# Supporting Information

# Synthesis of the C1-C26 Hexacyclic Subunit of Pectenotoxin 2

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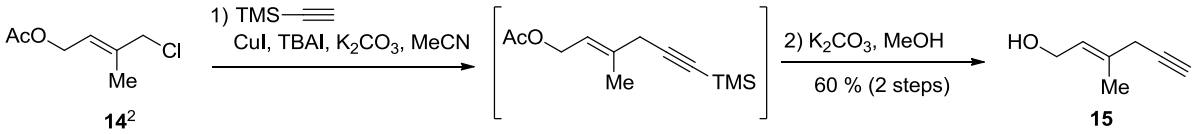
## General Information

$^{1}H$ NMR data were recorded at 400 MHz on a Bruker AM-400, and $^{13}C$ NMR data were recorded at 100 MHz on a Bruker AM-400. The spectra were calibrated using the solvent peak ($CDCl_3$, 7.26 ppm for $^{1}H$ and 77.16 ppm for $^{13}C$). Infrared spectra were acquired on a PerkenElmer SpectrumOne FT-IR instrument. Optical rotations were acquired on a Rudolph Research Analytical Autopol IV Automatic Polarimeter. Low-resolution mass spectrometry was measured on a Waters Micromass® ZQTM instrument using electrospray ionization. High resolution mass spectrometry was measured by the University of Illinois Mass Spectrometry Services.

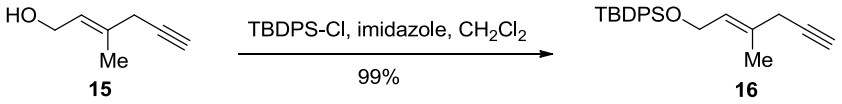
Tetrahydrofuran (THF) and dichloromethane ($CH_2Cl_2$) were dried over activated alumina columns and sparged with argon prior to use. Acetonitrile (MeCN) was distilled over calcium hydride under argon. All chemicals were purchased from Aldrich Chemical Co. and used as received except the following: $CrCl_2$ and ($n$-$Bu_3Sn)_2$ were purchased from Strem Chemicals Inc; Ti(O$i$-Pr)$_4$ was distilled prior to use. All reactions were conducted in flame-dried glass flasks under an argon atmosphere unless otherwise indicated. Asymmetric Nozaki-Hiyama-Kishi reaction was conducted in a glove box. Flash column chromatography was performed using Silacycle SilaFlash P60 silica gel, 40-63 μm particle size, and TLC was performed using EMD Chemicals Inc. TLC Silica Gel 60 F254 glass plates visualized by UV light (254 nm) or *p*-anisaldehyde, phosphomolybdic acid, and potassium permanganate. Compounds **4**[1], **14**[2], **21**[3], **22**[4], chiral sulfonamide *ligand* **S1**[5], $NiCl_2$·DMP[5], and 2-iodo-allylbromide[6] were prepared according to literature procedures.

## Experimental Procedures




**(*E*)-3-methylhex-2-en-5-yn-1-ol (15):**

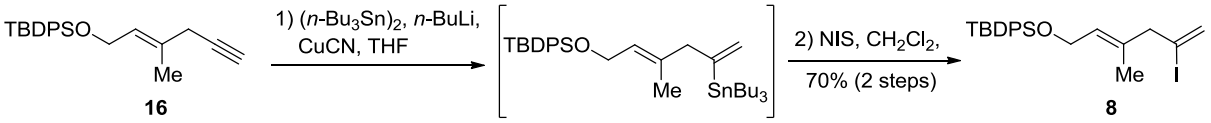
According to the literature[7], CuI (4.88 g, 25.64 mmol), tetrabutylammonium iodide (9.47 g, 25.64 mmol), $K_2CO_3$ (6.38 g, 46.15 mmol), and TMS-acetylene (5.0 mL, 38.46 mmol) were added successively to a solution of **14**[2] (4.17 g, 25.64 mmol) in MeCN (85 mL) at rt. The resulting slurry was stirred for 27 h, then quenched with sat. $NH_4Cl$ aq. After evaporation of MeCN, the residue was extracted with $Et_2O$. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. The rsulting oil was dissolved in MeOH (128 mL), and $K_2CO_3$ (5.32 g, 38.46 mmol) was added at rt. After stirring for 2 h, $K_2CO_3$ was filtered and sat. $NH_4Cl$ aq. was added to the mixture. After evaporation of MeOH, the residue was extracted with EtOAc, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 4/1 to 2/1) provided **15** (898.4 mg, 60%, 2 steps) as a pale yellow oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.34 (1 H, s), 1.76 (3 H, t, $J$ = 0.6 Hz), 2.13 (1 H, t, $J$ = 2.7 Hz), 2.93 (2 H, m), 4.20 (2 H, dd, $J$= 6.9, 0.6 Hz), 5.70-5.75 (1 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 16.1, 28.4, 58.9, 70.9, 81.2, 125.2, 133.2; **IR** (neat): 3294, 2882, 2118, 1675, 1419 $cm^{-1}$; **HRMS** (EI): Calcd for $C_7H_9O$ [M – H] 109.0653 found 109.0646.




**(*E*)-*tert*-butyl((3-methylhex-2-en-5-yn-1-yl)oxy)diphenylsilane (16):**

TBDPS-Cl (3.6 mL, 13.89 mmol) was added to a solution of **15** (1.02 g, 9.26 mmol) and imidazole (1.58 g, 23.15 mmol) in $CH_2Cl_2$ (18 mL) at 0 $^oC$. After stirring at same temperature for 2 h, the mixture was quenched with sat. $NH_4Cl$ aq., and extracted with $CH_2Cl_2$. The organic layer

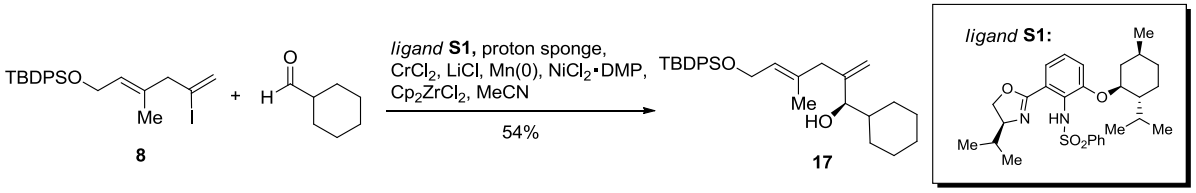
was dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 25/1) provided **16** (3.20 g, 99%) as a pale yellow oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.05 (9 H, s), 1.52 (3 H, s), 2.10 (1 H, t, $J$ = 2.7 Hz), 2.87 (2 H, s), 4.24 (2 H, dd, $J$ = 6.3, 0.8 Hz), 5.65-5.70 (1 H, m), 7.36-7.44 (6 H, m), 7.68-7.70 (4 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 16.3, 19.3, 27.0, 28.6, 61.1, 70.7, 81.5, 126.0, 127.8, 129.7, 131.5, 134.0, 135.7; **IR** (neat): 3307, 2858, 1428, 1108, 1051 cm$^{-1}$; **LRMS** (ESI): Calcd for $C_{23}H_{29}OSi$ [M + H] 349.20, found 349.3.




**(*E*)-*tert*-butyl((5-iodo-3-methylhexa-2,5-dien-1-yl)oxy)diphenylsilane (8):**

According to the literature[8], *n*-BuLi (2.5 M in hexanes, 2.34 mL, 5.85 mmol) was added dropwise to a solution of (*n*-$Bu_3Sn)_2$ (3.0 mL, 5.94 mmol) in THF (7.0 mL) at −40 °C. The reaction mixture was stirred at −40 °C for 1.5 h. Copper (I) cyanide (267.6 mg, 2.99 mmol) was added to the solution, and the reaction mixture was cooled to −78 °C. A solution of alkyne **12** (347.0 mg 0.996 mmol) in THF (2.0 mL + 1.0 mL rinse) was added to the resultant suspension, and stirred at −78 °C for 2.5 h. The reaction mixture was quenched with $H_2O$. The mixture was extracted with $Et_2O$, and the organic layer was washed with sat. KF aq. and brine, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc = 100/1) to give the vinyl stannane. To a solution of vinyl stannane in $CH_2Cl_2$ (7.0 mL) was added NIS (342 mg, 1.52 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, then quenched with sat. $Na_2S_2O_3$ aq. The mixture was extracted with $CH_2Cl_2$, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 40/1) provided **8** (333.0 mg, 70%, 2 steps) as a pale yellow oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.05 (9 H, s), 1.42 (3 H, s), 3.08 (2 H, s), 4.25 (2 H, d, $J$ = 6.2 Hz), 5.54 (1 H, t, $J$ = 6.2 Hz), 5.78 (1 H, s), 6.06 (1 H, d, $J$ = 1.2 Hz), 7.36-7.44 (6 H, m), 7.70-7.72 (4 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ:

15.7, 19.3, 27.0, 55.5, 61.2, 110.2, 127.1, 127.8, 128.9, 129.7, 133.0, 134.1, 135.8; **IR** (thin film): 2931, 2858, 1614, 1429, 1112, 1057 $cm^{-1}$; **HRMS** (ESI): Calcd for $C_{23}H_{29}INaOSi$ [M + Na] 499.0930 found 499.0936.

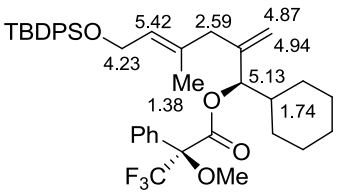



**(*R*,*E*)-6-*tert*-butyldiphenylsilyloxy-1-cyclohexyl-4-methyl-2-methylenehex-4-en-1-ol (17):**

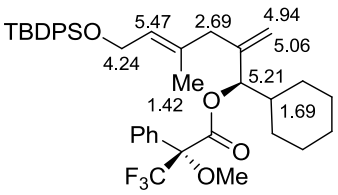
$CrCl_2$ (16.4 mg, 0.133 mmol) was added to a solution of sulfonamide *ligand* **S1**[5] (71.7 mg, 0.144 mmol) and proton sponge (30.4 mg, 0.142 mmol) in MeCN (1.7 mL) at rt. After stirring for 1 h, the reaction mixture was transferred into a separate flask containing cyclohexanecarboxyaldehyde (90 μL, 0.682 mmol), vinyl iodide **8** (651.1 mg, 1.367 mmol), anhydrous LiCl (57.9 mg, 1.366 mmol), Mn (75.2 mg, 1.369 mmol), $NiCl_2$·DMP[5] (9.0 mg, 0.027 mmol), and $Cp_2ZrCl_2$ (68.9 mg, 0.235 mmol). After stirring for 3 h, the reaction flask was removed from glove box, and diluted with EtOAc. Florisil was added, and the reaction mixture was stirred for 30 min, filtered through glass filter, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc = 15/1) to give **17** (170.0 mg, 54%, 87% ee) as a colorless oil. (Enantiomeric excess of **17** was determined by Mosher ester analysis[8]);$^1$H NMR (400 MHz, $CDCl_3$) δ: 0.94-1.07 (11 H, m), 1.12-1.30 (3 H, m), 1.43-1.56 (5 H, m), 1.66-1.68 (1 H, m), 1.72-1.80 (2 H, m), 1.86-1.90 (1 H, m), 2.65 (1 H, A in ABq, $J$ = 15.2 Hz), 2.77 (1 H, B in ABq, $J$ = 15.2 Hz), 3.78 (1 H, d, $J$ = 6.7 Hz), 4.25 (2 H, d, $J$ = 5.9 Hz), 4.87 (1 H, d, $J$ = 1.4 Hz), 5.03 (1 H, d, $J$ = 0.6 Hz), 5.48-5.51 (1 H, m), 7.36-7.45 (6 H, m), 7.69-7.72 (4 H, m); $^{13}$C NMR (100 MHz, $CDCl_3$) δ:16.2, 19.3, 26.2, 26.5, 27.0, 30.1, 41.1, 42.6, 61.2, 79.9, 112.7, 127.2, 127.8, 129.7, 134.1, 135.1, 135.7, 148.1; IR (thin film): 3436, 2930, 2856, 1428, 1112, 1055 $cm^{-1}$; $[\alpha]_D^{28}$ = -4.4 ($c$ = 1.08, $CHCl_3$); **LRMS** (ESI): Calcd for $C_{30}H_{41}O_2Si$ [M – H] 461.29, found 461.7.

**Determination of absolute stereochemistry of 17**

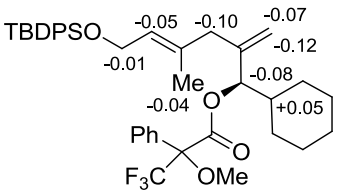
Stereochemistry of **17** was determined by modified Mosher's method[9]. Derivatization of **17** to the corresponding (*S*)-MTPA Ester, and (*R*)-MTPA Ester was conducted according to a usual method, and $^1$H NMR data are as follows.




(S)-MTPA ester of **17**



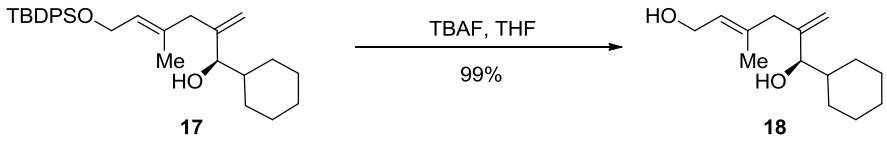

(R)-MTPA ester of **17**




$\Delta\delta = \delta_S - \delta_R$

**(*S*)-MTPA ester of 17**; $^1$H NMR (400 MHz, $CDCl_3$) δ: 1.05 (9 H, s), 1.09-1.30 (5 H, m), 1.38 (3 H, s), 1.57-1.74 (6 H, m), 2.56 (1 H, A in ABq, *J* = 15.6 Hz), 2.62 (1 H, B in ABq, *J* = 15.6 Hz), 3.55 (3 H, d, *J* = 1.0 Hz), 4.23 (2 H, d, *J* = 6.1 Hz), 4.87 (1 H, d, *J* = 1.2 Hz), 4.94 (1 H, s), 5.13 (1 H, d, *J* = 7.2 Hz), 5.41-5.44 (1 H, m), 7.35-7.44 (9 H, m), 7.49-7.51 (2 H, m), 7.68-7.70 (4 H, m).

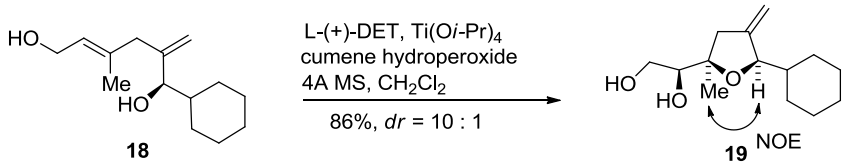
**(*R*)-MTPA ester of 17**; $^1$H NMR (400 MHz, $CDCl_3$) δ: 1.05 (9 H, s), 1.09-1.29 (5 H, m), 1.42 (3 H, s), 1.51-1.71 (6 H, m), 2.69 (2 H, s), 3.53 (3 H, d, *J* = 0.9 Hz), 4.24 (2 H, d, *J* = 6.1 Hz), 4.94 (1 H, d, *J* = 1.3 Hz), 5.06 (1 H, s), 5.21 (1 H, d, *J* = 7.1 Hz), 5.46-5.49 (1 H, m), 7.36-7.42 (9 H, m), 7.50-7.52 (2 H, m), 7.68-7.70 (4 H, m).




**(*R*, *E*)-6-cyclohexyl-3-methyl-5-methylenehex-2-ene-1,6-diol (18):**

TBAF (1.0 M solution in THF, 0.51 mL, 0.510 mmol) was added dropwise to a solution of **17** (117.8 mg, 0255 mmol) in THF (2.5 mL) at 0 °C. After stirring at rt for 13 h, the mixture was quenched with sat. $NH_4Cl$ aq. and extracted with EtOAc. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 3/2) provided **18**

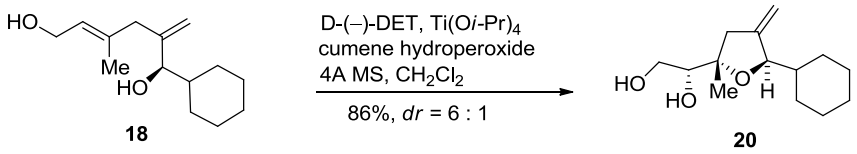
(56.8 mg, 99%) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.92-1.05 (2 H, m), 1.10-1.27 (3 H, m), 1.40-1.55 (2 H, m), 1.66 (3H, s), 1.66-1.77 (3 H, m), 1.89 (1 H, d, *J* = 12.8 Hz), 2.14 (2 H, s), 2.66 (1 H, A in ABq, *J* = 15.2 Hz), 2.80 (1 H, B in ABq, *J* = 15.2 Hz), 3.77 (1 H, d, *J* = 7.0 Hz), 4.16 (2 H, d, *J* = 6.8 Hz), 4.88 (1 H, s), 5.04 (1 H, s), 5.49 (1 H, t, *J* = 6.8 Hz); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 16.2, 26.2, 26.4, 26.5, 28.2, 30.0, 41.2, 42.5, 59.3, 79.8, 112.9, 126.4, 137.2, 148.0; **IR** (thin film): 3352, 2924, 2853, 1645, 1450, 1016 $cm^{-1}$; $[\alpha]_D^{29}$ = -0.14 (*c* = 0.94, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{14}H_{24}NaO_2$ [M + Na] 247.1674 found 247.1666.




**(*S*)-1-((2*R*,5*R*)-5-cyclohexyl-2-methyl-4-methylenetetrahydrofuran-2-yl)ethane-1,2-diol (19):**

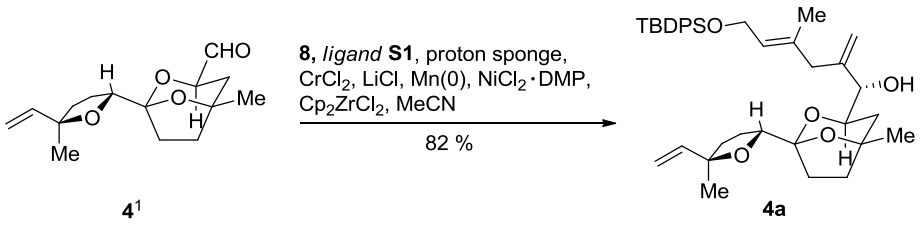
Ti(O*i*-Pr)$_4$ (22 μL, 0.112 mmol) and cumene hydroperoxide (0.06 mL, 0.375 mmol) were added successively to a solution of L-(+)-DET (22 μL, 0.127 mmol) and 4 Å molecular sieves (27.2 mg) in $CH_2Cl_2$ (0.29 mL) at -10 °C, and the resulting solution was stirred for 20 min. The reaction mixture was cooled to -25 °C, and a solution of the allylic alcohol **18** (16.8 mg, 0.0749 mmol) in $CH_2Cl_2$ (0.40 mL + 0.25 mL rinse) was added. After stirring for 13 h, the mixture was warmed to 0 °C. The reaction was quenched with aq. 30% NaOH (0.5 ml, saturated with NaCl), diluted with $CH_2Cl_2$, and stirred for 0.5 h. The mixture was filtered, and extracted with $CH_2Cl_2$. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 3/2) provided **19** (15.4 mg, 86%, *dr* = 10 : 1) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.02-1.28 (8.8 H, m), 1.39-1.48 (1.1 H, m), 1.65-1.76 (5.5 H, m), 2.12 (1 H, d, *J* = 14.8 Hz), 2.26 (0.1 H, dt, *J* = 15.6, 1.4 Hz), 2.34 (1 H, brs), 2.65 (1 H, dd, *J* = 14.8, 2.4 Hz), 2.74 (1 H, brs), 2.76 (0.1 H, dq, *J* = 15.6, 1.9 Hz), 3.53-3.62 (1.1 H, m), 3.72-3.78 (2.2 H, m), 4.15-4.19 (1.1 H, m), 4.83-4.85 (0.1 H, m), 4.87 (1 H, t-like, *J* = 1.5 Hz), 5.01 (0.1 H, q-like, *J* = 1.9 Hz), 5.05 (1 H, s); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 21.4, 26.5, 26.6 (2 C), 27.6, 29.7,

40.0, 43.3, 63.2, 76.2, 83.2, 83.5, 106.6, 149.8; **IR** (thin film): 3401, 2927, 2854, 1589, 1451, 1024 $cm^{-1}$; **HRMS** (ESI): $C_{14}H_{24}NaO_3$ [M + Na] 263.1623 found 263.1622.




**(*R*)-1-((2*S*,5*R*)-5-cyclohexyl-2-methyl-4-methylenetetrahydrofuran-2-yl)ethane-1,2-diol (20):**

Ti(O*i*-Pr)$_4$ (25 μL, 0.087mmol) and cumene hydroperoxide (0.05 mL, 0.29 mmol) were added successively to a solution of D-(–)-DET (17 μL, 0.029 mmol) and 4 Å molecular sieves (21.0 mg) in $CH_2Cl_2$ (0.22 mL) at -10 $^oC$, and the resulting solution was stirred for 20 min. The reaction mixture was cooled to -25 $^oC$, and a solution of the allylic alcohol **18** (13.0 mg, 0.058 mmol) in $CH_2Cl_2$ (0.3 mL + 0.2 ml rinse) was added. After stirring for 13 h, the temperature was raised to 0 $^oC$. The reaction was quenched with aq. 30% NaOH (0.5 ml, saturated with NaCl), diluted with $CH_2Cl_2$, and stirred for 0.5 h. The mixture was filtered, and extracted with $CH_2Cl_2$. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 3/2) provided **20** (11.9 mg, 86%, *dr* = 6 : 1) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.02-1.28 (9.33 H, m), 1.39-1.48 (1.17 H, m), 1.65-1.76 (5.83 H, m), 2.12 (0.17 H, d, *J* = 14.8 Hz), 2.26 (1 H, dt, *J* = 15.6, 1.4 Hz), 2.41 (2 H, brs), 2.65 (0.17 H, dd, *J* = 14.8, 2.4 Hz), 2.76 (1 H, dq, *J* = 15.6, 1.9 Hz), 3.53-3.62 (2.17 H, m), 3.72-3.78 (1.34 H, m), 4.15-4.19 (1.17 H, m), 4.83-4.85 (1 H, m), 4.87 (0.17 H, t-like, *J* = 1.5 Hz), 5.01 (1 H, q-like, *J* = 1.9 Hz), 5.05 (0.17 H, s); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 22.4, 26.4, 26.6 (2 C), 27.1, 29.6, 42.6, 43.1, 63.6, 75.1, 83.4, 85.9, 106.3, 149.7; **IR** (thin film): 3393, 2927, 2854, 1667, 1451, 1024 $cm^{-1}$; **HRMS** (ESI): Calcd for $C_{14}H_{24}NaO_3$ [M + Na] 263.1623 found 263.1619.



