Supporting Information

Construction of the septahydroxylated ABC-ring system of dihydro-β-agarofurans: application of 6-*exo*-*dig* radical cyclization

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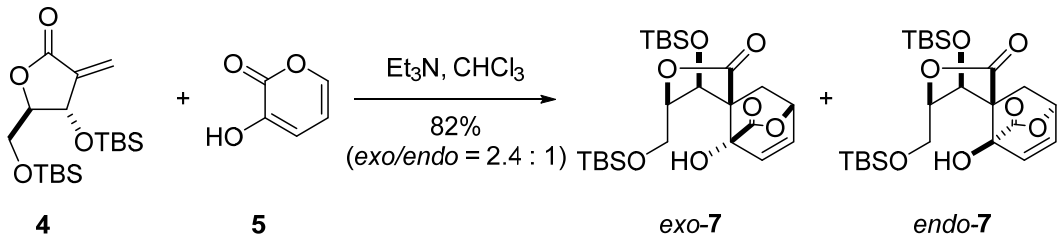
General methods.

All reactions sensitive to air or moisture were carried out in dry solvents under argon atmosphere, unless otherwise noted. THF, CH_2Cl_2, toluene, DMF and Et_2O were purified by Glass Contour solvent dispensing system (Nikko Hansen & Co., Ltd., Osaka, Japan). All other reagents were used as supplied unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using E. Merck Silica gel 60 F254 pre-coated plates (0.25 mm). Flash chromatography was performed using 40-50 μm Silica Gel 60N (Kanto Chemical Co., Inc.). Melting points were measured on Yanaco MP-J3 micro melting point apparatus, and are uncorrected. Optical rotations were measured on a JASCO P-2200 Digital Polarimeter at room temperature using the sodium D line. Infrared (IR) spectra were recorded as a thin film on a KBr disk using JASCO FT/IR-4100 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECX-500, JNM-ECA-500 or JNM-ECS-400 spectrometer at room temperature. Chemical shifts were reported in ppm on the δ scale relative to $CHCl_3$ (δ = 7.26 for ^{1}H NMR), C_6D_5H (δ = 7.16 for ^{1}H NMR) and $CDCl_3$ (δ = 77.0 for ^{13}C NMR) as internal references. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broaden peak. The numbering of compounds corresponds to that of dihydro-β-agarofurans. High resolution mass spectra were measured on JEOL JMS-T100LP (ESI-TOF).



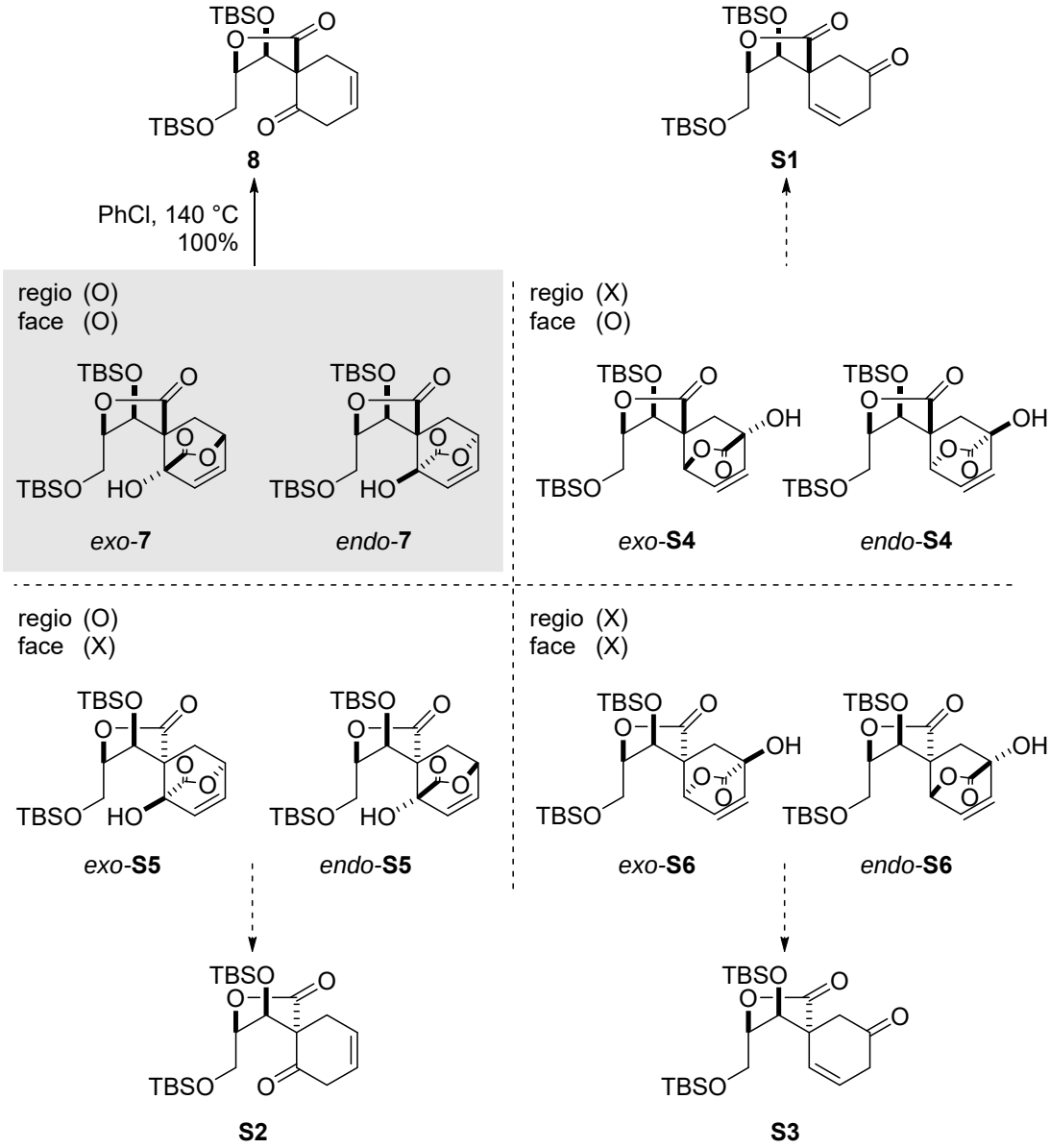
4 **5** *exo*-**7** *endo*-**7**

Diels-Alder adducts 7. Et_3N (1.80 mL, 12.9 mmol) was added to a solution of dienophile **4** (4.82 g, 12.9 mmol) and diene **5** (1.44 g, 12.9 mmol) in $CHCl_3$ (26 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated. The residue was purified by flash column chromatography on silica gel (60 g, hexane/EtOAc 8/1) to afford a 2.4 : 1 mixture of *exo*-**7** and *endo*-**7** (5.13 g, 10.6 mmol) in 82% yield. For characterizations of *exo*-**7** and *endo*-**7**, a small amount of the mixture was purified by flash column chromatography on silica gel. The structure of *exo*-**7** and *endo*-**7** were assigned as shown in page S4. *exo*-**7**: white solid; m.p. 121-125 °C; $[\alpha]_D^{27}$ 20 (*c* 1.2, $CHCl_3$); IR (film) ν 2954, 2930, 2886, 2858, 1780, 1472, 1464, 1362, 1257, 1230, 1190, 1134, 1107, 1070, 1052, 941 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.085 (3H, s, C*H*$_3$ of TBS), 0.089 (6H, s, C*H*$_3$ of TBS x2), 0.15 (3H, s, C*H*$_3$ of TBS), 0.86 (9H, s, *t*-Bu of TBS), 0.91 (9H, s, *t*-Bu of TBS), 2.35 (1H, dd, *J* = 13.7, 3.6 Hz, H9a), 2.68 (1H, dd, *J* = 13.7, 1.8 Hz, H9b), 3.84 (1H, dd, *J* = 11.9, 4.1 Hz, H3a), 3.87 (1H, s, O*H*), 3.98 (1H, dd, *J* = 11.9, 4.1 Hz, H3b), 4.07 (1H, ddd, *J* = 5.5,

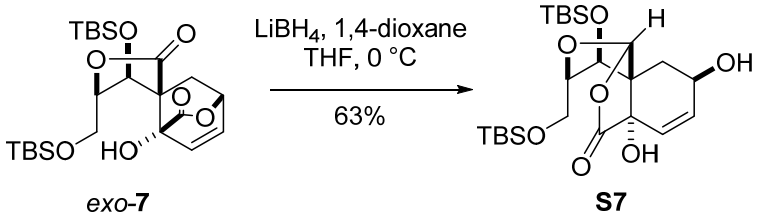
4.1, 4.1 Hz, H2), 4.73 (1H, d, *J* = 5.5 Hz, H1), 5.33 (1H, dddd, *J* = 5.0, 3.6, 1.8, 1.8 Hz, H8), 6.33 (1H, dd, *J* = 7.8, 1.8 Hz, H6), 6.50 (1H, dd, *J* = 7.8, 5.0 Hz, H7); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.42, -5.35, -4.4, -4.1, 17.9, 18.3, 25.75, 25.80, 32.5, 53.0, 60.8, 69.0, 72.9, 76.4, 85.2, 132.5, 135.3, 173.1, 176.2; HRMS (ESI) calcd for $C_{23}H_{40}O_7Si_2Na$ $[M+Na]^+$ 507.2205, found 507.2180. *endo*-**7**: white solid; m.p. 124-130 °C; $[\alpha]_D^{27}$ 15 (*c* 1.1, $CHCl_3$); IR (film) ν 3462, 2953, 2931, 2888, 2858, 1760, 1469, 1391, 1362, 1255, 1192, 1133, 1071, 1006, 977, 940 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (3H, s, C*H*$_3$ of TBS), 0.10 (3H, s, C*H*$_3$ of TBS), 0.12 (3H, s, C*H*$_3$ of TBS), 0.13 (3H, s, C*H*$_3$ of TBS), 0.90 (9H, s, *t*-Bu of TBS), 0.91 (9H, s, *t*-Bu of TBS), 1.79 (1H, d, *J* = 13.3 Hz, H9a), 3.16 (1H, dd, *J* = 13.3, 4.6 Hz, H9b), 3.87 (1H, s, O*H*), 3.89 (1H, dd, *J* = 12.4, 3.7 Hz, H3a), 3.98 (1H, dd, *J* = 12.4, 2.5 Hz, H3b), 4.04 (1H, ddd, *J* = 6.0, 3.7, 2.5 Hz, H2), 4.72 (1H, d, *J* = 6.0 Hz, H1), 5.33 (1H, m, H8), 6.53 (1H, dd, *J* = 7.8, 5.3 Hz, H7), 6.59 (1H, dd, *J* = 7.8, 2.0 Hz, H6); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.5, -5.4, -5.2, -4.1, 18.1, 18.3, 25.8, 25.9, 32.5, 51.9, 60.8, 67.5, 74.0, 76.1, 84.5, 130.0, 136.9, 172.9, 174.5; HRMS (ESI) calcd for $C_{23}H_{40}O_7Si_2Na$ $[M+Na]^+$ 507.2205, found 507.2193.

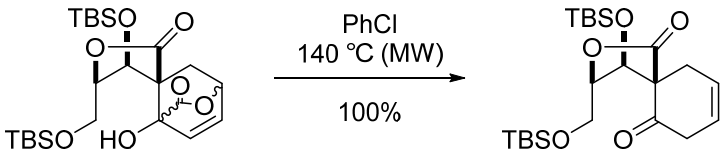
Structural assignment of Diels-Alder adducts 7.

Treatment of a 2.4 : 1 mixture of *exo/endo* **7** at 140 °C gave compound **8** as a single product through the thermal CO_2 loss. This conversion confirmed the formation of **7**, because other possible adducts *exo/endo*-**S4**, **S5** and **S6** should afford the different compounds **S1**, **S2** and **S3**, respectively.



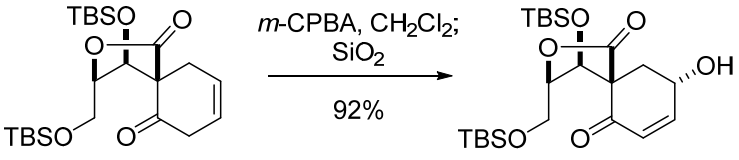
The structure of *exo*-**7** was assigned by the following derivatization into tricycle **S7**.





7 **8**

Ketone 8. A 20 mL Pyrex vessel was charged with compound **7** (a 2.4 : 1 mixture, 5.13 g, 10.6 mmol) and chlorobenzene (10 mL). The solution was degassed by freeze-thaw procedure (x3), and then was heated at 140 °C with microwave at normal absorption. The reaction mixture was stirred at 140 °C for 1 h, cooled to room temperature and concentrated. The residue was purified by flash column chromatography on silica gel (100 g, hexane/EtOAc 18/1) to afford ketone **8** (4.67 g, 10.6 mmol) in 100% yield: white solid; m.p. 62-68 °C; $[\alpha]_D^{26}$ 35 (*c* 1.1, $CHCl_3$); IR (film) ν 2954, 2931, 2888, 2858, 1781, 1720, 1470, 1391, 1256, 1165, 1144, 1118, 1096, 1066, 1008, 986, 941 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.03 (3H, s, C*H*$_3$ of TBS), 0.05 (3H, s, C*H*$_3$ of TBS), 0.07 (3H, s, C*H*$_3$ of TBS), 0.16 (3H, s, C*H*$_3$ of TBS), 0.87 (9H, s, *t*-Bu of TBS), 0.89 (9H, s, *t*-Bu of TBS), 2.62 (1H, brd, *J* = 19.7 Hz, H9a), 2.94 (1H, brd, *J* = 18.3 Hz, H6a), 2.97 (1H, brd, *J* = 19.7 Hz, H9b), 3.38 (1H, brd, *J* = 18.3 Hz, H6b), 3.77 (1H, dd, *J* = 11.9, 4.1 Hz, H3a), 3.84 (1H, dd, *J* = 11.9, 3.7 Hz, H3b), 4.14 (1H, ddd, *J* = 6.4, 4.1, 3.7 Hz, H2), 5.10 (1H, d, *J* = 6.4 Hz, H1), 5.80 (1H, d, *J* = 11.0 Hz, H6 or H7), 5.83 (1H, d, *J* = 11.0 Hz, H6 or H7); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.50, -5.47, -5.0, -4.8, 17.9, 18.2, 25.6, 25.8, 28.4, 39.3, 60.2, 60.6, 68.2, 83.8, 123.3, 124.0, 172.5, 203.3; HRMS (ESI) calcd for $C_{22}H_{40}O_5Si_2Na$ 463.2306 $[M+Na]^+$, found 463.2285.



