Highly Stereocontrolled Total Synthesis of Secodolastane Diterpenoid Isolinearol

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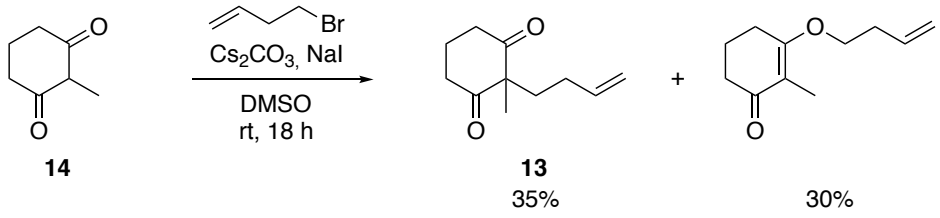
Experimental procedures

General

All reactions involving air- and moisture-sensitive reagents were carried out using standard syringe-septum cap techniques. Unless otherwise noted, all solvents and reagents were obtained from commercial suppliers and used without further purification. Routine monitoring of reactions were carried out Merck silica gel 50 F254 TLC plates. Column chromatography was performed on Kanto Chemical silica Gel 60N (spherical, neutral 60-230 μm) with the solvents indicated. Melting points were taken on Yanako MP-S3 micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a Jeol ECZ-400s (400 MHz) spectrometer. Chemical shifts were expressed in ppm using $CHCl_3$ (7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR) in $CDCl_3$ as an internal standard. Infrared spectral measurments were carried out with a JASCO FT/IR-4700 and only noteworthy absorptions were listed. HRMS spectra measured on a Micromass LCT spectrometer.

Synthesis of 2-(but-3-en-1-yl)-2-methylcyclohexane-1,3-dione (**13**).



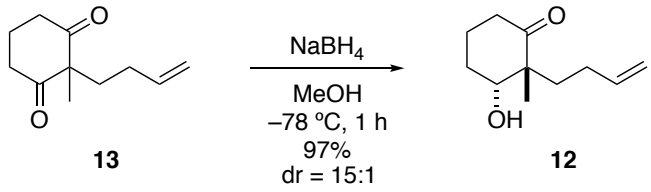
14 **13** 35% 30%

To a stirred solution of 2-methyl-1,3-cyclohexane-1,3-dione **14** (10.0 g, 79.3 mmol) in DMSO (80 mL) was added 4-bromo-1-butene (21.4 g, 16.0 mL, 158.5 mmol), Cs_2CO_3 (31.0 g, 95.1 mmol), NaI (17.8 g, 118.9 mmol) at room temperature under Ar, and the mixture was stirred for 18 h at same temperature. The reaction was quenched with H_2O at 0 ºC and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 3:1) to afford **13** (5.06 g, 35%) as yellow oil and *O*-butenyl compound (4.29 g, 30%) as yellow oil.

Data for **13**: IR (neat) 2944, 1726, 1695, 1456, 1026 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.82-1.93 (5H, m), 1.96-2.06 (1H, m), 2.58-2.74 (4H, m), 4.92-5.00 (2H, m), 5.65-5.76 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 19.8, 29.0, 36.2, 38.0 (2C), 65.1, 115.4, 137.4, 210.3 (2C); HRESIMS calcd for $C_{11}H_{16}O_2Na$ $[M+Na]^+$ 203.1048 found 203.1047.

Data for *O*-butenyl compound: IR (neat) 2947, 1617, 1377, 1354, 1095 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.69 (3H, t, J = 1.8 Hz), 1.97 (2H, td, J = 6.4, 1.9 Hz), 2.34 (2H, t, J = 6.9 Hz), 2.46 (2H, qt, J = 6.4, 1.4 Hz), 2.54 (2H, td, J = 6.4, 1.9 Hz), 4.04 (2H, t, J = 6.4 Hz), 5.09-5.18 (2H, m), 5.84 (1H, tdd, J = 16.9, 10.0, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.4, 21.0, 25.4, 34.1, 36.3, 67.0, 115.4, 117.6, 133.7, 171.1, 198.9; HRESIMS calcd for $C_{11}H_{16}O_2Na$ $[M+Na]^+$ 203.1048 found 203.1040.

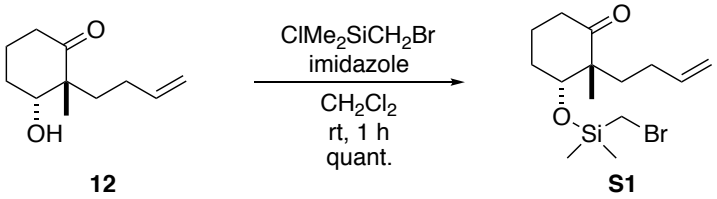
Synthesis of (2*R**,3*R**)-2-(but-3-en-1-yl)-3-hydroxy-2-methylcyclohexan-1-one (**12**).



To a stirred solution of **13** (3.67 g, 20.4 mmol) in MeOH (200 mL) was added $NaBH_4$ (231 mg, 6.12 mmol) at –78 ºC, and the mixture was stirred for 1 h at same temperature. The reaction was quenched with 1 M HCl aq. and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 6:1) to afford **12** (3.62 g, 97%, 15:1 diastereomer mixture) as colorless oil.

IR (neat) 3464, 2941, 1695, 1454, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.17 (3H, s), 1.54-1.63 (2H, m), 1.70-1.85 (2H, m), 1.88-2.06 (4H, m), 2.32-2.44 (2H, m), 3.70 (1H, dd, J = 8.5, 3.9 Hz), 4.94-5.05 (2H, m), 5.75-5.85 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 20.6, 27.6, 28.7, 30.7, 37.6, 54.5, 77.4, 114.7, 138.4, 213.8; HRESIMS calcd for $C_{11}H_{18}O_2Na$ $[M+Na]^+$ 205.1204, found 205.1196.

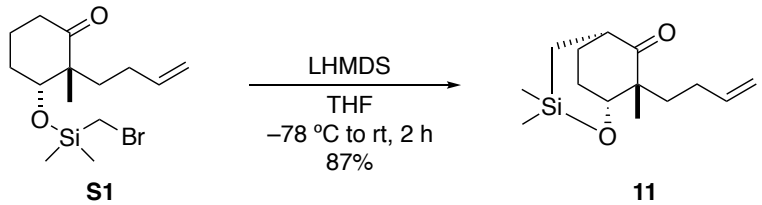
Synthesis of
(2*R**,3*R**)-3-(((bromomethyl)dimethylsilyl)oxy)-2-(but-3-en-1-yl)-2-methylcyclohexan-1-one (**S1**).



12 **S1**

To a stirred solution of **12** (3.79 g, 20.8 mmol) in CH_2Cl_2 (104 mL) was added imidazole (3.40 g, 49.9 mmol) and $ClMe_2SiCH_2Br$ (4.68 g, 3.40 mL, 24.9 mmol) at room temperature under Ar, and the mixture was stirred for 1 h at same temperature. The reaction was quenched with H_2O and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 20:1) to afford **S1** (6.90 g, quantitative yield) as colorless oil.
IR (neat) 2952, 1706, 1255, 1082 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.26 (6H, s), 1.10 (3H, s), 1.50-1.59 (3H, m), 1.67-1.81 (2H, m), 1.89-2.01 (3H, m), 2.29-2.40 (2H, m), 2.45 (2H, s), 3.72 (1H, t, *J* = 6.4 Hz), 4.93-5.03 (2H, m), 5.79 (1H, tdd, *J* = 16.9, 10.5, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –2.6, –2.5, 16.2, 19.1, 20.4, 27.7, 29.4, 30.9, 37.6, 54.8, 78.7, 114.5, 138.6, 213.7; HRESIMS calcd for $C_{14}H_{26}O_2BrSi$ $[M+H]^+$ 333.0885 found 333.0879.

Syntnesis of
(1*R**,5*S**,7*R**)-7-(but-3-en-1-yl)-3,3,7-trimethyl-2-oxa-3-silabicyclo[3.2.2]nonan-6-one (**11**).

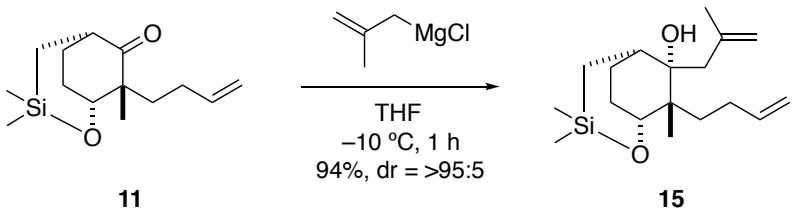


S1 **11**

To a stirred solution of **S1** (10.0 g, 30.0 mmol) in THF (300 mL) was added dropwise LHMDS (1.0 M THF, 60 mL, 60.0 mmol) at –78 ºC room temperature under Ar, and the mixture was stirred for 10 min at same temperature. After the reaction mixture was stirred for 2 h at room temperature, the reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 20:1) to afford **11** (6.56 g, 87%) as colorless oil.

IR (neat) 2952, 1706, 1252, 1088 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s), 0.28 (3H, s), 0.94 (1H, dd, *J* = 15.1, 6.0 Hz), 1.02 (3H, s), 1.08 (1H, ddd, *J* = 15.1, 4.4, 1.6 Hz), 1.64-1.72 (1H, m), 1.78-1.93 (2H, m), 2.02-2.25 (5H, m), 2.85 (1H, dd, *J* = 10.3, 5.3 Hz), 4.12 (1H, dd, *J* = 4.4, 1.6 Hz), 4.92-5.06 (2H, m), 5.83 (1H, tdd, *J* = 16.9, 10.1, 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.2, 3.5, 20.0, 21.2, 23.2, 24.0, 27.2, 33.7, 44.1, 52.0, 73.9, 114.3, 139.0, 218.9; HRESIMS calcd for $C_{14}H_{24}O_2NaSi$ $[M+Na]^+$ 275.1443 found 275.1436.

Synthesis of (1*R**,5*S**,6*S**,7*R**)-7-(but-3-en-1-yl)-3,3,7-trimethyl-6-(2-methylallyl)-2-oxa-3-silabicyclo[3.2.2]nonan-6-ol (**15**).

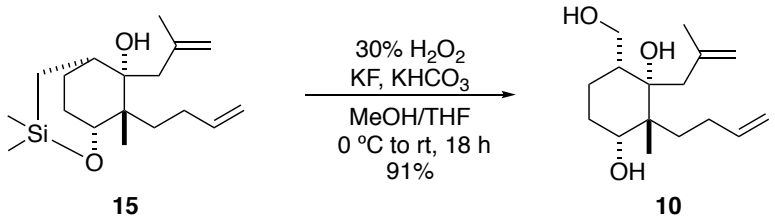


11 **15**

To a stirred solution of **11** (2.80 g, 11.1 mmol) in Et_2O (55 mL) was added dropwise a 2-methylallylmagnesium chloride (0.5 M THF, 44.4 mL, 22.3 mmol) at –10 ºC under Ar, and the mixture was stirred for 1 h at same temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 40:1) to afford **15** (3.20 g, 94%) as colorless oil.

IR (neat) 3548, 3067, 2919, 1639, 1477, 1244, 1102 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.16 (3H, s), 0.17 (3H, s), 0.53 (1H, dd, *J* = 14.6, 2.7 Hz), 0.88 (3H, s), 1.21 (1H, ddd, *J* = 14.6, 6.8, 1.8 Hz), 1.51-1.69 (3H, m), 1.74-1.81 (1H, m), 1.86 (3H, s), 1.97-2.16 (4H, m), 2.25 (1H, 1/2ABq, *J* = 13.3 Hz), 2.34 (1H, 1/2ABq, *J* = 13.3 Hz), 2.61-2.65 (1H, m), 3.82 (1H, t, *J* = 3.7 Hz), 4.79 (1H, brs), 4.93 (1H, d, *J* = 10.5 Hz), 5.00-5.08 (2H, m), 5.87 (1H, tdd, *J* = 17.2, 10.3, 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.5, 4.2, 20.5, 20.9, 23.9, 25.4, 26.0, 28.5, 33.9, 38.5, 44.8, 45.4, 74.9, 75.5, 113.8, 116.3, 140.1, 143.1; HRESIMS calcd for $C_{18}H_{32}O_2NaSi$ $[M+Na]^+$ 331.2069 found 331.2060.

Synthesis of (1*S**,2*R**,3*R**,6*R**)-2-(but-3-en-1-yl)-6-(hydroxymethyl)-2-methyl-1-(2-methylallyl)cyclohexane-1,3-diol (**10**).

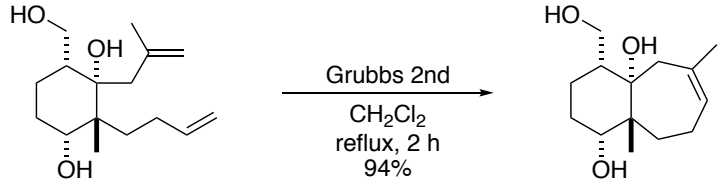


15 **10**

To a stirred solution **15** (100 mg, 0.32 mmol) in MeOH (0.3 mL) and THF (0.3 mL) was added $KHCO_3$ (32.0 mg, 0.32 mmol), KF (40.0 mg, 0.65 mmol) and 30% H_2O_2 (36.0 mg, 0.08 mL, 1.07 mmol) at 0 ºC, and the mixture was stirred for 30 min at same temperature. After the reaction mixture was stirred for 18 h at room temperature, the reaction was quenched with 50% $Na_2S_2O_3$ aqueous solution at 0 ºC and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 1:1) to afford **10** (79.0 mg, 91%) as a white solid.
M.p. 67-72 ºC; IR (KBr disk) 3323, 2939, 1739, 1640, 1446, 1243 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, s), 1.34-1.40 (1H, m), 1.46-1.56 (1H, m), 1.71-1.86 (3H, m), 1.90 (3H, s), 1.93-2.06 (1H, m), 2.16-2.23 (2H, m), 2.31 (1H, td, *J* = 13.3, 5.0 Hz), 2.36 (1H, 1/2ABq, *J* = 14.6 Hz), 2.52 (1H, 1/2ABq, *J* = 14.6 Hz), 3.61 (1H, dd, *J* = 11.4, 1.8 Hz), 3.66 (1H, t, *J* = 2.5 Hz), 4.42 (1H, dd, *J* = 11.4, 2.7 Hz), 4.86 (2H, d, *J* = 13.3 Hz), 4.92-4.97 (1H, m), 5.01-5.08 (1H, m), 5.89 (1H, tdd, *J* = 16.9, 10.5, 6.4 Hz); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 19.3, 20.2, 24.9, 27.4, 28.2, 30.3, 42.0, 43.7 (2C), 65.6, 73.2, 81.8, 113.9, 114.6, 139.8, 145.0; HRESIMS calcd for $C_{16}H_{28}O_3Na$ $[M+Na]^+$ 291.1936 found 291.1928.

Synthesis of (1*R**,4*R**,4a*S**,9a*R**)-4-(hydroxymethyl)-6,9a-dimethyl-1,2,3,4,5,8,9,9a-octahydro-4a*H*-benzo[7]annulene-1,4a-diol (**16**).

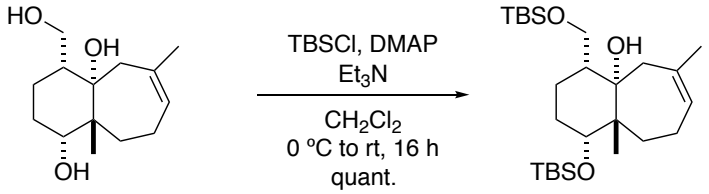


10 **16**

To a stirred solution of **10** (2.00 g, 7.45 mmol) in CH_2Cl_2 (750 mL) was added Grubbs 2nd generation catalyst (316 mg, 0.37 mmol) at room temperature under Ar, and the mixture was refluxed for 2 h. The solvent was concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 1:1) to afford **16** (1.68 g, 94%) as a white solid.

M.p. 149-151 ºC; IR (KBr disk) 3269, 2922, 1596, 1434, 1057, 1031 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, s), 1.07 (1H, dd, *J* = 13.5, 5.7 Hz), 1.49 (1H, d, *J* = 13.7 Hz), 1.66 (1H, d, *J* = 13.3 Hz), 1.76-1.79 (4H, m), 1.93-2.04 (2H, m), 2.24-2.49 (5H, m), 3.32 (1H, brs), 3.62 (1H, d, *J* = 11.0 Hz), 4.25 (1H, dd, *J* = 11.4, 2.3 Hz), 5.79 (1H, d, *J* = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 20.1, 22.9, 27.8, 28.6, 31.5, 38.5, 39.9, 44.1, 65.2, 79.1, 79.3, 127.4, 134.7; HRESIMS calcd for $C_{14}H_{24}O_3Na$ $[M+Na]^+$ 263.1623 found 263.1617.

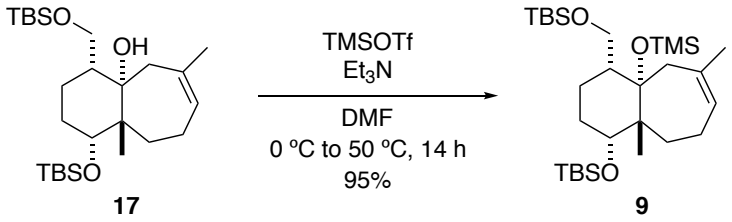
Synthesis of
(1*R**,4*R**,4a*S**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-1,2,3,4,5,8,9,9a-octahydro-4a*H*-benzo[7]annulen-4a-ol (**17**).



To a stirred solution of **16** (1.68 g, 6.99 mmol) in CH_2Cl_2 (35 mL) was added Et_3N (8.49 g, 11.6 mL, 83.9 mmol), 4,4-dimethylaminopyridine (2.56 g, 21.0 mmol) and *tert*-butyldimethylsilyl chloride (4.21 g, 28.0 mmol) at 0 ºC under Ar, and the mixture was stirred for 16 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 20:1) to afford **17** (3.27 g, quantitative yield) as a white crystal.

M.p. 52-54 ºC; IR (KBr disk) 3488, 2929, 2857, 1471, 1389, 1256, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (3H, s), 0.06 (3H, s), 0.07 (3H, s), 0.07 (3H, s), 0.90 (18H, s), 0.99 (3H, s), 1.50-1.57 (2H, m), 1.62-1.76 (2H,m), 1.71 (3H, s), 1.83-1.92 (1H, m), 1.94-2.02 (1H, m), 2.19-2.34 (3H, m), 2.43 (1H, td, *J* = 13.5, 2.7 Hz), 3.37 (1H, dd, *J* = 10.1, 6.4 Hz), 3.40-3.43 (1H, m), 4.04 (1H, dd, *J* = 10.1, 4.6 Hz), 4.25 (1H, d, *J* = 2.3 Hz), 5.53 (1H, d, *J* = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.34, –5.29, –5.0, –4.7, 17.9, 18.3, 18.7, 19.6, 25.0, 25.8 (3C), 26.0 (3C), 28.64, 28.65, 32.8, 35.7, 43.8, 44.3, 64.7, 77.2, 81.4, 126.7, 130.6; HRESIMS calcd for $C_{26}H_{52}O_3NaSi_2$ $[M+Na]^+$ 491.3353 found 491.3355.

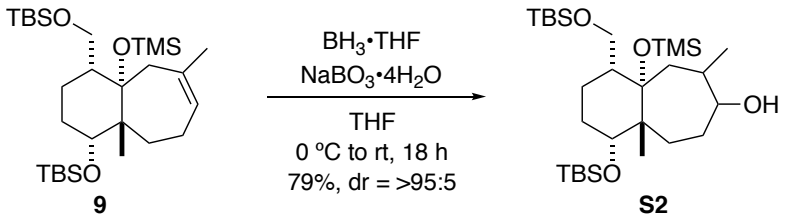
Synthesis of
tert-butyl(((1*R**,4*R**,4a*R**,9a*S**)-4-((*tert*-butyldimethylsilyl)oxy)-4a,8-dimethyl-9a-((trimethylsilyl)oxy)-2,3,4,4a,5,6,9,9a-octahydro-1*H*-benzo[7]annulen-1-yl)methoxy)dimethylsilane (**9**).



To a stirred solution of **17** (2.60 g, 5.55 mmol) in *N*,*N*-dimethylformamide (28 mL) was added Et_3N (5.62 g, 7.70 mL, 55.5 mmol) and trimethylsilyl trifluoromethanesulfonate (4.93 g, 4.00 mL, 22.2 mmol) at 0 ºC under Ar, and the mixture was stirred for 14 h at 50 ºC. The reaction mixture was added into the saturated $NaHCO_3$ aqueous solution at 0 ºC and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 60:1) to afford **9** (2.85 g, 95%) as colorless oil.

IR (neat) 2955, 2930, 1684 cm^{-1}; IR (neat) 2930, 2857, 1255, 1077 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s), 0.03 (3H, s), 0.05 (3H, s), 0.07 (6H, s), 0.09 (6H, s), 0.89 (9H, s), 0.90 (3H, s), 0.91 (9H, s), 1.44-1.54 (1H, m), 1.54-1.61 (2H, m), 1.61-1.80 (3H, m), 1.67 (3H, s), 2.07-2.17 (3H, m), 2.39-2.51 (2H, m), 3.27-3.34 (2H, m), 3.96 (1H, dd, *J* = 9.8, 3.9 Hz), 5.39-5.43 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.25, –5.22, –4.6, –4.5, 2.8 (3C), 18.3, 19.47, 19.50, 26.0 (4C), 26.2 (3C), 26.3, 28.5, 30.2, 31.8, 44.1, 44.7, 47.2, 65.3, 79.8, 81.6, 125.4, 130.2; HRESIMS calcd for $C_{29}H_{60}O_3NaSi_3$ $[M+Na]^+$ 563.3748 found 563.3748.

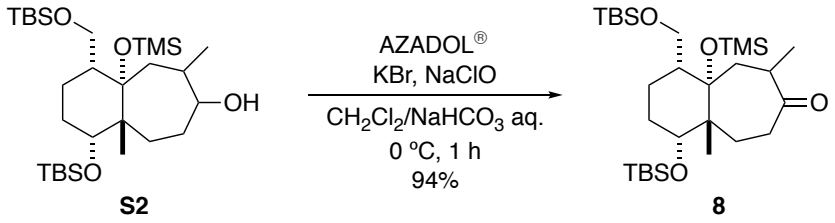
Synthesis of
(1*R**,4*R**,4a*S**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-1*H*-benzo[7]annulen-7-ol (**S2**).



To a stirred solution of **9** (1.56 g, 2.88 mmol) in THF (29 mL) was added dropwise BF_3•THF(1 M THF, 4.00 mL, 4.03 mmol) at 0 ºC under Ar, and the mixture was stirred for 18 h at room temperature. To a reaction mixture was added $NaBO_3$•$4H_2O$ (2.20 g, 14.4 mmol) at 0 ºC and the mixture was stirred for 4 h at room temperature. The reaction was quenched with H_2O and the mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 50:1) to afford **S2** (1.27 g, 79%) as colorless amorphous.

IR (neat) 3347, 2929, 2857, 1471, 1253, 1129, 1075 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.02 (3H, s), 0.03 (3H, s), 0.07 (6H, s), 0.14 (3H, s), 0.16 (6H, s), 0,90 (9H, s), 0.91 (9H, s), 0.94 (3H, s), 1.00 (3H, d, *J* = 6.0 Hz), 1.45-1.70 (6H, m), 1.71-1.99 (5H, m), 2.52 (1H, td, *J* = 14.6, 4.1 Hz), 3.24-3.38 (2H, m), 3.64 (1H, td, *J* = 10.1, 2.0 Hz), 3.99 (1H, dd, *J* = 9.4, 3.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.2 (2C), –4.8, –4.3, 0.4, 3.5 (3C), 18.3, 19.1, 19.9, 20.6, 26.0 (3C), 26.2 (3C), 30.3, 32.1, 36.9, 39.9, 45.0, 46.0, 49.5, 64.4, 72.8, 79.3, 82.9; HRESIMS calcd for $C_{29}H_{62}O_4NaSi_3$ $[M+Na]^+$ 581.3854 found 581.3856.

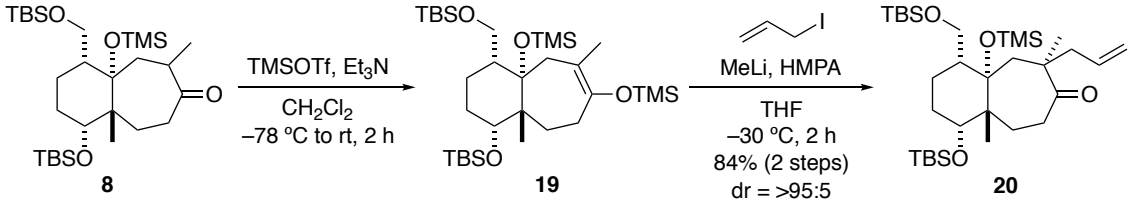
Synthesis of
(1*R**,4*R**,4a*S**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**8**)



To a stirred solution of **S2** (1.11 g, 1.99 mmol) in CH_2Cl_2 (5 mL) was added 2-hydroxy-2-azaadamantane (3.00 mg, 19.9 μmol), KBr (24.0 mg, 199 μmol) in $NaHCO_3$ aqueous solution (2.5 mL), and mixture of NaClO (223 mg, 0.19 mL, 2.99 mmol) aqueous solution and $NaHCO_3$ aqueous solution (2.5 mL) at 0 ºC and the mixture was stirred for 1 h at same temperature. The reaction was quenched with $Na_2S_2O_3$ aqueous solution and the mixture was extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 30:1) to afford **8** (1.04 g, 94%) as colorless oil.