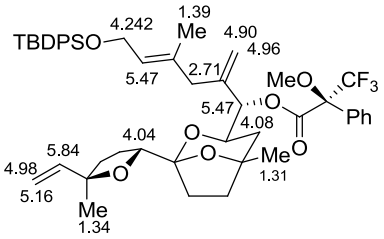

**4**[1] **4a**

**(*S*,*E*)-6-*tert*-butyldiphenylsilyloxy-4-methyl-1-((1*S*,3*R*,5*S*)-5-methyl-1-((2*R*,5*R*)-5-methyl-5-vinyltetrahydrofuran-2-yl)-2,8-dioxabicyclo[3.2.1]octan-3-yl)-2-methylenehex-4-en-1-ol (4a):**

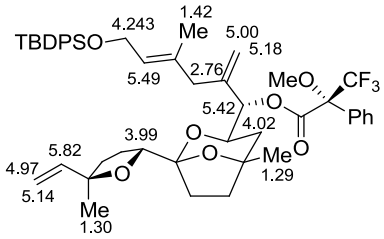
$CrCl_2$ (47.1 mg, 0.383 mmol) was added to a solution of sulfonamide *ligand* **S1**[5] (244.9 mg, 0.514 mmol) and proton sponge (84,1mg, 0.392 mmol) in MeCN (0.65 mL). After stirring for 1 h at rt, the reaction mixture was transferred into a separate flask containing aldehyde **4**[1] (68.9 mg, 0.259 mmol), vinyl iodide **5** (244.9 mg, 0.514 mmol), anhydrous LiCl (22.1 mg, 0.521 mmol), Mn (28.9 mg, 0.526 mmol), $NiCl_2$·DMP[5] (26.8 mg, 0.079 mmol), and $Cp_2ZrCl_2$ (90.9 mg, 0.311 mmol). After stirring for 2 h, the reaction flask was removed from glove box, and diluted with EtOAc. Florisil was added, and the reaction mixture was stirred for 0.5 h, filtered through glass filter, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc = 5/1) to give **4a** (131.2 mg, 82%, *dr* > 20 : 1) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.04 (9 H, s), 1.17-1.21 (1 H, m), 1.33 (3 H, s), 1.37 (3 H, s), 1.43 (3 H, s), 1.66-1.85 (5 H, m), 1.94-2.05 (3 H, m), 2.16-2.22 (1 H, m), 2.24 (1 H, s), 2.65 (1 H, A in ABq, $J$ = 15.0 Hz), 2.74 (1 H, B in ABq, $J$ = 15.0 Hz), 3.98-4.03 (1 H, m), 4.09 (1 H, t, $J$ = 7.1 Hz), 4.15 (1 H, d, $J$ = 3.9 Hz), 4.24 (2 H, d, $J$ = 6.1 Hz), 4.94 (1 H, s), 4.98 (1 H, dd, $J$ = 10.7, 1.5 Hz), 5.18 (1 H, dd, $J$ = 17.3, 1.5 Hz), 5.24 (1 H, s), 5.47-5.50 (1 H, m), 5.84 (1 H, dd, $J$ = 17.3, 10.7 Hz), 7.36-7.44 (6 H, m), 7.68-7.70 (4 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 16.0, 19.3, 26.3, 26.7, 26.9, 27.2, 31.4, 34.4, 35.8, 37.0, 43.8, 61.2, 70.4, 74.8, 80.7, 80.8, 84.2, 108.0, 111.6, 113.6, 127.2, 127.7, 129.7, 134.0, 134.5, 135.7, 143.6, 143.8; **IR** (thin film): 3445, 2930, 2858, 1646, 1428, 1110, 1053 $cm^{-1}$; $[\alpha]_D^{25}$ = -14.2 ($c$ = 1.08, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{38}H_{52}NaO_5Si$ [M + Na] 639.3482 found 639.3491.

**Determination of absolute stereochemistry of 4a**

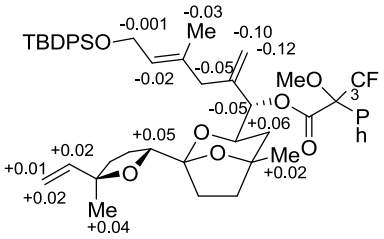
Stereochemistry of **4a** was determined by modified Mosher's method[9]. Derivatization of **4a** to the corresponding (*S*)-MTPA Ester, and (*R*)-MTPA Ester was conducted according to a usual method, and $^1$H NMR data are as follows.




(*S*)-MTPA ester of **4a**



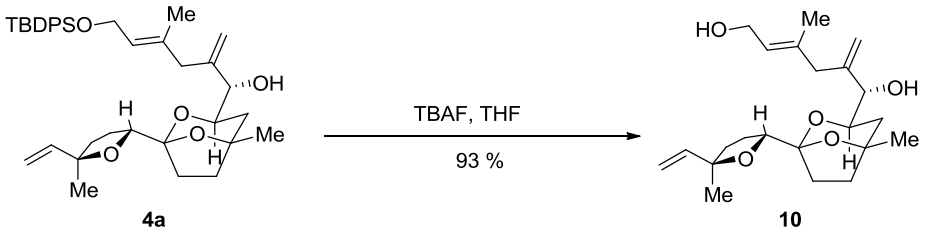

(*R*)-MTPA ester of **4a**




$\Delta\delta = \delta_S - \delta_R$

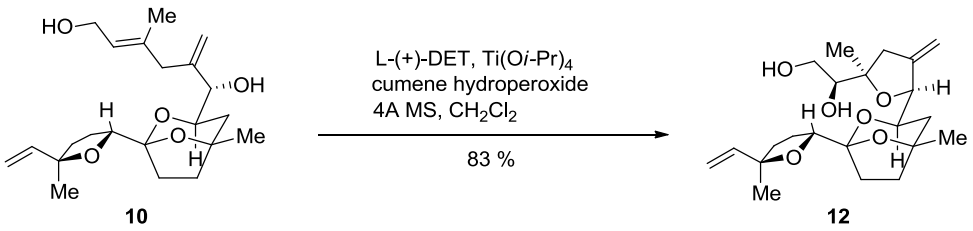
**(*S*)-MTPA ester of S2**;$^1$H NMR (400 MHz, $CDCl_3$) δ: 1.05 (9 H, s), 1.23-1.28 (1 H, m), 1.31 (3 H, s), 1.34 (3 H, s), 1.39 (3 H, s), 1.65-1.82 (5 H, m), 1.90-2.00 (3 H, m), 2.16-2.24 (1 H, m), 2.69 (1 H, A in ABq, *J* = 15.3 Hz), 2.74 (1 H, B in ABq, *J* = 15.3 Hz), 3.59 (3 H, s), 4.03-4.10 (2 H, m), 4.24 (1 H, d, *J* = 6.1 Hz), 4.90 (1 H, s), 4.96 (1 H, s), 4.98 (1 H, dd, *J* = 10.6, 1.5 Hz), 5.16 (1 H, dd, *J* = 17.3, 1.5 Hz), 5.46-5.49 (2 H, m), 5.84 (1 H, dd, *J* = 17.3, 10.6 Hz), 7.35-7.44 (9 H, m), 7.58-7.60 (2 H, m), 7.68-7.70 (4 H, m).

**(*R*)-MTPA ester of S2**; $^1$H NMR (400 MHz, $CDCl_3$) δ: 1.05 (9 H, s), 1.12-1.16 (1 H, m), 1.29 (3 H, s), 1.30 (3 H, s), 1.42 (3 H, s), 1.45-1.51 (1 H, m), 1.63-1.79 (4 H, m), 1.87-1.97 (3 H, m), 2.12-2.20 (1 H, m), 2.74 (1 H, A in ABq, *J* = 15.6 Hz), 2.79 (1 H, B in ABq, *J* = 15.6 Hz), 3.52 (3 H, s), 3.98-4.05 (2 H, m), 4.24 (2 H, d, *J* = 6.2 Hz), 4.97 (1 H, dd, *J* = 10.6, 1.5 Hz), 5.00 (1 H, d, *J* = 1.0 Hz), 5.14 (1 H, dd, *J* = 17.3, 1.5 Hz), 5.18 (1 H, s), 5.42 (1 H, d, *J* = 6.0 Hz), 5.47-5.50 (1 H, m), 5.82 (1 H, dd, *J* = 17.3, 10.6 Hz), 7.34-7.44 (9 H, m), 7.52-7.54 (2 H, m), 7.68-7.70 (4 H, m).



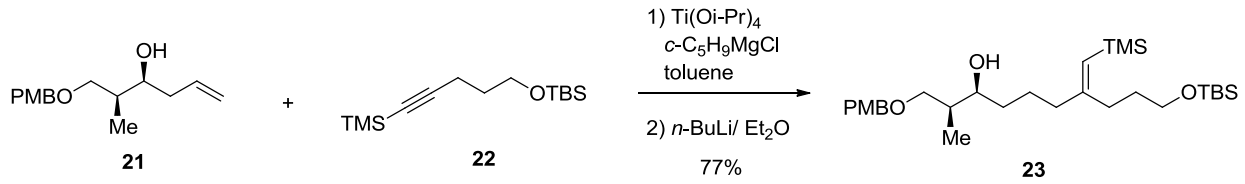

**(*S*,*E*)-3-methyl-6-((1*S*,3*R*,5*S*)-5-methyl-1-((2*R*,5*R*)-5-methyl-5-vinyltetrahydrofuran-2-yl)-2,8-dioxabicyclo[3.2.1]octan-3-yl)-5-methylenehex-2-ene-1,6-diol (10):**

TBAF (1.0 M solution in THF, 0.24 mL, 0.24 mmol) was added dropwise to a solution of **4a** (74.5 mg, 0.121 mmol) in THF (1.2 mL) at 0 °C. After stirring at rt for 18.5 h, the mixture was quenched with sat. $NH_4Cl$ aq. and extracted with EtOAc. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (Pretreated with 1% $Et_3N$ in hexane, hexane/EtOAc = 1/1) provided **10** (42.6 mg, 93%) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.19-1.24 (1 H, m), 1.33 (3 H, s), 1.36 (3 H, s), 1.64 (3 H, s), 1.67-1.74 (3 H, m), 1.77-1.85 (2 H, m), 1.94-2.06 (3 H, m), 2.12-2.19 (1H, m), 2.66 (1 H, A in ABq, $J$ = 15.0 Hz), 2.78 (1 H, B in ABq, $J$ = 15.0 Hz), 3.93-3.98 (1 H, m), 4.07 (1 H, t, $J$ = 6.6 Hz), 4.13 (1 H, d, $J$ = 4.1 Hz), 4.16 (2 H, d, $J$ = 6.7 Hz), 4.96-4.99 (2 H, m), 5.16 (1 H, dd, $J$ = 17.3, 1.5 Hz), 5.24 (1 H, s), 5.47-5.50 (1 H, m), 5.83 (1 H, dd, $J$ = 17.3, 10.7 Hz); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 16.2, 26.3, 26.6, 27.1, 31.6, 34.4, 36.0, 37.0, 43.7, 59.4, 70.6, 74.9, 80.8, 81.0, 84.2, 107.9, 111.7, 113.9, 126.4, 136.7, 143.5, 143.9; **IR** (thin film): 3402, 2972, 2924, 1589, 1455, 1051 cm$^{-1}$; $[\alpha]_D^{29}$ = -3.30 ($c$ = 0.37, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{22}H_{34}NaO_5$ [M + Na] 401.2304 found 401.2303.



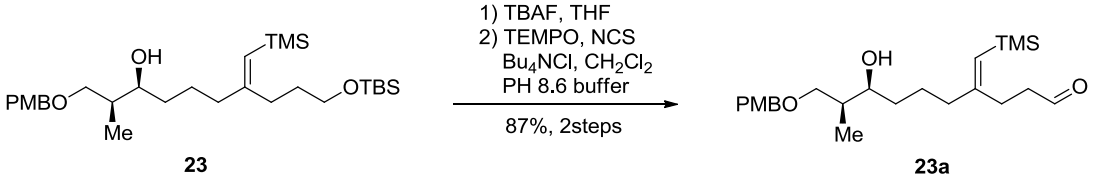

**(1*S*)-1-((2*R*)-2-methyl-5-((1*S*,3*R*,5*S*)-5-methyl-1-((2*R*,5*R*)-5-methyl-5-vinyltetrahydrofuran-2-yl)-2,8-dioxabicyclo[3.2.1]octan-3-yl)-4-methylenetetrahydrofuran-2-yl)ethane-1,2-diol (12):**

$Ti(O\textit{i}\text{-}Pr)_4$ (35 μL, 0.119 mmol) and cumene hydroperoxide (0.07 mL, 0.398 mmol) were added successively to a solution of L-(+)-DET (23 μL, 0.135 mmol) and 4 Å molecular sieves (30.8 mg) in $CH_2Cl_2$ (0.3 mL) at -10 $^oC$, and the resulting solution was stirred for 20 min. The reaction mixture was cooled to -25 $^oC$, and a solution of the allylic alcohol **10** (30.1 mg, 0.0795 mmol) in $CH_2Cl_2$ (0.3 mL + 0.2 ml rinse) was added. After stirring for 1 h, the temperature was raised to 0 $^oC$. The reaction was quenched with aq. 30% NaOH (0.5 ml, satursted with NaCl), diluted with $CH_2Cl_2$, and stirred for 0.5 h. The mixture was filtered, and extracted with $CH_2Cl_2$. The organic layer was washed with sat. aq. $NH_4Cl$, brine, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (Pretreated with 1% $Et_3N$ in hexane, hexane/EtOAc = 1/1) provided **12** (26.0 mg, 83%) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 1.13 (3 H, s), 1.30-1.33 (1 H, m), 1.35 (3 H, s), 1.38 (3 H, s), 1.66-1.92 (7 H, m), 1.95-2.10 (3 H, m), 2.17-2.26 (1 H, m), 2.82-2.86 (1H, m), 3.50 (1 H, dd, *J* = 11.3, 6.9 Hz), 3.71 (1 H, dd, *J* = 11.3, 3.3 Hz), 3.77 (1 H, dd, *J* = 6.9, 3.3 Hz), 3.99-4.06 (2 H, m), 4.20-4.22 (2 H, m), 4.97 (1 H, dd, *J* = 10.7, 1.4 Hz), 5.03 (1 H, s), 5.13 (1 H, s), 5.17 (1 H, dd, *J* = 17.3, 1.4 Hz), 5.82 (1 H, dd, *J* = 17.3, 10.7 Hz); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 22.3, 26.3, 26.6, 27.2, 30.7, 34.2, 36.7, 37.8, 39.4, 63.3, 72.2, 75.9, 80.0, 80.7, 81.2, 84.0, 84.3, 108.5, 109.1, 111.8, 143.4, 147.4; **IR** (thin film): 3437, 2970, 2929, 2874, 1456, 1379, 1051 $cm^{-1}$; $[\alpha]_D^{29}$ = +0.33 (*c* = 0.74, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{22}H_{34}NaO_6$ [M + Na] 417.2253 found 417.2251.



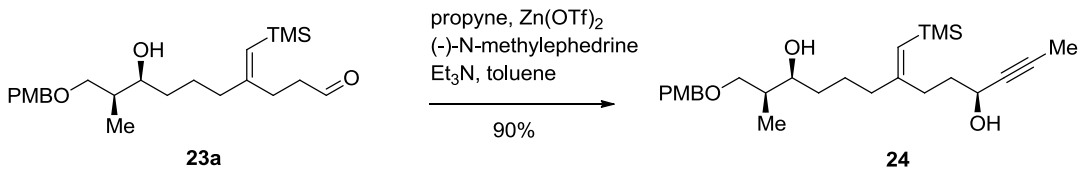

**(2S,3S,Z)-10-*tert*-butyldimethylsilyloxy-1-(4-methoxybenzyloxy)-2-methyl-7-(trimethylsilyl methylene)decan-3-ol (23):**

According to the literature[10], Ti(O*i*-Pr)$_4$ (8.36 mL, 28.53 mmol) was added to a solution of alkyne **22**[4] (7.72 g, 28.53 mmol) in toluene (220 mL) at rt. The colorless solution was cooled to -78 °C and *c*-$C_5H_9MgCl$ (2.0 M in $Et_2O$, 28.5 mL, 57.05 mmol) was added dropwise to generate a bright yellow solution. The resulting solution was allowed to slowly warm to -30°C over an hour, and stirred at -30 °C for 2 h. In a separate flask, the lithium alkoxide of homoallylic alcohol **21**[3] was generated by the addition of *n*-BuLi (2.5M in hexanes, 3.6 mL, 8.97 mmol) to alcohol **21**[3] (2.04 g, 8.15 mmol) in $Et_2O$ (20 mL) at -78 °C. The titanium complex was cooled to -78 °C, and the separate alkoxide solution was warmed to 0 °C and stirred at this temperature for 20 min, whereupon it was transferred dropwise via syringe to the titanium complex at -78 °C, using an additional 5 mL $Et_2O$ to aid in the transfer. The resulting dark brown/black solution was allowed to slowly warm to -30 °C and stirred at this temperature for 9 h. The reaction was quenched with 1M HCl, warmed to rt, and stirred for 1h. The resulting mixture was diluted with $H_2O$ and extracted with EtOAc. The organic layer was washed with brine, dried over $Na_2SO_4$ and concentrated. Column chromatography (hexane/EtOAc = 8/1 to 6/1 to 2/1) provided **23** (3.30 g, 77%) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.05 (6 H, s), 0.09 (9 H, s), 0.89-0.91 (12 H, m), 1.32-1.46 (3 H, m), 1.56-1.66 (3 H, m), 1.84-1.91 (1 H, m), 2.07-2.17 (4 H, m), 2.57 (1 H, d, *J* = 4.6 Hz), 3.49 (2 H, d, *J* = 5.5 Hz), 3.61 (2 H, t, *J* = 6.4 Hz), 3.74 (1 H, m), 3.80 (3 H, s), 4.44 (2 H, s), 5.19 (1 H, s), 6.86-6.89 (2 H, m), 7.22-7.25 (2 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: -5.1, 0.5, 10.9, 18.5, 24.9, 26.1, 32.6 (2C), 33.7, 37.9, 38.9, 55.4, 63.5, 73.2, 74.3, 74.6, 114.0, 123.4, 129.4, 130.3, 159.4 (2C); **IR** (neat): 3496, 2951, 2932, 2857, 1612, 1514, 1245 cm$^{-1}$; $[\alpha]_D^{28}$ = -6.5 (*c* = 0.60, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{29}H_{55}O_4Si_2$ [M + H] 523.3639 found 523.3638.



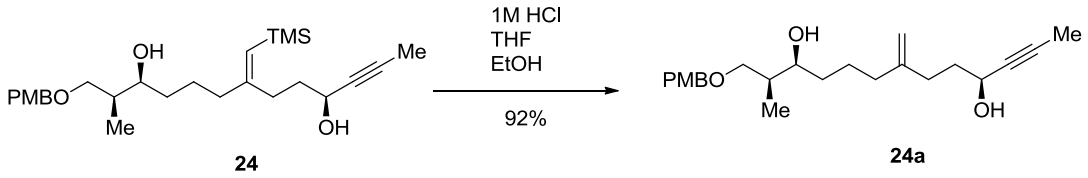

**(8S,9S,Z)-8-hydroxy-10-(4-methoxybenzyloxy)-9-methyl-4-(trimethylsilylmethylene)decanal (23a):**

TBAF (1.0 M in THF, 6.6 mL, 6.64 mmol) was added dropwise to a solution of **23** (2.89 g, 5.53 mmol) in THF (18 mL) at 0 °C. After stirring at rt for 14 h, the reaction was quenched with sat. $NH_4Cl$ aq. and the mixture was extracted with EtOAc. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. The resulting diol was dissolved in $CH_2Cl_2$ (55 mL) and pH 8.6 buffer (55 mL, 0.5 M $NaHCO_3$/0.05 M $K_2CO_3$). TEMPO (86.4 mg, 0.553 mmol), $Bu_4NCl$ (154.0 mg, 0.554 mmol), and NCS (1.11 g, 8.30 mmol) were wdded to the mixture. The mixture was vigorously stirred for 19 h, diluted and extracted with $CH_2Cl_2$. The combined organic solutions were washed with brine, dried over $Na_2SO_4$, and concentrated. Column chromatography (hexane/EtOAc = 3/1 to 2/1) provided **23a** (1.74 g, 87%, 2steps) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.09 (9 H, s), 0.90 (3 H, d, *J* = 7.1 Hz), 1.33-1.44 (2 H, m), 1.57-1.66 (2 H, m), 1.86-1.91 (1 H, m), 2.04-2.07 (2 H, m), 2.41-2.45 (2 H, m), 2.50-2.55 (2 H, m), 2.61 (1 H, d, *J* = 4.7 Hz), 3.47-3.51 (2 H, m), 3.73 (1 H, m), 3.81 (3 H, s), 4.43 (1 H, A in ABq, *J* = 11.6 Hz), 4.45 (1 H, B in ABq, *J* = 11.6 Hz), 5.28 (1 H, s), 6.87-6.90 (2 H, m), 7.23-7.25 (2 H, m), 9.79 (1 H, s); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ:0.4, 11.0, 24.8, 28.3, 33.6, 38.0, 38.6, 43.5, 55.4, 73.2, 74.2, 74.6, 113.9, 125.3, 129.4, 130.2, 156.8, 159.4, 201.9; **IR** (neat): 3470, 2951, 1724, 1613, 1514, 1248 $cm^{-1}$; $[\alpha]_D^{28}$ = -2.5 (*c* = 0.60, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{23}H_{39}O_4Si$ [M + H] 407.2618 found 407.2624.



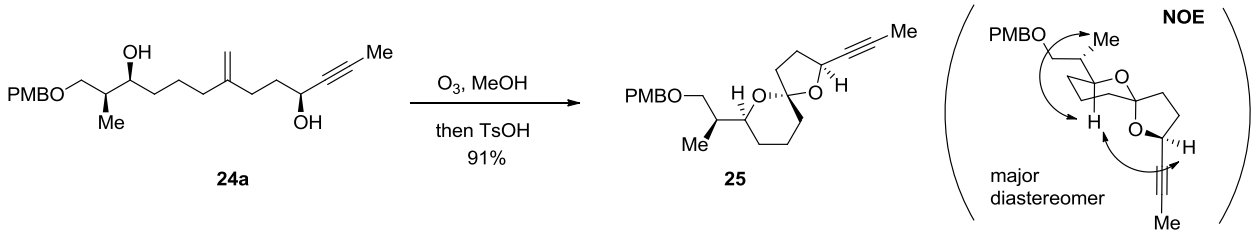

**(2S,3S,10S,Z)-1-(4-methoxybenzyloxy)-2-methyl-7-(trimethylsilylmethylene)tridec-11-yne-3,10-diol (24):**

According to the literature[11], $Zn(OTf)_2$ (617.4 mg, 1.70 mmol) and (-)-N-methylephedrine (335.6 mg, 1.87 mmol) were added to a flame-dried round bottom flask and purged with argon 3 times. Toluene (2.3 mL) and distilled $Et_3N$ (0.25 ml, 1.79 mmol) were added, and the mixture was stirred vigorously for 2 h at rt. Then, excess propyne (~ 0.2 mL) in toluene (0.5 mL) was added to the mixture at −78 °C via cannula. The reaction mixture was slowly warmed to rt and stirred for 10 min. Aldehyde **23a** (345.8 mg, 0.850 mmol) in toluene (1.3 mL + 0.2 mL rinse) was added to the mixture over 5 h by syringe pump and further stirred for another 19 h. The reaction was diluted with sat. $NH_4Cl$ aq., extracted with EtOAc, dried over $Na_2SO_4$, filtered, and concentrated in *vacuo*. Column chromatography (hexane/EtOAc = 2/1) provided **24** (341.1 mg, 90%, dr>20:1) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.10 (9 H, s), 0.90 (3 H, d, $J$ = 7.1 Hz), 1.35-1.45 (2 H, m), 1.60-1.67 (2 H, m), 1.72-1.79 (2 H, m), 1.84-1.91 (4 H, m), 2.07-2.11 (2 H, m), 2.27 (2 H, t, $J$ = 8.6 Hz), 2.60 (1 H, d, $J$ = 4.7 Hz), 3.48-3.51 (2 H, m), 3.73-3.76 (1 H, m), 3.81 (3 H, s), 4.31-4.36 (1 H, m), 4.39 (1 H, A in ABq, $J$ = 11.7 Hz), 4.41 (1 H, B in ABq, $J$ = 11.7 Hz), 5.23 (1 H, s), 6.87-6.89 (2 H, m), 7.23-7.25 (2 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 0.4, 3.6, 11.0, 24.8, 31.6, 33.6, 37.5, 37.9, 38.9, 55.4, 62.7, 73.2, 74.1, 74.4, 80.5, 81.4, 113.9, 124.2, 129.4, 130.2, 158.6, 159.3; **IR** (neat): 3423, 2949, 2321, 1611, 1514, 1246 cm$^{-1}$; $[\alpha]_D^{28}$ = -11.8 ($c$ = 0.60, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{26}H_{42}NaO_4Si$ [M + Na] 469.2750 found 469.2745.




