Total synthesis of (-)-borrelidin

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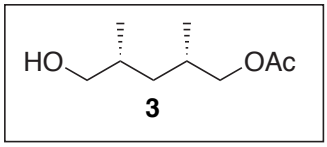
Supporting Information

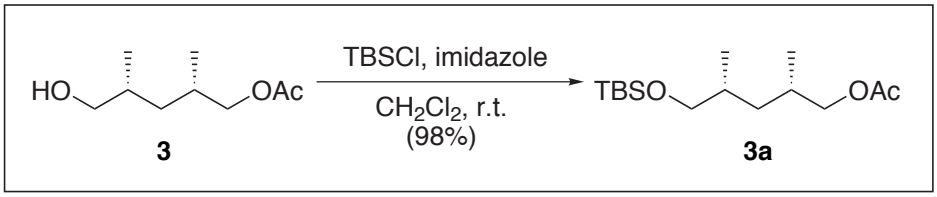
General Information. All non-aqueous reactions were carried out under an inert atmosphere of argon. Organic solvents were dried over molecular sieves 3A or 4A. Other reagents were commercially available and used without further purification. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter with a sodium lamp. Infrared spectra were recorded on a Horiba FT-210 and JASCO FT/IR-460. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a JEOL JNM-EX270. Ambiguous assignments were resolved on the basis of two-dimensional COSY experiments. High-resolution mass spectra were obtained on JEOL JMS-700 (FAB) and JEOL JMS-AX505HA (EI).

(2*R*,4*S*)-5-Acetoxy-2,4-dimethylpentane-1-ol (3)



This compound was prepared according to Mori's procedure. (Fujita, K.; Mori, K. Eur. *J. Org. Chem.* **2001**, *66*, 493-502.)

(2*S*,4*R*)-1-Acetoxy-5-(*tert*-butyldimethylsilyloxy)-2,4-dimethylpentane (3a)

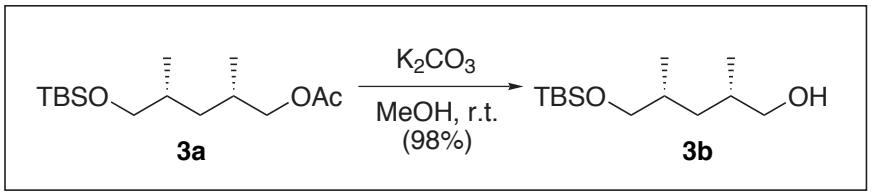


To a solution of **3** (1.01 g, 5.83 mmol) in CH_2Cl_2 (20 ml) were added imidazole (790 mg, 11.6

mmol) and TBSCl (1.30 g, 8.74 mmol) at r.t.. The resulting solution was stirred for 30 min and quenched with water. The aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded **3a** (1.64 g, 98%) as a colorless oil.

$[\alpha]_D^{22}$ = +5.6° (*c* = 0.24, $CHCl_3$); **IR (KBr)** 2956, 2931, 2892, 2888, 1743, 1251, 1238 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.01 (s, 6H, C**H$_3$**Si), 0.87 (s, 9H, C**H$_3$**CSi), 0.88 (d, 3H, *J* = 6.6 Hz, C_4-C**H$_3$**), 0.90 (m, 1H, 1/2 C_3-**H**), 0.92 (d, 3H, *J* = 6.6 Hz, C_2-C**H$_3$**), 1.44 (m, 1H, 1/2 C_3-**H**), 1.67 (m, 1H, C_4-**H**), 1.88 (m, 1H, C_2-**H**), 2.02 (s, 3H, COC**H$_3$**), 3.34 (dd, 1H, *J* = 9.6, 6.3 Hz, 1/2 C_5-**H**), 3.41 (dd, 1H, *J* = 9.6, 5.6 Hz, 1/2 C_5-**H**), 3.80 (dd, 1H, *J* = 10.9, 6.9 Hz, 1/2 C_1-**H**), 3.94 (dd, 1H, *J* = 10.9, 5.3 Hz, 1/2 C_1-**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -5.4, 17.4, 17.8, 18.2, 20.9, 25.9, 30.0, 33.0, 37.4, 68.0, 69.3, 171.2; **HRMS [FAB, m-NBA]** calcd for $C_{15}H_{33}O_3Si$ [M+H$^+$]: 289.2199; found: 289.2193.

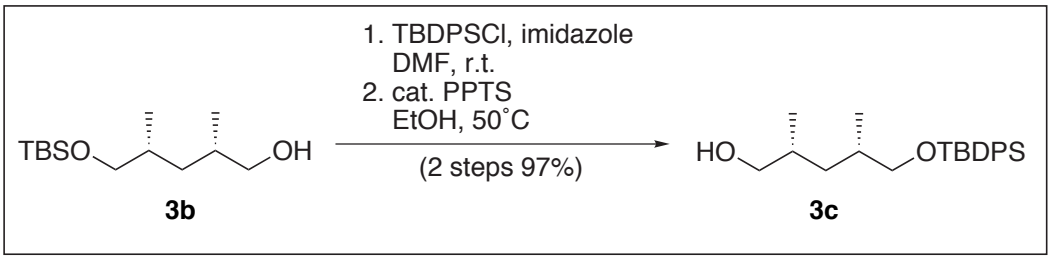
(2*S*,4*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylpentan-1-ol (3b)



To a stirred solution of **3a** (1.64 g, 5.72 mmol) in MeOH (6 ml) was added potassium carbonate (870 mg, 6.29 mmol). The reaction was stirred at r.t. for 2h, and then diluted with water. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (10:1 hexanes/EtOAc) afforded **3b** (1.47 g, 98%) as a colorless oil.

$[\alpha]_D^{22}$ = +0.8° (*c* = 0.32, $CHCl_3$); **IR (KBr)** 3411, 2956, 2929, 2858, 1471, 1255, 1093, 837 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.03 (s, 6H, C**H$_3$**Si), 0.88 (m, 1H, 1/2 C_3-**H**), 0.89 (s, 9H, C**H$_3$**CSi), 0.90 (d, 3H, *J* = 6.6 Hz, C**H$_3$**), 0.93 (d, 3H, *J* = 6.6 Hz, C**H$_3$**), 1.42 (m, 1H, 1/2 C_3-**H**), 1.70 (m, 1H, C**H**), 1.81 (m, 1H, C**H**), 3.32-3.52 (m, 4H, C**H$_2$** x 2); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -5.4, 17.7, 17.8, 18.3, 25.9, 33.2, 33.3, 37.3, 68.1, 68.3; **HRMS [FAB, m-NBA]** calcd for $C_{13}H_{31}O_2Si$ [M+H$^+$]: 247.2093; found: 247.2079.

(2*R*,4*S*)-5-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylpentan-1-ol (3c)

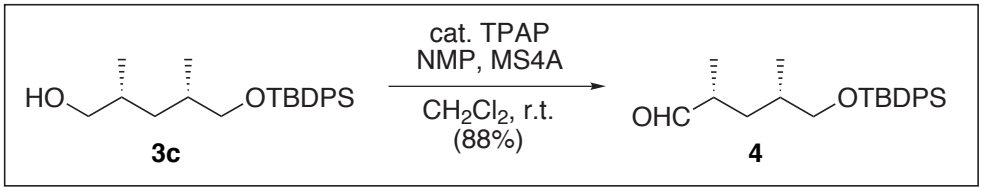


To a solution of **3b** (3.10 g, 12.6 mmol) in DMF (63 ml) were added imidazole (1.70 g, 25.2 mmol) and TBDPSCl (4.9 ml, 18.9 mmol) at 0°C. The reaction was allowed to warm to r.t. and stirred for 30 min. After addition of water, the reaction mixture was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (50:1 hexanes/EtOAc) afforded the corresponding disilyl ether (5.52 g) including unseparable impurities.

