2.2 g) that could be resubjected for further material throughput.

Notes: Incomplete conversion is typically observed. Removal of starting material can be challenging on larger scale. 1,2-Addition into the methyl ketone appears to occur with complete diastereoselectivity, although the absolute configuration at the newly formed (albeit inconsequential given the subsequent step) stereocenter could not be unambiguously assigned via 2D-NMR spectroscopic techniques.

TLC (40% EtOAc/Hexanes), R_f: 0.40 (UV, *p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.27 (m, 10H, **H**-Ar), 5.13 (d, *J* = 6.9 Hz, 1H, BnOC***H***$_2$O), 5.11 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.99 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.95 (d, *J* = 6.9 Hz, 1H, BnOC***H***$_2$O), 4.88 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.81 (d, *J* = 11.7 Hz, 1H,

PhC***H***$_2$O), 4.74 (d, *J* = 11.6 Hz, 1H, PhC***H***$_2$O), 4.60 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.50 (s, 1H, O***H***), 4.03 (q, *J* = 7.1 Hz, 2H, OC***H***$_2$CH$_3$), 3.70 (s, 1H, O***H***), 3.56 (d, *J* = 10.6 Hz, 1H, ***H***C$_{10}$), 2.27 (dt, *J* = 15.6, 3.4 Hz, 1H, ***H***$_A$C$_7$), 2.12 (ddd, *J* = 15.4, 13.8, 4.3 Hz, 1H, ***H***$_B$C$_7$), 1.88 – 1.81 (m, 1H, ***H***C$_9$), 1.84 (s, 3H, ***H***$_3$C$_{17}$), 1.80 (s, 3H, ***H***$_3$C$_{20}$), 1.55 (dq, *J* = 11.8, 4.1 Hz, 1H, ***H***$_A$C$_8$), 1.35 – 1.25 (m, 1H, ***H***$_B$C$_8$), 1.31 (t, *J* = 7.1 Hz, 3H, OCH$_2$C***H***$_3$), 1.03 (d, *J* = 6.5 Hz, 3H, ***H***$_3$C$_{21}$); **^{13}C NMR (126 MHz, CDCl$_3$):** 137.9 (**C**$_{Ar\text{-}ipso}$), 137.7 (**C**$_{Ar\text{-}ipso}$), 128.4 (**C**$_{Ar}$H), 128.3 (**C**$_{Ar}$H), 128.0 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 127.6 (**C**$_{Ar}$H), 127.6 (**C**$_{Ar}$H), 97.0 (BnO**C**H$_2$O), 94.4 (**C**$_{15}$), 89.2 (BnO**C**H$_2$O), 87.5 (**C**$_{10}$H), 84.1 (**C**$_6$), 83.3 (**C**$_{12}$), 81.7 (**C**$_{11}$), 75.4 (**C**$_1$), 74.8 (**C**$_5$), 74.2 (O**C**H$_2$CH$_3$), 70.6 (Ph**C**H$_2$O), 70.2 (Ph**C**H$_2$O), 42.5 (**C**$_{14}$), 31.6 (**C**$_9$H), 28.9 (**C**$_{20}$H$_3$), 27.0 (**C**$_8$H$_2$), 22.8 (**C**$_7$H$_2$), 18.7 (**C**$_{21}$H$_3$), 14.5 (OCH$_2$**C**H$_3$), 3.9 (**C**$_{17}$H$_3$); **FTIR (NaCl, thin film):** 3402, 2983, 2929, 2262, 1457, 1022 cm^{-1}; **HRMS:** calc'd for [M+Na]$^+$: 559.2666, found: 559.2662; **[α]$_D^{25}$:** +11 (*c* = 1.1, CHCl$_3$).

Preparation of Lactone 15:



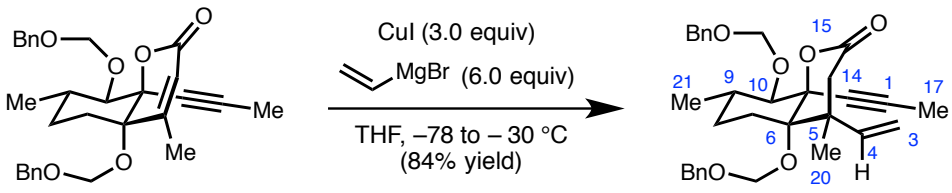
SI-2 **15**

To a 200 mL, round-bottomed flask was added diyne **SI-2** (8.97 g, 16.7 mmol, 1.0 equiv) and anhydrous PhMe (84 mL). The solution was stirred vigorously at 23 °C for 15 minutes to ensure complete dissolution of the starting material, then the flask was submerged in an ice/water bath and allowed to cool over 15 minutes. AgOTf (85.6 mg, 0.334 mmol, 0.02 equiv) was weighed into a 1-dram vial in a nitrogen-filled glovebox and then added directly to the solution against a positive pressure of Argon, and the resulting mixture stirred vigorously at 0 °C for 20 min. The entire cold solution was then directly and rapidly loaded onto a silica gel column pre-equilibrated with 20% EtOAc in hexanes, and the compound purified by silica gel chromatography (20 to 30 to 40% EtOAc in hexanes) to provide lactone **15** as a pale yellow oil (7.38 g, 15.0 mmol, 90% yield).

Notes: The reaction is challenging to monitor by TLC since the product and starting material have nearly identical R_f's. Since the reaction is purified directly by chromatography on scale, it is recommended that preparation of the silica gel column is performed prior to the addition of AgOTf so that the reaction can be immediately purified. Prolonged reaction times (>1 h) can result in the acid-catalyzed, hydrolytic cleavage of the benzyloxymethyl groups.

TLC (40% EtOAc/Hexanes), R_f: 0.40 (UV, *p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.27 (m, 10H, **H-**Ar), 5.85 (q, *J* = 1.5 Hz, 1H, ***H***C_{14}), 5.12 (d, *J* = 7.3 Hz, 1H, BnOC***H***$_2$O), 5.08 (d, *J* = 6.6 Hz, 1H, BnOC***H***$_2$O), 5.06 (d, *J* = 6.6 Hz, 1H, BnOC***H***$_2$O), 4.91 (d, *J* = 7.3 Hz, 1H, BnOC***H***$_2$O), 4.84 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.76 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.65 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.59 (d, *J* = 12.0 Hz, 1H, PhC***H***$_2$O), 3.70 (d, *J* = 10.1 Hz, 1H, ***H***C_{10}), 2.07 (m, ***H***C_9), 2.01 (d, *J* = 1.5 Hz, 3H, ***H***$_3C_{20}$), 2.02 – 1.96 (m, 1H ***H***$_A$$C_7$), 1.77 (s, 3H, ***H***$_3C_{17}$), 1.71 – 1.47 (m, 3H, ***H***$_B$$C_7$, ***H***$_2$$C_8$), 1.12 (d, *J* = 6.6 Hz, 3H, ***H***$_3C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 162.5 (**C_{15}**=O), 160.9 (br s, **C_5**) 138.1 (**$C_{Ar\text{-}ipso}$**), 137.4 (**$C_{Ar\text{-}ipso}$**), 128.5 (**C_{Ar}**H), 128.4 (**C_{Ar}**H), 127.9 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.7 (**C_{Ar}**H), 127.5 (**C_{Ar}**H), 118.6 (**C_{14}**H), 96.8 (BnO**C**H_2O), 91.5 (BnO**C**H_2O), 85.2 (**C_{12}**), 83.8 (**C_{10}**H), 81.4 (**C_{11}**), 80.6 (**C_6**), 76.6 (**C_1**), 70.6 (Ph**C**H_2O), 70.5 (Ph**C**H_2O), 32.4 (**C_9**H), 32.3 (**C-**$_7H_2$), 27.2 (**C_8H_2**), 18.5 (**$C_{21}H_3$**), 17.9 (**$C_{20}H_3$**), 3.8 (**$C_{17}H_3$**); **FTIR (NaCl, thin film):** 2954, 2927, 2245, 1727, 1247, 1167, 1025 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 513.2248, found: 513.2236;**$[\alpha]_D^{25}$:** +34 (*c* = 0.50, $CHCl_3$).

Preparation of Enyne 16:



15 **16**

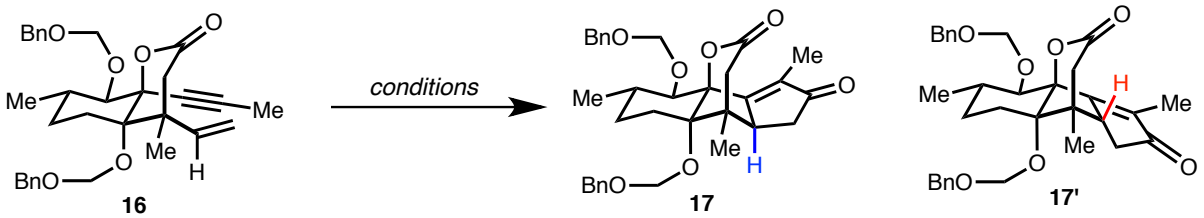
To a flame-dried, 1-liter, round-bottomed flask was charged CuI (8.46 g, 44.4 mmol, 3.0 equiv) and THF (400 mL). The suspension was cooled to –78 °C in a dry ice/acetone bath and vinylmagnesium bromide (1 M in THF, 89 mL, 89 mmol, 6.0 equiv) was added dropwise by syringe. Upon completion of the addition, the mixture was stirred for an additional 15 minutes, then a solution of lactone **15** (7.26 g, 14.8 mmol, 1.0 equiv) in THF (100 mL) was added dropwise by cannula transfer. The resulting mixture was maintained at –78 °C for 15 minutes, then the mixture was gradually warmed to –30 °C over 30 minutes, and stirring maintained at –30 °C for 30 minutes. The reaction was then carefully quenched by the addition of sat. aq. NH_4Cl (300 mL) and warmed to ambient temperature. The reaction was then diluted with Et_2O (400 mL) and the biphasic mixture filtered through a short pad of Celite to remove precipitated red copper solids. The resulting mixture was then poured into a separatory funnel and washed with sat. aq. NH_4Cl (2 x 200 mL), and the combined aqueous layers extracted with additional Et_2O (2 x 200 mL). The combined organic layers were then washed with brine (400 mL), dried over anhydrous $MgSO_4$ and filtered over a short pad of silica gel to remove additional red copper-based precipitates, and the resultant solution concentrated *in vacuo* to afford a colorless oil. Purification of the crude residue by silica gel chromatography (20 to 30% EtOAc in hexanes) afforded enyne **16** as a slightly yellow oil (6.45 g, 12.4 mmol, 84% yield).

TLC (40% EtOAc/Hexanes), R_f: 0.53 (UV, *p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.27 (m, 10H, **H-**Ar), 6.81 (dd, *J* = 17.7, 10.8 Hz, 1H, ***H***C_4), 5.16 (d, *J* = 7.2 Hz, 1H, BnOC***H***$_2$O), 5.09 (dd, *J* = 4.0, 0.8 Hz, 1H), 5.08 (dd, *J* = 17.7 Hz, 0.8 Hz, 1H, ***H***$_A$$C_3$), 5.08 (dd, *J* =10.8, 0.8 Hz, 1H, ***H***$_B$$C_3$), 4.99 (d, *J* = 7.2 Hz, 1H, BnOC***H***$_2$O), 4.89 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.82 (d, *J* = 7.1 Hz, 1H, BnOC***H***$_2$O), 4.77 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.71 (d, *J* = 7.1 Hz, 1H, BnOC***H***$_2$O), 4.60 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.51 (d, *J* = 11.8 Hz, 1H, PhC***H***$_2$O), 3.66 (d, *J* = 10.7 Hz, 1H, ***H***C_{10}), 3.49 (d, *J* = 15.6 Hz, 1H, ***H***$_A$$C_{14}$), 2.13 (d, *J* = 15.6 Hz, 1H, ***H***$_B$$C_{14}$), 2.07 – 1.94 (m, 2H, ***H***C_9, ***H***$_A$$C_7$), 1.91 (s, 3H, ***H***$_3$$C_{17}$), 1.56 – 1.46 (m, 3H, ***H***$_b$$C_7$, ***H***$_2$$C_8$), 1.26 (s, 3H, ***H***$_3$$C_{20}$), 1.08 (d, *J* = 6.5 Hz, 3H, ***H***$_3$$C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 170.6 (**C_{15}**=O), 144.9 (**C_4**H), 138.0 (**$C_{Ar\text{-}ipso}$**), 137.4 (**$C_{Ar\text{-}ipso}$**), 128.4 (**C_{Ar}**H), 128.4 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 127.6 (**C_{Ar}**H), 111.6 (**C_3**H_2), 97.6 (BnO**C**H_2O), 90.5 (BnO**C**H_2O), 86.0 (**C_{10}**H), 85.8 (**C_{12}**), 83.3 (**C_6**), 81.3 (**C_{11}**), 77.2 (**C_1**), 71.0 (Ph**C**H_2O), 70.5 (Ph**C**H_2O), 44.2 (**C_{14}**H_2), 43.7 (**C_5**), 31.0 (**C_9**H), 27.4 (**C_8**H_2), 26.7 (**C_7**H_2), 24.1 (**C_{20}**H_3), 18.8 (**C_{21}**H_3), 3.9 (**C_{17}**H_3); **FTIR (NaCl, thin film):** 2954, 2928, 2871, 1752, 1454, 1237, 1026 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 541.2561, found: 541.2539; **$[\alpha]_D^{25}$:** +76 (*c* = 1.0, $CHCl_3$).

Evaluation of Pauson–Khand Reaction Conditions

Evaluation of Pauson–Khand reaction conditions were performed with enyne **16** on 0.20 mmol scale (104 mg). A variety of conditions employing cobalt (*38, 39*), molybdenum (*40, 47*), and rhodium complexes (*41*) were surveyed following literature precedent. Isolated yields are indicated for the combined mixture of diastereomers, and were obtained after purification by silica gel chromatography. In entries **1** and **2** (cobalt-mediated), the diastereomeric ratios were obtained by ^{1}H NMR after silica gel purification due to the presence of paramagnetic Co-species, whereas in the remainder of the entries, diastereomeric ratios were obtained from ^{1}H NMR analysis of the crude reaction mixtures.

Table S1. Evaluation of Pauson–Khand Reaction Conditions



Conditions	dr	Yield **17+17'**
1. $Co_2(CO)_8$ (1.2 equiv), THF, 12 h; then DMSO, 65 °C	2.2 :1	46%
2. $Co_2(CO)_8$ (1.2 equiv), CH_2Cl_2, 9 h; then NMO, 23 °C	4.5 :1	78%
3. $Mo(CO)_6$ (1.2 equiv), DMSO, PhMe, 110 °C	--	*trace*
4. $Mo(CO)_3(DMF)_3$ (1.1 equiv), CH_2Cl_2, 23 °C	>20:1	67%
5. $[RhCl(CO)_2]_2$ (1 mol %), CO (1 atm), *m*-xylene, 110 °C	>20:1	85%

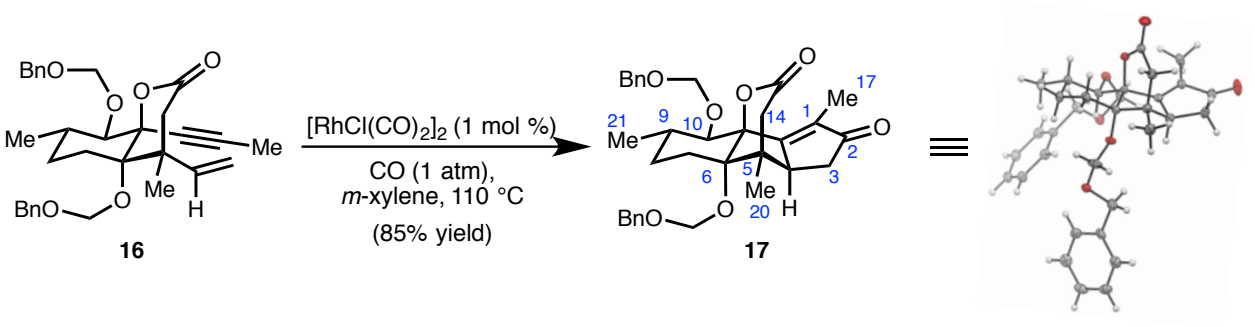
A sample of the minor diastereomer (**17'**) was obtained via purification of entry **2** for characterization purposes.

Minor Diastereomer (17'):

TLC (70% EtOAc/Hexanes), R_f: 0.52 (UV, *p*-anisaldehyde). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38 – 7.26 (m, 8H, **H**-Ar), 7.25 – 7.20 (m, 2H, **H**-Ar), 5.24 (d, *J* = 5.9 Hz, 1H, BnOC***H***$_2$O), 5.06 (d, *J* = 6.0 Hz, 1H, BnOC***H***$_2$O), 4.83 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.77 (d, *J* = 11.8 Hz, 1H, PhC***H***$_2$O), 4.70 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.64 (d, *J* = 11.8 Hz, 1H, PhC***H***$_2$O), 4.47 (d, *J* = 11.5 Hz, 1H, PhC***H***$_2$O), 4.41 (d, *J* = 11.5 Hz, 1H, PhC***H***$_2$O), 4.02 (d, *J* = 11.0 Hz, 1H, ***H***C$_{10}$), 2.83 (dddd, *J* = 6.7, 5.1, 2.4, 1.0 Hz, 1H, ***H***C$_4$), 2.69 (dd, *J* = 18.6, 1.0 Hz, 1H, ***H***$_A$C$_{14}$), 2.65 (dd, *J* = 16.4, 6.7 Hz, 1H, ***H***$_A$C$_3$), 2.63 (d, *J* = 18.7 Hz, 1H, ***H***$_B$C$_{14}$), 2.35 – 2.23 (m, 1H, ***H***C$_9$), 2.33 (dd, *J* = 16.4, 5.1 Hz, 1H, ***H***$_B$C$_3$), 2.08 (d, *J* = 2.4 Hz, 3H, ***H***$_3$C$_{17}$), 2.02 – 1.91 (m, 1H, ***H***$_A$C$_7$), 1.79 – 1.64 (m, 2H, ***H***$_B$C$_7$, ***H***$_A$C$_8$), 1.63 – 1.52 (m, 1H, ***H***$_B$C$_8$), 1.19 (d, *J* = 6.5 Hz, 3H, ***H***$_3$C$_{21}$), 1.11 (s, 3H, ***H***$_3$C$_{20}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 208.8 (**C**$_2$=O), 172.3 (**C**$_{15}$=O), 168.0 (**C**$_{12}$), 137.9 (**C**$_{Ar\text{-}ipso}$), 136.4 (**C**$_{Ar\text{-}ipso}$), 135.9 (**C**$_1$), 128.6 (**C**$_{Ar}$H),

128.3 (**C**$_{Ar}$H), 128.2 (**C**$_{Ar}$H), 128.1 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 127.6 (**C**$_{Ar}$H), 91.8 (BnO**C**H$_2$O), 90.6 (**C**), 89.3 (BnO**C**H$_2$O), 89.0 (**C**), 78.2 (**C**$_{10}$H), 70.5 (Ph**C**H$_2$O), 70.5 (Ph**C**H$_2$O), 51.1 (**C**$_4$H), 48.0 (**C**$_{14}$H$_2$), 42.8 (**C**$_5$), 41.8 (**C**$_3$H$_2$), 30.0 (**C**$_9$H), 28.7 (**C**$_8$H$_2$), 21.9 (**C**$_7$H$_2$), 18.5 (**C**$_{21}$H$_3$), 16.7 (**C**$_{20}$H$_3$), 9.4 (**C**$_{17}$H$_3$); **FTIR (NaCl, thin film):** 2929, 1748, 1707, 1453, 1234, 1025, 1008 cm^{-1}; **HRMS:** calc'd for [M+Na]$^+$: 569.2510, found: 569.2510; **[α]$_D^{25}$:** –140 (*c* = 0.20, $CHCl_3$).

Preparation of Enone 17:

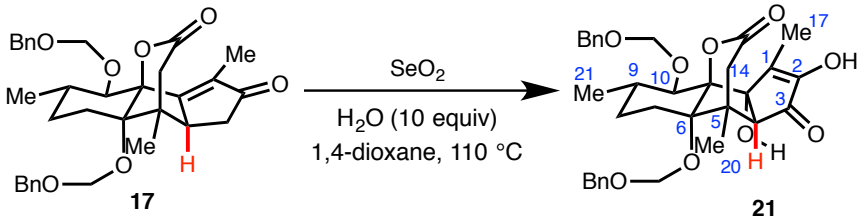


To a 500-mL, round-bottomed flask containing enyne **16** (6.33 g, 12.2 mmol, 1.0 equiv) was added $[RhCl(CO)_2]_2$ (47.4 mg, 0.122 mmol, 0.01 equiv) in a nitrogen-filled glovebox. The flask was capped with a rubber septum, removed from the glovebox, and anhydrous *m*-xylene (120 mL) was added via syringe. The flask was equipped with an outlet needle and dry argon was bubbled through the solution for five minutes, followed by carbon monoxide for five minutes [Caution! Carbon monoxide is highly toxic. This reaction must be run in an efficient fume hood!]. The vent needle was removed and a CO atmosphere was maintained in the flask by means of a double-walled balloon, then the flask was submerged into a preheated oil bath at 110 °C. After heating for 2 h, the reaction was cooled to ambient temperature, sparged with N_2 to thoroughly expel excess CO gas, then the solvent was removed *in vacuo* (an efficient rotovap was utilized with a bath temperature at 50 °C) to afford a thick, dark orange oil. ^{1}H NMR analysis of the unpurified reaction mixture could not identify traces of the undesired diastereomer, **17'**. Purification by silica gel chromatography (30 to 50 to 70 % EtOAc in hexanes) afforded enone **17** as a crunchy foam. Dissolution of the resulting foam in Et_2O followed by reevaporation (2 x 100 mL) affords enone **17** as an off-white powder (5.66 g, 10.4 mmol, 85% yield). Single crystals suitable for X-ray diffraction were obtained from this material by crystallization from Et_2O (See p. **S32** for data).

TLC (70% EtOAc/Hexanes), R$_f$: 0.60 (UV, *p*-anisaldehyde); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.37 – 7.27 (m, 10H, **H**-Ar), 5.02 (d, *J* = 6.9 Hz, 1H, BnOC***H***$_2$O), 4.98 (d, *J* = 6.9 Hz, 1H, BnOC***H***$_2$O), 4.85 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.85 (d, *J* = 6.7 Hz, 1H, BnOC***H***$_2$O), 4.78 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.70 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.63 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.59 (d, *J* = 11.9 Hz, 1H, PhC***H***$_2$O), 4.13 (d, *J* = 10.4 Hz, 1H,

HC_{10}), 3.63 (dddd, *J* = 6.6, 3.3, 2.7, 1.3 Hz, 1H, ***H***C_4), 2.48 (dd, *J* = 18.4, 6.6 Hz, 1H, ***H***$_A C_3$), 2.32 (dd, *J* = 19.5, 1.3 Hz, 1H, ***H***$_B C_{14}$), 2.28 – 2.21 (m, 1H, ***H***C_9), 2.25 (d, *J* = 19.6 Hz, 1H, ***H***$_A C_{14}$), 2.06 (dd, *J* = 18.4, 3.3 Hz, 1H, ***H***$_B C_3$), 2.03 – 1.96 (m, 1H, ***H***$_A C_7$), 1.93 (d, *J* = 2.7 Hz, 3H, ***H***$_3 C_{17}$), 1.75 (dtd, *J* = 11.5, 4.3, 2.6 Hz, 1H, ***H***$_A C_8$), 1.71 – 1.57 (m, 2H, ***H***$_B C_7$, ***H***$_B C_7$), 1.16 (d, *J* = 6.6 Hz, 3H, ***H***$_3 C_{21}$), 1.14 (s, 3H, ***H***$_3 C_{20}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 209.2 (**C_2**=O), 174.1 (**C_{15}**=O), 168.8 (**C_{12}**), 140.9 (**C_1**), 137.6 (**$C_{Ar\text{-}ipso}$**), 137.0 (**$C_{Ar\text{-}ipso}$**), 128.5 (**C_{Ar}**H), 128.4 (**C_{Ar}**H), 128.0 (**C_{Ar}**H), 127.9 (**C_{Ar}**H), 127.7 (**C_{Ar}**H), 127.6 (**C_{Ar}**H), 95.5 (BnO**C**H_2O), 90.1 (BnO**C**H_2O), 89.3 (**C_6**), 87.1 (**C_{11}**), 79.2 (**C_{10}**H), 71.2 (Ph**C**H_2O), 70.7 (Ph**C**H_2O), 51.0 (**C_4**H), 45.4 (**C_5**), 37.3 (**$C_{14}H_2$**), 35.6 (**C_3H_2**), 32.1 (**C_9**H), 28.5 (**C_8H_2**), 20.6 (**C_7H_2**), 18.8 (**$C_{21}H_3$**), 18.2 (**$C_{20}H_3$**), 10.1 (**$C_{17}H_3$**); **FTIR (NaCl, thin film):** 2954, 2872, 1748, 1707, 1454, 1209, 1154, 1042, 1025 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 569.2510, found: 569.2523; **$[\alpha]_D^{25}$:** +180 (*c* = 1.0, $CHCl_3$).

Preparation of Diosphenol 21:



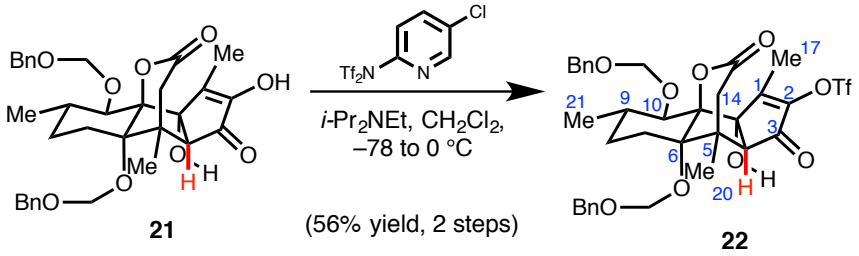
To a 2-dram vial was added enone **17** (109.0 mg, 0.200 mmol, 1.0 equiv), SeO_2 (222 mg, 20.0 mmol, 10 equiv), dioxane (4.0 mL), and H_2O (36 µL, 2.00 mmol, 10 equiv). The vial was sealed with a Teflon cap, then submerged in an oil bath preheated to 110 °C for 1 h. The vial was then cooled to ambient temperature, diluted with EtOAc (50 mL) and washed with sat. aq. $NaHCO_3$ (2 x 50 mL). The combined aqueous layers were then extracted with EtOAc (15 mL), the combined organics dried over anhydrous Na_2SO_4, and the solution filtered and concentrated *in vacuo* to afford a dark orange foam. Purification by silica gel chromatography (2% MeOH in CH_2Cl_2) affords an orange foam that was used in the subsequent reaction without additional purification.

Notes: Large amounts of Se-based byproducts (both selenium black and selenium red) are produced during the course of this reaction. Although material post-chromatography appears to be pure by ^{1}H NMR spectroscopy, integration of purified material against an internal standard indicates that a significant amount of selenium red (colloidal) is co-eluted during silica gel chromatography, and thus a two-step yield is obtained after triflation (see next step).

A sample of diosphenol **21** was futher purified by repeated chromatography to remove Se-based byproducts to afford an analytically pure sample for characterization purposes, affording **21** as a colorless foam.