**(2S,3S,10S)-1-(4-methoxybenzyloxy)-2-methyl-7-methylenetridec-11-yne-3,10-diol (24a):**

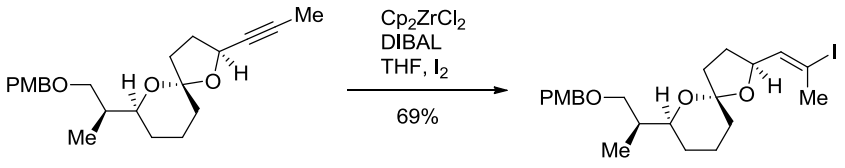
1M HCl (0.55 mL) was added to a solution of **24** (99.3 mg, 0.222 mmol) in THF (0.55 mL) and 1 drop of EtOH at rt. The resulting mixture was stirred for 13 h, then 0.55 mL EtOH was added. The resulting mixture was stirred for 11 h, then 0.55 mL 1 M HCl was added, and stirred for additional 45 h. The reaction was quenched with sat. $NaHCO_3$ aq., and extracted with $CH_2Cl_2$, dried over $Na_2SO_4$, filtered and concentrated in *vacuo*. Column chromatography (EtOAc/hexane = 2/1) provided **24a** (73.2 mg, 92%) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.90 (3 H, d, *J* = 7.1 Hz), 1.39-1.47 (2 H, m), 1.60-1.67 (2 H, m), 1.77-1.95 (6 H, m), 2.03-2.07 (2 H, m), 2.17 (2 H, t, *J* = 8.1 Hz), 2.60 (1 H, brs), 3.48-3.49 (2 H, m), 3.74 (1 H, m), 3.80 (3 H, s), 4.34 (1 H, m), 4.42 (1 H, A in ABq, *J* = 11.6 Hz), 4.45 (1 H, B in ABq, *J* = 11.7 Hz), 4.75 (2 H, s), 6.87-6.89 (2 H, m), 7.23-7.25 (2 H, m); **$^{13}$C NMR** (100 MHz, $CD_3OD$) δ: 3.1, 11.5, 25.4, 32.5, 35.2, 37.1, 37.6, 39.8, 55.7, 62.6, 73.0, 73.8, 74.2, 81.0, 81.4, 109.9, 114.7, 130.4, 131.8, 150.2, 160.7; **IR** (neat): 3418, 2936, 1613, 1514, 1456, 1248 $cm^{-1}$; $[\alpha]_D^{28}$ = -10.6 (*c* = 0.50, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{23}H_{34}NaO_4$ [M + Na] 397.2355 found 397.2353.




**(2S,5S,7S)-7-((S)-1-(4-methoxybenzyloxy)propan-2-yl)-2-(prop-1-yn-1-yl)-1,6-dioxaspiro[4.5] decane (25):**

According to the literature[12], $O_3$ was bubbled through a solution of diol **24a** (22.8 mg, 0.0609 mmol) and Sudan Red 7B (0.0018 M stock solution in MeOH, 0.1 mL, 0.00018 mmol) in MeOH

(3.0 mL) at -78 °C until the pink color just disappeared (~ 1 min). The solution was purged with Ar, then the ozonide was reduced by the addition of 0.5 mL dimethyl sulfide. After stirring for 3 h at rt, TsOH (4.6 mg, 0.024 mmol) was added, and the resulting solution was stirred for 1 h. Sat. $NaHCO_3$ was added and the mixture was extracted with $CH_2Cl_2$, dried over $Na_2SO_4$ and concentrated. Column chromatography (EtOAc/hexane = 9/1) provided **25** (19.8 mg, 91% *dr* = 14 : 1 ) as a colorless oil.; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.91 (3 H, d, *J* = 6.9 Hz), 1.25-1.32 (1 H, m), 1.46-1.49 (1 H, m), 1.61-1.68 (2 H, m), 1.72-1.92 (9 H, m), 2.21-2.31 (1 H, m), 3.25 (1 H, dd, *J* = 6.5, 9.0 Hz), 3.41 (1 H, dd, *J* = 6.2, 9.0 Hz), 3.76-3.80 (4 H, m), 4.39 (1 H, A in ABq, *J* = 11.5 Hz), 4.42 (1 H, B in ABq, *J* = 11.5 Hz), 4.54-4.58 (1 H, m), 6.86-6.89 (2 H, m), 7.24-7.28 (2 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 4.0, 12.5, 20.5, 27.9, 31.9, 33.1, 37.8, 38.4, 55.4, 66.9, 71.1, 72.8, 72.9, 79.1, 81.4, 106.5, 113.9, 129.4, 130.9, 159.2; **IR** (neat): 2941, 2870, 2248, 1612, 1514, 1459, 1247 $cm^{-1}$; **HRMS** (ESI): Calcd for $C_{22}H_{30}NaO_4$ [M + Na] 381.2042 found 381.2034.

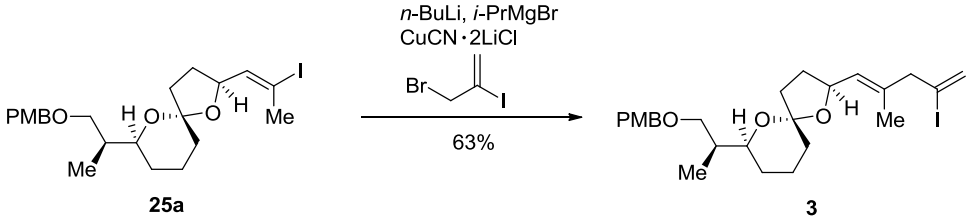



**25** **25a**

**(2S,5R,7S)-2-((E)-2-iodoprop-1-en-1-yl)-7-((S)-1-(4-methoxybenzyloxy)propan-2-yl)-1,6-dioxaspiro[4.5]decane (25a)**

DIBAL (1.0 M in hexane, 0.14 mL, 0.144 mmol) was added to a solution of $Cp_2ZrCl_2$ (44.1 mg, 0.151 mmol) and 4 Å molecular sieves (13.3mg) in THF (0.5 ml) at rt. A solution of alkyne **25** in THF (0.4 mL + 0.1 mL rinse) was added, the mixture was then warmed to 55 °C, and stirred for 30 min. After cooling to 0 °C, $I_2$ (32.1 mg, 0.126 mmol) in THF (0.4 ml) was added and the resulting mixture was stirred for additional 30 min. Sat. $Na_2S_2O_3$ aq. was added and the biphasic mixture was extracted with $Et_2O$. The organic layer was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in *vacuo*. Column chromatography (hexane/EtOAc = 10/1) provided **25a** (12.7 mg, 69%, *dr* = 10:1 ) as a pale yellow oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.94 (3 H, d, *J* = 6.8 Hz),

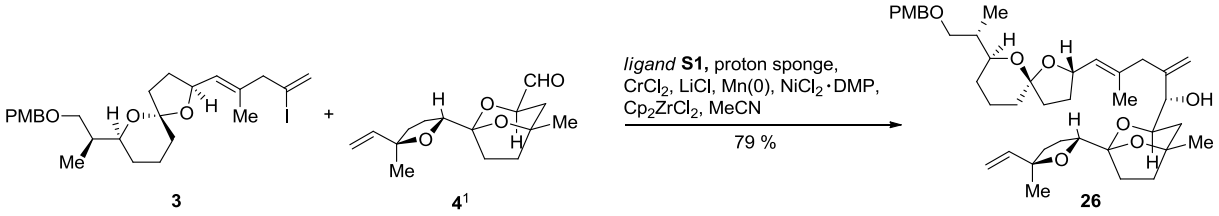
1.23-1.34 (1 H, m), 1.47-1.50 (1 H, m), 1.61-1.92 (8 H, m), 2.14-2.20 (1 H, m), 2.39 (3 H, d, $J$ = 1.4 Hz), 3.27 (1 H, dd, $J$ = 6.5, 9.2 Hz), 3.44 (1 H, dd, $J$ = 6.2, 9.2 Hz), 3.77-3.81 (4 H, m), 4.39 (1 H, A in ABq, $J$ = 11.5 Hz), 4.42 (1 H, B in ABq, $J$ = 11.5 Hz), 4.63 (1 H, q, $J$ = 7.4 Hz), 6.21-6.24 (1 H, m), 6.85-6.89 (2 H, m), 7.22-7.25 (2 H, m); **$^{13}$C NMR** (100 MHz, $C_6D_6$) δ: 12.6, 21.0, 28.3 (2C), 30.6, 33.6, 38.0, 38.7, 54.8, 71.1, 72.8, 73.0, 74.9, 97.8, 106.3, 114.1, 129.3, 131.3, 142.8, 159.7; **IR** (neat): 2940, 2868, 1613, 1458, 1514, 1248 cm$^{-1}$; **HRMS** (ESI): Calcd for $C_{22}H_{32}IO_4$ [M + H] 487.1345 found 487.1344.




**(2S,5R,7S)-2-((E)-4-iodo-2-methylpenta-1,4-dien-1-yl)-7-((S)-1-(4-methoxybenzyloxy)propan-2-yl)-1,6-dioxaspiro[4.5]decane (3):**

According to the literature[13], *n*-BuLi (2.5 M in hexanes, 0.40 mL, 1.01 mmol) was added dropwise to a solution of *i*-PrMgBr (2.9 M in 2-Me THF, 0.17 mL, 0.540 mmol) in THF (2.0 mL) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C. After cooling to −78 °C, a solution of vinyl iodide **25a** (204.2 mg, 0.420 mmol) in THF (0.8 mL + 0.2 mL rinse) was added and the mixture was and stirred for 2 h at −78 °C. CuCN·2LiCl (1.0 M in THF, 0.46 mL, 0.462 mmol) was then added and resulting solution was stirred for 15 min at −78 °C. Finally, a solution of 2-iodo-allylbromide[6] (368.5 mg, 1.49 mmol) in THF (0.6 mL + 0.2 mL rinse) was added and the mixture was further diluted with 1.0 mL THF. The solution was warmed to 0 °C and stirred for 2 h. Then sat. $NH_4Cl$ aq. was added and the biphasic solution was extracted with EtOAc. The organic layer was dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (Benzene/EtOAc = 50/1) provided **3** (138.5 mg, 63%) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.97 (3 H, d, $J$ = 6.8 Hz), 1.23-1.34 (1 H, m), 1.47-1.51 (1 H, m), 1.57-1.94 (11 H, m), 2.16-2.25 (1 H, m), 3.05 (1 H, A in ABq, $J$ = 15.0 Hz), 3.11 (1 H, B in ABq, $J$ = 15.0 Hz), 3.29 (1

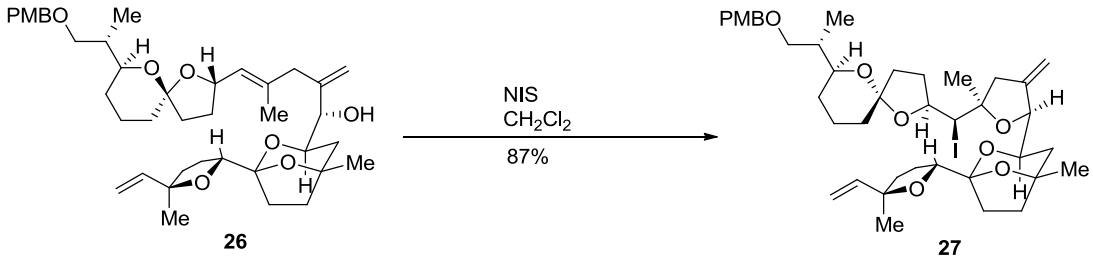
H, dd, $J$ = 6.7, 9.1 Hz), 3.46 (1 H, dd, $J$ = 5.8, 9.1 Hz), 3.78-3.82 (4 H, m), 4.39 (1 H, A in ABq, $J$ = 11.6 Hz), 4.45 (1 H, B in ABq, $J$ = 11.6 Hz), 4.71 (1 H, q-like, $J$ = 7.3 Hz), 5.38-5.40 (1 H, m), 5.79 (1 H, s), 6.08 (1 H, d, $J$ = 1.3 Hz), 6.85-6.88 (2 H, m), 7.24-7.26 (2 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 12.8, 16.0, 20.6, 28.1, 30.9, 33.4, 38.2, 38.5, 55.4, 55.5, 71.3, 72.8, 72.9, 74.2, 106.3, 110.3, 113.8, 127.2, 129.3, 130.8, 131.0, 134.2, 159.2; **IR** (neat): 2937, 2868, 1612, 1513, 1457, 1247 cm$^{-1}$; $[\alpha]_D^{28}$ = -14.3 ($c$ = 0.30, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{25}H_{36}IO_4$ [M + H] 527.1658 found 527.1664.




**Allylic alcohol 26:**

$CrCl_2$ (28.0 mg, 0.228 mmol) was added to a solution of sulfonamide *ligand* **S1**[2] (115.5 mg, 0.232 mmol) and proton sponge (49.6 mg, 0.231 mmol) in MeCN (0.4 mL). After stirring for 1 h at rt, the reaction mixture was transferred into a separate flask containing aldehyde **4**[1] (40.8 mg, 0.153 mmol), vinyl iodide **3** (116.5 mg, 0.221 mmol), anhydrous LiCl (13.4 mg, 0.316 mmol), Mn (16.8 mg, 0.306 mmol), $NiCl_2$·DMP[2] (15.4 mg, 0.046 mmol), and $Cp_2ZrCl_2$ (54.2 mg, 0.185 mmol). After stirring for 2 h, the reaction flask was removed from the glove box, and diluted with EtOAc. Florisil was added, and the reaction mixture was stirred for 0.5 h, filtered through a glass filter, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane/EtOAc = 5/1 to 3/1) to give **26** (80.6 mg, 79%, $dr$ > 20 : 1) as a colorless oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.96 (3 H, d, $J$ = 6.8 Hz), 1.16 (1 H, dd, $J$ = 3.8, 13.2 Hz), 1.25-1.32 (1 H, m), 1.33 (1 H, s), 1.36 (1 H, s), 1.46-1.53 (2 H, m), 1.61-2.03 (18 H, m), 2.11-2.23 (2 H, m), 2.71 (1 H, A in ABq, $J$ = 14.8 Hz), 2.74 (1 H, B in ABq, $J$ = 14.8 Hz), 3.28 (1 H, dd, $J$ = 6.8, 9.1 Hz), 3.45 (1 H, dd, $J$ = 5.7, 9.1 Hz), 3.75-3.80 (4 H, m), 3.94-4.04 (1 H, m), 4.08 (1 H, t-like, $J$ = 5.2

Hz), 4.15 (1 H, d-like, $J$ = 3.7 Hz), 4.39 (1 H, A in ABq, $J$ = 11.6 Hz), 4.44 (1 H, B in ABq, $J$ = 11.6 Hz), 4.70 (1 H, q-like, $J$ = 7.4 Hz), 4.97-5.00 (2 H, m), 5.17 (1 H, dd, $J$ = 1.5, 17.2 Hz), 5.26 (1 H, s), 5.32-5.35 (1 H, m), 5.84 (1 H, dd, $J$ = 10.6, 17.2 Hz), 6.84-6.88 (2 H, m), 7.22-7.26 (2 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 12.9, 16.3, 20.5, 26.3, 26.7, 27.2, 28.1, 31.1, 31.6, 33.4, 34.4, 35.5, 37.1, 38.2, 38.5, 44.4, 55.4, 70.3, 71.4, 72.8, 72.9, 74.0, 74.5, 80.8, 81.0, 84.2, 106.2, 108.0, 111.7, 113.7, 113.8, 129.2 (2 C), 131.0, 136.0, 143.5, 143.6, 159.2; **IR** (neat): 3436, 2936, 1614, 1514, 1458, 1248 cm$^{-1}$; $[\alpha]_D^{28}$ = -5.3 ($c$ = 0.60, $CHCl_3$); **HRMS** (ESI): Calcd for $C_{40}H_{58}NaO_8$ [M + Na] 689.4029 found 689.4023.




**Hexacyclic compound 27:**

NIS (10.0 mg, 0.0444 mmol) was added to a solution of allylic alcohol **26** (10.0 mg, 0.0150 mmol) in $CH_2Cl_2$ (0.5 mL) at -78 °C. After stirring for 2.5 h at same temperature, NIS (10.2 mg, 0.0453 mmol) was added to the mixture. After stirring for 3 h at same temperature, NIS (10.7 mg, 0.0476 mmol) was added to the mixture and stirred for 2 h. The mixture was warmed to 0 °C, then quenched with sat. $Na_2S_2O_3$ aq. After extraction with $CH_2Cl_2$, the organic layer was dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. Column chromatography (hexane/EtOAc = 6/1) provided **27** (10.3 mg, 87%, $dr$ = 12:1) as a pale yellow oil; **$^1$H NMR** (400 MHz, $CDCl_3$) δ: 0.94 (3 H, d, $J$ = 6.8 Hz), 1.30-1.32 (1 H, m), 1.34 (3 H, s), 1.36 (3H, s), 1.37 (3H, s), 1.50-1.87 (16 H, m), 1.95-2.02 (3 H, m), 2.08-2.23 (2 H, m), 2.42 (1 H, d, $J$ = 15.0 Hz), 2.77 (1 H, d, $J$ = 15.0 Hz), 3.26 (1 H, dd, $J$ = 6.6, 9.1 Hz), 3.40 (1 H, dd, $J$ = 5.5, 9.1 Hz), 3.66-3.70 (1 H, m), 3.77-3.83 (5 H, m), 4.09 (1 H, t, $J$ = 6.8 Hz), 4.20 (1 H, d-like, $J$ = 7.2Hz), 4.37 (1 H, A in ABq, $J$ = 11.7 Hz), 4.45

(1 H, B in ABq, $J$ = 11.7 Hz), 4.51 (1 H, d, $J$ = 3.8 Hz), 4.83 (1 H, dd, $J$ = 1.5, 10.6 Hz), 5.03 (1 H, s), 5.15 (3 H, s), 5.23 (1 H, dd, $J$ = 1.5, 17.3 Hz), 5.83 (1 H, dd, $J$ = 10.6, 17.3 Hz), 6.86-6.88 (2 H, m), 7.23-7.25 (2 H, m); **$^{13}$C NMR** (100 MHz, $CDCl_3$) δ: 13.1, 20.6, 23.1, 26.3, 26.7, 27.2, 28.0, 30.5, 30.7, 31.7, 32.9, 34.3, 36.7, 37.8, 38.5, 39.8, 46.2, 53.5, 55.4, 71.7, 71.8, 72.7, 72.9, 80.6, 80.9, 82.9, 83.2, 84.3, 106.0, 108.1, 108.9, 111.7, 113.9, 129.3, 130.9, 143.5, 147.4, 159.2; **IR** (neat): 2918, 2850, 1613, 1519, 1462, 1377, 1249 $cm^{-1}$; **HRMS** (ESI): Calcd for $C_{40}H_{58}IO_8$ [M + H] 793.3176 found 793.3181.