To a solution of the disilyl ether in EtOH (40 ml) was added PPTS (1.43 g, 5.70 mmol), and the mixture was allowed to warm up to 50˚C. After 7h, water was added and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (15:1 hexanes/EtOAc) afforded **3c** (4.19 g, 2 steps 97%) as a colorless oil.

$[\alpha]_D^{23}$ = +1.8° (*c* = 0.23, $CHCl_3$); **IR (KBr)** 3455, 2931, 2856, 1112, 1091, 702 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.91 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.95 (m, 1H, 1/2 C_3-**H**), 0.98 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 1.08 (s, 9H, C**H**$_3$CSi), 1.49 (m, 1H, 1/2 C_3-**H**), 1.65 (m, 1H, C**H**), 1.76 (m, 1H, C**H**), 3.36 (dd, 1H, *J* = 10.2, 6.6 Hz, 1/2 C**H**$_2$), 3.45 (m, 1H, 1/2 C**H**$_2$), 3.51 (dd, 1H, *J* = 9.6, 5.3 Hz, 1/2 C**H**$_2$), 3.55 (dd, 1H, *J* = 9.6, 5.3 Hz, 1/2 C**H**$_2$), 7.35-7.72 (m, 10H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 17.4, 17.9, 19.3, 26.9, 33.1, 37.1, 68.2, 68.7, 127.6, 129.5, 134.0, 135.6; **HRMS [FAB, m-NBA]** calcd for $C_{23}H_{35}O_2Si$ [M+H$^+$]: 371.2406; found: 371.2415.

(2R,4S)-5-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethylpentanal (4)

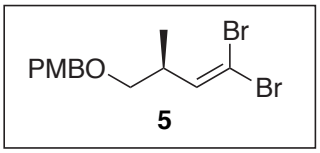


To a solution of **3c** (89.3 mg, 0.241 mmol) in CH_2Cl_2 (2.5 ml) were added dried MS4A (500 mg),

NMO (31.1 mg, 0.265 mmol) and TPAP (4.2 mg, 12.0 μmol) at r.t.. The resulting solution was stirred for 30 min and the reaction mixture was filtered through a silica pad. After evaporation of the filtrate, the residue was purified by flash chromatography (50:1 hexanes/EtOAc) to afford **4** (78.0 mg, 88%) as a colorless oil.

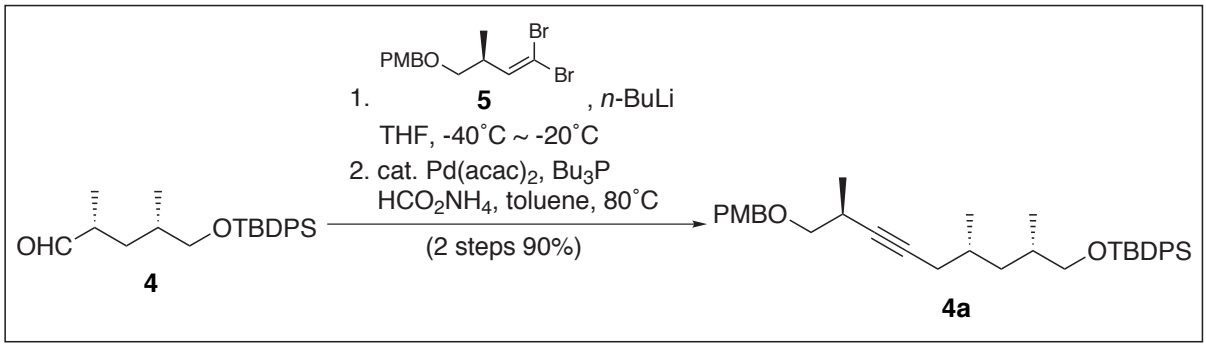
$[\alpha]_D^{23}$ = -6.3° (*c* = 0.40, $CHCl_3$); **IR (KBr)** 2960, 2931, 2858, 1727, 1427, 1112, 1089 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.94 (d, 3H, *J* = 6.6 Hz, C_4-C**H$_3$**), 1.04 (d, 3H, *J* = 6.6 Hz, C_2-C**H$_3$**), 1.06 (s, 9H, C**H$_3$**CSi), 1.14 (m, 1H, 1/2 C_3-**H**), 1.75 (m, 1H, C_4-**H**), 1.90 (m, 1H, 1/2 C_3-**H**), 2.39 (m, 1H, C_2-**H**), 3.49 (d, 2H, *J* = 5.6 Hz, C_5-**H**), 7.34-7.70 (m, 10H, Ar**H**), 9.54 (d, 1H, *J* = 2.3 Hz, C**H**O); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 14.1, 17.2, 19.3, 26.9, 33.3, 34.5, 44.1, 68.4, 127.6, 129.6, 133.7, 135.6, 205.2; **HRMS [FAB, m-NBA]** calcd for $C_{23}H_{32}O_2Si$ [M^+]: 368.2171; found: 368.2142.

(3*S*)-1,1-Dibromo-4-(4'-methoxybenzyloxy)-3-methylbut-1-ene (5)



This compound was prepared by using a known method. (Paquette, L. A.; Guevel, R.; Sakamoto, S.; Kim, I. H.; Crawford, J. *J. Org. Chem.* **2003**, *68*, 6096-6107.)

(2*S*,6*R*,8*S*)-9-(*tert*-Butyldiphenylsilyloxy)-1-(4'-methoxybenzyloxy)-2,6,8-trimethylnona-3-yne (4a)



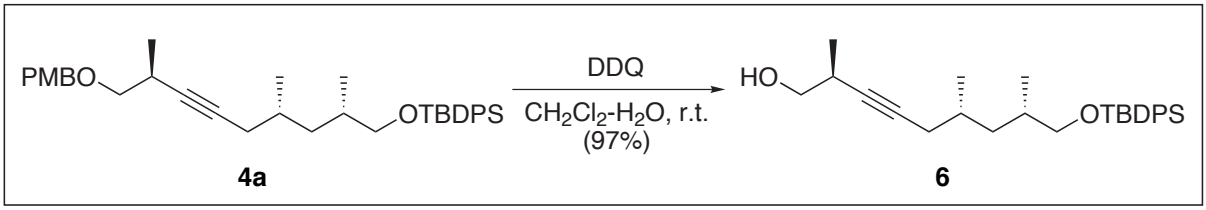
To a solution of **5** (83.0 mg, 0.229 mmol) in THF (700 μl) was added *n*-BuLi (1.58 M solution in hexane, 290 μl, 0.459 mmol) at –78˚C, and the mixture was allowed to warm up to –40˚C. The reaction was stirred for 1 h, and then treated with a solution of **4** (56.3 mg, 0.153 mmol) in THF

(700 μl). The reaction was continued for 1 h at –30˚C, and methyl chloroformate (90 μl, 1.15 mmol) was added at –20˚C. The reaction was quenched with sat. aq. NH_4Cl, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded the corresponding carbonate (100.8 mg) including unseparable impurities.

To a solution of palladium acetylacetonate (2.3 mg, 7.65 μmol) and tributylphosphine (8 μl, 30.6 μmol) in toluene (700 μl) were added a solution of the crude carbonate in toluene (700 μl) and ammonium formate (24.1 mg, 0.382 mmol). The resulting solution was warmed up to 70˚C and stirred for 1 hr. Concentration in vacuo gave a yellow oil, which upon flash chromatography (50:1 hexanes/EtOAc) afforded **4a** (76,3 mg, 2 steps 90%) as a colorless oil.