TLC (70% EtOAc/Hexanes), R_f: 0.50 (UV, $KMnO_4$); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.27 (m, 10H, ***H***-Ar), 5.39 (s, 1H, ***H***OC_2), 5.09 (d, *J* = 5.4 Hz, 1H, BnOC***H***$_2$O), 5.01 (d, *J* = 6.8 Hz, 1H, BnOC***H***$_2$O), 4.97 (d, *J* = 6.8 Hz, 1H), 4.84 (d, *J* = 5.4 Hz, 1H, BnOC***H***$_2$O), 4.76 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.71 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.71 (d, *J* = 12.2 Hz, 1H, PhC***H***$_2$O), 4.64 (d, *J* = 12.2 Hz, 1H, PhC***H***$_2$O), 4.55 (s, 1H, O***H***), 3.99 (d, *J* = 10.5 Hz, 1H, ***H***C_{10}), 2.92 (s, 1H, ***H***C_4), 2.29 (dd, *J* = 19.9, 1.2 Hz, 1H, ***H***$_B$$C_{14}$), 2.24 (d, *J* = 19.9 Hz, 1H, ***H***$_A$$C_{14}$), 2.11 – 2.03 (m, 1H, ***H***C_9), 2.10 (s, 3H, ***H***$_3$$C_{17}$), 1.96 – 1.88 (m, 1H, ***H***$_A$$C_7$), 1.69 – 1.47 (m, 3H, ***H***$_B$$C_7$, ***H***$_2$$C_8$), 1.28 (s, 3H, ***H***$_3$$C_{20}$), 1.05 (d, *J* = 6.6 Hz, 3H, ***H***$_3$$C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 200.1 (**C_3**=O), 166.9 (**C_{15}**=O), 150.0 (**C_2**), 143.9 (**C_1**), 137.0 (**$C_{Ar\text{-}ipso}$**), 136.9 (**$C_{Ar\text{-}ipso}$**), 128.7 (**C_{Ar}**H), 128.6 (**C_{Ar}**H), 128.2 (**C_{Ar}**H), 128.1 (**C_{Ar}**H), 128.0 (**C_{Ar}**H), 127.7 (**C_{Ar}**H), 97.0 (BnO**C**H_2O), 91.4 (**C_6**), 90.6 (**C_{11}**), 89.8 (BnO**C**H_2O), 87.1 (**C_{12}**), 80.0 (**C_{10}**H), 71.1 (Ph**C**H_2O), 70.3 (Ph**C**H_2O), 64.4 (**C_4**H), 45.1 (**C_5**), 39.1 (**C_{14}**H_2), 33.3 (**C_9**H), 27.9 (**C_8**H_2), 21.3 (**C_7**H_2), 19.9 (**C_{20}**H_3), 18.5 (**C_{21}**H_3), 11.2 (**C_{17}**H_3); **FTIR (NaCl, thin film):** 3350, 2926, 1744, 1707, 1405, 1240, 1157, 1034 cm^{-1}; **HRMS:** calc'd for $[M+NH_4]^+$: 596.2871, found: 596.2854; **$[\alpha]_D^{25}$:** +79 (*c* = 0.55, $CHCl_3$).

Preparation of Triflate 22:

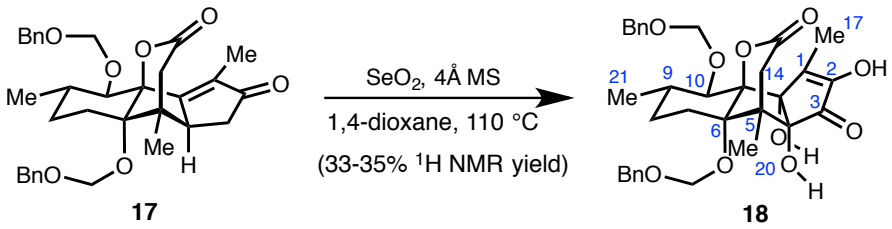


To a 25-mL, round-bottomed flask was added **21** (material directly isolated from the previous reaction) and anhydrous CH_2Cl_2 (4.0 mL). *i*-Pr_2NEt (0.18 ml) was added and then the solution was cooled to –78 °C in a dry ice/acetone bath. *N*-(5-chloro-2-pyridyl)bis(trifluoromethanesulfonimide) (Comins' reagent, 78.5 mg, 0.20 mmol, 1.0 equiv) was then added in a single portion and the solution stirred for 5 minutes, then the cold bath removed and replaced with an ice/water bath at 0 °C. After 1 h, the solution was directly loaded onto a silica gel column (30 to 40% EtOAc in hexanes) to afford triflate **22** as a colorless foam (79.4 mg, 0.111 mmol, 56% yield).

TLC (40% EtOAc/Hexanes), R_f: 0.40 (UV, $KMnO_4$); **^{1}H NMR ($CDCl_3$, 400 MHz):** δ 7.41 – 7.29 (m, 10H, ***H***-Ar), 5.33 (s, 1H, O***H***), 5.05 (d, *J* = 4.7 Hz, 1H, BnOC***H***$_2$O), 4.99 (d, *J* = 6.8 Hz, 1H BnOC***H***$_2$O), 4.95 (d, *J* = 6.9 Hz, 1H, BnOC***H***$_2$O), 4.79 (d, *J* = 4.8 Hz, 1H, BnOC***H***$_2$O), 4.77 (d, *J* = 11.8 Hz, 1H, PhC***H***$_2$O), 4.71 (d, *J* = 11.7 Hz, 1H, PhC***H***$_2$O), 4.64 (s, 2H, PhC***H***$_2$O), 4.01 (d, *J* = 10.5 Hz, 1H, ***H***C_{10}), 3.03 (d, *J* = 1.5 Hz, 1H, ***H***C_4), 2.49 (d, *J* = 19.9 Hz, 1H, ***H***$_A$$C_{14}$), 2.31 (dd, *J* = 19.9, 1.5 Hz, 1H, ***H***$_B$$C_{14}$), 2.26 (s, 3H, ***H***$_3$$C_{17}$), 2.15 – 2.05 (m, 1H, ***H***C_9), 1.96 – 1.88 (m, 1H, ***H***$_A$$C_7$), 1.70 – 1.46 (m, 3H, ***H***$_B$$C_7$, ***H***$_2$$C_8$), 1.30 (s, 3H, ***H***$_3$$C_{20}$), 1.01 (d, *J* = 6.5 Hz, 3H, ***H***$_3$$C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 195.5 (**C_3**=O), 166.0 (**C_{15}**=O), 164.0 (**C**), 144.8 (**C**), 137.0 (**$C_{Ar\text{-}ipso}$**), 136.1 (**C_{Ar}**-

ipso), 128.8 ($\mathbf{C}_{Ar}$H), 128.7 ($\mathbf{C}_{Ar}$H), 128.4 ($\mathbf{C}_{Ar}$H), 128.2 ($\mathbf{C}_{Ar}$H), 128.0 ($\mathbf{C}_{Ar}$H), 127.8 ($\mathbf{C}_{Ar}$H), 118.3 (q, $J_{C\text{-}F}$ = 321 Hz, $SO_2\mathbf{C}F_3$), 96.6 (BnO$\mathbf{C}H_2$O), 90.5 ($\mathbf{C}_6$), 90.5 ($\mathbf{C}_{11}$), 89.5 (BnO$\mathbf{C}H_2$O), 86.0 ($\mathbf{C}_{12}$), 79.5 ($\mathbf{C}_{10}$H), 70.8 (Ph$\mathbf{C}H_2$O), 70.0 (Ph$\mathbf{C}H_2$O), 63.6 ($\mathbf{C}_4$H), 45.7 ($\mathbf{C}_5$), 38.8 ($\mathbf{C}_{14}H_2$), 33.2 ($\mathbf{C}_9$H), 27.8 ($\mathbf{C}_8H_2$), 21.2 ($\mathbf{C}_7H_2$), 19.8 ($\mathbf{C}_{20}H_3$), 18.2 ($\mathbf{C}_{21}H_3$), 12.6 ($\mathbf{C}_{17}H_3$); **FTIR (NaCl, thin film):** 3368, 2930, 2875, 1756, 1732, 1426, 1216, 1038 cm^{-1}; **HRMS:** calc'd for $[M+NH_4]^+$: 728.2347, found 728.2359; **$[\alpha]_D^{25}$:** +83 (*c* = 1.0 $CHCl_3$).

Preparation of Diosphenol 18:



To an oven-dried, 48-mL, heavy-walled pressure vessel equipped with a magnetic stirbar was charged enone **17** (1.09 g, 2.00 mmol, 1.0 equiv), anhydrous SeO_2 (2.22 g, 20.0 mmol, 10.0 equiv), and freshly activated 4Å molecular sieves (prepared via vigorous flame-drying at <200 mTorr for 10 minutes, 2.18 g, 200 wt % relative to substrate) in a nitrogen-filled glovebox. Anhydrous 1,4-dioxane (20 mL) was then added and the vessel was tightly sealed, removed from the glovebox, and submerged in a preheated oil bath at 110 °C. After 9.0 h, the vessel was allowed to cool to ambient temperature, diluted with EtOAc (100 mL), and filtered through a short pad of Celite, rinsing with additional EtOAc (50 mL). The resulting filtrate was then washed with sat. aq. $NaHCO_3$ (2 x 50 mL), H_2O (50 mL), and the combined aqueous layers back extracted with EtOAc (2 x 25 mL). The combined organics were then dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to afford an orange foam. ^{1}H NMR analysis of this crude reaction mixture, integrating an external standard of phenyltrimethylsilane, indicated that **18** had been produced in 34% ^{1}H NMR yield. The crude residue was purified via silica gel chromatography (slurry packed column, 2% MeOH in CH_2Cl_2) to afford a pale orange-tan foam. The isolated material (typically ~575 mg) was carried to the next reaction without further purification.

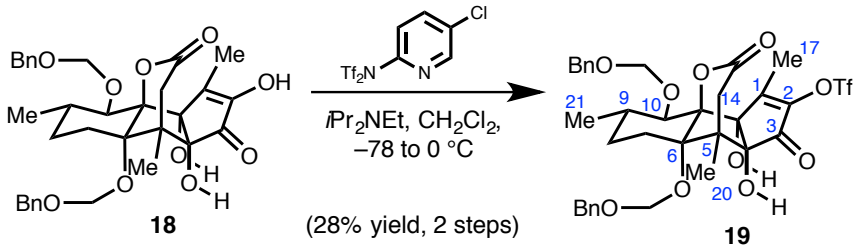
Notes: It is critical that the reaction is rigorously anhydrous. Strictly anhydrous solvent and adequately activated 4Å molecular sieves are necessarily for complete conversion to **18**. Failure to use rigorously anhydrous solvent or adequately flame-dried 4Å molecular sieves can result in contaminated material (containing up to ~7% **21**), which is extremely challenging to separate by silica gel chromatography. Furthermore, failure to remove residual **21** from samples carried through the triflation results in an inseparable mixture of vinyl triflates **19** and **22**.

As above, Se-based byproducts (both selenium black and selenium red) are produced during the course of this reaction. Although material post-chromatography appears to be pure by ^{1}H NMR spectroscopy, integration of purified material against an internal standard indicates that a significant amount of red selenium (colloidal) is co-eluted during silica gel chromatography, and thus a two-step yield is obtained after triflation (see next step).

A sample of this material was further purified by repeated silica gel chromatography for characterization purposes:

TLC (70% EtOAc/Hexanes), R_f: 0.36 (UV, $KMnO_4$); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.27 (m, 10H, ***H***-Ar), 5.66 (br s, 1H, ***H***OC_2), 5.15 (d, J = 5.7 Hz, 1H, BnOC***H***$_2$O), 4.96 (d, J = 6.1 Hz, 1H, BnOC***H***$_2$O), 4.93 (d, J = 6.2 Hz, 1H, BnOC***H***$_2$O), 4.89 (d, J = 5.7 Hz, 1H, BnOC***H***$_2$O), 4.76 (d, J = 12.1 Hz, 1H, PhC***H***$_2$O), 4.72 (d, J = 11.7 Hz, 1H, PhC***H***$_2$O), 4.68 (d, J = 11.7 Hz, 1H, PhC***H***$_2$O), 4.65 (d, J = 12.1 Hz, 1H, PhC***H***$_2$O), 4.60 (s, 1H, O***H***), 4.08 (s, 1H, O***H***), 4.00 (d, J = 10.5 Hz, 1H, ***H***C_{10}), 2.41 (d, J = 19.8 Hz, 1H, ***H***$_A$$C_{14}$), 2.25 (d, J = 19.9 Hz, 1H, ***H***$_B$$C_{14}$), 2.14 (s, 3H, ***H***$_3$$C_{17}$), 2.13 – 2.00 (m, 1H, ***H***C_9), 1.92 – 1.81 (m, 1H, ***H***$_A$$C_7$), 1.64 (dtd, J = 6.7, 4.6, 2.1 Hz, 1H, ***H***$_A$$C_8$), 1.56 – 1.42 (m, 2H, ***H***$_B$$C_7$, ***H***$_B$$C_8$), 1.27 (s, 3H, ***H***$_3$$C_{20}$), 1.08 (d, J = 6.6 Hz, 3H, ***H***$_3$$C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 197.2 (**C_3**=O), 166.7 (**C_{15}**=O), 149.3 (**C_2**), 146.0 (**C_1**), 137.0 (**$C_{Ar\text{-}ipso}$**), 136.4 (**$C_{Ar\text{-}ipso}$**), 128.7 (**C_{Ar}**H), 128.6 (**C_{Ar}**H), 128.4 (**C_{Ar}**H), 128.1 (**C_{Ar}**H), 128.0 (**C_{Ar}**H), 127.8 (**C_{Ar}**H), 97.1 (BnO**C**H_2O), 91.2 (**C_6**), 90.6 (**C_{11}**), 90.2 (BnO**C**H_2O), 86.6 (**C_{12}**), 84.6 (**C_4**), 79.9 (**C_{10}**H), 71.7 (Ph**C**H_2O), 70.4 (Ph**C**H_2O), 47.3 (**C_5**), 40.8 (**C_{14}**H_2), 33.1 (**C_9**H), 27.9 (**C_8**H_2), 21.5 (**C_7**H_2), 18.6 (**C_{21}**H_3), 15.1 (**C_{20}**H_3), 11.3 (**C_{17}**H_3); **FTIR (NaCl, thin film):** 3368, 2928, 1747, 1717, 1659, 1454, 1405, 1360, 1155, 1035 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 617.2357, found: 617.2367; **$[\alpha]_D^{25}$:** +120 (c = 0.86, $CHCl_3$).

Preparation of Vinyl Triflate 19:

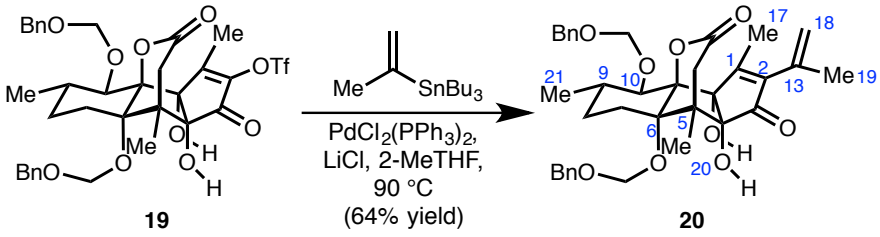


To a 50-mL, round-bottomed flask was added **18** (directly from the previous reaction, approximately 575 mg) and anhydrous CH_2Cl_2 (20 mL). *i*Pr_2NEt (0.89 mL) was added, and then the solution was cooled to –78 °C in a dry ice/acetone bath. *N*-(5-chloro-2-pyridyl) bis(trifluoromethanesulfonimide) (Comins' reagent, 589 mg, 1.50 mmol) was then added in a single portion and the solution stirred for five minutes, then the cold bath removed and replaced with an ice/water bath at 0 °C. After 1 h, the solution was directly purified by silica gel chromatography

(30 to 40% EtOAc in Hwexanes) to afford triflate **19** as a slightly off white foam (413 mg, 0.568 mmol, 28% yield, 2 steps).

TLC(40% EtOAc/Hexanes), R_f: 0.36 (UV, $KMnO_4$); **^{1}H NMR ($CDCl_3$, 400 MHz):** δ 7.41 – 7.28 (m, 10H, **H**-Ar), 5.09 (d, *J* = 5.4 Hz, 1H, BnOC***H***$_2$O), 4.98 (s, 1H, O***H***), 4.95 (d, *J* = 6.2 Hz, 1H, BnOC***H***$_2$O), 4.93 (d, *J* = 6.2 Hz, 1H, BnOC***H***$_2$O), 4.88 (d, *J* = 5.4 Hz, 1H, BnOC***H***$_2$O), 4.73 (d, *J* = 12.2 Hz, 1H, PhC***H***$_2$O), 4.69 (m, 2H, PhC***H***$_2$O), 4.65 (d, *J* = 12.0 Hz, 1H, PhC***H***$_2$O), 4.21 (s, 1H, O***H***), 3.98 (d, *J* = 10.5 Hz, 1H, ***H***C_{10}), 2.53 (d, *J* = 20.3 Hz, 1H, ***H***$_A$$C_{14}$), 2.44 (d, *J* = 20.2 Hz, 1H, ***H***$_B$$C_{14}$), 2.30 (s, 3H, **H**$_3$$C_{17}$), 2.08 (tdd, *J* = 13.8, 7.0, 3.9 Hz, 1H, ***H***C_9), 1.93 – 1.83 (m, 1H, ***H***$_A$$C_7$), 1.70 – 1.60 (m, 1H, ***H***$_A$$C_8$), 1.54 – 1.44 (m, 2H, ***H***$_B$$C_7$, ***H***$_B$$C_8$), 1.28 (s, 3H, ***H***$_3$$C_{20}$), 1.07 (d, *J* = 6.6 Hz, 3H, ***H***$_3$$C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 192.9 (**C**$_3$=O), 165.6 (**C**$_{15}$=O), 164.6 (**C**), 144.4 (**C**), 136.6 (**C**$_{Ar\text{-}ipso}$), 136.2 (**C**$_{Ar\text{-}ipso}$), 128.8 (**C**$_{Ar}$H), 128.7 (**C**$_{Ar}$H), 128.5 (**C**$_{Ar}$H), 128.2 (**C**$_{Ar}$H), 128.1 (**C**$_{Ar}$H), 127.8 (**C**$_{Ar}$H), 118.3 (q, $J_{C\text{-}F}$ = 321 Hz, SO_2**C**F_3), 96.8 (BnO**C**H_2O), 90.6 (**C**$_6$), 90.4 (**C**$_{11}$), 90.2 (BnO**C**H$_2$O), 85.7 (**C**$_{12}$), 84.4 (**C**$_4$), 79.5 (**C**$_{10}$H), 71.8 (Ph**C**H_2O), 70.4 (Ph**C**H_2O), 47.6 (**C**$_5$), 40.1 (**C**$_{14}$$H_2$), 33.0 (**C**$_9$H), 27.8 (**C**$_8$$H_2$), 21.4 (**C**$_7$$H_2$), 18.4 (**C**$_{21}$$H_3$), 15.1 (**C**$_{20}$$H_3$), 12.7 (**C**$_{17}$$H_3$); **FTIR (NaCl, thin film):** 3368, 2931, 1743, 1650, 1429, 1243, 1216, 1040 cm^{-1}; **HRMS:** calc'd for $[M+NH_4]^+$: 744.2313, found: 744.2296; **$[\alpha]_D^{25}$:** +58 (*c* = 0.74, $CHCl_3$).

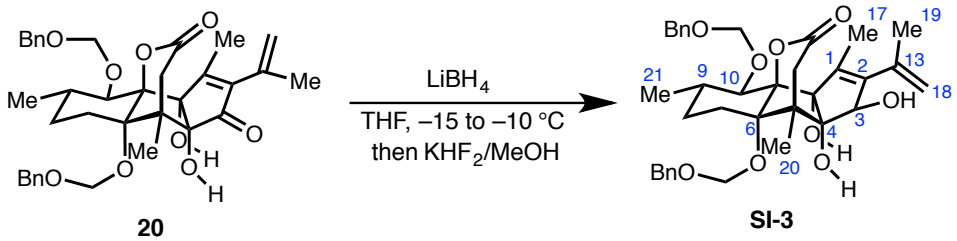
Preparation of Enone 20:



In a nitrogen-filled glovebox, an oven-dried, 48-mL capacity heavy-walled pressure vessel was charged with vinyl triflate **19** (413 mg, 0.568 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (159 mg, 0.227 mmol, 40 mol %), anhydrous LiCl (192 mg, 4.54 mmol, 8.0 equiv), tributyl(2-propenyl)stannane (752 mg, 2.27 mmol, 4.0 equiv), and anhydrous 2-methyltetrahydrofuran (11 mL). The vial was sealed with a PTFE-lined cap, and submerged in a preheated oil bath at 90 °C. After 14 h, the vial was removed from the bath and allowed to cool to ambient temperature, then sat. aq. KF (15 mL) was added. The solution was stirred for 45 minutes, diluted with EtOAc (50 mL) and washed with sat. aq. KF (20 mL). The combined aqueous layers were extracted with additional EtOAc (25 mL), and the combined organics washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered over Celite, and concentrated *in vacuo* to afford a red-brown oil. Purification by silica gel chromatography (30 to 40% EtOAc in hexanes) afforded enone **20** as an off-white foam (224 mg, 0.363 mmol, 64% yield).

TLC (40% EtOAc/Hexanes), R_f: 0.32 (UV, $KMnO_4$); **^{1}H NMR ($CDCl_3$, 400 MHz):** 7.40 – 7.27 (m, 10H, **H**-Ar), 5.24 (p, *J* = 1.6 Hz, 1H, $\mathbf{H_A}C_{18}$), 5.15 (d, *J* = 5.9 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.96 (d, *J* = 6.3 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.94 (d, *J* = 6.3 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.92 (d, *J* = 5.9 Hz, 1H, BnOC$\boldsymbol{H}_2$O), 4.82 (dq, *J* = 2.0, 1.0 Hz, 1H, $\mathbf{H_A}C_{18}$), 4.78 (d, *J* = 12.1 Hz, 1H, PhC$\boldsymbol{H}_2$O), 4.70 (s, 2H, PhC$\boldsymbol{H}_2$O), 4.64 (d, *J* = 12.1 Hz, 1H, PhC$\boldsymbol{H}_2$O), 4.27 (s, 1H, O***H***), 4.01 (d, *J* = 10.5 Hz, 1H), 3.94 (s, 1H, O***H***), 2.42 (d, *J* = 19.8 Hz, 1H, $\boldsymbol{H_A}C_{14}$), 2.32 (d, *J* = 19.8 Hz, 1H, $\boldsymbol{H_B}C_{14}$), 2.25 (s, 3H, $\boldsymbol{H_3}C_{17}$), 2.14 – 2.01 (m, 1H, ***H***C_9), 1.89 – 1.82 (m, 1H, $\boldsymbol{H_A}C_7$), 1.87 (q, *J* = 1.5 Hz, 3H, $\boldsymbol{H_3}C_{19}$), 1.65 (dtt, *J* = 7.9, 4.9, 2.2 Hz, 1H, $\boldsymbol{H_A}C_8$), 1.54 – 1.46 (m, 2H, $\boldsymbol{H_B}C_8$, $\boldsymbol{H_B}C_8$), 1.26 (s, 3H, $\boldsymbol{H_3}C_{20}$), 1.10 (d, *J* = 6.5 Hz, 3H, $\boldsymbol{H_3}C_{21}$); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 202.1 ($\mathbf{C_3}$**=O**), 171.0 ($\mathbf{C_{15}}$**=O**), 166.8 ($\mathbf{C_1}$), 143.7 ($\mathbf{C_2}$), 137.3 (**C**), 136.5 (**C**), 135.6 (**C**), 128.7 ($\mathbf{C_{Ar}}$H), 128.5 ($\mathbf{C_{Ar}}$H), 128.4 ($\mathbf{C_{Ar}}$H), 128.1 ($\mathbf{C_{Ar}}$H), 127.9 ($\mathbf{C_{Ar}}$H), 127.7 ($\mathbf{C_{Ar}}$H), 118.2 ($\mathbf{C_{18}}H_2$), 97.1 (BnO**C**H_2O), 91.3 ($\mathbf{C_6}$), 91.2 ($\mathbf{C_{11}}$), 90.3 (BnO**C**H_2O), 88.1 (**C**), 85.5 (**C**), 79.9 (**H**C_{10}), 71.8 (Ph**C**H_2O), 70.5 (Ph**C**H_2O), 47.6 ($\mathbf{C_5}$), 40.9 ($\mathbf{C_{14}}H_2$), 33.1 ($\mathbf{C_9}$H), 27.9 ($\mathbf{C_8}H_2$), 21.6 ($\mathbf{C_{19}}H_3$), 21.4 ($\mathbf{C_7}H_2$), 18.7 ($\mathbf{C_{21}}H_3$), 15.0 ($\mathbf{C_{20}}H_3$), 15.0 ($\mathbf{C_{17}}H_3$); **FTIR (NaCl, thin film):** 3412, 2953, 2925, 1749, 1709, 1037, 1026 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 641.2721, found: 641.2729; **$[\alpha]_D^{25}$:** +100 (*c* = 0.67, $CHCl_3$).

Preparation of Enone SI-3:



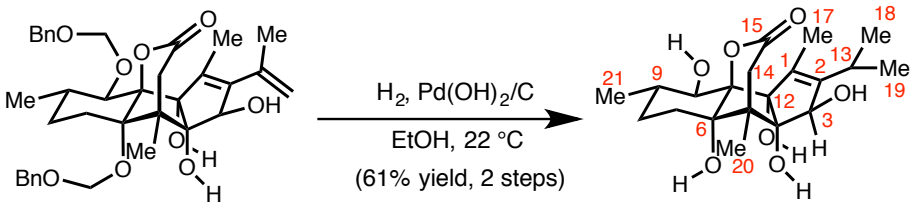
20 **SI-3**

To an oven-dried, 2-dram vial was added enone **20** (250 mg, 0.404 mmol, 1.00 equiv), and anhydrous THF (16 mL). The solution was cooled to –15 °C in an ice/MeOH bath and solid $LiBH_4$ (132 mg, 6.06 mmol, 15 equiv) was added in a single portion. The temperature was carefully maintained between –10 and –15 °C. After 2 h, TLC analysis indicated full consumption of the starting material. Sat. aq. NH_4Cl was then slowly added to the reaction [Caution! Vigorous evolution of H_2 gas occurs, particularly in the initial stages of addition. Careful, controlled dropwise addition of NH_4Cl solution is advised in order to avoid a violent reaction]. The mixture was diluted with EtOAc (30 mL), and washed thoroughly with sat. aq. NH_4Cl (2 x 20 mL), and the combined organic layers extracted with additional EtOAc (20 mL). The solution was then concentrated *in vacuo*, redissolved in MeOH (45 mL) and KHF_2 (3 M in H_2O, 3 mL) was then added and the solution vigorously swirled for two minutes and the entire mixture concentrated *in vacuo* [rotary evaporator bath temperature at 35 °C]. The resultant residue was suspended in EtOAc (50 mL), anhydrous Na_2SO_4 added, then filtered through a short pad of silica gel to remove salts, and rinsed with additional EtOAc (25 mL), concentrated *in vacuo*. The resulting off-white foam was carried onto the next step without further purification.

A sample of allylic alcohol **SI-3** could be additionally purified by preparative thin-layer chromatography (30% EtOAc in CH_2Cl_2) for characterization purposes.