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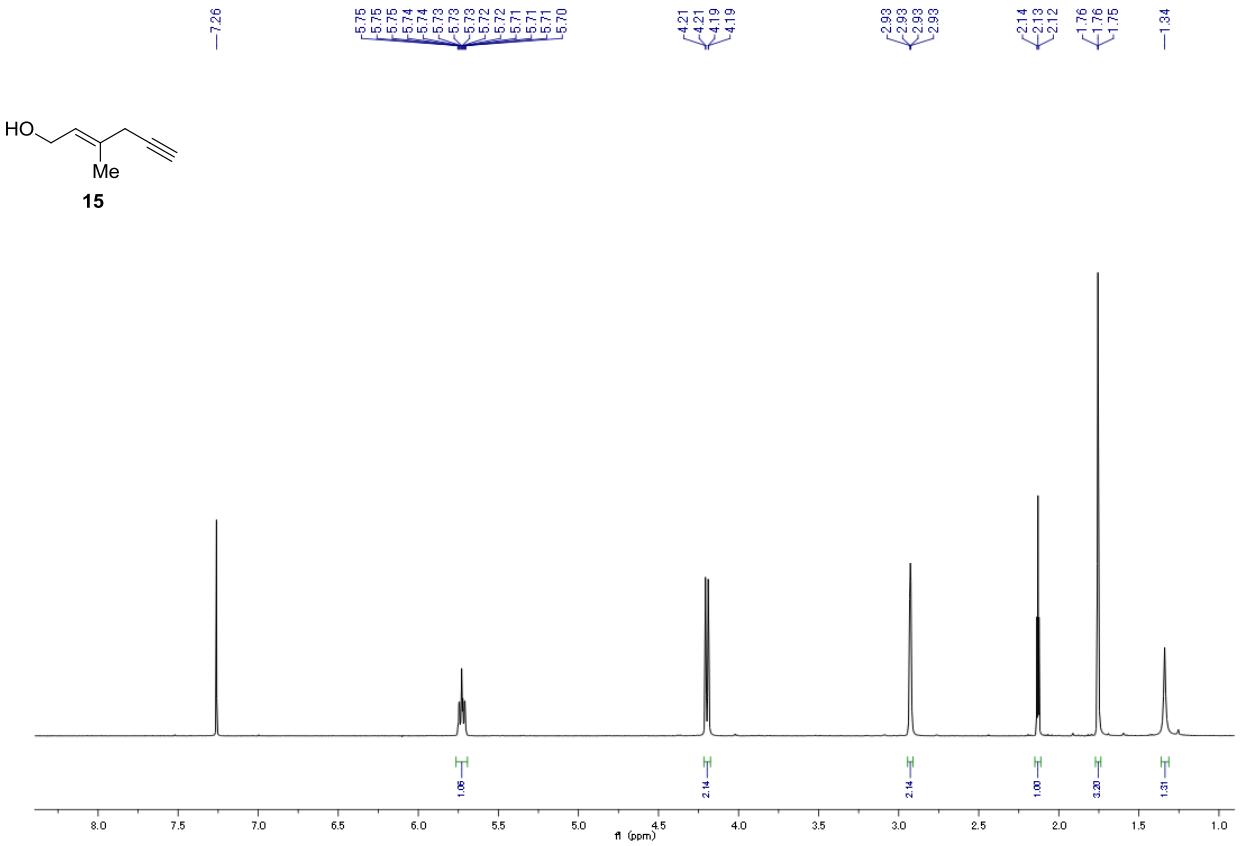
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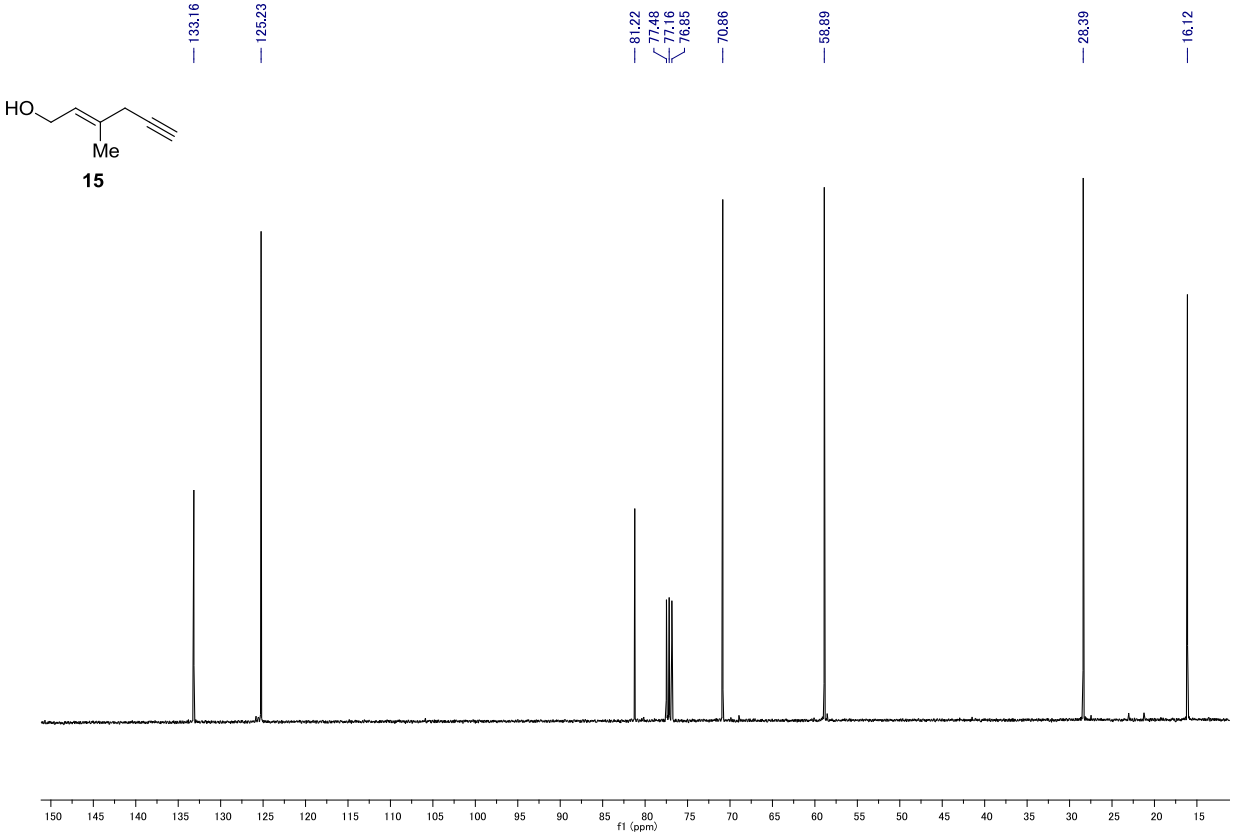
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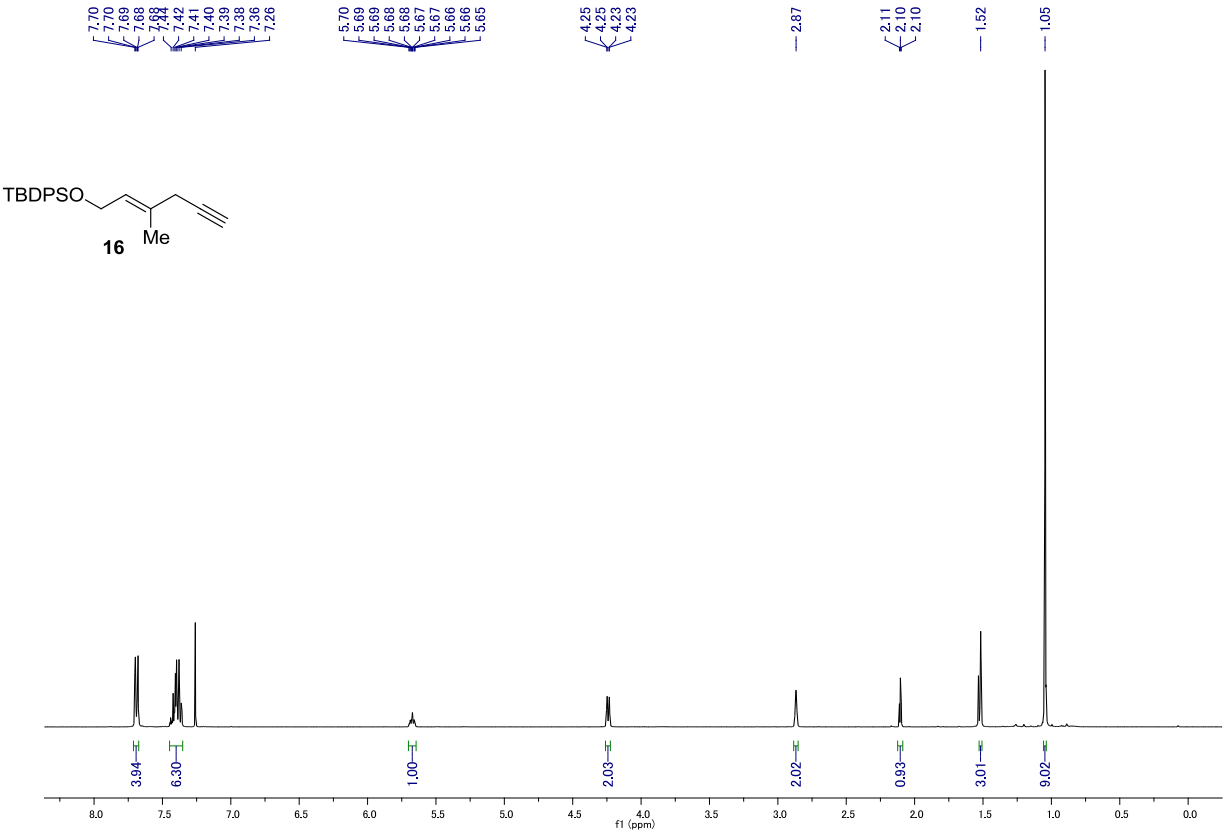
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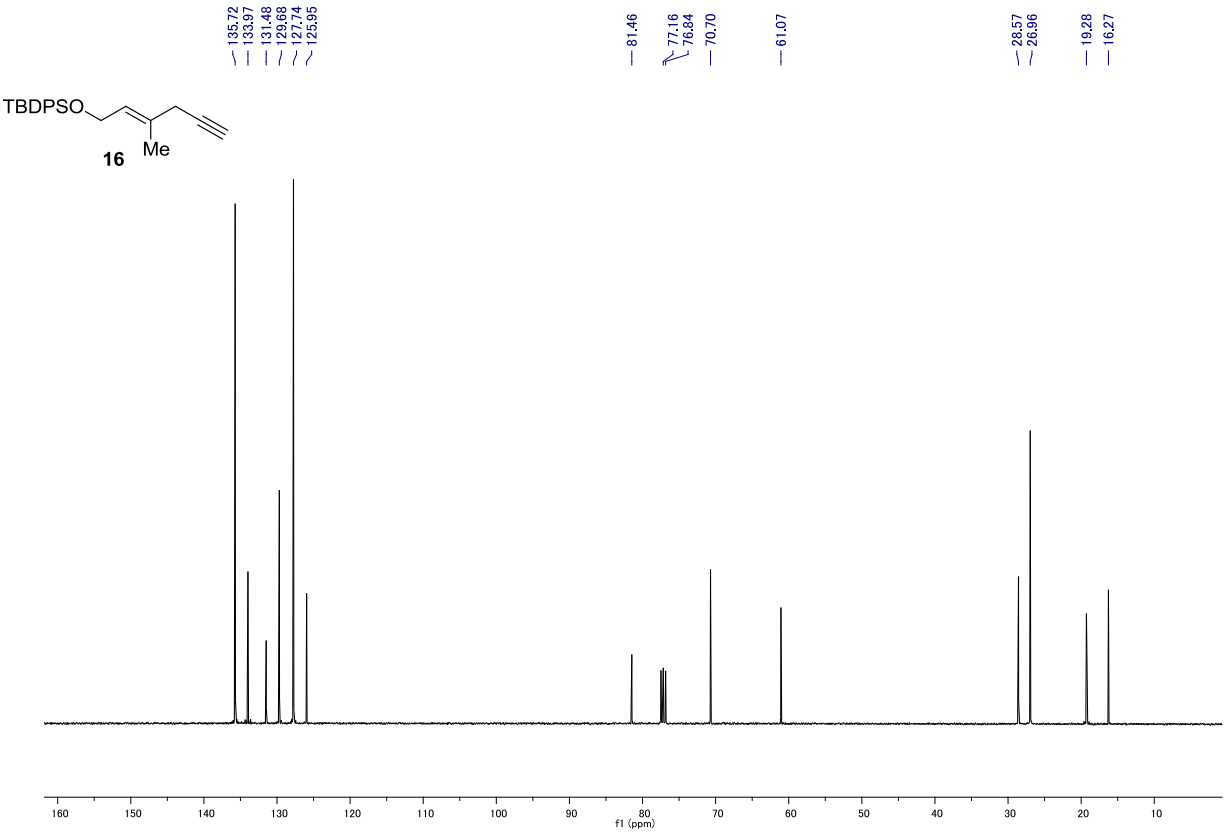
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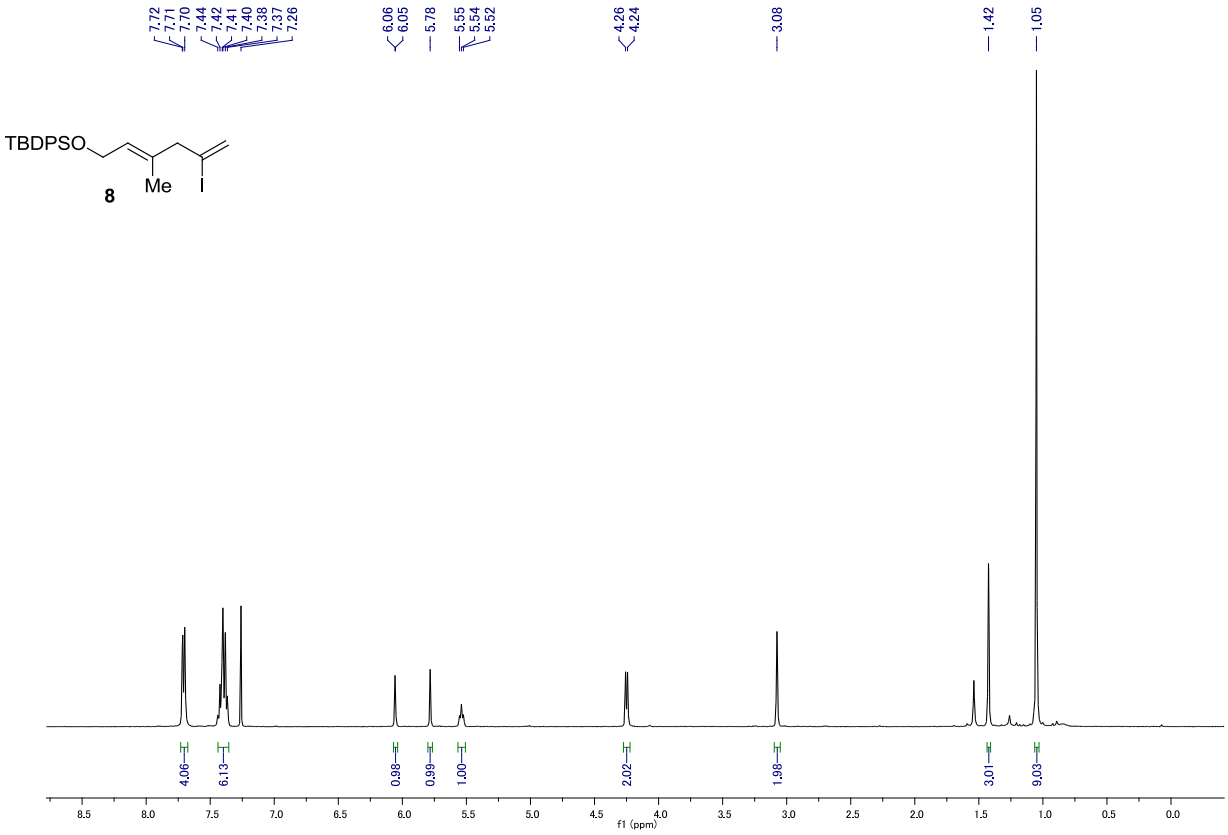
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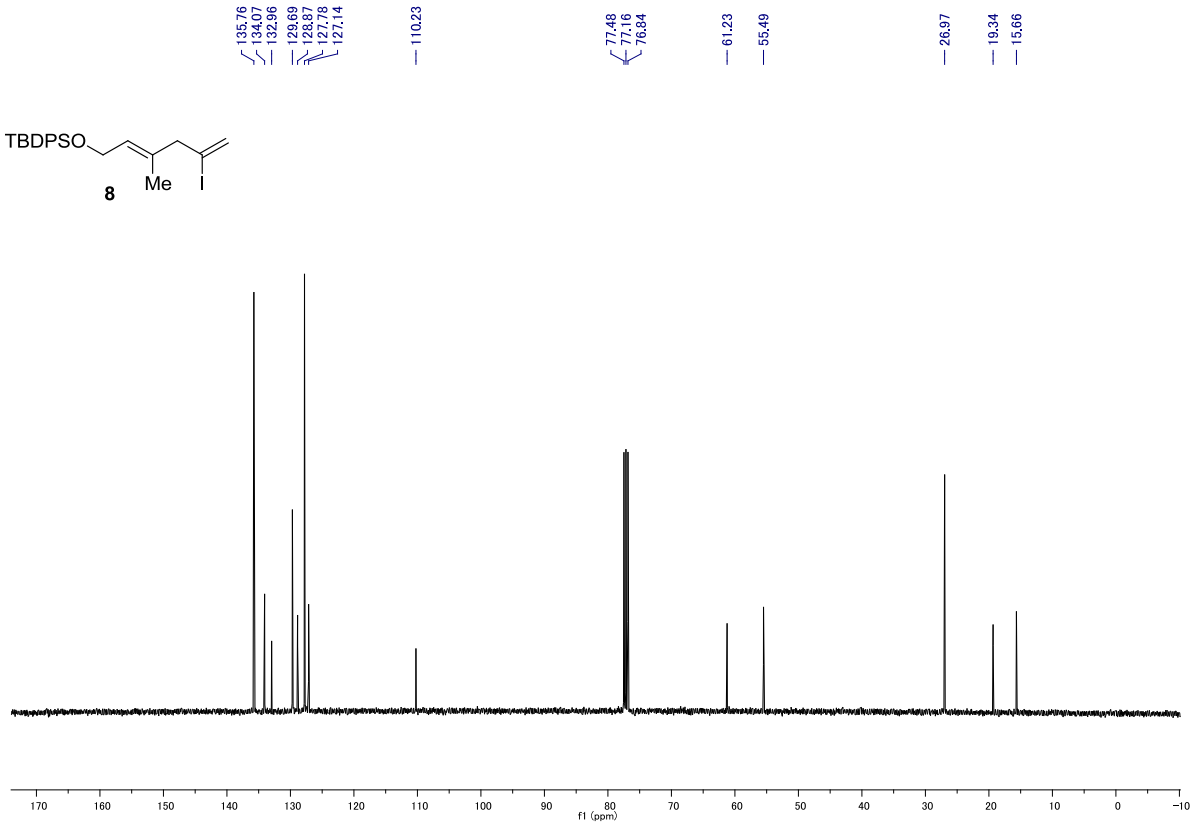
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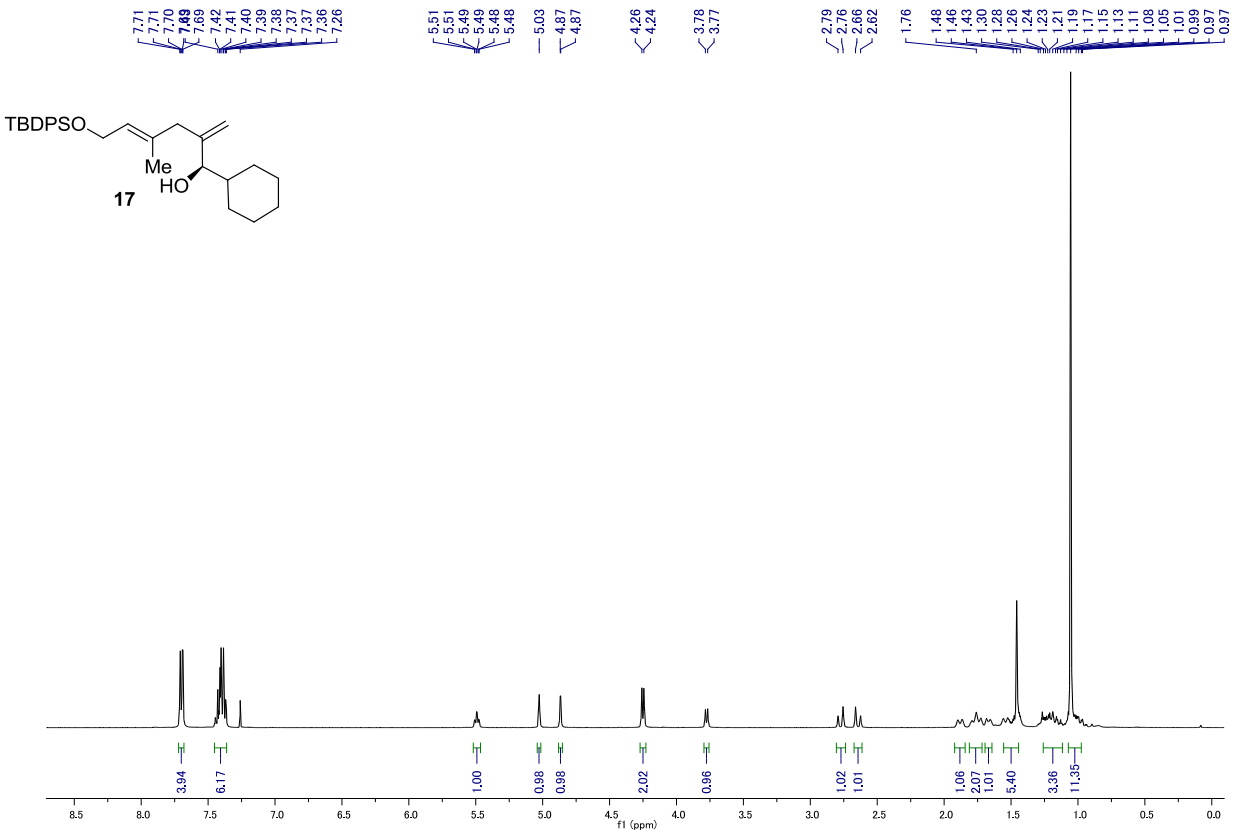
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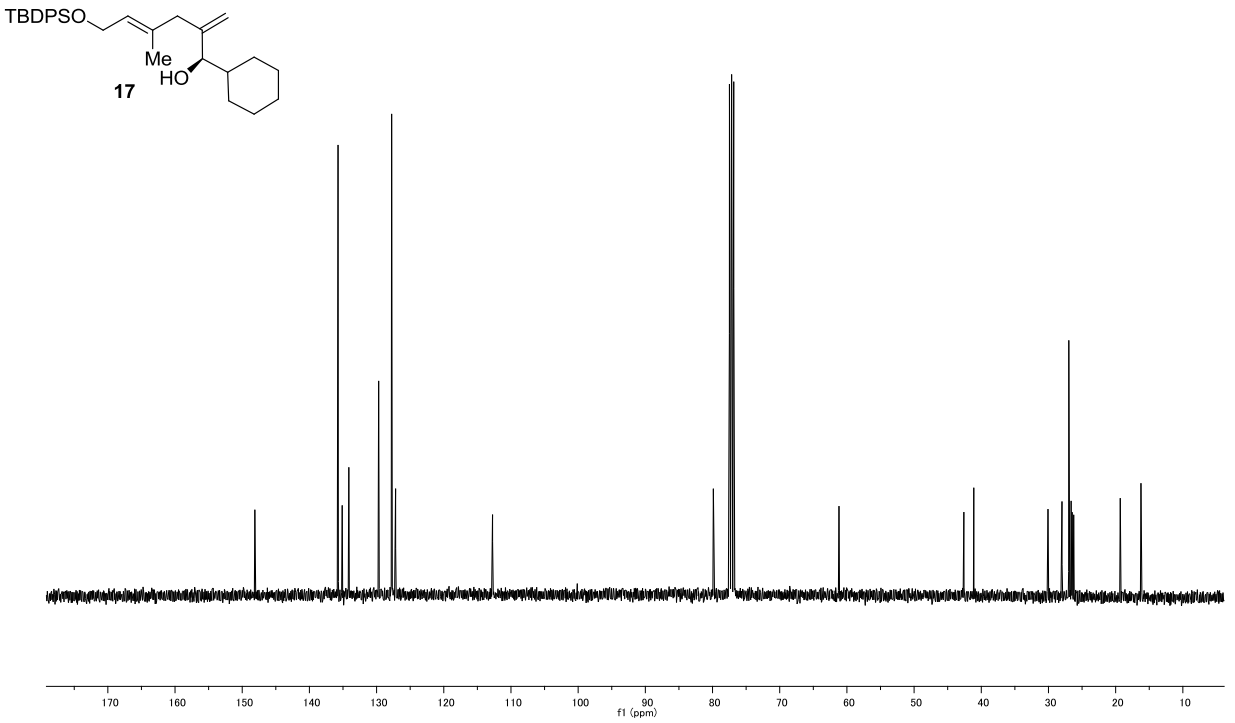
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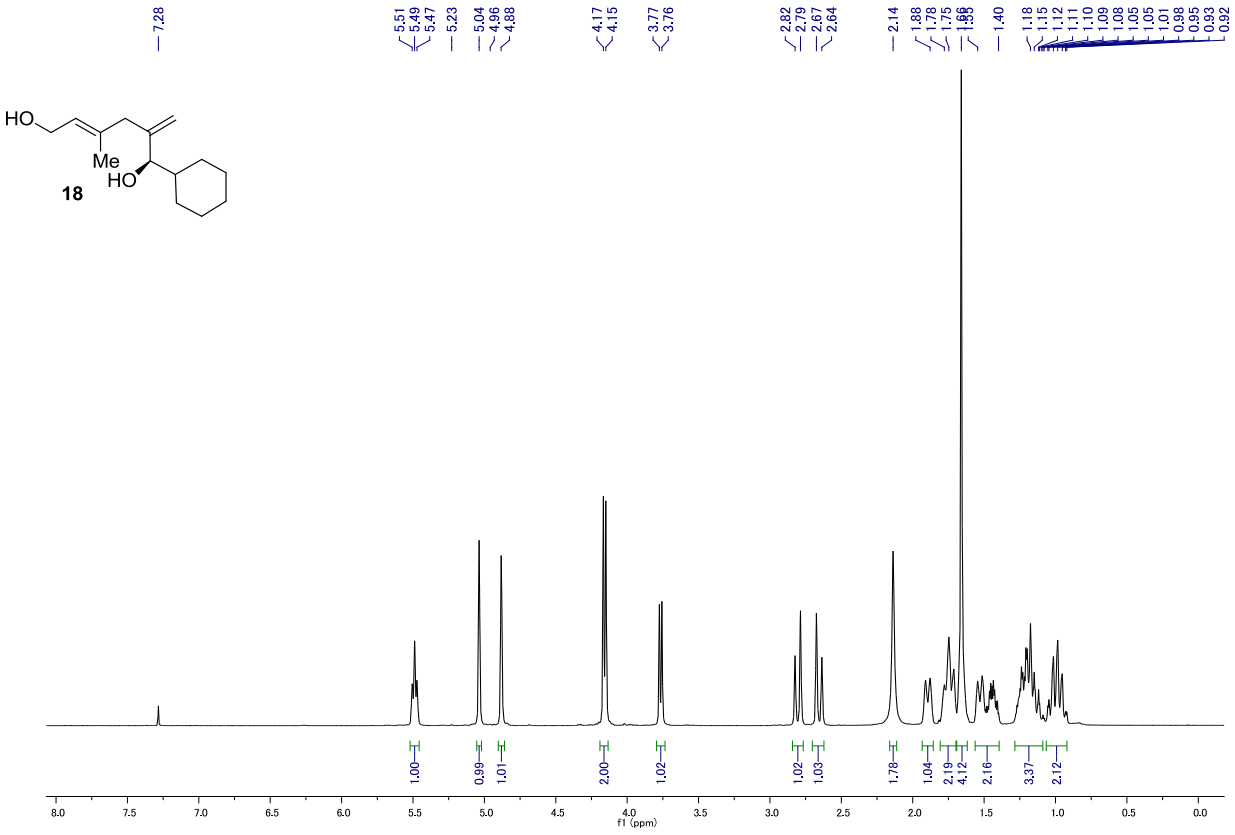
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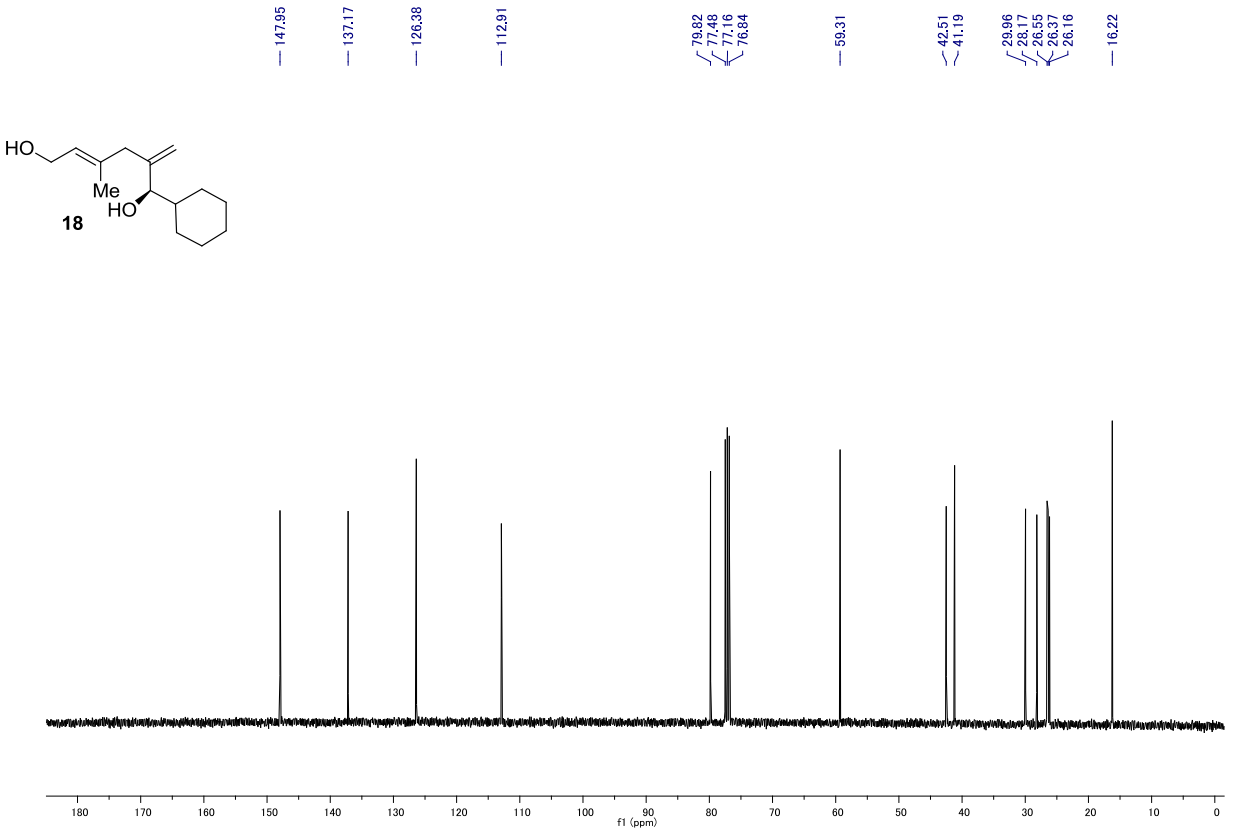
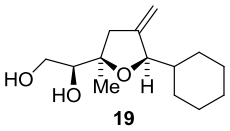
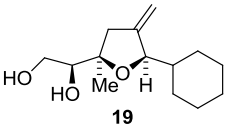