$[\alpha]_D^{24}$ = -3.1˚ (*c* = 0.29, $CHCl_3$); **IR (KBr)** 2910, 2898, 2856, 1513, 1459, 1112, 1106, 1091 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.95 (d, 6H, *J* = 6.6 Hz, C_6-C**H$_3$** and C_8-C**H$_3$**), 0.98 (m, 1H, 1/2 C_7-**H**), 1.08 (s, 9H, C**H$_3$**CSi), 1.17 (d, 3H, *J* = 6.9 Hz, C_2-C**H$_3$**), 1.46 (m, 1H, 1/2 C_7-**H**), 1.68 (m, 1H, C_6-**H**), 1.75 (m, 1H, C_8-**H**), 1.97 (ddd, 1H, *J* = 16.2, 7.3, 1.7 Hz, 1/2 C_5-**H**), 2.15 (ddd, 1H, *J* = 16.5, 4.9, 1.7 Hz, 1/2 C_5-**H**), 2.70 (m, 1H, C_2-**H**), 3.30 (m, 1H, 1/2 C_1-**H**), 3.48 (m, 3H, C_9-**H** and 1/2 C_1-**H**), 3.81 (s, 3H, OC**H$_3$**), 4.48 (s, 2H, C**H$_2$**Ph), 6.89 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.28 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.37-7.71 (m, 10H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ ; 17.5, 18.3, 19.3, 20.1, 25.9, 26.7, 26.9, 30.1, 33.2, 40.1, 55.2, 69.0, 72.6, 74.3, 79.7, 83.0, 113.7, 127.5, 129.2, 129.5, 130.5, 134.0, 135.6, 159.1 **HRMS [FAB, m-NBA]** calcd for $C_{36}H_{48}O_3Si$ [M+H$^+$]: 556.3372; found: 556.3364.

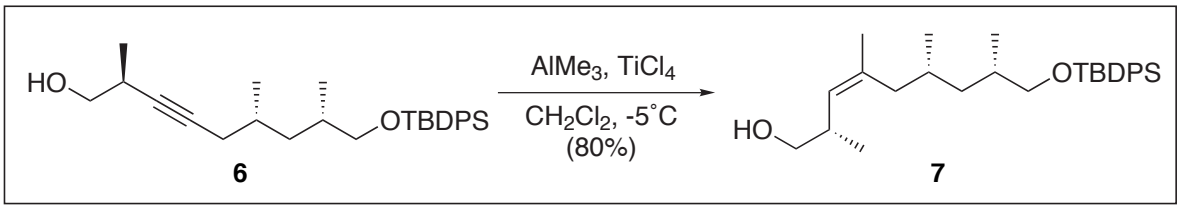
(2*S*,6*R*,8*S*)-9-(*tert*-Butyldiphenylsilyloxy)-2,6,8-trimethylnona-3-yn-1-ol (6)



To a solution of **4a** (648.6 mg, 1.16 mmol) in CH_2Cl_2 (12 ml) and H_2O (1.2 ml) was added DDQ (344.0 mg, 1.51 mmol) at r.t.. The reaction mixture was stirred for 30 min, and then diluted with water. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded **6** (494.1 mg, 97%) as a colorless oil.

$[\alpha]_D^{24}$ = -11.6° (*c* = 0.26, $CHCl_3$); **IR (KBr)** 3644, 2964, 2960, 2931, 2325, 1112, 761 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.96 (d, 6H, *J* = 6.6 Hz, C_6-C**H**$_3$ and C_8-C**H**$_3$), 0.98 (m, 1H, 1/2 C_7-**H**), 1.08 (s, 9H, C**H**$_3$CSi), 1.14 (d, 3H, *J* = 6.9 Hz, C_2-C**H**$_3$), 1.47 (m, 1H, 1/2 C_7-**H**), 1.70 (m, 1H, C_6-**H**), 1.75 (m, 1H, C_8-**H**), 1.98 (ddd, 1H, *J* = 16.5, 6.9, 1.7 Hz, 1/2 C_5-**H**), 2.17 (ddd, 1H, *J* = 16.1, 5.0, 1.7 Hz, 1/2 C_5-**H**), 2.64 (m, 1H, C_2-**H**), 3.49 (m, 4H, C_1-**H** and C_9-**H**), 7.37-7.71 (m, 10H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 17.3, 17.5, 19.3, 20.2, 25.8, 26.9, 29.5, 30.0, 33.2, 40.1, 67.1, 68.9, 81.1, 82.4, 127.6, 129.5, 134.0, 135.6; **HRMS [FAB, m-NBA]** calcd for $C_{28}H_{40}O_2SiNa$ [M+Na^+]: 459.2695; found: 459.2677.

(2*S*,6*R*,8*S*)-9-(*tert*-Butyldiphenylsilyloxy)-2,4,6,8-tetramethylnona-3*Z*-en-1-ol (7)

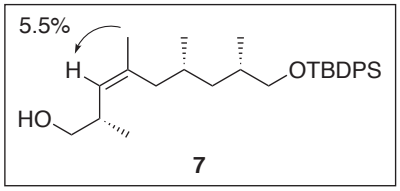


To a solution of trimethylaluminium (1.0 M solution in hexanes, 6.2 ml, 6.20 mmol) was added a solution of **6** (672.5 mg, 1.54 mmol) in CH_2Cl_2 (3 ml) at 0°C. The mixture was allowed to warm to r.t., stirred for 20 min, and then cooled to –15°C. The resulting solution was treated with titanium tetrachloride (1.0 M solution in CH_2Cl_2, 3.1 ml, 3.10 mmol) and continued for 15 min. The reaction was cooled to –40°C and then cautiously quenched with ice-cooled MeOH (3 ml) followed by Celite® (10 g) and $Na_2SO_4 \cdot 10H_2O$ (10 g). The mixuture was allowed to warm to r.t. and stirred for 2 hr. The mixture was filtered through Celite® and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (40:1 hexanes/EtOAc) to afford **7** (557.1 mg, 80%) as a colorless oil.

$[\alpha]_D^{24}$ = -9.1° (*c* = 0.17, $CHCl_3$); **IR (KBr)** 3444, 2960, 2931, 2896, 2869, 1473, 1459, 1450, 1427, 1105 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.77 (d, 3H, *J* = 6.3 Hz, C_6-C**H**$_3$), 0.90 (d, 3H, *J* = 6.6 Hz, C_2-C**H**$_3$), 0.95 (d, 3H, *J* = 6.6 Hz, C_8-C**H**$_3$), 0.98 (m, 1H, 1/2 C_7-**H**), 1.06 (s, 9H, C**H**$_3$CSi), 1.34 (m, 1H, 1/2 C_7-**H**), 1.66 (s, 3H, C_4-C**H**$_3$), 1.70 (m, 1H, C_6-**H**), 1.79 (m, 1H, C_8-**H**), 1.90 (m, 2H, C_5-**H**), 2.62 (m, 1H, C_2-**H**), 3.28 (dd, 1H, *J* = 10.2, 8.2 Hz, 1/2 C_1-**H**), 3.43 (m, 2H, 1/2 C_1-**H** and 1/2 C_9-**H**), 3.52 (dd, 1H, *J* = 9.8, 5.1 Hz, 1/2 C_9-**H**), 4.93 (d, 1H, *J* = 9.6 Hz, C_3-**H**), 7.30-7.70 (m, 10H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 17.1, 17.7, 19.3, 19.7, 23.7, 27.0, 28.3, 33.2, 35.2, 39.5, 41.5, 67.9, 68.9, 127.5, 128.8, 129.5, 134.0, 135.5, 137.0; **HRMS [FAB, m-**

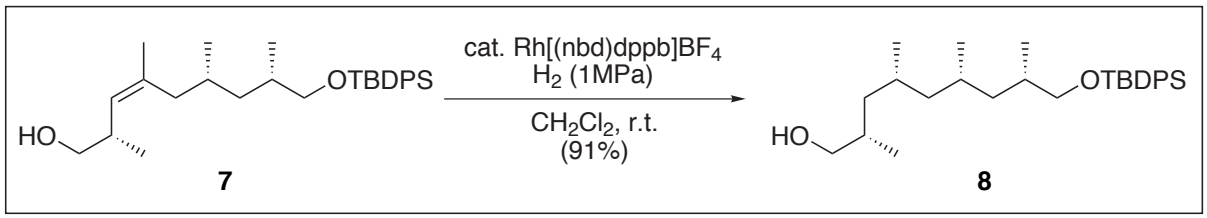
NBA] calcd for $C_{29}H_{44}O_2SiNa$ [M+Na$^+$]: 475.3008; found: 475.3022.