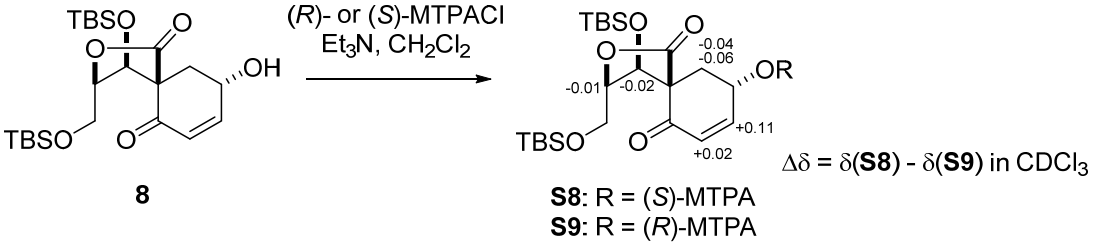
8 **9**

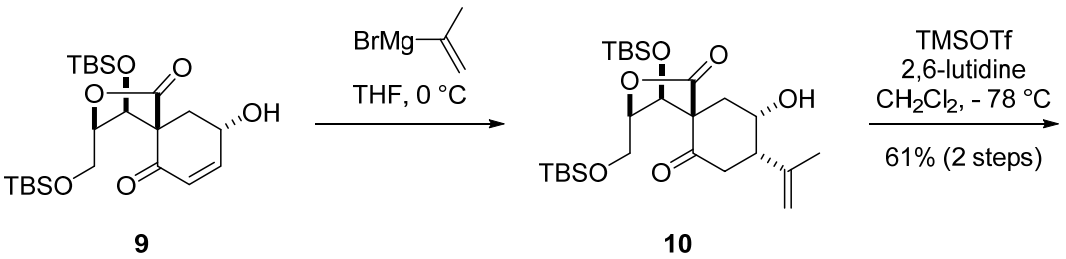
Enone 9. *m*-CPBA (77% purity, 3.56 g, 15.9 mmol) was added to a solution of ketone **8** (4.67 g, 10.6 mmol) in CH_2Cl_2 (106 mL) at room temperature. The reaction mixture was stirred at room temperature for 18 h, and then *m*-CPBA (77% purity, 1.56 g, 6.96 mmol) was added. The reaction mixture was stirred at room temperature for 4 h, and then saturated aqueous $NaHCO_3$ (40 mL) and saturated aqueous $Na_2S_2O_3$ (40 mL) were successively added. The resultant solution was extracted with CH_2Cl_2 (50 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was treated with silica gel (80 g) for 12 h at room temperature and eluted with EtOAc (1 L). Concentration of the solution afforded enone **9** (4.45 g, 9.74 mmol) in 92% yield. The C8-configuration was determined by the modified Mosher method as described page S6: white solid; m.p. 103-108 °C; $[\alpha]_D^{28}$ 0.41 (*c* 1.0, $CHCl_3$); IR (film) ν 3484, 2954, 2931, 2888, 2859, 1774, 1684,

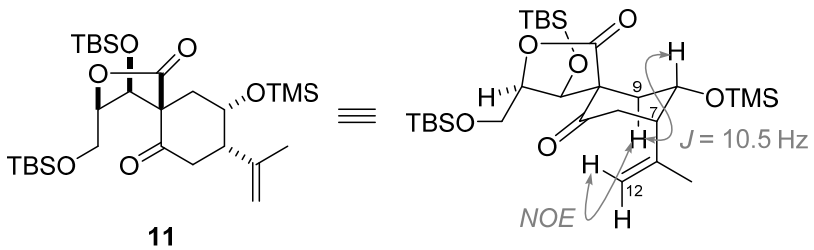
1470, 1408, 1390, 1363, 1325, 1257, 1235, 1142, 1121, 1069, 1034, 1011, 949 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.04 (3H, s, C*H*$_3$ of TBS), 0.06 (3H, s, C*H*$_3$ of TBS), 0.08 (3H, s, C*H*$_3$ of TBS), 0.12 (3H, s, C*H*$_3$ of TBS), 0.86 (9H, s, *t*-Bu of TBS), 0.90 (9H, s, *t*-Bu of TBS), 2.18 (1H, dd, *J* = 13.7, 11.0 Hz, H9a), 2.19 (1H, d, *J* = 5.9 Hz, O*H*), 2.41 (1H, ddd, *J* = 13.7, 5.3, 1.8 Hz, H9b), 3.80 (1H, dd, *J* = 12.4, 3.7 Hz, H3a), 4.01 (1H, dd, *J* = 12.4, 1.8 Hz H3b), 4.17 (1H, ddd, *J* = 7.8, 3.7, 1.8 Hz, H2), 4.96 (1H, m, H8), 5.37 (1H, d, *J* = 7.8 Hz, H1), 6.13 (1H, dd, *J* = 10.5, 2.1 Hz, H6), 7.07 (1H, ddd, *J* = 10.5, 2.1, 1.8 Hz, H7); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.5, -5.4, -5.3, -4.5, 17.8, 18.2, 25.6, 25.7, 33.1, 58.4, 60.1, 64.5, 68.6, 83.3, 128.2, 154.8, 171.7, 192.0; HRMS (ESI) calcd for $C_{22}H_{40}O_6Si_2Na$ $[M+Na]^+$ 479.2256, found 479.2234.

Determination of the C8-configuration.

The C8-configuration of **8** was determined to be *S* by the modified Mosher method.[S1] (*S*)- and (*R*)-MTPA esters **S8** and **S9** were synthesized by treatment of **8** with (*R*)- and (*S*)-MTPACl, respectively.



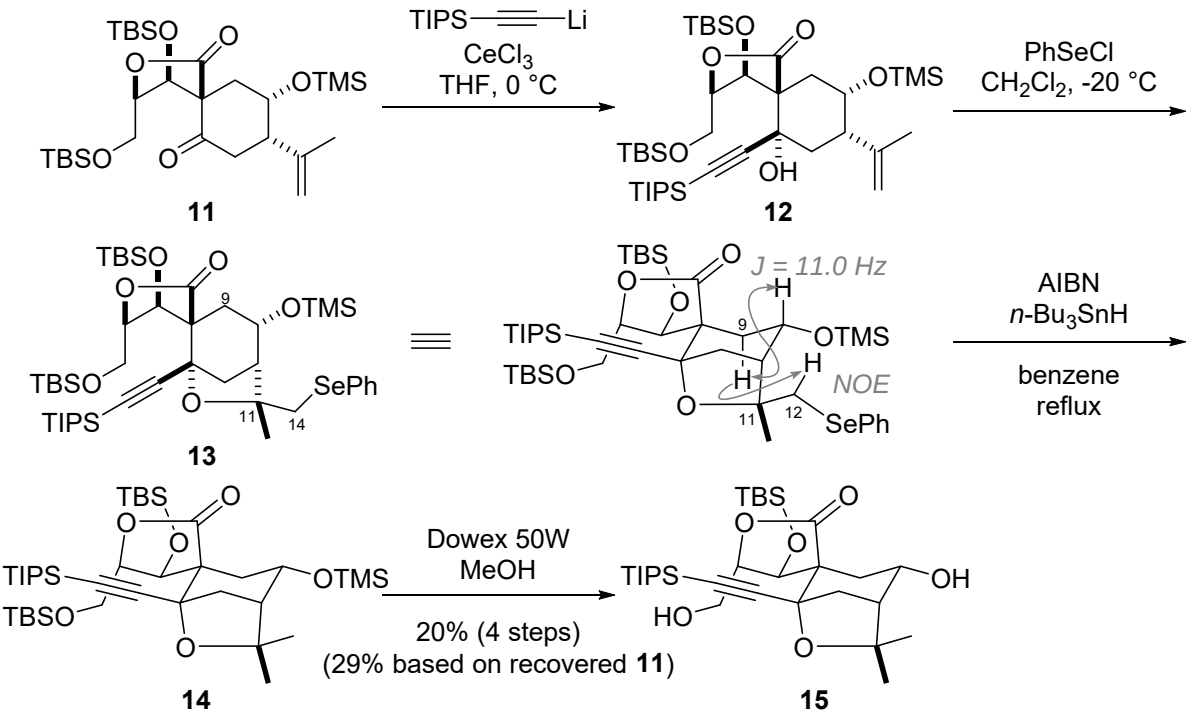




Ketone 11. Isopropenylmagnesium bromide (0.5 M in THF, 55.0 mL, 27.5 mmol) was added to a solution of enone **9** (4.22 g, 9.24 mmol) in THF (92 mL) at -78 °C. The reaction mixture was warmed to 0 °C and stirred for 10 min, and then poured into pH 7 phosphate buffer (150 mL). The resultant solution was extracted with EtOAc (200 mL x3), and the

combined organic layers were dried over Na_2SO_4, filtered and concentrated to afford the crude ketone **10**, which was used in the next reaction without further purification.

TMSOTf (2.50 mL, 13.8 mmol) was added to a solution of the above crude ketone **10** and 2,6-lutidine (3.20 mL, 27.5 mmol) in CH_2Cl_2 (92 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, and then saturated aqueous NH_4Cl (100 mL) was added. The resultant solution was extracted with EtOAc (100 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (100 g, hexane/EtOAc 100/1) to afford ketone **11** (3.23 g, 5.66 mmol) in 61% yield over 2 steps. The C7-configuration was determined by the NOE correlation between α-H9 and H12 of **11**: white solid; m.p. 87.0-88.0 °C; $[\alpha]_D^{22}$ -4.6 (*c* 1.0, $CHCl_3$); IR (film) ν 2954, 2931, 2895, 2858 1767, 1712, 1647, 1559, 1536, 1512, 1467, 1406, 1326, 1254, 1149, 1118, 1088, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.01 (3H, s, C*H*$_3$ of TBS), 0.04 (3H, s, C*H*$_3$ of TBS), 0.07 (3H, s, C*H*$_3$ of TBS), 0.13 (9H, s, C*H*$_3$ of TMS), 0.14 (3H, s, C*H*$_3$ of TBS), 0.86 (9H, s, *t*-Bu of TBS), 0.88 (9H, s, *t*-Bu of TBS), 1.82 (1H, ddd, *J* = 14.2, 4.1, 0.9 Hz, H9a), 1.85 (3H, s, H13), 2.41 (1H, dd, *J* = 14.2, 10.5 Hz, H9b), 2.69 (1H, dd, *J* = 16.0, 4.1 Hz, H6a), 2.94 (1H, m, H7), 3.11 (1H, dd, *J* = 16.0, 6.4 Hz, H6b), 3.77 (1H, dd, *J* = 12.4, 3.6 Hz, H3a), 3.96 (1H, dd, *J* = 12.4, 2.3 Hz, H3b), 4.09 (1H, ddd, *J* = 7.8, 3.6, 2.3 Hz, H2), 4.59 (1H, s, H12a), 4.79 (1H, ddd, *J* = 10.5, 8.7, 4.1 Hz, H8), 4.94 (1H, s, H12b) 5.24 (1H, d, *J* = 7.8 Hz, H1); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.5, -5.4, -5.0, -4.5, -0.1, 17.8, 18.2, 25.4, 25.70, 25.73, 31.3, 42.7, 46.2, 60.1, 60.8, 67.2, 67.8, 83.2, 114.1, 145.4, 172.9, 203.6; HRMS (ESI) calcd for $C_{28}H_{54}O_6Si_3Na$ 593.3120 $[M+Na]^+$, found 593.3097.



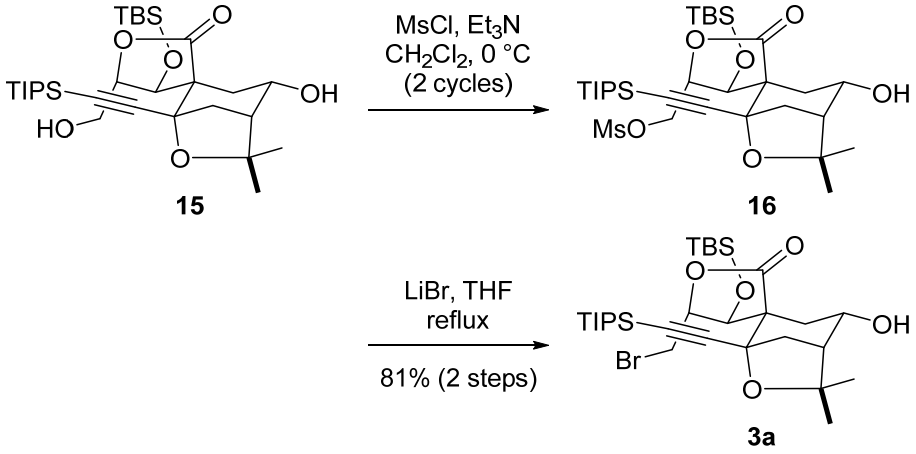
Diol 15. *n*-BuLi (1.6 M in hexane, 18 mL, 29.0 mmol) was added to a solution of triisopropylsilyl acetylene (7.0 mL, 31 mmol) in THF (35 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 15 min, and then anhydrous $CeCl_3$ (0.6 M in THF, 48 mL, 29.0 mmol), which was prepared according to the reported procedure,[S2] was added. The resultant mixture was at -78 °C for 1 h, and then a solution of ketone **11** (3.63 g, 6.36 mmol) in THF (5 mL) was added. The reaction mixture was warmed to 0 °C and stirred for 1 h, and then saturated aqueous NH_4Cl (100 mL) was added. The resultant solution was extracted with EtOAc (100 mL x3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (60 g, hexane/EtOAc 100/1) to afford the unreacted ketone **11** (1.10 g, 1.93 mmol) and the crude alcohol **12**, which was used in the next reaction without further purification.

PhSeCl (914 mg, 4.77 mmol) was added to a solution of the above crude alcohol **12** in CH_2Cl_2 (32 mL) at -20 °C. The reaction mixture was stirred at -20 °C for 10 min, and then saturated aqueous $NaHCO_3$ (15 mL) and saturated aqueous $Na_2S_2O_3$ (15 mL) were successively added. The resultant solution was extracted with EtOAc (20 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated to afford the crude selenide **13**, which was used in the next reaction without further purification. The C11-configuration was determined by the NOE correlation between α-H9 and H12 of the pure selenide **13**, which was obtained by PTLC purification of a small amount of the crude selenide **13**. Selenide **13**: ^{1}H NMR (400 MHz, C_6D_6) δ 0.13 (9H, s, C*H*$_3$ of TMS x3), 0.18 (3H, s, C*H*$_3$ of TBS), 0.19 (3H, s, C*H*$_3$ of TBS), 0.22 (3H, s, C*H*$_3$ of TBS), 0.36 (3H, s, C*H*$_3$ of TBS), 0.95 (9H, s, *t*-Bu of TBS), 1.00 (9H, s, *t*-Bu of TBS), 1.05-1.08 (3H, m, C*H* of TIPS x3), 1.12-1.16 (18H, m, C*H*$_3$ of TIPS x 6), 1.47 (3H, s, H13), 1.90 (1H, dd, *J* = 14.6, 6.9 Hz,

H9a), 2.34 (1H, m, H7), 2.53 (1H, dd, *J* = 13.2, 5.0 Hz, H6a), 2.80 (1H, dd, *J* = 14.6, 11.0 Hz, H9b), 3.20 (1H, d, *J* = 11.4 Hz, H12a), 3.82 (1H, d, *J* = 13.2 Hz, H6b), 3.97 (1H, dd, *J* = 12.4, 8.2 Hz, H3a), 4.18-4.25 (3H, m, H2, H3 and H12b), 4.36 (1H, m, H8), 4.95 (1H, d, *J* = 7.8 Hz, H1), 7.57 (3H, m, aromatic), 7.58 (2H, m, aromatic); HRMS (ESI) calcd for $C_{45}H_{80}O_6Si_4Na$ 931.4089 $[M+Na]^+$, found 931.4106.

A solution of the above crude selenide **13**, *n*-Bu_3SnH (4.5 mL, 17 mmol) and AIBN (522 mg, 3.18 mmol) in benzene (32 mL) was degassed by freeze-thaw procedure (x3). The reaction mixture was heated to reflux, stirred for 2 h, cooled to room temperature and concentrated to afford the crude **14**, which was used in the next reaction without further purification.