TLC (40% EtOAc/Hexanes), R_f: 0.12 (UV, $KMnO_4$); **^{1}H NMR (CDCl3, 400 MHz):** δ 7.42 – 7.26 (m, 10H, **H**-Ar), 5.17 (d, *J* = 6.5 Hz, 1H, BnOC***H***$_2$O), 5.16 – 5.14 (m, 1H, ***H***$_A$C$_{18}$), 4.99 (d, *J* = 5.9 Hz, 1H, BnOC***H***$_2$O), 4.95 (d, *J* = 5.8 Hz, 1H, BnOC***H***$_2$O), 4.87 (d, *J* = 6.3 Hz, 1H, BnOC***H***$_2$O), 4.89 – 4.87 (m, 1H, ***H***$_B$C$_{18}$), 4.86 – 4.83 (m, 1H, ***H***C$_3$), 4.79 (d, *J* = 12.3 Hz, 1H, PhC***H***$_2$O), 4.73 (d, *J* = 11.8 Hz, 1H, PhC***H***$_2$O), 4.69 (d, *J* = 11.8 Hz, 1H, PhC***H***$_2$O), 4.61 (d, *J* = 12.2 Hz, 1H, PhC***H***$_2$O), 4.41 (s, 1H, O***H***), 3.91 (d, *J* = 10.3 Hz, 1H, ***H***C$_{10}$), 3.89 (s, 1H, O***H***), 3.53 (d, *J* = 19.8 Hz, 1H, ***H***$_A$C$_{14}$), 2.26 (d, *J* = 19.8 Hz, 1H, ***H***$_B$C$_{14}$), 2.13 – 2.03 (m, 1H, ***H***C$_9$), 2.08 (d, *J* = 4.6 Hz, 1H, C$_3$O***H***), 1.85 (d, *J* = 2.3 Hz, 3H, ***H***$_3$C$_{17}$), 1.85 – 1.83 (m, 3H, ***H***$_3$C$_{19}$), 1.79 (ddd, *J* = 14.9, 4.4, 2.1 Hz, 1H, ***H***$_A$C$_7$), 1.71 – 1.63 (m, 1H, ***H***$_A$C$_8$), 1.56 (ddd, *J* = 14.9, 12.9, 4.6 Hz, 1H, ***H***$_B$C$_7$), 1.38 – 1.27 (m, 1H, ***H***$_B$C$_8$), 1.30 (s, 3H, ***H***$_3$C$_{20}$), 1.09 (d, *J* = 6.5 Hz, 3H, ***H***$_3$C$_{21}$); **^{13}C NMR (126 MHz, CDCl$_3$):** δ 168.5 (**C**$_{15}$=O), 143.4 (**C**), 138.4 (**C**), 137.7 (**C**), 136.6 (**C**), 136.4 (**C**), 128.7 (**C**$_{Ar}$H), 128.4 (**C**$_{Ar}$H), 128.2 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 127.7 (**C**$_{Ar}$H), 117.0 (**C**$_{18}$H$_2$), 97.3 (BnO**C**H$_2$O), 91.5 (**C**), 91.2 (**C**), 91.1 (**C**), 90.4 (BnO**C**H$_2$O), 88.7 (**C**), 83.0 (**C**$_3$H), 80.6 (**C**$_{10}$H), 72.1 (PhC***H***$_2$O), 70.5 (PhC***H***$_2$O), 49.2 (**C**$_5$), 39.6 (**C**$_{14}$H$_2$), 33.2 (**C**$_9$H), 28.3 (**C**$_8$H$_2$), 21.3 (**C**$_{19}$H$_3$), 21.2 (**C**$_7$H$_2$), 18.9 (**C**$_{21}$H$_3$), 16.0 (**C**$_{20}$H$_3$), 13.0 (**C**$_{17}$H$_3$); **FTIR (NaCl, thin film):** 3453, 2923, 2872, 1742, 1026 cm^{-1}; **HRMS:** calc'd for $[M+Na]^+$: 643.2878, found: 643.2886; **$[\alpha]_D^{25}$:** –29 (*c* = 0.33, $CHCl_3$).

Preparation of Anhydroryanodol (3):



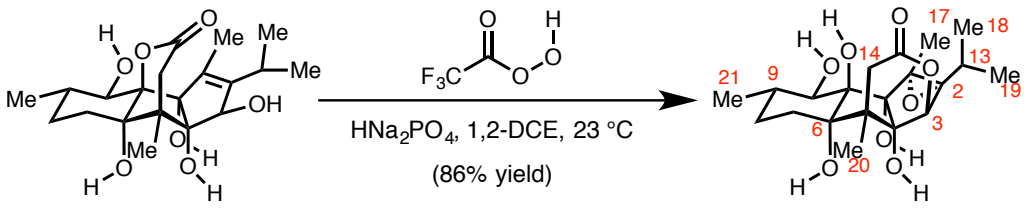
SI-3 *(+)-anhydroryanodol* (**3**)

To a 25-mL, round-bottomed flask was charged crude triol **SI-3**. $Pd(OH)_2/C$ (20 wt %, 375 mg) was added, followed by absolute EtOH (16 mL). The suspension was sparged with N_2 for five minutes, then H_2 for 5 minutes via a double-walled balloon. The suspension was subsequently stirred for 2 h at 20 °C under H_2, sparged with N_2 to remove excess hydrogen gas, then diluted with EtOAc (50 mL), filtered through a short pad of Celite and concentrated *in vacuo*. Purification of the crude residue by silica gel chromatography (slurry packed column, 4% MeOH in $CHCl_3$) affords (+)-anhydroryanodol (**3**) (94.1 mg, 0.246 mmol, 61% yield) as a colorless foam.

Note: Soda-lime (Flint) disposable culture tubes were purchased from Kimble Chase and used during silica gel chromatography for fraction collection in order to prevent formation of borate complexes formed with leached B_2O_3 from borosilicate (Pyrex) glassware. In some instances, leached B_2O_3 from use of borosilicate glass resulted in up to 10% of a stable borate. Treatment with aq. 3 M KHF_2 in MeOH followed by dilution with EtOAc and filtration over silica gel allowed for clean liberation of the reactive triol (as described above). The chloroform employed for silica gel chromatography contains 0.75 % EtOH as a stabilizer.

TLC (10% MeOH/CH_2Cl_2), R_f: 0.32 ($KMnO_4$); **^{1}H NMR (500 MHz, CD_3OD):** δ 4.71 (q, *J* = 2.3 Hz, 1H, ***H***C_3), 3.98 (d, *J* = 10.4 Hz, 1H, ***H***C_{10}), 3.62 (d, *J* = 19.9 Hz, 1H, ***H***$_A$$C_{14}$), 2.75 (hept, *J* = 7.0 Hz, 1H, ***H***C_{13}), 2.30 (d, *J* = 19.8 Hz, 1H, ***H***$_B$$C_{14}$), 1.84 – 1.74 (m, 1H, ***H***C_9), 1.77 (d, *J* = 2.4 Hz, 3H, ***H***$_3$$C_{17}$), 1.62 – 1.43 (m, 4H, ***H***$_2$$C_7$, ***H***$_2$$C_8$), 1.18 (s, 3H, ***H***$_3$$C_{20}$), 1.15 (d, *J* = 7.0 Hz, 3H, ***H***$_3$$C_{18}$), 1.11 (d, *J* = 7.0 Hz, 3H, ***H***$_3$$C_{19}$), 1.08 (d, *J* = 6.5 Hz, 3H, ***H***$_3$$C_{21}$); **^{13}C NMR (126 MHz, CD_3OD):** δ 173.2 (**C_{15}**=O), 148.3 (**C_2**), 134.2 (**C_1**), 93.4 (**C_{12}**), 92.8 (**C_{11}**), 90.3 (**C_4**), 84.7 (**C_6**), 84.0 (**C_3**H), 72.8 (**C_{10}**H), 48.9 (**C_5**), 40.3 (**C_{14}**H_2), 35.2 (**C_9**H), 28.8 (**C_8**H_2), 28.5 (**C_{13}**H), 26.1 (**C_7**H_2), 21.6 (**C_{19}**H_3), 19.3 (**C_{18}**H_3), 18.8 (**C_{21}**H_3), 14.7 (**C_{20}**H_3), 12.2 (**C_{17}**H_3); **FTIR (NaCl, thin film):** 3450, 1735 cm^{-1}; **HRMS:** calc'd for $[M–H]^-$: 381.1919, found: 381.2045; **$[\alpha]_D^{25}$:** +54 (*c* = 0.45, MeOH).

Preparation of Epianhydroryanodol Epoxide (SI-4):



(+)-anhydroryanodol (**3**) **SI-4**

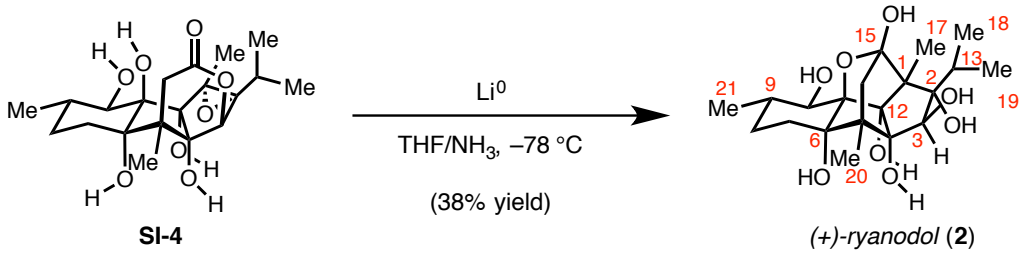
Deslongchamps et. Al (*28*) reported the use of a 1.09 M solution of trifluoroperacetic acid in 1,2-dichloroethane, prepared according to the procedure of Emmons and Pagano (*48*). In this report, trifluoroperacetic acid is prepared from 90% H_2O_2 (aq.) and trifluoroacetic anhydride. Given the high hazards of preparing and handling 90% H_2O_2, which has been known detonate explosively during its preparation, we prepared trifluoroperacetic acid utilizing commercially available urea hydrogen peroxide.

An approximately 1M solution of trifluoroperacetic acid was prepared according to the following procedure: to a 25-mL, round-bottomed flask was added urea hydrogen peroxide (940 mg, 10.0 mmol, 1.00 equiv) and anhydrous 1,2-dichloroethane (10.0 mL). The suspension was cooled to 0 °C in an ice/water bath and trifluoroacetic anhydride (1.56 mL, 11 mmol, 1.1 equiv) added dropwise by syringe. The solution was stirred at 0 °C for 1 h, then the ice bath removed and stirred at 20 °C for 1 h, by which time the white suspension had changed into a biphasic mixture. Stirring was stopped to allow the layers to separate before addition.

To a 100-mL, round-bottomed flask was added anhydroryanodol (76.4 mg, 0.200 mmol, 1.00 equiv), HNa_2PO_4 (170 mg, 1.20 mmol, 6.0 equiv) and 1,2-dichloroethane (30 mL). The suspension was stirred vigorously at 20 °C, then trifluoroperacetic acid (1M solution in 1,2-DCE, as prepared above, 0.40 mL, ~0.40 mmol, ~2 equiv) was added dropwise by syringe. The solution was stirred for 3 h at 20 °C, by which time TLC analysis had indicated consumption of the starting material, then filtered over a short pad of Celite to remove solids, rinsing with 1,2-dichloroethane (20 mL) and concentrated *in vacuo* to afford a white foam [Caution! Trifluoroperacetic acid, like other organic peroxides, is potentially explosive and should be used with caution. Although no incidents involving this peroxide were encountered during these studies, rotary evaporation was conducted behind a blast shield as a precaution]. Purification of the crude foam by silica gel chromatography (5% MeOH in $CHCl_3$) afforded epianhydroryanodol epoxide **SI-4** as a colorless semicrystalline solid (68.5 mg, 0.172 mmol, 86% yield).
Note: Soda-lime (Flint) disposable culture tubes were purchased from Kimble Chase and used during silica gel chromatography for fraction collection in order to prevent formation of borate complexes formed with leached B_2O_3 from borosilicate (Pyrex) glassware. The chloroform employed for silica gel chromatography contains 0.75 % EtOH as a stabilizer.

TLC (5% MeOH/CH_2Cl_2), R_f 0.20 ($KMnO_4$); **^{1}H NMR (CD_3OD, 400 MHz):** δ 4.58 (s, 1H, ***H***C_3), 4.07 (d, *J* = 10.1 Hz, 1H, ***H***C_{10}), 3.66 (d, *J* = 16.0 Hz, 1H, ***H$_A$***C_{14}), 2.18 (d, *J* = 16.1 Hz, 1H, ***H$_B$***C_{14}), 1.87 – 1.76 (m, 2H, ***H$_A$***C_7, ***H***C_{13}), 1.73 – 1.64 (m, 1H, ***H***C_9), 1.63 (s, 3H, ***H$_3$***C_{17}), 1.59 – 1.41 (m, 2H, ***H$_2$***C_8), 1.29 (ddd, *J* = 13.0, 4.5, 2.1 Hz, 1H, ***H$_B$***C_7), 1.22 (d, *J* = 7.0 Hz, ***H$_3$***C_{19}), 1.06 (d, *J* = 7.3 Hz, 3H, ***H$_3$***C_{18}), 1.06 (d, *J* = 6.3 Hz, 3H, ***H$_3$***C_{21}), 1.01 (s, 3H, ***H***$_3C_{20}$); **^{13}C NMR (CD_3OD, 400 MHz):** 174.2 (**C_{15}**=O), 94.7 (**C**), 89.8 (**C_3**H), 89.1 (**C**), 88.1 (**C**), 85.1 (**C**), 77.4 (**C**), 74.8 (**C**), 74.3 (**C_{10}**H), 51.0 (**C_5**), 38.4 (**$C_{14}H_2$**), 34.6 (**C_9**H), 30.6 (**C_{13}**H), 28.5 (**C_8H_2**), 24.7 (**C_7H_2**), 19.1 (**$C_{19}H_3$**), 18.3 (**$C_{20}H_3$**), 17.4 (**$C_{18}H_3$**), 17.1 (**$C_{21}H_3$**), 15.2 (**$C_{17}H_3$**); **FTIR (NaCl, thin film):** 3462, 1736 cm^{-1}; **HRMS:** calc'd for $[M+H]^+$: 399.2013, found: 399.2034. **$[\alpha]_D^{25}$:** –39 (*c* = 0.40, MeOH).

Preparation of (+)-Ryanodol (2):



SI-4 *(+)-ryanodol* (**2**)

An oven-dried, 100-mL, three-necked, round-bottomed flask containing a borosilicate glass-coated magnetic stirbar was equipped with an oven-dried cold-finger condenser and allowed to cool under dry Argon. While cooling, the flask was directly connected to a gas cylinder of ammonia (Matheson anhydrous ammonia) by means of a gas inlet adapter connected to a piece of dry Tygon tubing. Once the glassware had completely cooled, the flask was submerged into a dry-ice/acetone bath (–78 °C) and the cold finger filled with dry-ice/acetone. Ammonia was carefully condensed into the flask by opening the tank, until ~50 mL had accumulated, and both the ammonia inlet and cold finger condenser were removed and replaced with rubber septa. Freshly cut sodium metal (200 mg cut into six pieces, hexanes washed) was then added piecewise to the ammonia, which resulted immediately in a deep blue solution. This solution was maintained at –78 °C for 30 min for drying.

A separate oven-dried, 100-mL, three-necked, round-bottomed flask containing a borosilicate glass coated magnetic stirbar was equipped with an oven-dried cold-finger condenser, and was allowed to cool under an Ar atmosphere. The distilling flask prepared above was then connected by means of a dry piece of Tygon tubing under a positive pressure of Argon. The receiving flask was submerged into a dry-ice/acetone bath, and the cold finger condenser filled with dry ice/acetone. The distilling flask was then removed from the cold bath, allowing for the slow distillation of anhydrous ammonia from sodium metal, until ~20 mL of ammonia had condensed into the receiving flask (approximately 30 minutes). A solution of epianhydroryanodol epoxide (**SI-4**, 15.3 mg, 38.7 μmol, 1.0 equiv) in THF (4.0 mL) was then added dropwise by syringe to the freshly distilled ammonia, which was allowed to stir for an additional 15 minutes –78 °C.

A fresh piece of lithium^0-wire (30.5 mg, stored in mineral oil), was rinsed with hexanes, then cut into a pre-tared 25-mL beaker containing hexanes (15 mL). Immediately prior to addition, this piece of wire was further cut into four pieces (~ 7-8 mg each) and added to the flask above within two minutes, and the deep blue mixture stirred for 60 min at –78 °C. Ammonium chloride (solid, 750 mg) was then added slowly as a solid. The deep blue color faded within 90 seconds, producing a colorless suspension. The cold bath was then removed and the flask was opened to atmosphere, allowing for the evaporation of ammonia as the flask warmed to ambient temperature (45 min). The resulting slurry, consisting primarily of some residual THF, LiCl, and NH_4Cl salts, was then carefully diluted with H_2O (20 mL), and additional THF (5 mL). The mixture was extracted with CH_2Cl_2 (3 x 15

mL), and the combined organics concentrated *in vacuo*. ^{1}H NMR analysis of this organic layer indicated the presence of a carbonyl reduction product and a small amount of starting material.

Carbon dioxide (g) was then bubbled through the aqueous layer (20 mL) for 10 minutes to neutralize the pH below 8 and the aqueous layer saturated with NaCl. This aqueous solution was then transferred into a continuous extraction apparatus equipped with an efficient reflux condenser and 100 mL round bottomed flask that had been pre-filled with $CHCl_3$ (50 mL in the flask, 100 mL in the extraction body). The round-bottomed flask was then heated in an oil bath at 100 °C, allowing for vigorous reflux of the chloroform, and the apparatus maintained for 40 h under a nitrogen atmosphere. The flask was then removed from the apparatus and the solvent removed *in vacuo* affording a solid residue. ^{1}H NMR analysis of this organic residue indicated that it was ~90% pure by NMR. The residue was again dissolved in H_2O (20 mL) and THF (5 mL) and washed with CH_2Cl_2 (3 x 15 mL). Concentration of the aqueous layer (rotovap temperature at 50 °C) and drying under high vacuum affords (+)-ryanodol (**2**) as a white solid (95% purity by ^{1}H NMR, 7.4 mg, 47% yield) that contains minor salt impurities and is further purified by silica gel chromatography (3 g of slurry packed silica, 10% MeOH in $CHCl_3$) to afford ryanodol (**2**) as a white film (5.9 mg, 14.8 μmol, 38% yield).

Notes: Deslongchamps and coworkers (*28*) report a detailed procedure for this reductive cyclization on 20 mg scale, to produce 12 mg of (+)-ryanodol, isolated in pure fashion directly after continuous extraction. In our hands, the reaction profile of this transformation was determined to be highly dependent on the purity of the ammonia, which we attribute to trace iron impurities and water. Control experiments with added H_2O (10 equiv) after distillation of NH_3 from sodium indicates that proton sources, as may be expected, favor the formation of carbonyl reduction products, whereas the addition of Fe-salts or the use of ammonia directly following condensation from the cylinder result in diminished reactivity, presumably due to the rapid formation of $LiNH_2$ (catalyzed by trace metals). Redistillation of the condensed ammonia from Na^0 to remove water and trace impurities yields the most reproducible results. Despite these precautions, an identical reaction profile to that described by Deslongchamps was not obtained.

A continuous extractor consisting of a 14/20 ground glass attachment (see photo on p. **S28**) was used for the extraction process. This particular extractor had a volume of approximately 120 mL, allowing for an aqueous phase of approximately 20 mL and a heavy-organic phase of 100 mL. Material obtained after continuous extraction was typically of ~90% purity by ^{1}H NMR. Most organic impurities were readily removed by washing with THF/DCM, as described above. However, dissolution of this material in MeOH typically left trace inorganic residues (potentially trace salts from the aqueous phase) that affect an accurate mass. The material obtained after column chromatography does not produce the same residue, lending further evidence to trace inorganic salt impurities.

^{1}H NMR (CD_3OD, 400 MHz): δ 4.12 (s, 1H, ***H***C_3), 3.78 (d, *J* = 10.2 Hz, 1H, ***H***C_{10}), 2.51 (d, *J* = 13.4 Hz, 1H, ***H***$_A$$C_{14}$), 2.15 (hept, *J* = 6.7 Hz, 1H, ***H***C_{13}), 2.08 (td, *J* =12.9, 5.3 Hz, 1H, ***H***$_B$$C_7$), 1.90 – 1.76 (m, 1H, ***H***C_9), 1.74 (d, *J* = 13.4 Hz, 1H, ***H***$_B$$C_{14}$), 1.53 (dtd, *J* = 12.7, 5.2, 1.6 Hz, 1H, ***H***$_B$$C_8$), 1.46 (qd, *J* = 12.9, 4.7 Hz, 1H, ***H***$_A$$C_8$), 1.33 (s, 3H, ***H***$C_{17}$), 1.26 (ddd, *J* = 12.7, 4.6, 2.0 Hz, 1H, ***H***$_A$$C_7$), 1.12 (s, 3H, ***H***$_3$$C_{20}$), 1.08 (d, *J* = 6.8 Hz, 3H, ***H***$_3$$C_{19}$), 1.01 (d, *J* = 6.5 Hz, 3H, ***H***$_3$$C_{21}$), 1.00 (d, *J* = 6.5 Hz, 3H, ***H***$_3$$C_{18}$). **^{13}C NMR ($CD_3OD$, 400 MHz):** δ 103.1 (**C_{15}**), 96.3 (**C_{12}**), 92.6 (**C_4**), 91.6 (**C_3**H), 87.3 (**C_{11}**), 86.6 (**C_6**), 84.9 (**C_2**), 72.9 (**C_{10}**H), 65.4 (**C_1**), 49.7 (**C_5**), 41.5 (**C_{14}**H_2), 35.4 (**C_9**H), 30.7 (**C_{13}**H), 29.4 (**C_8**H_2), 26.6 (**C_7**H_2), 19.5 (**C_{19}**H_3), 19.4 (**C_{18}**H_3), 19.0 (**C_{21}**H_3), 13.2 (**C_{20}**H_3), 10.2 (**C_{17}**H_3); **HRMS:** calc'd for $[M–H]^-$: 399.2024, found: 399.2028; **$[\alpha]_D^{25}$:** +37 (*c* = 0.30, MeOH).

^{1}H and ^{13}C Data Comparison Tables for Authentic vs. Synthetic (+)-Ryanodol

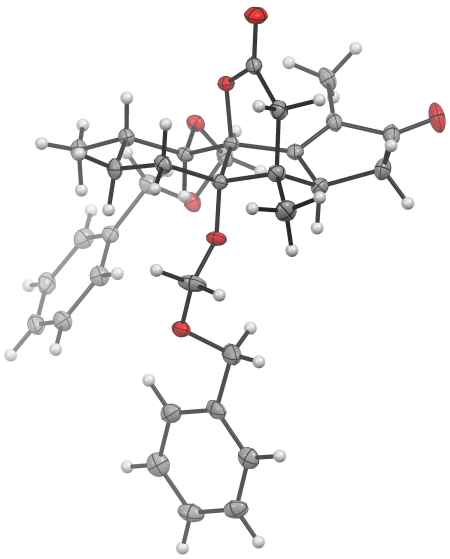
Table S2. Comparison of ^{1}H NMR data for Authentic vs. Synthetic (+)-Ryanodol

Carbon No.	Authentic Ryanodol (from hydrolysis of ryanodine) Inoue, 2014 (*ref. 29*) (400 MHz, CD_3OD) $[\alpha]_D^{22}$ = +36 (c 0.41, MeOH)	Synthetic (+)-Ryanodol This Report (500 MHz, CD_3OD) $[\alpha]_D^{25}$: +37 (*c* = 0.30, MeOH)
	^{1}H [δ, multi., *J* (Hz)]	^{1}H [δ, multi., *J* (Hz)]
1	–	–
2	–	–
3	4.12 (s, 1H)	4.12 (s, 1H)
4	–	–
5	–	–
6	–	–
7a	1.26 (1H, ddd, *J* = 12.8, 4.6, 1.7 Hz)	1.26 (ddd, *J* = 12.7, 4.6, 2.0 Hz, 1H)
7b	2.08 (ddd, *J* = 12.8, 12.8, 5.5 Hz, 1H)	2.08 (td, *J* =12.9, 5.3 Hz, 1H)
8a	1.45 (dddd, *J* = 13.2, 3.2, 12.8, 4.6 Hz, 1H)	1.46 (qd, *J* = 12.9, 4.7 Hz, 1H)
8b	1.51 (dddd, J = 13.2, 5.8, 5.5, 1.7 Hz, 1H)	1.53 (dtd, *J* = 12.7, 5.2, 1.6 Hz, 1H)
9	1.83 (ddqd, *J* =13.2, 10.4, 6.3, 5.8 Hz, 1H)	1.90 – 1.76 (m, 1H)
10	3.77 (d, *J* = 10.4 Hz, 1H)	3.78 (d, *J* = 10.2 Hz, 1H)
11	–	–
12	–	–
13	2.15 (qq, *J* = 6.8, 6.3 Hz)	2.15 (hept, *J* = 6.7 Hz, 1H)
14a	1.73 (d, *J* = 13.1 Hz, 1H)	1.74 (d, *J* = 13.4 Hz, 1H)
14b	2.51 (d, *J* = 13.1 Hz, 1H)	2.51 (d, *J* = 13.4 Hz, 1H)
15	–	–
17	1.33 (s, 3H)	1.33 (s, 3H)
18	1.00 (d, *J* = 6.3 Hz, 3 H)	1.00 (d, *J* = 6.5 Hz, 3H)
19	1.08 (d, *J* = 6.8 Hz, 3H)	1.08 (d, *J* = 6.8 Hz, 3H)
20	1.12 (s, 3H)	1.12 (s, 3H)
21	1.01 (d, *J* = 6.3 Hz, 3H)	1.01 (d, *J* = 6.5 Hz, 3H)

Table S3. Comparison of ^{13}C NMR data for Authentic vs. Synthetic (+)-Ryanodol

Carbon No.	Authentic Ryanodol (from hydrolysis of ryanodine) Inoue, 2014 (*ref. 29*) (100 MHz, CD_3OD) $[\alpha]_D^{22}$ = +36 (c 0.41, MeOH)	Synthetic (+)-Ryanodol This Report (500 MHz, CD_3OD) $[\alpha]_D^{25}$: +37 (*c* = 0.30, MeOH)	Chemical Shift Difference, Δδ
	^{13}C (δ) ppm	^{13}C (δ) ppm	^{13}C (Δδ) ppm
1	65.4	65.4	0
2	84.9	84.9	0
3	91.6	91.6	0
4	92.6	92.6	0
5	49.6	49.7	0.1
6	86.6	86.6	0
7	26.6	26.6	0
8	29.4	29.4	0
9	35.4	35.4	0
10	72.9	72.9	0
11	87.3	87.3	0
12	96.3	96.3	0
13	30.7	30.7	0
14	41.5	41.5	0
15	103.1	103.1	0
17	10.2	10.2	0
18	19.4	19.4	0
19	19.5	19.5	0
20	13.2	13.2	0
21	19.0	19.0	0

X-Ray Structure Determination for 17



Crystals of **15** were grown by slow, repeated crystallization from Et_2O and found to be suitable for X-ray diffraction. Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Cu-$K\alpha$ radiation (λ = 1.54178 Å) from an $I_\mu S$ micro-source. All diffractometer manipulations, including data collection, integration, and scaling were carried out using the Bruker APEXII software (*49*). Absorption corrections were applied using SADABS (*50*). The structure was solved by intrinsic phasing using SHELXT (*51*) and refined against F^2 on all data by full-matrix least squares with SHELXL-2014 using established refinement techniques and with an extinction correction of 0.00106(15) (*52*). All non-hydrogen atoms were refined using anisotropic displacement parameters. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. Compound **17** crystallizes in the orthorhombic space group $P2_12_12_1$ and absolute configuration was determined by anomalous dispersion (Flack = -0.02(8)) (*53*). CCDC deposition number 1478621 contains the supplementary crystallographic data for **17**. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S4. Crystal data and structure refinement for p16083_O_a.