IR (neat) 2929, 2857, 1714, 1252, 1129, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03-0.11 (21H, m), 0.90 (18H, s), 1.03 (3H, d, J = 6.4 Hz), 1.14 (3H, s), 1.41-1.86 (7H, m), 2.01 (1H, dd, J = 14.9, 9.8 Hz), 2.38-2.59 (3H, m), 2.89-2.98 (1H, m), 3.31-3.44 (2H, m), 3.91 (1H, dd, J = 9.6, 2.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.22, –5.20, –4.7, –4.3, 2.9 (3C), 17.4, 18.2, 18.3, 19.4, 21.6, 26.0 (3C), 26.2 (3C), 30.3, 31.9, 41.9, 42.1, 44.5, 45.6, 48.4, 64.3, 79.3, 82.7, 212.9; HRESIMS calcd for $C_{29}H_{60}O_4NaSi_3$ $[M+Na]^+$ 579.3697 found 579.3699.

Synthesis of (1*R**,4*R**,4a*S**,6*R**,9a*R**)-6-allyl-1-((*tert*-butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**20**).



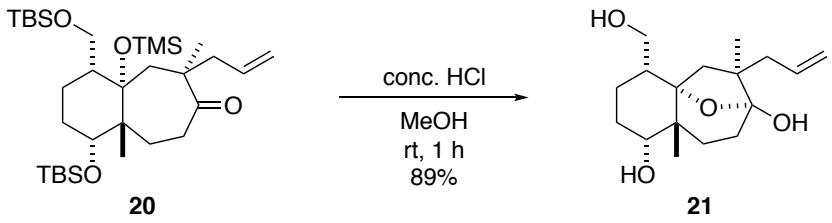
To a stirred solution of **8** (212 mg, 0.38 mmol) in CH_2Cl_2 (3 mL) was added Et_3N (461 mg, 0.63 mL, 4.56 mmol) at –78 ºC under Ar, and the mixture was stirred for 30 min at same temperature. To a reaction mixture was added trimethylsilyl trifluoromethanesulfonate (338 mg, 0.27 mL, 1.52 mmol) at –78 ºC, and the mixture was stirred for 30 min at same temperature. After the mixture was stirred for 1 h at room temperature, the mixture was added to saturated $NaHCO_3$ aqueous solution and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give the compound **19**. The obtained **19** was used for next reaction without further purification.

To a solution of **19** obtained above in tetrahydrofuran (4 mL) was added MeLi (1.1 M Et_2O, 0.71 mL, 0.78 mmol) at 0 ºC under Ar, and the mixture was stirred for 20 min at same temperature. To a reaction mixture was added hexamethylphosphoric triamide (140 mg, 0.14 mL, 0.78 mmol) and allyl iodide (197 mg, 0.11 mL, 1.17 mmol) at –30 ºC, and the mixture was stirred for 2 h at same temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 60:1) to afford **20** (191 mg, 84% for 2 steps) as a white solid.

M.p. 96-100 ºC; IR (KBr disk) 2929, 1697, 1471, 1253, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (9H, s), 0.08 (3H, s), 0.20 (9H, s), 0.86 (3H, s), 0.90 (9H, s), 0.91 (9H, s), 1.08-1.12 (1H, m), 1.30 (3H, s), 1.55-1.87 (6H, m), 1.94 (1H, d, *J* = 15.6 Hz), 2.14 (1H, 1/2ABqd, *J* = 13.7, 7.8 Hz), 2.28 (1H ,1/2ABqd, *J* = 13.7, 6.8 Hz), 2.46-2.51 (1H, m), 2.59-2.74 (2H, m), 3.35 (1H, dd, *J* = 10.5, 6.9 Hz), 3.45-3.48 (1H, m), 3.94 (1H, dd, *J* =

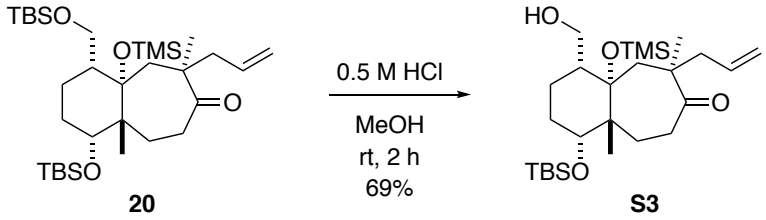
9.6, 3.7 Hz), 4.99-5.06 (2H, m), 5.67-5.77 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.2 (2C), –4.2, –4.1, 4.1 (3C), 18.3, 18.7, 19.6, 21.6, 22.7, 26.0 (3C), 26.5 (3C), 29.1, 29.6, 38.3, 45.0, 46.0, 46.3, 46.5, 49.7, 65.0, 79.4, 83.1, 118.0, 134.6, 215.6; HRESIMS calcd for $C_{32}H_{64}O_4NaSi_3$ $[M+Na]^+$ 619.4010 found 619.4019.

Synthesis of (1*R**,4*R**,4a*S**,6*R**,7*R**,9a*R**)-6-allyl-4-(hydroxymethyl)-6,9a-dimethyloctahydro-4a,7-epoxybenzo[7]annulene-1,7(2*H*)-diol (**21**).



To a stirred solution of **20** (43.0 mg, 72.0 μmol) in MeOH (0.4 mL) was added a drop of conc. HCl at room temperature and the mixture was stirred for 1 h at same temperature. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 2:1) to afford **21** (19.0 mg, 89%) as a white solid.
M.p. 154-159 ºC; IR (KBr disk) 3365, 2924, 1417, 1024 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (3H, s), 1.08 (3H, s), 1.62-1.71 (3H, m), 1.75-1.99 (6H, m), 2.04-2.25 (4H, m), 3.58 (1H, t, *J* = 2.7 Hz), 3.68 (1H, dd, *J* = 11.4, 3.2 Hz), 3.98 (1H, dd, *J* = 11.4, 3.7 Hz), 5.05-5.13 (2H, m), 5.84 (1H, tdd, *J* = 16.9, 10.1, 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 22.3, 23.3, 28.7, 32.4, 33.3, 38.1, 38.9, 40.9, 41.1, 43.8, 63.8, 78.2, 86.7, 106.1, 117.5, 134.9; HRESIMS calcd for $C_{17}H_{28}O_4Na$ $[M+Na]^+$ 319.1885 found 319.1877.

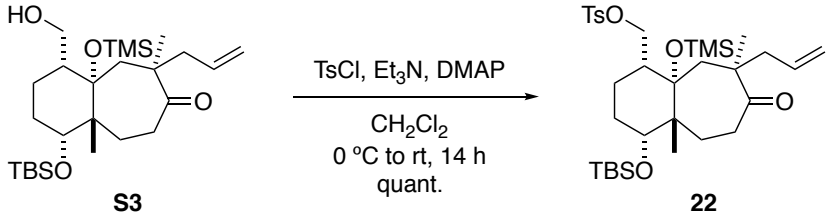
Synthesis of
(1*R**,4*R**,4a*S**,6*R**,9a*R**)-6-allyl-1-((*tert*-butyldimethylsilyl)oxy)-4-(hydroxymethyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**S3**).



To a stirred solution of **20** (29.2 mg, 49.0 μmol) in MeOH (0.5 mL) was added 0.5 M HCl aqueous solution (0.2 mL) at room temperature and the mixture was stirred for 2 h at same temperature. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 10:1) to afford **S3** (16.3 mg, 69%) as a white solid.

IR (neat) 3444, 2930, 1694, 1252, 1077 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (3H, s), 0.08 (3H, s), 0.21 (9H, s), 0.87 (3H, s), 0.92 (9H, s), 1.09-1.15 (1H, m), 1.31 (3H, s), 1.53-1.71 (4H, m), 1.78-1.88 (2H, m), 1.92 (1H, d, *J* = 15.6 Hz), 2.16 (1H, 1/2ABqd, *J* = 13.7, 8.2 Hz), 2.27 (1H, 1/2ABqd, *J* = 13.7, 6.9 Hz), 2.47-2.53 (1H, m), 2.59-2.76 (2H, m), 3.44 (1H, dd, *J* = 10.3, 8.0 Hz), 3.47-3.49 (1H, m), 4.01 (1H, dd, *J* = 10.3, 3.9 Hz), 4.99-5.08 (2H, m), 5.72 (1H, tdd, *J* = 17.2, 9.8, 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.2, –4.1, 4.1 (3C), 18.7, 19.7, 21.6, 22.6, 26.5 (3C), 29.1, 29.5, 38.3, 45.0, 46.0, 46.3, 46.6, 49.7, 64.6, 79.3, 83.0, 118.2, 134.5, 215.5; HRESIMS calcd for $C_{26}H_{50}O_4NaSi_2$ $[M+Na]^+$ 505.3145 found 505.3147.

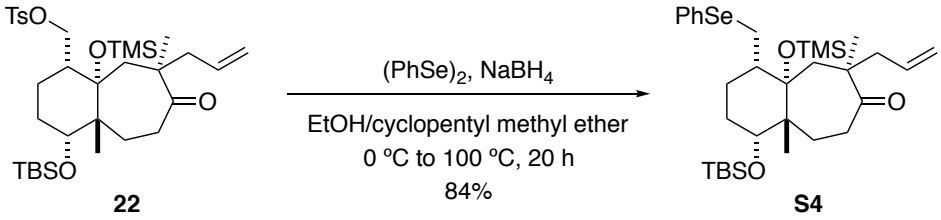
Synthesis of
((1*R**,4*R**,4a*R**,8*R**,9a*S**)-8-allyl-4-((*tert*-butyldimethylsilyl)oxy)-4a,8-dimethyl-7-oxo-9a-((trimethylsilyl)oxy)decahydro-1*H*-benzo[7]annulen-1-yl)methyl 4-methylbenzenesulfonate (**22**).



To a stirred solution of **S3** (20.0 mg, 41.4 μmol) in CH_2Cl_2 (2 mL) was added Et_3N (16.6 mg, 0.02 mL, 0.16 mmol), 4,4-dimethylaminopyridine (5.5 mg, 45.0 μmol) and *p*-toluenesulfonyl chloride (16.0 mg, 82.8 μmol) at 0 ºC and the mixture was stirred for 2 h at room temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 10:1) to afford **22** (26.0 mg, 99%) as a white solid.

M.p. 79-89 ºC; IR (KBr disk) 2932, 1703, 1357, 1254, 1181, 1128 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ –0.06 (3H, d, *J* = 2.7 Hz), 0.03 (3H, s), 0.05 (3H, s), 0.09 (9H, s), 0.80 (3H, s), 0.84-0.90 (10H, m), 0.97 (1H, d, *J* = 6.4 Hz), 1.06-1.13 (1H, m), 1.20 (3H, s), 1.43-1.51 (1H, m), 1.56-1.64 (4H, m), 1.65-1.97 (2H, m), 2.07 (1H, dd, *J* = 13.7, 8.2 Hz), 2.22 (1H, dd, *J* = 13.7, 6.9 Hz), 2.40-2.50 (3H, m), 2.54-2.70 (2H, m), 3.42-3.46 (1H, m), 3.72-3.79 (1H, m), 4.28 (1H, dd, *J* = 9.4, 3.9 Hz), 4.94-5.08 (2H, m), 5.58-5.72 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.3, –4.1, 3.9 (3C), 18.6, 19.7, 21.5, 21.6, 22.6, 26.4 (3C), 29.0, 38.0, 43.2, 45.0, 46.0, 46.2, 49.5, 72.5, 77.2, 78.9, 82.7, 118.4, 128.0 (2C), 129.9 (2C), 132.7, 134.2, 145.0, 214.8; HRESIMS calcd for $C_{33}H_{56}O_6NaSSi_2$ $[M+Na]^+$ 659.3234 found 659.3242.

Synthesis of
(1*R**,4*S**,4a*S**,6*R**,9a*R**)-6-allyl-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-4-((phenylselanyl)methyl)-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**S4**).

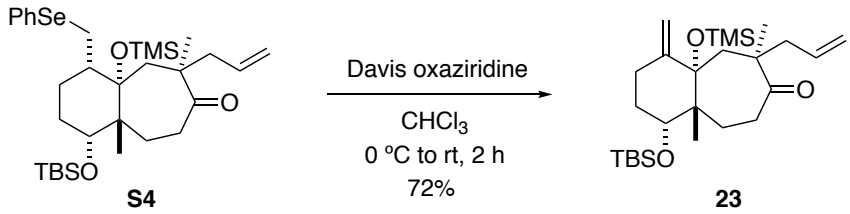


To a stirred solution of diphenyl diselenide (26.5 mg, 84.8 μmol) in EtOH (0.4 mL) was added sodium borohydride (6.43 mg, 0.17 mmol) at 0 ºC and the mixture was stirred for 10 min at room temperature. The mixture was added dropwise to a stirred solution of **22** (27.0 mg, 42.4 μmol) in cyclopentyl methyl ether (0.2 mL) at room temperature and the mixture was stirred for 20 h at 100 ºC. To the reaction mixture was added Et_2O and saturated NH_4Cl aqueous solution then the mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 20:1) to afford **S4** (22.1 mg, 84%) as colorless oil.

IR (neat) 2928, 1696, 1472, 1253, 1132, 1080 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (3H, s), 0.07 (3H, s), 0.22 (9H, s), 0.76 (3H, s), 0.91 (9H, s), 0.96-1.17 (2H, m), 1.25-1.30 (1H, m), 1.29 (3H, s), 1.58-1.87 (5H, m), 2.08 (1H, 1/2ABqd, *J* = 13.7, 8.2 Hz), 2.19 (1H, 1/2ABqd, *J* = 13.5, 6.6 Hz), 2.44-2.74 (4H, m), 3.30 (1H, dd, *J* = 11.7, 2.1 Hz), 3.43-3.48 (1H, m), 4.97-5.07 (2H, m), 5.62-5.74 (1H, m), 7.25-7.28 (3H, m), 7.46-7.51 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.2, –4.0, 4.3 (3C), 18.7, 21.7, 21.9, 22.8, 26.5 (3C), 29.4, 29.7, 31.3, 38.2, 44.8 (2C), 46.2, 46.3, 49.5, 77.2, 79.5, 83.8, 118.2, 127.1, 129.2 (2C), 133.0 (2C), 134.4, 215.3; HRESIMS calcd for $C_{32}H_{54}O_3NaSeSi_2$ $[M+Na]^+$ 645.2674 found 645.2679.

Synthesis of

(1*R**,4a*S**,6*R**,9a*R**)-6-allyl-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-4-methylene-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**23**).

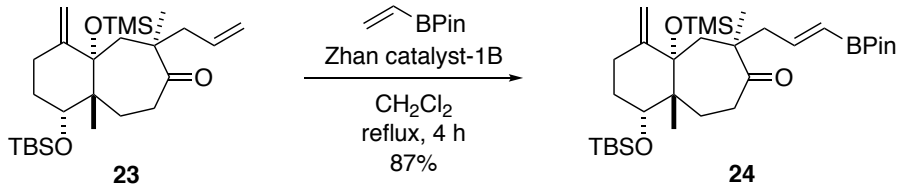


To a stirred solution of **S4** (11.0 mg, 17.9 μmol) in $CHCl_3$ (2 mL) was added Davis oxaziridine (11.7 mg, 44.8 μmol) at 0 ºC under Ar and the mixture was stirred for 2 h at room temperature. The mixture was concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 40:1) to afford **23** (6.0 mg, 72%) as colorless amorphous.

IR (neat) 2930, 1695, 1464, 1251, 1017 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (3H, s), 0.06 (3H, s), 0.15 (9H, s), 0.65 (3H, s), 0.93 (9H, s), 1.15-1.18 (1H, m), 1.39 (3H, s), 1.60-1.63 (1H, m), 1.71 (1H, 1/2ABq, *J* = 15.1 Hz), 1.75-1.90 (2H, m), 1.95 (1H, 1/2ABq, *J* = 15.1 Hz), 2.20 (1H, 1/2ABqd, *J* = 13.5, 8.0 Hz), 2.32 (1H, 1/2ABqd, *J* = 13.7, 6.9 Hz), 2.54-2.57 (2H, m), 2.94-3.02 (2H, m), 3.41-3.44 (1H, m), 4.84 (1H, s), 4.96 (1H, s), 5.02-5.08 (2H, m), 5.80 (1H, tdd, *J* = 17.2, 9.4, 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.0, –4.1, 3.2 (3C), 18.3, 19.7, 22.0, 26.1 (3C), 27.6, 28.1, 31.4, 38.9, 43.2, 46.4, 46.5, 49.9, 79.8, 80.6, 110.8, 118.0, 135.1, 151,7, 216.1; HRESIMS calcd for $C_{26}H_{48}O3NaSi_2$ $[M+Na]^+$ 487.3040 found 487.3038.

Synthesis of

(1*R**,4a*S**,6*R**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-4-methylene-6-((*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**24**).

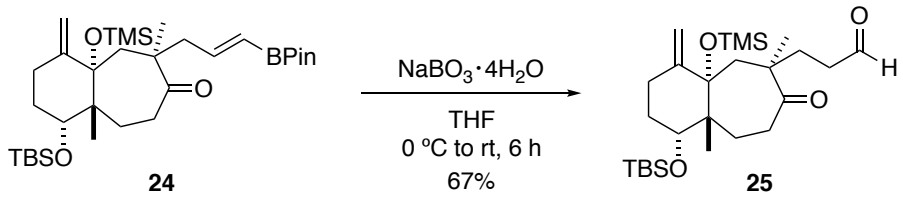


To a stirred solution of **23** (6.0 mg, 12.9 μmol) in CH_2Cl_2 (0.2 mL) was added 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (2.98 mg, 19.4 μmol) and Zhan catalyst-1B (0.50 mg, 0.65 μmol) at room temperature under Ar and the mixture was refluxed for 4 h. The mixture was cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 60:1) to afford **24** (6.7 mg, 87%) as colorless oil.

IR (neat) 2931, 1742, 1695, 1635, 1362, 1251, 1146 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.05 (3H, s), 0.06 (3H, s), 0.13 (9H, s), 0.63 (3H, s), 0.93 (9H, s), 1.09-1.21 (1H, m), 1.25 (12H, s), 1.42 (3H, s), 1.55-1.61 (H, m), 1.64 (1H, 1/2ABq, *J* = 15.1 Hz), 1.75-1.89 (2H, m), 1,97 (1H, 1/2ABq, *J* = 15.1 Hz), 2.31 (1H, 1/2ABqd, *J* = 13,7, 8.8 Hz), 2.43 (1H, 1/2ABqdd, *J* = 13.6, 6.2, 1.1 Hz), 2.50-2.64 (2H, m), 2.94-3.04 (2H, m), 3.39-3.44 (1H, m), 4.83 (1H, s), 4.94 (1H, s), 5.48 (1H, d, *J* = 17.9 Hz), 6.61 (1H, ddd, *J* = 17.5, 8.3, 6.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.0, –4.1, 3.2 (3C), 18.3, 19.6, 21.6, 24.7 (4C), 26.1 (3C), 27.3, 28.1, 31.3, 39.1, 42.7, 46.5, 48.0, 50.3, 79.9, 80.6, 83.1 (2C), 110.9, 122.2, 150.8, 151.5, 216.1; HRESIMS calcd for $C_{32}H_{59}O_5NaSi_2B$ $[M+Na]^+$ 613.3892 found 613.3899.

Synthesis of

3-((1*R**,4a*S**,6*R**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-4-methylene-7-oxo-4a-((trimethylsilyl)oxy)decahydro-1*H*-benzo[7]annulen-6-yl)propanal (**25**).

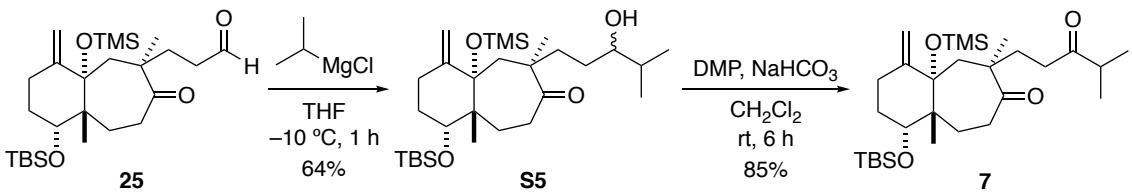


To a stirred solution of **24** (56.8 mg, 96.1 μmol) in tetrahydrofuran (0.5 mL) and H_2O (0.5 mL) was added sodium peroxoborate tetrahydrate (59.0 mg, 0.38 mmol) at 0 ºC and the mixture was stirred for 6 h at room temperature. The reaction was quenched with H_2O and the mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 30:1) to afford **25** (31.0 mg, 67%) as white amorphous.

IR (neat) 2930, 1707, 1251, 1103 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (3H, s), 0.05 (3H, s), 0.14 (9H, s), 0.64 (3H, s), 0.92 (9H, s), 1.13-1.20 (1H, m), 1.41 (3H, s), 1.56-1.73 (2H, m), 1.74-1.83 (2H, m), 1.86-2.03 (3H, m), 2.40-2.44 (2H, m), 2.51-2.55 (2H, m), 2.92-3.02 (2H, m), 3.39-3.44 (1H, m), 4.83 (1H, s), 4.96 (1H, s), 9.77 (1H, brs); ^{13}C NMR (100 MHz, $CDCl_3$) δ –5.0, –4.1, 3.2 (3C), 18.3, 19.6, 21.5, 26.1 (3C), 27.6, 28.1, 31.3, 33.9, 38.9, 39.5, 44.2, 46.6, 49.5, 79.8, 80.7, 110.9, 151.4, 202.3, 215.8; HRESIMS calcd for $C_{26}H_{48}O_4NaSi_2$ $[M+Na]^+$ 503.2989 found 503.2989.

Synthesis of

(1*R**,4a*S**,6*R**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-6-(4-methyl-3-oxopentyl)-4-methylene-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (**7**).

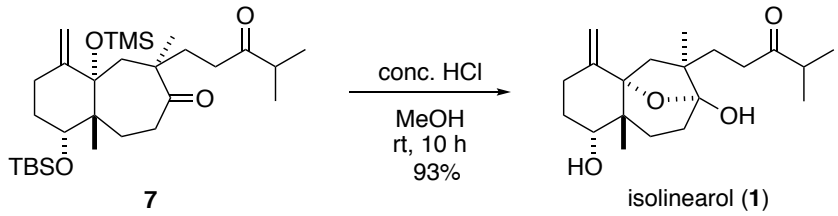


To a stirred solution of **25** (9.4 mg, 19.5 μmol) in tetrahydrofuran (0.2 mL) was added dropwise isopropylmagnesium chloride (2.0 M THF, 0.01 mL, 20.0 μmol) at –10 ºC under Ar, and the mixture was stirred for 1 h at same temperature. The reaction was quenched with saturated NH_4Cl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 30:1) to afford **S5** (6.7 mg, 64%, 1:1 diastereomixture) as colorless amorphous. The obtained **S5** was used for next reaction with out further separation.

To a solution of **S5** (15.0 mg, 28.6 μmol) in CH_2Cl_2 (1.5 mL) was added $NaHCO_3$ (7.21 mg, 85.8 μmol) and Dess-Martin periodinane (12.1 mg, 28.6 μmol) at room temperature under Ar, and the mixture was stirred for 6 h at same temperature. The reaction was quenched with 50% $Na_2S_2O_3$ aqueous solution and saturated $NaHCO_3$ aqueous solution and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 30:1) to afford **7** (12.9 mg, 85%) as colorless amorphous.

IR (neat) 2929, 1251, 1075 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (3H, s), 0.06 (3H, s), 0.14 (9H, s), 0.67 (3H, s), 0.92 (9H, s), 1.05-1.18 (1H, m), 1.08 (6H, d, J = 6.9 Hz), 1.37 (3H, s), 1.54-1.69 (3H, m), 1.75-1.97 (4H, m), 2.36-2.50 (3H, m), 2.53-2.64 (2H, m), 2.88-3.02 (2H, m), 3.40-3.43 (1H, m), 4.85 (1H, s), 4.96 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ –4.9, –4.1, 3.2 (3C), 18.29, 18.34, 18.4, 19.8, 22.0, 26.2 (3C), 28.16, 28.21, 31.5, 35.6, 36.0, 38.6, 40.9, 44.6, 46.7, 49.4, 79.7, 80.8, 111.0, 151.5, 214.9, 215.8; HRESIMS calcd for $C_{29}H_{54}O_4NaSi_2$ $[M+Na]^+$ 545.3458 found 545.3460.

Synthesis of isolinearol (**1**).



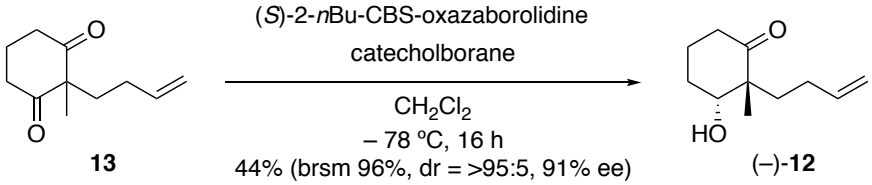
7 isolinearol (**1**)

To a stirred solution of **7** (3.0 mg, 5.74 μmol) in methol (0.3 mL) was added a drop of

conc. HCl at room temperature and the mixture was stirred for 20 min at same temperature. The reaction was quenched with saturated $NaHCO_3$ aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 2:1) to afford **1** (1.8 mg, 93%) as a white solid.