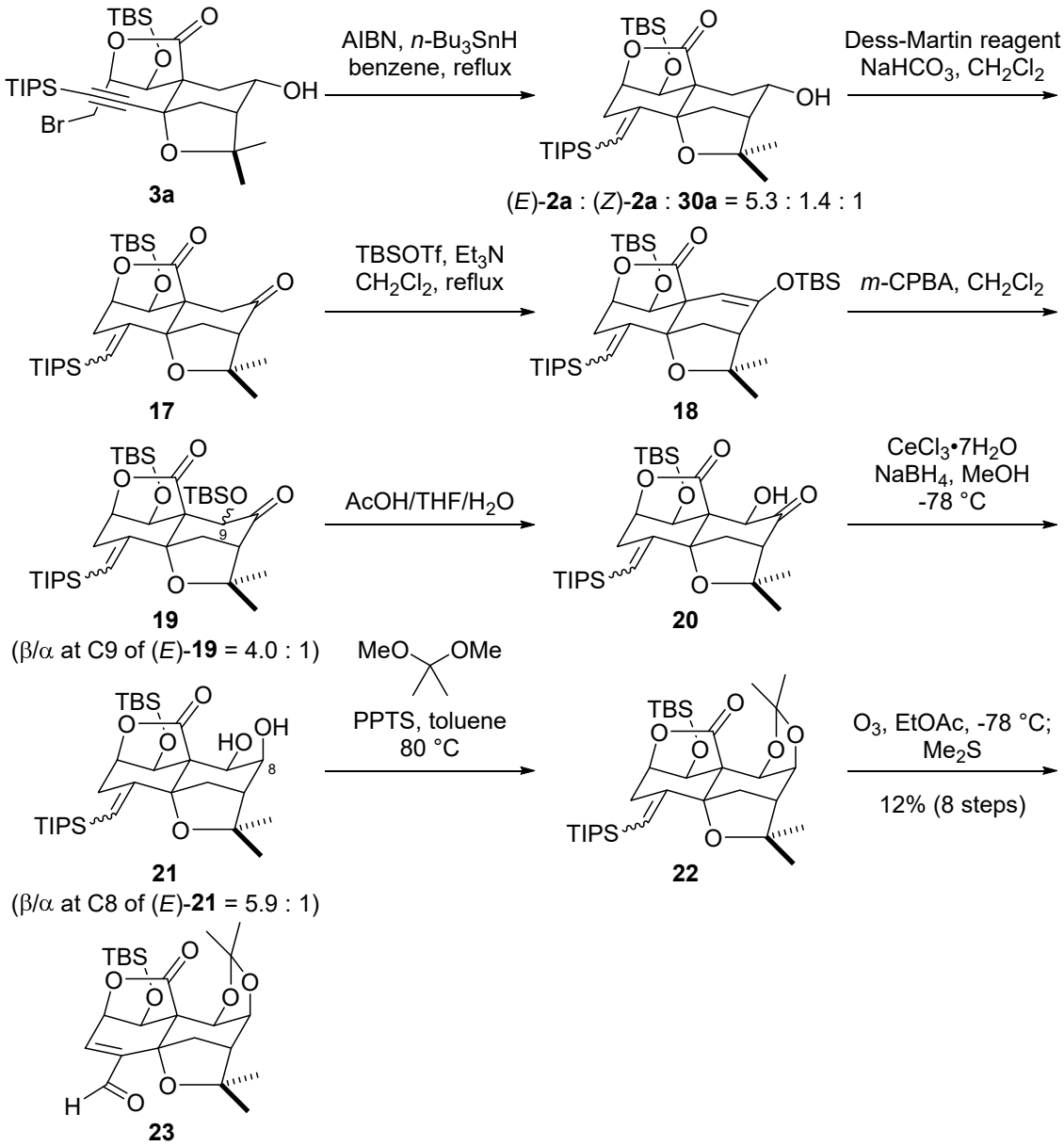
Dowex-50W (2.4 g) was added to a solution of the above crude **14** in MeOH (32 mL) at room temperature. The reaction mixture was stirred at room temperature for 18 h, filtered and concentrated. The residue was purified by flash column chromatography [a column consecutively packed with silica gel (50 g) and 50% (w/w) KF contained silica gel (50 g), hexane/EtOAc 3/1] to afford diol **15** (721 mg, 1.27 mmol) in 20% yield over 4 steps. The yield was calculated to be 29% over 4 steps based on the recovered ketone **11**: white solid; m.p. 158.0-160.0 °C; $[\alpha]_D^{17}$ 32 (*c* 0.50, $CHCl_3$); IR (film) ν 3438, 2940, 2864, 2170, 1756, 1463, 1386, 1364, 1255, 1191, 1149, 1120, 1066, 1008, 938 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.15 (3H, s, C*H*$_3$ of TBS), 0.21 (3H, s, C*H*$_3$ of TBS), 0.91 (9H, s, *t*-Bu of TBS), 1.05 (21H, br s, TIPS), 1.30 (3H, s, C*H*$_3$), 1.51 (3H, s, C*H*$_3$), 1.76 (1H, dd, *J* = 14.4, 6.6 Hz, H9a), 2.14 (1H, dd, *J* = 5.5, 3.2 Hz, H7), 2.47 (1H, dd, *J* = 13.0, 5.5 Hz, H6a), 2.55 (1H, dd, *J* = 14.4, 11.7 Hz, H9b), 3.33 (1H, d, *J* = 13.0 Hz, H6b), 3.77 (1H, dd, *J* = 12.4, 5.3 Hz, H3a), 3.98 (1H, dd, *J* = 12.4, 2.3 Hz, H3b), 4.02 (1H, ddd, *J* = 7.8, 5.3, 2.3 Hz, H2), 4.25 (1H, ddd, *J* = 11.7, 6.6, 3.2 Hz, H8), 4.89 (1H, d, *J* = 7.8 Hz, H1); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.5, -3.4, 11.0, 18.0, 18.5, 24.7, 25.9, 29.5, 31.5, 38.6, 48.9, 55.0, 61.2, 69.9, 71.9, 79.3, 82.3, 84.0, 88.0, 106.8, 175.3; HRMS (ESI) calcd for $C_{30}H_{54}O_6Si_2Na$ 589.3351 $[M+Na]^+$, found 589.3328.



Bromide 3a. MsCl (57 μL, 740 μmol) was added to a solution of diol **15** (691 mg, 1.22 mmol) and Et_3N (200 μL, 1.44 mmol) in CH_2Cl_2 (12 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 5 min, and then saturated aqueous NH_4Cl (15 mL) was added. The resultant solution was extracted with EtOAc (10 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (15 g, CH_2Cl_2/EtOAc 35/1) to afford the crude mesylate **16** and the unreacted diol **15** (307 mg, 542 μmol). According to the above procedure, the recovered diol **15** (307 mg, 542 μmol) was mesylated by using MsCl (29 μL, 370 μmol) and Et_3N (106 μL, 761 μmol) in CH_2Cl_2 (5.5 mL). The residue was purified by flash column chromatography on silica gel (6 g, CH_2Cl_2/EtOAc 35/1) to give the crude mesylate **16** and the unreacted diol **15** (101 mg, 178 μmol). The combined crude mesylate **16** was used in the next reaction without further purification.

LiBr (4.56 g, 52.5 mmol) was added to a solution of the above crude mesylate **16** in THF (11 mL) at room temperature. The reaction mixture was heated to reflux and stirred for 14 h. After the mixture was cooled to room temperature, saturated aqueous $NaHCO_3$ (12 mL) was added. The resultant solution was extracted with EtOAc (20 mL x3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (15 g, hexane/EtOAc 6/1) to afford bromide **3a** (622 mg, 987 μmol) in 81% yield over 2 steps: white solid; m.p. 120.0-122.0 °C; $[\alpha]_D^{30}$ 23 (*c* 0.50, $CHCl_3$); IR (film) ν 3437, 2941, 2892, 2864, 2169, 1774, 1463, 1387, 1366, 1318, 1294, 1256, 1221, 1192, 1149, 1119, 1065, 1037, 1009, 970, 922 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.18 (3H, s, C*H*$_3$ of TBS), 0.23 (3H, s, C*H*$_3$ of TBS), 0.92 (9H, s, *t*-Bu of TBS), 1.06 (21H, br s, TIPS), 1.30 (3H, s, C*H*$_3$), 1.50 (3H, s, C*H*$_3$), 1.75 (1H, dd, *J* = 14.2, 6.4 Hz, H9a), 2.14 (1H, dd, *J* = 5.3, 3.2 Hz, H7), 2.479 (1H, dd, *J* = 14.2, 11.4 Hz, H9b), 2.481 (1H, dd, *J* = 13,3, 5.3 Hz, H6a), 3.32 (1H, d, *J* = 13.3 Hz, H6b), 3.54 (1H, dd, *J* = 11.4, 7.1 Hz, H3a), 3.77 (1H, dd, *J* = 11.4, 2.7 Hz, H3b), 4.16 (1H, ddd, *J* = 7.1, 6.8, 2.7 Hz, H2), 4.27 (1H, ddd, *J* = 11.4, 6.4, 3.2 Hz, H8), 4.77 (1H, d, *J* = 6.8 Hz, H1); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.2, -3.4, 11.1, 18.0, 18.6, 24.7, 25.9, 29.9, 31.0, 31.4, 38.8, 48.9, 55.6, 69.9, 75.1, 79.2, 81.3, 84.3, 88.6,

106.9, 174.6; HRMS (ESI) calcd for $C_{30}H_{53}BrO_5Si_2Na$ 651.2507 and 653.2487 $[M+Na]^+$, found 651.2487 and 653.2467.



Enal 23. A solution of bromide **3a** (230 mg, 365 μmol) and AIBN (30.0 mg, 182 μmol) in benzene (34 mL) was degassed by freeze-thaw procedure (x3). The mixture was heated to reflux, and then a degassed solution of *n*-Bu_3SnH (980 μL, 3.6 mmol) and AIBN (30.0 mg, 182 μmol) in benzene (2.5 mL) by freeze-thaw procedure (x3) was added over 30 min. After the addition was completed, the reaction mixture was stirred at the reflux temperature for further 1 h. The mixture was cooled to room temperature and concentrated. The residue was purified by flash column chromatography [a column consecutively packed with silica gel (5 g) and 50% (w/w) KF contained silica gel (5 g), hexane/EtOAc 10/1] to afford a 5.3 : 1.4 : 1 mixture of (*E*)-**2a**, (*Z*)-**2a**, and the 7-membered compound **30a**, which was used in

the next reaction without further purification. The combined yield of (*E*)-**2a**, (*Z*)-**2a**, and **30a** was calculated to be 83% by ^{1}H NMR analysis of the crude mixture using CH_2Br_2 as an internal standard. For the structural confirmation of the products, see page S13.

Dess-Martin periodinane (276 mg, 651 μmol) was added to a solution of the above crude mixture and $NaHCO_3$ (546 mg, 6.50 mmol) in CH_2Cl_2 (3.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, and then saturated aqueous $Na_2S_2O_3$ (4 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (4 g, hexane/EtOAc 20/1) to afford the crude **17**, which was used in the next reaction without further purification.

TBSOTf (1.4 mL, 6.1 mmol) was added to a solution of the above crude ketone **17** and Et_3N (1.7 mL, 12 mmol) in CH_2Cl_2 (3 mL) at room temperature. The reaction mixture was heated to reflux and stirred for 1 h. After the mixture was cooled to room temperature, pH 7 phosphate buffer (1.5 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (4 g, hexane/EtOAc 50 /1) to afford the crude TBS-enol ether **18**, which was used in the next reaction without further purification.

m-CPBA (79.2 mg, 459 μmol) was added to a solution of the above TBS-enol ether **18** in CH_2Cl_2 (3 mL) at room temperature. The reaction mixture was stirred for 2 h at room temperature, and then saturated aqueous $NaHCO_3$ (1.5 mL) and saturated aqueous $Na_2S_2O_3$ (1.5 mL) were successively added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated to afford the crude ketone **19**, which was used in the next reaction without further purification. The β/α C9-diastereomeric ratio of the major compound (*E*)-**19** was determined to be 4.0 : 1 by the ^{1}H NMR analysis of the crude mixture.

A solution of the above crude **19** mixture in THF (1 mL), H_2O (1 mL) and AcOH (1 mL) was stirred for 24 h at room temperature, and then saturated aqueous $NaHCO_3$ (5 mL) was added. The resultant solution was extracted with EtOAc (10 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (4 g, hexane/EtOAc 15/1) to afford the crude ketone **20**, which was used in the next reaction without further purification. The β/α C9-diastereomeric ratio of the major compound (*E*)-**20** was over 20 : 1 from the ^{1}H NMR analysis of the crude mixture.

$NaBH_4$ (31.6 mg, 836 μmol) was added to a solution of the above crude ketone **20** and $CeCl_3 \cdot 7H_2O$ (311 mg, 834 μmol) in MeOH (2.1 mL) at -78 °C. The reaction mixture was stirred for 5 min at -78 °C, and then saturated aqueous potassium sodium tartrate (3.0 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined

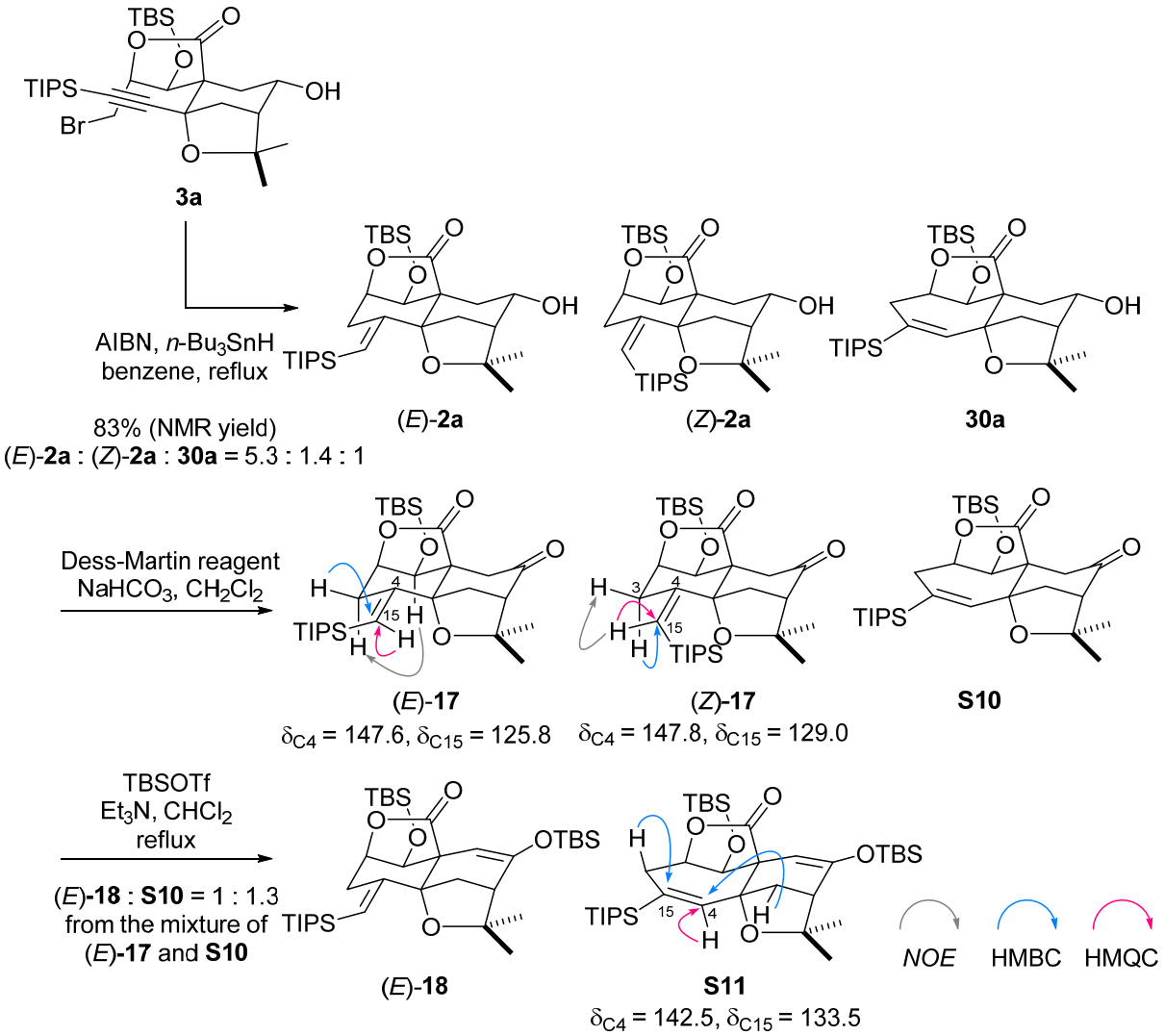
organic layers were dried over Na_2SO_4, filtered and concentrated to afford the crude diol **21**, which was used in the next reaction without further purification. The β/α C8-diastereomeric ratio of the major compound (*E*)-**21** was determined to be 5.9 : 1 by the ^{1}H NMR analysis of the crude mixture. The β-orientation of the *cis*-C8, 9-diol was established by the NOESY spectra of the target compound **1**. For the key NOESY correlations, see page S18.

PPTS (26.2 mg, 104 μmol) was added to a solution of the above crude diol **21** and 2,2-dimethoxypropane (510 μL, 4.2 mmol) in toluene (2.1 mL) at room temperature. The reaction mixture was heated to 80 °C and stirred for 2 h. After the mixture was cooled to room temperature, saturated aqueous $NaHCO_3$ (3 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (2 g, hexane/EtOAc 30/1) to afford the crude acetonide **22**, which was used in the next reaction without further purification.