147.95
137.17
126.38
112.91
79.82
77.48
77.16
76.84
59.31
42.51
41.19
29.96
28.17
26.55
26.37
26.16
16.22
HO
Me
HO
18
f1 (ppm)


HO
HO
Me
O
H

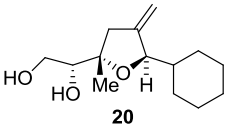
**19**


7.26
5.05
5.02
5.01
5.01
5.00
4.87
4.84
4.17
4.16
3.59
3.59
3.57
3.56
3.54
2.67
2.66
2.63
2.34
2.27
2.25
2.10
1.50
1.46
1.43
1.40
1.26
1.21
1.16
1.12
1.09
1.06
1.02
0.01
1.00
0.10
1.00
0.10
0.07
1.00
2.18
1.14
0.88
1.06
0.73
0.10
1.03
5.53
1.13
8.80
f1 (ppm)


HO
HO
Me
O
H

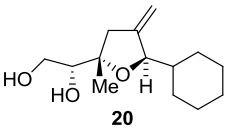
**19**


149.77
106.64
83.50
83.19
77.48
77.16
76.84
76.15
63.21
43.26
39.98
29.69
27.61
26.59
26.55
26.46
21.44
f1 (ppm)


HO
HO
Me
O
H

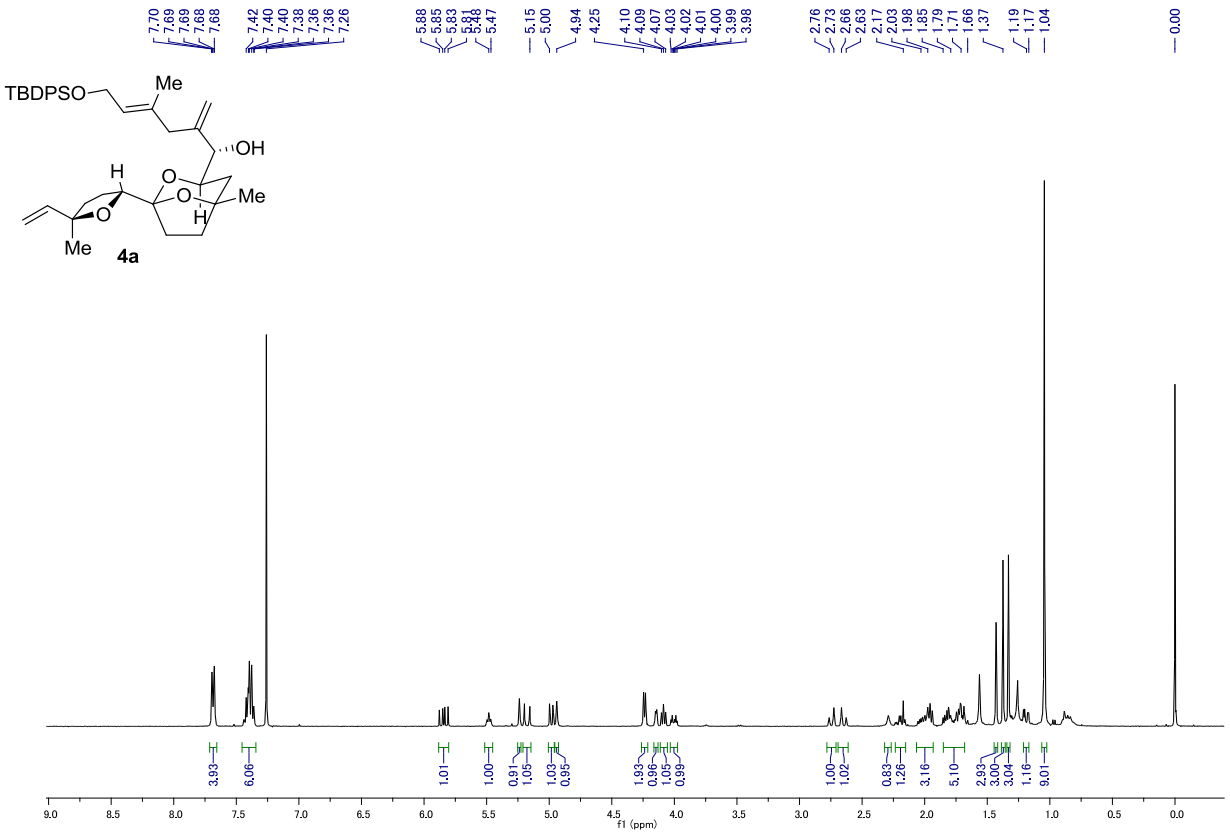
**20**

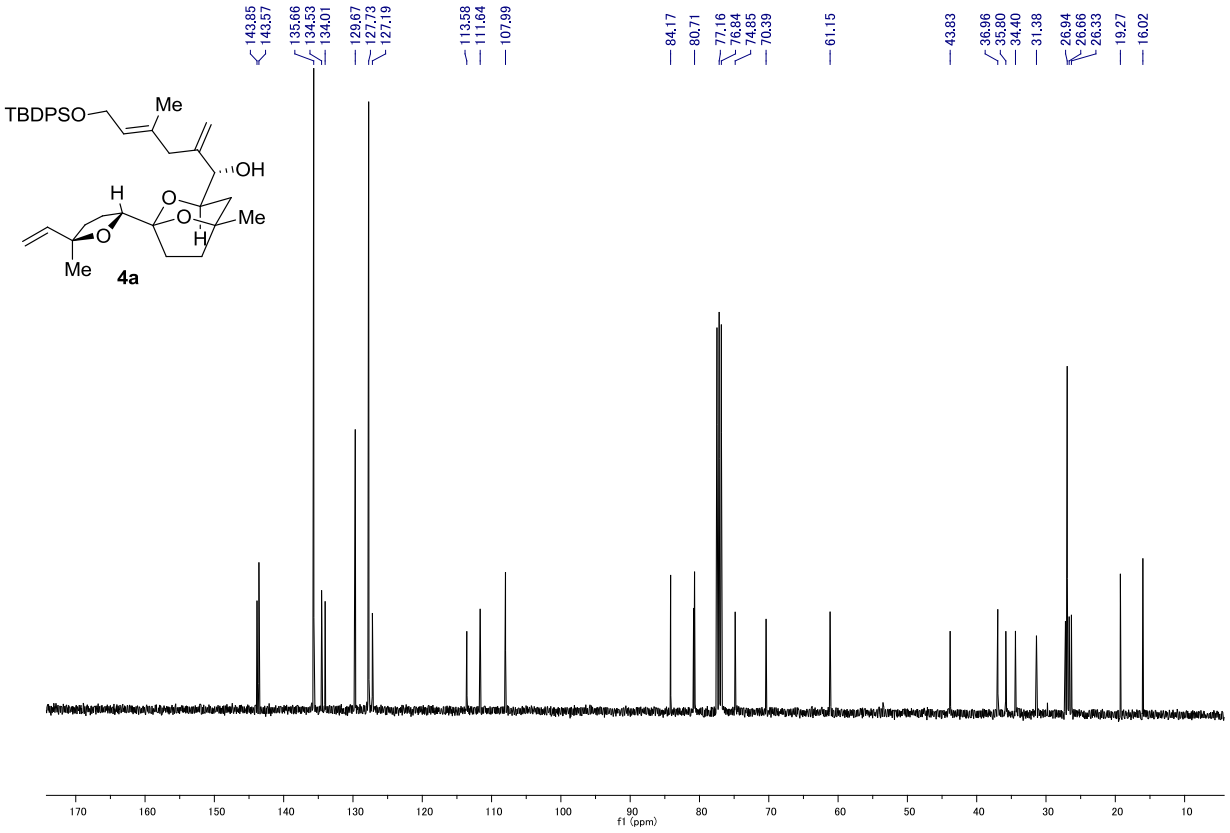

7.26
5.06
5.02
5.02
5.01
5.01
4.84
4.84
4.84
4.33
4.19
4.18
4.18
4.16
3.77
3.73
3.82
3.60
3.57
3.55
2.74
2.74
2.74
2.67
2.63
2.24
2.18
1.73
1.68
1.65
1.43
1.26
1.21
1.16
1.13
1.12
1.10
1.06
1.03
0.00
-0.01
-0.01
0.17
1.00
0.17
1.00
1.17
1.35
2.17
1.00
0.17
1.73
1.08
0.18
5.83
1.16
9.33
f1 (ppm)

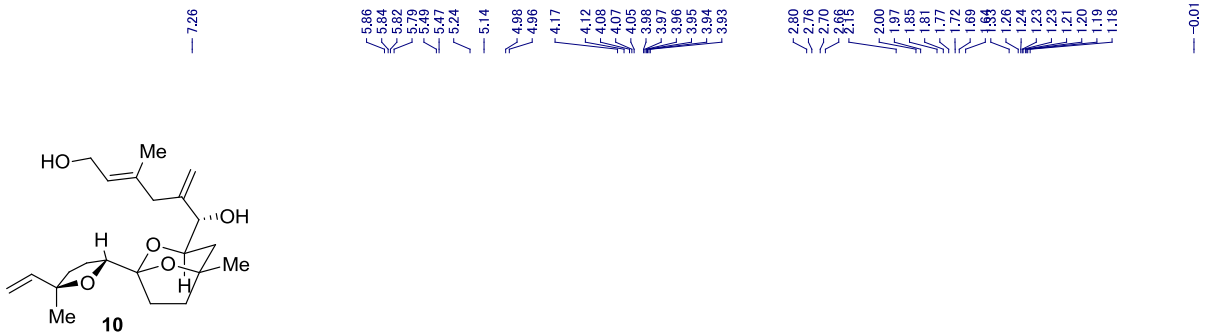

HO
HO
Me
O
H

**20**

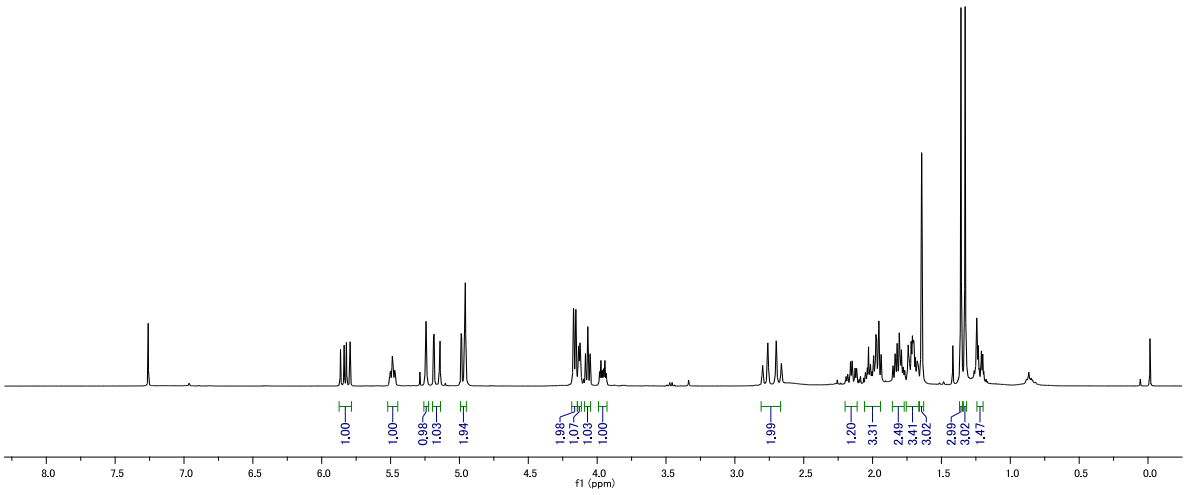

149.71
106.27
85.89
83.34
77.48
77.16
76.84
75.08
63.62
43.07
42.57
29.63
26.59
26.58
26.42
22.38
f1 (ppm)


TBDPSO
Me
OH
H
O
O
Me
O
H
Me
4a
7.70 7.69 7.69 7.68 7.68 7.42 7.40 7.40 7.38 7.36 7.36 7.26
5.88 5.85 5.83 5.81 5.48 5.47 5.15 5.00 4.94 4.25 4.10 4.09 4.07 4.03 4.02 4.01 4.00 3.99 3.98
2.76 2.73 2.66 2.63 2.17 2.03 1.98 1.85 1.79 1.71 1.66 1.37 1.19 1.17 1.04 0.00
3.93 6.06 1.01 1.00 0.91 1.05 1.03 0.95 1.93 0.96 1.05 0.99 1.00 1.02 0.83 1.26 3.16 5.10 2.93 3.00 3.04 1.16 9.01
f1 (ppm)

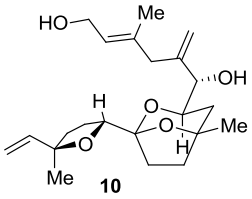

TBDPSO
Me
OH
H
O
O
Me
O
H
Me
4a
143.85 143.57 135.66 134.53 134.01 129.67 127.73 127.19 113.58 111.64 107.99 84.17 80.71 77.16 76.84 74.85 70.39 61.15 43.83 36.96 35.80 34.40 31.38 26.94 26.66 26.33 19.27 16.02
f1 (ppm)


7.26
5.86
5.84
5.82
5.79
5.49
5.47
5.24
5.14
4.98
4.96
4.17
4.12
4.08
4.07
4.05
3.98
3.97
3.96
3.95
3.94
3.93
2.80
2.76
2.70
2.66
2.15
2.00
1.97
1.85
1.81
1.77
1.72
1.69
1.64
1.33
1.26
1.24
1.23
1.23
1.21
1.20
1.19
1.18
0.01

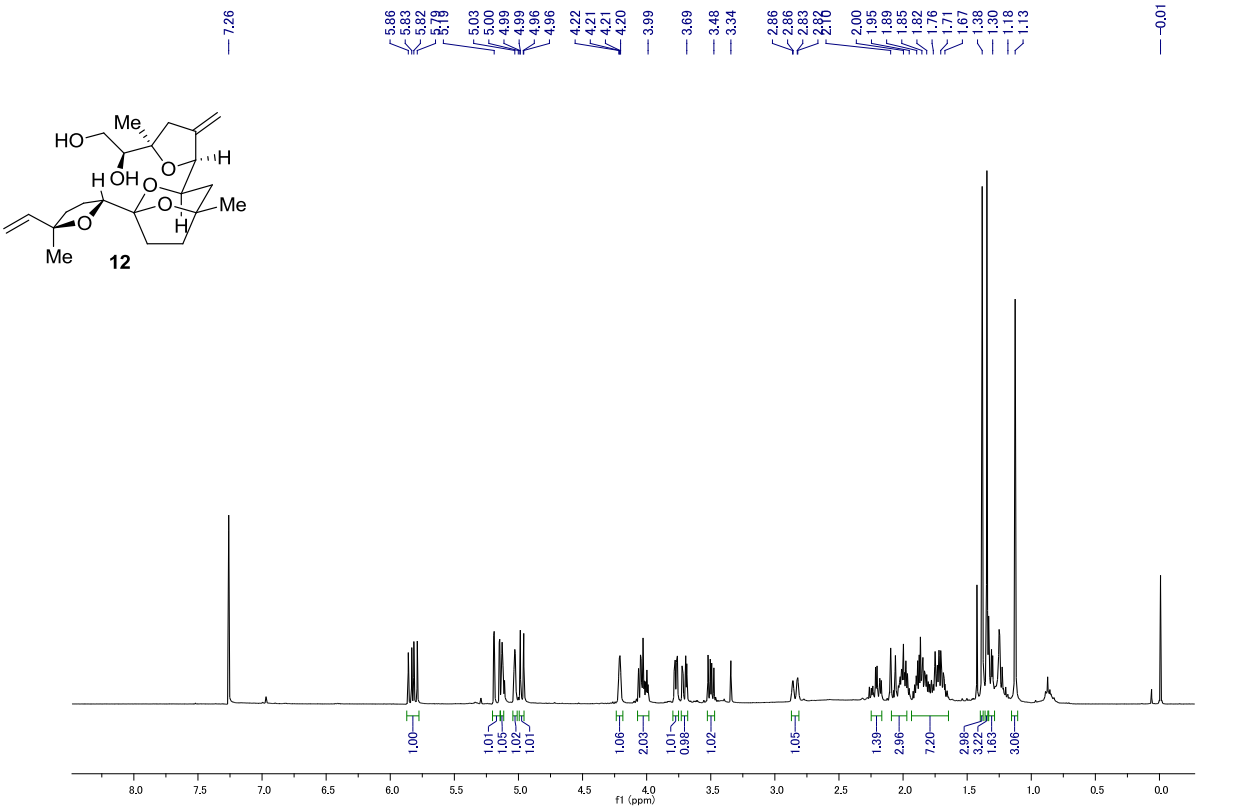

HO
Me
OH
H
O
O
O
H
Me
Me
10

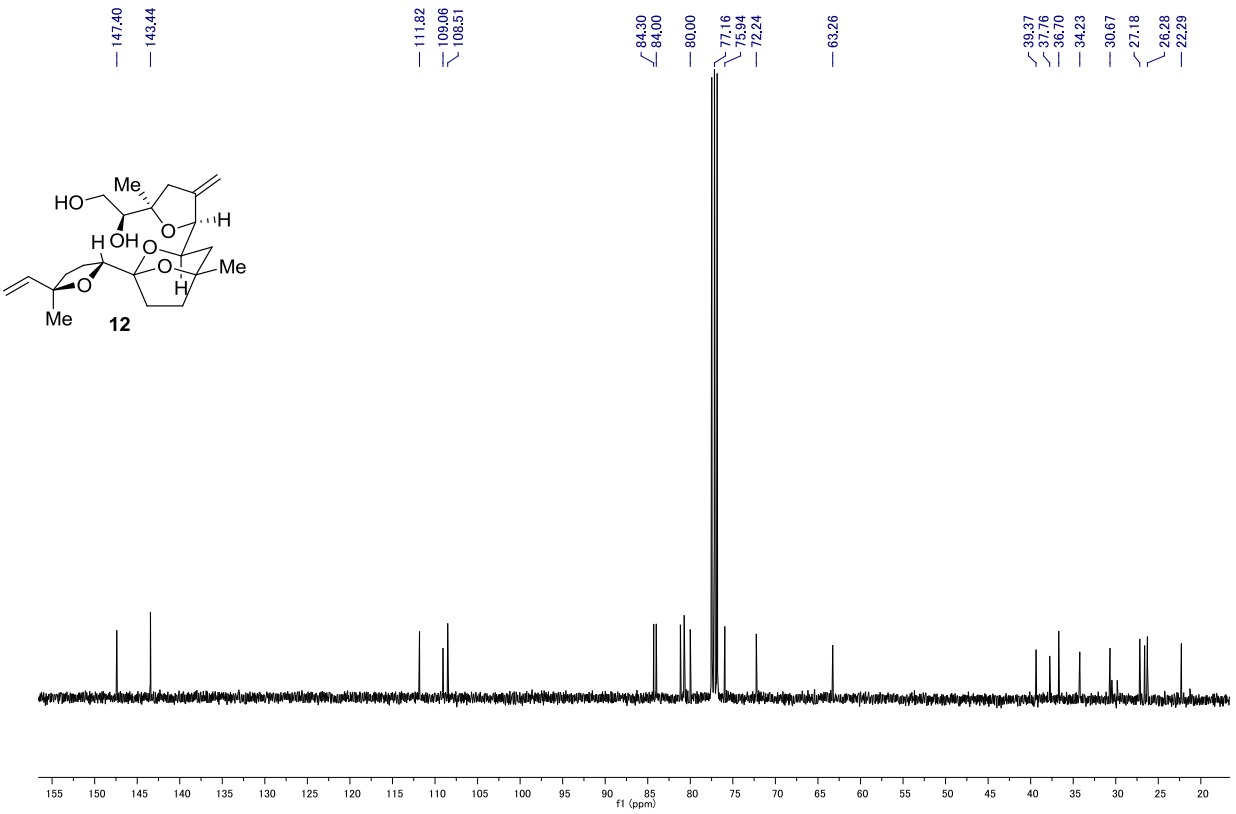

1.00
1.00
0.98
1.03
1.94
1.98
1.07
1.03
1.00
1.99
1.20
3.31
2.49
3.41
3.02
2.99
3.02
1.47
f1 (ppm)


143.94
143.54
136.68
126.43
113.94
111.70
107.88
84.24
80.80
77.16
76.84
74.90
70.56
59.41
43.72
36.98
35.96
34.42
31.61
27.12
26.61
26.32
16.20

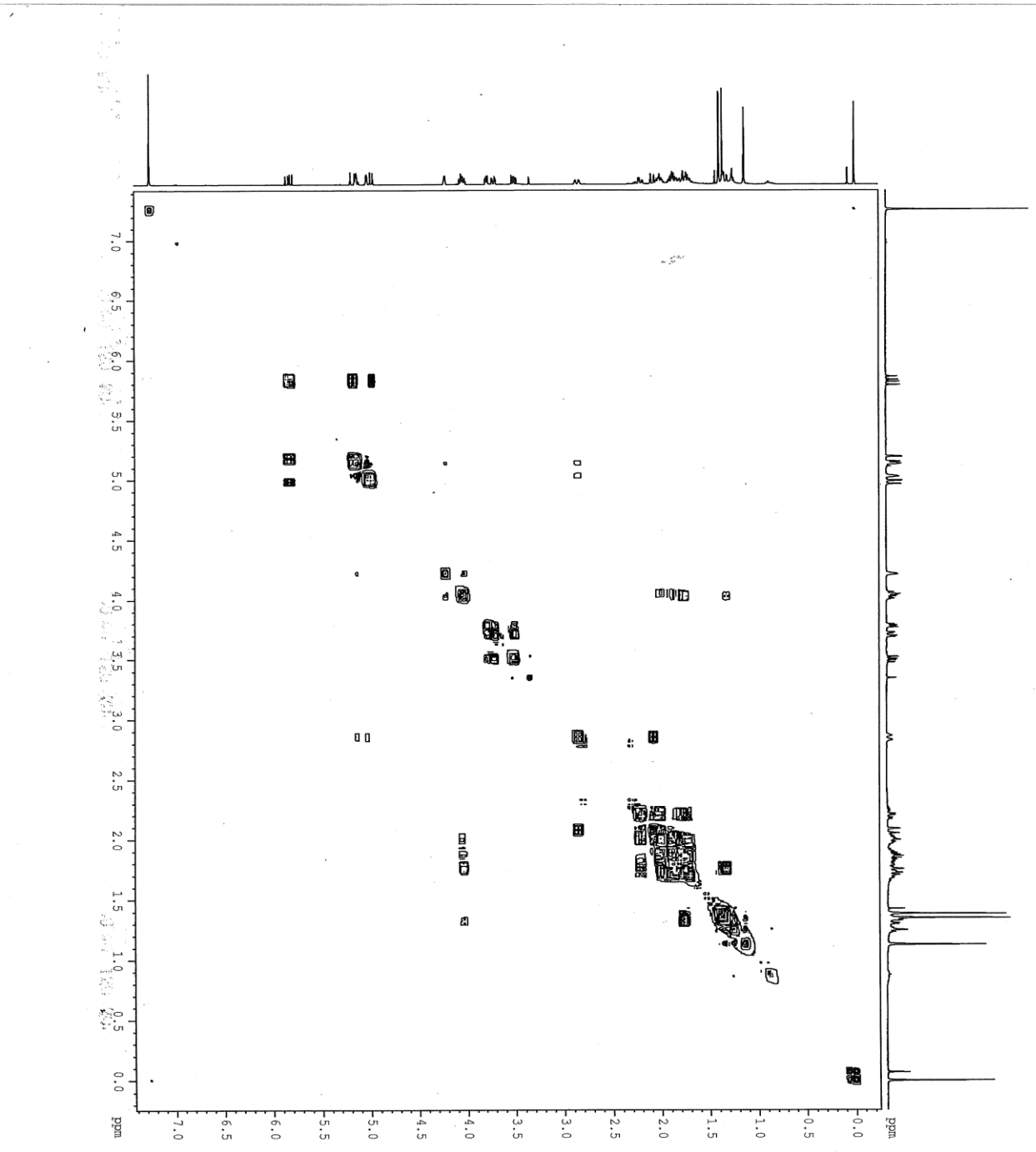

HO
Me
OH
H
O
O
O
H
Me
Me
10

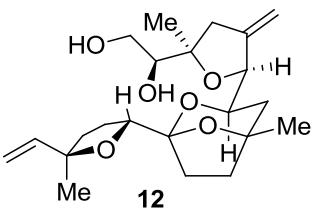

f1 (ppm)