M.p. 91-99 ºC; IR (KBr disk) 3355, 2947, 1705, 1472, 1089, 1023 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.67 (3H, s), 1.01 (3H, s), 1.11 (6H, d, J = 6.9 Hz), 1.63-1.78 (4H, m), 1.80-1.86 (2H, m), 1.88-2.01 (3H, m), 2.14-2.28 (2H, m), 2.48 (1H, qq, J = 6.9, 6.9 Hz), 2.56-2.68 (2H, m), 2.69-2.79 (1H, m), 3.55-3.59 (1H, m), 4.82 (1H, brs), 4.97 (1H, brs); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3, 18.4, 22.3, 22.6, 27.3, 29.5, 31.9, 32.0, 33.1, 35.8, 39.8, 40.9, 41.0, 43.2, 78.6, 86.0, 105.5, 110.2, 146.5, 214.8; HRESIMS calcd for $C_{20}H_{32}O_4Na$ $[M+Na]^+$ 359.2198 found 359.2191.

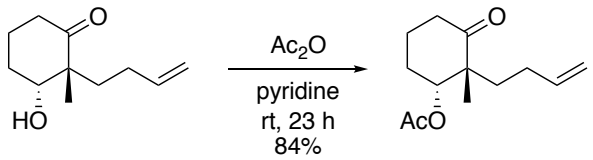
Synthesis of (2*R*,3*R*)-2-(but-3-en-1-yl)-3-hydroxy-2-methylcyclohexan-1-one (–)-(**12**).



To a stirred solution of (*S*)-2-*n*Bu-CBS-oxazaborolidine (1 M toluene, 0.14 mL, 0.14 mmol) in CH_2Cl_2 (3 mL) was added dropwise catecholborane (66.0 mg, 0.06 mL, 0.55 mmol) at 0 ºC under Ar and the mixture was stirred for 30 min at same temperature. The mixture was added dropwise to a stirred solution of **13** (740 mg, 4.10 mmol) in CH_2Cl_2 (3 mL) at –78 ºC under Ar and the mixture was stirred for 16 h at same temperature. The reaction was quenched with MeOH and 1 M HCl and the mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 10:1) to afford (–)-**12** (328 mg, 44%, brsm 96%) as colorless oil and **13** (397 mg, 54%) as yellow oil.

Optical rotation of (2*R*,3*R*)-2-(but-3-en-1-yl)-3-hydroxy-2-methylcyclohexan-1-one (–)-(**12**); $[\alpha]_D^{25}$ = –38.5 (*c* 1.01, $CHCl_3$).

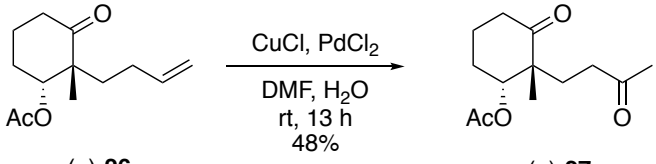
Synthesis of (1*R*,2*R*)-2-(but-3-en-1-yl)-2-methyl-3-oxocyclohexyl acetate (–)-(**26**).



(–)-**12** (–)-**26**

To a stirred solution of (–)-**12** (56.5 mg, 0.31 mmol) in CH_2Cl_2 (1 mL) was added pyridine (1 mL) and acetic anhydride (108 mg, 0.1 mL, 1.06 mmol) at room temperature under Ar and the mixture was stirred for 23 h at same temperature. The reaction was quenched with H_2O and 1 M HCl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 3:1) to afford (–)-**26** (58.6 mg, 84%) as colorless oil. $[\alpha]_D^{25}$ = –27.4 (c = 0.30, $CHCl_3$); IR (neat) 2952, 1739, 1713, 1374, 1237, 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13 (3H, s), 1.56-2.03 (8H, m), 2.05 (3H, s), 2.33-2.54 (2H, m), 4.89 (1H, dd, *J* = 7.8, 3.7 Hz), 4.92-5.05 (2H, m), 5.71-5.85 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 20.6, 21.0, 25.6, 27.5, 31.5, 37.5, 52.5, 78.2, 114.7, 138.3, 170.1, 212.4; HRESIMS calcd for $C_{13}H_{20}O_3Na$ $[M+Na]^+$ 247.1310 found 247.1303.

Synthesis of (1*R*,2*R*)-2-methyl-3-oxo-2-(3-oxobutyl)cyclohexyl acetate (–)-(**27**).



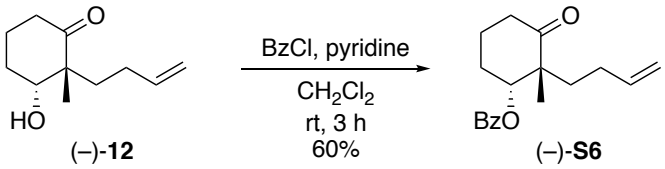
(–)-**26** (–)-**27**

To a stirred solution of CuCl (15.9 mg, 0.16 mmol) in *N*,*N*-dimethylformamide (0.3 mL) and H_2O (0.2 mL) was added $PdCl_2$ (4.8 mg, 26.8 μmol) at room temperature and the mixture was stirred for 24 h at same temperature. To a stirred mixture was added

solution of (–)-**26** (30.0 mg, 0.13 mmol) in *N*,*N*-dimethylformamide (0.2 mL) at room temperature and mixture was stirred for 13 h at same temperature under O_2. The reaction was quenched with H_2O and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 10:1) to afford (–)-**27** (15.6 mg, 48%) as colorless oil.

$[\alpha]_D^{25}$ = –39.3 (c = 0.24, $CHCl_3$); IR (neat) 2952, 1738, 1712, 1373, 1237, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.07 (3H, s), 1.62-1.73 (1H, m), 1.75-1.83 (1H, m), 1.91-2.09 (4H, m), 2.05 (3H, s), 2.12 (3H, s), 2.20-2.42 (4H, m), 4.86 (1H, dd, *J* = 8.0, 3.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.0, 20.4, 21.0, 25.5, 25.7, 30.0, 37.5, 37.7, 52.0, 78.2, 170.1, 208.0, 212.2; HRESIMS calcd for $C_{13}H_{20}O_4Na$ $[M+Na]^+$ 263.1259 found 263.1250.

Synthesis of (1*R*,2*R*)-2-(but-3-en-1-yl)-2-methyl-3-oxocyclohexyl benzoate (–)-**S6**.



To a stirred solution of (–)-**12** (13.8 mg, 75.7 μmol) in CH_2Cl_2 (0.6 mL) was added pyridine (0.1 mL) and benzoyl chloride (21.0 mg, 0.02 mL, 0.15 mmol) at room temperature under Ar and the mixture was stirred for 3 h at same temperature. The reaction was quenched with 1 M HCl aqueous solution and the mixture was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by column chromatography (hexane-AcOEt, 20:1) to afford (–)-**S6** (16.7 mg, 60%) as colorless oil.

$[\alpha]_D^{25}$ = –43.1 (c = 0.82, $CHCl_3$); IR (neat) 2951, 2874, 1790, 1714, 1641, 1453, 1272 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (3H, s), 1.73-1.90 (4H, m), 1.95-2.20 (4H, m), 2.42-2.57 (2H, m), 4.93 (1H, dd, *J* = 10.3, 1.1 Hz), 5.00 (1H, dd, *J* = 16.9, 1.4 Hz), 5.16 (1H, dd, *J* = 7.3, 3.7 Hz), 5.72-5.83 (1H, m), 7.45 (2H, t, *J* = 7.6 Hz), 7.58 (1H, t, *J* = 7.5 Hz), 8.01 (2H, d, *J* = 8.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 20.7, 25.6, 27.6, 31.8, 37.6, 52.7, 78.8, 114.8, 128.5 (2C), 129.6 (2C), 129.9, 133.2, 138.2, 165.5, 212.5;

HRESIMS calcd for $C_{18}H_{22}O_3Na$ $[M+Na]^+$ 309.1467 found 309.1458.

Optical rotation of
(2*R*,3*R*)-2-(But-3-en-1-yl)-3-(((bromomethyl)dimethylsilyl)oxy)-2-methylcyclohexan-1-one (–)-(**S1**)
$[\alpha]_D^{25}$ = –26.2 (*c* 1.03, $CHCl_3$)

Optical rotation of
(1*R*,5*S*,7*R*)-7-(But-3-en-1-yl)-3,3,7-trimethyl-2-oxa-3-silabicyclo[3.2.2]nonan-6-one (–)-(**11**)
$[\alpha]_D^{25}$ = –46.8 (*c* 0.86, $CHCl_3$)

Optical rotation of
(1*R*,5*S*,6*S*,7*R*)-7-(But-3-en-1-yl)-3,3,7-trimethyl-6-(2-methylallyl)-2-oxa-3-silabicyclo[3.2.2]nonan-6-ol (+)-(**15**)
$[\alpha]_D^{25}$ = +53.6 (*c* 0.95, $CHCl_3$)

Optical rotation of
(1*S*,2*R*,3*R*,6*R*)-2-(But-3-en-1-yl)-6-(hydroxymethyl)-2-methyl-1-(2-methylallyl)cyclohexane-1,3-diol (–)-(**10**)
$[\alpha]_D^{25}$ = –6.6 (*c* 1.00, $CHCl_3$)

Optical rotation of
(1*R*,4*R*,4a*S*,9a*R*)-4-(Hydroxymethyl)-6,9a-dimethyl-1,2,3,4,5,8,9,9a-octahydro-4a*H*-benzo[7]annulene-1,4a-diol (–)-(**16**)
$[\alpha]_D^{25}$ = –56.1 (*c* 0.70, $CHCl_3$)

Optical rotation of
(1*R*,4*R*,4a*S*,9a*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-1,2,3,4,5,8,9,9a-octahydro-4a*H*-benzo[7]annulen-4a-ol (–)-(**17**)
$[\alpha]_D^{25}$ = –23.0 (*c* 0.95, $CHCl_3$)

Optical rotation of
tert-Butyl(((1*R*,4*R*,4a*R*,9a*S*)-4-((*tert*-butyldimethylsilyl)oxy)-4a,8-dimethyl-9a-((trimethylsilyl)oxy)-2,3,4,4a,5,6,9,9a-octahydro-1*H*-benzo[7]annulen-1-yl)methoxy)dimethylsilane (–)-(**9**)
$[\alpha]_D^{25}$ = –18.9 (*c* 1.16, $CHCl_3$)

Optical rotation of
(1*R*,4*R*,4a*S*,9a*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-1*H*-benzo[7]annulen-7-ol (+)-(**S2**)
$[\alpha]_D^{25}$ = +1.84 (*c* 1.16, $CHCl_3$)

Optical rotation of
(1*R*,4*R*,4a*S*,9a*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (+)-(**8**)
$[\alpha]_D^{25}$ = +4.45 (*c* 0.90, $CHCl_3$)

Optical rotation of
(1*R*,4*R*,4a*S*,6*R*,9a*R*)-6-Allyl-1-((*tert*-butyldimethylsilyl)oxy)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (–)-(**20**)
$[\alpha]_D^{25}$ = –12.6 (*c* 0.90, $CHCl_3$)

Optical rotation of
(1*R*,4*R*,4a*S*,6*R*,9a*R*)-6-Allyl-1-((*tert*-butyldimethylsilyl)oxy)-4-(hydroxymethyl)-6,9a-dimethyl-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (–)-(**S4**)
$[\alpha]_D^{25}$ = –15.9 (*c* 0.45, $CHCl_3$)

Optical rotation of
((1*R*,4*R*,4a*R*,8*R*,9a*S*)-8-Allyl-4-((*tert*-butyldimethylsilyl)oxy)-4a,8-dimethyl-7-oxo-9a-((trimethylsilyl)oxy)decahydro-1*H*-benzo[7]annulen-1-yl)methyl
4-methylbenzenesulfonate (–)-(**21**)
$[\alpha]_D^{25}$ = –10.3 (*c* 0.36, $CHCl_3$)

Optical rotation of
(1*R*,4*S*,4a*S*,6*R*,9a*R*)-6-Allyl-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-4-((phenylselanyl)methyl)-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (+)-(**22**)
$[\alpha]_D^{25}$ = +1.1 (*c* 0.23, $CHCl_3$)

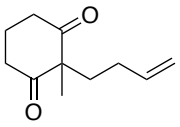
Optical rotation of
(1*R*,4a*S*,6*R*,9a*R*)-6-Allyl-1-((*tert*-butyldimethylsilyl)oxy)-6,9a-dimethyl-4-methylene-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (–)-(**23**)
$[\alpha]_D^{25}$ = –63.4 (*c* 0.42, $CHCl_3$)

Optical rotation of
(1*R*,4a*S*,6*R*,9a*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-6,9a-dimethyl-4-methylene-6-((*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (–)-(**24**)
$[\alpha]_D^{25}$ = –33.2 (*c* 0.53, $CHCl_3$)

Optical rotation of
3-((1*R*,4a*S*,6*R*,9a*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-6,9a-dimethyl-4-methylene-7-oxo-4a-((trimethylsilyl)oxy)decahydro-1*H*-benzo[7]annulen-6-yl)propanal (–)-(**25**)
$[\alpha]_D^{25}$ = –54.0 (*c* 0.29, $CHCl_3$)

Optical rotation of
(1*R*,4a*S*,6*R*,9a*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-6,9a-dimethyl-6-(4-methyl-3-oxopentyl)-4-methylene-4a-((trimethylsilyl)oxy)decahydro-7*H*-benzo[7]annulen-7-one (–)-(**7**)
$[\alpha]_D^{25}$ = –38.2 (*c* 0.15, $CHCl_3$)

Optical rotation of Isolinearol (–)-(**1**)
$[\alpha]_D^{25}$ = –47.4 (*c* 0.12, $CHCl_3$)



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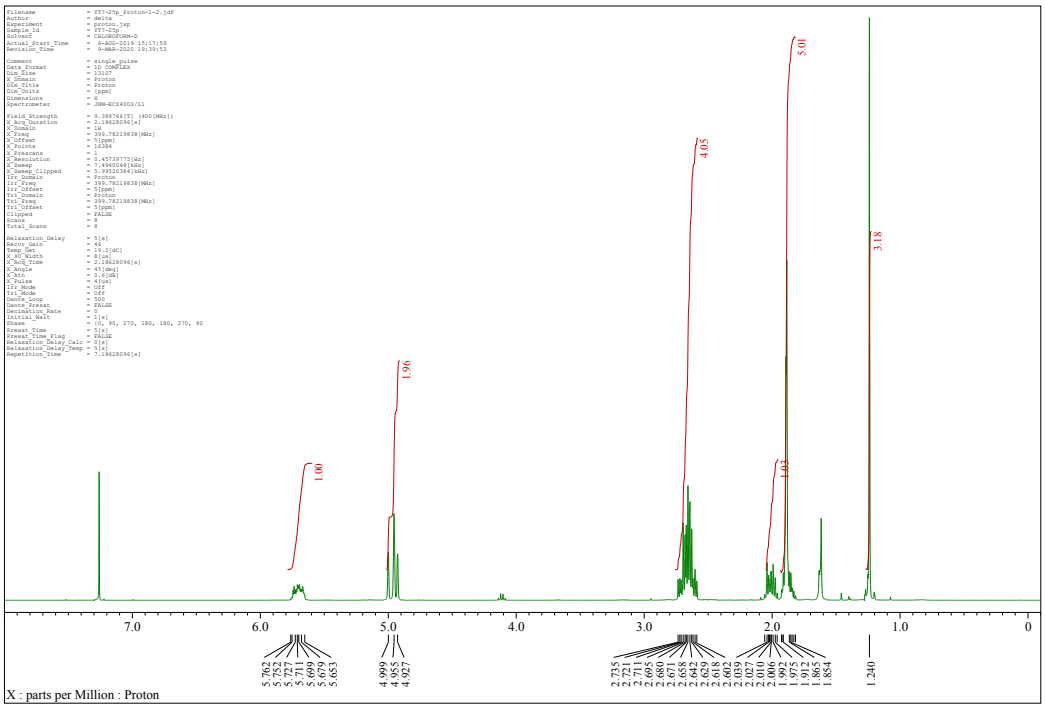
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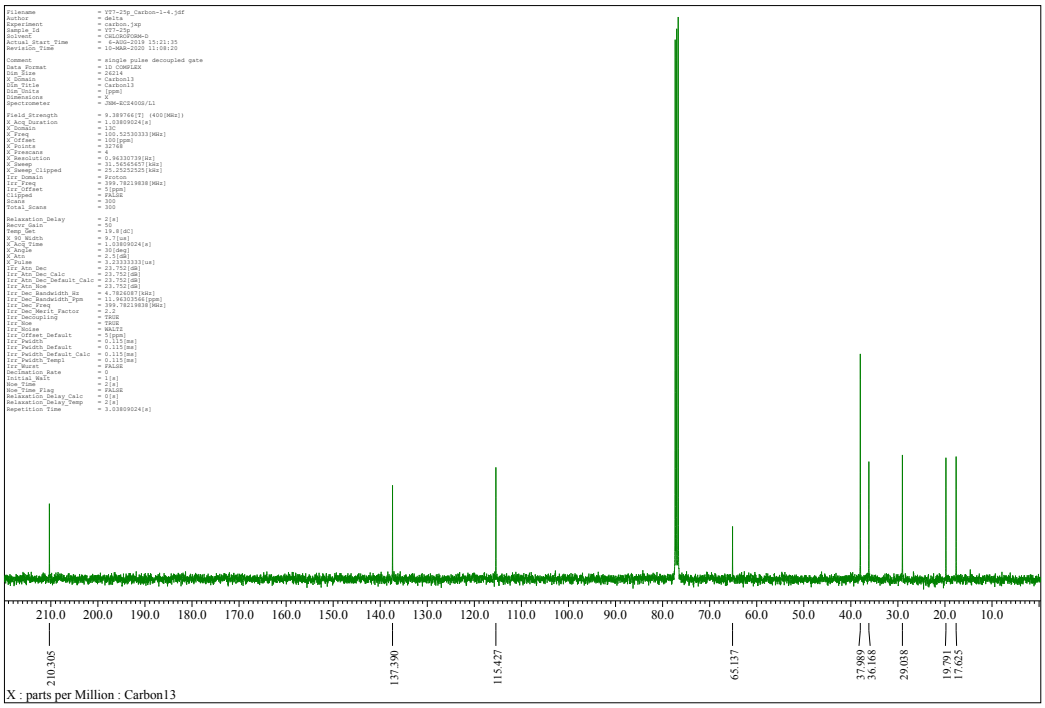
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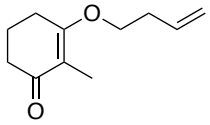
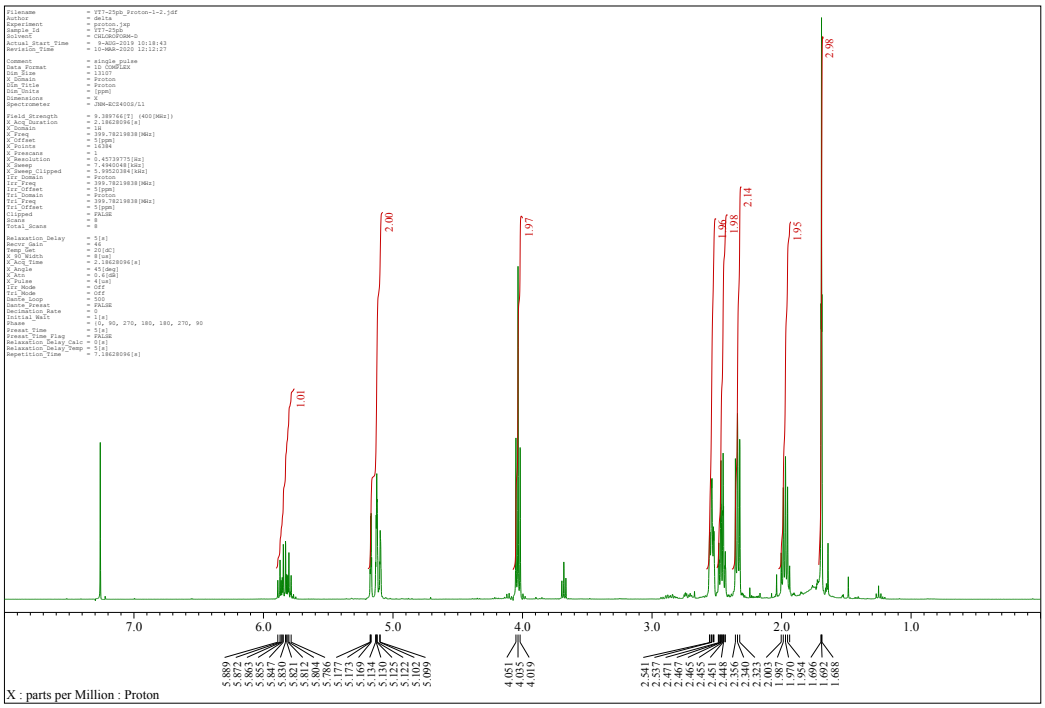
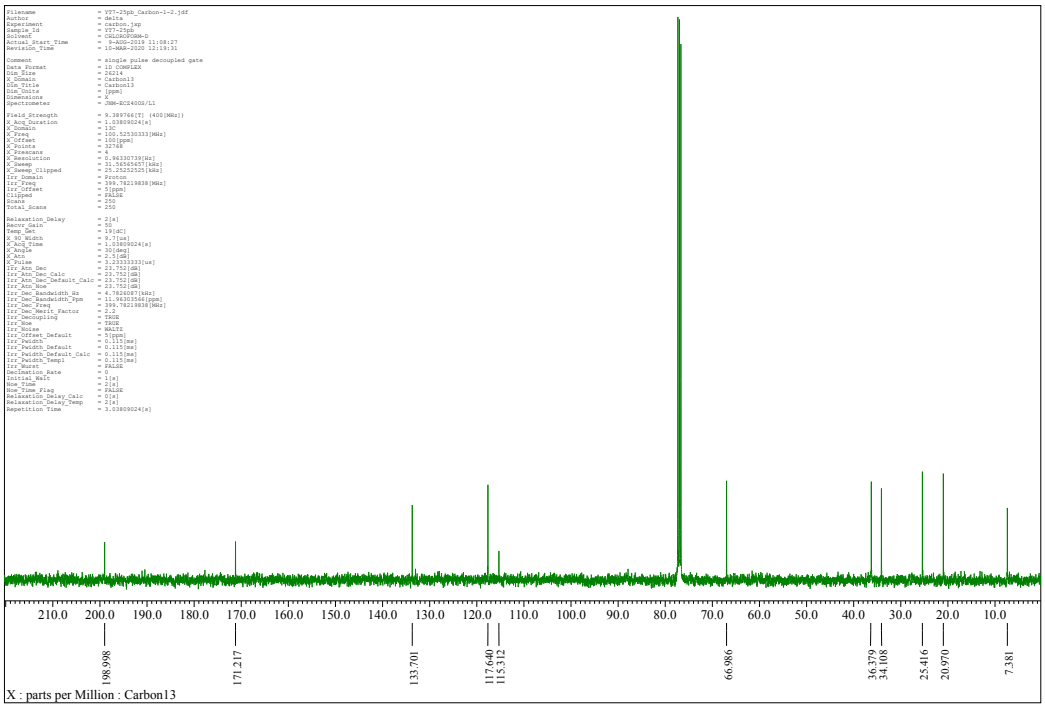
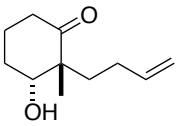
17.625
X : parts per Million : Carbon13