Ozone was bubbled into a solution of the above crude acetonide **22** in EtOAc (5 mL) for 1.5 min at -78 °C. Excess ozone was removed by bubbling O_2 at -78 °C for 5 min, and then Me_2S (730 μL, 9.8 mmol) was added. The reaction mixture was warmed to room temperature and stirred for 22 h. After toluene (5 mL) was added, the resultant mixture was concentrated at 20 °C. This procedure was repeated twice to remove excess Me_2S. the residue was purified by flash column chromatography on silica gel (0.25 g, hexane/EtOAc 15/1) to afford enal **23** (20.5 mg, 44.1 μmol) in 12% yield over 8 steps: **23** colorless oil; $[\alpha]_D^{27}$ 9.4 (*c* 1.0, $CHCl_3$); IR (film) ν 2931, 2858, 1789, 1706, 1469, 1382, 1369, 1327, 1303, 1262, 1214, 1139, 1096, 1064, 1037, 1011, 937 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.13 (3H, s, C*H*$_3$ of TBS), 0.14 (3H, s, C*H*$_3$ of TBS), 0.92 (9H, s, *t*-Bu of TBS), 1.33 (3H, s, C*H*$_3$), 1.37 (3H, s, C*H*$_3$), 1.43 (3H, s, C*H*$_3$), 1.66 (3H, s, C*H*$_3$), 2.58 (1H, dd, *J* = 4.6, 2.7 Hz, H7), 2.65 (1H, d, *J* = 12.8 Hz, H6a), 3.07 (1H, dd, *J* = 12.8, 4.6 Hz, H6b), 4.34 (1H, d, *J* = 6.9 Hz, H9), 4.57 (1H, dd, *J* = 6.9, 2.7 Hz, H8), 4.61 (1H, s, H1), 4.67 (1H, d, *J* = 5.9 Hz, H2), 7.08 (1H, d, *J* = 5.9 Hz, H3), 9.47 (1H, s, H15); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -4.5, 18.0, 24.5, 24.8, 24.9, 25.4, 28.2, 29.1, 46.1, 61.3, 71.9, 73.8, 75.2, 76.2, 82.5, 83.6, 110.5, 141.0, 149.3, 171.9, 191.1; HRMS (ESI) calcd for $C_{24}H_{36}O_7SiNa$ 487.2123 $[M+Na]^+$, found 487.2125.

Structural assignment of 2a and 30a: Inseparable (*E*)-**2a**, (*Z*)-**2a** and **30a** were oxidized into (*E*)-**17**, (*Z*)-**17** and **S10**, respectively. Flash column chromatography of a small amount of the crude products gave pure (*E*)-**17** and (*Z*)-**17** along with the crude mixture of (*E*)-**17** and **S10**. An inseparable 1 : 1.3 mixture of (*E*)-**18** and **S11** was synthesized from the crude mixture of (*E*)-**17** and **S10** by treatment with TBSOTf and Et_3N in refluxing CH_2Cl_2. The 6-membered ring structures of (*E*)-**17** and (*Z*)-**17** were elucidated by the 1D and 2D NMR experiments, and the stereochemistries of the vinyl silane of (*Z*)-**17** was determined by the

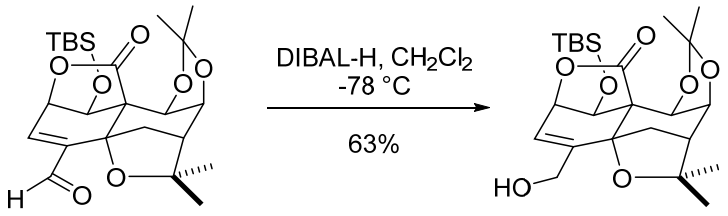
NOE correlation between H3 and H15. The 7-membered ring formation was also established by the 1D and 2D NMR experiments of the mixture of (*E*)-**18** and **S11**.



(*E*)-**17**: colorless oil; $[\alpha]_D^{25}$ 53 (*c* 0.15, $CHCl_3$); IR (film) ν 2933, 2894, 2864, 1779, 1721, 1622, 1465, 1386, 1364, 1257, 1212, 1187, 1137, 1120, 1089, 1058, 1032, 997, 973 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (3H, s, C*H*$_3$ of TBS), 0.10 (3H, s, C*H*$_3$ of TBS), 0.87 (9H, s, *t*-Bu of TBS), 1.05 (9H, d, *J* = 6.8 Hz, C*H*$_3$ of TIPS x3), 1.06 (9H, d, *J* = 6.8 Hz, C*H*$_3$ of TIPS x3), 1.13 (3H, m, C*H* of TIPS x3), 1.22 (3H, s, C*H*$_3$), 1.23 (3H, s, C*H*$_3$), 2.28 (1H, br d, *J* = 15.1 Hz, H6a), 2.55 (1H, d, *J* = 20.6 Hz, H9a), 2.73-2.80 (3H, m, H3a, H6b and H7), 2.85 (1H, d, *J* = 20.6 Hz, H9b), 2.99 (1H, dd, *J* = 15.1, 5.3 Hz, H3b), 4.56 (1H, d, *J* = 5.3 Hz, H2), 4.64 (1H, s, H1), 5.77 (1H, d, *J* = 1.8 Hz, H15); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, -4.6, 12.2, 17.9, 18.7, 18.8, 25.6, 25.7, 29.1, 31.2, 35.9, 36.2, 57.9, 58.9, 80.8, 82.4, 86.1, 125.8, 147.6, 176.6, 208.6; HRMS (ESI) calcd for $C_{30}H_{52}O_5Si_2Na$ 571.3245 $[M+Na]^+$, found 571.3236.

(*Z*)-**17**: colorless oil; $[\alpha]_D^{25}$ 29 (*c* 0.28, $CHCl_3$); IR (film) ν 2949, 2929, 2863, 1772, 1722, 1608, 1465, 1389, 1367, 1257, 1202, 1180, 1122, 1085, 1059, 1024, 1002, 971 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (3H, s, C*H*$_3$ of TBS), 0.11 (3H, s, C*H*$_3$ of TBS), 0.88 (9H, s, *t*-Bu of

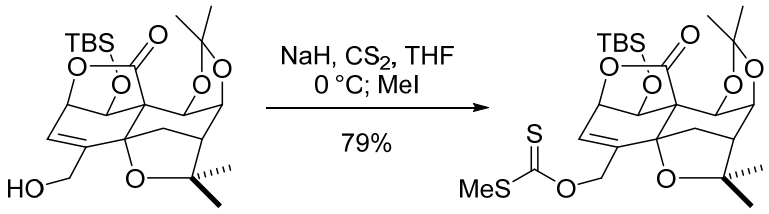
TBS), 1.06-1.08 (21H, m, TIPS), 1.22 (3H, s, CH_3), 1.27 (3H, s, CH_3), 2.34 (1H, d, J = 12.1 Hz, H6a), 2.60 (1H, dd, J = 12.1, 5.0 Hz, H6b), 2.62 (1H, d, J = 21.0 Hz, H9a), 2.75 (1H, d, J = 5.0 Hz, H7), 2.76 (1H, dd, J = 14.6, 5.5 Hz, H3a), 2.89 (1H, d, J = 21.0 Hz, H9b), 3.10 (1H, dd, J = 14.6, 1.7 Hz, H3b), 4.52 (1H, d, J = 5.5 Hz, H2), 4.68 (1H, s, H1), 5.50 (1H, d, J = 1.7 Hz, H15); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.7, -4.4, 13.8, 17.9, 19.1, 19.4, 25.6, 26.1, 29.7, 29.8, 32.4, 35.8, 44.2, 58.1, 59.2, 80.6, 81.3, 85.5, 129.0, 147.8, 176.5, 208.2; HRMS (ESI) calcd for $C_{30}H_{52}O_5Si_2Na$ 571.3245 $[M+Na]^+$, found 571.3242. (*E*)-**18**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.079 (3H, s, CH_3 of TBS), 0.085 (3H, s, CH_3 of TBS), 0.19 (3H, s, CH_3 of TBS), 0.22 (3H, s, CH_3 of TBS), 0.89 (9H, s, *t*-Bu of TBS), 0.93 (9H, s, *t*-Bu of TBS), 1.03-1.06 (21H, m, TIPS), 1.22 (3H, s, CH_3), 1.33 (3H, s, CH_3), 2.12 (1H, d, J = 11.4 Hz, H6a), 2.24 (1H, d, J = 4.6 Hz, H7), 2.52 (1H, dd, J = 11.4, 4.6 Hz, H6b), 2.72 (1H, dd, J = 15.1, 1.4 Hz, H3a), 2.93 (1H, dd, J = 15.1, 5.0 Hz, H3b), 4.48 (1H, d, J = 5.0 Hz, H2), 4.60 (1H, s, H9), 4.61 (1H, d, J = 1.4 Hz, H1), 5.74 (1H, brs, H15). **S11**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (3H, s, CH_3 of TBS), 0.09 (3H, s, CH_3 of TBS), 0.18 (3H, s, CH_3 of TBS), 0.20 (3H, s, CH_3 of TBS), 0.90 (9H, s, *t*-Bu of TBS), 0.93 (9H, s, *t*-Bu of TBS), 1.03-1.08 (21H, m, TIPS), 1.25 (3H, s, CH_3), 1.32 (3H, s, CH_3), 2.05 (1H, dd, J = 11.0 , 4.1 Hz, H6a), 2.21 (1H, d, J = 4.1 Hz, H7), 2.42 (1H, ddd, J = 18.3, 2.8, 1.8 Hz, H3a), 2.82 (1H, dd, J = 18.3, 5.0 Hz, H3b), 2.84 (1H, d, J = 11.0 Hz, H6b), 4.52 (1H, s, H9), 4.53 (1H, dd, J = 5.0, 2.8 Hz, H2), 4.67 (1H, brs, H1), 5.66 (1H, d, J = 1.8 Hz, H4). The ^{13}C NMR peaks at C4 and C15 of **S11** were deduced from the 2D NMR data of the mixture of (*E*)-**18** and **S11**.



23 **24**

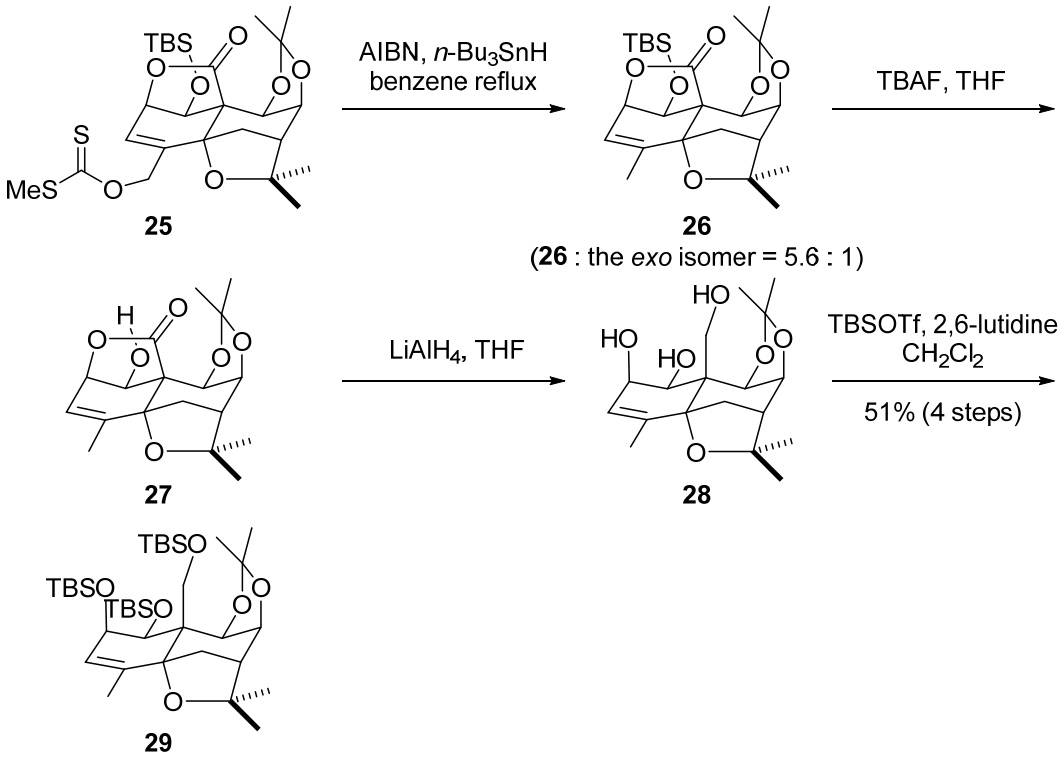
Alcohol 24. DIBAL-H (1.0 M in hexane, 64 μL, 64 μmol) was added to a solution of enal **23** (29.9 mg, 64.4 μmol) in CH_2Cl_2 (640 μL) at -78 °C. The reaction mixture was stirred at -78 °C for 5 min, and then saturated aqueous potassium sodium tartrate (3 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (1 g, hexane/EtOAc 2/1) to afford alcohol **24** (18.9 mg, 40.5 μmol) in 63% yield: colorless oil; $[\alpha]_D^{27}$ 6.6 (*c* 0.050, $CHCl_3$); IR (film) ν 2977, 2931, 2861, 1781, 1469, 1381, 1258, 1212, 1124, 1066 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (3H, s, CH_3 of TBS), 0.13 (3H, s, CH_3 of TBS), 0.91 (9H, s, *t*-Bu of TBS), 1.32 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.66 (3H, s, CH_3), 2.22 (1H, dd, J = 12.8, 4.6 Hz, H6a), 2.54 (1H, dd, J = 4.6, 2.8 Hz, H7), 2.72 (1H, d, J = 12.8 Hz, H6b), 4.15-4.19 (2H, m, H15),

4.34 (1H, d, *J* = 6.9 Hz, H9), 4.48 (1H, d, *J* = 6.0 Hz, H2), 4.53 (1H, s, H1), 4.56 (1H, dd, *J* = 6.9, 2.8 Hz, H8), 6.35 (1H, ddd, *J* = 6.0, 1.4, 1.4 Hz, H3); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.1, -4.4, 18.0, 24.3, 24.8, 24.9, 25.4, 29.2, 29.3, 45.8, 60.51, 60.54, 61.5, 72.1, 73.9, 76.2, 82.3, 84.3, 110.4, 127.4, 142.4, 173.0; HRMS (ESI) calcd for $C_{24}H_{38}O_7SiNa$ 489.2279 $[M+Na]^+$, found 489.2281.



24 **25**

Xanthate 25. CS_2 (25 μL, 410 μmol) was added to a solution of alcohol **24** (18.9 mg, 40.5 μmol) and NaH (70% purity, 13.9 mg, 405 μmol) in THF (405 μL) at 0 °C. The reaction mixture was stirred at 0 °C for 13 min, and then MeI (25 μL, 410 μmol) was added. The reaction mixture was stirred at 0 °C for 1 h, and then saturated aqueous NH_4Cl (1.5 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (0.5 g, hexane/EtOAc 15/1) to afford xanthate **25** (17.8 mg, 32.0 μmol) in 79% yield: colorless oil; IR (film) ν 2924, 2852, 1771, 1460, 1382, 1258, 1213, 1064, 1004 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.12 (3H, s, C*H*$_3$ of TBS), 0.13 (3H, s, C*H*$_3$ of TBS), 0.91 (9H, s, *t*-Bu of TBS), 1.32 (3H, s, C*H*$_3$), 1.32 (3H, s, C*H*$_3$), 1.38 (3H, s, C*H*$_3$), 1.67 (3H, s, C*H*$_3$), 2.12 (1H, dd, *J* = 13.3, 4.6 Hz, H6a), 2.52-2.56 (1H, m, H7), 2.56 (3H, s, SC*H*$_3$), 2.76 (1H, d, *J* = 13.3 Hz, H6b), 4.34 (1H, d, *J* = 6.9 Hz, H9), 4.49 (1H, d, *J* = 6.4 Hz, H2), 4.53 (1H, s, H1), 4.56 (1H, dd, *J* = 6.9, 2.7 Hz, H8), 4.98 (1H, d, *J* = 13.8 Hz, H15a), 5.16 (1H, d, *J* = 13.8 Hz, H15b), 6.41 (1H, d, *J* = 6.4 Hz, H3); HRMS (ESI) calcd for $C_{26}H_{40}O_7S_2SiNa$ 579.1877 $[M+Na]^+$, found 579.1870.