Identification code	p16083_o_a	
Empirical formula	C33 H38 O7	
Formula weight	546.63	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.5193(3) Å	α= 90°.
	b = 9.9691(4) Å	β= 90°.
	c = 37.1447(17) Å	γ = 90°.
Volume	2784.4(2) $Å^3$	
Z	4	
Density (calculated)	1.304 Mg/m^3	
Absorption coefficient	0.735 mm^{-1}	
F(000)	1168	
Crystal size	0.22 x 0.15 x 0.12 mm^3	
Theta range for data collection	2.379 to 78.722°.	
Index ranges	-9<=h<=8, -11<=k<=12, -44<=l<=46	
Reflections collected	25520	
Independent reflections	5891 [R(int) = 0.0654]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7542 and 0.6748	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5891 / 0 / 369	
Goodness-of-fit on F^2	1.054	
Final R indices [I>2sigma(I)]	R1 = 0.0332, wR2 = 0.0756	
R indices (all data)	R1 = 0.0395, wR2 = 0.0783	
Absolute structure parameter	-0.02(8)	
Extinction coefficient	0.00106(15)	
Largest diff. peak and hole	0.388 and -0.305 e.$Å^{-3}$	

Table S5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for p16083_O_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(4)	2446(2)	7582(1)	3543(1)	18(1)
O(3)	4(2)	4472(1)	3389(1)	16(1)
O(5)	3759(2)	9341(2)	3828(1)	21(1)
O(6)	2900(2)	3729(1)	3863(1)	17(1)
O(7)	5698(2)	4343(2)	4094(1)	20(1)
O(2)	-2174(2)	3906(2)	3026(1)	27(1)
O(1)	4183(3)	3802(2)	2313(1)	34(1)
C(10)	2201(3)	5059(2)	3829(1)	15(1)
C(29)	6237(3)	5835(2)	4718(1)	20(1)
C(15)	-1057(3)	4716(2)	3102(1)	18(1)
C(28)	6510(3)	4451(2)	4716(1)	18(1)
C(9)	664(3)	5251(2)	4097(1)	17(1)
C(16)	4771(3)	3678(2)	3818(1)	20(1)
C(6)	919(3)	6838(2)	3422(1)	16(1)
C(12)	2662(3)	5171(2)	3110(1)	16(1)
C(5)	684(3)	6979(2)	3008(1)	19(1)
C(33)	7460(3)	3870(2)	4998(1)	22(1)
C(1)	3222(3)	4090(2)	2927(1)	19(1)
C(22)	6786(3)	10036(2)	3812(1)	24(1)
C(4)	2507(3)	6424(2)	2883(1)	20(1)
C(14)	-850(3)	6035(2)	2901(1)	20(1)
C(31)	7840(3)	6022(2)	5278(1)	24(1)
C(19)	5755(3)	3586(2)	4421(1)	21(1)
C(11)	1544(3)	5350(2)	3447(1)	14(1)
C(7)	-659(3)	7050(2)	3672(1)	18(1)
C(30)	6905(3)	6619(2)	4997(1)	23(1)
C(27)	7190(3)	9695(2)	4167(1)	26(1)
C(21)	1297(3)	5035(2)	4483(1)	22(1)
C(32)	8119(3)	4649(2)	5278(1)	24(1)
C(2)	3570(3)	4510(2)	2549(1)	23(1)
C(8)	-140(3)	6662(2)	4058(1)	20(1)

C(3)	2884(3)	5936(2)	2500(1)	25(1)
C(25)	9588(3)	11287(2)	4169(1)	28(1)
C(23)	7809(3)	10996(2)	3640(1)	24(1)
C(20)	311(3)	8385(2)	2862(1)	26(1)
C(17)	3378(3)	2659(2)	3039(1)	23(1)
C(24)	9198(3)	11617(2)	3817(1)	26(1)
C(26)	8583(3)	10318(2)	4347(1)	27(1)
C(13)	2247(3)	8959(2)	3642(1)	28(1)
C(18)	5294(3)	9365(3)	3607(1)	33(1)

Table S6. Bond lengths [Å] and angles [°] for p16083_O_a.

O(4)-C(6)	1.439(2)
O(4)-C(13)	1.429(2)
O(3)-C(15)	1.354(2)
O(3)-C(11)	1.467(2)
O(5)-C(13)	1.384(3)
O(5)-C(18)	1.416(3)
O(6)-C(10)	1.432(2)
O(6)-C(16)	1.418(3)
O(7)-C(16)	1.406(2)
O(7)-C(19)	1.430(2)
O(2)-C(15)	1.199(3)
O(1)-C(2)	1.217(3)
C(10)-H(10)	1.0000
C(10)-C(9)	1.536(3)
C(10)-C(11)	1.532(3)
C(29)-H(29)	0.9500
C(29)-C(28)	1.395(3)
C(29)-C(30)	1.391(3)
C(15)-C(14)	1.521(3)
C(28)-C(33)	1.393(3)
C(28)-C(19)	1.507(3)
C(9)-C(21)	1.528(3)
C(9)-C(8)	1.537(3)
C(9)-H(9)	0.94(3)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(6)-C(5)	1.556(3)
C(6)-C(11)	1.559(3)
C(6)-C(7)	1.521(3)
C(12)-C(1)	1.340(3)
C(12)-C(4)	1.511(3)
C(12)-C(11)	1.518(3)
C(5)-C(4)	1.549(3)
C(5)-C(14)	1.541(3)

C(5)-C(20)	1.528(3)
C(33)-H(33)	0.9500
C(33)-C(32)	1.387(3)
C(1)-C(2)	1.490(3)
C(1)-C(17)	1.491(3)
C(22)-C(27)	1.397(3)
C(22)-C(23)	1.384(3)
C(22)-C(18)	1.510(3)
C(4)-H(4)	1.0000
C(4)-C(3)	1.529(3)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(31)-H(31)	0.9500
C(31)-C(30)	1.390(3)
C(31)-C(32)	1.385(3)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(7)-C(8)	1.537(3)
C(30)-H(30)	0.9500
C(27)-H(27)	0.9500
C(27)-C(26)	1.389(3)
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800
C(32)-H(32)	0.9500
C(2)-C(3)	1.523(3)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(25)-H(25)	0.9500
C(25)-C(24)	1.379(3)
C(25)-C(26)	1.392(3)
C(23)-H(23)	0.9500

C(23)-C(24)	1.381(3)
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(24)-H(24)	0.9500
C(26)-H(26)	0.9500
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900

C(13)-O(4)-C(6)	119.45(16)
C(15)-O(3)-C(11)	118.19(15)
C(13)-O(5)-C(18)	112.66(18)
C(16)-O(6)-C(10)	112.76(15)
C(16)-O(7)-C(19)	112.65(16)
O(6)-C(10)-H(10)	108.6
O(6)-C(10)-C(9)	109.59(15)
O(6)-C(10)-C(11)	111.99(15)
C(9)-C(10)-H(10)	108.6
C(11)-C(10)-H(10)	108.6
C(11)-C(10)-C(9)	109.48(16)
C(28)-C(29)-H(29)	119.8
C(30)-C(29)-H(29)	119.8
C(30)-C(29)-C(28)	120.5(2)
O(3)-C(15)-C(14)	118.85(18)
O(2)-C(15)-O(3)	118.52(19)
O(2)-C(15)-C(14)	122.55(19)
C(29)-C(28)-C(19)	120.96(19)
C(33)-C(28)-C(29)	118.8(2)
C(33)-C(28)-C(19)	120.19(19)
C(10)-C(9)-C(8)	110.51(16)
C(10)-C(9)-H(9)	108.2(15)

C(21)-C(9)-C(10)	110.86(17)
C(21)-C(9)-C(8)	109.77(16)
C(21)-C(9)-H(9)	108.1(15)
C(8)-C(9)-H(9)	109.4(15)
O(6)-C(16)-H(16A)	109.0
O(6)-C(16)-H(16B)	109.0
O(7)-C(16)-O(6)	112.95(17)
O(7)-C(16)-H(16A)	109.0
O(7)-C(16)-H(16B)	109.0
H(16A)-C(16)-H(16B)	107.8
O(4)-C(6)-C(5)	110.72(16)
O(4)-C(6)-C(11)	103.40(15)
O(4)-C(6)-C(7)	111.10(16)
C(5)-C(6)-C(11)	100.27(15)
C(7)-C(6)-C(5)	120.16(17)
C(7)-C(6)-C(11)	109.33(16)
C(1)-C(12)-C(4)	114.03(17)
C(1)-C(12)-C(11)	133.24(19)
C(4)-C(12)-C(11)	108.62(17)
C(4)-C(5)-C(6)	99.35(16)
C(14)-C(5)-C(6)	106.56(16)
C(14)-C(5)-C(4)	111.53(17)
C(20)-C(5)-C(6)	116.95(17)
C(20)-C(5)-C(4)	112.65(18)
C(20)-C(5)-C(14)	109.38(18)
C(28)-C(33)-H(33)	119.6
C(32)-C(33)-C(28)	120.8(2)
C(32)-C(33)-H(33)	119.6
C(12)-C(1)-C(2)	107.81(19)
C(12)-C(1)-C(17)	130.82(19)
C(2)-C(1)-C(17)	121.18(18)
C(27)-C(22)-C(18)	121.9(2)
C(23)-C(22)-C(27)	118.9(2)
C(23)-C(22)-C(18)	119.2(2)
C(12)-C(4)-C(5)	101.40(16)
C(12)-C(4)-H(4)	108.9

C(12)-C(4)-C(3)	103.95(17)
C(5)-C(4)-H(4)	108.9
C(3)-C(4)-C(5)	123.74(19)
C(3)-C(4)-H(4)	108.9
C(15)-C(14)-C(5)	118.56(17)
C(15)-C(14)-H(14A)	107.7
C(15)-C(14)-H(14B)	107.7
C(5)-C(14)-H(14A)	107.7
C(5)-C(14)-H(14B)	107.7
H(14A)-C(14)-H(14B)	107.1
C(30)-C(31)-H(31)	120.0
C(32)-C(31)-H(31)	120.0
C(32)-C(31)-C(30)	120.0(2)
O(7)-C(19)-C(28)	109.14(17)
O(7)-C(19)-H(19A)	109.9
O(7)-C(19)-H(19B)	109.9
C(28)-C(19)-H(19A)	109.9
C(28)-C(19)-H(19B)	109.9
H(19A)-C(19)-H(19B)	108.3
O(3)-C(11)-C(10)	106.06(15)
O(3)-C(11)-C(6)	108.76(15)
O(3)-C(11)-C(12)	104.30(15)
C(10)-C(11)-C(6)	109.37(15)
C(12)-C(11)-C(10)	124.31(17)
C(12)-C(11)-C(6)	103.31(16)
C(6)-C(7)-H(7A)	109.7
C(6)-C(7)-H(7B)	109.7
C(6)-C(7)-C(8)	109.69(17)
H(7A)-C(7)-H(7B)	108.2
C(8)-C(7)-H(7A)	109.7
C(8)-C(7)-H(7B)	109.7
C(29)-C(30)-H(30)	120.0
C(31)-C(30)-C(29)	120.0(2)
C(31)-C(30)-H(30)	120.0
C(22)-C(27)-H(27)	119.7
C(26)-C(27)-C(22)	120.6(2)

C(26)-C(27)-H(27)	119.7
C(9)-C(21)-H(21A)	109.5
C(9)-C(21)-H(21B)	109.5
C(9)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(33)-C(32)-H(32)	120.0
C(31)-C(32)-C(33)	120.0(2)
C(31)-C(32)-H(32)	120.0
O(1)-C(2)-C(1)	125.7(2)
O(1)-C(2)-C(3)	125.8(2)
C(1)-C(2)-C(3)	108.36(17)
C(9)-C(8)-H(8A)	108.6
C(9)-C(8)-H(8B)	108.6
C(7)-C(8)-C(9)	114.61(16)
C(7)-C(8)-H(8A)	108.6
C(7)-C(8)-H(8B)	108.6
H(8A)-C(8)-H(8B)	107.6
C(4)-C(3)-H(3A)	110.9
C(4)-C(3)-H(3B)	110.9
C(2)-C(3)-C(4)	104.41(17)
C(2)-C(3)-H(3A)	110.9
C(2)-C(3)-H(3B)	110.9
H(3A)-C(3)-H(3B)	108.9
C(24)-C(25)-H(25)	120.0
C(24)-C(25)-C(26)	120.0(2)
C(26)-C(25)-H(25)	120.0
C(22)-C(23)-H(23)	119.7
C(24)-C(23)-C(22)	120.6(2)
C(24)-C(23)-H(23)	119.7
C(5)-C(20)-H(20A)	109.5
C(5)-C(20)-H(20B)	109.5
C(5)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20C)	109.5

H(20B)-C(20)-H(20C)	109.5
C(1)-C(17)-H(17A)	109.5
C(1)-C(17)-H(17B)	109.5
C(1)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(25)-C(24)-C(23)	120.4(2)
C(25)-C(24)-H(24)	119.8
C(23)-C(24)-H(24)	119.8
C(27)-C(26)-C(25)	119.4(2)
C(27)-C(26)-H(26)	120.3
C(25)-C(26)-H(26)	120.3
O(4)-C(13)-H(13A)	110.1
O(4)-C(13)-H(13B)	110.1
O(5)-C(13)-O(4)	107.86(18)
O(5)-C(13)-H(13A)	110.1
O(5)-C(13)-H(13B)	110.1
H(13A)-C(13)-H(13B)	108.4
O(5)-C(18)-C(22)	108.78(18)
O(5)-C(18)-H(18A)	109.9
O(5)-C(18)-H(18B)	109.9
C(22)-C(18)-H(18A)	109.9
C(22)-C(18)-H(18B)	109.9
H(18A)-C(18)-H(18B)	108.3

Symmetry transformations used to generate equivalent atoms:

Table S7. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for p16083_O_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(4)	17(1)	11(1)	24(1)	-3(1)	-1(1)	-1(1)
O(3)	15(1)	16(1)	16(1)	0(1)	-1(1)	-3(1)
O(5)	18(1)	19(1)	24(1)	-6(1)	2(1)	-3(1)
O(6)	18(1)	14(1)	19(1)	-1(1)	-1(1)	2(1)
O(7)	21(1)	23(1)	16(1)	-1(1)	-4(1)	2(1)
O(2)	27(1)	30(1)	25(1)	0(1)	-6(1)	-12(1)
O(1)	36(1)	46(1)	19(1)	-9(1)	4(1)	11(1)
C(10)	15(1)	14(1)	16(1)	-2(1)	0(1)	1(1)
C(29)	19(1)	21(1)	20(1)	1(1)	-2(1)	3(1)
C(15)	17(1)	22(1)	15(1)	-2(1)	1(1)	-1(1)
C(28)	17(1)	20(1)	17(1)	1(1)	0(1)	-1(1)
C(9)	18(1)	18(1)	15(1)	-2(1)	1(1)	-1(1)
C(16)	18(1)	22(1)	18(1)	-5(1)	-2(1)	6(1)
C(6)	15(1)	15(1)	17(1)	-2(1)	-1(1)	-1(1)
C(12)	14(1)	19(1)	16(1)	-1(1)	0(1)	-2(1)
C(5)	22(1)	16(1)	17(1)	2(1)	-1(1)	-1(1)
C(33)	22(1)	22(1)	22(1)	4(1)	-2(1)	1(1)
C(1)	18(1)	23(1)	17(1)	-4(1)	2(1)	1(1)
C(22)	18(1)	23(1)	30(1)	-13(1)	4(1)	3(1)
C(4)	22(1)	19(1)	17(1)	0(1)	2(1)	-4(1)
C(14)	23(1)	22(1)	16(1)	1(1)	-2(1)	0(1)
C(31)	22(1)	32(1)	17(1)	-5(1)	1(1)	-3(1)
C(19)	24(1)	19(1)	20(1)	1(1)	-5(1)	2(1)
C(11)	14(1)	13(1)	16(1)	-2(1)	1(1)	-2(1)
C(7)	17(1)	18(1)	20(1)	-4(1)	0(1)	3(1)
C(30)	25(1)	22(1)	24(1)	-3(1)	2(1)	1(1)
C(27)	25(1)	18(1)	34(1)	-4(1)	8(1)	1(1)
C(21)	24(1)	27(1)	16(1)	-2(1)	2(1)	1(1)
C(32)	21(1)	34(1)	16(1)	3(1)	-3(1)	-2(1)
C(2)	18(1)	32(1)	18(1)	-4(1)	2(1)	-1(1)
C(8)	19(1)	22(1)	19(1)	-3(1)	5(1)	5(1)

C(3)	30(1)	28(1)	17(1)	1(1)	6(1)	-3(1)
C(25)	21(1)	23(1)	39(1)	-5(1)	-7(1)	0(1)
C(23)	22(1)	21(1)	28(1)	-3(1)	0(1)	6(1)
C(20)	35(1)	20(1)	23(1)	6(1)	-1(1)	0(1)
C(17)	27(1)	22(1)	21(1)	-7(1)	0(1)	7(1)
C(24)	25(1)	16(1)	37(1)	0(1)	2(1)	1(1)
C(26)	26(1)	25(1)	29(1)	1(1)	-2(1)	7(1)
C(13)	24(1)	15(1)	46(1)	-7(1)	-6(1)	0(1)
C(18)	26(1)	42(1)	31(1)	-16(1)	9(1)	-9(1)

Table S8. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for p16083_O_a.

	x	y	z	U(eq)
H(10)	3165	5713	3890	18
H(29)	5591	6245	4528	24
H(16A)	5153	2728	3811	23
H(16B)	5086	4090	3584	23
H(33)	7660	2929	4999	26
H(4)	3460	7067	2956	24
H(14A)	-1976	6540	2927	24
H(14B)	-715	5823	2642	24
H(31)	8288	6556	5469	29
H(19A)	6507	2780	4388	25
H(19B)	4541	3288	4486	25
H(7A)	-1673	6492	3591	22
H(7B)	-1032	8002	3665	22
H(30)	6721	7562	4996	28
H(27)	6506	9030	4287	31
H(21A)	1624	4092	4517	33
H(21B)	339	5271	4651	33
H(21C)	2334	5605	4530	33
H(32)	8761	4240	5469	28
H(8A)	-1211	6719	4213	24
H(8B)	731	7325	4149	24
H(3A)	1787	5946	2353	30
H(3B)	3791	6507	2383	30
H(25)	10541	11720	4290	33
H(23)	7554	11230	3397	29
H(20A)	-674	8787	2998	39
H(20B)	-10	8328	2607	39
H(20C)	1376	8942	2889	39
H(17A)	4612	2466	3107	35
H(17B)	3028	2077	2838	35

H(17C)	2597	2491	3245	35
H(24)	9888	12275	3696	31
H(26)	8849	10086	4589	32
H(13A)	2100	9520	3424	34
H(13B)	1182	9074	3796	34
H(18A)	5044	9865	3383	40
H(18B)	5641	8438	3542	40
H(9)	-210(30)	4610(20)	4046(6)	17(6)

Table S9. Torsion angles [°] for p16083_O_a.

O(4)-C(6)-C(5)-C(4)	58.24(19)
O(4)-C(6)-C(5)-C(14)	174.15(16)
O(4)-C(6)-C(5)-C(20)	-63.2(2)
O(4)-C(6)-C(11)-O(3)	170.36(14)
O(4)-C(6)-C(11)-C(10)	54.95(19)
O(4)-C(6)-C(11)-C(12)	-79.25(17)
O(4)-C(6)-C(7)-C(8)	-56.4(2)
O(3)-C(15)-C(14)-C(5)	6.1(3)
O(6)-C(10)-C(9)-C(21)	59.6(2)
O(6)-C(10)-C(9)-C(8)	-178.50(15)
O(6)-C(10)-C(11)-O(3)	66.60(19)
O(6)-C(10)-C(11)-C(6)	-176.28(15)
O(6)-C(10)-C(11)-C(12)	-53.9(2)
O(2)-C(15)-C(14)-C(5)	-177.2(2)
O(1)-C(2)-C(3)-C(4)	-172.6(2)
C(10)-O(6)-C(16)-O(7)	66.2(2)
C(10)-C(9)-C(8)-C(7)	51.7(2)
C(29)-C(28)-C(33)-C(32)	0.3(3)
C(29)-C(28)-C(19)-O(7)	31.6(3)
C(15)-O(3)-C(11)-C(10)	166.62(15)
C(15)-O(3)-C(11)-C(6)	49.1(2)
C(15)-O(3)-C(11)-C(12)	-60.6(2)
C(28)-C(29)-C(30)-C(31)	-0.5(3)
C(28)-C(33)-C(32)-C(31)	-0.3(3)
C(9)-C(10)-C(11)-O(3)	-55.16(19)
C(9)-C(10)-C(11)-C(6)	61.96(19)
C(9)-C(10)-C(11)-C(12)	-175.67(17)
C(16)-O(6)-C(10)-C(9)	-143.36(17)
C(16)-O(6)-C(10)-C(11)	94.94(19)
C(16)-O(7)-C(19)-C(28)	-171.20(17)
C(6)-O(4)-C(13)-O(5)	165.61(17)
C(6)-C(5)-C(4)-C(12)	46.43(18)
C(6)-C(5)-C(4)-C(3)	161.92(18)
C(6)-C(5)-C(14)-C(15)	-35.0(2)

C(6)-C(7)-C(8)-C(9)	-52.8(2)
C(12)-C(1)-C(2)-O(1)	175.9(2)
C(12)-C(1)-C(2)-C(3)	-8.8(2)
C(12)-C(4)-C(3)-C(2)	-10.5(2)
C(5)-C(6)-C(11)-O(3)	-75.25(17)
C(5)-C(6)-C(11)-C(10)	169.34(16)
C(5)-C(6)-C(11)-C(12)	35.13(18)
C(5)-C(6)-C(7)-C(8)	172.11(17)
C(5)-C(4)-C(3)-C(2)	-124.8(2)
C(33)-C(28)-C(19)-O(7)	-150.05(19)
C(1)-C(12)-C(4)-C(5)	135.25(18)
C(1)-C(12)-C(4)-C(3)	5.9(2)
C(1)-C(12)-C(11)-O(3)	-47.8(3)
C(1)-C(12)-C(11)-C(10)	73.5(3)
C(1)-C(12)-C(11)-C(6)	-161.5(2)
C(1)-C(2)-C(3)-C(4)	12.0(2)
C(22)-C(27)-C(26)-C(25)	-0.3(3)
C(22)-C(23)-C(24)-C(25)	0.1(3)
C(4)-C(12)-C(1)-C(2)	1.7(2)
C(4)-C(12)-C(1)-C(17)	-173.2(2)
C(4)-C(12)-C(11)-O(3)	107.26(18)
C(4)-C(12)-C(11)-C(10)	-131.43(19)
C(4)-C(12)-C(11)-C(6)	-6.4(2)
C(4)-C(5)-C(14)-C(15)	72.4(2)
C(14)-C(5)-C(4)-C(12)	-65.6(2)
C(14)-C(5)-C(4)-C(3)	49.9(3)
C(19)-O(7)-C(16)-O(6)	76.3(2)
C(19)-C(28)-C(33)-C(32)	-178.1(2)
C(11)-O(3)-C(15)-O(2)	170.39(18)
C(11)-O(3)-C(15)-C(14)	-12.7(2)
C(11)-C(10)-C(9)-C(21)	-177.25(16)
C(11)-C(10)-C(9)-C(8)	-55.3(2)
C(11)-C(6)-C(5)-C(4)	-50.44(17)
C(11)-C(6)-C(5)-C(14)	65.47(19)
C(11)-C(6)-C(5)-C(20)	-171.89(19)
C(11)-C(6)-C(7)-C(8)	57.1(2)

C(11)-C(12)-C(1)-C(2)	155.8(2)
C(11)-C(12)-C(1)-C(17)	-19.2(4)
C(11)-C(12)-C(4)-C(5)	-25.1(2)
C(11)-C(12)-C(4)-C(3)	-154.45(17)
C(7)-C(6)-C(5)-C(4)	-170.07(17)
C(7)-C(6)-C(5)-C(14)	-54.2(2)
C(7)-C(6)-C(5)-C(20)	68.5(3)
C(7)-C(6)-C(11)-O(3)	52.0(2)
C(7)-C(6)-C(11)-C(10)	-63.5(2)
C(7)-C(6)-C(11)-C(12)	162.34(16)
C(30)-C(29)-C(28)-C(33)	0.0(3)
C(30)-C(29)-C(28)-C(19)	178.5(2)
C(30)-C(31)-C(32)-C(33)	-0.2(4)
C(27)-C(22)-C(23)-C(24)	-0.6(3)
C(27)-C(22)-C(18)-O(5)	47.4(3)
C(21)-C(9)-C(8)-C(7)	174.31(18)
C(32)-C(31)-C(30)-C(29)	0.5(4)
C(23)-C(22)-C(27)-C(26)	0.7(3)
C(23)-C(22)-C(18)-O(5)	-134.1(2)
C(20)-C(5)-C(4)-C(12)	170.93(17)
C(20)-C(5)-C(4)-C(3)	-73.6(3)
C(20)-C(5)-C(14)-C(15)	-162.34(18)
C(17)-C(1)-C(2)-O(1)	-8.6(4)
C(17)-C(1)-C(2)-C(3)	166.7(2)
C(24)-C(25)-C(26)-C(27)	-0.2(3)
C(26)-C(25)-C(24)-C(23)	0.3(3)
C(13)-O(4)-C(6)-C(5)	88.7(2)
C(13)-O(4)-C(6)-C(11)	-164.68(18)
C(13)-O(4)-C(6)-C(7)	-47.5(2)
C(13)-O(5)-C(18)-C(22)	169.40(19)
C(18)-O(5)-C(13)-O(4)	67.5(2)
C(18)-C(22)-C(27)-C(26)	179.2(2)
C(18)-C(22)-C(23)-C(24)	-179.2(2)

Symmetry transformations used to generate equivalent atoms:

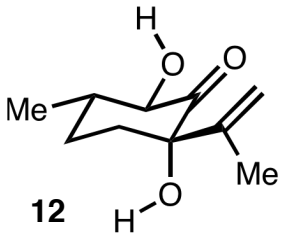
KVC25-169

Sample Name:
KVC25-169
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-169
FidFile: PROTON02