7.26
5.86
5.83
5.82
5.79
5.19
5.03
5.00
4.99
4.99
4.96
4.96
4.22
4.21
4.21
4.20
3.99
3.69
3.48
3.34
2.86
2.86
2.83
2.82
2.10
2.00
1.95
1.89
1.85
1.82
1.76
1.71
1.67
1.38
1.30
1.18
1.13
0.01
HO
Me
H
OH
O
O
O
H
Me
O
Me
12
1.00
1.01
1.05
1.02
1.01
1.06
2.03
1.01
0.98
1.02
1.05
1.39
2.96
7.20
2.98
3.22
1.63
3.06
f1 (ppm)

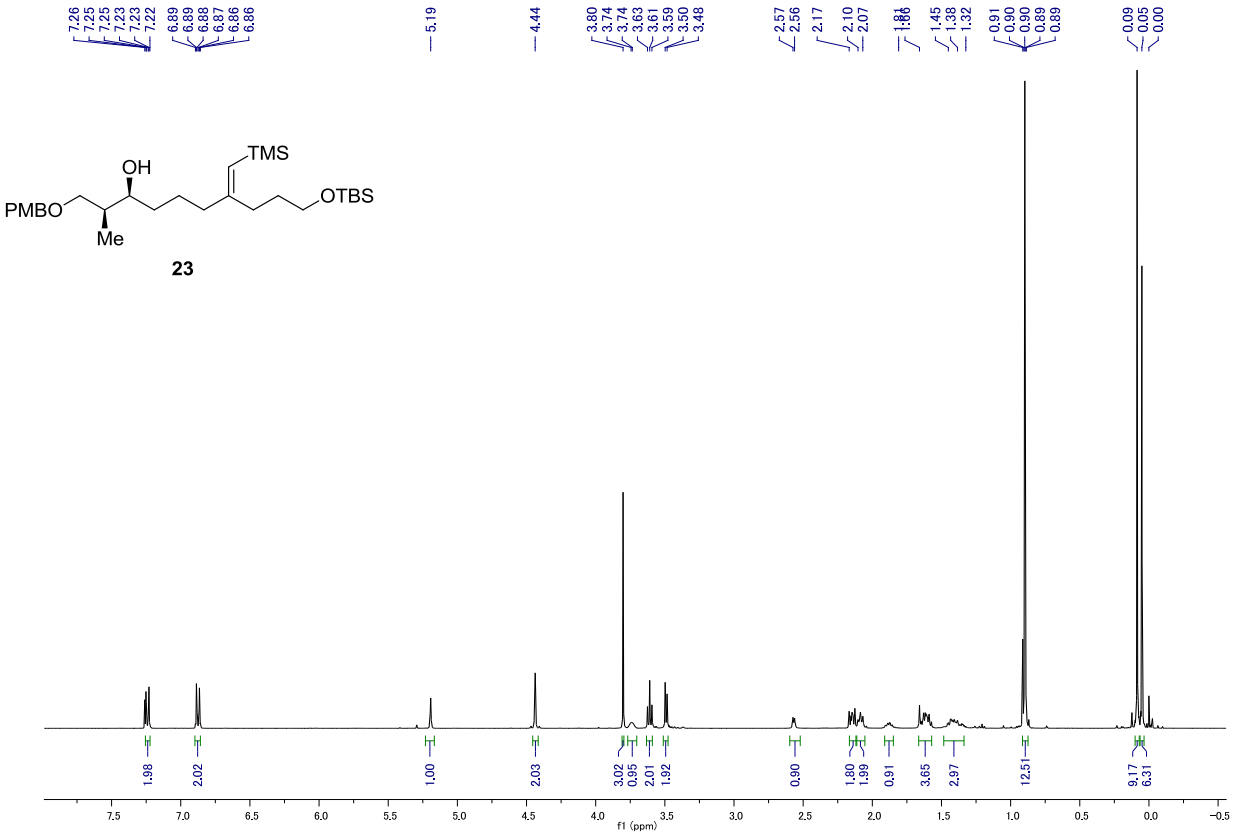

147.40
143.44
111.82
109.06
108.51
84.30
84.00
80.00
77.16
75.94
72.24
63.26
39.37
37.76
36.70
34.23
30.67
27.18
26.28
22.29
HO
Me
H
OH
O
O
O
H
Me
O
Me
12
f1 (ppm)

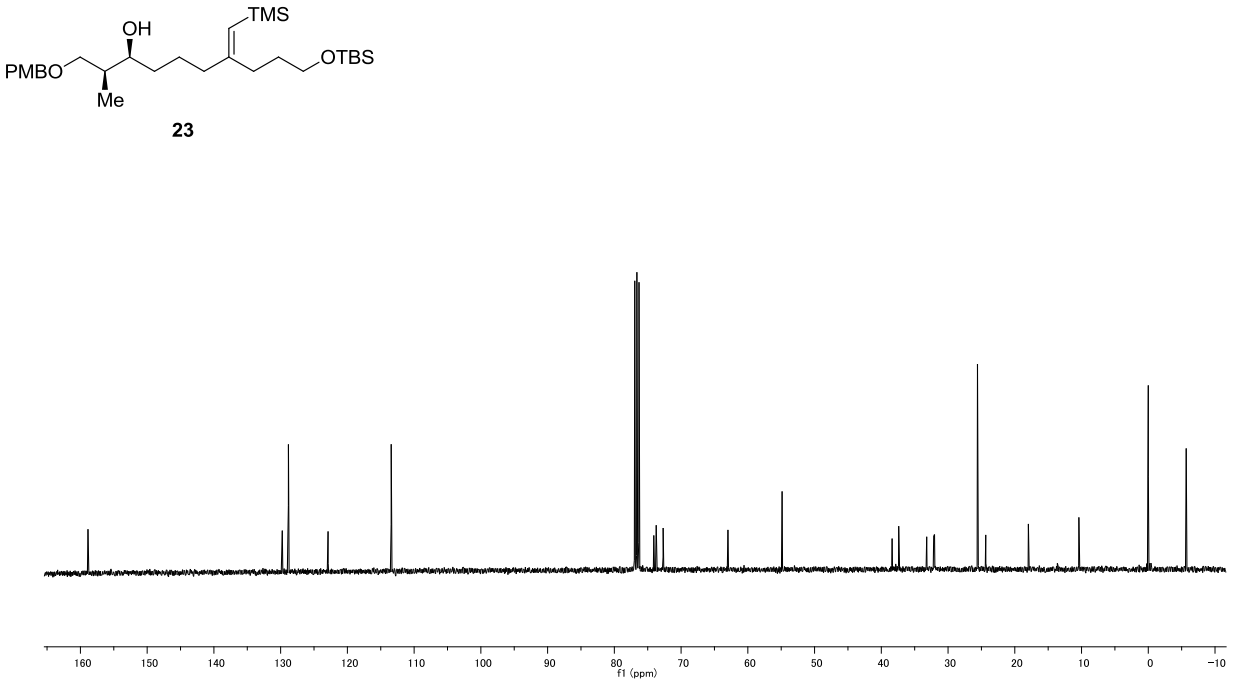
**H-H COSY** of compound **12**

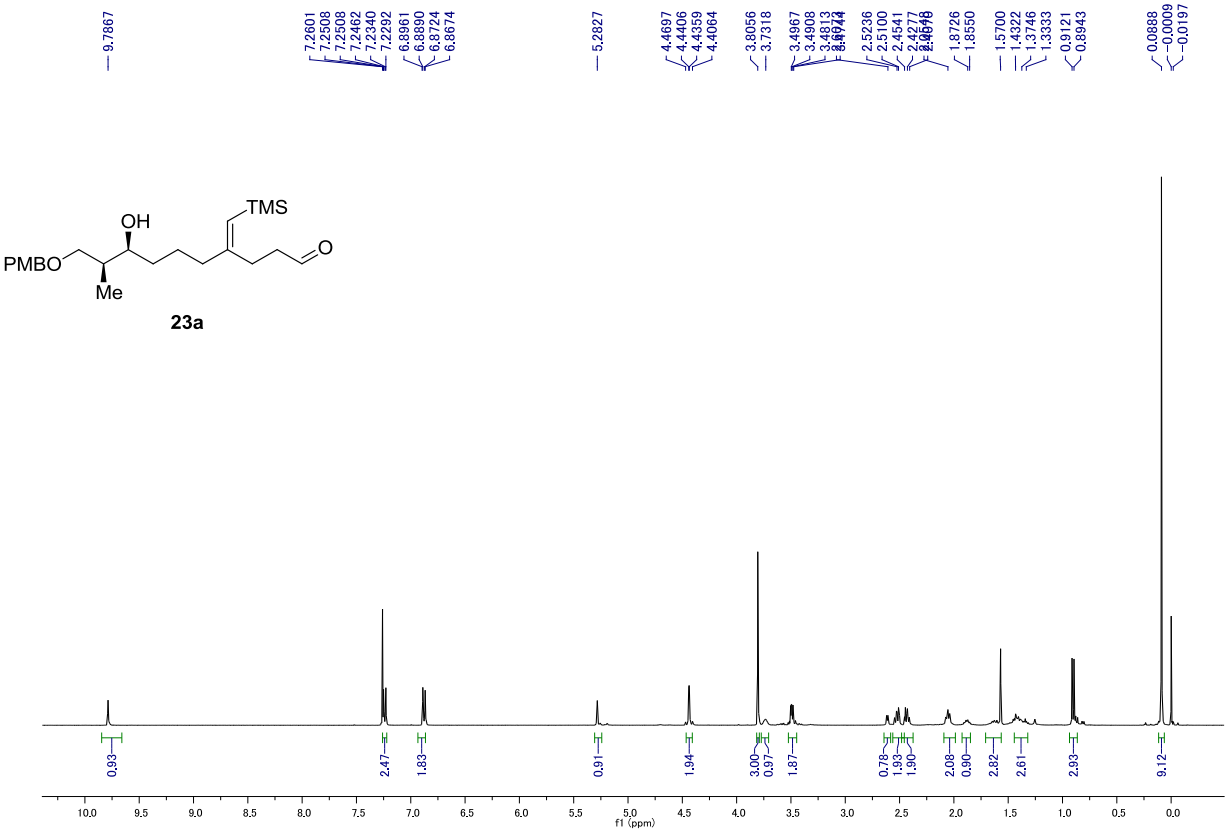


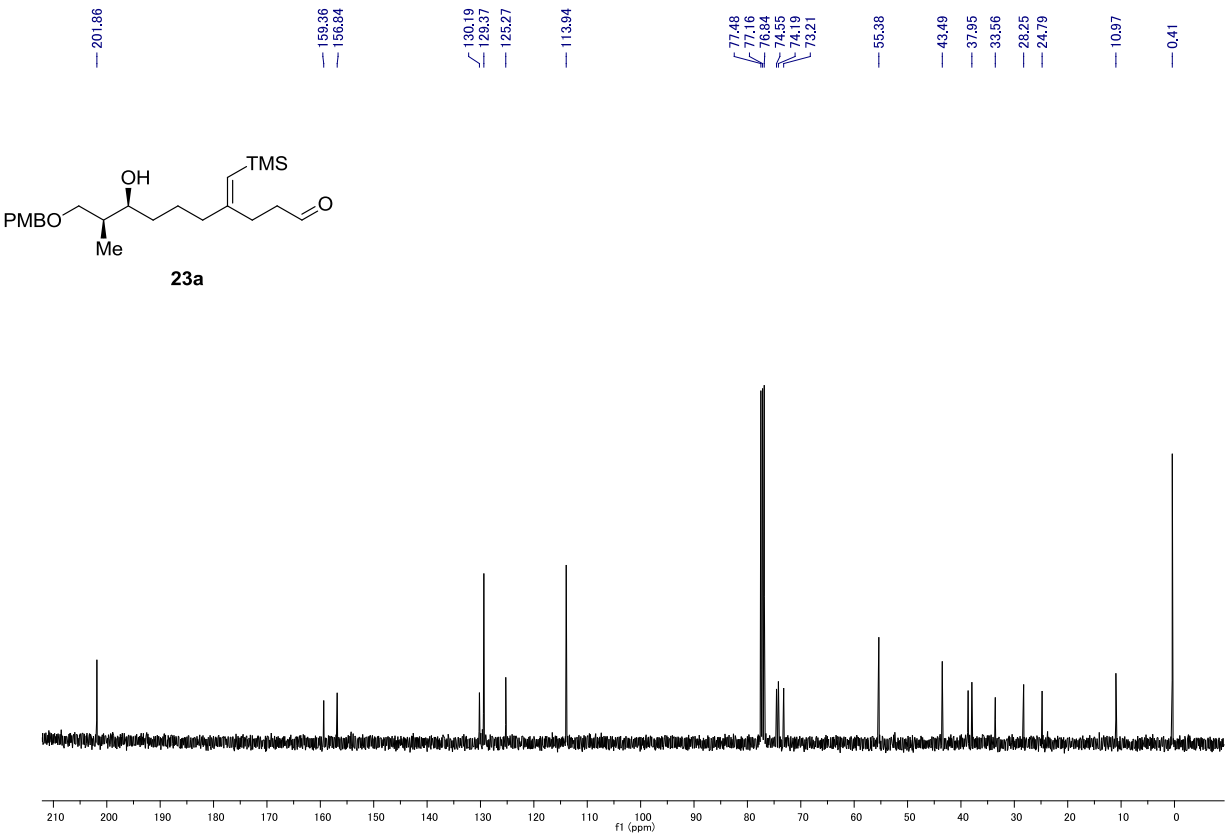

**12**


TMS
OH
PMBO
OTBS
Me
23
f1 (ppm)

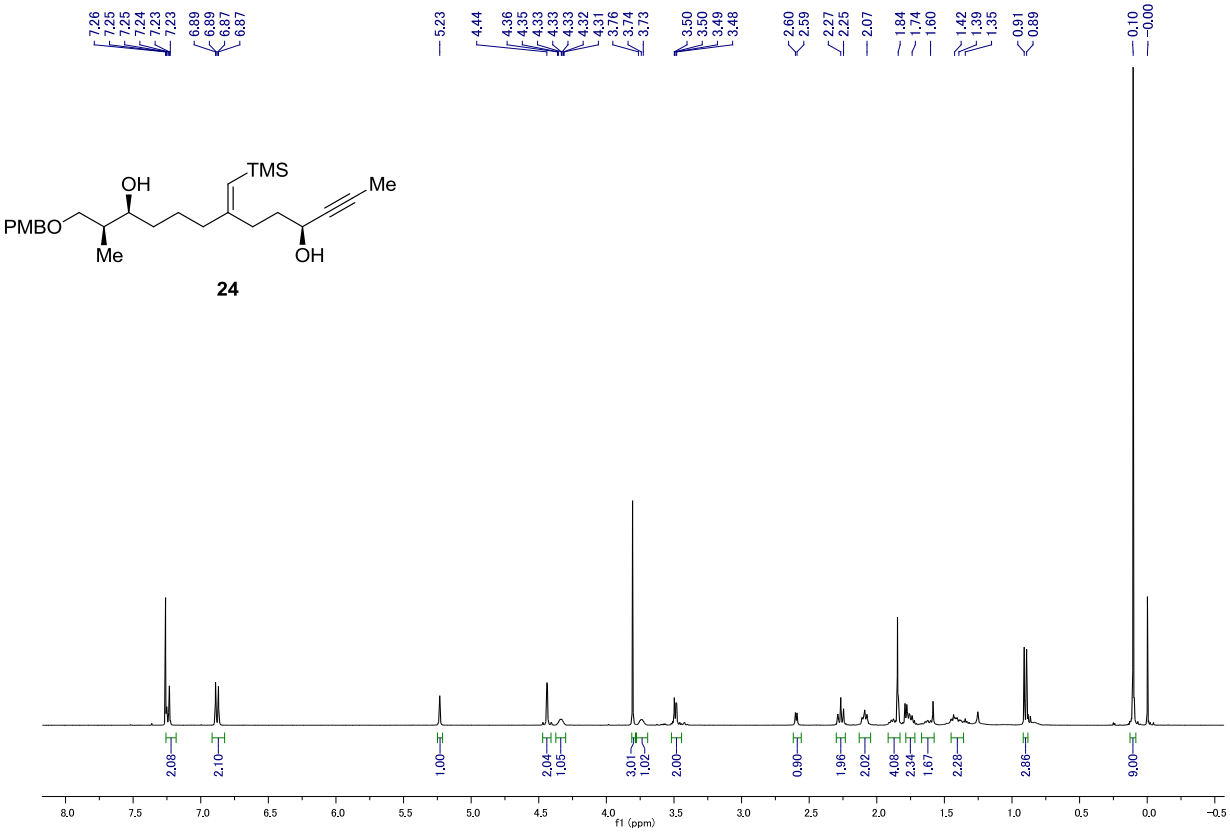

TMS
OH
PMBO
OTBS
Me
23
f1 (ppm)


9.7867
7.2601
7.2508
7.2462
7.2340
7.2292
6.8961
6.8890
6.8724
6.8674
5.2827
4.4697
4.4406
4.4359
4.4064
3.8056
3.7318
3.4967
3.4908
3.4813
2.5236
2.5100
2.4541
2.4277
1.8726
1.8550
1.5700
1.4322
1.3746
1.3333
0.9121
0.8943
0.0888
-0.0009
-0.0197
TMS
OH
PMBO
Me
O
0.93
2.47
1.83
0.91
1.94
3.00
0.97
1.87
0.78
1.93
1.90
2.08
0.90
2.82
2.61
2.93
9.12
f1 (ppm)

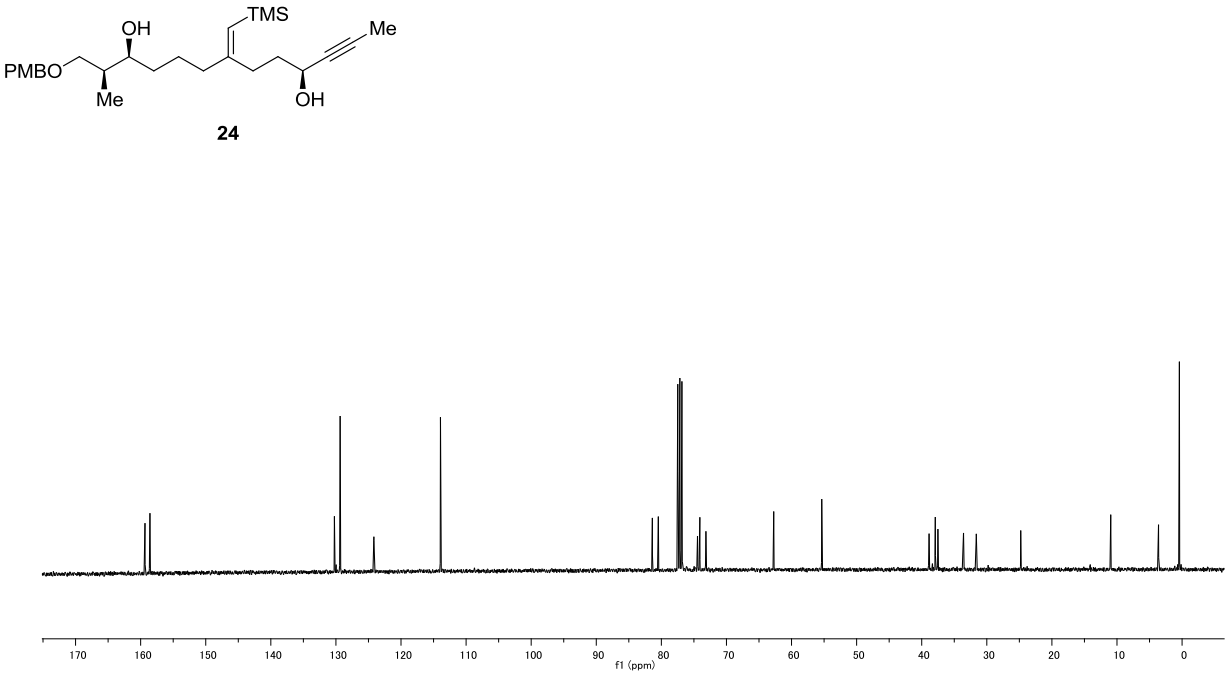
**23a**


201.86
159.36
156.84
130.19
129.37
125.27
113.94
77.48
77.16
76.84
74.55
74.19
73.21
55.38
43.49
37.95
33.56
28.25
24.79
10.97
0.41
TMS
OH
PMBO
Me
O
f1 (ppm)