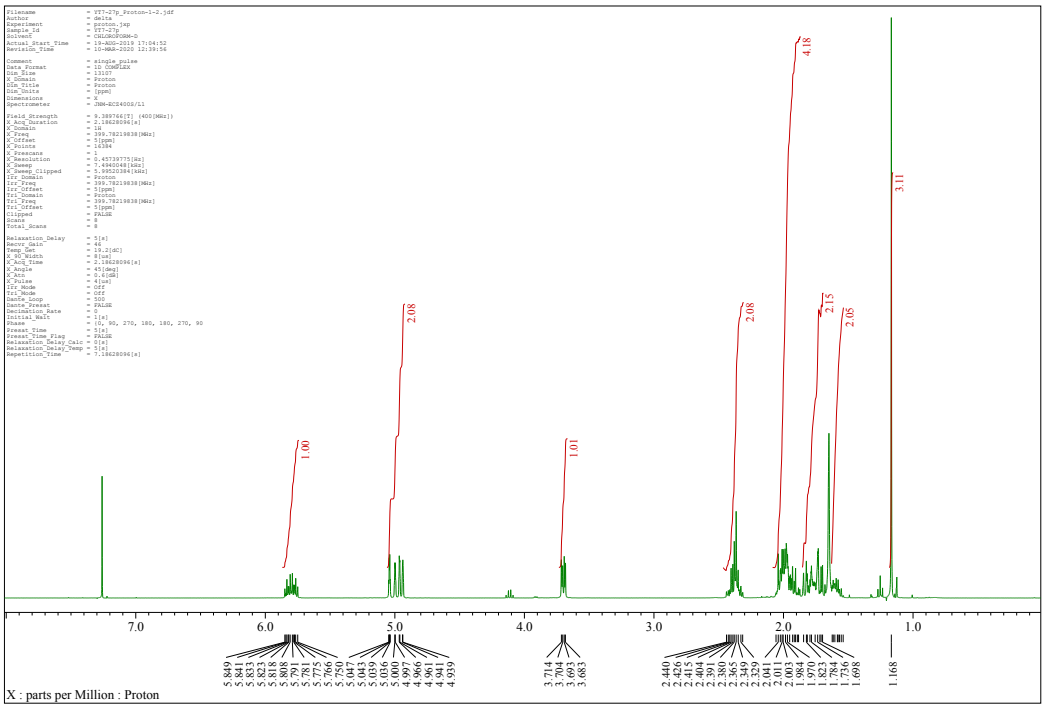


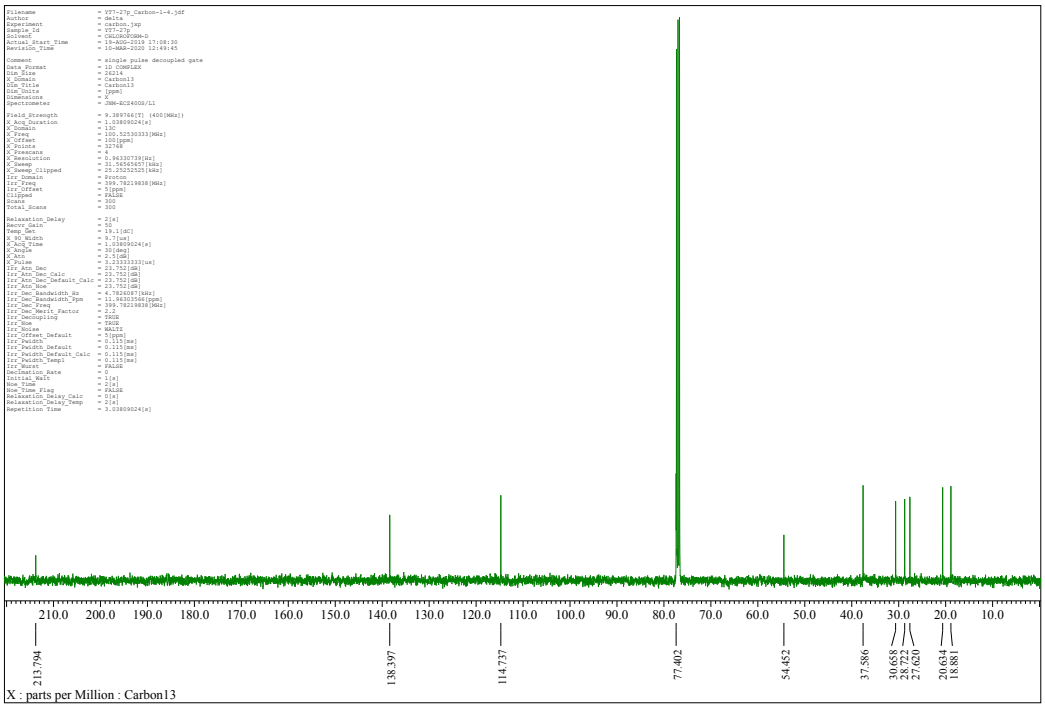

X : parts per Million : Proton

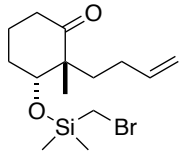

X : parts per Million : Carbon13


O
OH

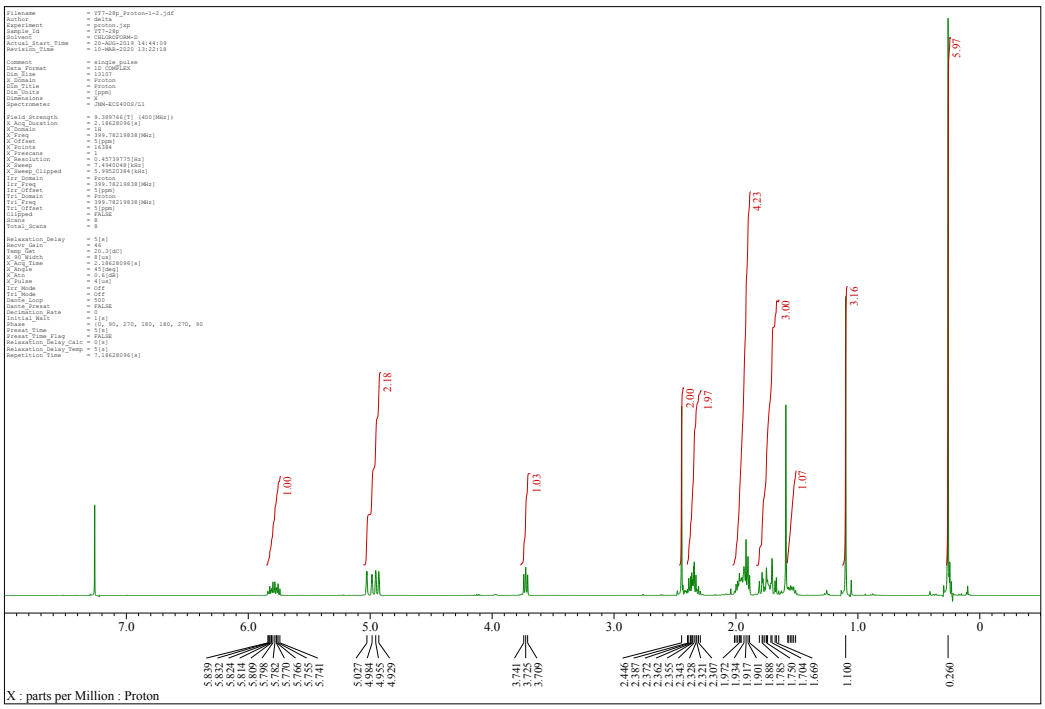
12

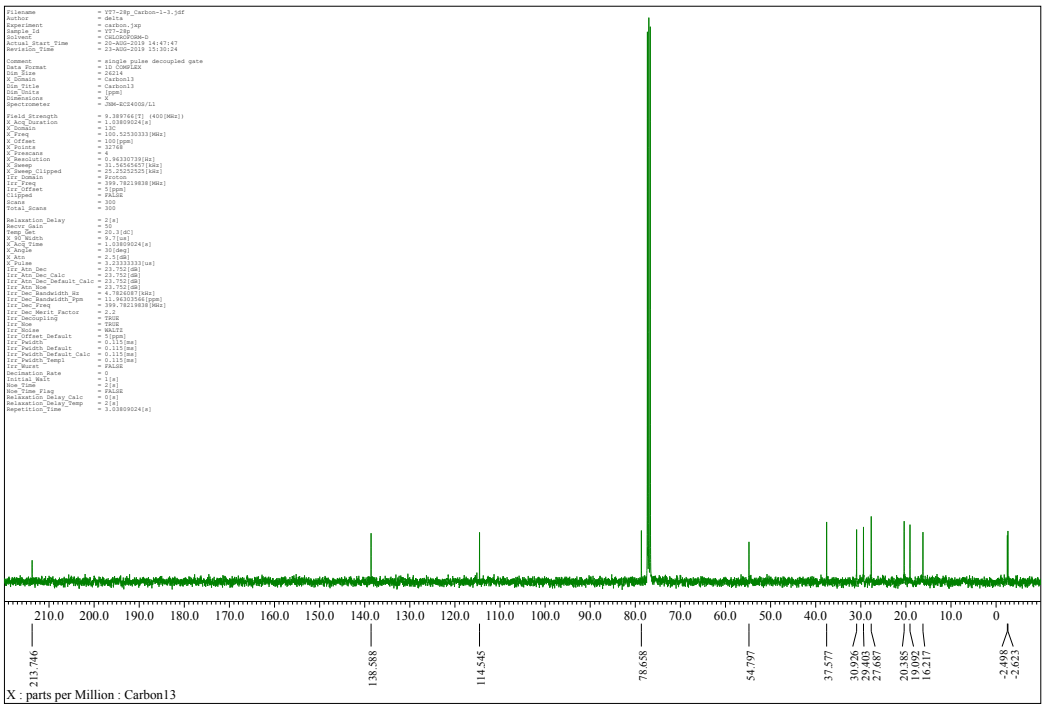

1.00
2.08
1.01
2.08
4.18
2.15
2.05
3.11
7.0
6.0
5.0
4.0
3.0
2.0
1.0
X : parts per Million : Proton

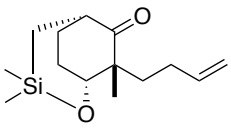

213.794
138.397
114.737
77.402
54.452
37.586
30.658
28.722
27.620
20.634
18.881
X : parts per Million : Carbon13


O
O
Si
Br

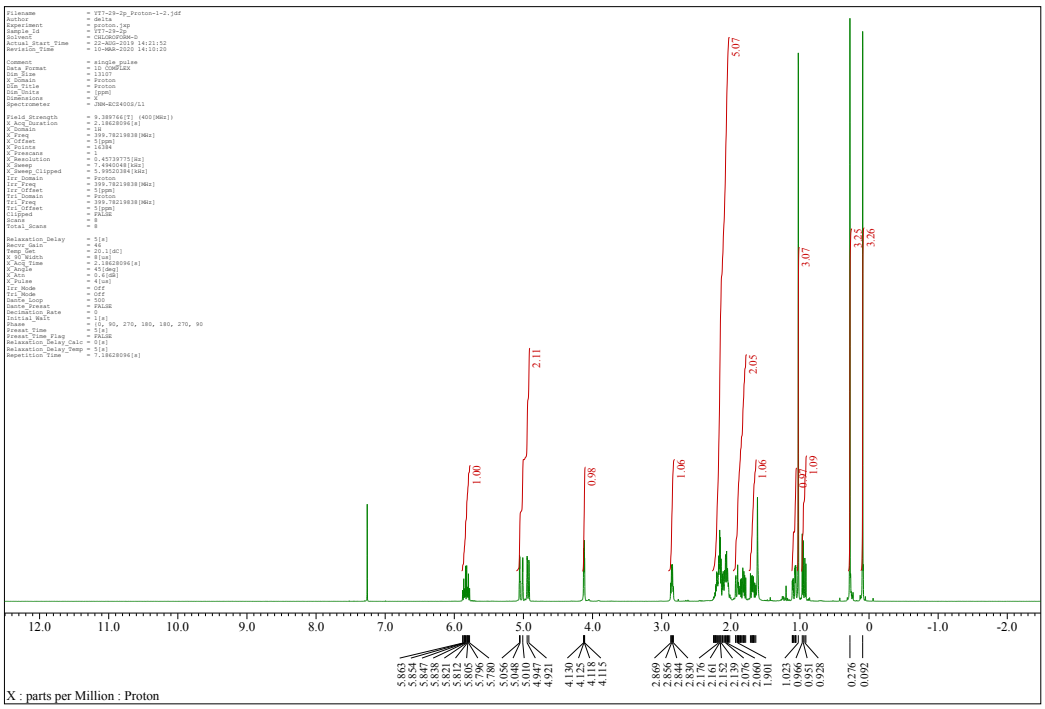
S1

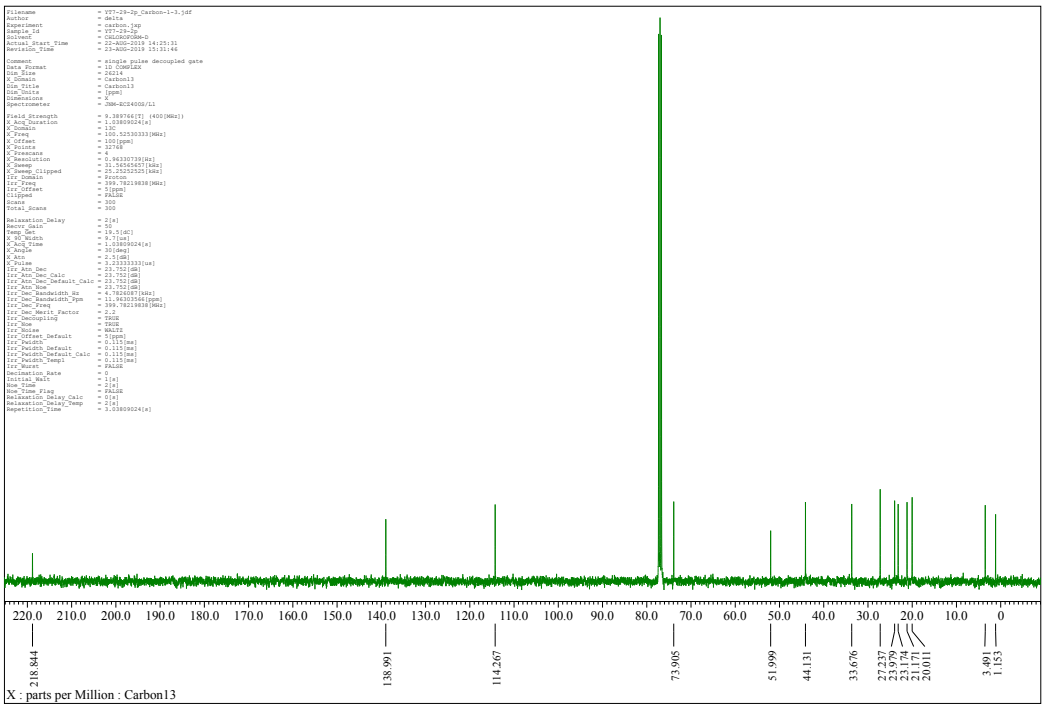

5.97
4.23
3.16
3.00
2.18
2.00
1.97
1.07
1.03
1.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

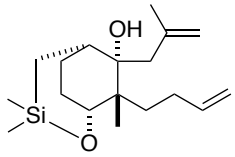

213.746
138.588
114.545
78.658
54.797
37.577
30.926
29.403
27.687
20.385
19.002
16.217
-2.498
-2.623
X : parts per Million : Carbon13


O
Si
O

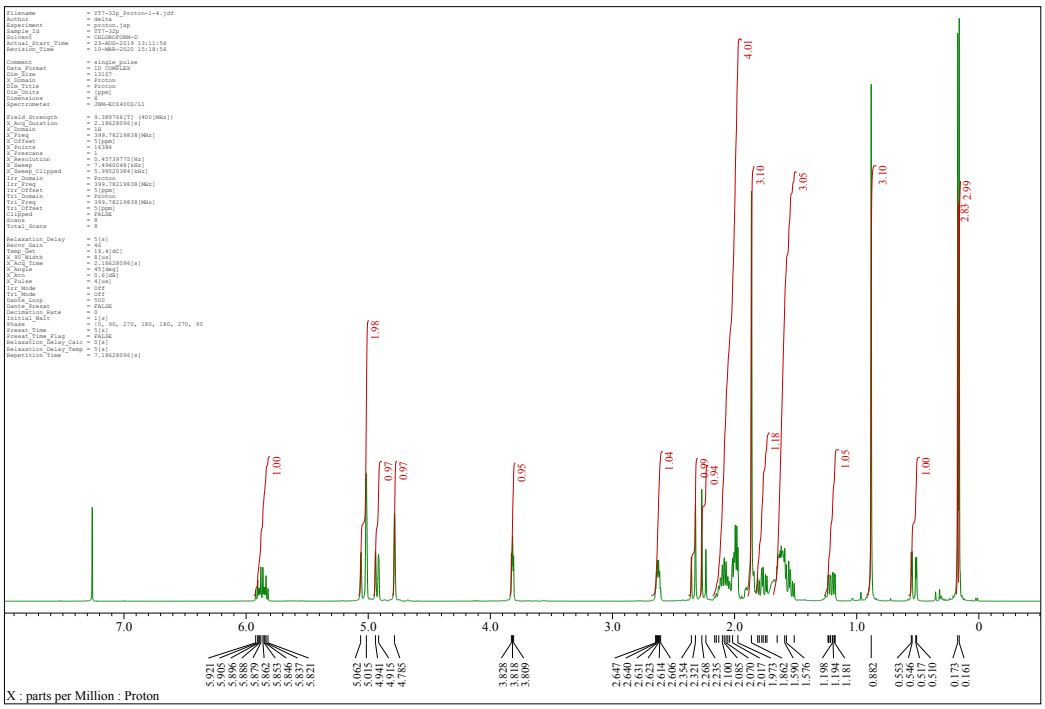
11

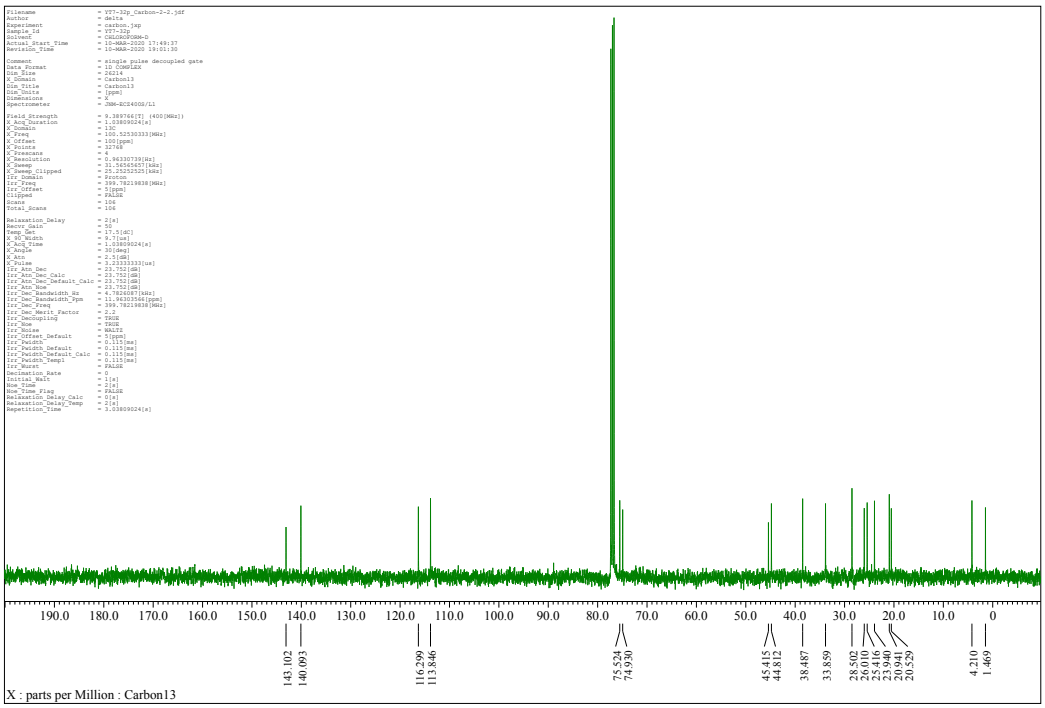

5.07
3.07
3.25
3.26
2.11
2.05
1.00
0.98
1.06
1.06
0.97
1.09
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-1.0
-2.0
X : parts per Million : Proton

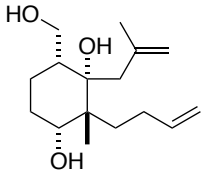

220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
218.844
138.991
114.267
73.905
51.999
44.131
33.676
27.237
23.979
23.174
21.171
20.011
3.491
1.153
X : parts per Million : Carbon13