The stereochemistry of C8-9 olefin was determined by NOE experiment.



NOE experiment of **7**

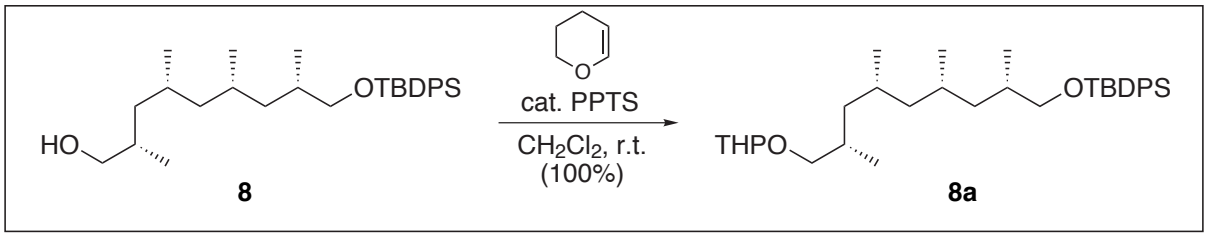
(2*S*,4*R*,6*S*,8*S*)-9-(*tert*-Butyldiphenylsilyloxy)–2,4,6,8–tetramethylnonan-1-ol (8)



A solution of **7** (941.3 mg, 2.08 mmol) and Rh[(nbd)dppb]BF_4 (147.5 mg, 0.208 mmol) in CH_2Cl_2 (4 ml) was stirred under 1 Mpa of H_2 gas for 2 hr. The resulting solution was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (40:1 hexanes/EtOAc) to afford **8** (928.5 mg, 91%) as a colorless oil.

$[\alpha]_D^{25}$ = -16.6° (*c* = 0.15, $CHCl_3$); **IR (KBr)** 3425, 2958, 2929, 2858, 1461, 1427, 1112, 1081 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.83 (d, 3H, *J* = 6.3 Hz, C**H**$_3$), 0.84 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.85 (m, 1H, 1/2 C**H**$_2$), 0.89 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 0.93 (m, 1H, 1/2 C**H**$_2$), 0.95 (d, *J* = 6.6 Hz, C**H**$_3$), 1.03 (m, 2H, C**H**$_2$), 1.07 (s, 9H, C**H**$_3$CSi), 1.12 (m, 1H, 1/2 C**H**$_2$), 1.33 (m, 1H, 1/2 C**H**$_2$), 1.52 (m, 1H, C**H**), 1.57 (m, 1H, C**H**), 1.70 (m 2H, C**H** x 2), 3.36-3.59 (m, 4H, C**H**$_2$ x 2), 7.30-7.74 (m, 10H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 16.0, 18.0, 19.2, 20.2, 20.5, 26.8, 27.0, 27.4, 33.1, 33.2, 39.9, 41.5, 46.1, 68.8, 69.2, 127.5, 129.4, 134.0, 135.5; **HRMS [FAB, m-NBA]** calcd for $C_{29}H_{46}O_2SiNa$ [M+Na$^+$]: 477.3164; found: 477.3266.

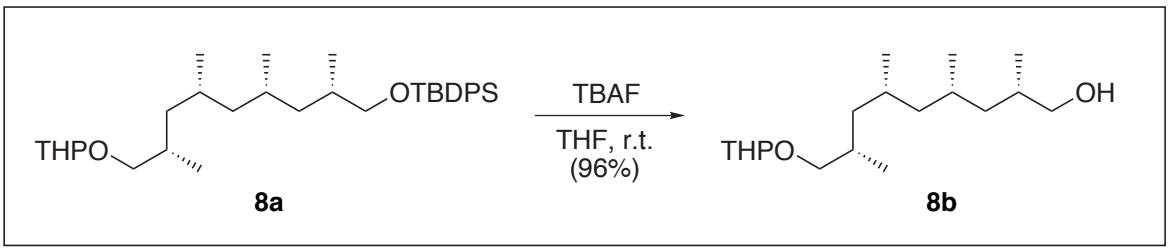
(2*S*,4*S*,6*R*,8*S*)-1-(*tert*-Butyldiphenylsilyloxy)-2,4,6,8-tetramethyl-9-(tetrahydropyran-2'-yloxy)nonane (8a)



To a solution of **8** (928. 5 mg, 2.05 mmol) in CH_2Cl_2 (20 ml) were added dihydropyrane (1.85 ml, 20.5 mmol) and PPTS (51 mg, 0.205 mmol). The resulting solution was stirred at r.t. for 2 hr. The reaction was quenched with sat. aq. $NaHCO_3$ solution and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (50:1 hexanes/EtOAc) afforded **8a** (1.10 g, 100%) as a colorless oil.

$[\alpha]_D^{25}$ = -10.5° (*c* = 0.19, $CHCl_3$); **IR (KBr)** 3450, 2956, 2929, 2366, 1473, 1461, 1079 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.82 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.83 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.84 (m, 1H, 1/2 C**H**$_2$), 0.91 (d, 3H, *J* = 6.3 Hz, C**H**$_3$), 0.92 (m, 1H, 1/2 C**H**$_2$), 0.94 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 1.03 (m, 2H, C**H**$_2$), 1.07 (s, 9H, C**H**$_3$CSi), 1.09 (m, 1H, 1/2 C**H**$_2$), 1.29 (m, 1H, 1/2 C**H**$_2$), 1.47-1.80 (m, 10H, THP(6H) and C**H** x 4), 3.17 (m, 1H, THP(1H)), 3.39-3.61 (m, 4H, 1/2 C**H**$_2$, C**H**$_2$ and THP(1H)), 3.87 (m, 1H, 1/2 C**H**$_2$), 4.58 (m, 1H, THP(1H)), 7.35-7.71 (m, 10H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 16.7, 16.8, 17.9, 18.0, 19.3, 19.5, 19.6, 20.3, 20.6, 20.7, 25.6, 26.8, 27.0, 27.1, 27.4, 30.7, 30.8, 30.9, 33.1, 40.6, 41.4, 46.1, 62.0, 62.2, 68.8, 73.8, 74.0, 98.6, 99.0, 127.5, 129.5, 134.1, 135.6; **HRMS [FAB, m-NBA]** calcd for $C_{34}H_{54}O_3SiNa$ [M+Na^+]: 561.3739; found: 561.3741.