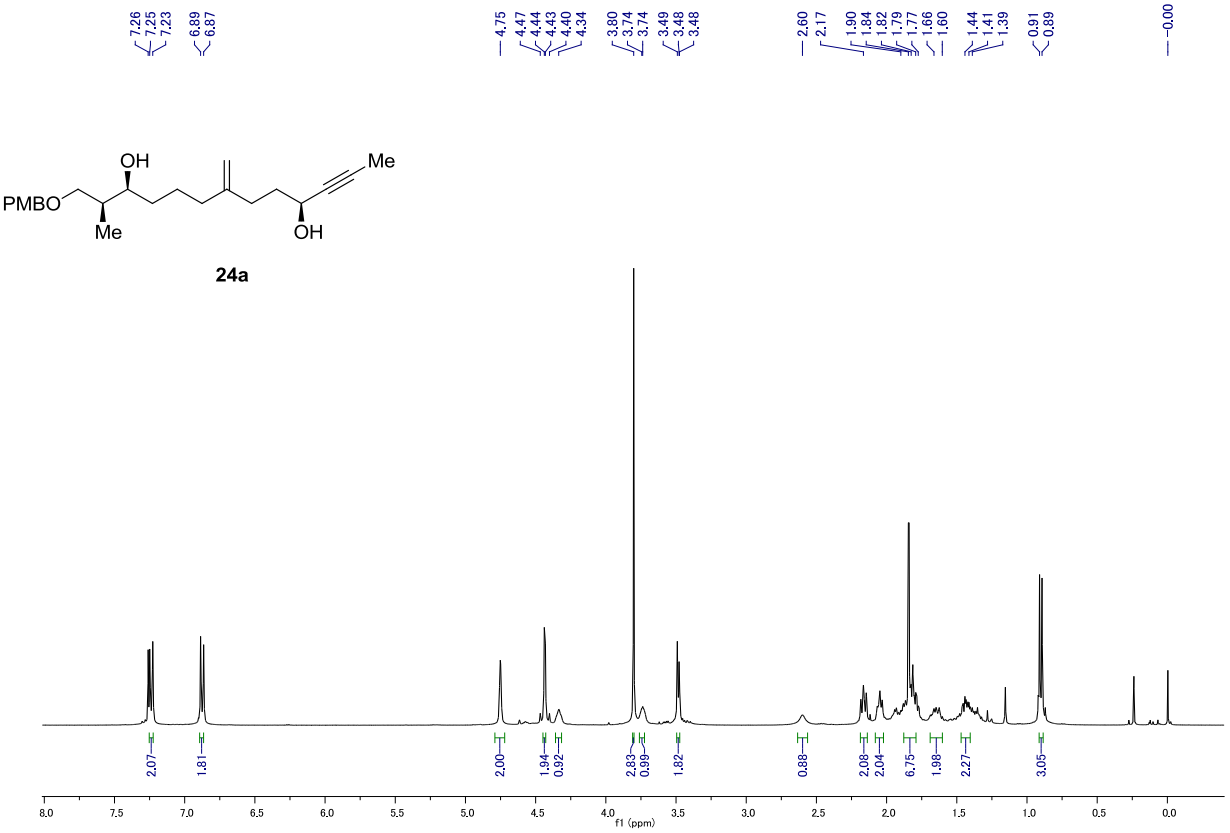
**23a**



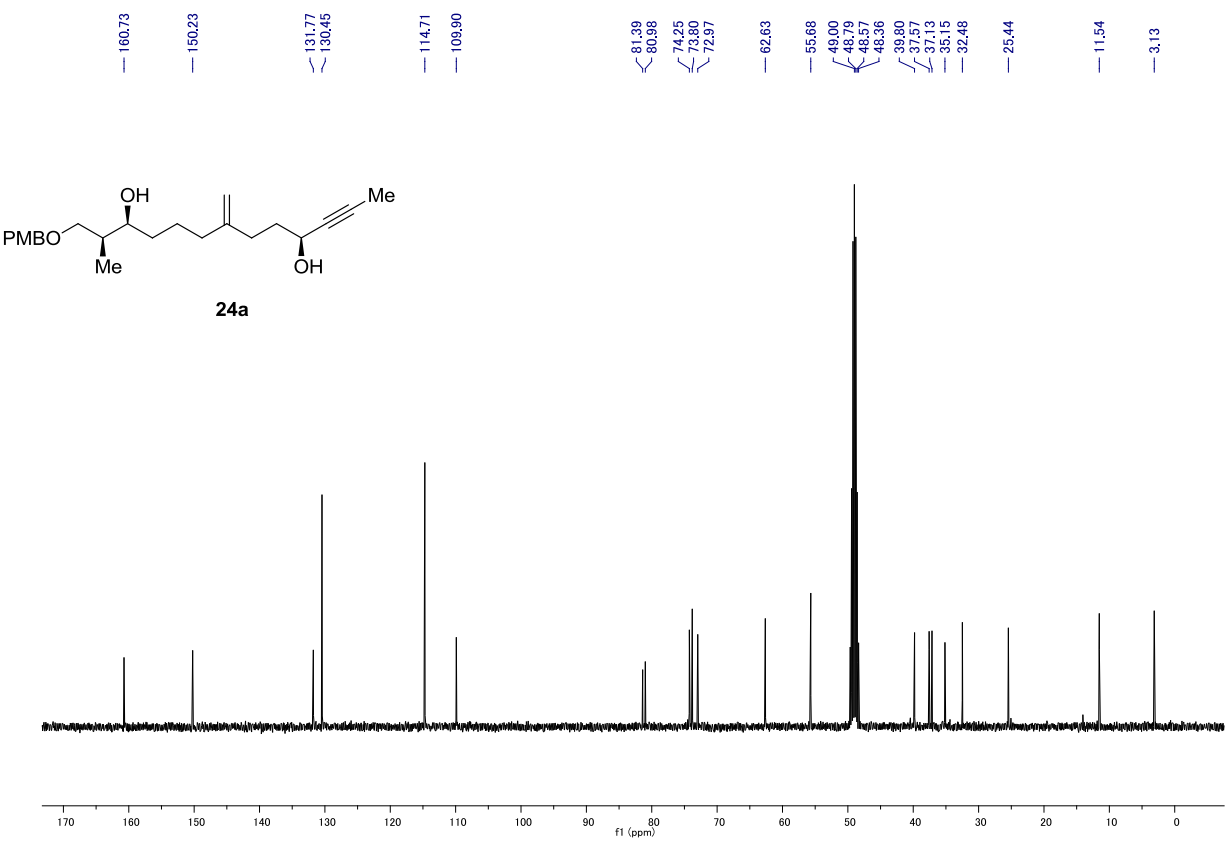

**24**



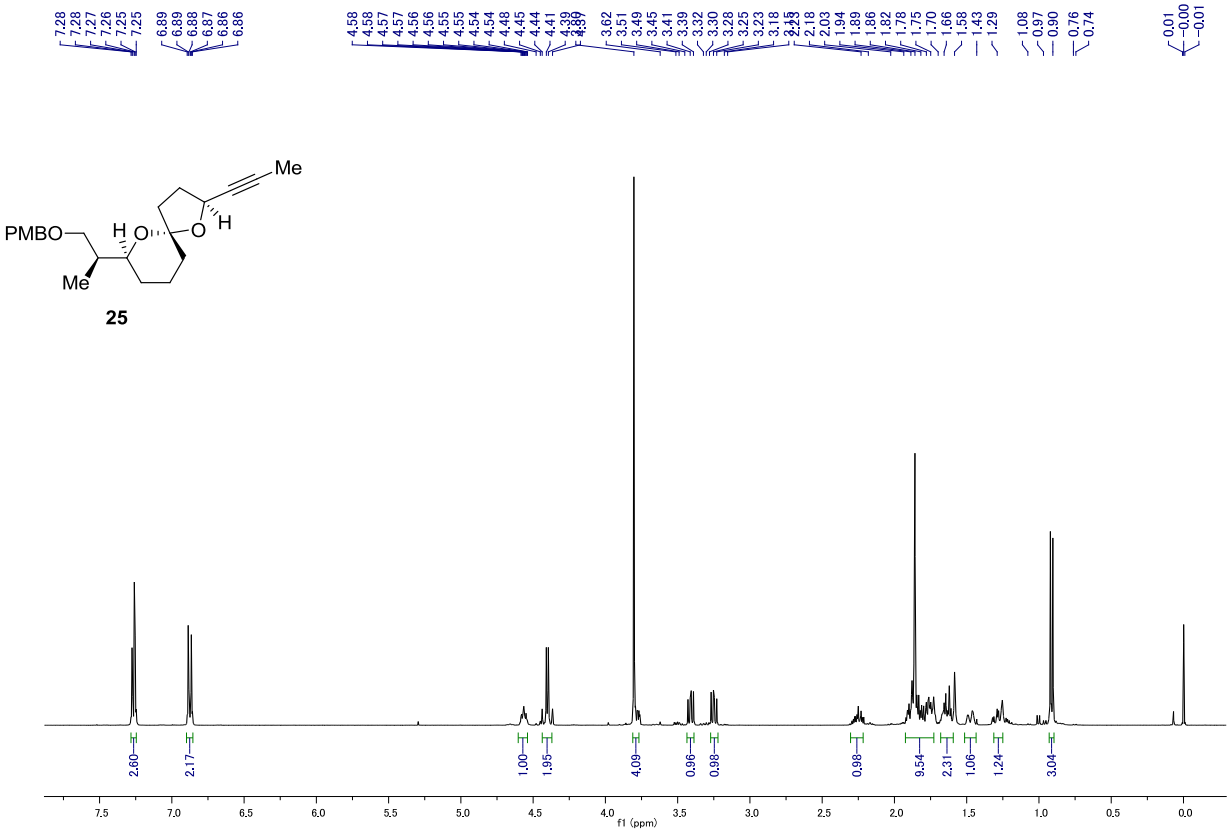

**24**

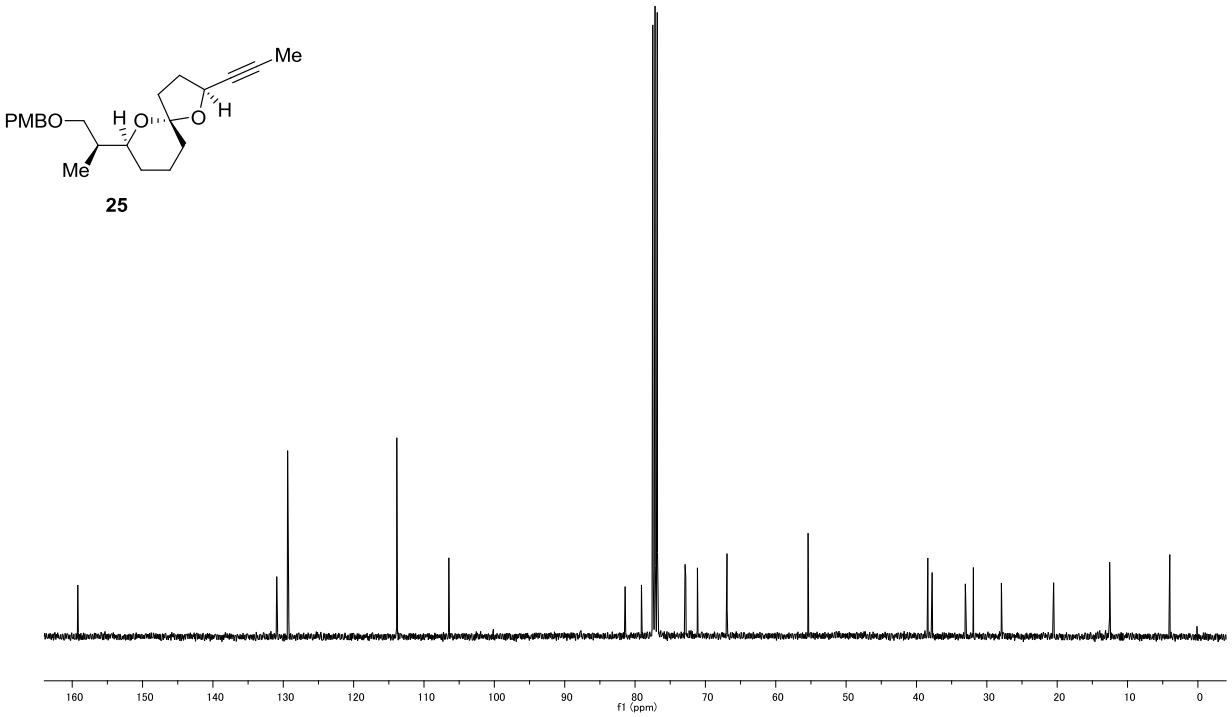

7.26
7.25
7.23
6.89
6.87
4.75
4.47
4.44
4.43
4.40
4.34
3.80
3.74
3.74
3.49
3.48
3.48
2.60
2.17
1.90
1.84
1.82
1.79
1.77
1.66
1.60
1.44
1.41
1.39
0.91
0.89
0.00
OH
Me
PMBO
Me
OH
2.07
1.81
2.00
1.94
0.92
2.83
0.99
1.82
0.88
2.08
2.04
6.75
1.98
2.27
3.05
f1 (ppm)

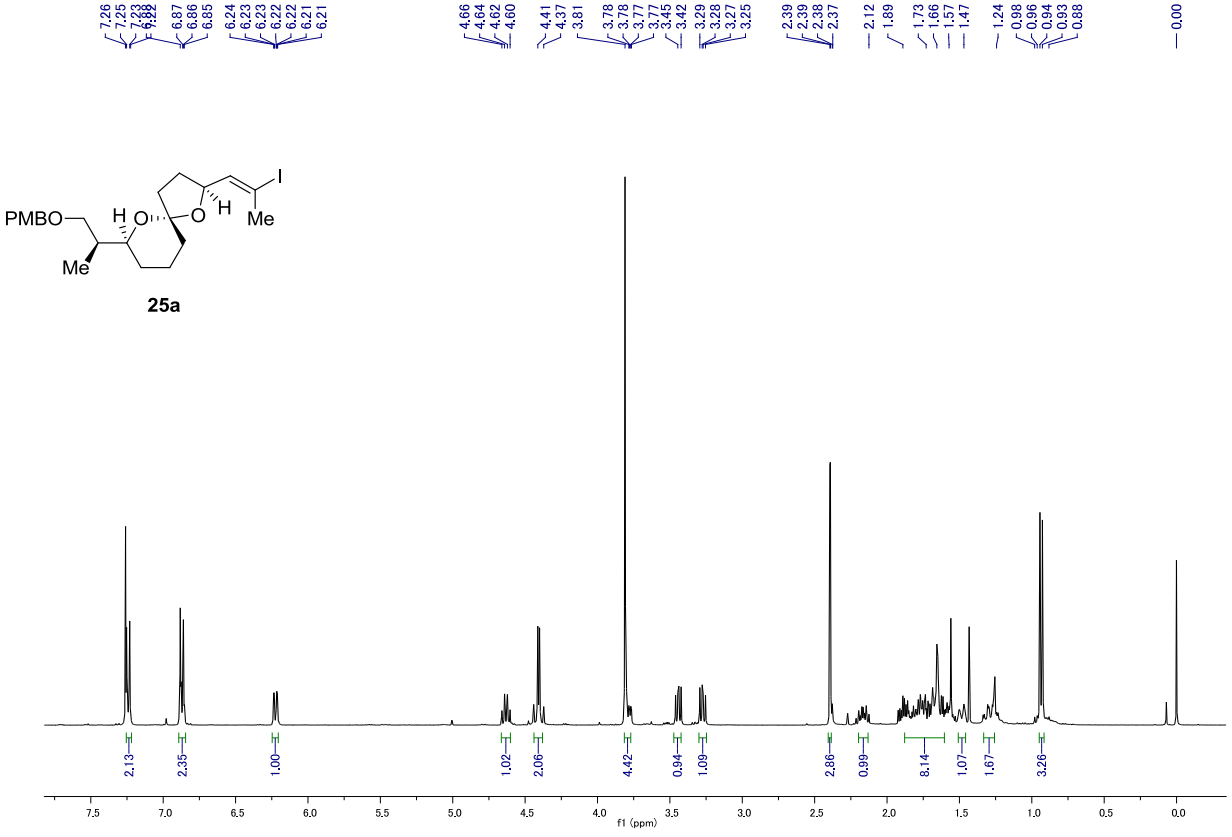
**24a**


160.73
150.23
131.77
130.45
114.71
109.90
81.39
80.98
74.25
73.80
72.97
62.63
55.68
49.00
48.79
48.57
48.36
39.80
37.57
37.13
35.15
32.48
25.44
11.54
3.13
OH
Me
PMBO
Me
OH
f1 (ppm)