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 17 2016

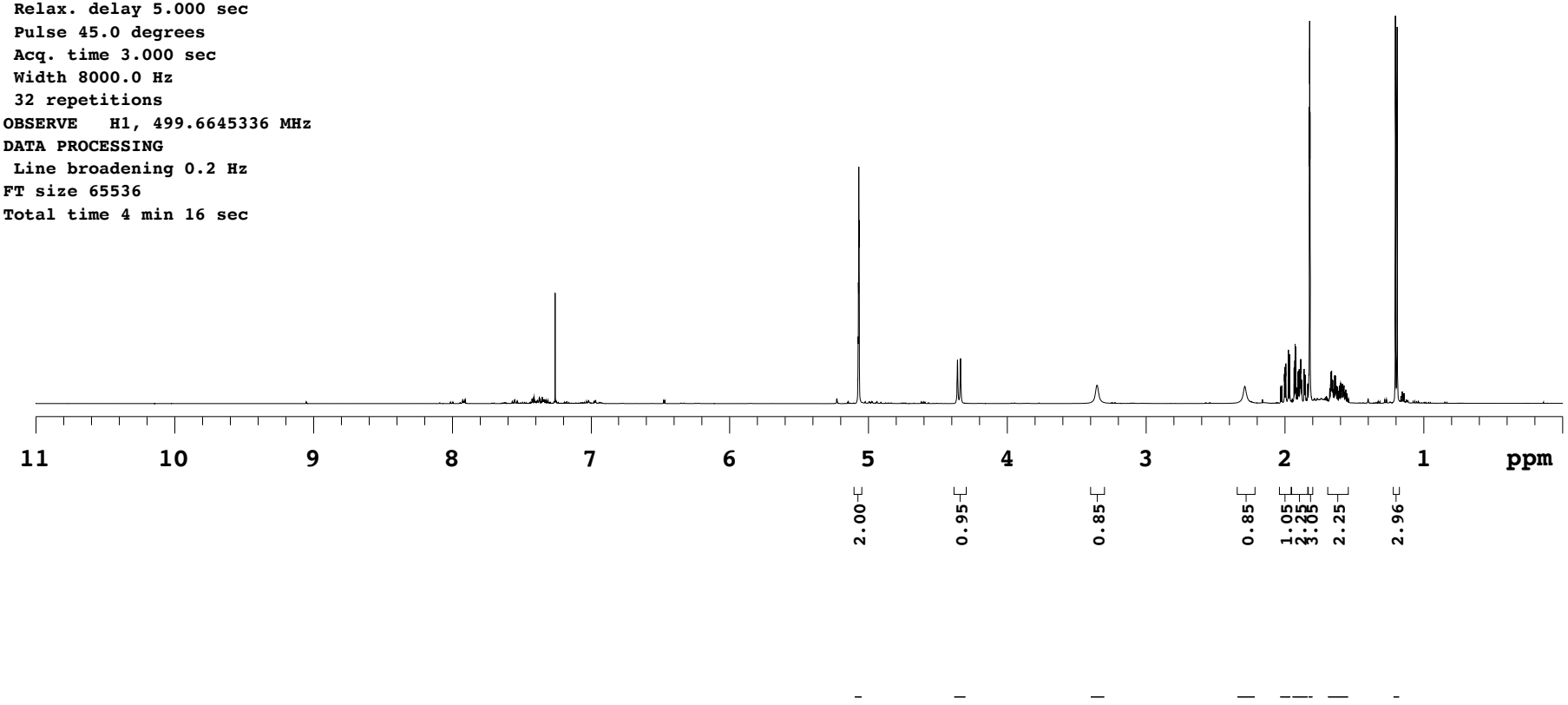
Sample #22, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645336 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



12

(120 mmol scale reaction)



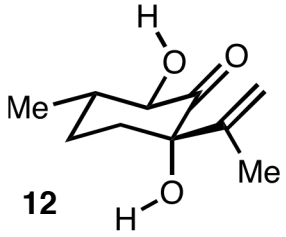
KVC25-169-Repurified

Sample Name:
KVC25-169-Repurified
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-169-Repurified
FidFile: PROTON01

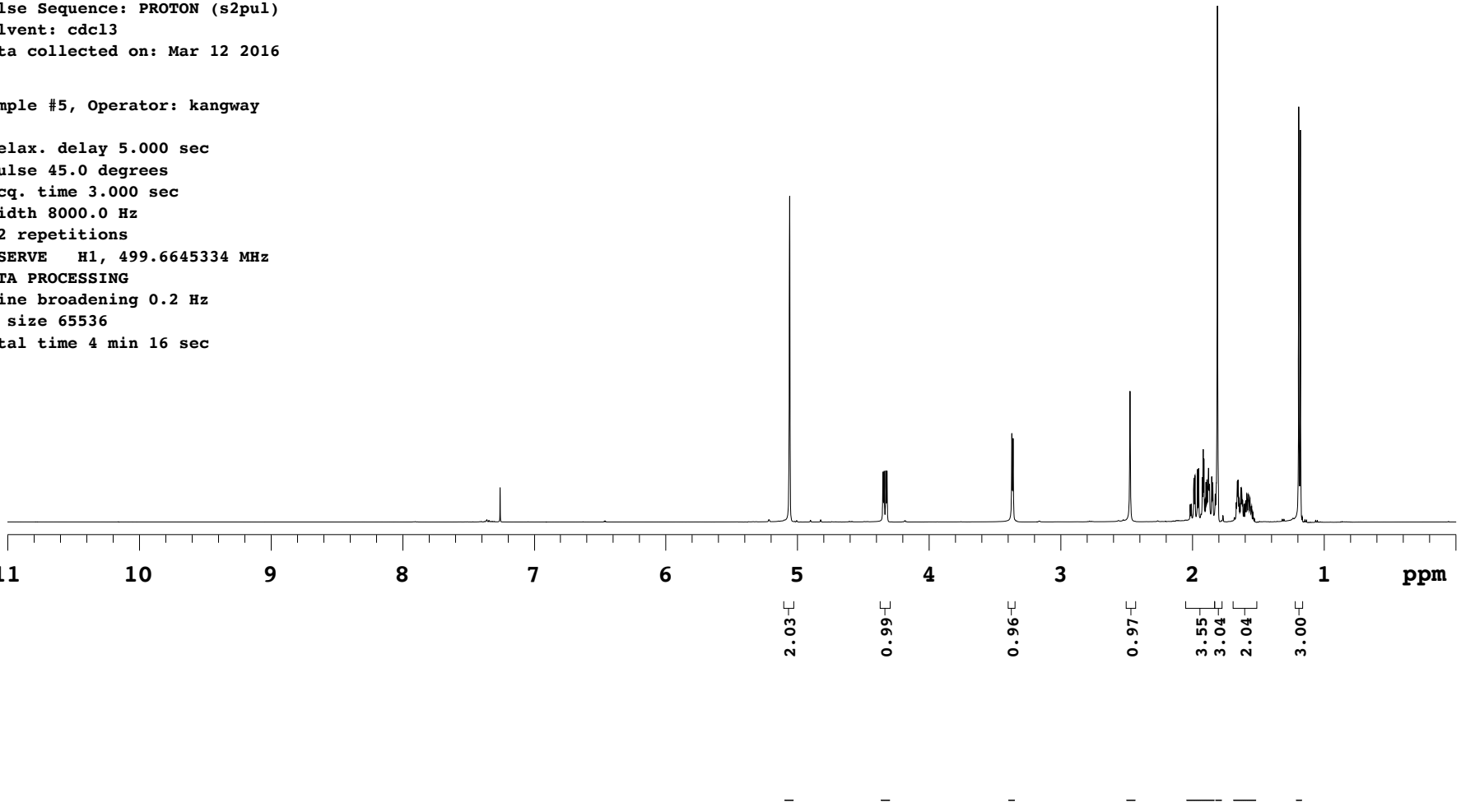
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 12 2016

Sample #5, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645334 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



12



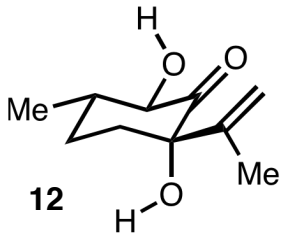
KVC25-169-Repurified

Sample Name:
KVC25-169-Repurified
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-169-Repurified
FidFile: CARBON01

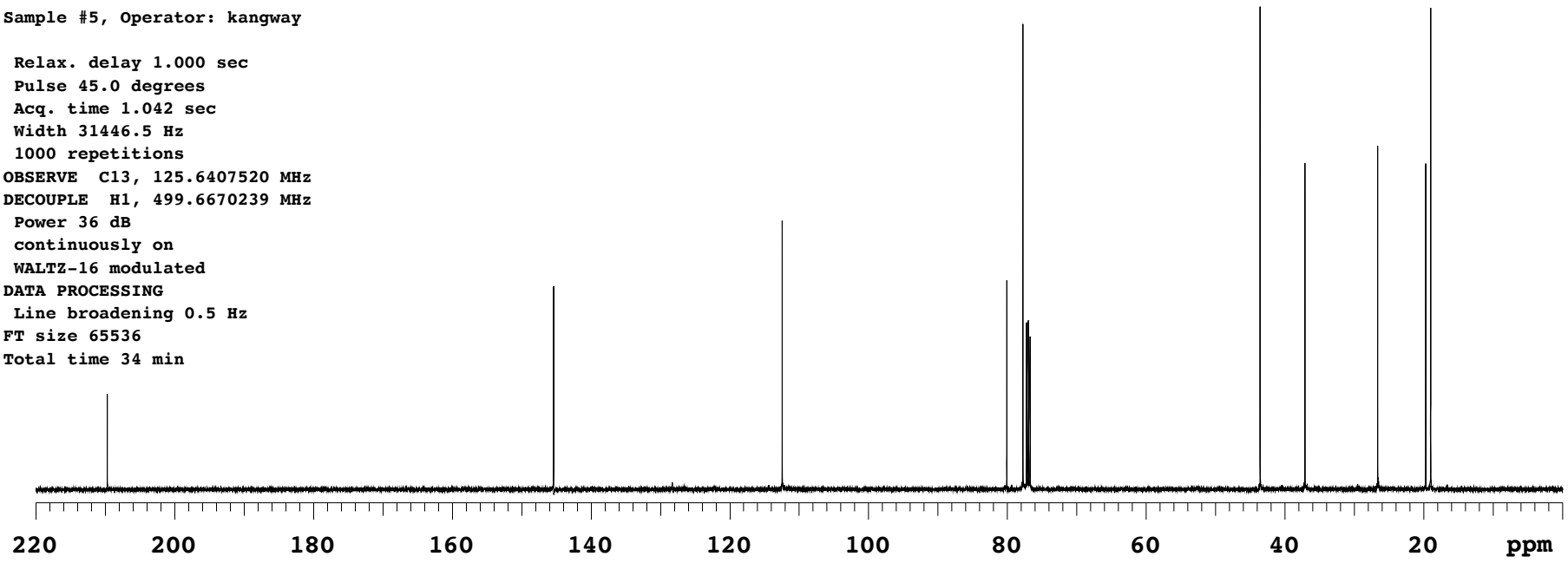
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 12 2016

Sample #5, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407520 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



12



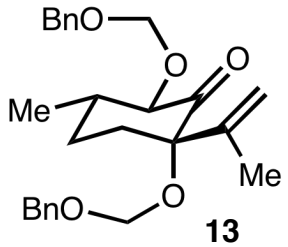
KVC25-171

Sample Name:
KVC25-171
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-171
FidFile: PROTON02

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 20 2016

Sample #28, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec



13

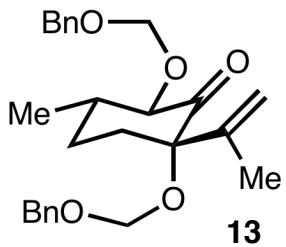
KVC25-171

Sample Name:
KVC25-171
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-171
FidFile: CARBON01

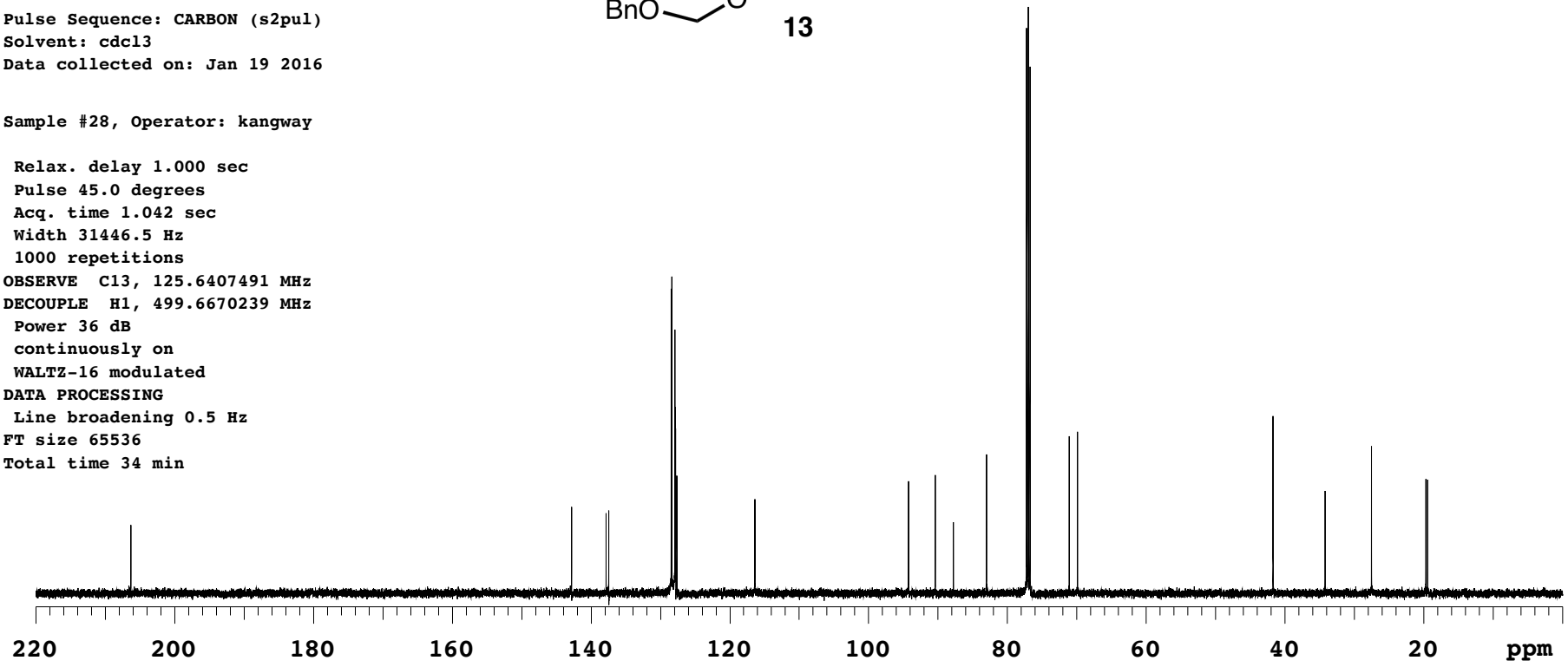
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 19 2016

Sample #28, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407491 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



13



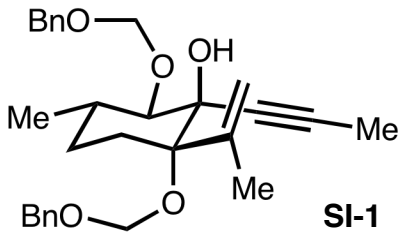
Major Diastereomer

Sample Name:
KVC25-173-Major
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-173-Major
FidFile: PROTON01

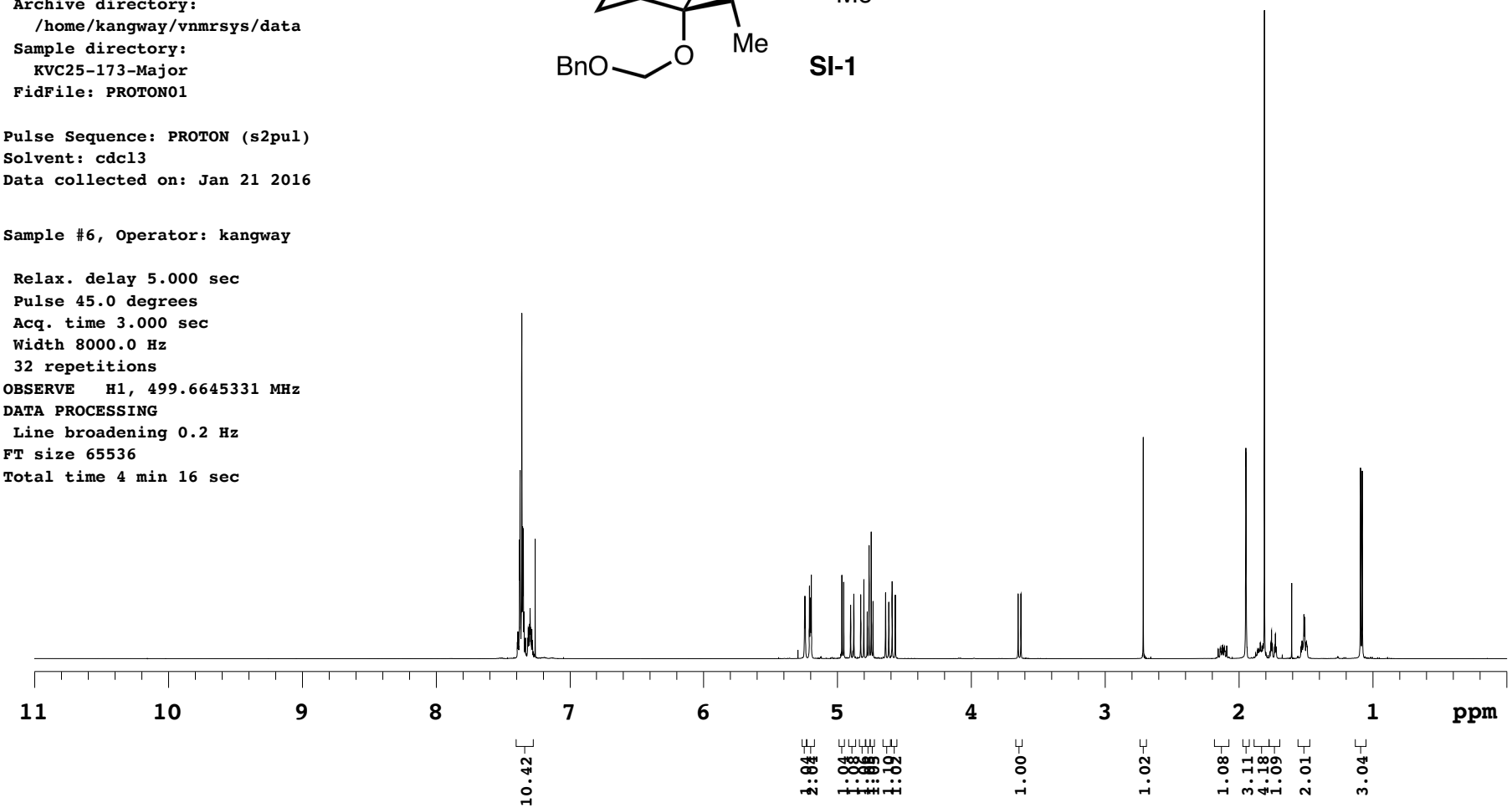
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #6, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



SI-1



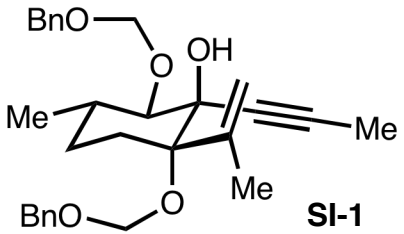
Major Diastereomer

Sample Name:
KVC25-173-Major
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-173-Major
FidFile: CARBON01

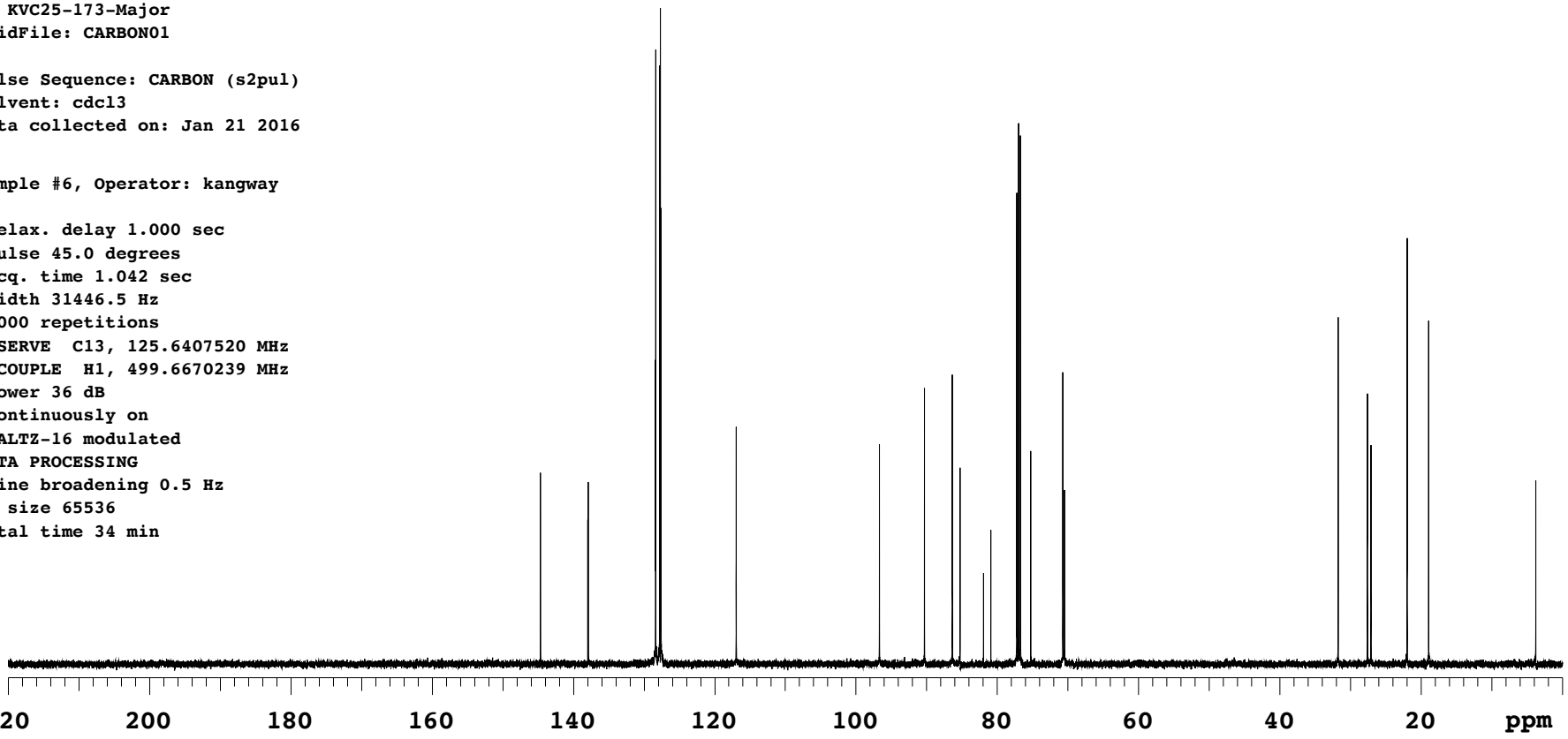
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #6, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407520 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



SI-1



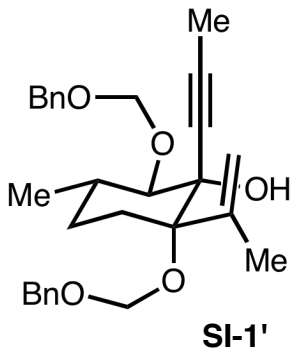
Minor Diastereomer

Sample Name:
KVC25-173-Minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-173-Minor
FidFile: PROTON01

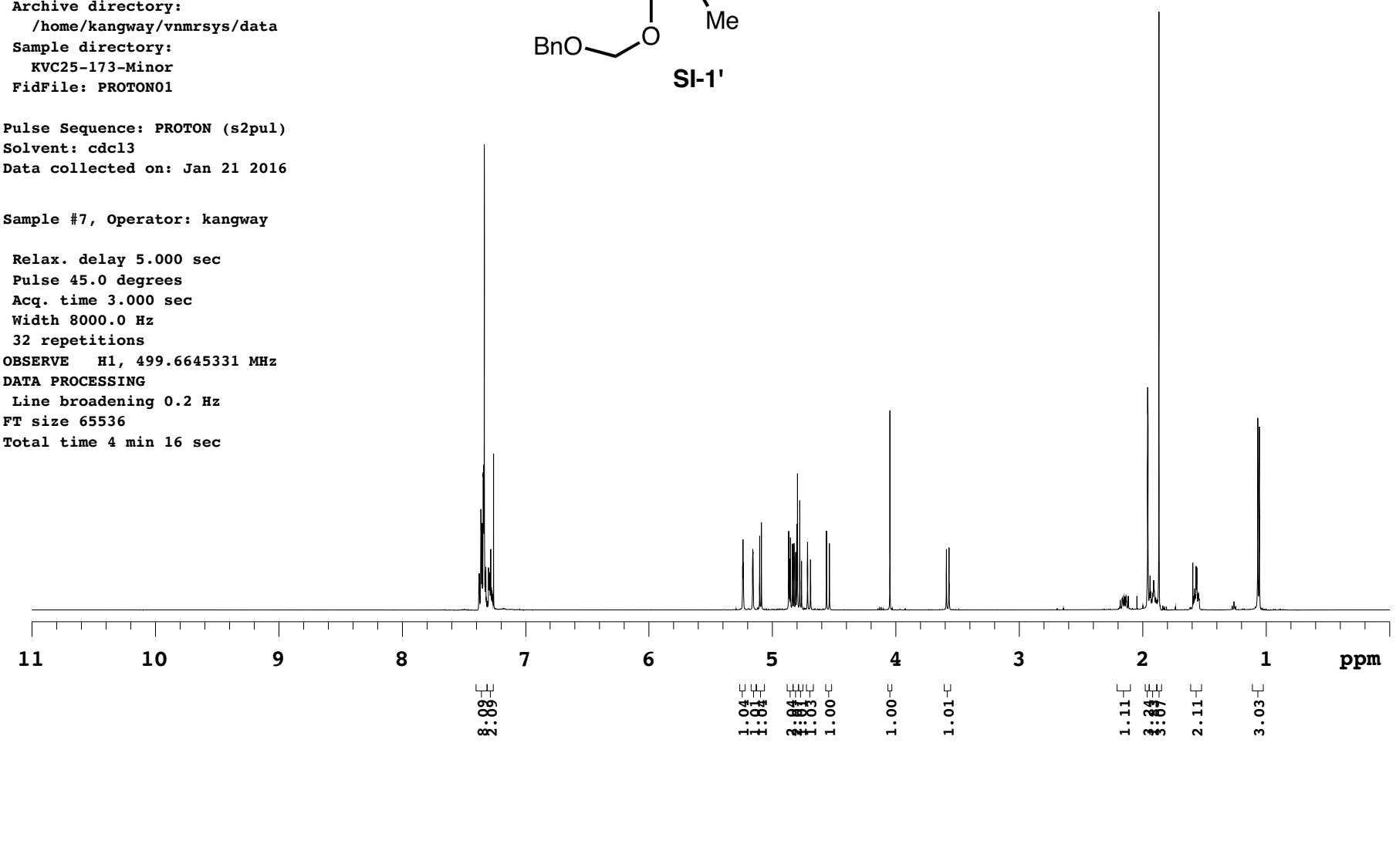
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #7, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



SI-1'



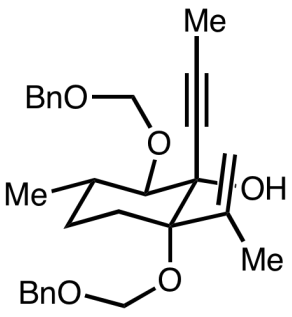
Minor Diastereomer

Sample Name:
KVC25-173-Minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-173-Minor
FidFile: CARBON01