(2*S*,4*S*,6*R*,8*S*)–2,4,6,8–Tetramethyl-9-(tetrahydropyran-2'-yloxy)nonan-1-ol (8b)

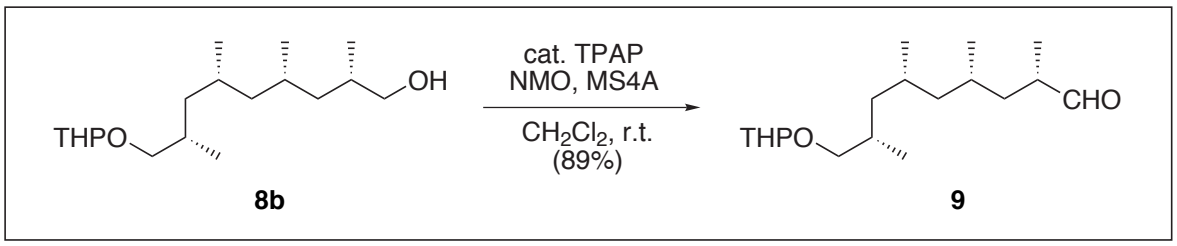


To a stirred solution of **8a** (1.10 g, 2.05 mmol) in THF (20 ml) was added TBAF (1.0 M solution

in THF, 5 ml, 5.00 mmol). The resulting solution was stirred for 3 hr, quenched with sat. aq. NH_4Cl solution, and extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (10:1 hexanes/EtOAc) afforded **8b** (590.3 mg, 96%) as a colorless oil.

$[\alpha]_D^{25}$ = -13.7° (*c* = 0.29, $CHCl_3$); **IR (KBr)** 3422, 2957, 2922, 2871, 2359, 1457, 1377, 1261, 1201, 1118 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.81 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 0.84 (d, 3H, *J* = 7.3 Hz, C**H**$_3$), 0.89 (d, 3H, *J* = 6.0 Hz, C**H**$_3$), 0.90 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 0.92 (m, 2H, 1/2 C**H**$_2$ x 2), 1.01-1.32 (m, 4H, 1/2 C**H**$_2$ x 2 and C**H**$_2$), 1.48-1.86 (m, 10H, C**H** x 4 and THP(6H)), 3.15 (m, 1H, THP(1H)), 3.34 (dd, 1H, *J* = 10.2, 6.9 Hz, 1/2 C**H**$_2$), 3.41-3.58 (m, 3H, THP(1H) and 1/2 C**H**$_2$ x 2), 3.84 (m, 1H, 1/2 C**H**$_2$), 4.54 (m, 1H, THP(1H)); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** 16.7, 16.8, 17.4, 17.5, 19.4, 19.6, 20.3, 20.6, 20.8, 25.5, 27.1, 27.2, 27.4, 30.6, 30.7, 30.8, 33.0, 40.5, 41.3, 45.8, 62.0, 68.1, 68.2, 73.6, 73.9, 98.6, 99.0; **HRMS [FAB, m-NBA]** calcd for $C_{18}H_{37}O_3$ [M+H$^+$]: 301.2742; found: 301.2746.

(2*S*,4*S*,6*R*,8*S*)–2,4,6,8–Tetramethyl-9-(tetrahydropyran-2'-yloxy)nonanal (9)



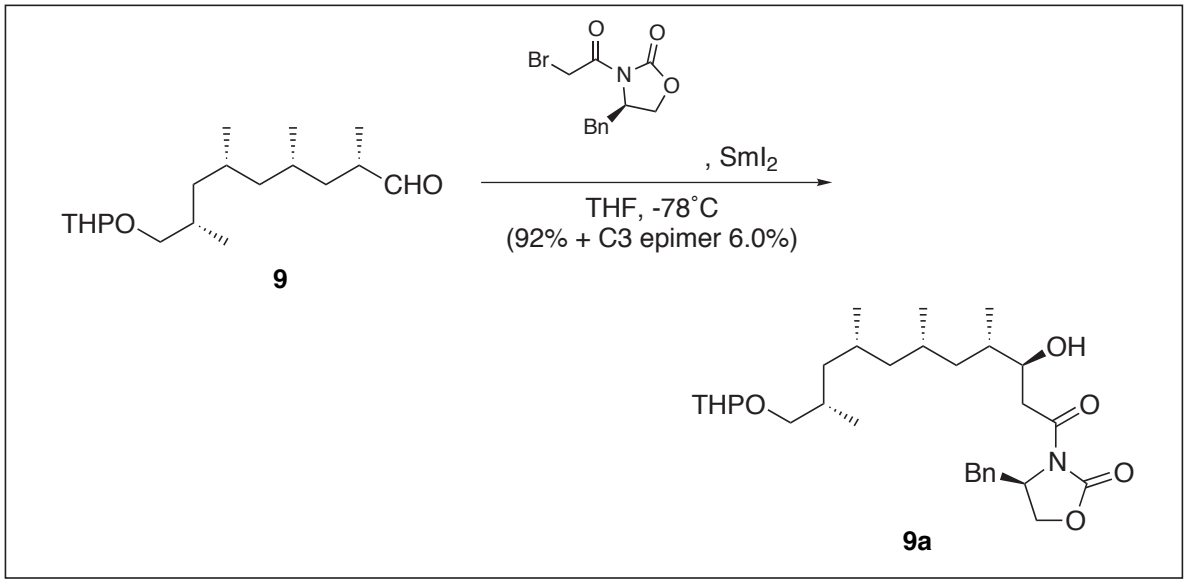
8b **9**

To a solution of **8b** (388.6 mg, 1.30 mmol) in CH_2Cl_2 (13 ml) were added MS4A (1 g), NMO (321 mg, 2.70 mmol) and TPAP (24.0 mg, 68.5 μmol). The reaction was stirred at r.t. for 30 min, and then filtered through a silica pad. After evaporation of the filtrate, the residue was purified by flash chromatography (40:1 hexanes/EtOAc) to afford **9** (343.6 mg, 89%) as a colorless oil.

$[\alpha]_D^{25}$ = +1.0° (*c* = 0.14, $CHCl_3$); **IR (KBr)** 2955, 2873, 1734, 1488, 1457, 1261, 1031 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.81 (d, 3H, *J* = 6.3 Hz, C**H**$_3$), 0.87 (d, 6H, *J* = 6.3 Hz, C**H**$_3$ x 2), 1.00-1.07 (m, 5H, C**H**$_2$ x 2 and 1/2 C**H**$_2$), 1.16 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 1.47-1.87 (m, 10H, THP(6H), C**H** x 3 and 1/2 C**H**$_2$), 2.56 (m, 1H, C**H**), 3.16 (m, 1H, THP(1H)), 3.40-3.58 (m, 2H, 1/2 C**H**$_2$ and THP(1H)), 3.85 (m, 1H, 1/2 C**H**$_2$), 4.56 (m, 1H, THP(1H)), 9.57 (d, 1H, *J* = 2.3 Hz, C**H**O); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 16.8, 16.9, 18.0, 19.4, 19.6, 19.8, 20.1, 25.5, 27.0, 27.1, 28.0, 30.6, 30.7, 30.8, 37.2, 40.9, 41.1, 45.9, 62.0, 62.2, 73.6, 73.9, 98.6, 99.0, 182.7; **HRMS**

[FAB, m-NBA] calcd for $C_{18}H_{34}O_3Na$ [M+Na$^+$]: 321.2405; found: 321.2391.

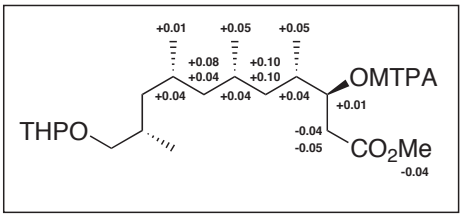
(3'*S*,4*R*,4'*S*,6'*S*,8'*R*,10'*S*)-4-Benzyl-3-[3'-hydroxy-4',6',8',10'-tetramethyl-11'-(tetrahydropyran-2''-yloxy)undecanoyl]-2-oxazolidinone (9a)



To a solution of samarium iodide (0.1 M solution in THF, 58.0 ml, 5.80 mmol) were added **9** (343.6 mg, 1.15 mmol) and (*R*)-4-benzyl-3-bromoacetyl-2-oxazolidinone (376.0 mg, 1.26 mmol) in THF (11 ml) at –78˚C. The reaction was stirred for 20 min and then treated with hexane (100 ml) followed by silica gel (50 g). The mixture was allowed to warm to r.t. and stirred for 30 min. The mixture was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (5:1 hexanes/EtOAc) to afford **9a** (550.7 mg, 92%) along with its epimer (40.0 mg, 6.2%).