OH
Si
O

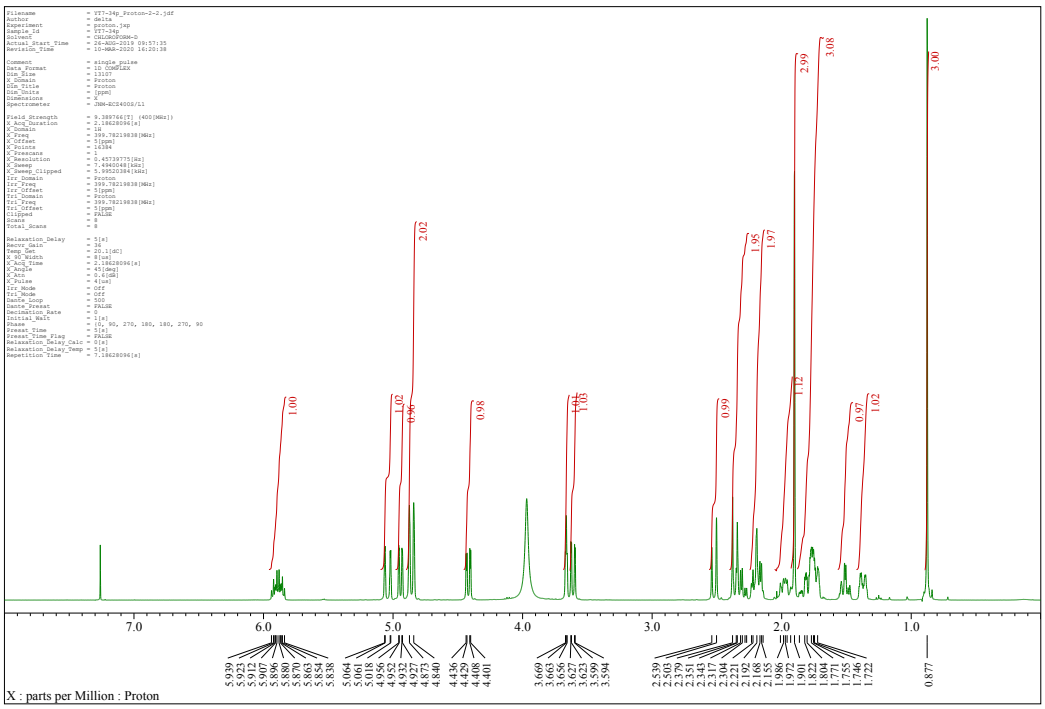
15

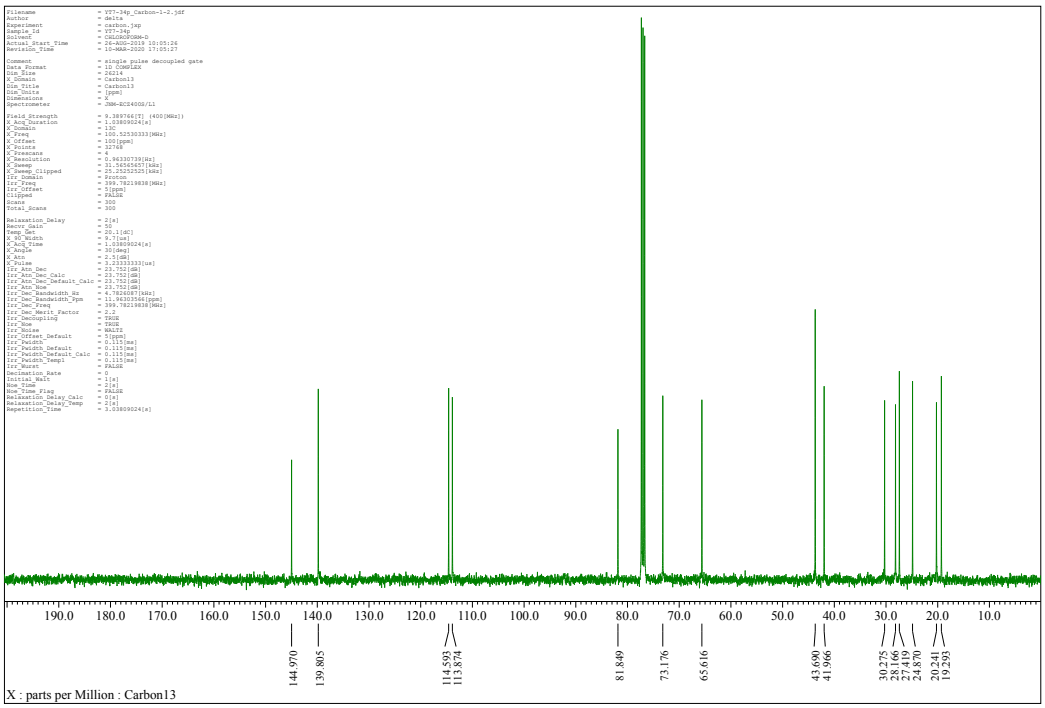

X : parts per Million : Proton

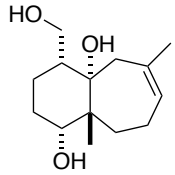

X : parts per Million : Carbon13


HO
OH
OH

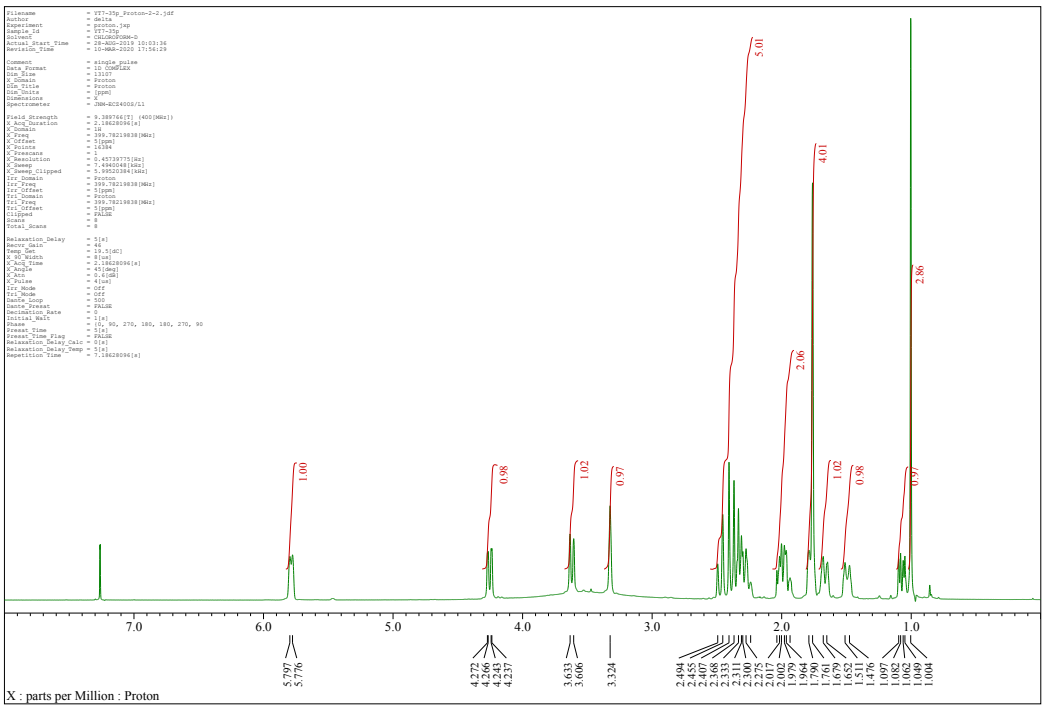
10

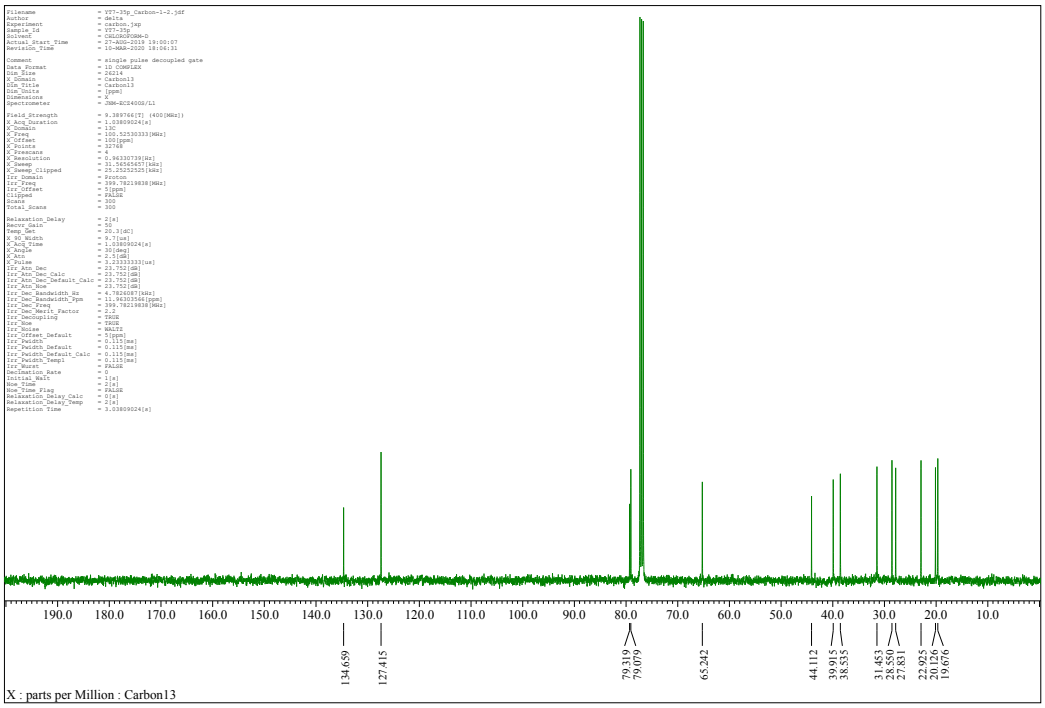

X : parts per Million : Proton

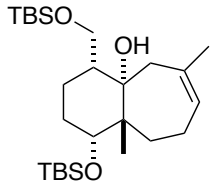

X : parts per Million : Carbon13


HO
OH
OH

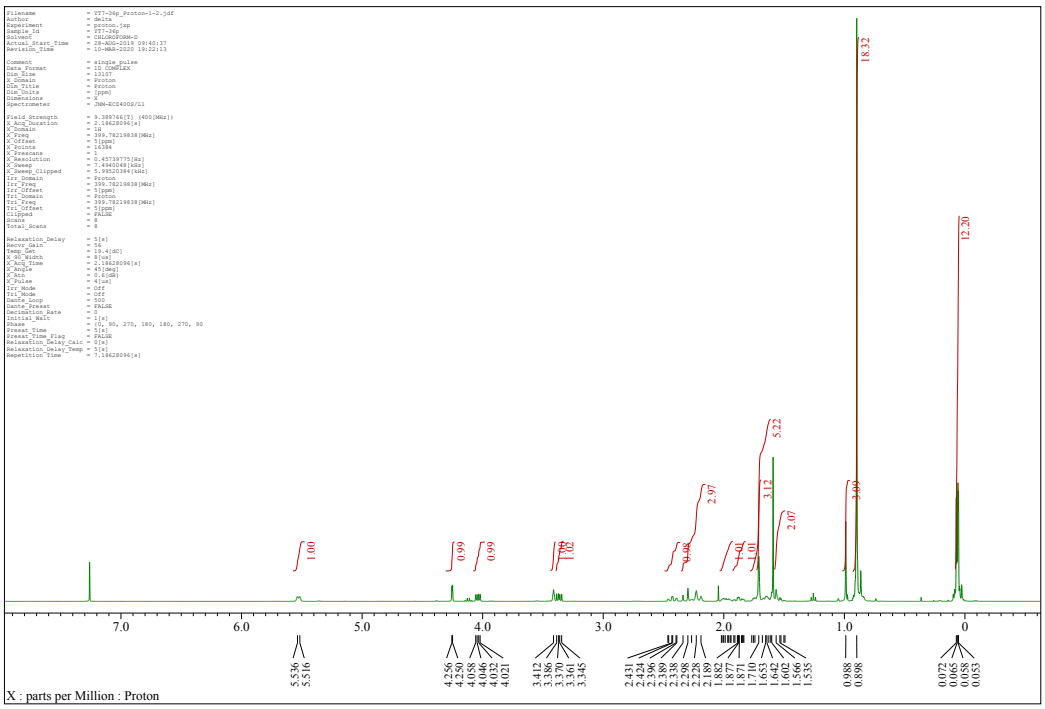
16

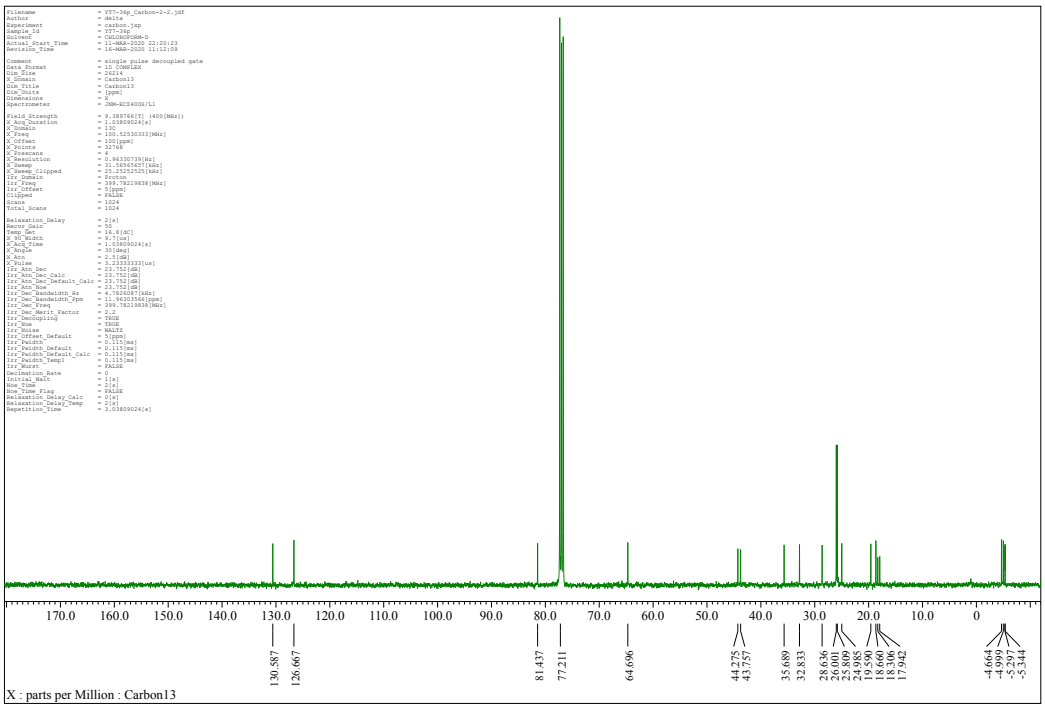

5.01
4.01
2.86
2.06
1.00
0.98
1.02
0.97
1.02
0.98
0.97
7.0
6.0
5.0
4.0
3.0
2.0
1.0
5.797
5.776
4.272
4.266
4.243
4.237
3.633
3.606
3.324
2.494
2.455
2.407
2.368
2.333
2.311
2.290
2.275
2.017
2.002
1.979
1.964
1.790
1.761
1.679
1.652
1.511
1.476
1.097
1.082
1.062
1.049
1.004
X : parts per Million : Proton

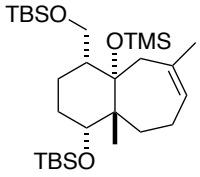

190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
134.659
127.415
79.319
79.079
65.242
44.112
39.915
38.555
31.453
28.550
27.851
22.925
20.126
19.676
X : parts per Million : Carbon13


TBSO
OH
TBSO

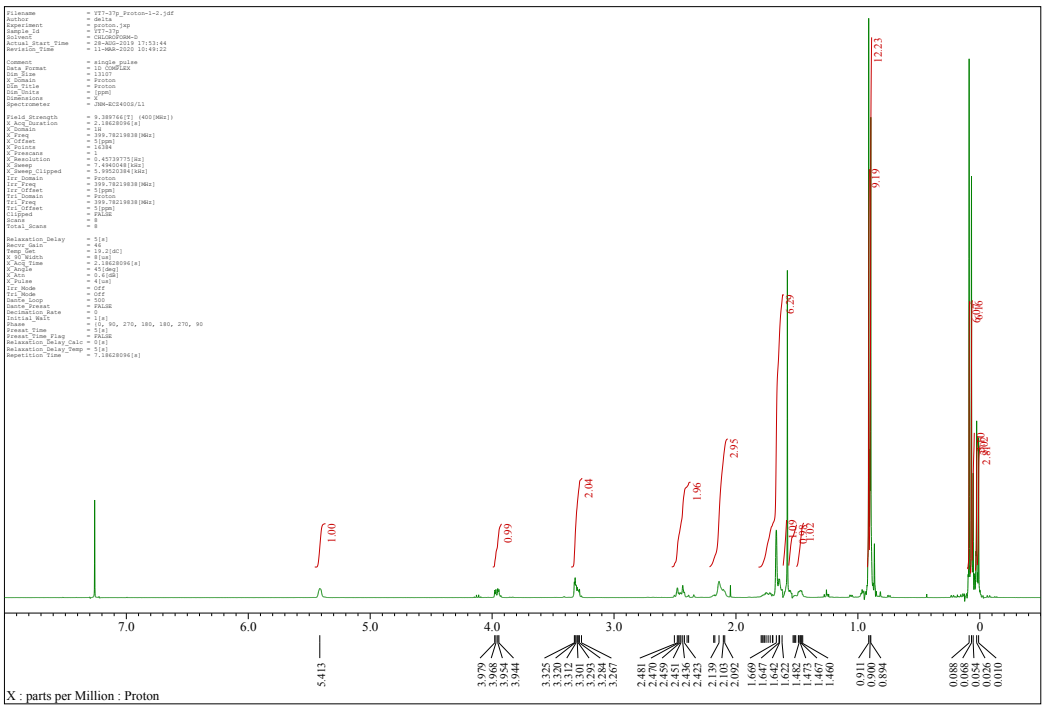
17

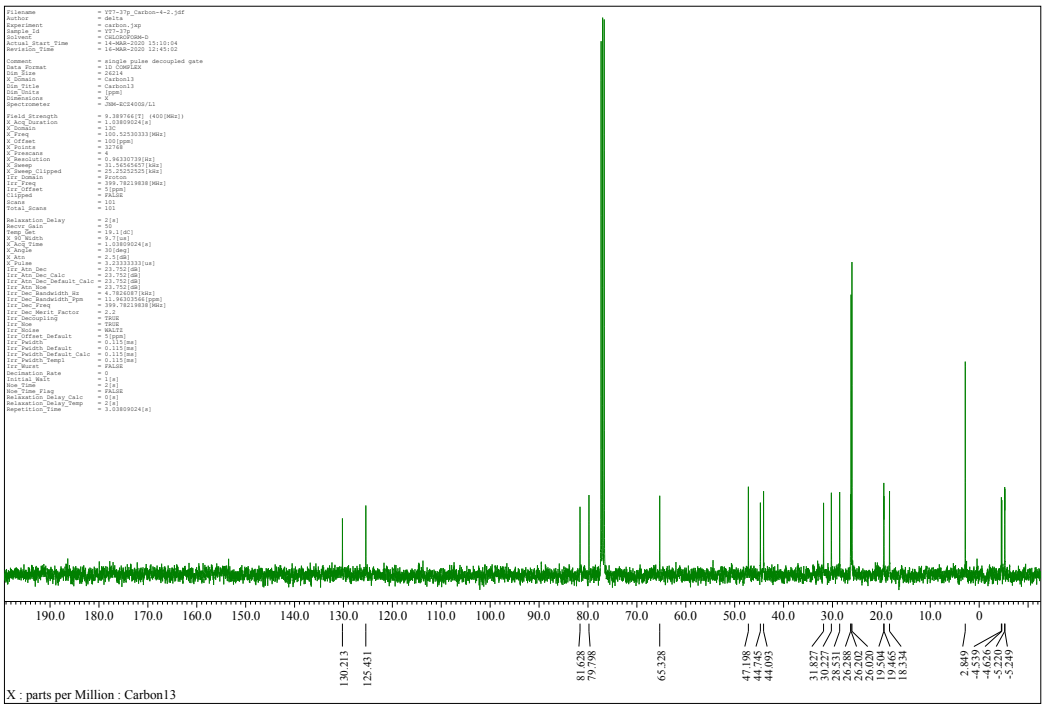

18.32
12.20
5.22
3.12
2.97
3.09
2.07
1.00
0.99
0.99
1.02
0.98
1.01
1.01
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

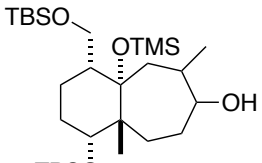

170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13


TBSO
OTMS
TBSO

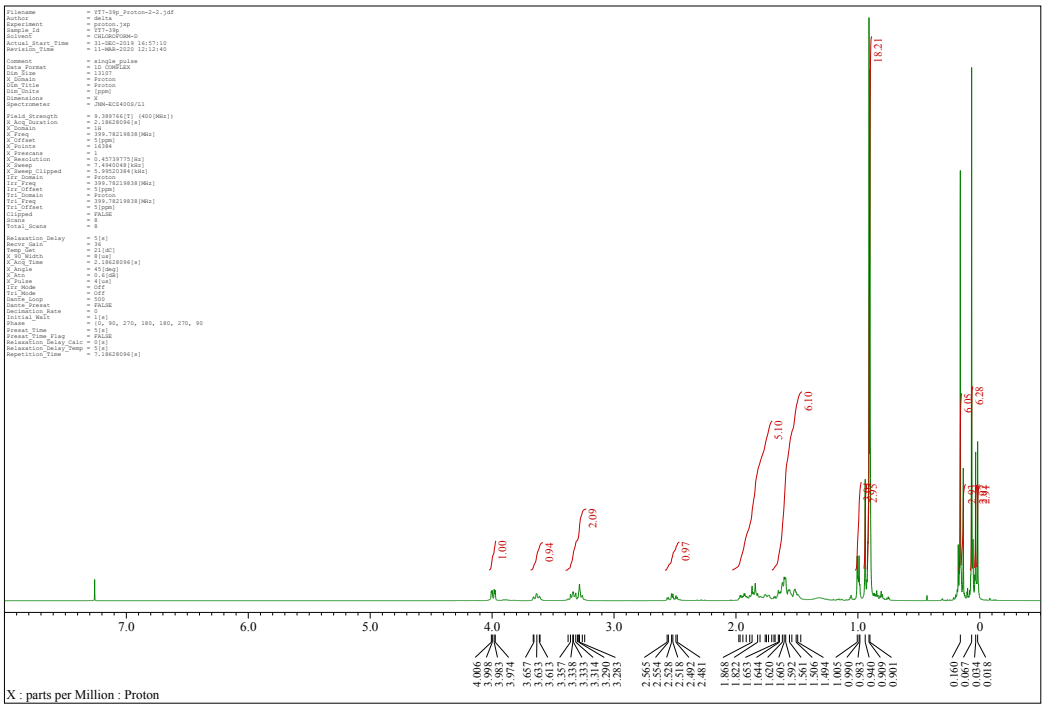
9

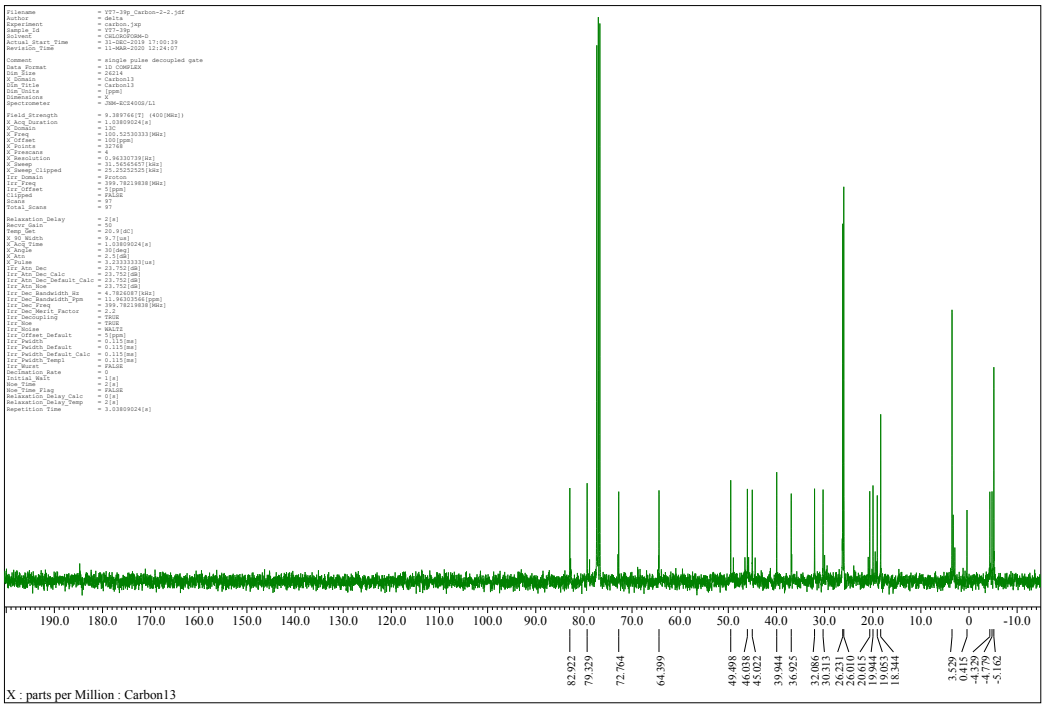

X : parts per Million : Proton

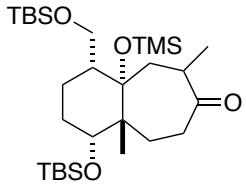

X : parts per Million : Carbon13


TBSO
OTMS
OH
TBSO

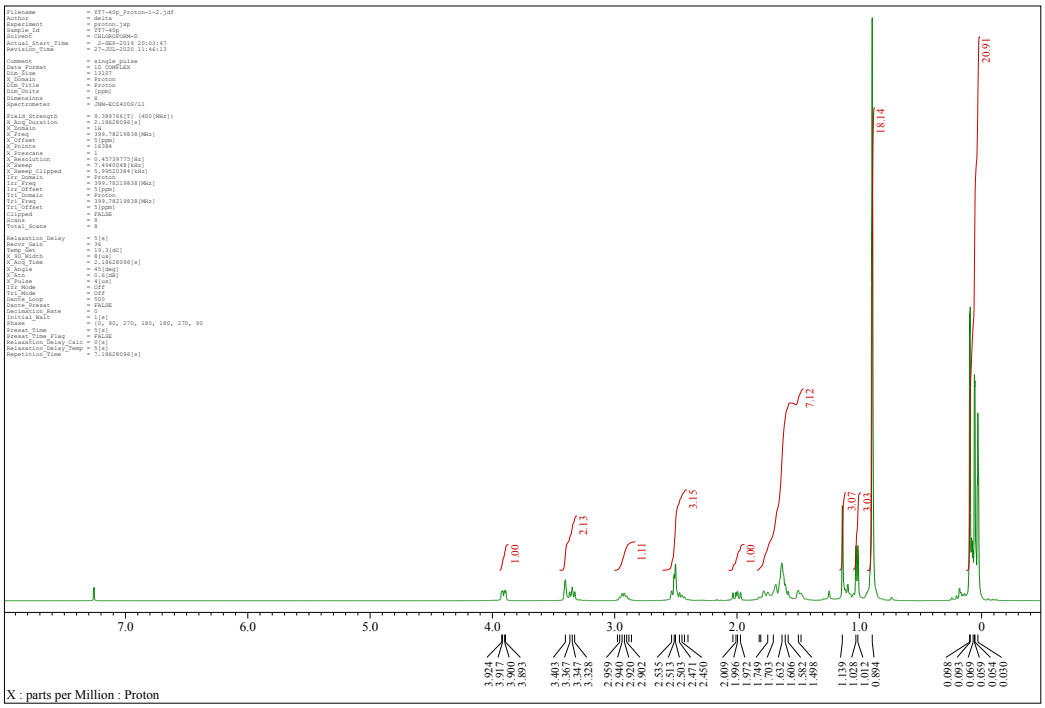
S2

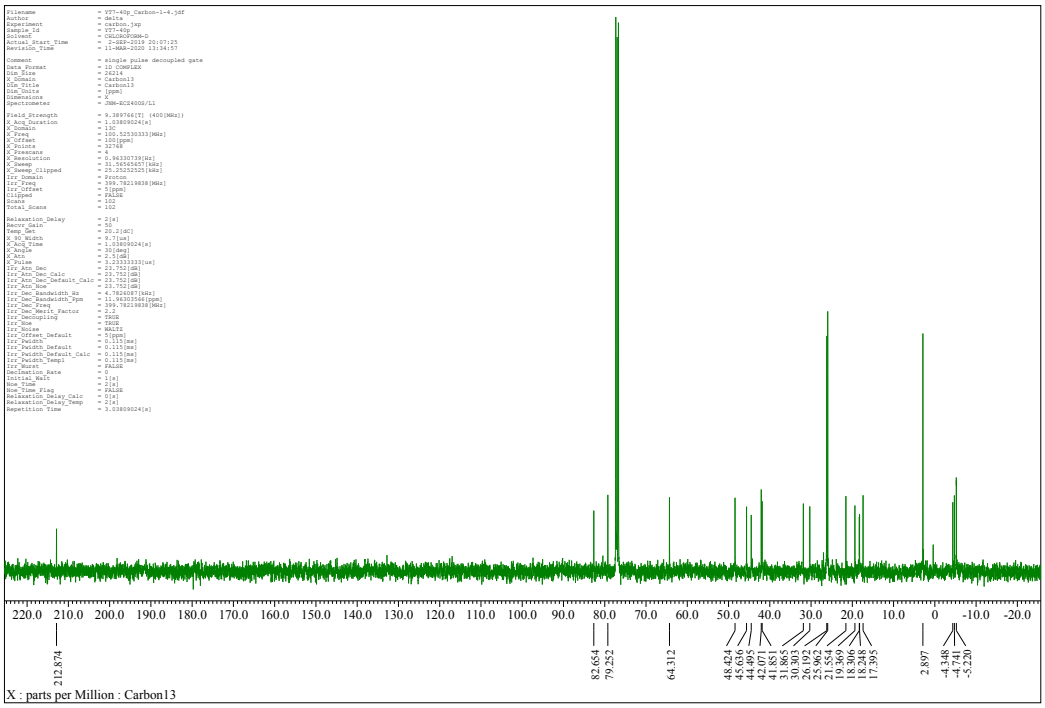

18.21
6.10
5.10
2.09
1.00
0.94
0.97
X : parts per Million : Proton

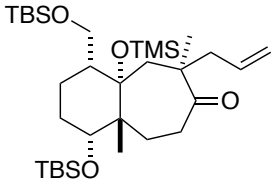

X : parts per Million : Carbon13


TBSO
OTMS
O
TBSO

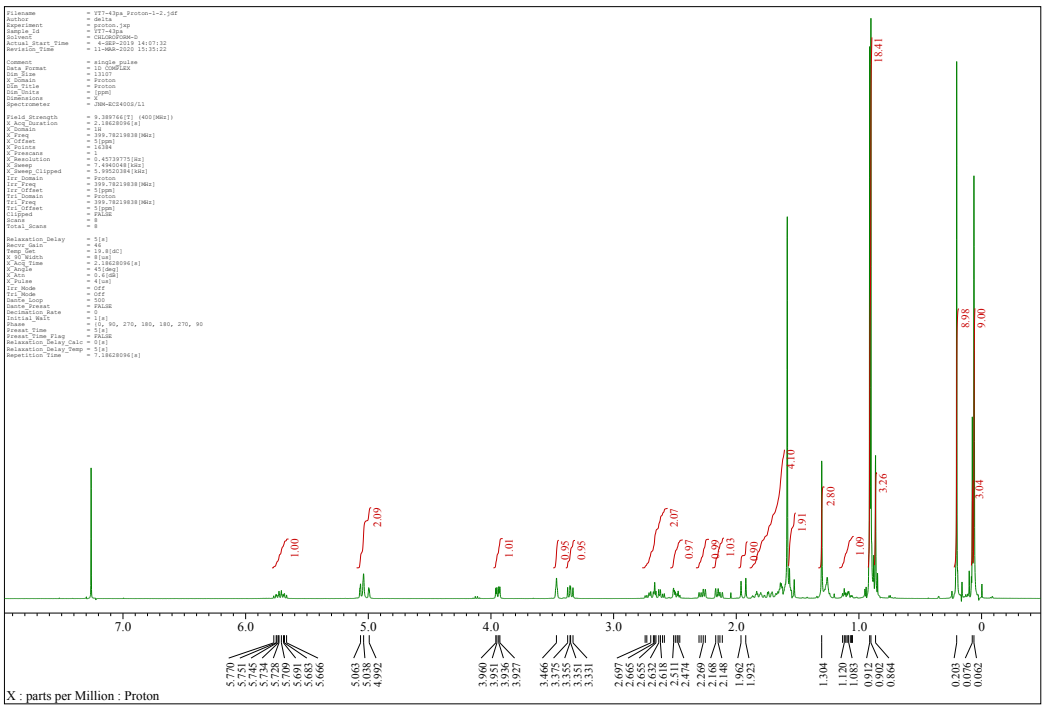
8

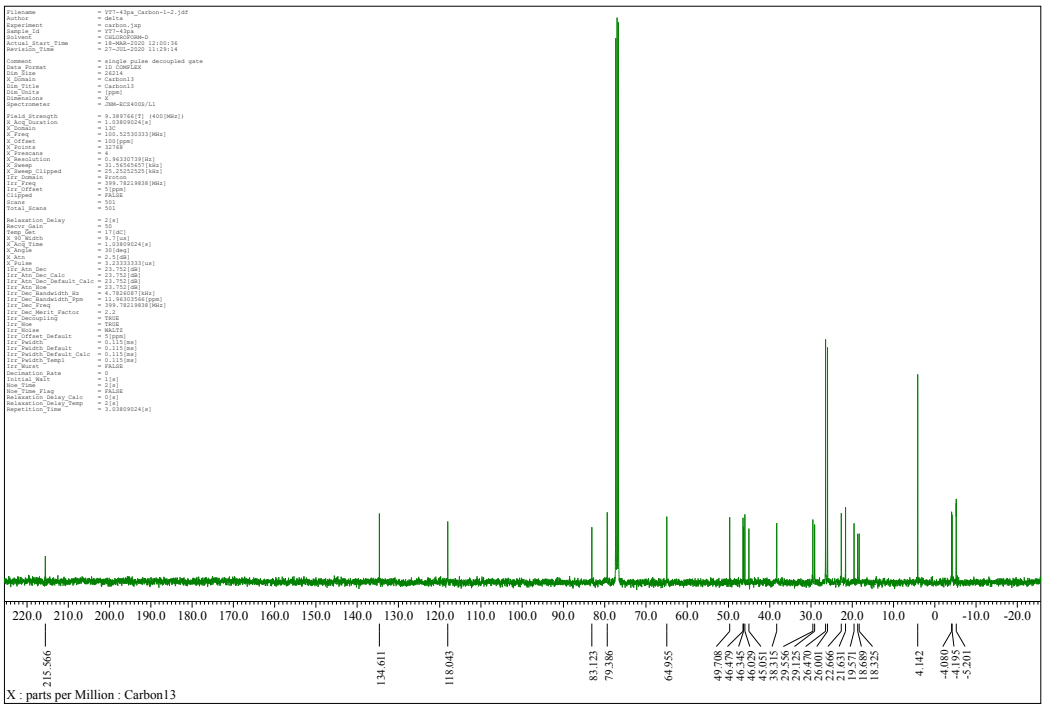

20.91
18.14
7.12
3.15
3.07
3.03
2.13
1.11
1.00
1.00
X : parts per Million : Proton