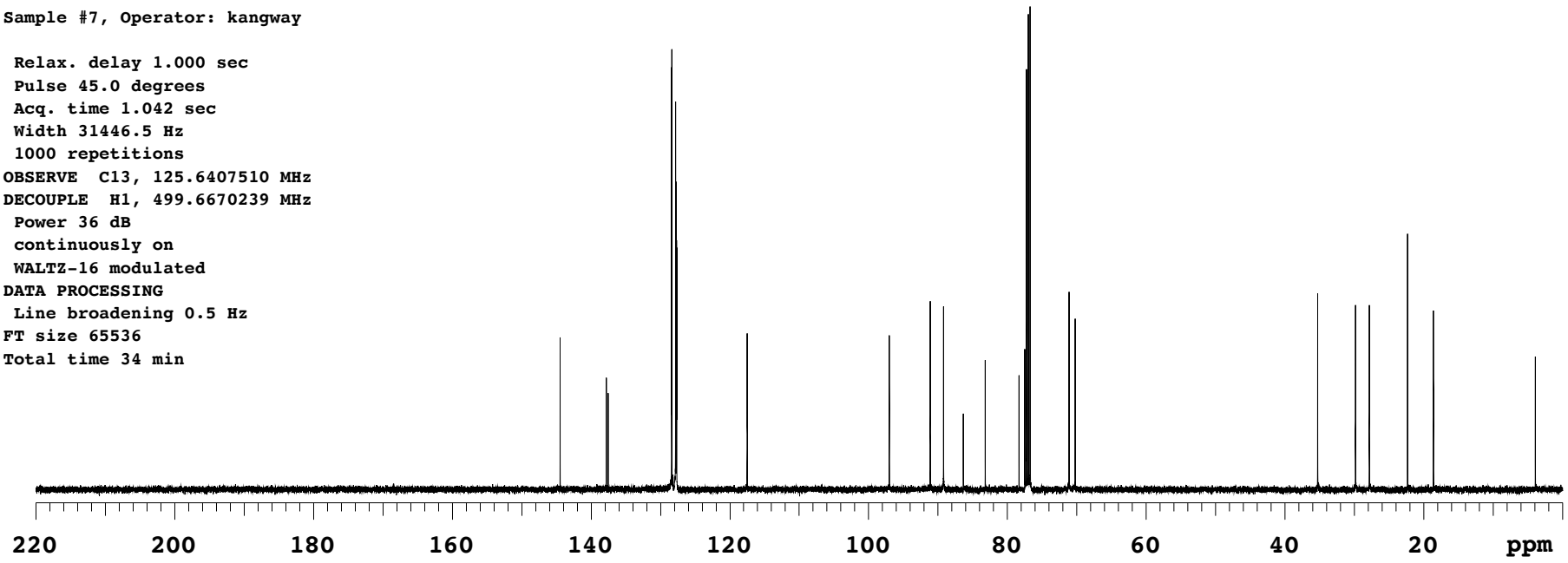
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #7, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407510 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



SI-1'



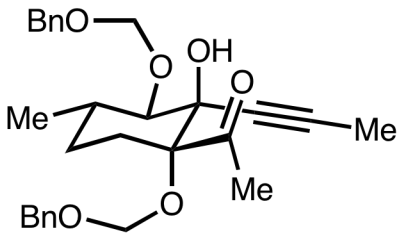
KVC25-175

Sample Name:
KVC25-175
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-175
FidFile: PROTON01

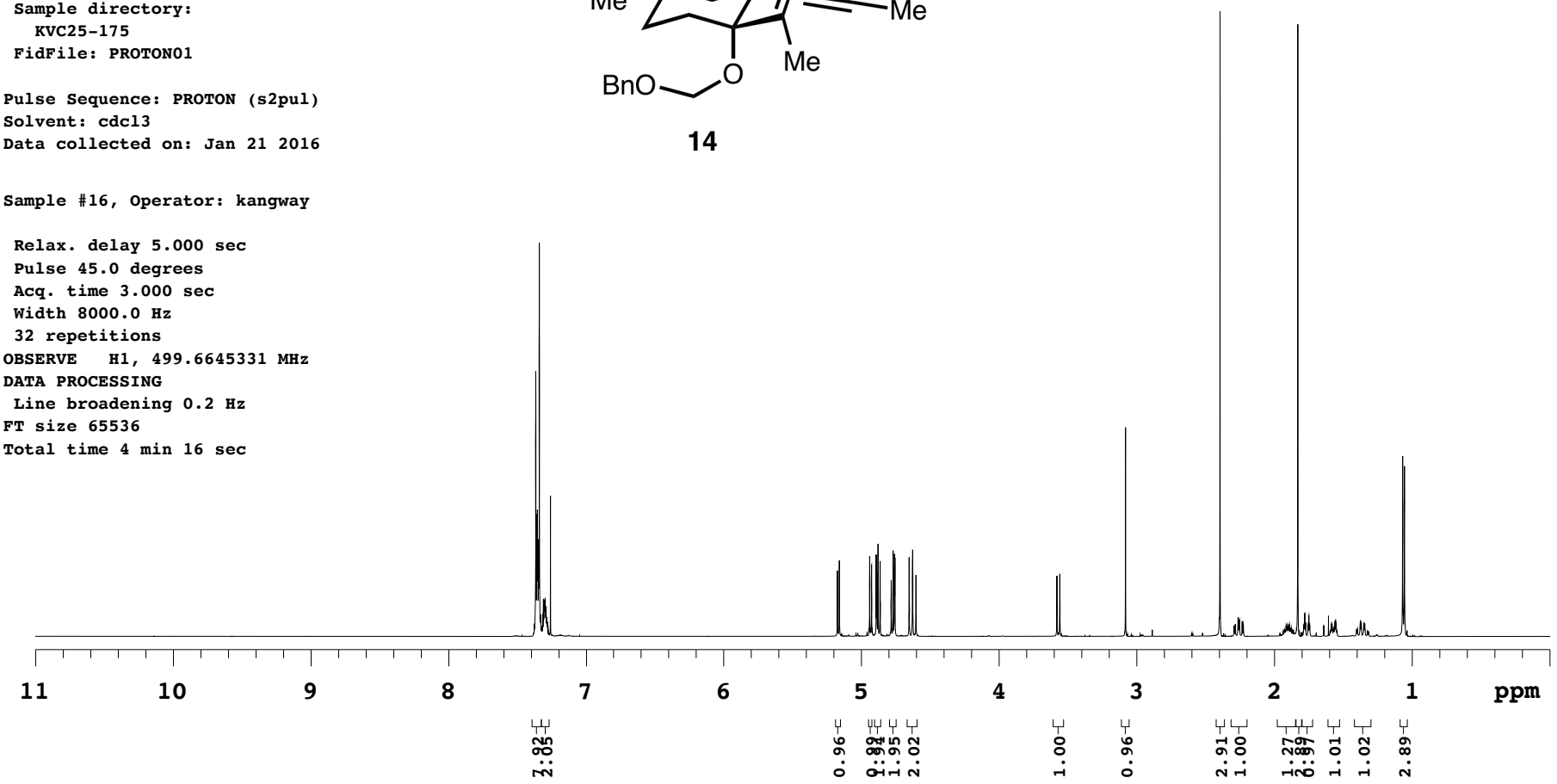
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #16, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



14



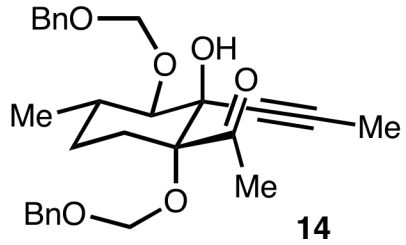
KVC25-175

Sample Name:
KVC25-175
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-175
FidFile: CARBON01

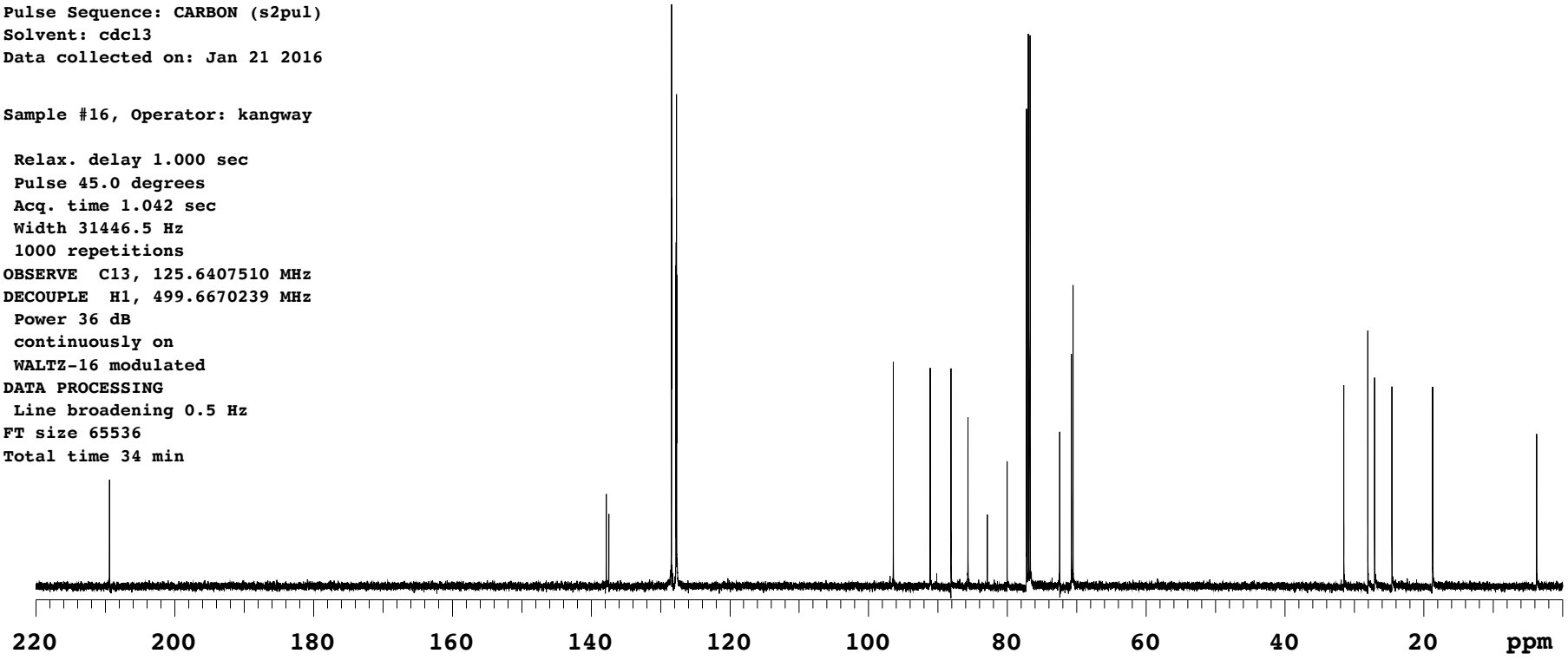
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #16, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407510 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



14



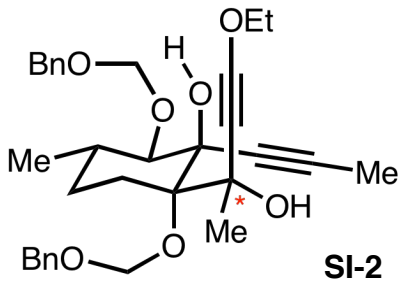
KVC25-177

Sample Name:
KVC25-177
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-177
FidFile: PROTON03

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 24 2016

Sample #28, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec



SI-2

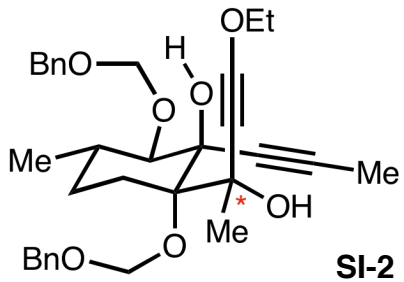
KVC25-177

Sample Name:
KVC25-177
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-177
FidFile: CARBON01

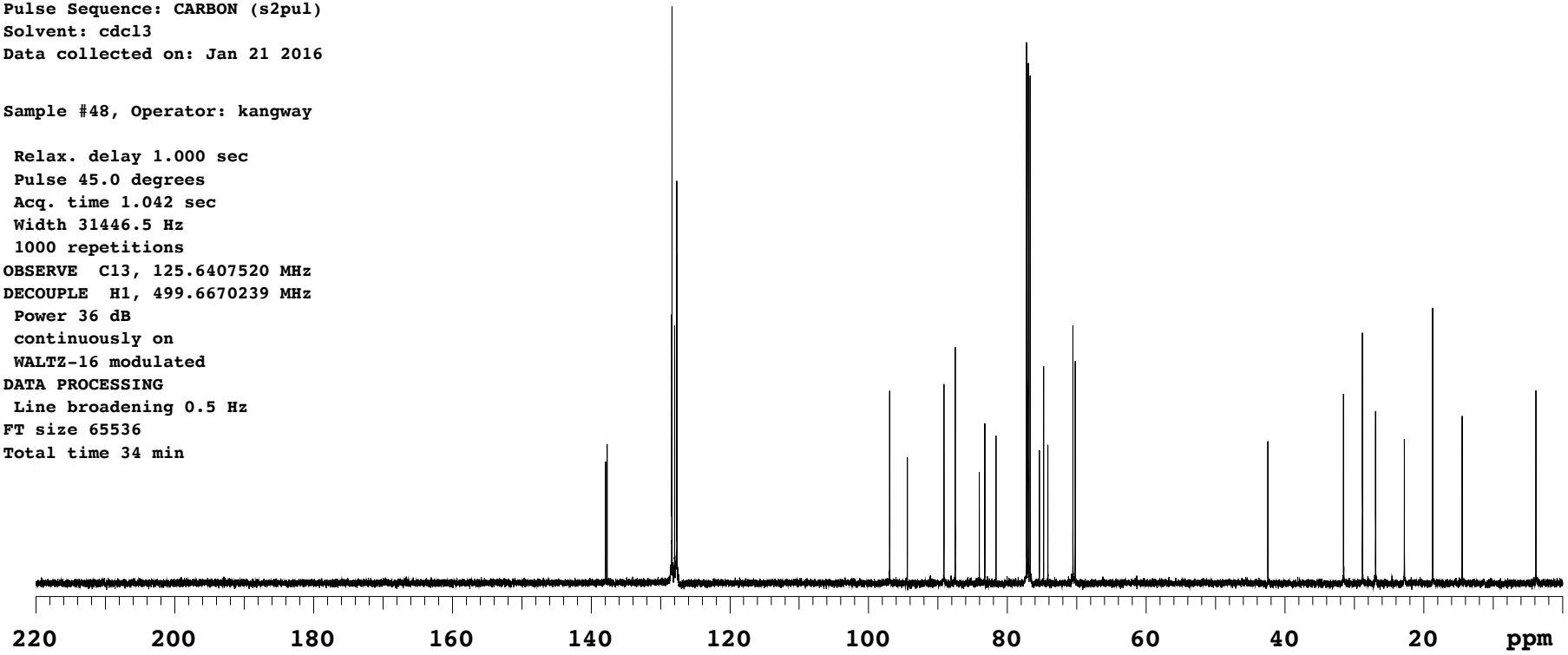
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2016

Sample #48, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407520 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



SI-2



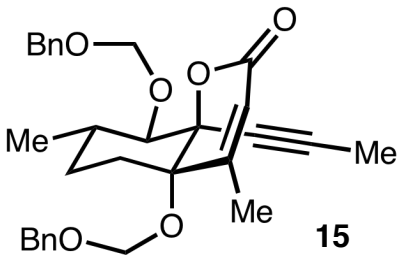
KVC25-179

Sample Name:
KVC25-179
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-179
FidFile: PROTON03

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 24 2016

Sample #29, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec



15

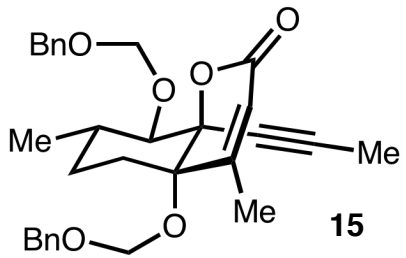
KVC25-179

Sample Name:
KVC25-179
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-179
FidFile: CARBON02

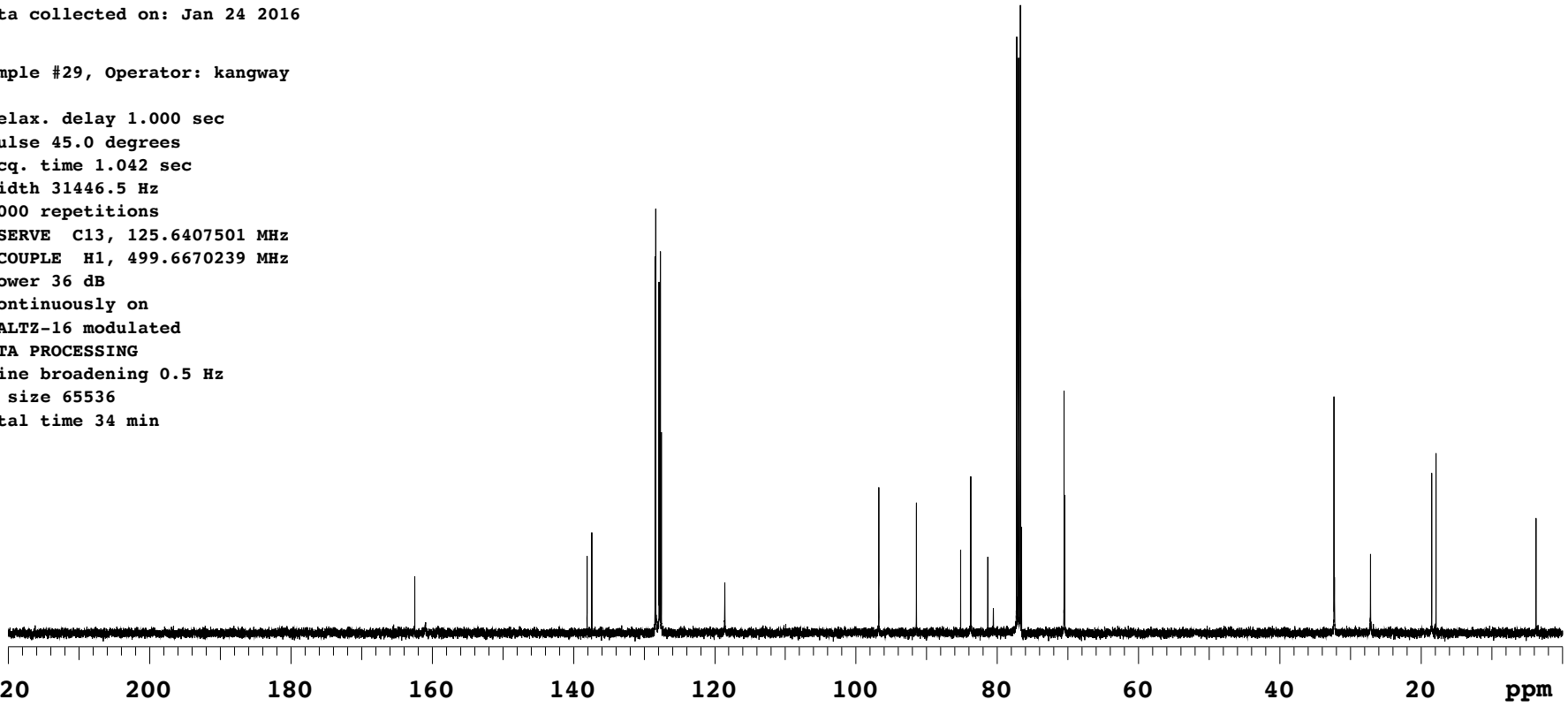
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 24 2016

Sample #29, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407501 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



15



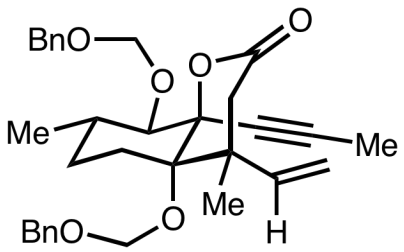
KVC25-181

Sample Name:
KVC25-181
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-181
FidFile: PROTON01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2016

Sample #21, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



16

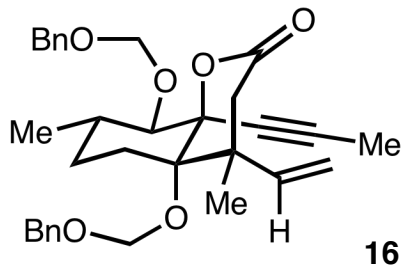
KVC25-181

Sample Name:
KVC25-181
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-181
FidFile: CARBON01

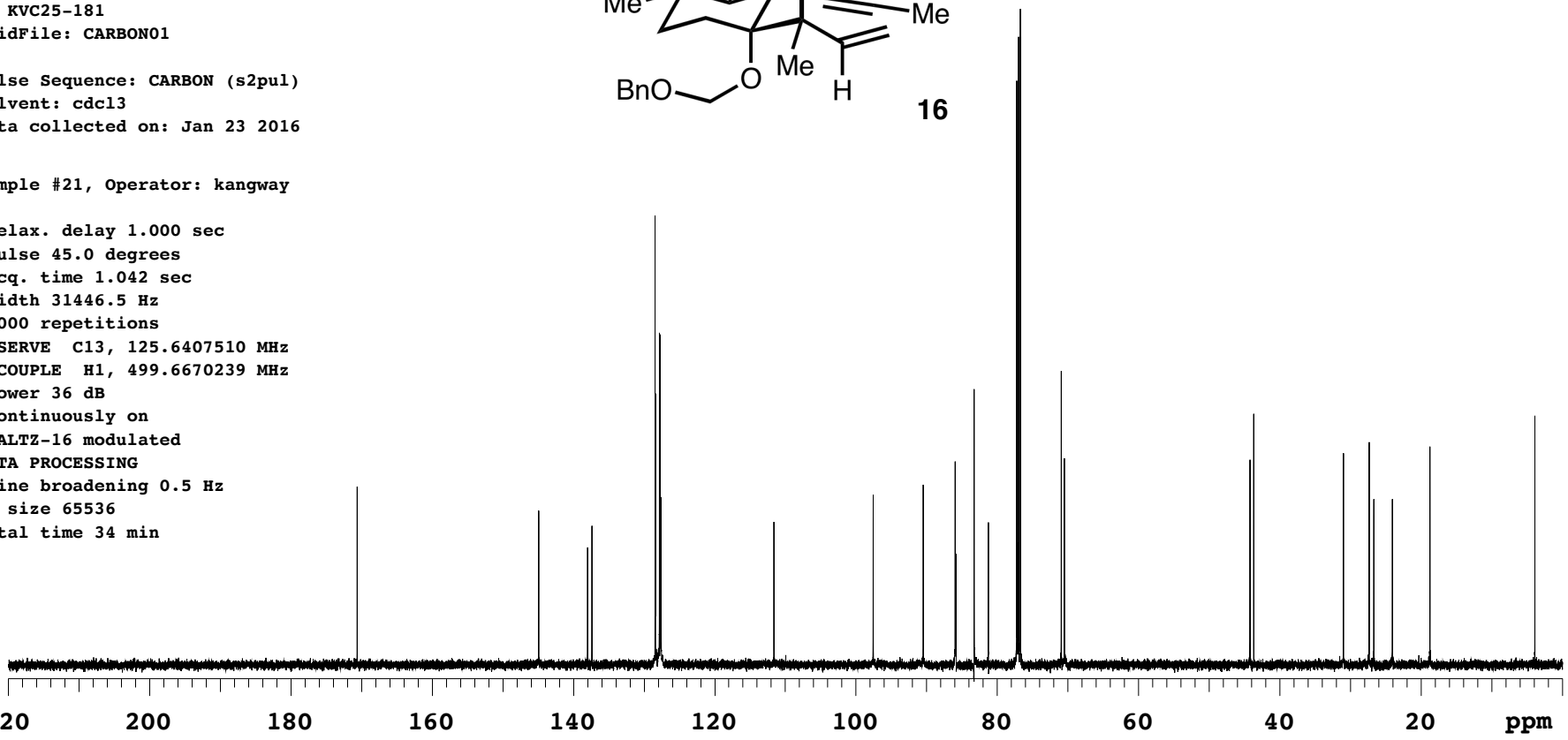
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2016

Sample #21, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407510 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



16



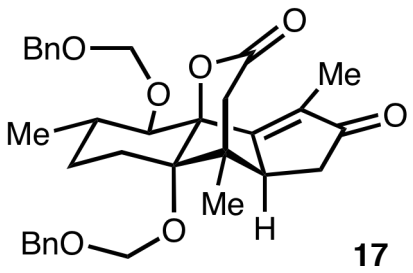
KVC25-183

Sample Name:
KVC25-183
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-183
FidFile: PROTON01

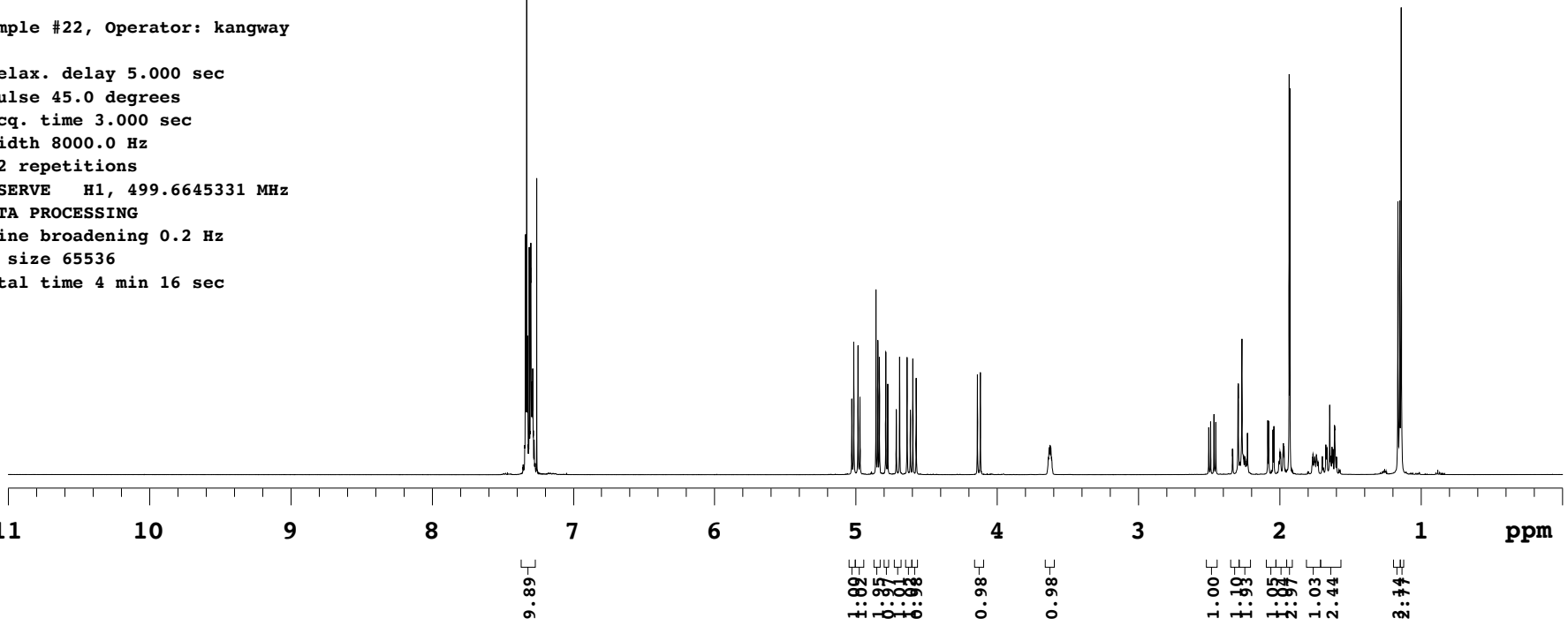
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 24 2016