$[\alpha]_D^{26}$ = -43.8° (*c* = 0.25, $CHCl_3$); **IR (KBr)** 3566, 2955, 1785, 1698, 1456, 1386, 1199, 1030 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.85 (d, 3H, *J* = 5.9 Hz, C**H$_3$**), 0.87 (d, 3H, *J* = 5.3 Hz, C**H$_3$**), 0.89 (d, 3H, *J* = 5.0 Hz, C**H$_3$**), 0.93 (d, 3H, *J* = 6.3 Hz, C**H$_3$**), 0.98-1.14 (m, 3H, C**H$_2$** and 1/2 C**H$_2$**), 1.25 (m, 2H, C**H$_2$**), 1.42-174 (m, 10H, THP(6H), C**H**x3 and 1/2 C**H$_2$**), 1.83 (m, 1H, C**H**), 2.79 (dd, 1H, *J* = 13.2, 9.6 Hz, 1/2 C**H$_2$**Ph), 3.07 (d, 2H, *J* = 6.3 Hz, $C_{2'}$-**H**), 3.19 (m, 1H, THP(1H)), 3.31 (dd, 1H, *J* = 13.2, 2.6 Hz, 1/2 C**H$_2$**Ph), 3.48 (m, 1H, 1/2 $C_{11'}$-**H**), 3.54 (m, 1H, THP(1H)), 3.86 (m, 1H, 1/2 $C_{11'}$-**H**), 4.10 (m, 1H, $C_{4'}$-**H**), 4.21 (m, 2H, NCHC**H$_2$**), 4.57 (m, 1H, THP(1H)), 4.69 (m, 1H, NC**H**), 7.18-7.36 (m, 5H, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 14.5, 16.7, 16.8, 19.4, 19.6, 20.3, 20.7, 25.5, 27.1, 27.2, 30.6, 30.8, 30.9, 35.2, 37.9, 40.4, 40.5, 40.9,

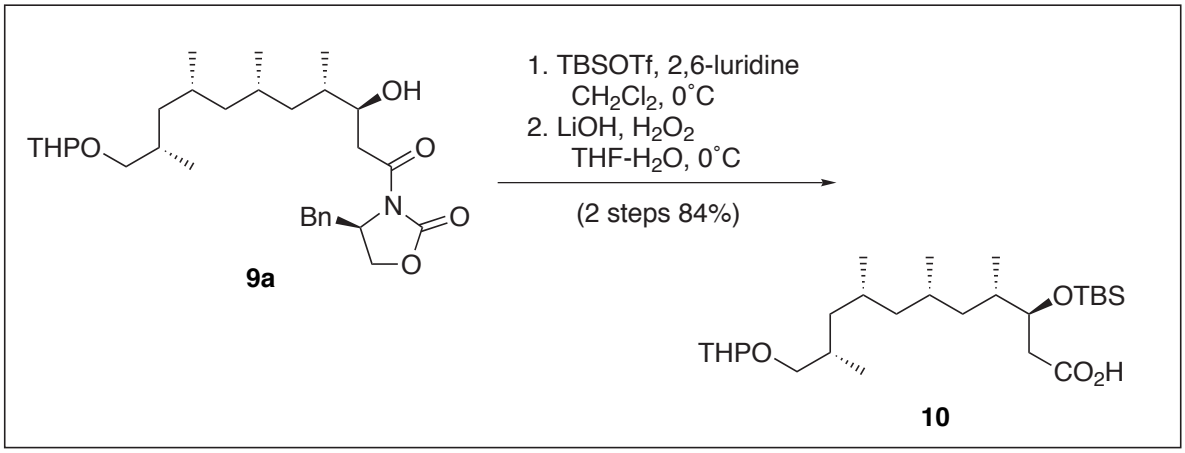
45.6, 55.1, 62.2, 61.9, 66.3, 70.2, 70.3, 73.7, 73.9, 98.6, 99.0, 127.3, 128.9, 129.3, 135.1, 153.4, 173.1; **HRMS [FAB, m-NBA]** calcd for $C_{30}H_{47}O_6NNa$ [M+Na$^+$]: 540.3301; found: 540.3309. Absolute configuration of C3 was determined by modified Mosher ester analysis.*



$\Delta\delta = (\delta_S - \delta_R)$ for (*R*)- and (*S*)-MTPA derivatives

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

(3*S*,4*S*,6*S*,8*R*,10*S*)-3-(*tert*-Butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-(tetrahydropyran-2'-yloxy)undecanoic acid (10)

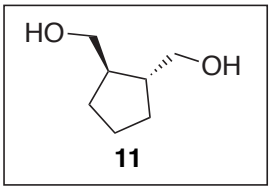


To a 0˚C stirred solution of **9a** (453.0 mg, 0.876 mmol) in CH_2Cl_2 (9 ml) was added 2,6-lutidine (170 μl, 1.49 mmol) followed by TBSOTf (260 μl, 1.14 mmol). After 30 min, the reaction was quenched with water and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. This residue was employed in the next reaction without further purification. The resulting silyl ether was dissolved in THF (6 ml) and H_2O (2 ml) at 0˚C. Lithium hydroxide (72.9 mg, 1.74 mmol) and hydrogen peroxide (30% solution in H_2O, 590 μl, 5. 21 mmol) were added to the solution. After 3 hr, the reaction was quenched with sat. aq. $Na_2S_2O_3$ solution, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in

vacuo. Flash chromatography (5:1 hexanes/EtOAc) afforded **10** (347.4 mg, 2 steps 84%) as a colorless oil.

$[\alpha]_D^{27}$ = -31.5° (*c* = 0.24, $CHCl_3$); **IR (KBr)** 3444, 2955, 2927, 1789, 1456, 1385, 1350, 1250, 1031 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.02 (s, 3H, C**H**$_3$Si), 0.05 (s, 3H, C**H**$_3$Si), 0.78-0.92 (m, 23H, C**H**$_3$ x 4, C**H**$_3$CSi and 1/2 C**H**$_2$ x 2), 0.95-0.92 (m, 3H, C**H**$_2$ and 1/2 C**H**$_2$), 1.33-1.88 (m, 11H, 1/2 C**H**$_2$, C**H** x 4 and THP(6H)), 2.42 (d, 2H, *J* = 5.9 Hz, C_2-**H**), 3.15 (m, 1H, THP(1H)), 3.50 (m, 2H, THP(1H) and 1/2 C_{11}-**H**), 3.85 (m, 1H, 1/2 C_{11}-**H**), 4.06 (m, 1H, C_3-**H**), 4.57 (m, 1H, THP(1H)); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -4.7, -4.6, 15.2, 16.6, 16.7, 18.0, 19.4, 19.5, 20.6, 20.7, 20.8, 25.5, 25.8, 27.2, 27.3, 27.5, 30.6, 30.8, 30.9, 35.9, 39.3, 40.1, 40.4, 45.7, 61.9, 62.1, 72.5, 73.8, 74.0, 98.6, 99.0, 177.9; **HRMS [FAB, m-NBA]** calcd for $C_{26}H_{52}O_5SiNa$ [M+H$^+$]: 495.3481; found: 495.3489.