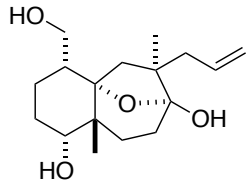

212.874
82.654
79.252
64.312
48.424
45.636
44.495
44.071
41.851
31.865
30.303
26.192
25.962
21.554
19.369
18.306
18.248
17.995
2.897
-4.348
-4.744
-5.220
X : parts per Million : Carbon13


TBSO
OTMS
O
TBSO

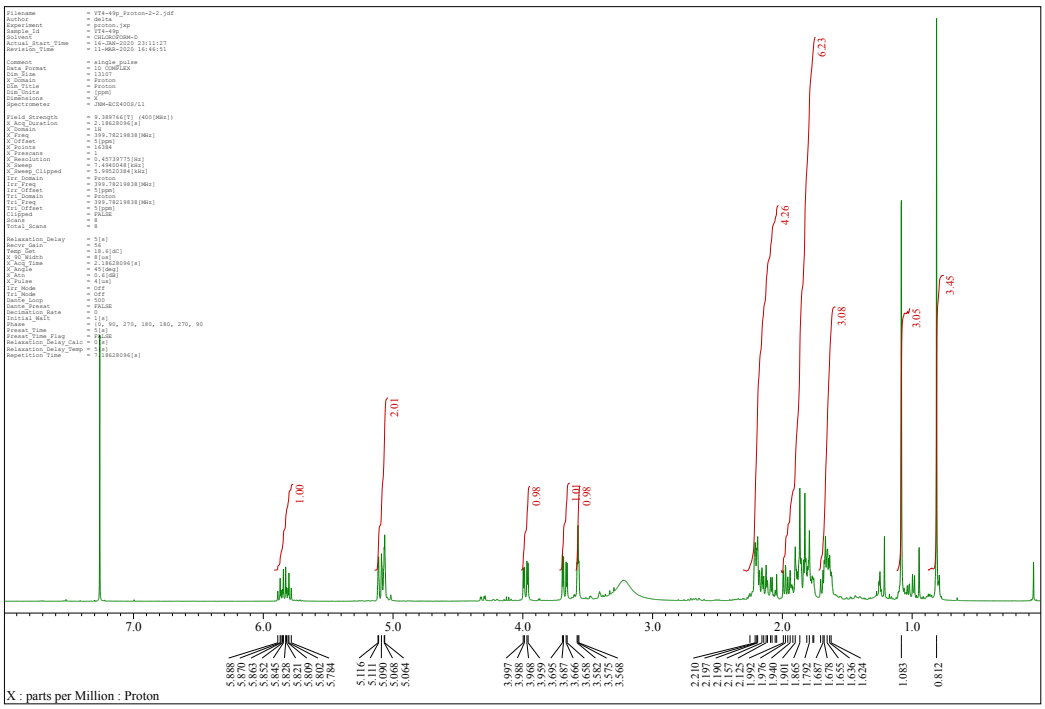
20

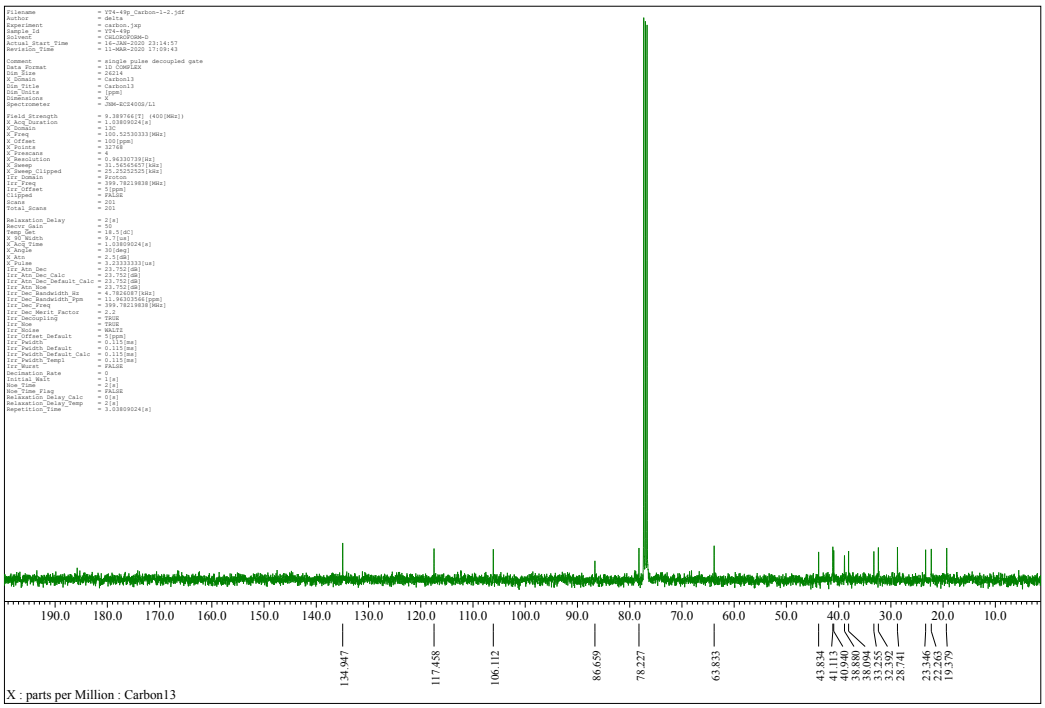

X : parts per Million : Proton

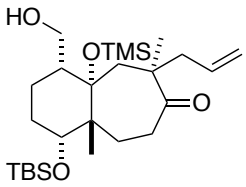

X : parts per Million : Carbon13


HO
O
OH
HO

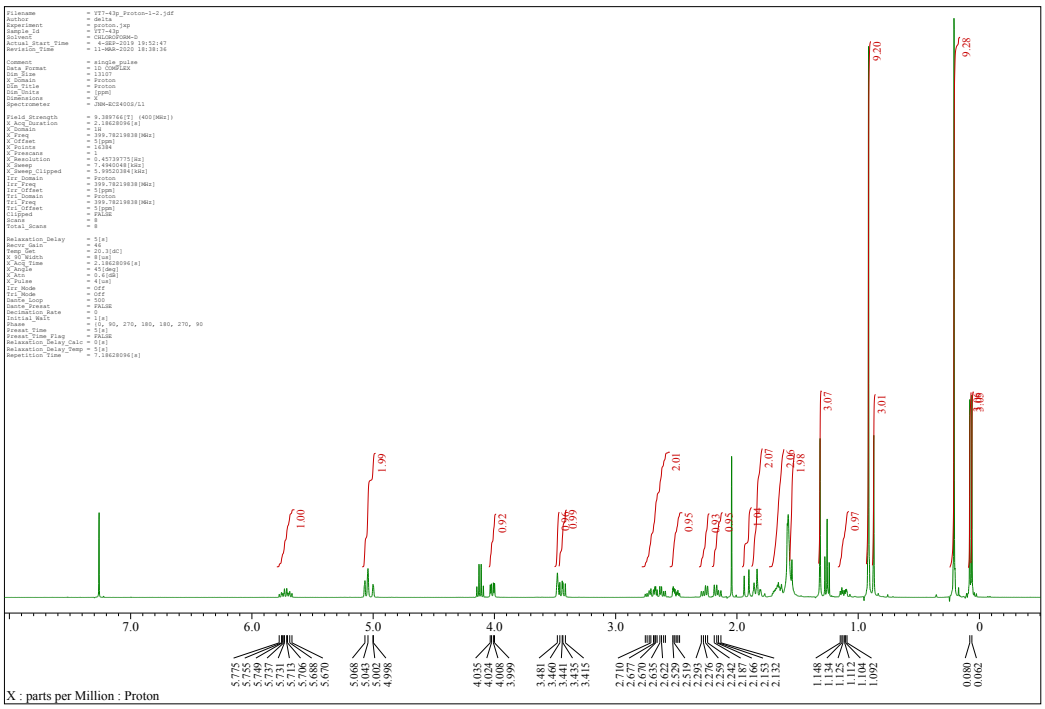
21

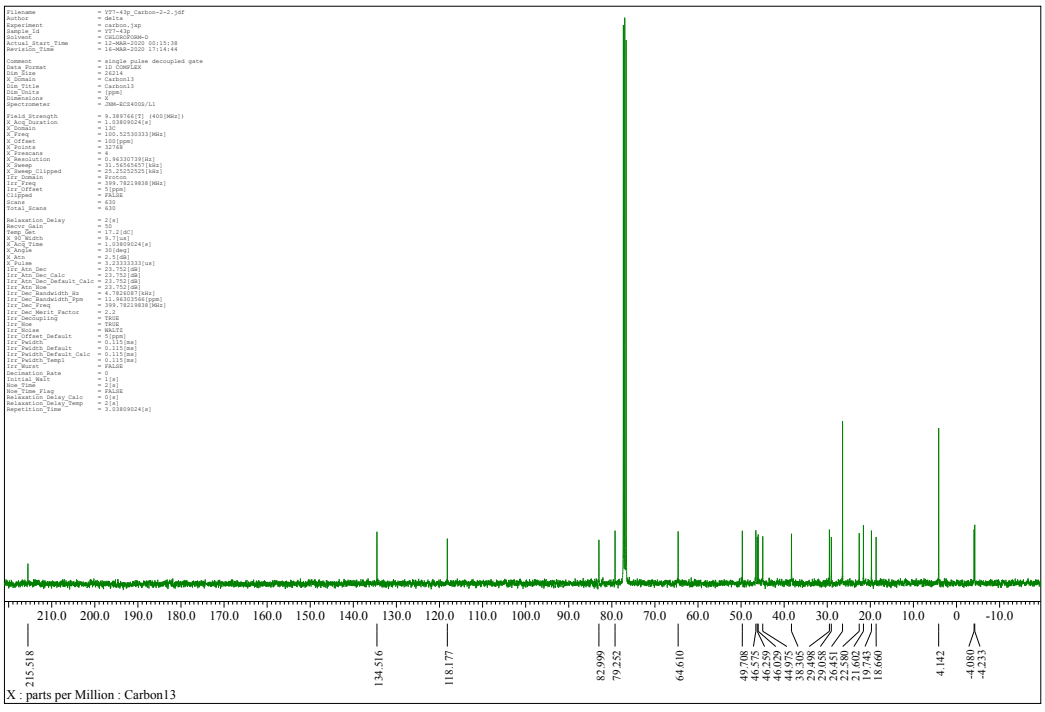

X : parts per Million : Proton

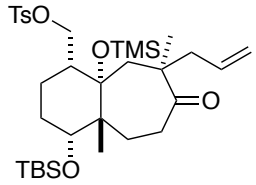

X : parts per Million : Carbon13


HO
OTMS
O
TBSO

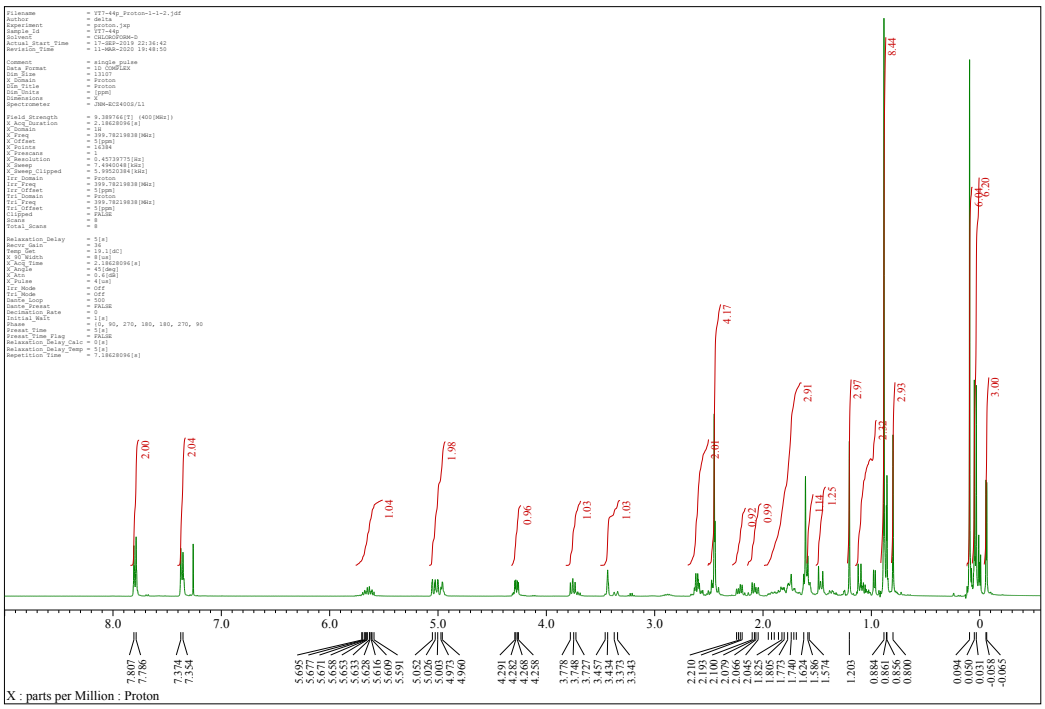
S3

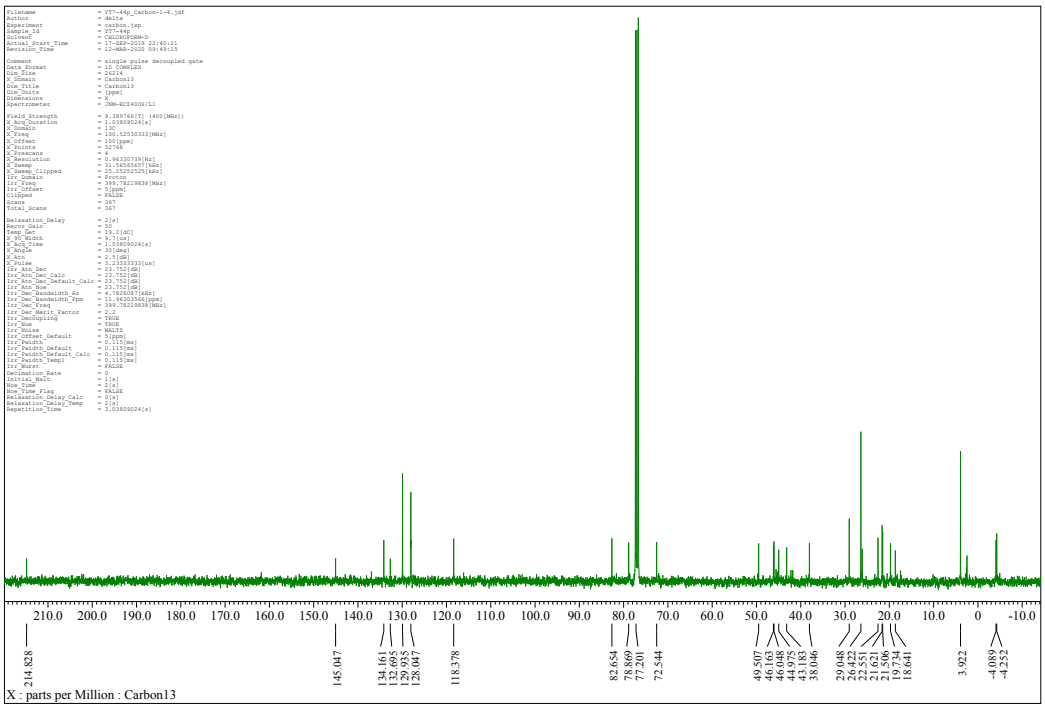

X : parts per Million : Proton

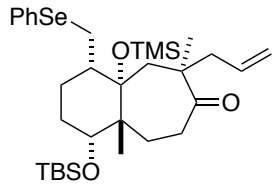

X : parts per Million : Carbon13


TsO
OTMS
O
TBSO

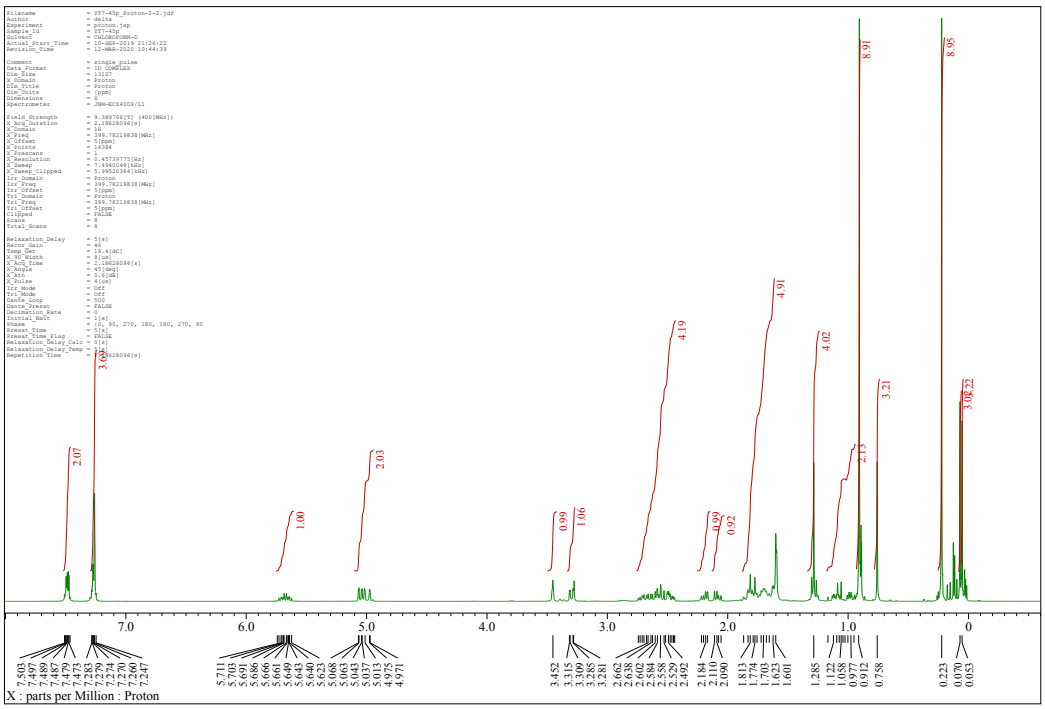
22

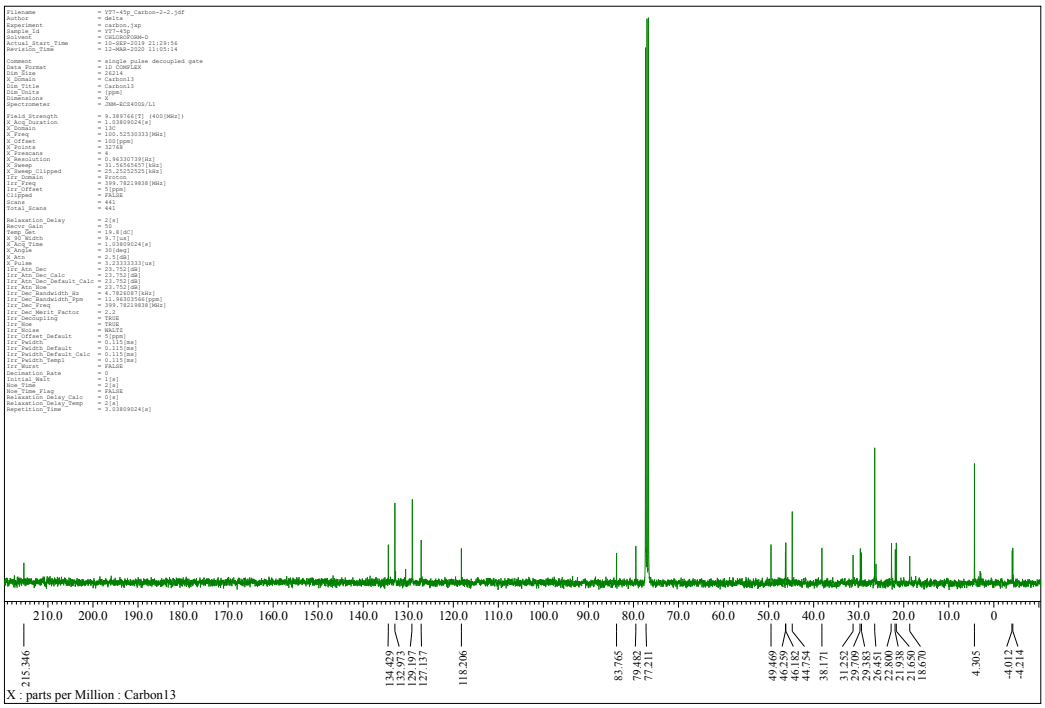

X : parts per Million : Proton

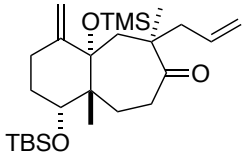

X : parts per Million : Carbon13


PhSe
OTMS
O
TBSO

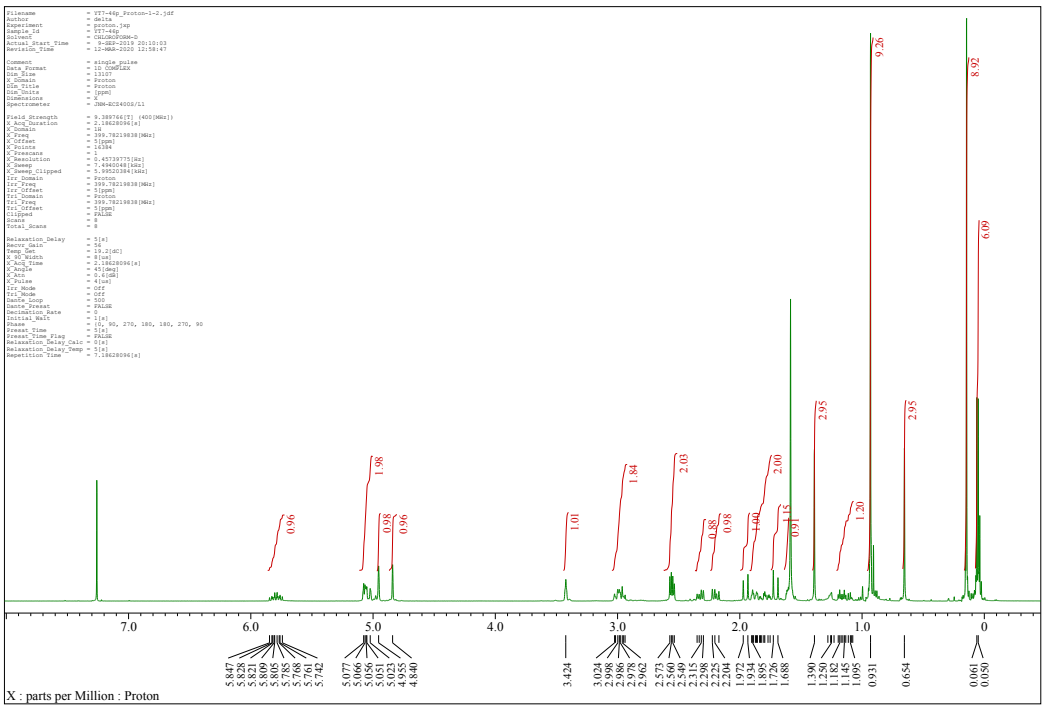
S4

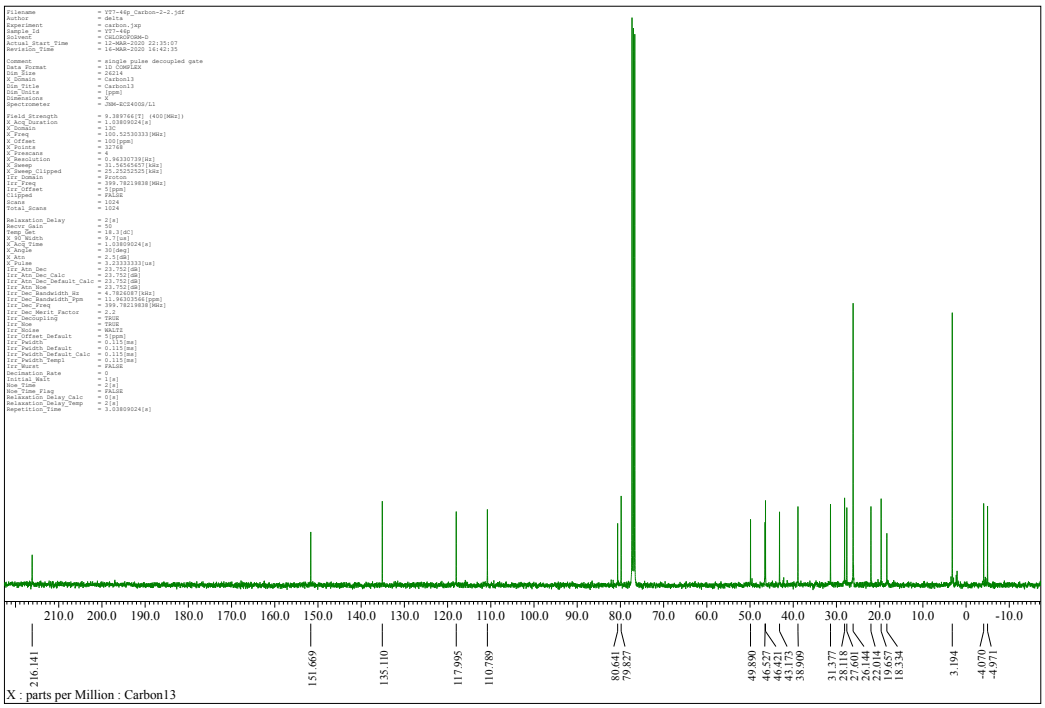

X : parts per Million : Proton

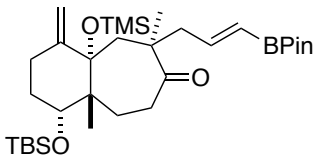

X : parts per Million : Carbon13


OTMS
O
TBSO

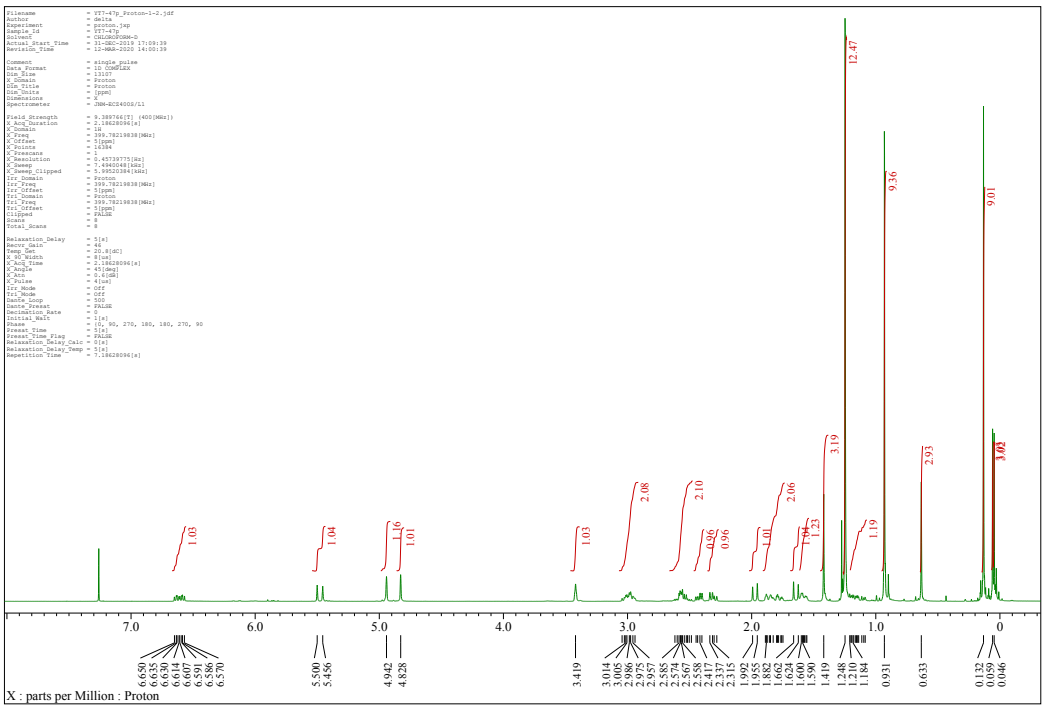