Sample #22, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



17



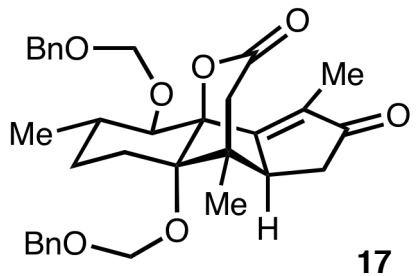
KVC25-183

Sample Name:
KVC25-183
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-183
FidFile: CARBON01

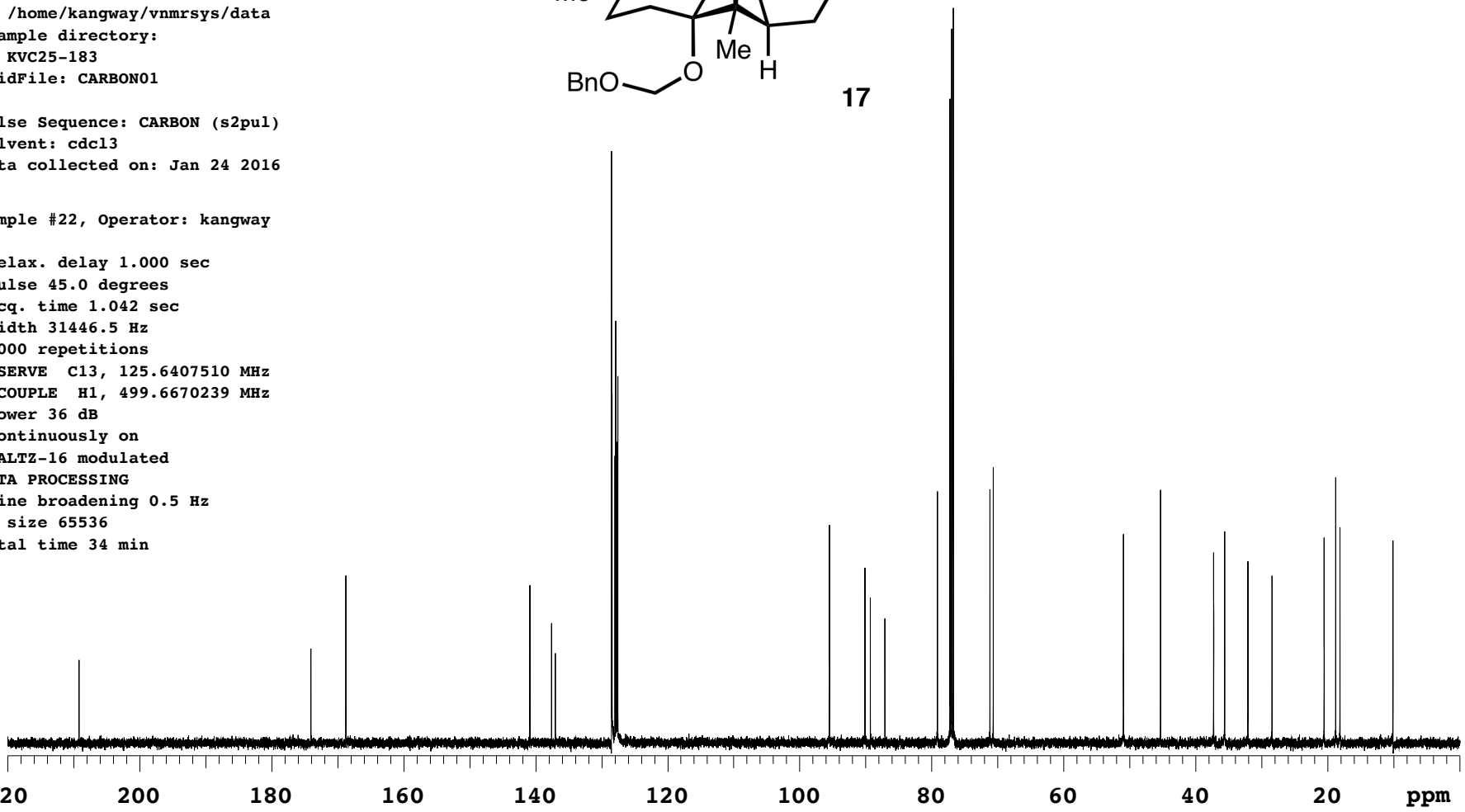
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 24 2016

Sample #22, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407510 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



17



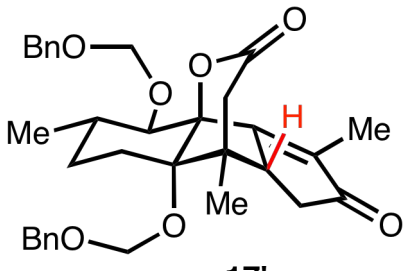
KVC25-217-Minor

Sample Name:
KVC25-217-Minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-217-Minor
FidFile: PROTON02

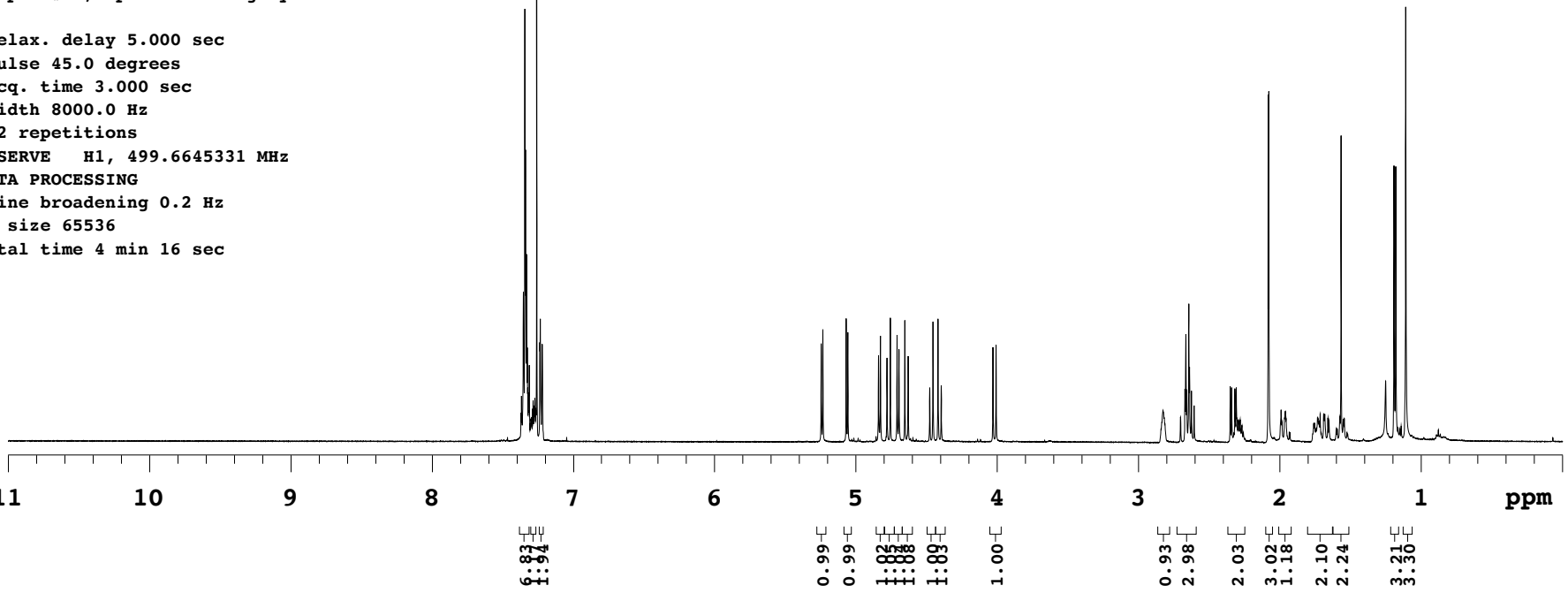
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 5 2016

Sample #36, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



17'



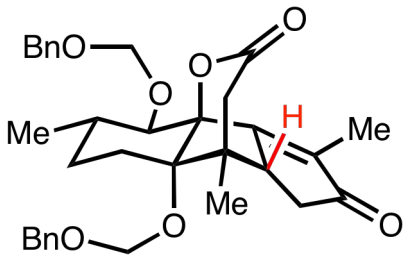
KVC25-217-Minor

Sample Name:
KVC25-217-Minor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-217-Minor
FidFile: CARBON02

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 5 2016

Sample #36, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6407482 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min



17'

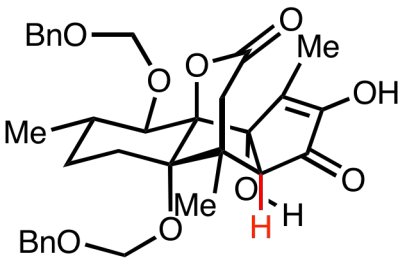
KVC25-227

Sample Name:
KVC25-227
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-227
FidFile: PROTON01

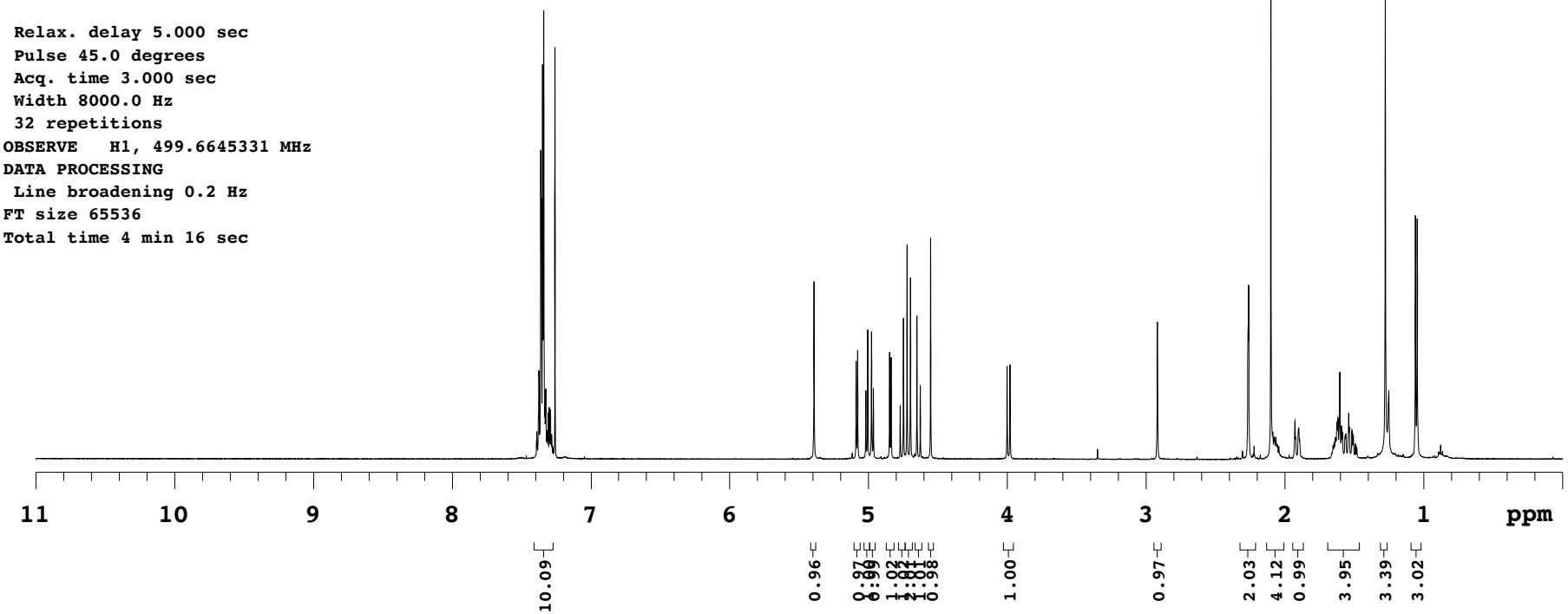
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 8 2016

Sample #19, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



21



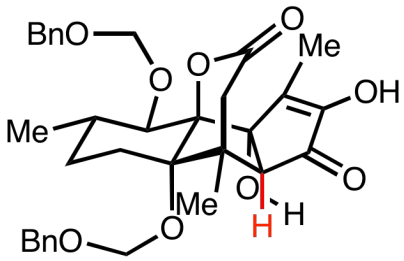
KVC25-227

Sample Name:
KVC25-227
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-227
FidFile: CARBON01

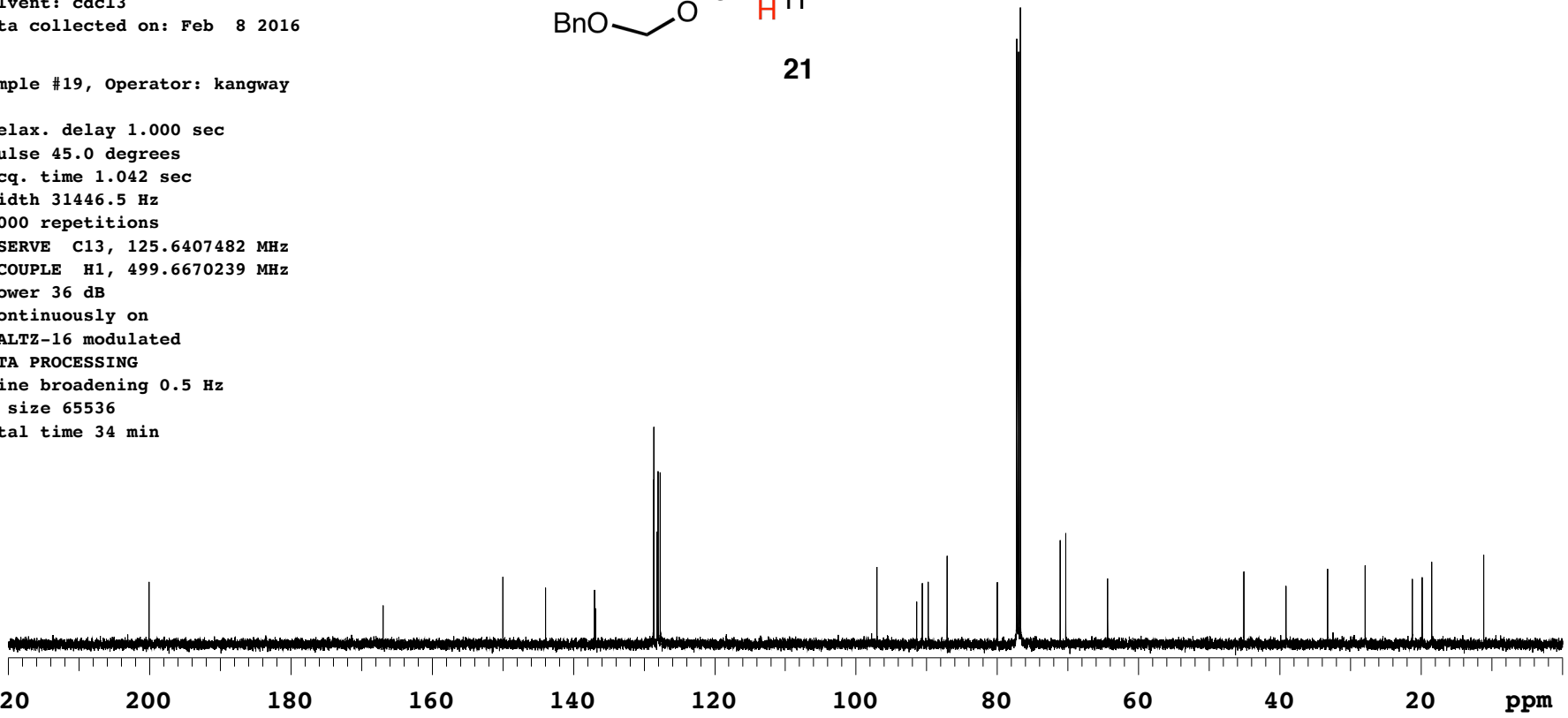
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 8 2016

Sample #19, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407482 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



21



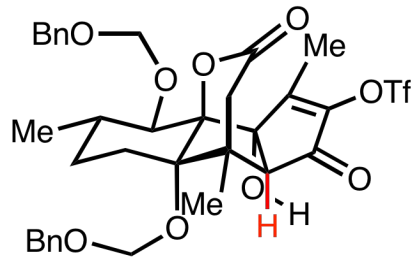
KVC25-259

Sample Name:
KVC25-259
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-259
FidFile: PROTON01

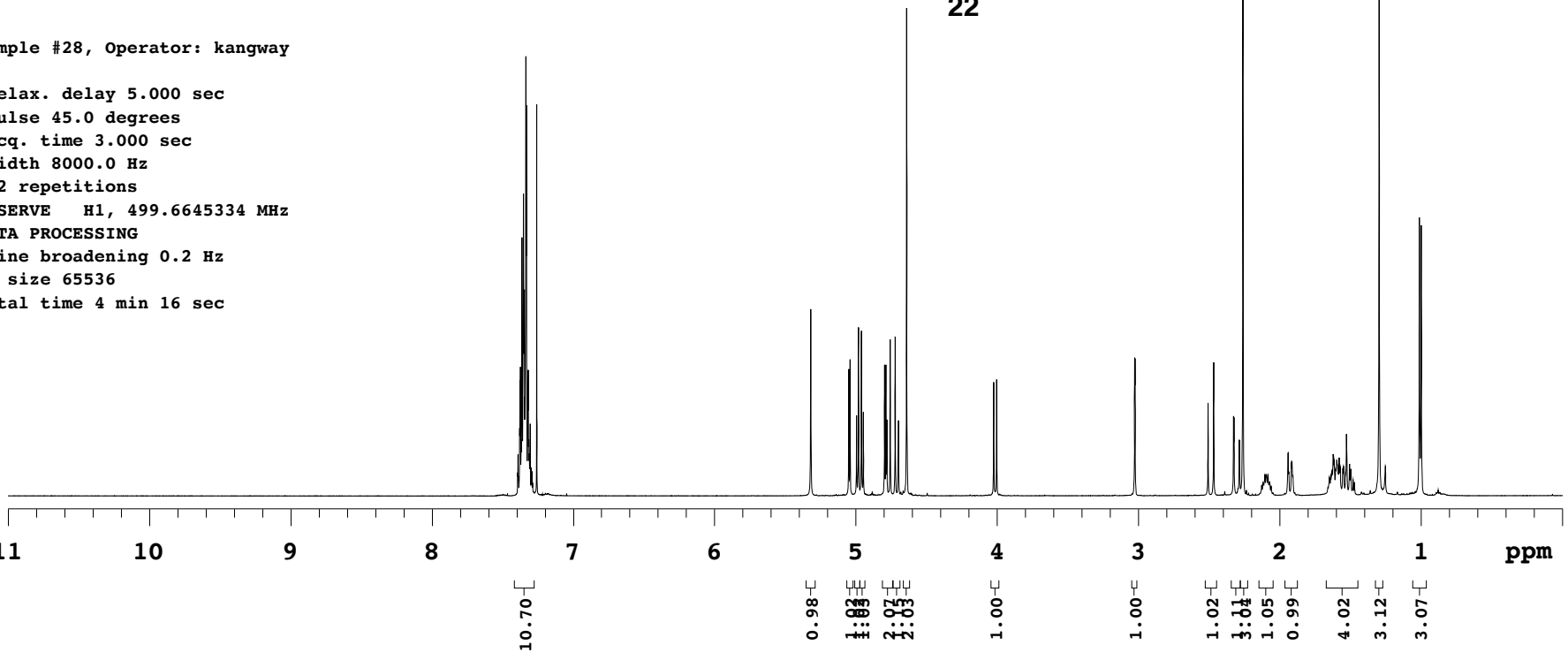
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 9 2016

Sample #28, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645334 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



22



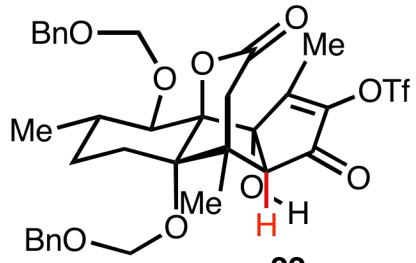
KVC25-259

Sample Name:
KVC25-259
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-259
FidFile: CARBON02

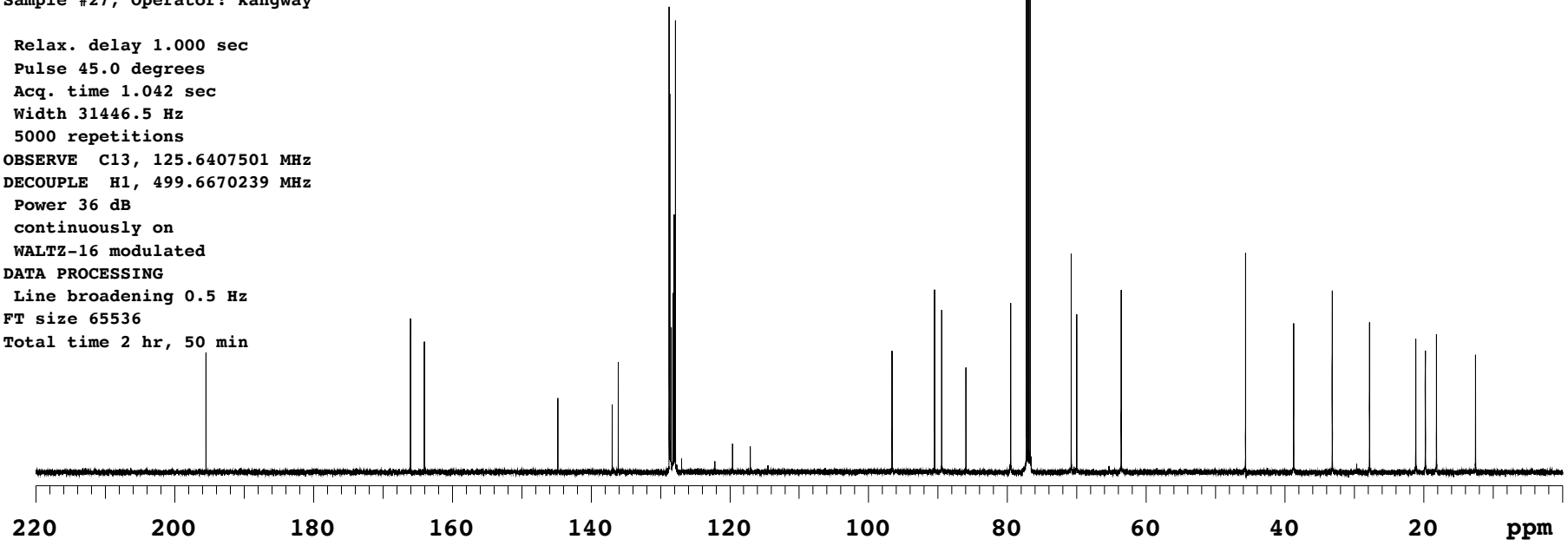
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 9 2016

Sample #27, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
5000 repetitions
OBSERVE C13, 125.6407501 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 2 hr, 50 min



22



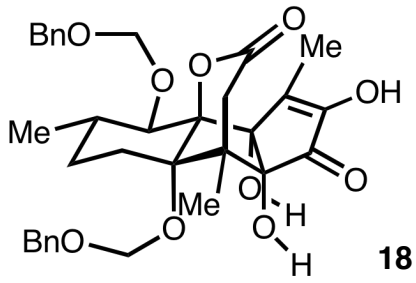
KVC25-221

Sample Name:
KVC25-221
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-221
FidFile: PROTON01

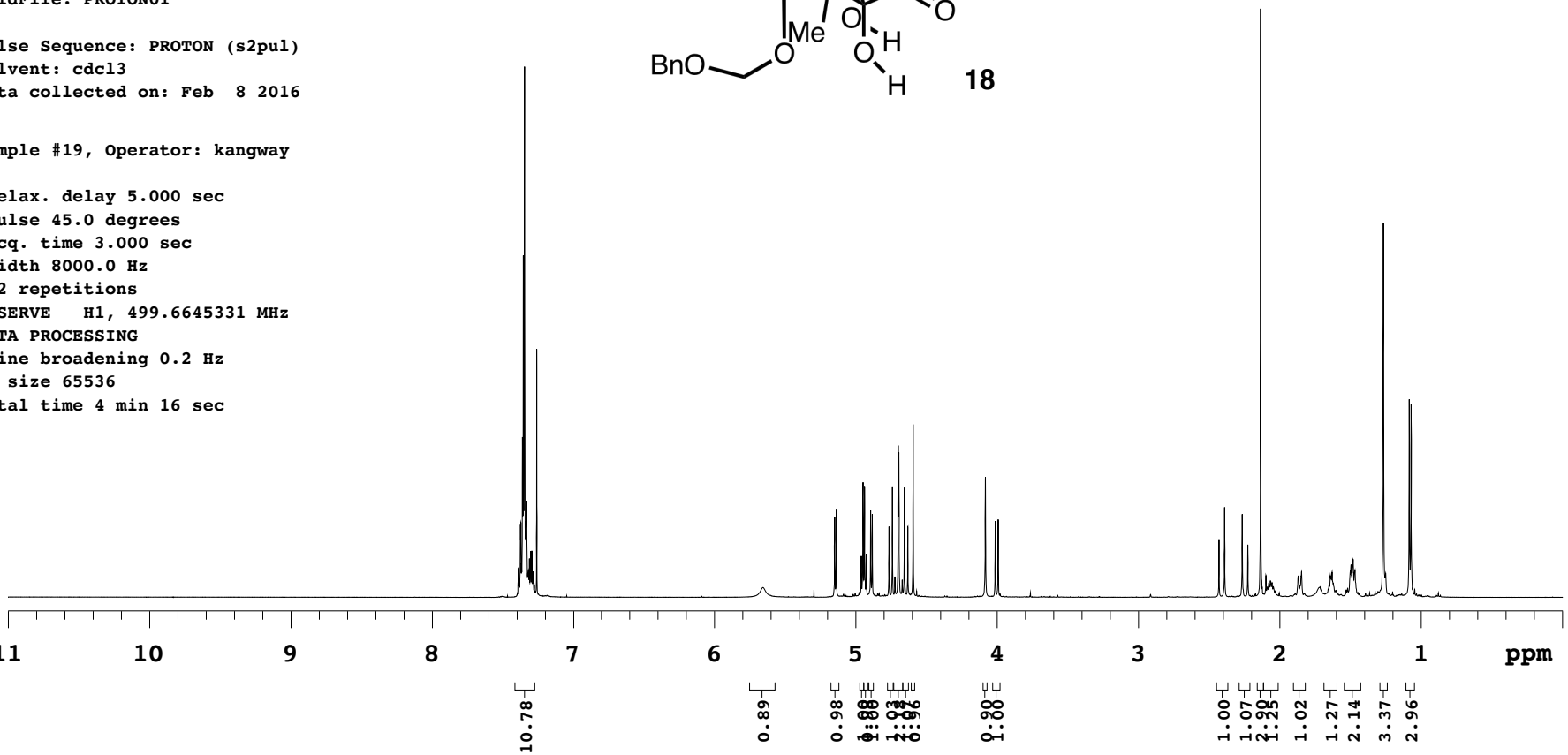
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 8 2016

Sample #19, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645331 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