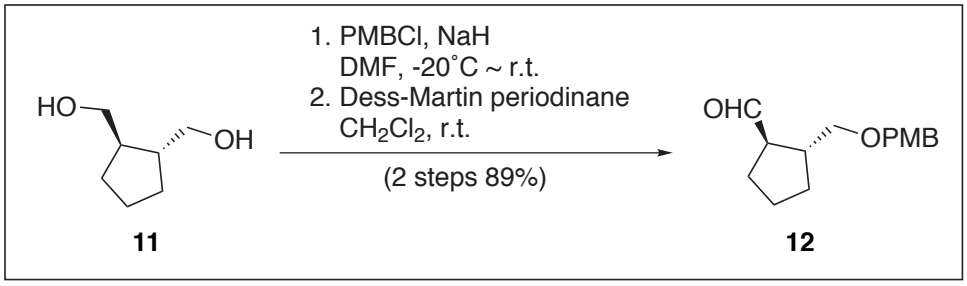
(1*R*,2*R*)-1,2-Dihydroxymethylcyclopentane (11)



11

This diol was synthesized according to known protcol. [(a) Misumi, A.; Iwanaga, K.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 3343-3345. (b) Fujimura, O.; de la Mata, F. J.; Grubbs, R. H. *Organometallics* **1996**, *15*, 1865-1871.]

(1*R*,2*R*)-2-(4'-Methoxybenzyloxymethyl)cyclopentanecarboaldehyde (12)

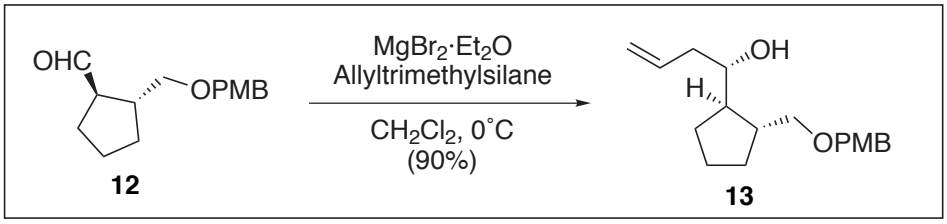


11 **12**

To a solution of **11** (55.0 mg, 0.42 mmol) in DMF (4.2 ml) was added sodium hydride (60% in oil, 20 mg, 0.47 mmol) at –20˚C. After being stirred for 30 min, the resulting suspension was added PMBCl (60 μL, 0.50 mmol) and then warmed to r.t.. The reaction was quenched with

water, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (7:1 hexanes/EtOAc) afforded the corresponding alcohol (111.4 mg) including unseparable impurities. To a solution of alcohol in CH_2Cl_2 (4.5 ml) was added Dess-Martin periodinane (283 mg, 0.67 mmol). After being stirred at r.t. for 30 min, the reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$, the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (20:1 hexanes/EtOAc) afforded **12** (94.5 mg, 2 steps 89%) as a colorless oil.
$[\alpha]_D^{21}$ = -25.9° (*c* = 0.27, $CHCl_3$); **IR (KBr)** 2955, 2854, 1721, 1613, 1513, 1247, 1095, 1034 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 1.31 (m, 1H, 1/2 C_3-**H**), 1.57 (m, 2H, C_4-**H**), 1.66-1.86 (m, 3H, 1/2 C_3-**H** and C_5-**H**), 2.33-2.51 (m, 2H, C_1-**H** and C_2-**H**), 3.25 (dd, 1H, *J* = 8.9, 7.3 Hz, 1/2 C**H**$_2$OPMB), 3.39 (dd, 1H, *J* = 8.9, 5.6 Hz, 1/2 C**H**$_2$OPMB), 3.72 (s, 3H, OC**H**$_3$), 4.36 (s, 2H, C**H**$_2$Ph), 6.79 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.15 (d, 2H, *J* = 8.6 Hz, Ar**H**), 9.75 (d, 1H, *J* = 2.0 Hz, C**H**O); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 24.9, 26.5, 29.3, 41.2, 55.2, 55.7, 72.6, 72.9, 113.7, 129.1, 130.4, 159.1, 203.7; **HRMS [EI]** calcd for $C_{15}H_{20}O_3$ [M^+]: 248.1412; found: 248.1407.

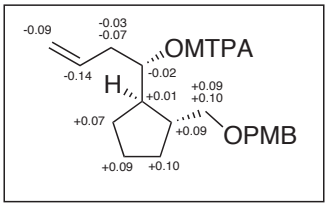
(1*S*,1'*R*,2'*R*)-1-[2'-(4''-Methoxybenzyloxymethyl)cyclopentyl]buta-3-en-1-ol (13)



To a stirred solution of **12** (111.8 mg, 0.45 mmol) in CH_2Cl_2 (4.5 ml) was added allyltrimethylsilane (110 μl, 0.67 mmol) and magnesium bromide diethyl etherate (116.4 mg, 0.45 mmol) at 0˚C. The reaction was stirred for 7 hr, then quenched with water. The aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 a**n**d concentrated in vacuo. Flash chromatography (25:1 hexanes/EtOAc) afforded **13** (117.3 mg, 90%) along with its epimer (6.0 mg, 4.5%).
$[\alpha]_D^{21}$ = +6.1° (*c* = 0.30, $CHCl_3$); **IR (KBr)** 3432, 2950, 2865, 1613, 1513, 1248, 1091, 1036 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 1.18-1.33 (m, 2H, 1/2 C**H**$_2$ x 2), 1.47 (m, 1H, 1/2 C**H**$_2$), 1.51-1.63 (m, 2H, 1/2 C**H**$_2$ and C_1-**H**), 1.72-1.84 (m, 2H, 1/2 C**H**$_2$ x 2), 2.02-2.17 (m, 2H, 1/2 C_2-**H**

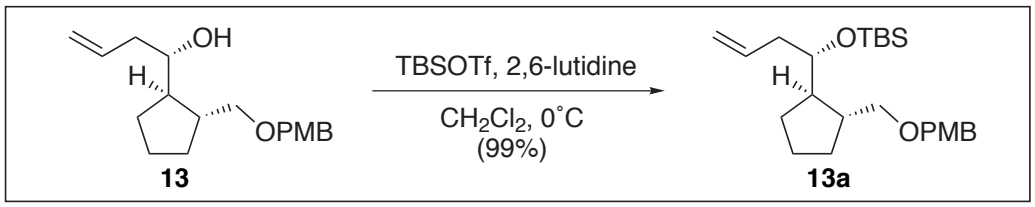
and $C_{2'}$-**H**), 2.39 (m, 1H, 1/2 C_2-**H**), 3.20 (t, 1H, *J* = 8.9 Hz, 1/2 C**H**$_2$OPMB), 3.41 (m, 1H, C_1-**H**), 3.53 (dd, 1H, *J* = 8.9, 4.6 Hz, 1/2 C**H**$_2$OPMB), 3.81 (s, 3H, OC**H**$_3$), 4.47 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.53 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 5.10 (m, 2H, C_4-**H**), 5.98 (m, 1H, C_3-**H**), 6.89 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.26 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, CDCl$_3$)** δ 24.5, 29.9, 30.9, 40.4, 43.9, 51.6, 55.2, 72.8, 74.2, 74.9, 113.8, 116.4, 129.4, 129.6, 135.7, 159.2; **HRMS [EI]** calcd for $C_{18}H_{26}O_3$ [M^+]: 290.1882; found: 290.1887.

Stereochemical assignment of the newly created asymmetric center was achieved by Mosher's method.