23

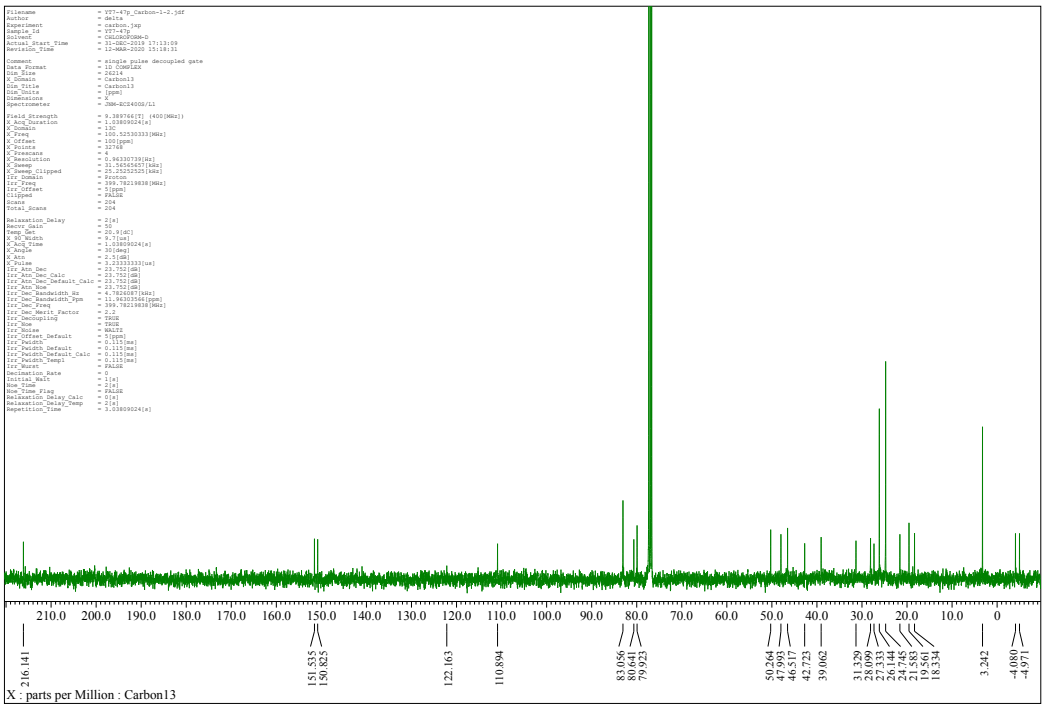

X : parts per Million : Proton

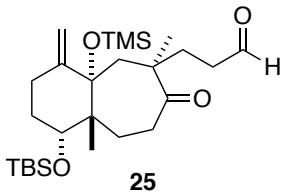

X : parts per Million : Carbon13


OTMS
BPin
O
TBSO

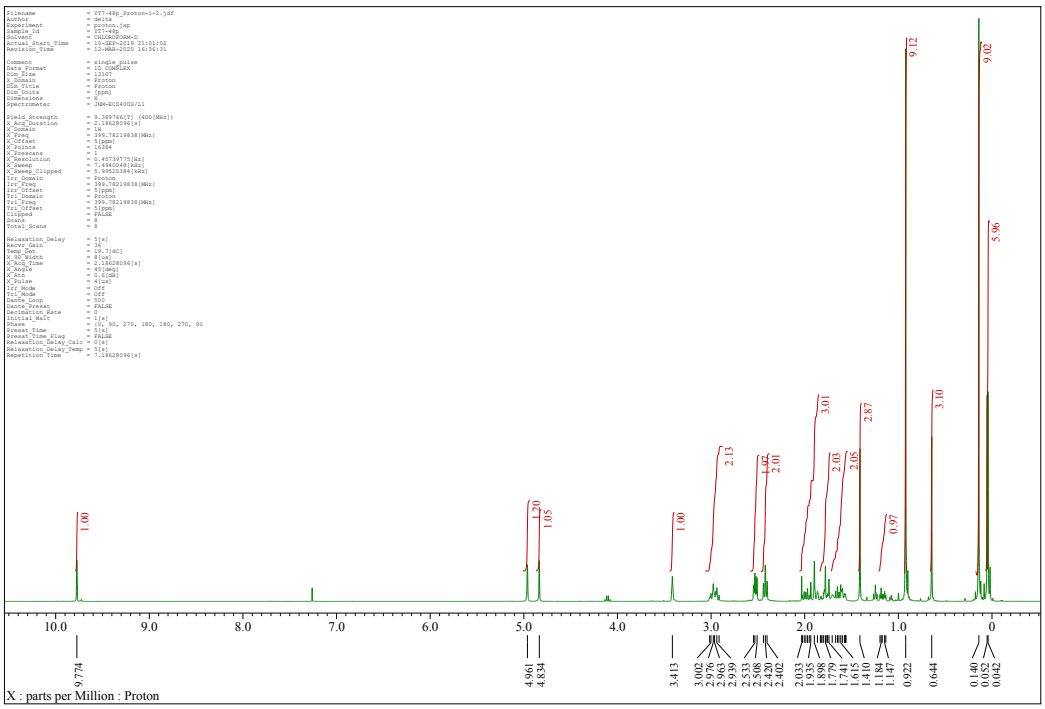
24

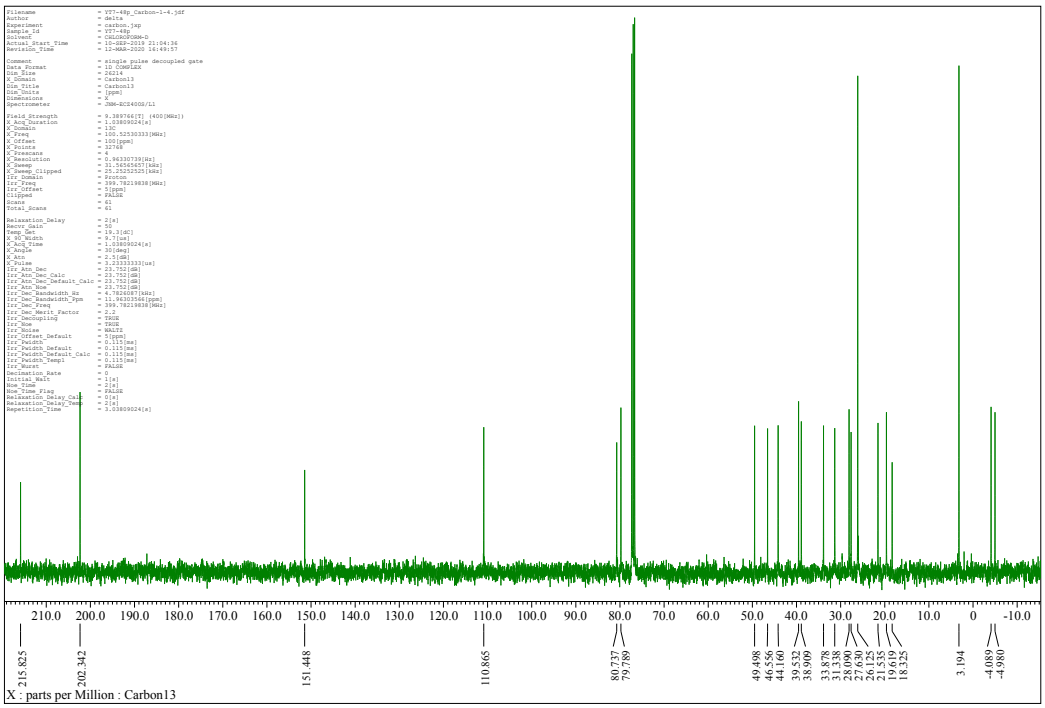

X : parts per Million : Proton

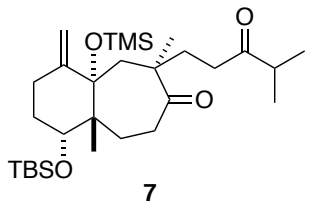

X : parts per Million : Carbon13


OTMS
O
H
O
TBSO

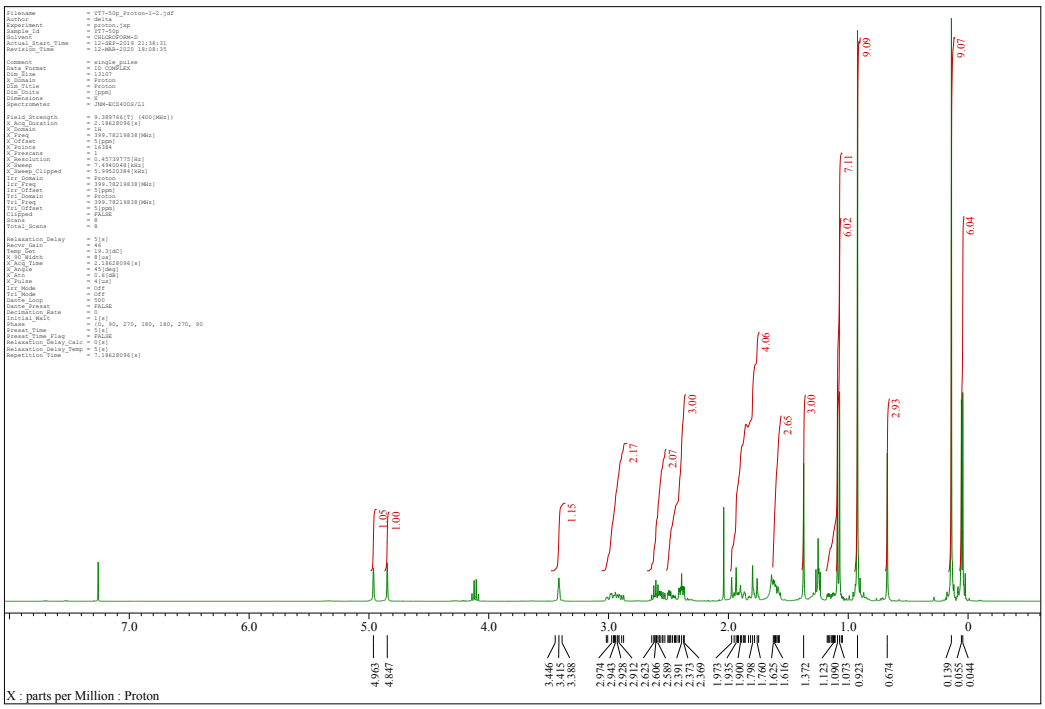
25

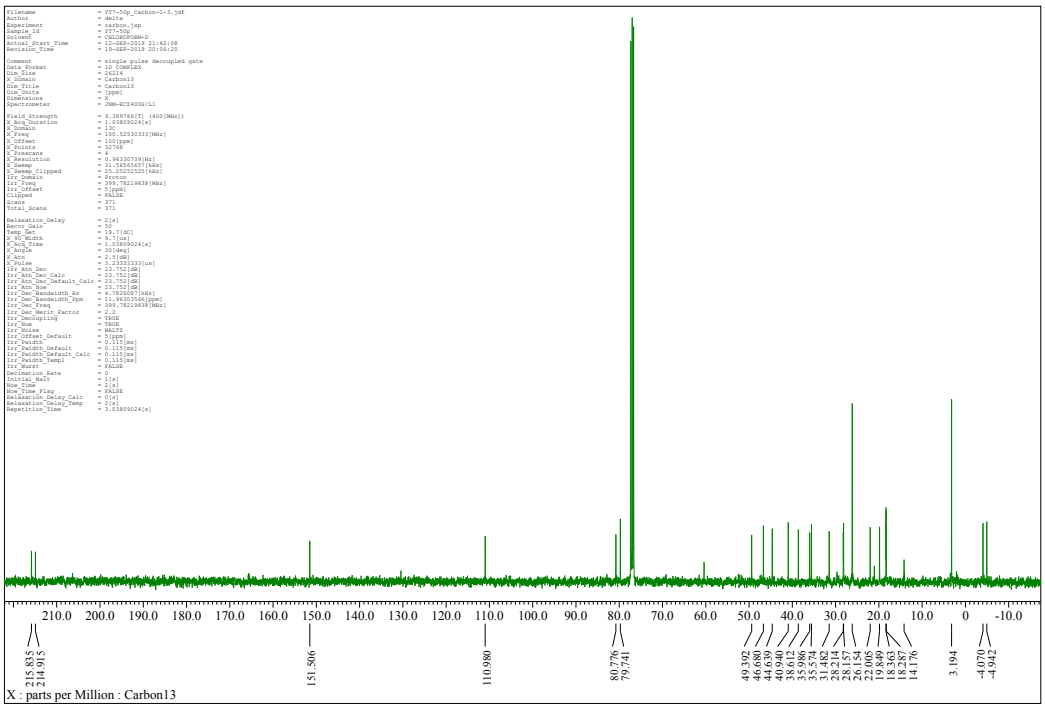

X : parts per Million : Proton

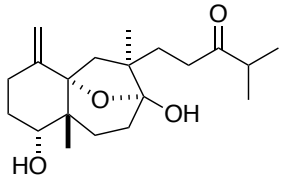

X : parts per Million : Carbon13


OTMS
O
O
TBSO

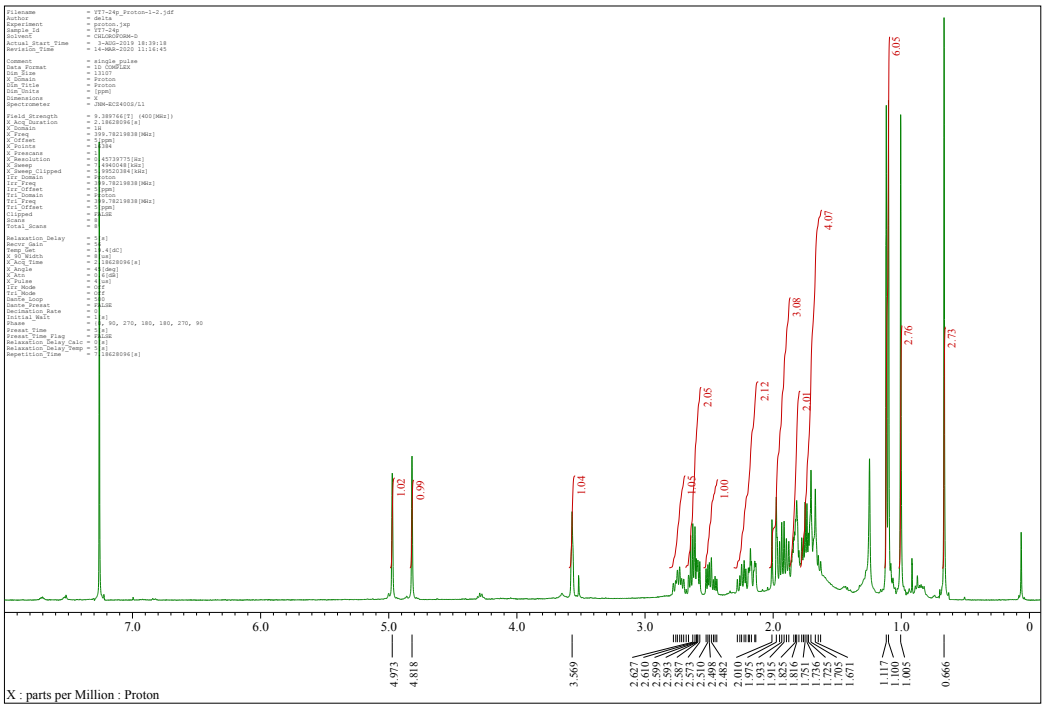
7

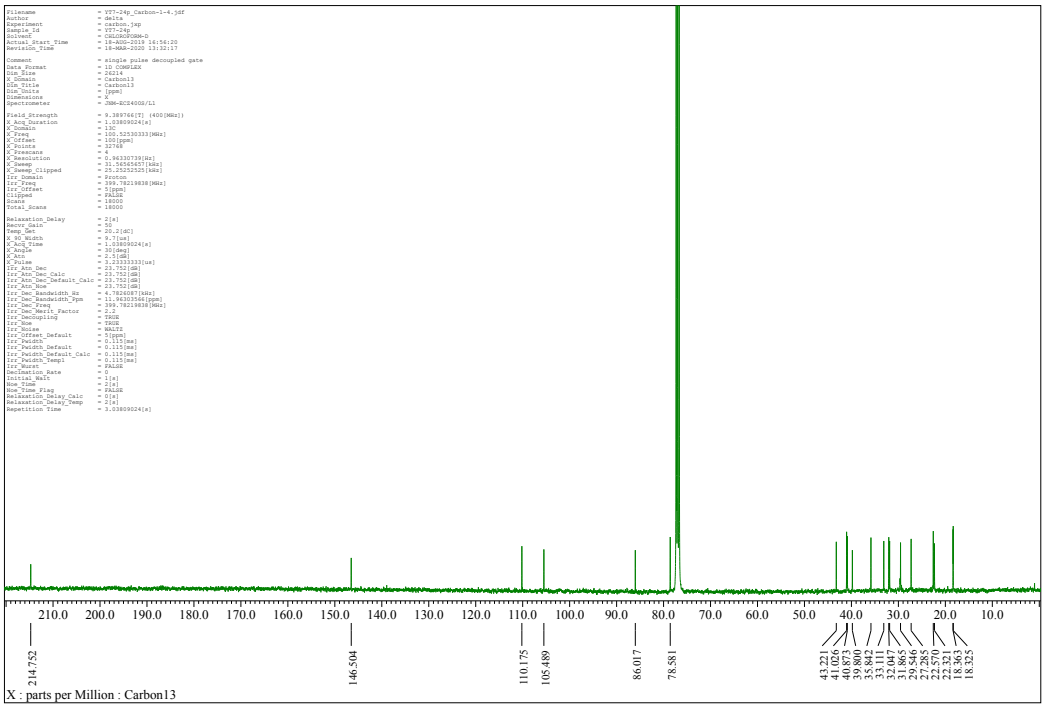

9.09
9.07
7.11
6.02
6.04
4.06
3.00
2.65
3.00
2.93
2.17
2.07
1.15
1.05
1.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
4.963
4.847
3.446
3.415
3.388
2.974
2.943
2.928
2.912
2.623
2.606
2.589
2.571
2.371
2.369
1.973
1.935
1.900
1.798
1.760
1.625
1.616
1.372
1.123
1.090
1.073
0.923
0.674
0.139
0.055
0.044
X : parts per Million : Proton

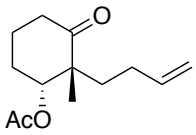

210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
215.835
214.915
151.506
110.980
80.776
79.741
49.392
46.680
44.639
40.940
38.642
35.960
35.574
31.482
28.214
26.157
26.157
22.005
19.849
18.363
18.167
14.176
3.194
-4.070
-4.942
X : parts per Million : Carbon13