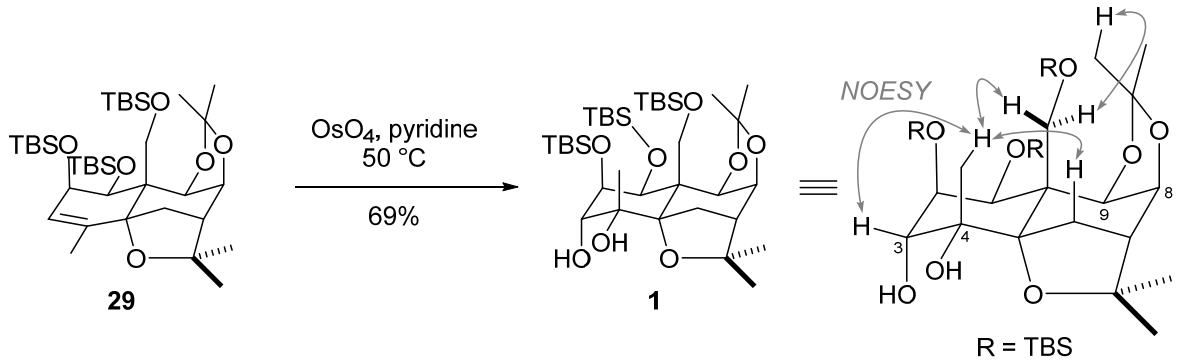
Tris-TBS ether 29. A solution of xanthate **25** (17.8 mg, 32.0 μmol), *n*-Bu_3SnH (86 μL, 320 μmol) and AIBN (5.3 mg, 32 μmol) in benzene (320 μL) was degassed by freeze-thaw procedure (x3). The reaction mixture was heated to reflux, stirred for 2 h and then concentrated. The residue was purified by flash column chromatography [a column consecutively packed with silica gel (1 g) and 50% (w/w) KF contained silica gel (1 g), hexane/EtOAc 10/1] to afford an inseparable 5.6 : 1 mixture of the *endo*-olefin **26** and the *exo*-olefin isomer, which was used in the next reaction without further purification.

TBAF (1.0 M in THF, 46 μL, 46 μmol) was added to a solution of the above crude mixture in THF (0.3 mL) at -20 °C. The reaction mixture was warmed to room temperature and stirred for 2 h, and then saturated aqueous NH_4Cl (3 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (0.5 g, hexane/EtOAc 2/1) to afford the crude alcohol **27**, which was used in the next reaction without further purification.

$LiAlH_4$ (16.4 mg, 432 μmol) was added to a solution of the above crude alcohol **27** in THF (0.3 mL) at room temperature. The reaction mixture was stirred at room temperature for 30 min. After the mixture was cooled to 0 °C, H_2O (5 drops) was added. The resultant solution was filtrated through a pad of Celite with EtOAc (30 mL). The filtrate was concentrated to afford the crude triol **28**, which was used in the next reaction without further purification.

TBSOTf (200 μL, 870 μmol) was added to a solution of the above crude triol **28** and 2,6-lutidine (200 μL, 1.7 mmol) in CH_2Cl_2 (290 μL) at room temperature. The reaction

mixture was stirred at room temperature for 30 min, and then pH 7 phosphate buffer (1.5 mL) was added. The resultant solution was extracted with EtOAc (5 mL x3), and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (0.5 g, hexane/EtOAc 180/1 to 50/1) to afford tris-TBS ether **29** (11.1 mg, 16.2 μmol) in 51% yield over 4 steps: colorless oil; $[\alpha]_D^{27}$ -2.8 (*c* 0.18, $CHCl_3$); IR (film) ν 2953, 2931, 2897, 2857, 1469, 1365, 1300, 1254, 1210, 1165, 1123, 1098, 1060, 1043, 923 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.01 (3H, s, C*H*$_3$ of TBS), 0.00 (3H, s, C*H*$_3$ of TBS), 0.03 (3H, s, C*H*$_3$ of TBS), 0.06 (3H, s, C*H*$_3$ of TBS), 0.09 (3H, s, C*H*$_3$ of TBS), 0.11 (3H, s, C*H*$_3$ of TBS), 0.89 (9H, s, *t*-Bu of TBS), 0.91 (9H, s, *t*-Bu of TBS), 0.93 (9H, s, *t*-Bu of TBS), 1.25 (3H, s, C*H*$_3$), 1.30 (3H, s, C*H*$_3$), 1.32 (3H, s, C*H*$_3$), 1.55 (3H, s, C*H*$_3$), 1.78 (3H, s, H15), 1.98 (1H, dd, *J* = 12.4, 4.6 Hz, H6a), 2.36 (1H, dd, *J* = 3.7, 2.3 Hz, H7), 3.41 (1H, d, *J* = 12.4 Hz, H6b), 4.01 (1H, d, *J* = 11.4 Hz, H14a), 4.18 (1H, d, *J* = 11.4 Hz, H14b), 4.18 (1H, d, *J* = 6.4 Hz, H9), 4.21-4.25 (1H, m, H2), 4.22 (1H, s, H1), 4.48 (1H, dd, *J* = 6.4, 2.3 Hz, H8), 5.62 (1H, m, H3); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.4, -5.0, -4.9, -4.7, -2.5, -2.2, 18.1, 18.2, 18.4, 19.1, 24.3, 24.5, 26.16, 26.25, 26.32, 26.6, 28.4, 29.7, 46.8, 51.1, 61.1, 68.2, 73.7, 74.7, 76.1, 78.8, 87.2, 108.2, 128.2, 135.0; HRMS (ESI) calcd for $C_{36}H_{70}O_6Si_3Na$ 705.4372 $[M+Na]^+$, found 705.4387.



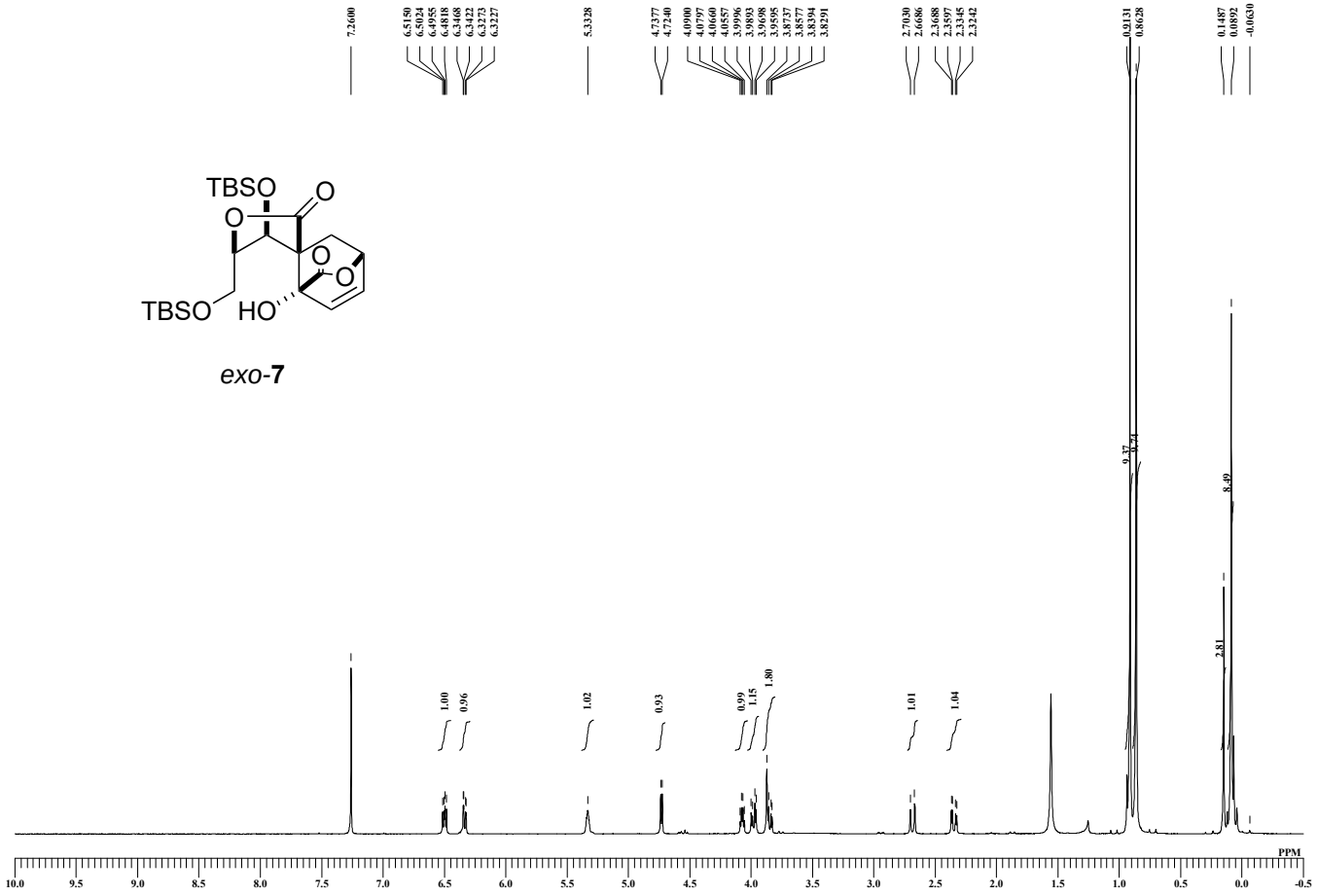
Compound 1. OsO_4 (0.5 M in pyridine, 64 μL, 32 μmol) was added to a solution of tris-TBS ether **29** (2.2 mg, 3.2 μmol) in pyridine (0.26 mL) at room temperature. The reaction mixture was warmed to 50 °C and stirred for 40 h. After the mixture was cooled to room temperature, EtOAc (0.25 mL) and saturated aqueous $NaHSO_3$ (1 mL) were successively added. The mixture was stirred for 18 h, and the resultant solution was extracted with EtOAc (5 mL x3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography on silica gel (0.5 g, hexane/EtOAc 50/1 to 15/1) to afford **1** (1.6 mg, 2.2 μmol) in 69% yield. The stereochemistry of the α-oriented *cis*-C3, 4-diol and β-oriented *cis*-C8, 9-diol were elucidated by the NOESY experiment of **1**: colorless oil; $[\alpha]_D^{26}$ 3.7 (*c* 0.21, $CHCl_3$); IR (film) ν 3442, 2929, 2857, 1469, 1378, 1256, 1213, 1108, 1039 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.02 (3H, s, C*H*$_3$ of TBS), 0.04 (3H, s, C*H*$_3$ of TBS), 0.08 (3H, s, C*H*$_3$ of TBS), 0.12 (3H, s,

C*H*$_3$ of TBS), 0.15 (6H, s, C*H*$_3$ of TBS x2), 0.93 (27H, s, *t*-Bu of TBS x 3), 0.131 (3H, s, C*H*$_3$), 0.135 (3H, s, C*H*$_3$), 1.36 (3H, s, C*H*$_3$), 1.43 (3H, s, C*H*$_3$), 1.53 (3H, s, C*H*$_3$), 2.14 (1H, dd, *J* = 12.4, 3.2 Hz, H6a), 2.29 (1H, m, H7), 3.04 (1H, s, O*H*), 3.38 (1H, d, *J* = 12.4 Hz, H6b), 3.54 (1H, dd, *J* = 11.4, 2.8 Hz, H3), 3.94 (1H, d, *J* = 7.3 Hz, H9), 4.01 (1H, d, *J* = 4.1 Hz, H1), 4.08 (1H, dd, *J* = 4.1, 2.8 Hz, H2), 4.10 (1H, d, *J* = 12.4 Hz, H14a), 4.24 (1H, d, *J* = 11.4 Hz, O*H*), 4.46 (1H, br d, *J* = 7.3, H8), 4.60 (1H, d, *J* = 12.4 Hz, H14b); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.2, -4.6, -4.3, -4.2, -4.0, -2.5, 18.07, 18.14, 18.5, 23.1, 24.2, 24.6, 26.3, 26.5, 26.6, 26.8, 29.0, 29.7, 44.8, 52.4, 59.0, 69.6, 74.5, 74.7, 77.9, 79.1, 80.2, 81.5, 96.2, 108.4; HRMS (ESI) calcd for $C_{36}H_{72}O_8Si_3Na$ 739.4427 $[M+Na]^+$, found 739.4449.