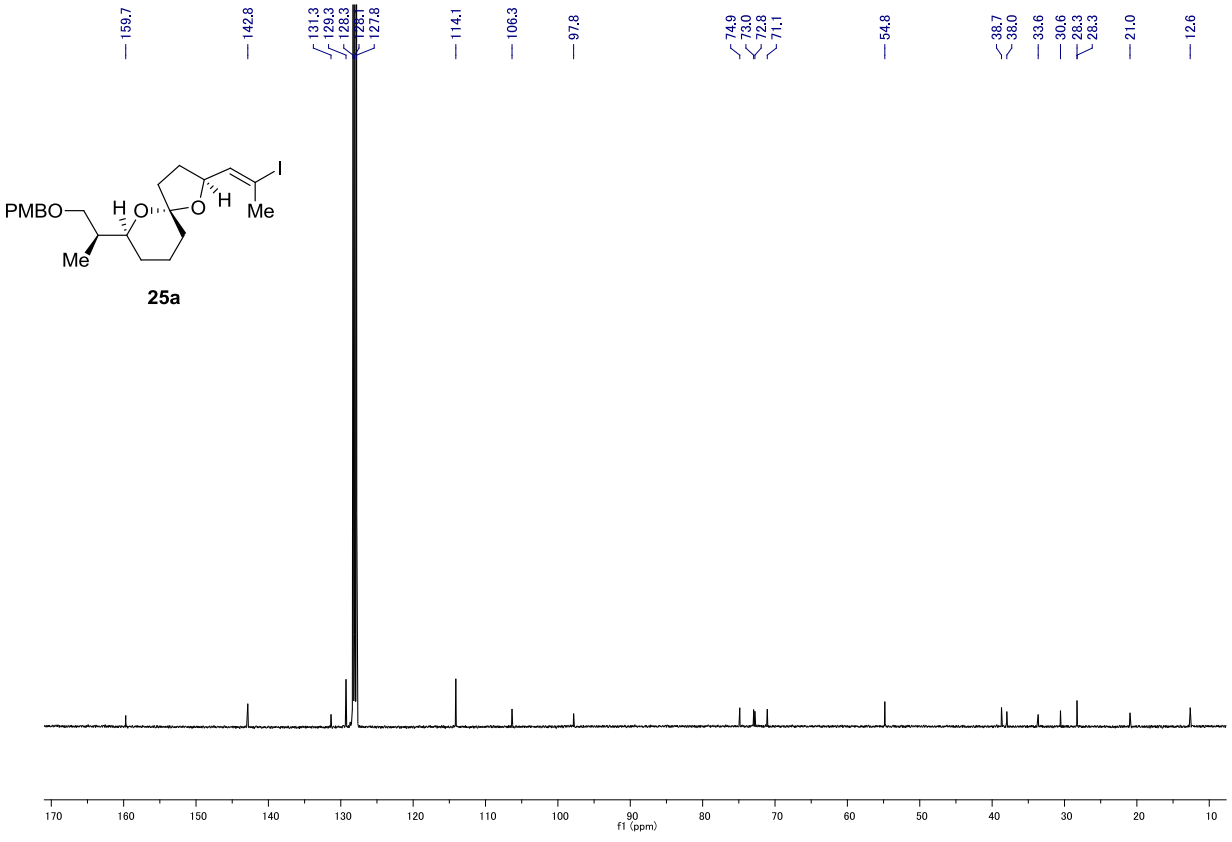
**24a**


PMBO
Me
H
O
O
H
Me
25

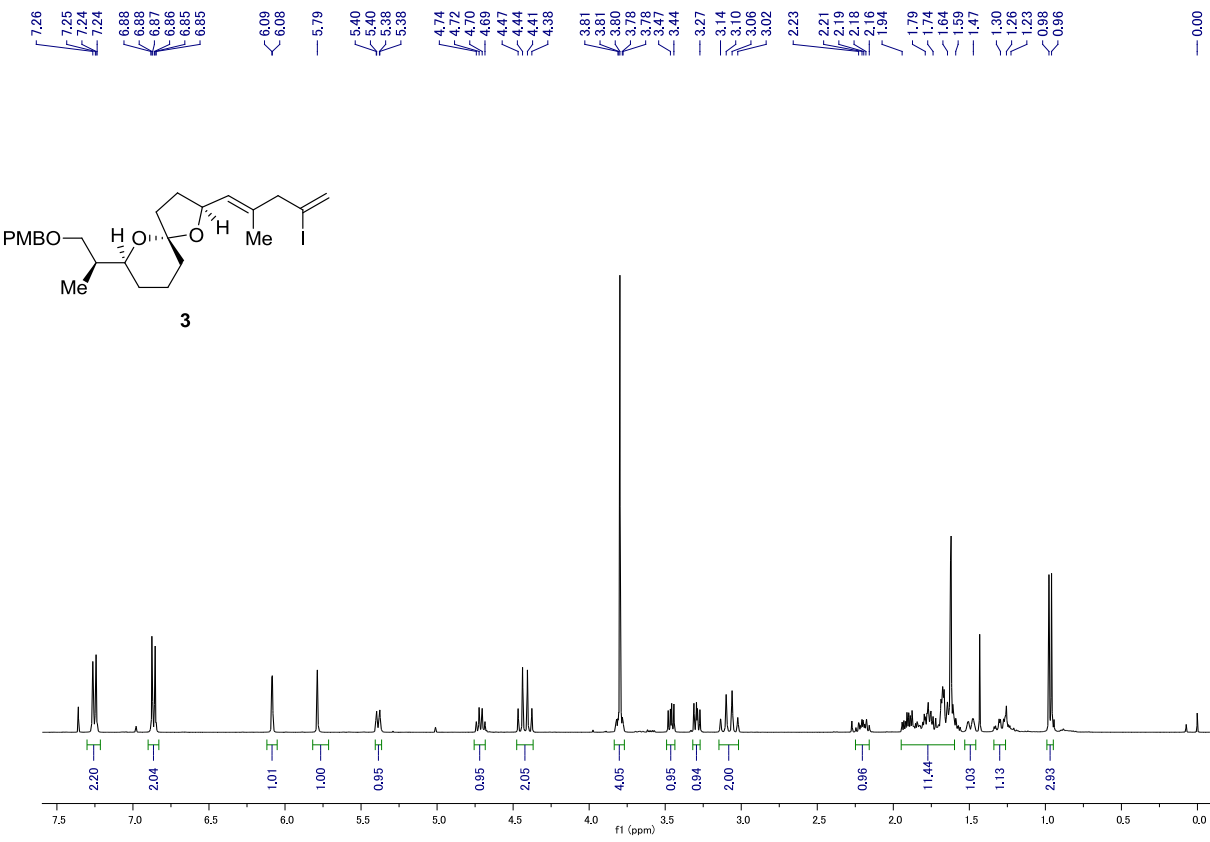

PMBO
Me
H
O
O
H
Me
25

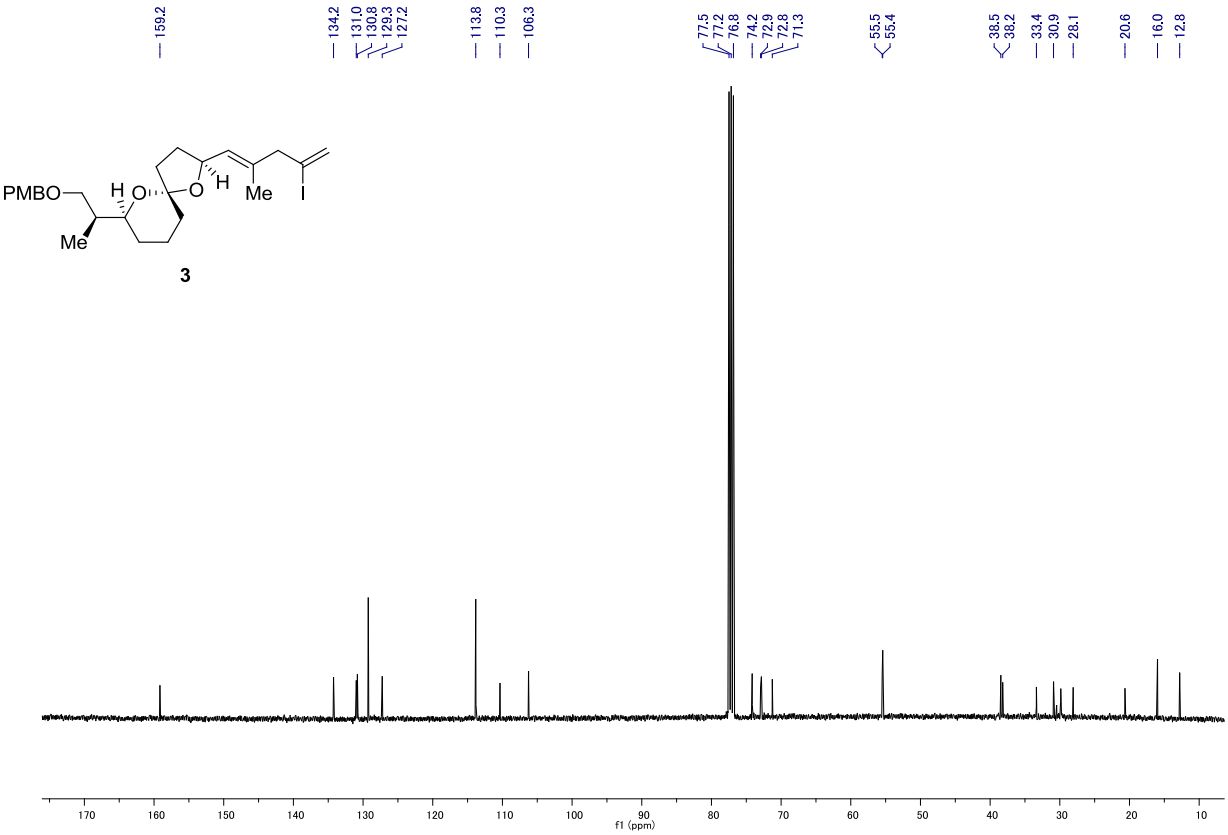


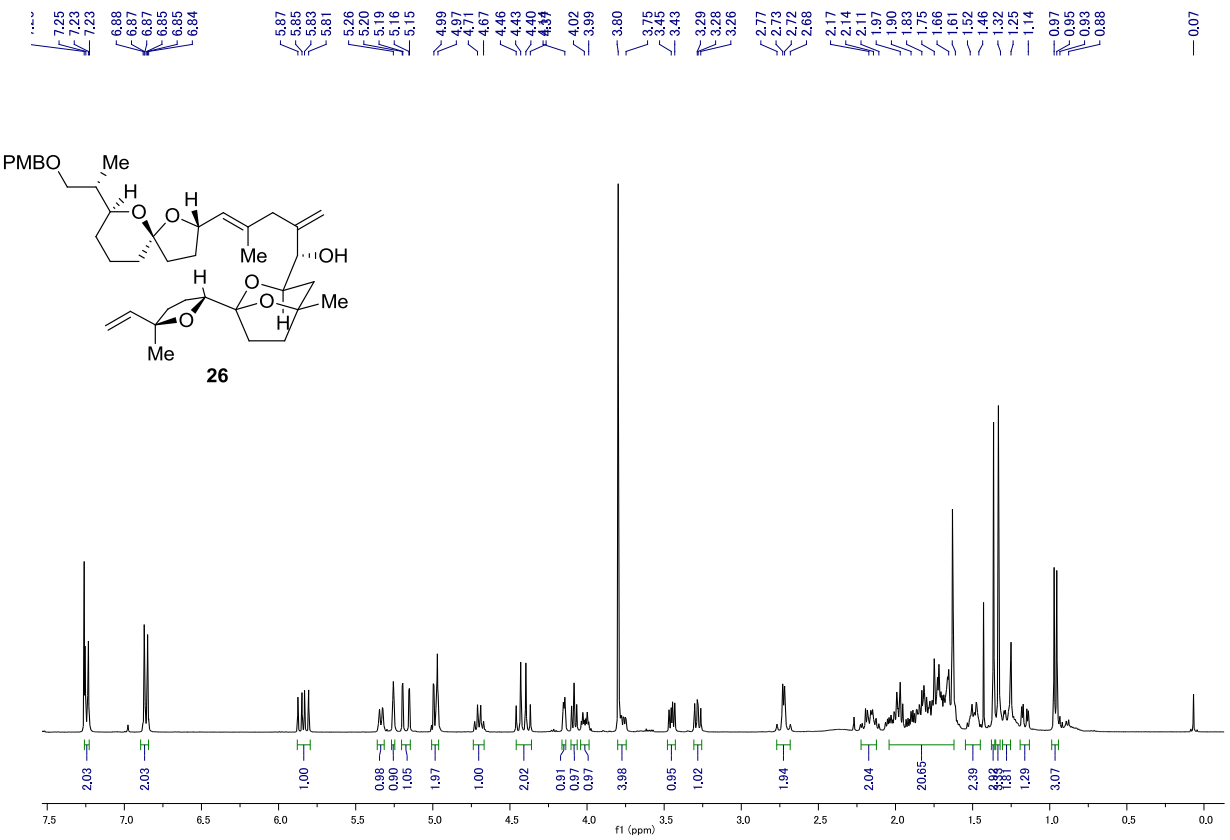

**25a**

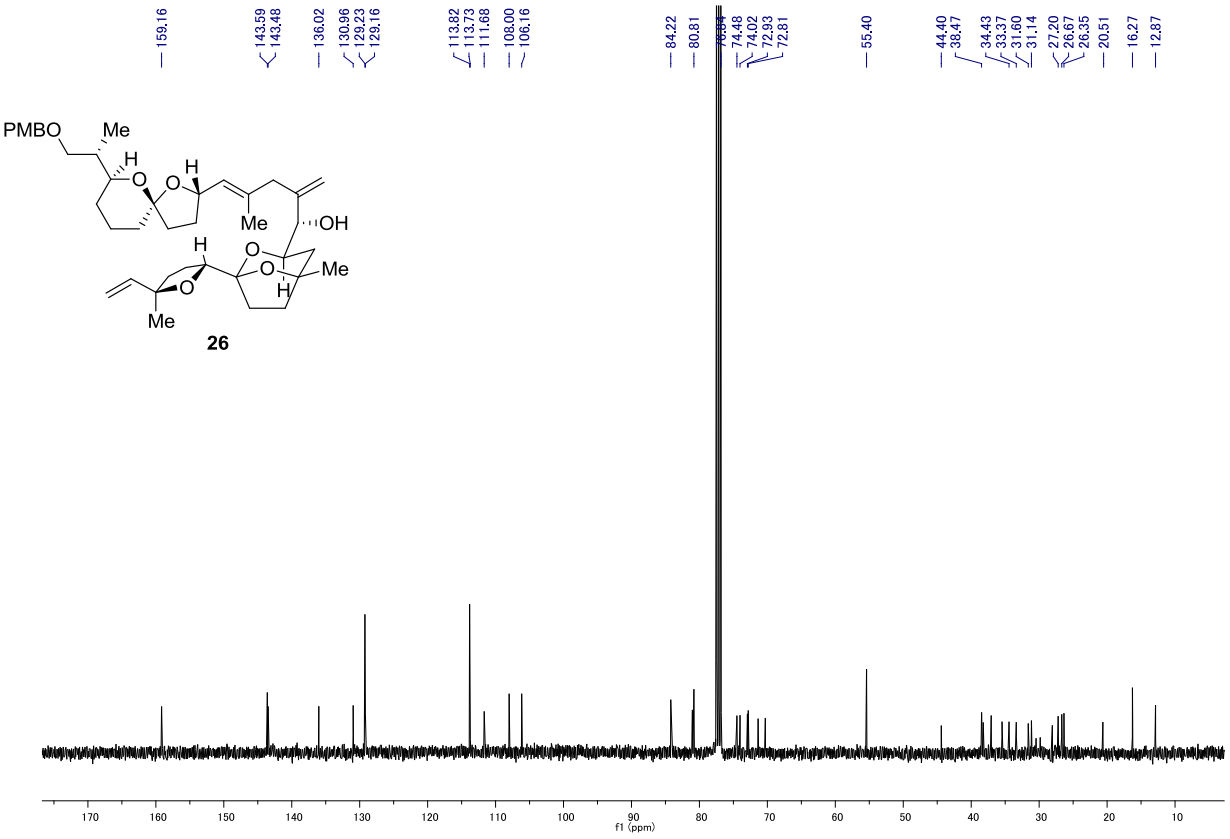



**25a**

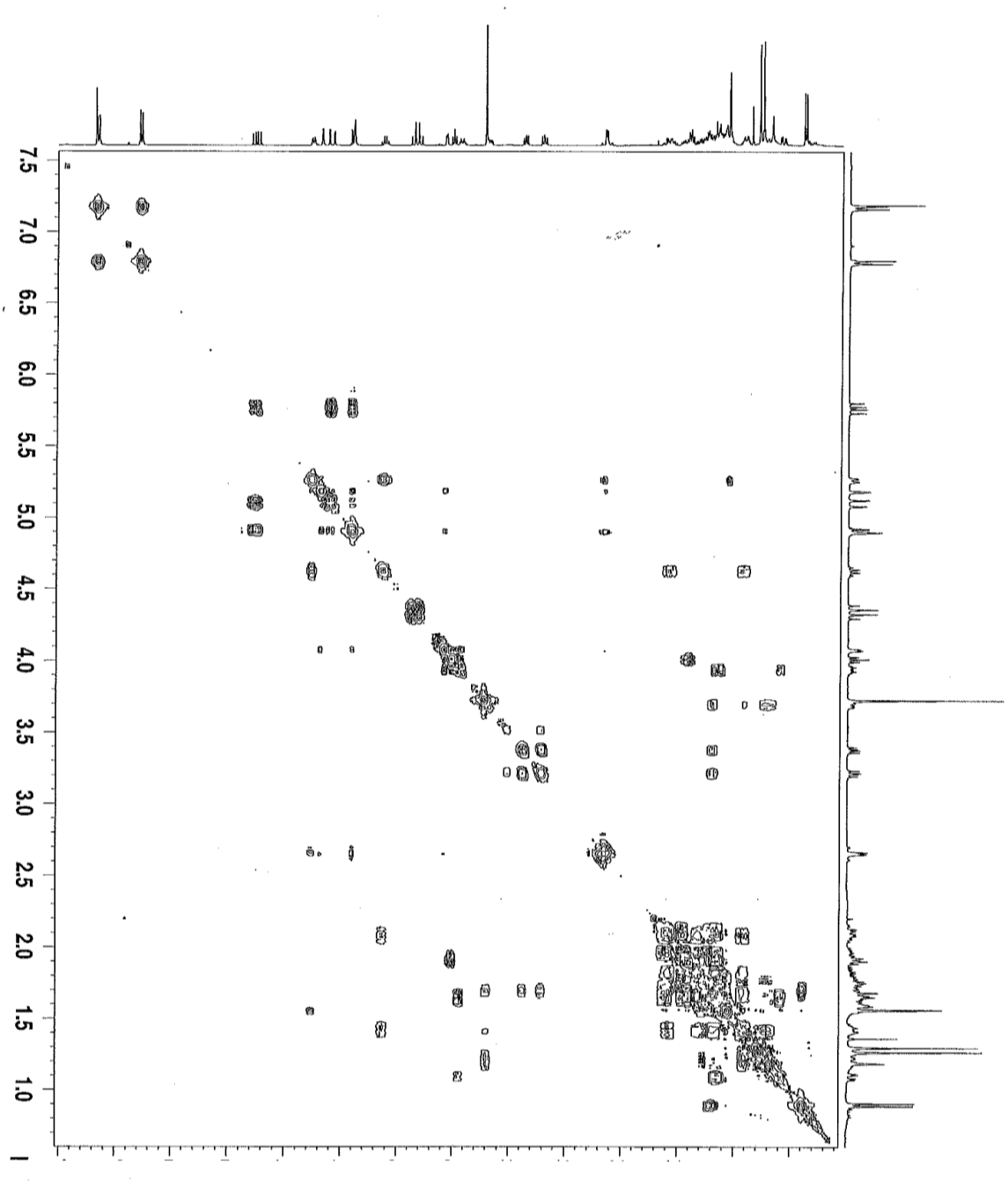

7.26
7.25
7.24
7.24
6.88
6.88
6.87
6.86
6.85
6.85
6.09
6.08
5.79
5.40
5.40
5.38
5.38
4.74
4.72
4.70
4.69
4.47
4.44
4.41
4.38
3.81
3.81
3.80
3.78
3.78
3.47
3.44
3.27
3.14
3.10
3.06
3.02
2.23
2.21
2.19
2.18
2.16
1.94
1.79
1.74
1.64
1.59
1.47
1.30
1.26
1.23
0.98
0.96
0.00
PMBO
H
O
O
H
Me
I
Me
3
2.20
2.04
1.01
1.00
0.95
0.95
2.05
4.05
0.95
0.94
2.00
0.96
11.44
1.03
1.13
2.93
f1 (ppm)

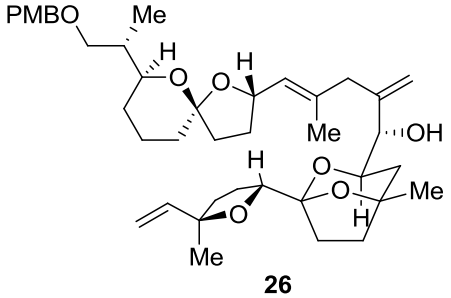

159.2
134.2
131.0
130.8
129.3
127.2
113.8
110.3
106.3
77.5
77.2
76.8
74.2
72.9
72.8
71.3
55.5
55.4
38.5
38.2
33.4
30.9
28.1
20.6
16.0
12.8
PMBO
H
O
O
H
Me
I
Me
3
f1 (ppm)


PMBO
Me
H
O
O
H
Me
OH
H
O
O
Me
H
O
Me
26
7.25
7.23
7.23
6.88
6.87
6.87
6.85
6.85
6.84
5.87
5.85
5.83
5.81
5.26
5.20
5.19
5.16
5.15
4.99
4.97
4.71
4.67
4.46
4.43
4.40
4.02
3.99
3.80
3.75
3.45
3.43
3.29
3.28
3.26
2.77
2.73
2.72
2.68
2.17
2.14
2.11
1.97
1.90
1.83
1.75
1.66
1.61
1.52
1.46
1.32
1.25
1.14
0.97
0.95
0.93
0.88
0.07
2.03
2.03
1.00
0.98
0.90
1.05
1.97
1.00
2.02
0.91
0.97
0.97
3.98
0.95
1.02
1.94
2.04
20.65
2.39
1.29
3.07
f1 (ppm)

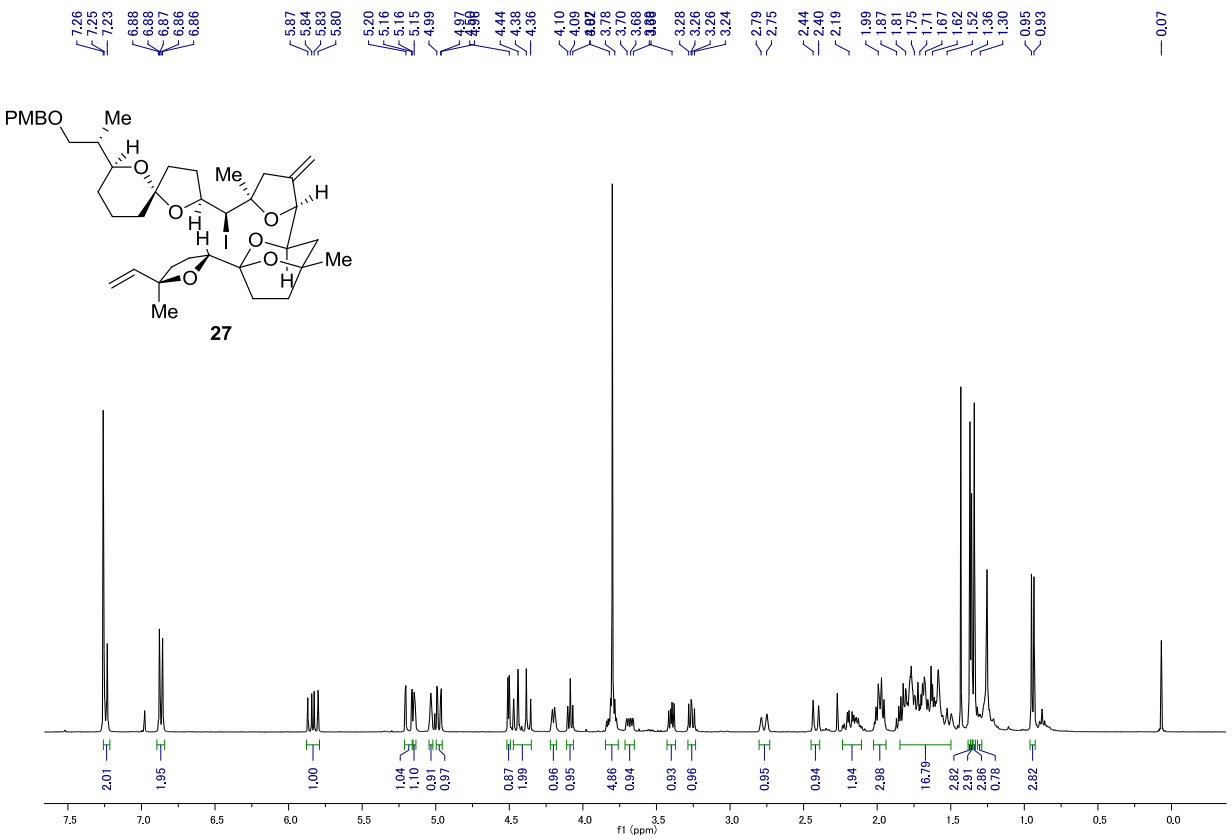

PMBO
Me
H
O
O
H
Me
OH
H
O
O
Me
H
O
Me
26
159.16
143.59
143.48
136.02
130.96
129.23
129.16
113.82
113.73
111.68
108.00
106.16
84.22
80.81
74.48
74.02
72.93
72.81
55.40
44.40
38.47
34.43
33.37
31.60
31.14
27.20
26.67
26.35
20.51
16.27
12.87
f1 (ppm)

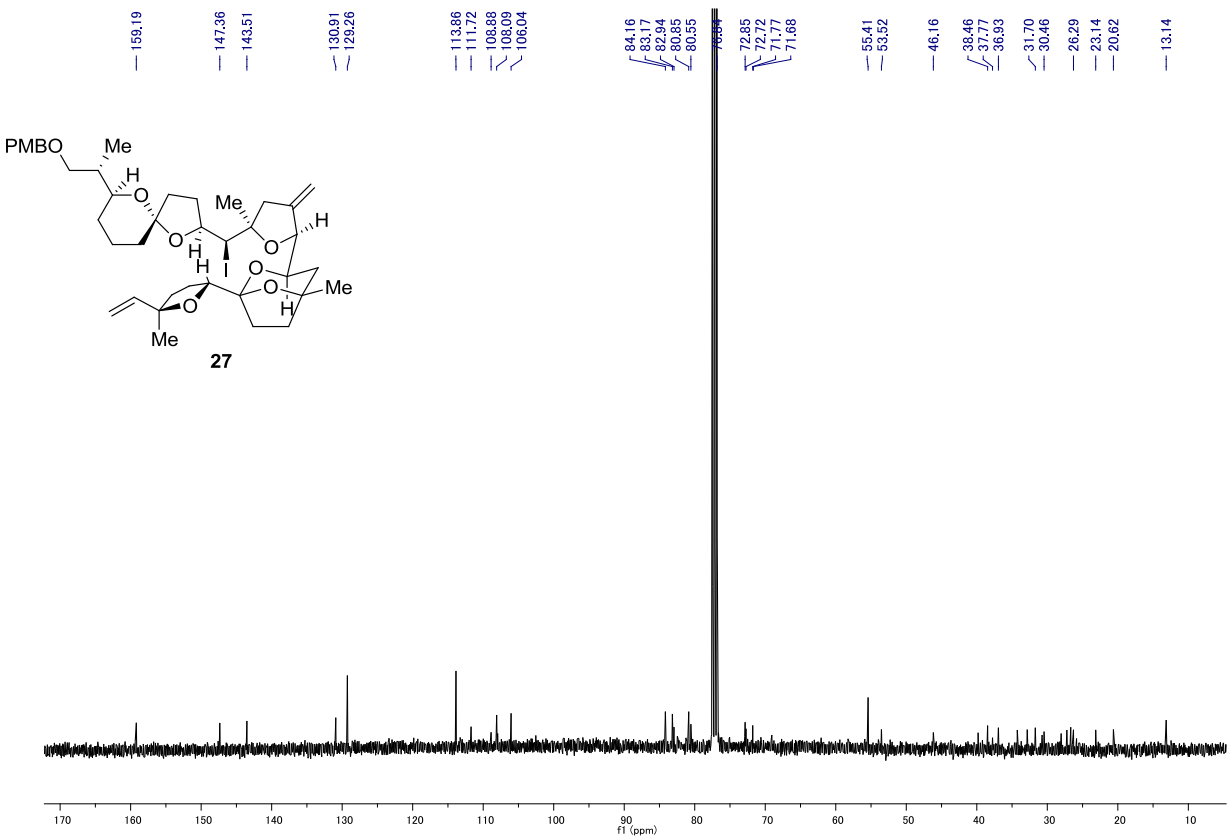
**H-H COSY** of compound **26**



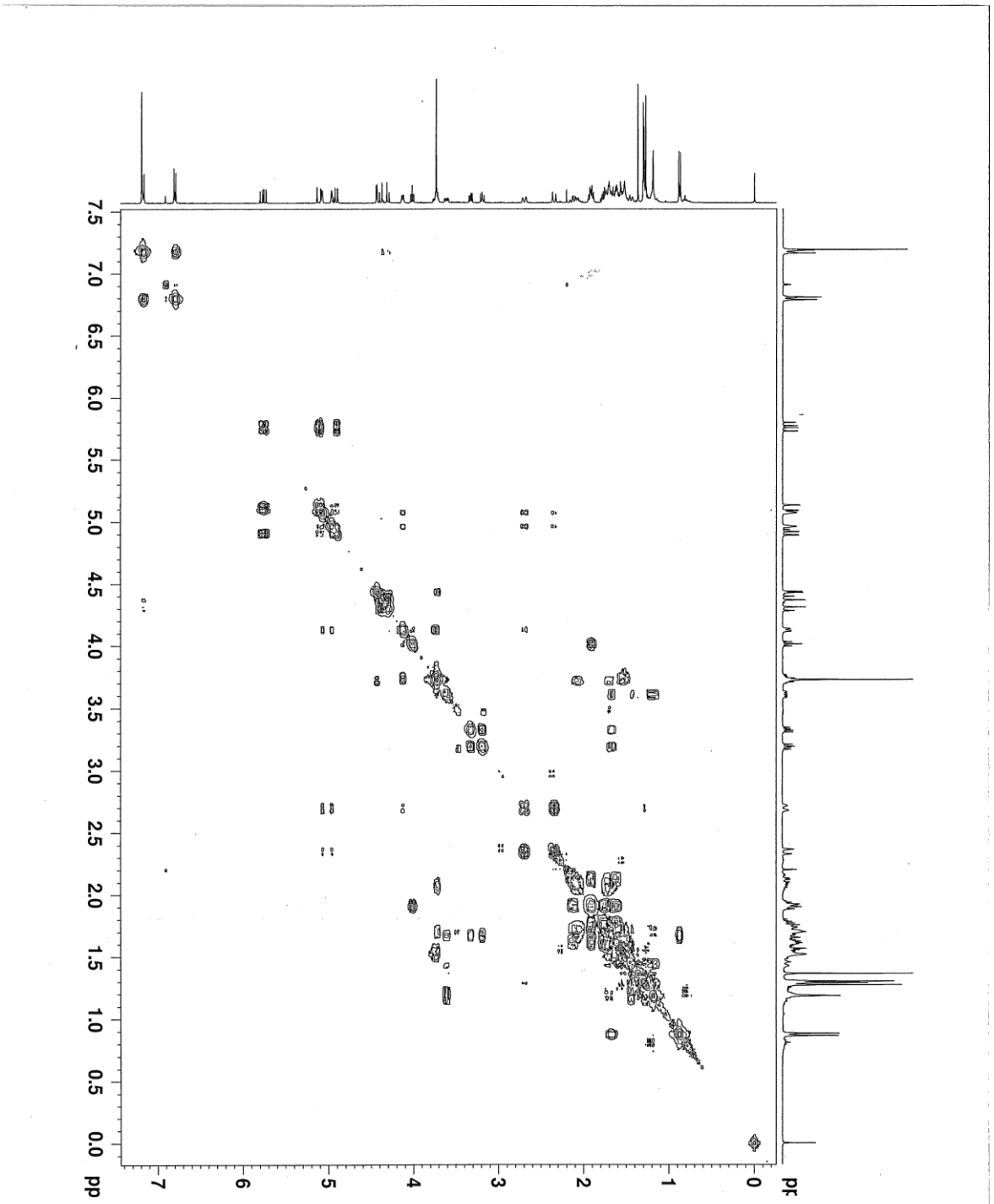



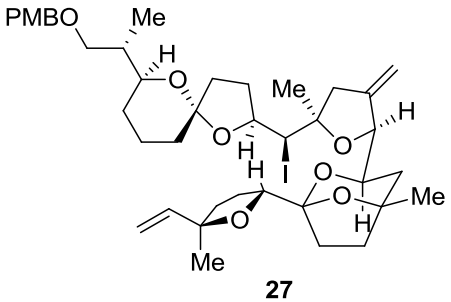

**26**


PMBO
Me
H
O
Me
H
O
H
I
O
O
Me
H
O
Me
Me
27


PMBO
Me
H
O
Me
H
O
H
I
O
O
Me
H
O
Me
Me
27

**H-H COSY** of compound **27**




**27**

Selected **NOEOSY spectra** of compound **27**