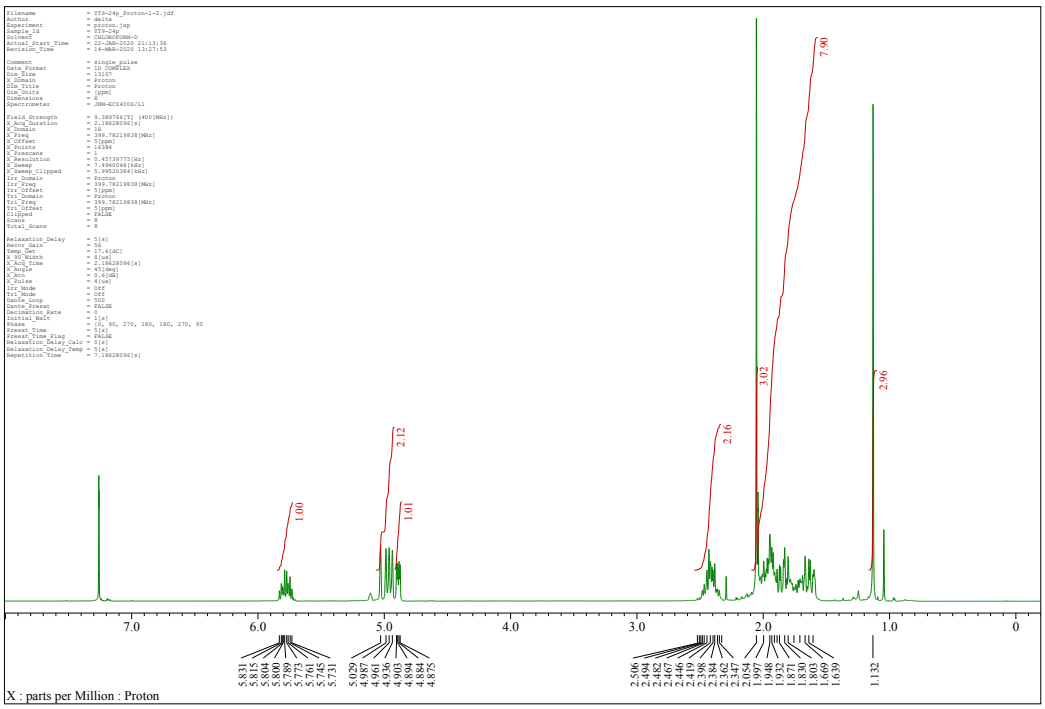
isolinearol (**1**)

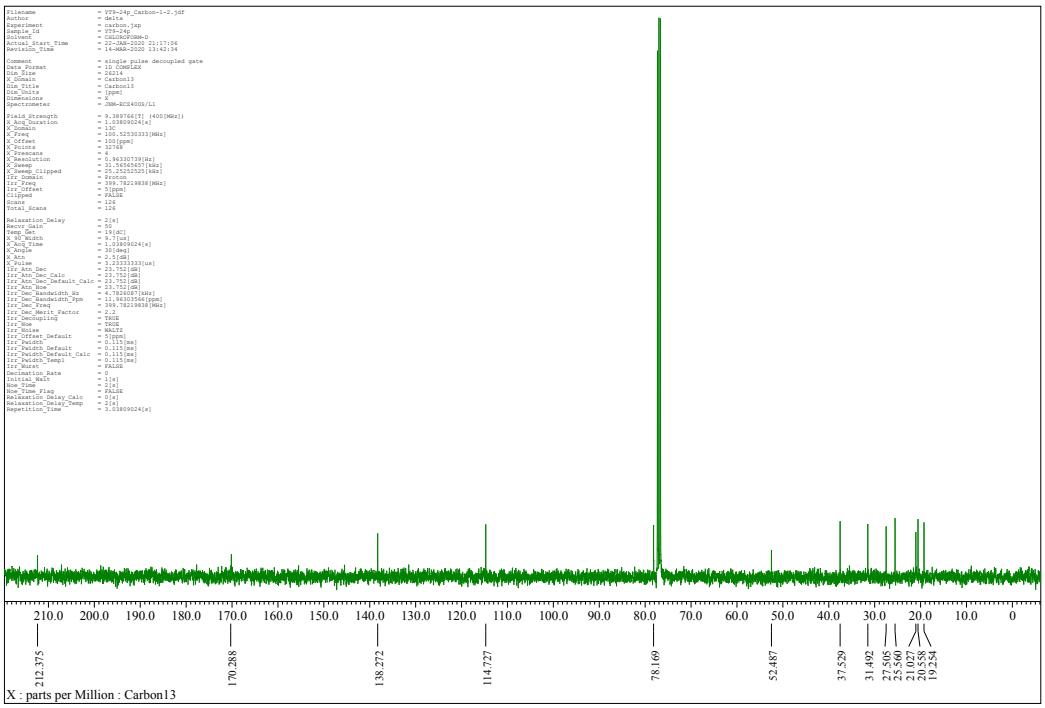


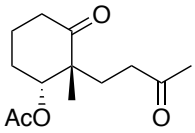



O
AcO

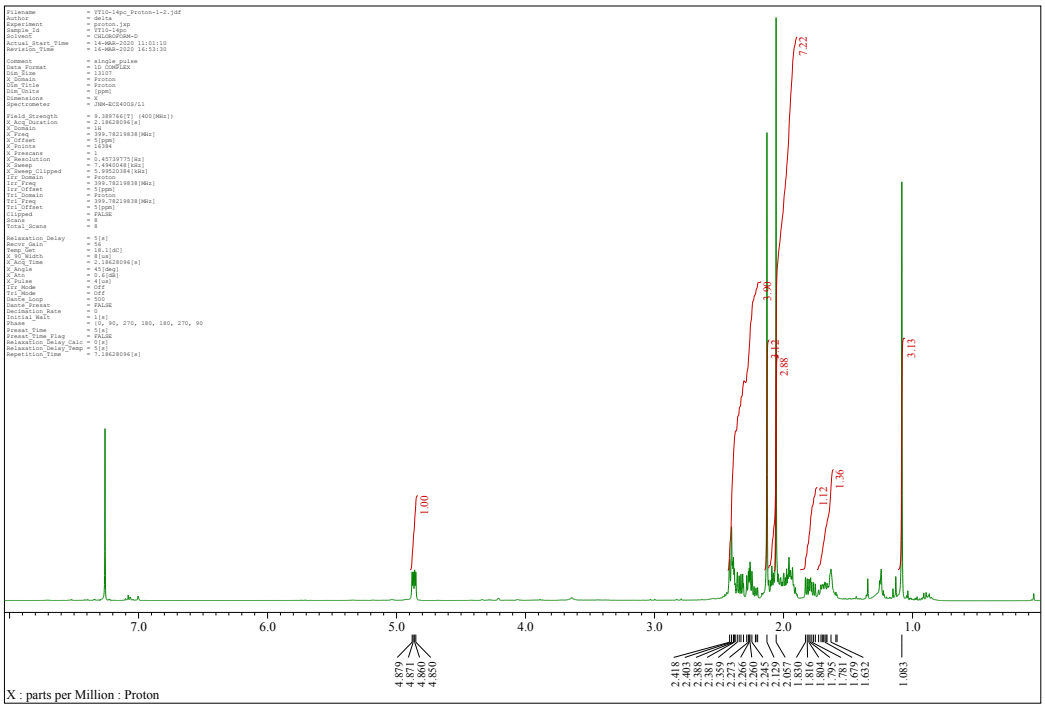
(–)-**26**

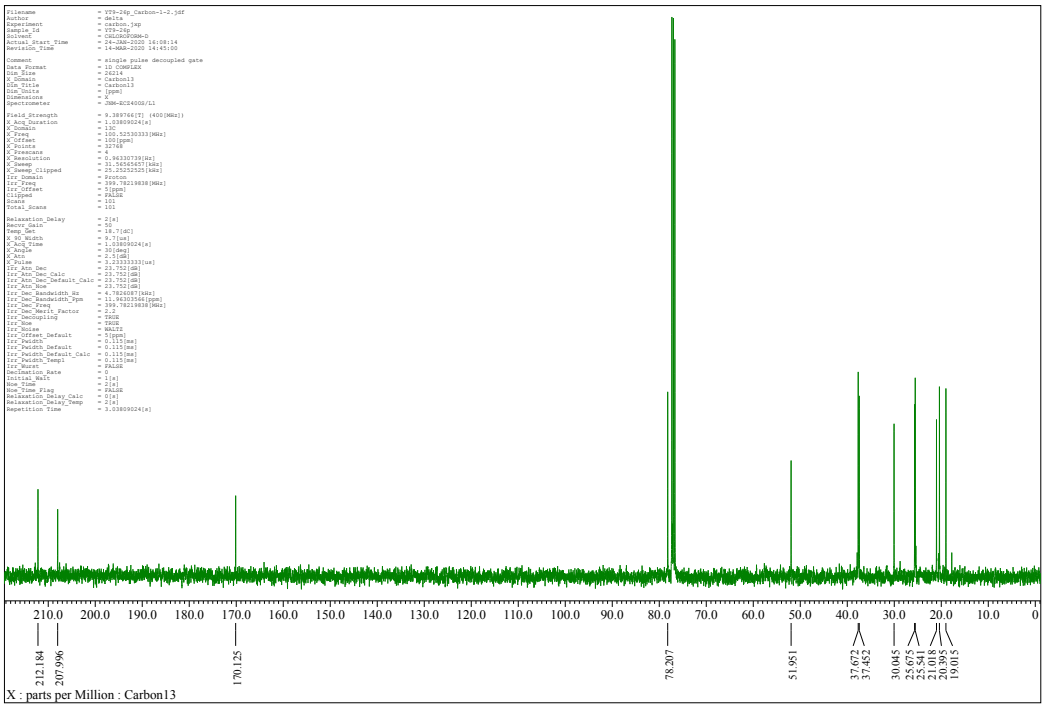

7.90
3.02
2.96
2.16
2.12
1.00
1.01
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

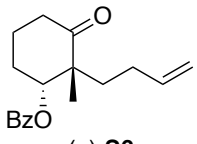

212.375
170.288
138.272
114.727
78.169
52.487
37.529
31.492
27.505
25.560
21.027
20.558
19.254
X : parts per Million : Carbon13


O
AcO
O

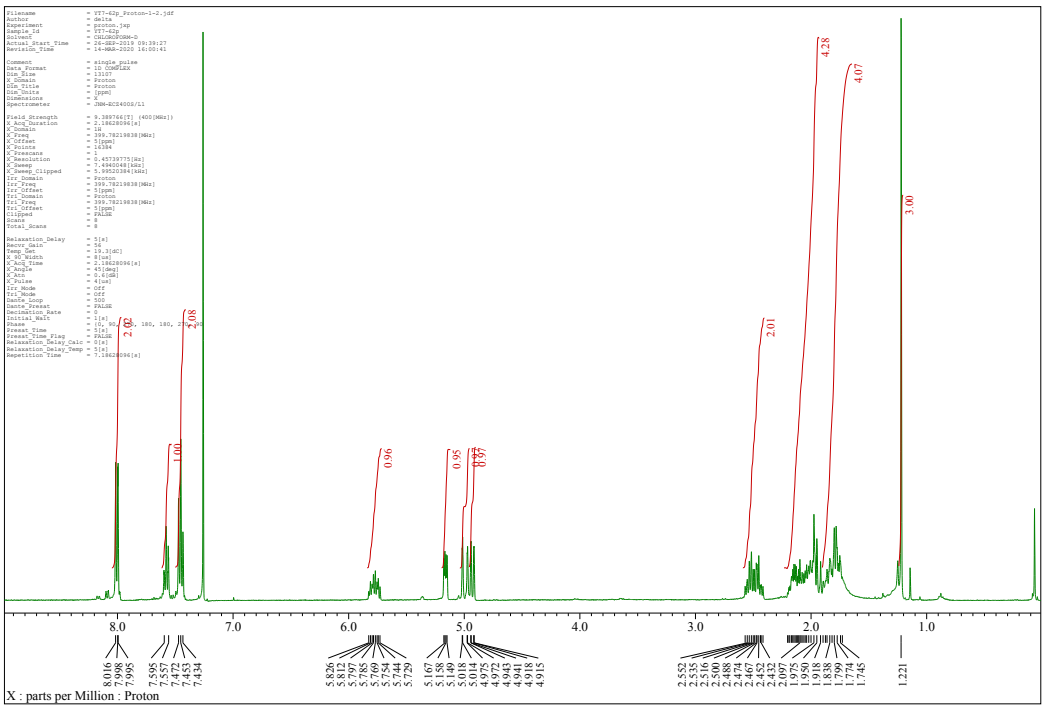
(–)-**27**

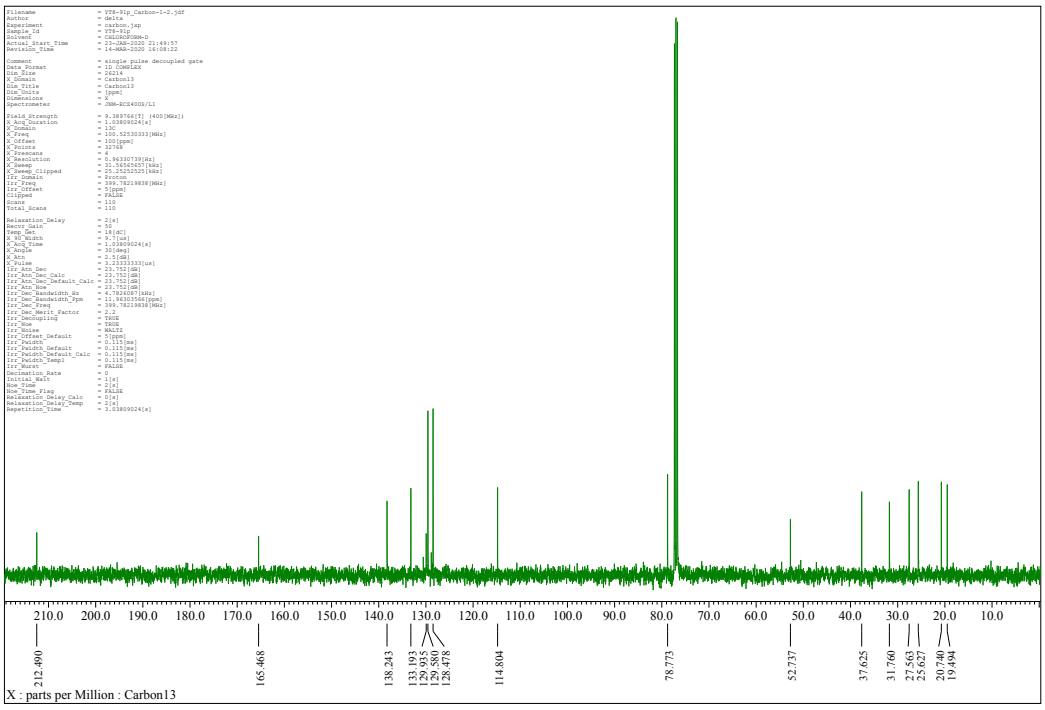

7.22
3.90
3.13
2.88
3.13
1.36
1.12
1.00
7.0
6.0
5.0
4.0
3.0
2.0
1.0
4.879
4.871
4.860
4.850
2.418
2.403
2.388
2.381
2.273
2.266
2.260
2.245
2.219
2.057
1.830
1.816
1.804
1.795
1.781
1.679
1.632
1.083
X : parts per Million : Proton


210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
212.184
207.996
170.125
78.207
51.951
37.672
37.452
30.045
25.675
25.541
21.018
20.385
19.015
X : parts per Million : Carbon13


O
BzO

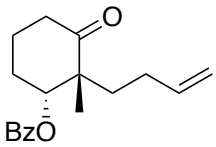
(–)-**S6**


4.28
4.07
3.00
2.01
2.08
2.00
1.00
0.96
0.95
0.97
X : parts per Million : Proton


212.490
165.468
138.243
133.193
130.935
129.580
128.478
114.804
78.773
52.737
37.625
31.760
27.563
25.627
20.740
19.494
X : parts per Million : Carbon13

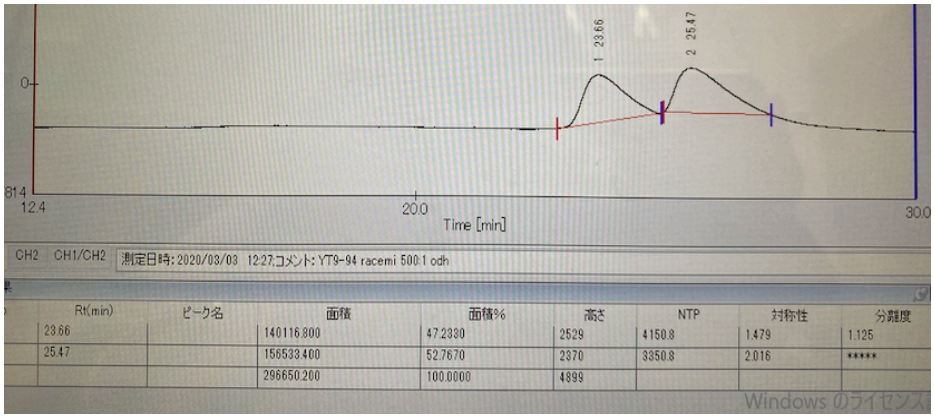
Chiralcel OD-H column, hexane : *i*PrOH = 50 : 1, 1.0 mL/min;

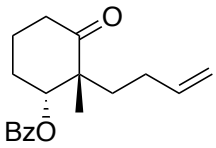
(+)-**S6** (minor) ; t_R = 23.7 min, (—)-S7 (major) ; t_R = 25.5 min



(–)-**S6**

racemic form





(–)-**S6**

optically active form

91% ee

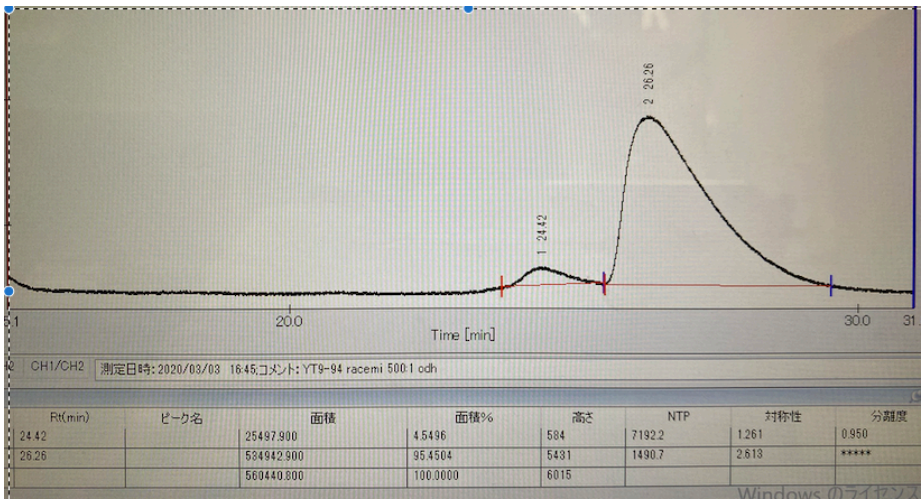
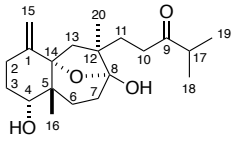


Table S1. Comparison of the chemical shift of ^{1}H and ^{13}C NMR spectra of isolated isolinearol with those of synthetic sample **1**.



isolinearol (**1**)

	isolated isolinearol			synthetic isolinearol				
C/H no.	δ_H (*J* in Hz) [a]	δ_C [a]	C/H no.	δ_H (*J* in Hz) [a]	δ_C [a]	C/H no.	$\Delta\delta_H$|iso-synth|	$\Delta\delta_C$|iso-synth|
1	–	146.6	1	–	146.5	1	–	0.1
2	N/A	33.3	2	1.63-1.78, m 1.88-2.01, m	33.1	2	–	0.2
3	N/A	32.2	3	1.80-1.86, m, 2H	32.0	3	–	0.2
4	3.57, t, (4.5)	78.7	4	3.55-3.59, m	78.6	4	–	0.1
5	–	39.8	5	–	39.8	5	–	0.0
6	N/A	31.9	6	1.88-2.01, m 2.14-2.28, m	31.9	6	–	0.0
7	N/A	29.8	7	1.63-1.78, m, 2H	29.5	7	–	0.3
8	–	105.5	8	–	105.5	8	–	0.0
9	–	214.5	9	–	214.8	9	–	0.3
10	N/A	27.4	10	2.14-2.28, m 2.69-2.79, m	27.3	10	–	0.1
11	N/A	35.9	11	2.56-2.68, m, 2H	35.8	11	–	0.1
12	–	43.4	12	–	43.2	12	–	0.2
13	N/A	41.0	13	1.63-1.78, m 1.88-2.01, m	40.9	13	–	0.1
14	–	86.0	14	–	86.0	14	–	0.0
15	4.82, bs 4.97, bs	109.8	15	4.82, bs 4.97, bs	110.2	15	0.00 0.00	0.4
16	0.66, s, 3H	22.6	16	0.67, s, 3H	22.3	16	0.01	0.3
17	2.63, h, (7)	41.0	17	2.62, qq, (6.9)	41.0	17	0.01	0.0
18	1.10, d, (7)	18.3	18	1.11, d, (6.9), 3H	18.3	18	0.01	0.0
19	1.10, d, (7)	18.3	19	1.11, d, (6.9), 3H	18.4	19	0.01	0.1
20	1.02,s, 3H	22.6	20	1.01, s, 3H	22.6	20	0.01	0.0

[a] $CDCl_3$

X-Ray Crystallographic Data

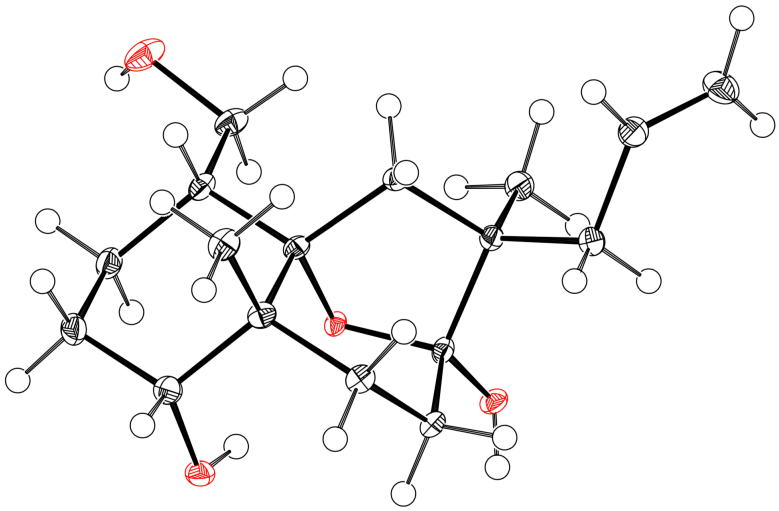


Figure S1. ORTEP drawing of **21**.

Table S2. Crystal data and structure refinement of **21**.

Crystal data	
Chemical formula	$C_{17}H_{28}O_4$
M_r	296.39
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	90
a, b, c (Å)	15.2304 (14), 9.1246 (8), 22.238 (2)
β (°)	95.627 (1)
V (Å^3)	3075.6 (5)
Z	8
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.09
Crystal size (mm)	0.32 × 0.31 × 0.12
Data collection	
Diffractometer	Bruker *SMART APEX* II Ultra
Absorption correction	Numerical *SADABS2016*/2 (Bruker,2016/2) was used for absorption correction. wR2(int) was 0.0920 before and 0.0451 after correction. The Ratio of minimum to maximum transmission is 0.9303. The λ/2 correction factor is Not present.
T_{min}, T_{max}	0.930, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	32814, 6332, 5308
R_{int}	0.031
(sin θ/λ)$_{max}$ (Å^{-1})	0.627
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.051, 0.143, 1.05
No. of reflections	6332
No. of parameters	389
No. of restraints	528
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.73, −0.27

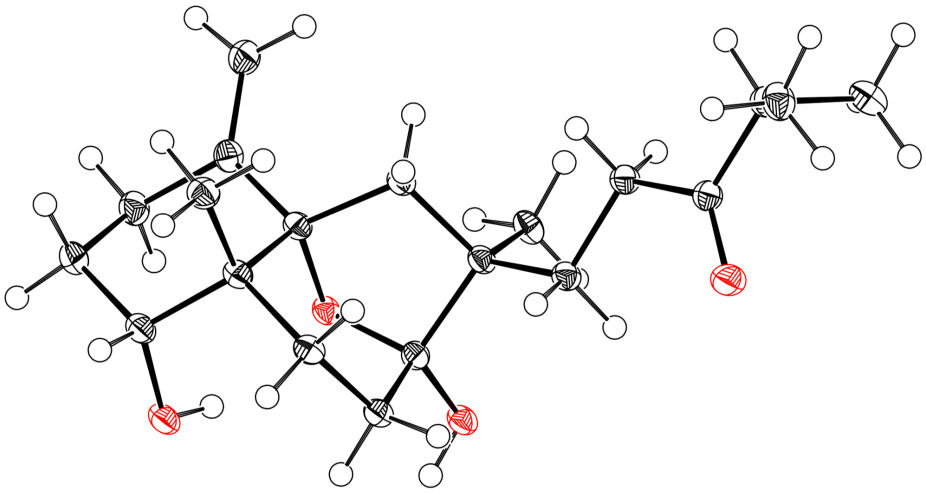


Figure S1. ORTEP drawing of **1**.

Table S3. Crystal data and structure refinement of **1**.

Crystal data	
Chemical formula	$C_{20}H_{32}O_4$
M_r	336.45
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	90
a, b, c (Å)	10.559 (2), 8.9149 (17), 19.341 (4)
β (°)	92.146 (2)
V (Å^3)	1819.3 (6)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.08
Crystal size (mm)	0.23 × 0.17 × 0.08
Data collection	
Diffractometer	Bruker *SMART APEX* II Ultra
Absorption correction	Numerical *SADABS2016*/2 (Bruker,2016/2) was used for absorption correction. wR2(int) was 0.1016 before and 0.0535 after correction. The Ratio of minimum to maximum transmission is 0.9601. The λ/2 correction factor is Not present.
T_{min}, T_{max}	0.960, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	16603, 3228, 2730
R_{int}	0.041
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.595
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.036, 0.096, 1.01
No. of reflections	3228
No. of parameters	223
No. of restraints	300
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.27, −0.21