References

S1 Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

S2 (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392. (b) Takeda, N.; Imamoto, T. *Org. Synth.* **1999**, *76*, 228.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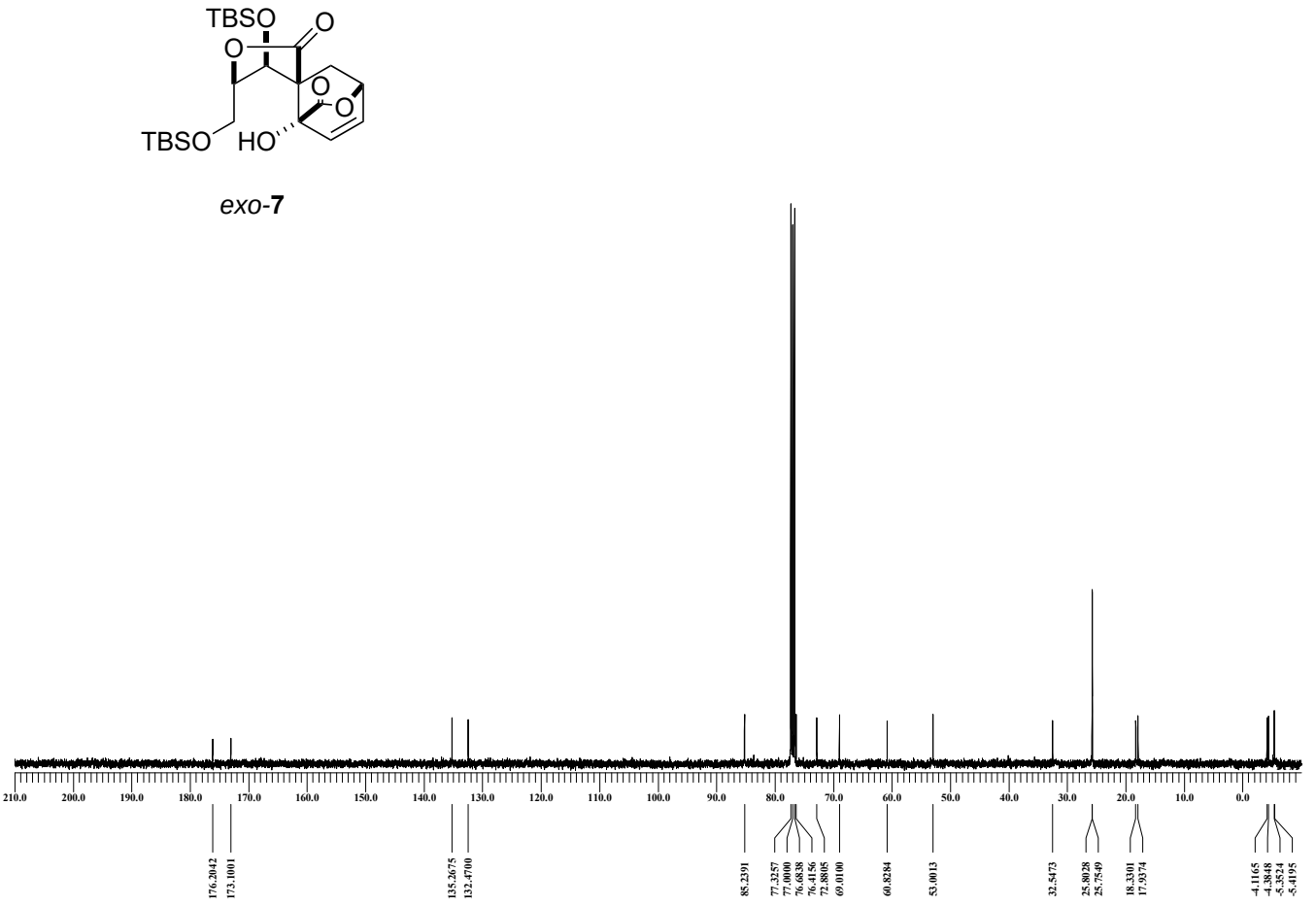
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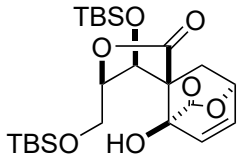
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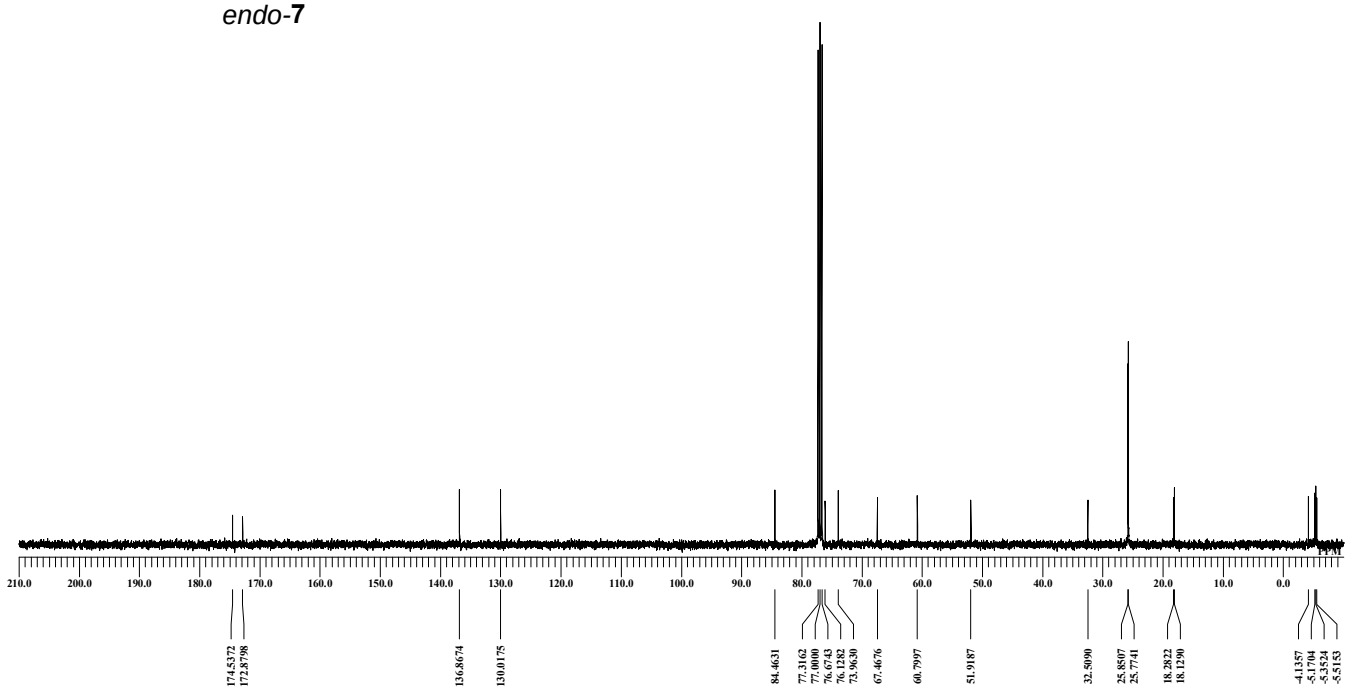
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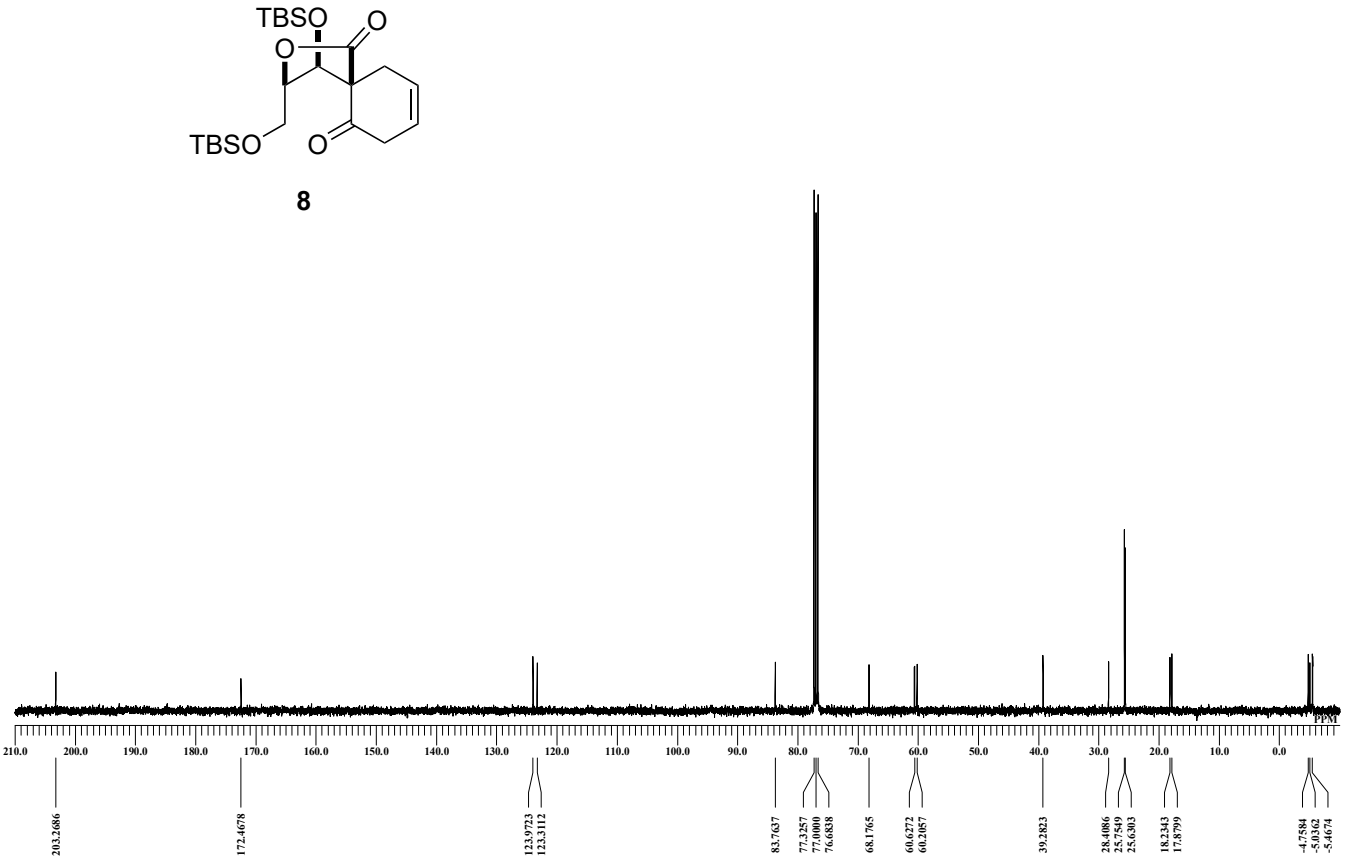
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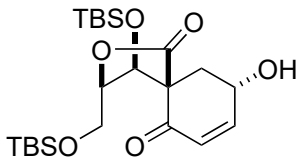
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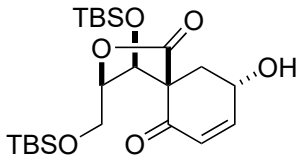
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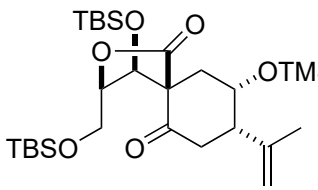

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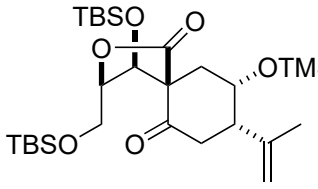

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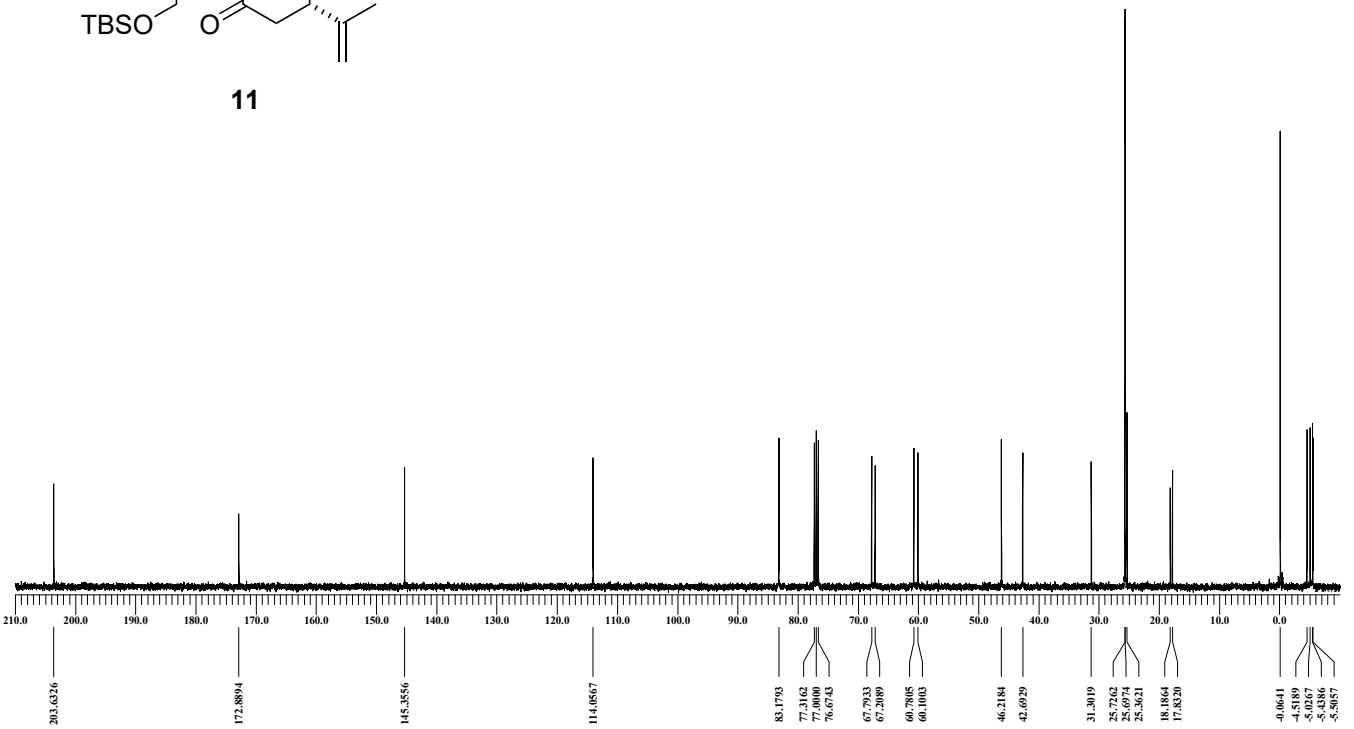

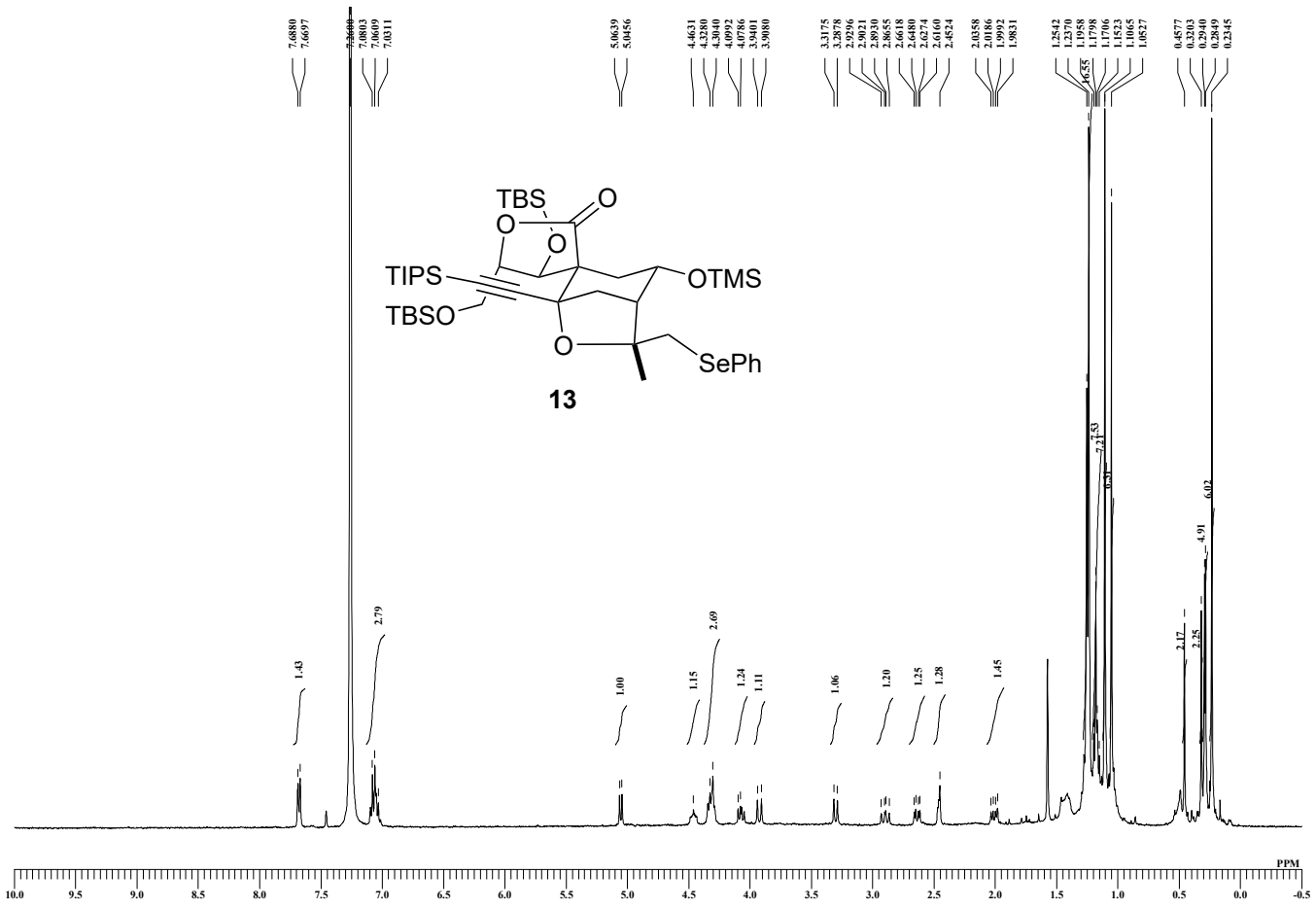
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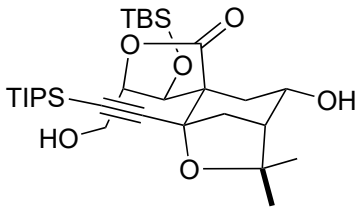
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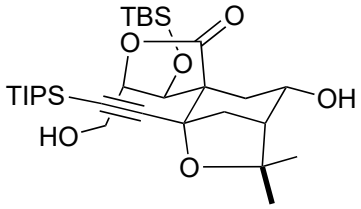
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HO
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15

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106.7948
87.9886
84.0128
82.2883
79.2610
77.2357
77.0000
76.6838
71.8937
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54.9844
48.9488
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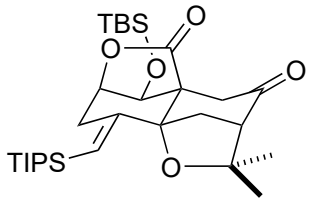
TBS
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TIPS
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(*E*)-**17**