18



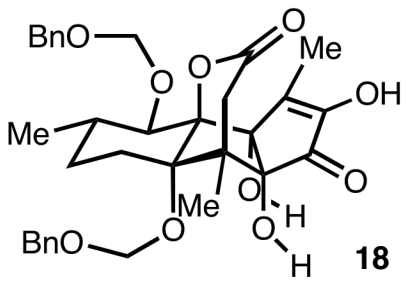
KVC25-221

Sample Name:
KVC25-221
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-221
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 8 2016

Sample #19, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6407501 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min



18

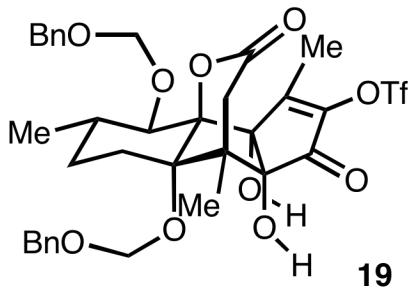
KVC25-255

Sample Name:
KVC25-255
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-255
FidFile: PROTON01

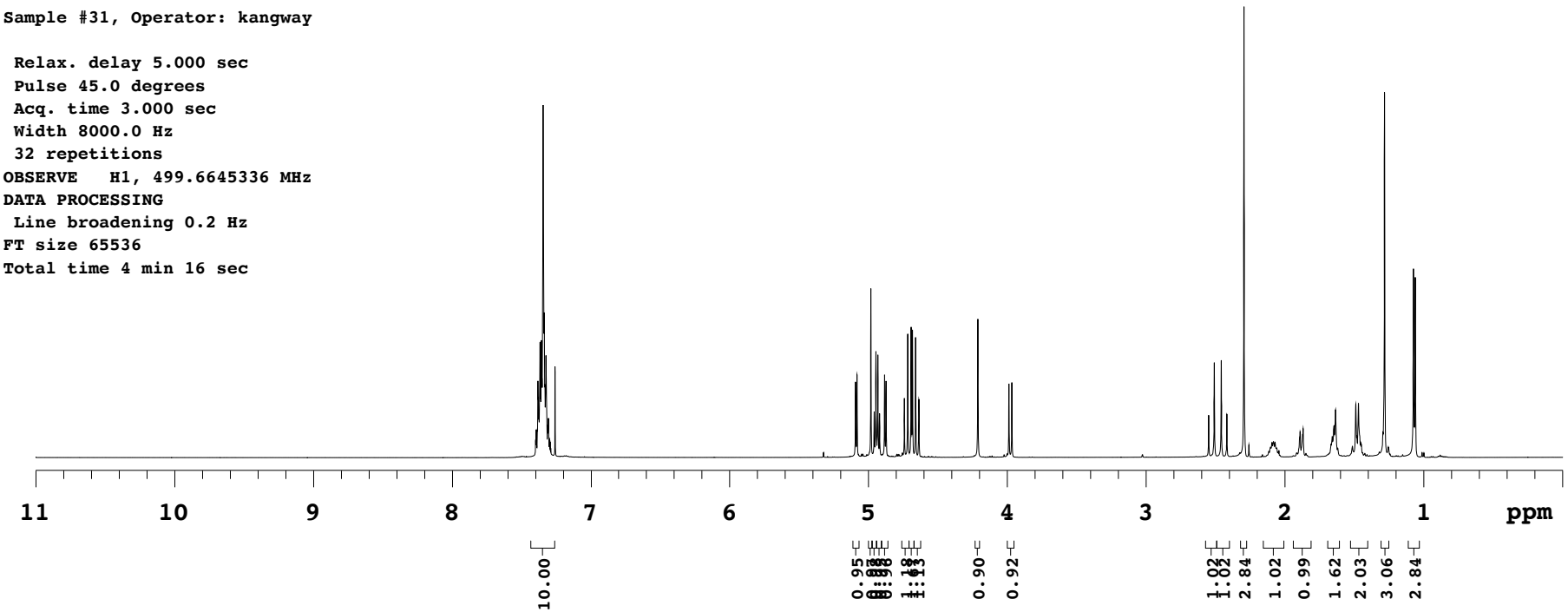
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 10 2016

Sample #31, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645336 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



19



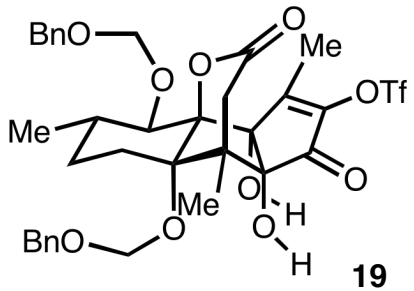
KVC25-255

Sample Name:
KVC25-255
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-255
FidFile: CARBON01

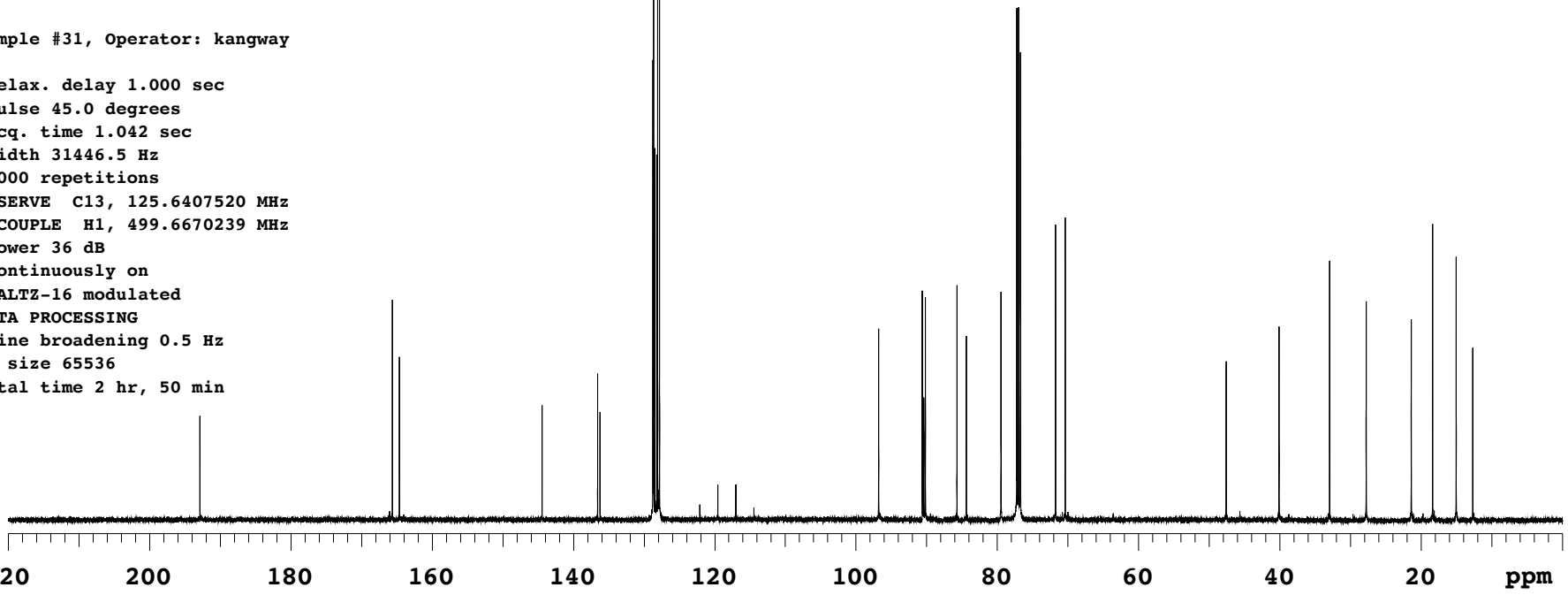
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 10 2016

Sample #31, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
5000 repetitions
OBSERVE C13, 125.6407520 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 2 hr, 50 min



19



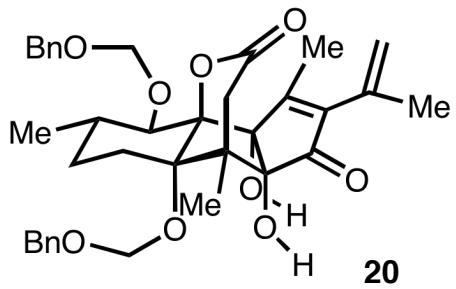
KVC25-269

Sample Name:
KVC25-269
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-269
FidFile: PROTON01

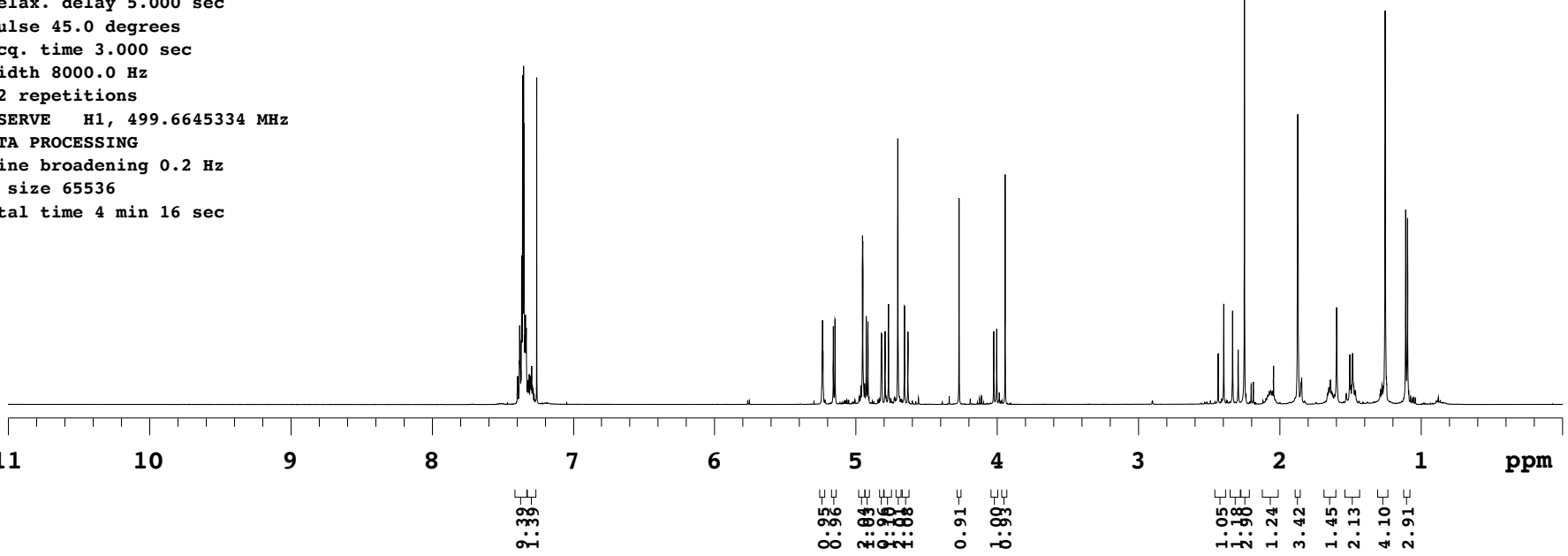
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 10 2016

Sample #32, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645334 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



20



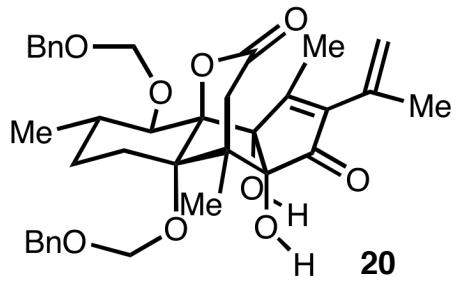
KVC25-269

Sample Name:
KVC25-269
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-269
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 10 2016

Sample #32, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6407501 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



20

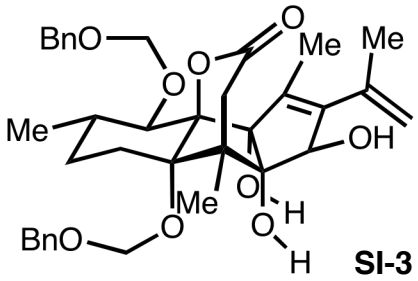
KVC25-261

Sample Name:
KVC25-261
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-261
FidFile: PROTON01

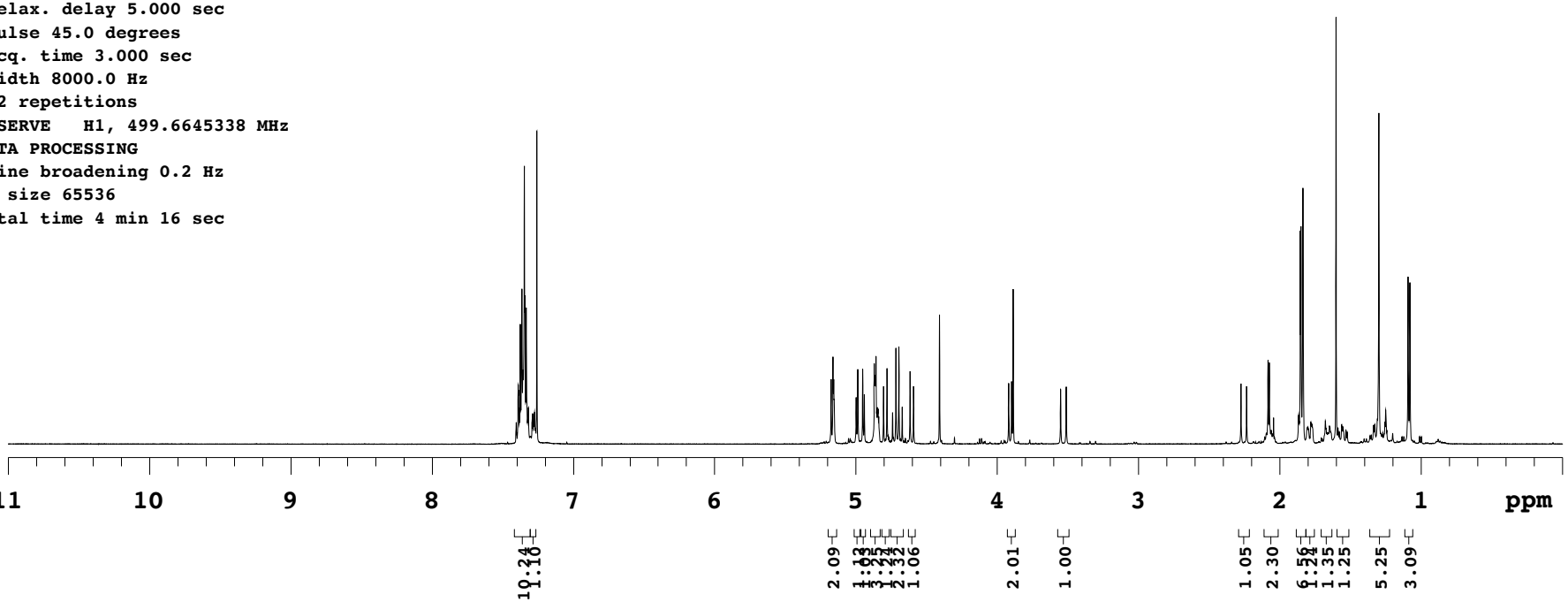
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 11 2016

Sample #34, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6645338 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



SI-3



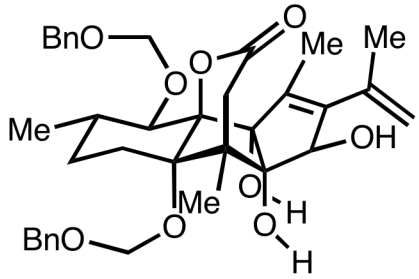
KVC25-261

Sample Name:
KVC25-261
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-261
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 11 2016

Sample #34, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6407491 MHz
DECOUPLE H1, 499.6670239 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min



SI-3

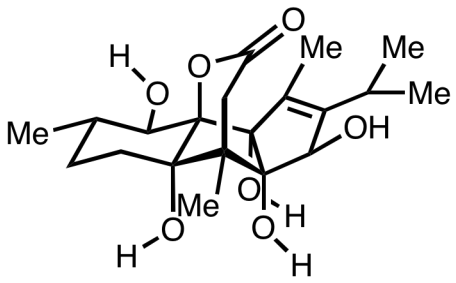
KVC25-263

Sample Name:
KVC25-263
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-263
FidFile: PROTON01

Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Mar 12 2016

Sample #11, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6664994 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



*(+)-anhydroryanodol (**3**)*

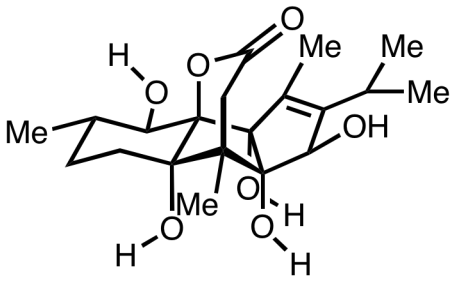
KVC25-263

Sample Name:
KVC25-263
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-263
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Mar 12 2016

Sample #11, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6410635 MHz
DECOUPLE H1, 499.6689926 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



*(+)-anhydroryanodol (**3**)*

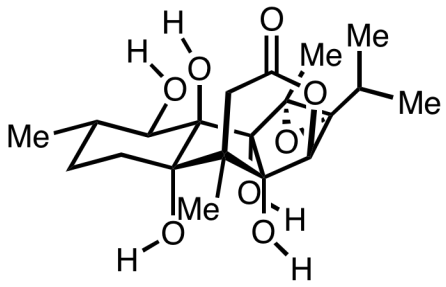
KVC25-265

Sample Name:
KVC25-265
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-265
FidFile: PROTON01

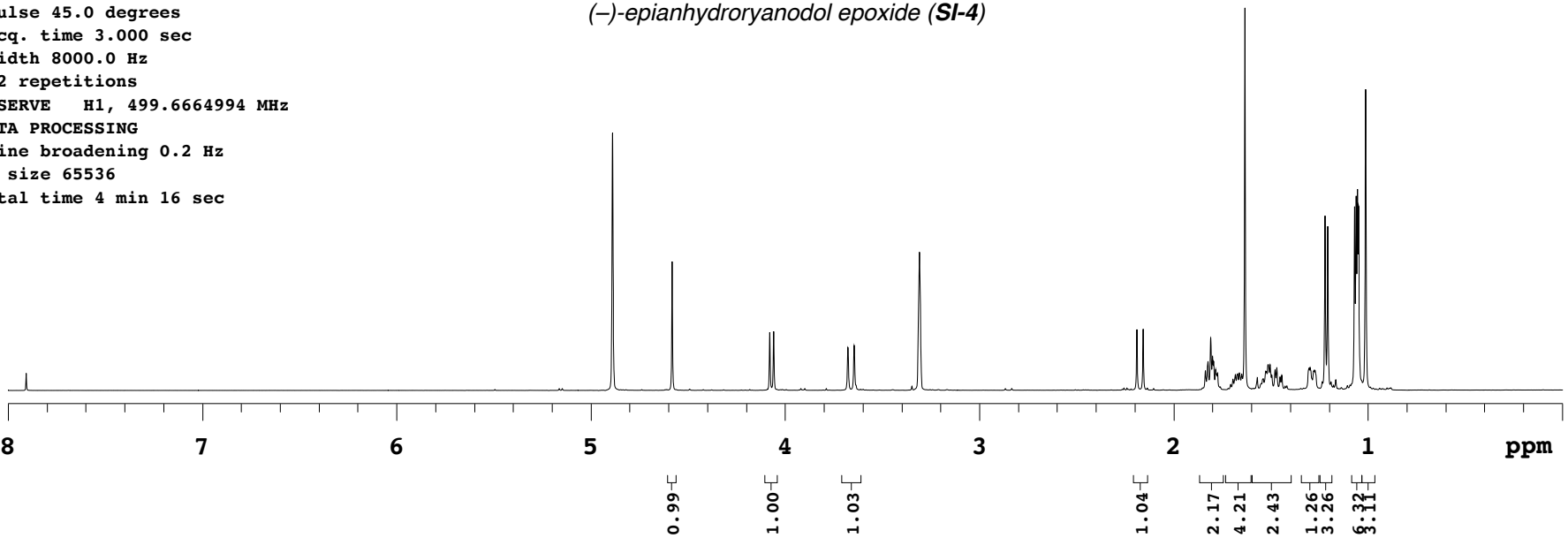
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Mar 13 2016

Sample #20, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6664994 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



*(–)-epianhydroryanodol epoxide (**SI-4**)*



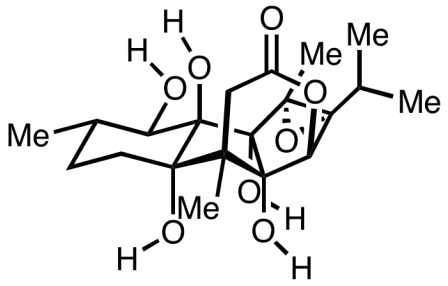
KVC25-265

Sample Name:
KVC25-265
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC25-265
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Mar 13 2016

Sample #20, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6410644 MHz
DECOUPLE H1, 499.6689926 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min



*(–)-epianhydroryanodol epoxide (**SI-4**)*

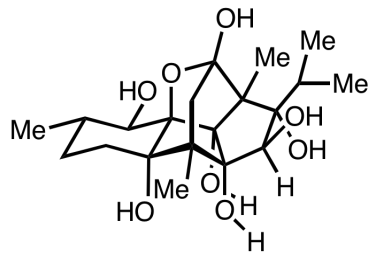
KVC26-031

Sample Name:
KVC26-031
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC26-031
FidFile: PROTON02

Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Apr 12 2016

Sample #47, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6580255 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



*(+)-ryanodol (**2**)*

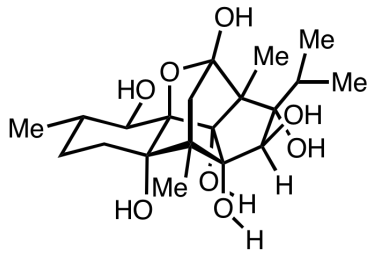
KVC26-031

Sample Name:
KVC26-031
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC26-031
FidFile: PROTON02

Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Apr 12 2016

Sample #47, Operator: kangway

Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6580255 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec



*(+)-ryanodol (**2**)*

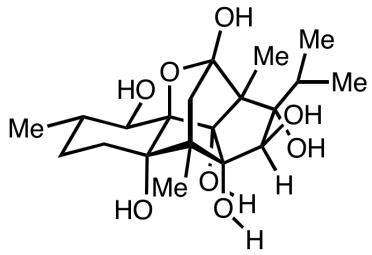
KVC26-031

Sample Name:
KVC26-031
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC26-031
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Apr 13 2016

Sample #47, Operator: kangway

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
12000 repetitions
OBSERVE C13, 125.6389340 MHz
DECOUPLE H1, 499.6605238 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 6 hr, 50 min



(+)-ryanodol (**2**)

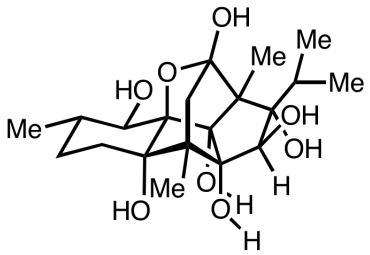
KVC26-031

Sample Name:
KVC26-031
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC26-031
FidFile: CARBON01

Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Apr 13 2016

Sample #47, Operator: kangway

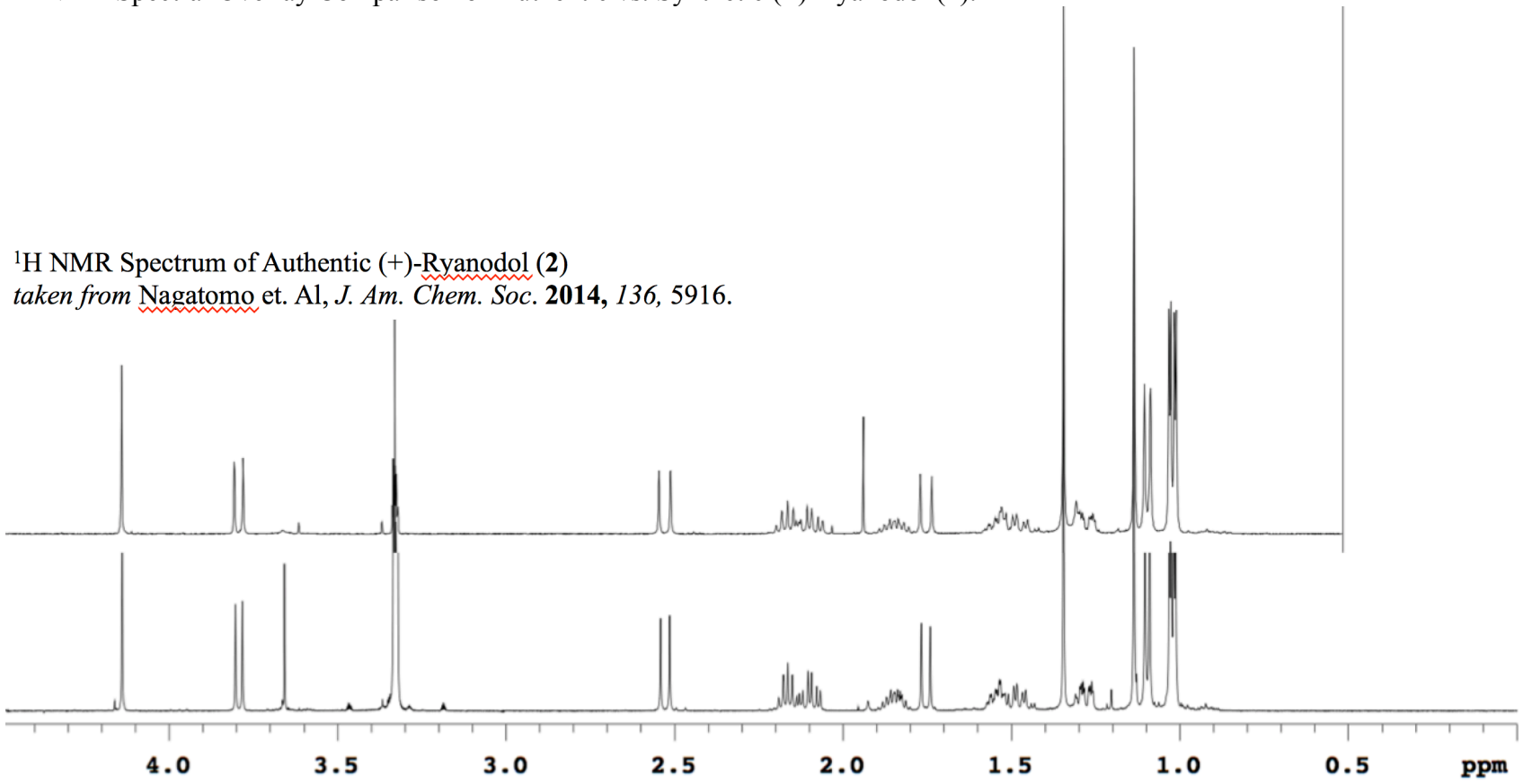
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
12000 repetitions
OBSERVE C13, 125.6389340 MHz
DECOUPLE H1, 499.6605238 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 6 hr, 50 min



(+)-ryanodol (**2**)

^{1}H NMR Spectral Overlay Comparison of Authentic vs. Synthetic (+)-Ryanodol (**2**).

^{1}H NMR Spectrum of Authentic (+)-Ryanodol (**2**)
taken from Nagatomo et. Al, *J. Am. Chem. Soc*. **2014,** *136,* 5916.



^{1}H NMR Spectrum of Synthetic (+)-Ryanodol (**2**)

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