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4.5672
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3.0005
2.9765
2.9628
2.8758
2.8243
2.7842
2.7728
2.7613
2.7350
2.5725
2.5210
2.2956
2.2647
1.2267
1.1855
1.1660
1.1477
1.1294
30.12
1.1145
1.0711
1.0550
1.0379
0.8719
0.0972
0.0880
11.00
8.88
6.52
3.81
3.29
1.00
1.03
0.99
1.03
1.12
1.13
1.23
PPM
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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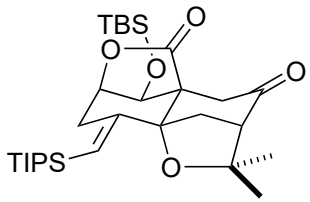
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TIPS
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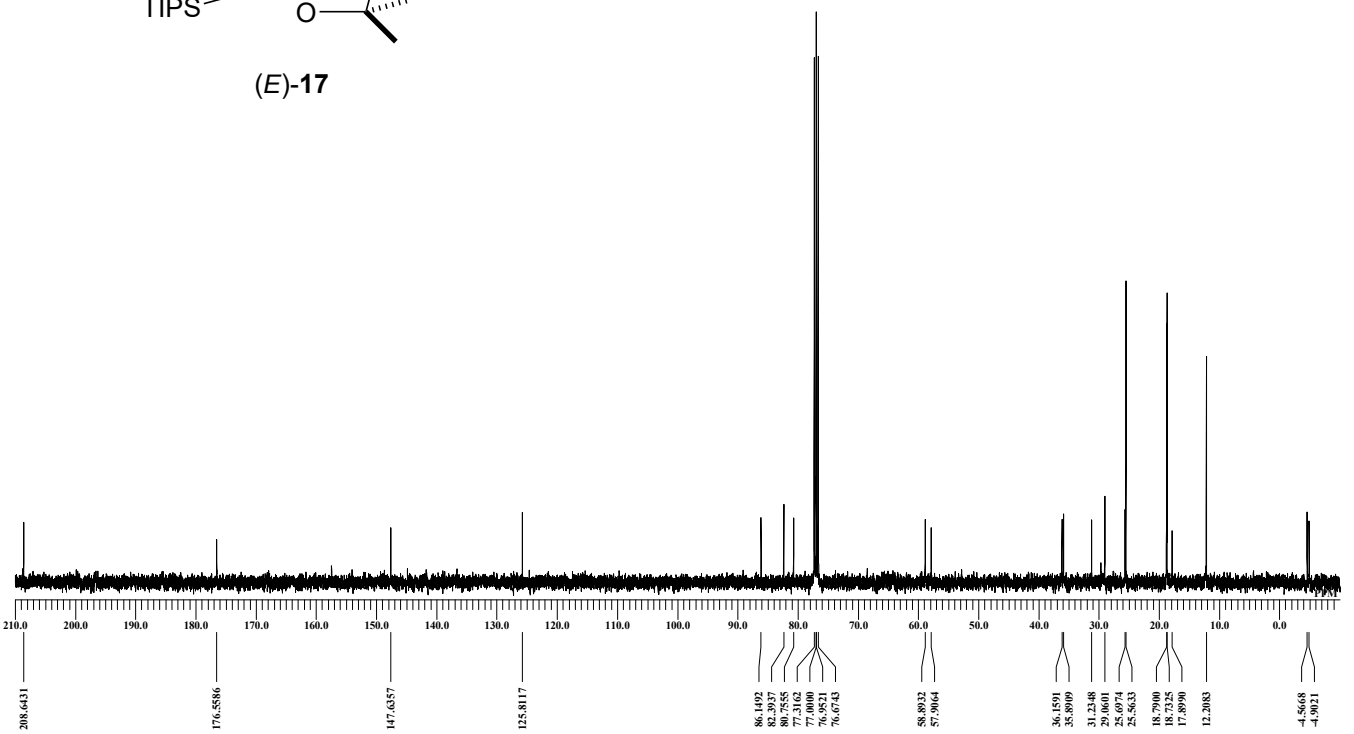
(*E*)-**17**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100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
208.6431
176.5586
147.6357
125.8117
86.1492
82.3937
80.7555
77.3162
77.0000
76.9521
76.6743
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57.9064
36.1591
35.8909
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25.5633
18.7900
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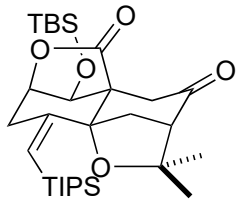
-4.5668
-4.9021


TBS
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TIPS

(*Z*)-**17**

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3.1161
3.0829
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2.7682
2.7591
2.7445
2.7316
2.6503
2.6240
2.6114
2.5977
2.5817
2.3539
2.3242
1.2702
1.2496
1.2198
1.1592
1.1397
1.1214
1.1077
1.0814
1.0699
0.8754
0.1052
0.0892
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5.69
1.00
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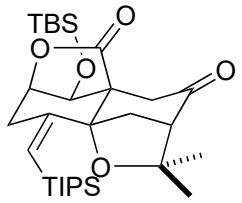
1.03
1.03
2.07
2.07
1.09
PPM


TBS
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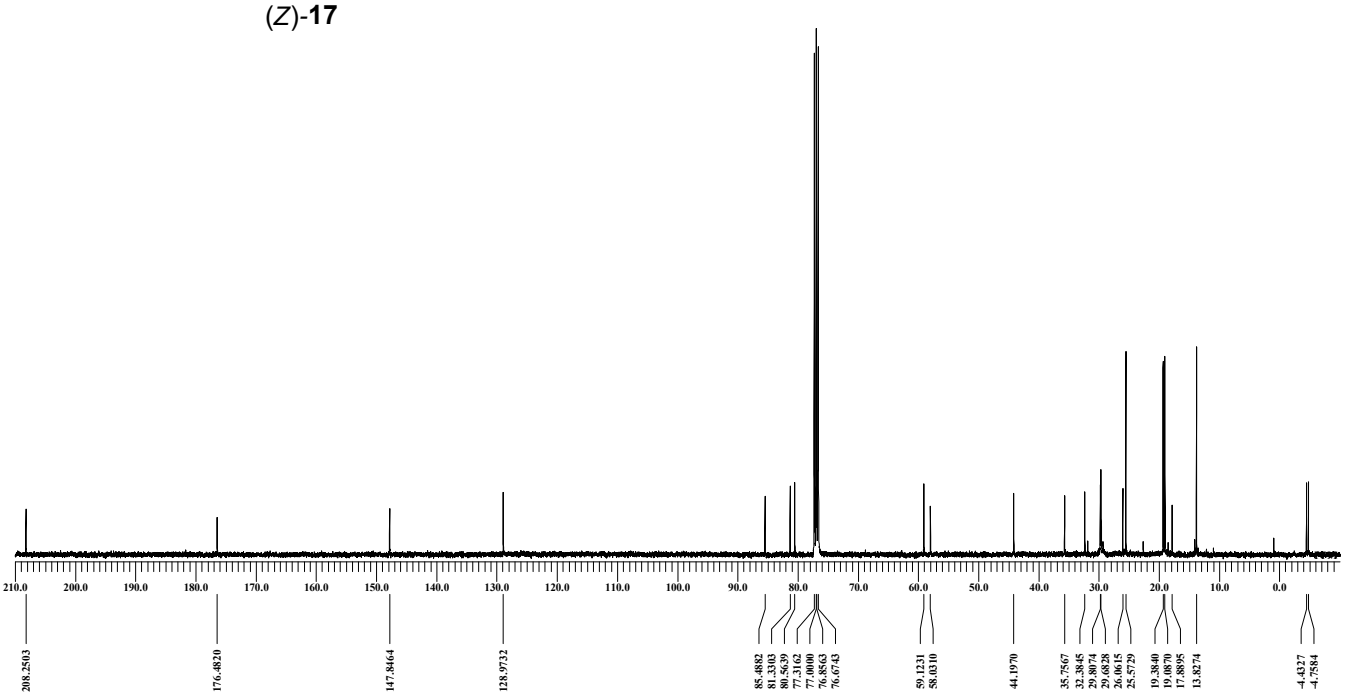
TIPS

(*Z*)-**17**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59.1231
58.0310
44.1970
35.7567
32.3845
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26.0615
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19.0870
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13.8274
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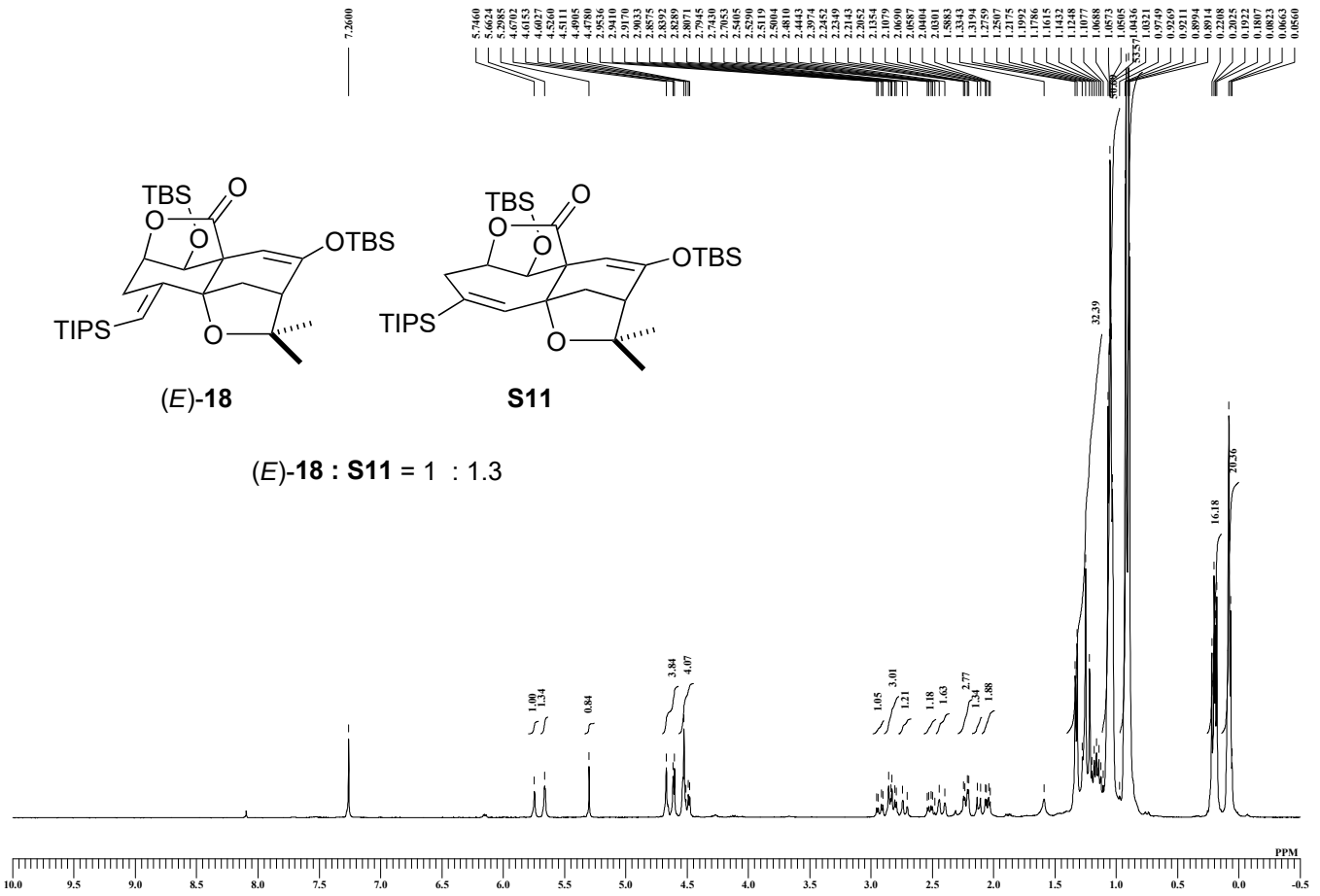
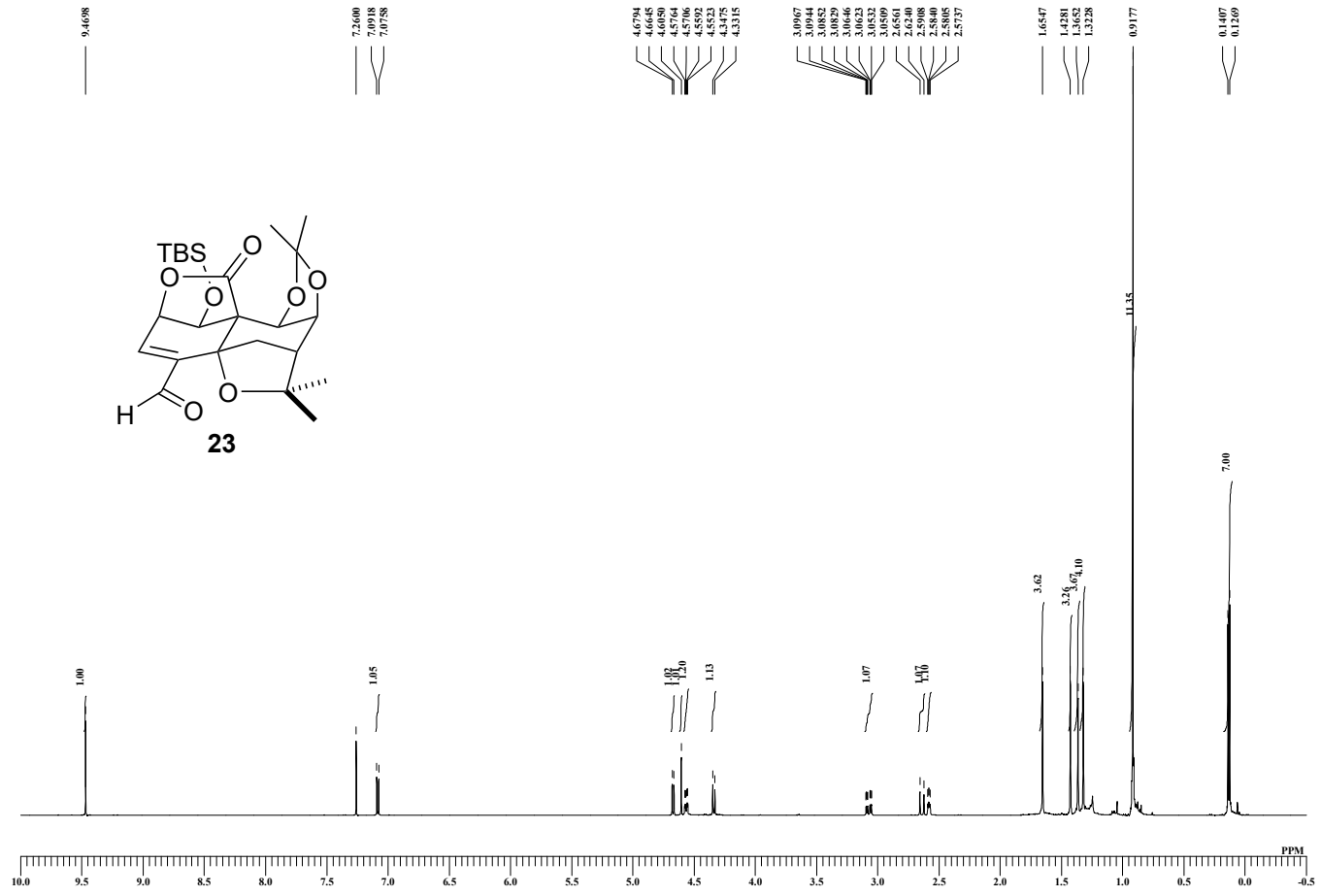
-4.7584



(*E*)-**18**

S11

(*E*)-**18 : S11** = 1 : 1.3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4.5523
4.3475
4.3315
3.0967
3.0944
3.0852
3.0829
3.0646
3.0623
3.0532
3.0509
2.6561
2.6140
2.5908
2.5840
2.5805
2.5737
1.6547
1.4281
1.3652
1.3228
0.9177
0.1407
0.1269
TBS
O
O
O
O
O
O
H
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7.00
3.62
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1.00
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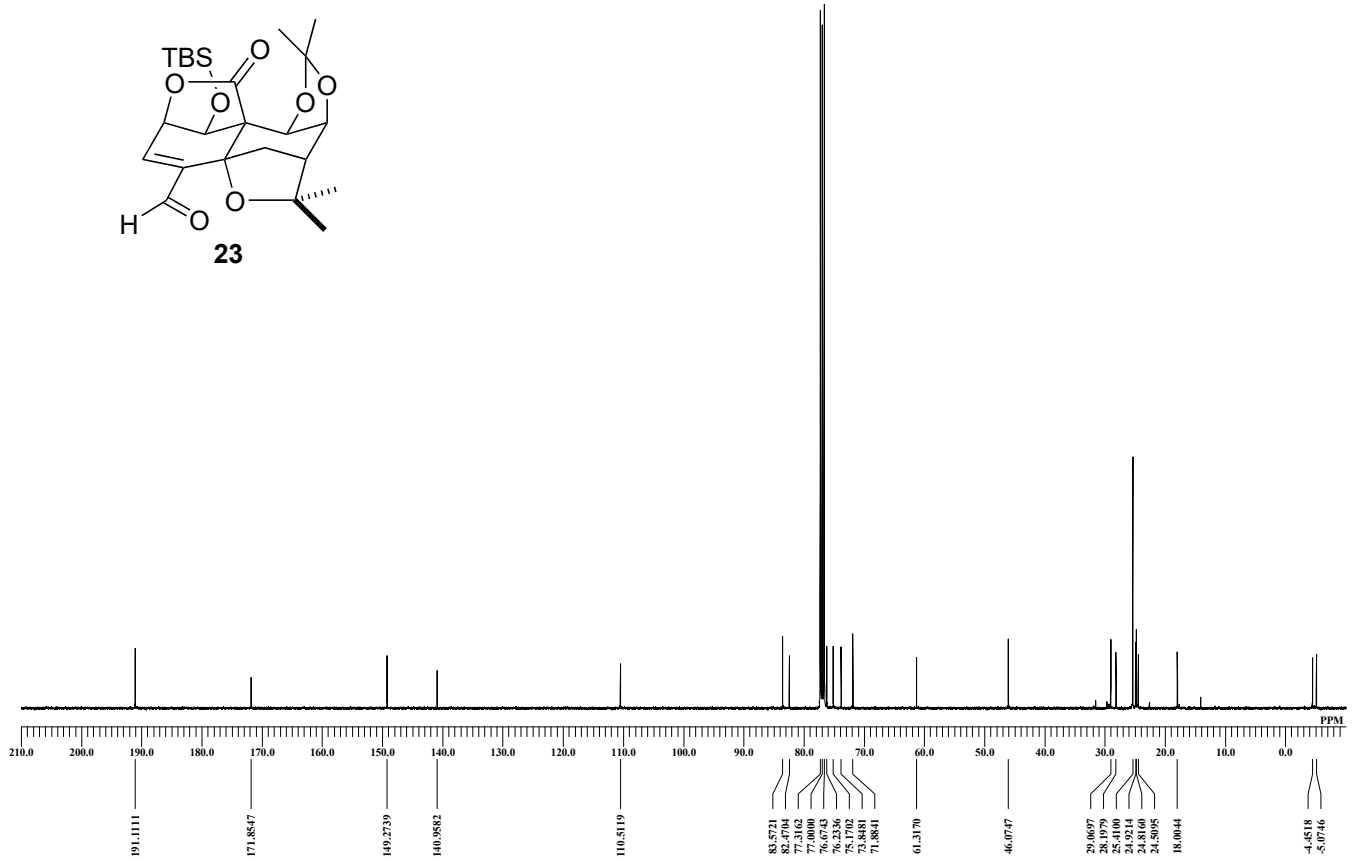
1.13
1.07
PPM


TBS
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O
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H
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23
PPM
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110.5119
83.5721
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77.0000
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61.3170
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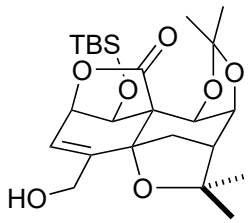
TBS
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24

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4.5672
4.5500
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4.4894
4.4745
4.3452
4.3200
4.1837
4.1701
4.1518
2.7407
2.7076
2.5370
2.3452
2.2338
2.2112
2.2017
1.6616
1.3778
1.3251
1.3217
0.9120
0.1292
0.1132
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2.52
2.13
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0.94
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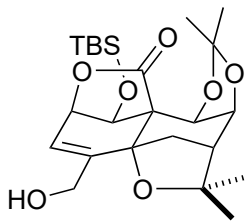
0.96
1.06
PPM


TBS
O
O
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O
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HO

24

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142.4257
127.4313
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84.2770
82.2758
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77.0000
76.7511
76.2340
73.8594
72.0689
61.5173
60.5406
60.5119
45.8431
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25.4484
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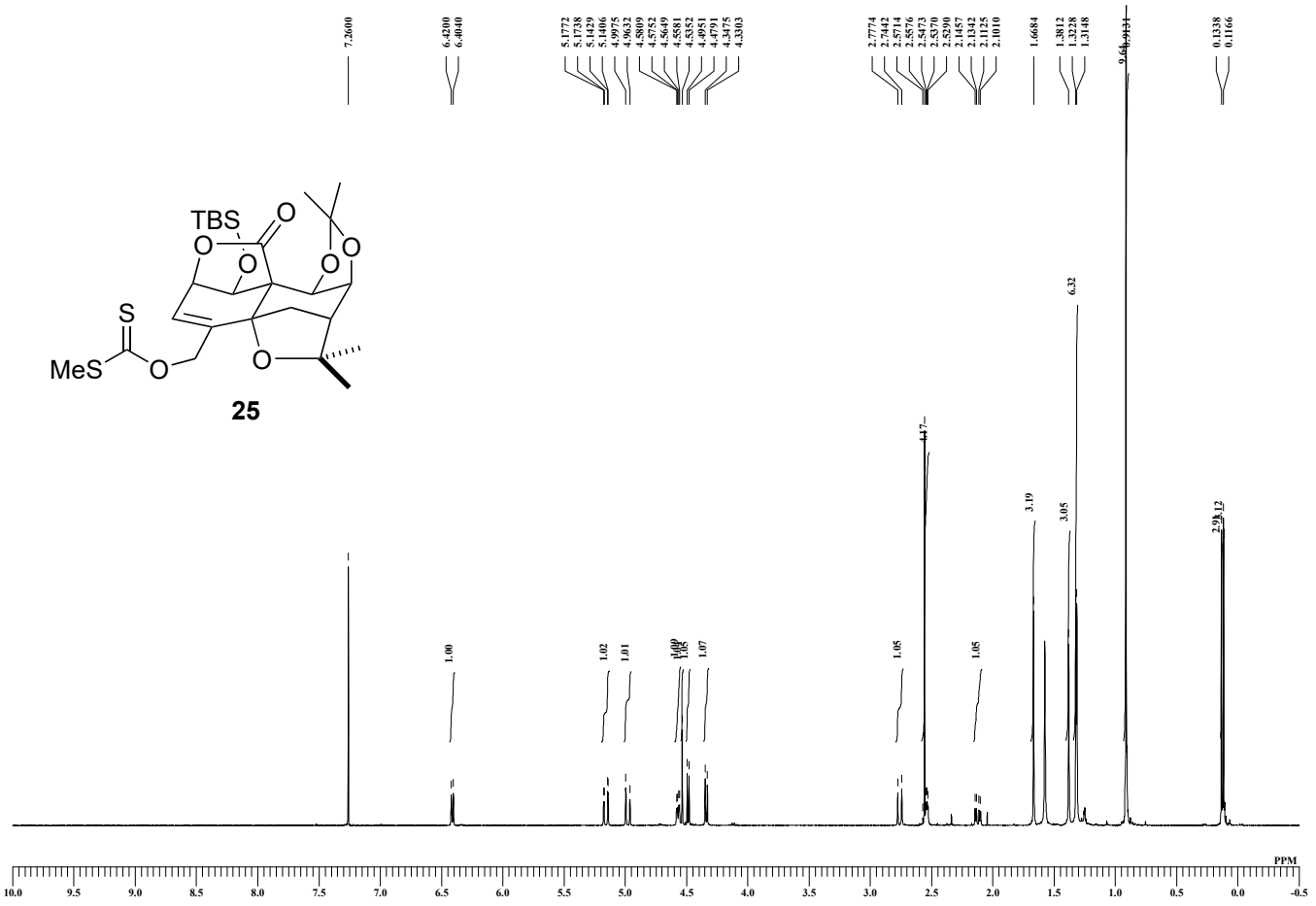
PPM


TBS
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S
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5.1738
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1.01
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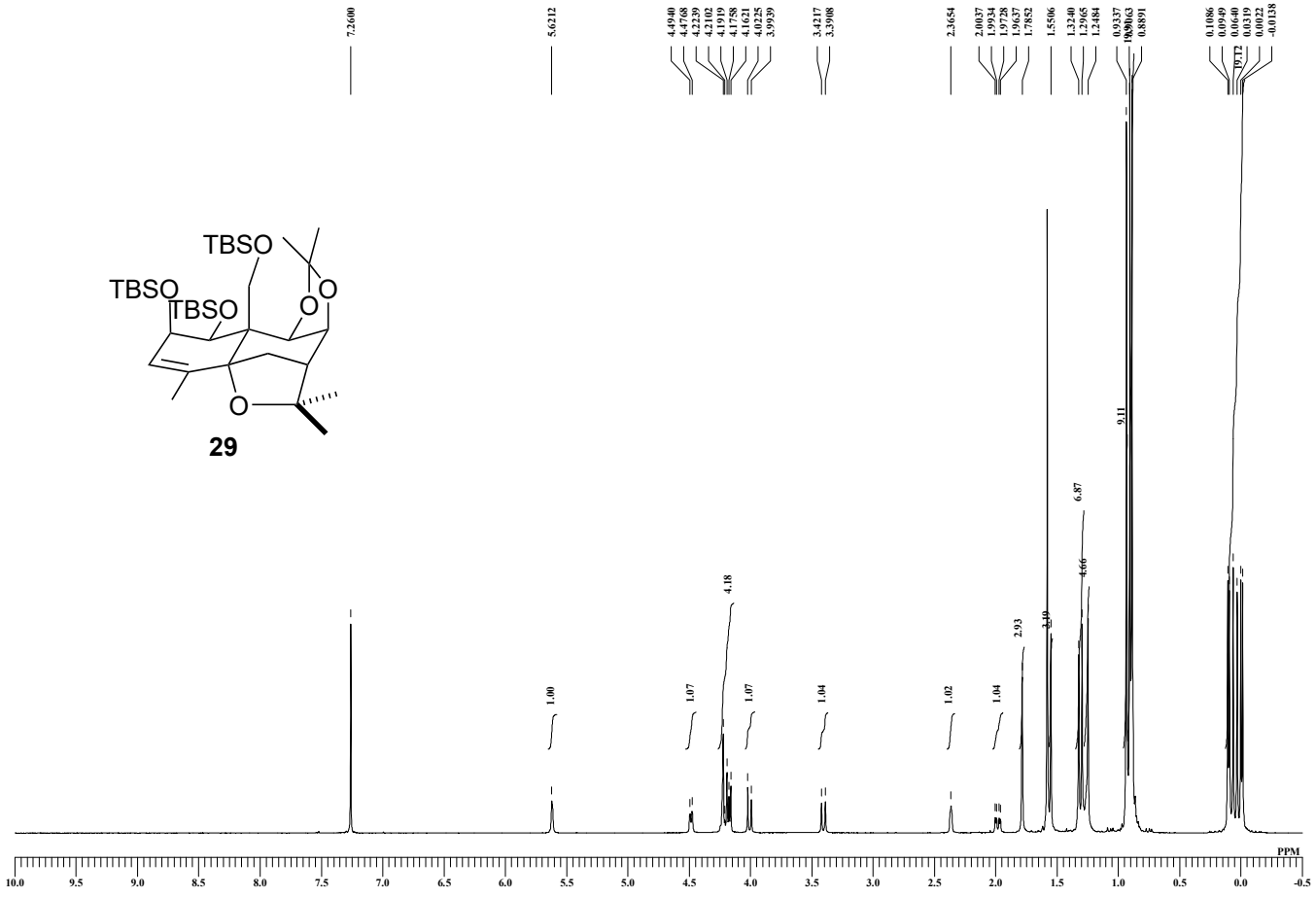
1.05
1.05
PPM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TBSO
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4.1621
4.0225
3.9939
3.4217
3.3908
2.3654
2.0037
1.9934
1.9728
1.9637
1.7852
1.5506
1.3240
1.2965
1.2484
0.9337
0.8891
0.1086
0.0949
0.0640
0.0319
0.0022
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1.04
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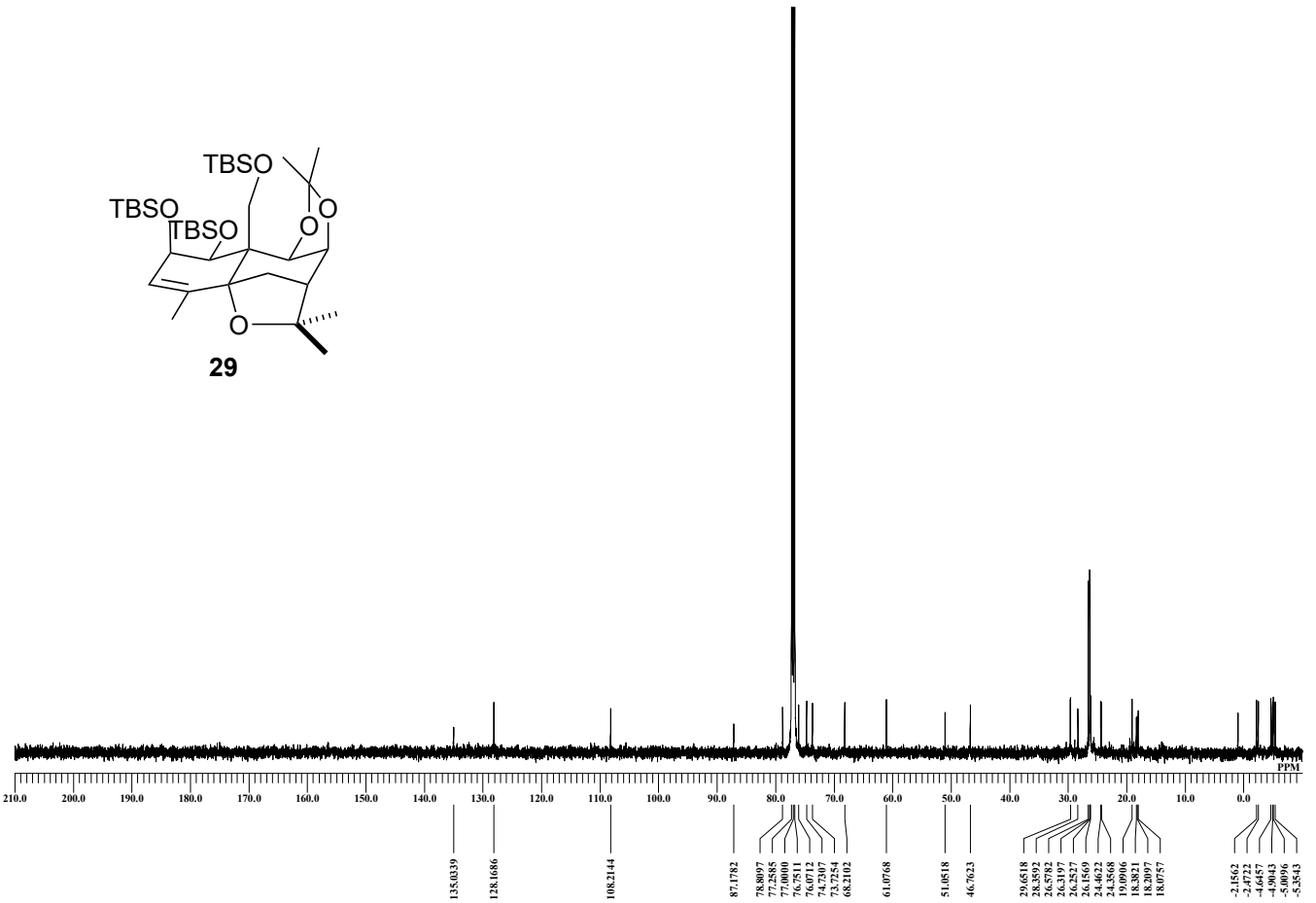
4.66
9.11
PPM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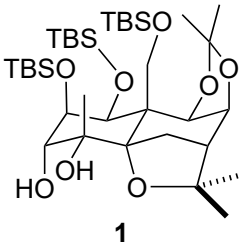
TBS
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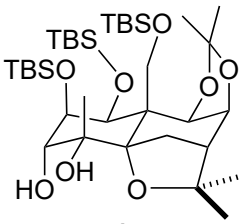
TBS
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HO
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O

1

PPM
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