$\Delta\delta = (\delta_S - \delta_R)$ for (*R*)- and (*S*)-MTPA ester of **13**

(1'*R*,2'*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-4-[2'-(4''-methoxybenzyloxymethyl)-cyclopentyl]butene (13a)

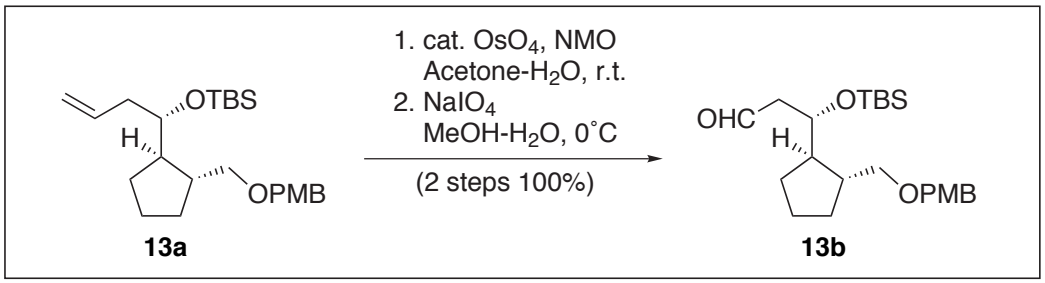


To a solution of **13** (1.91 g, 6.61 mmol) in CH_2Cl_2 (66 ml) at 0˚C was added 2,6-lutidine (1.1 ml, 9.92 mmol) followed by TBSOTf (2.0 ml, 8.59 mmol). After 1 hr, the reaction was quenched with water, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (50:1 hexanes/EtOAc) afforded **13a** (2.65 g, 99%) as a colorless oil.

$[\alpha]_D^{22}$ = -8.6˚ (*c* = 0.27, $CHCl_3$); **IR (KBr)** 2953, 2856, 1471, 1249, 1095 cm^{-1}; **^{1}H-NMR (270 MHz, CDCl$_3$)** δ 0.06 (s, 6H, C**H**$_3$Si), 0.90 (s, 9H, C**H**$_3$CSi), 1.23-1.36 (m, 2H, 1/2 $C_{3'}$-**H** and 1/2 $C_{5'}$-**H**), 1.44-1.74 (m, 5H, $C_{1'}$-**H**, 1/2 $C_{3'}$-**H**, $C_{4'}$-**H** and 1/2 $C_{5'}$-**H**), 2.15 (m, 1H, $C_{2'}$-**H**), 2.26 (m, 2H, C_3-**H**), 3,18 (t, 1H, *J* = 8.6 Hz, 1/2 C**H**$_2$OPMB), 3.46 (dd, 1H, *J* = 8.6, 4.9 Hz, 1/2 C**H**$_2$OPMB), 3.64 (m, 1H, C_4-**H**), 3.80 (s, 3H, OC**H**$_3$), 4.40 (d, 2H, *J* = 11.5 Hz, 1/2 C**H**$_2$Ph), 4.46

(d, 2H, *J* = 11.5 Hz, 1/2 C**H**$_2$Ph), 5.01 (m, 2H, C$_1$-**H**), 5.85 (m, 1H, C$_2$-**H**), 6.88 (d, 2H, *J* = 8.2 Hz, Ar**H**), 7.27 (d, 2H, *J* = 8.2 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, CDCl$_3$)** δ -4.6, -4.2, 18.0, 25.5, 25.9, 29.5, 30.5, 39.8, 41.0, 46.8, 55.2, 72.6, 74.7, 75.5, 113.7, 116.5, 129.1, 130.9, 135.2, 150.0; **HRMS [FAB, m-NBA]** calcd for $C_{24}H_{39}O_3Si$ [M-H$^+$]: 403.2668; found: 403.2669.

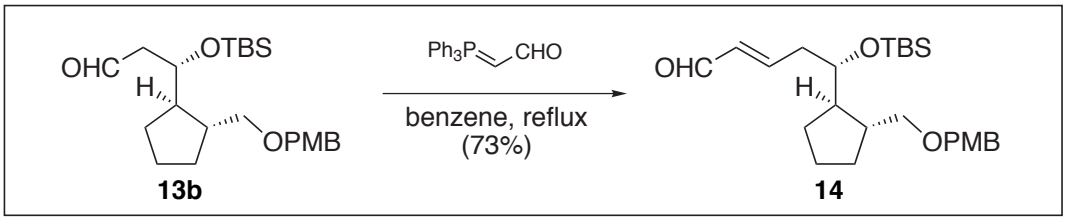
(1'*R*,2'*R*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-3-[2'-(4''-methoxybenzyloxymethyl)-cyclopentyl]propanal (13b)



To a solution of **13a** (515.8 mg, 1.27 mmol) in acetone (12 ml) and H_2O (12 ml) were added osmium tetraoxide (32.4 mg, 0.127 mmol) and NMO (600 mg, 5.10 mmol), and the reaction was stirred at r.t. for 4 hr. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give the corresponding diol as a yellow oil.

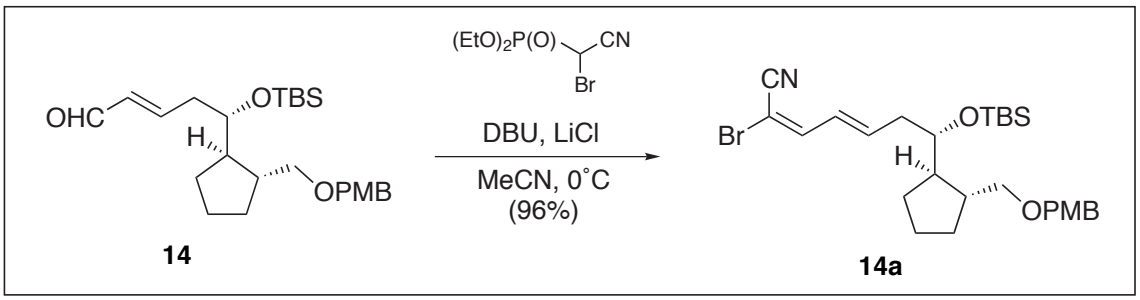
The crude diol was dissolved in MeOH (18 ml) and H_2O (6 ml). To the reaction mixture was added sodium metaperiodate (545 mg, 2.55 mmol) at 0˚C. The mixture was stirred for 2 hr, then quenched with sat. aq. $Na_2S_2O_3$ solution. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (40:1 hexanes/EtOAc) afforded **13b** (532.7 mg, 2 steps 100%) as a colorless oil. $[\alpha]_D^{22}$ = -14.4˚ (*c* = 0.36, $CHCl_3$); **IR (KBr)** 2954, 2857, 1725, 1614, 1513, 1249, 1093, 1037 cm^{-1}; **^{1}H-NMR (270 MHz, CDCl$_3$)** δ 0.03 (s, 3H, C**H$_3$**Si), 0.06 (s, 3H, C**H$_3$**Si), 0.86 (s, 9H, C**H$_3$**CSi), 1.32-1.75 (m, 6H, C$_{3'}$-**H**, C$_{4'}$-**H** and C$_{5'}$-**H**), 1.83 (m, 1H, C$_{1'}$-**H**), 2.04 (m, 1H, C$_{2'}$-**H**), 2.48 (ddd, 1H, *J* = 15.8, 5.9, 2.6 Hz, 1/2 C$_2$-**H**), 2.58 (ddd, 1H, *J* = 15.8, 4.9, 1.7 Hz, 1/2 C$_2$-**H**), 3.31 (m, 2H, C**H$_2$**OPMB), 3.80 (s, 3H, OC**H$_3$**), 4.20 (m, 1H, C$_3$-**H**), 4.41 (m, 2H, C**H$_2$**Ph), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.24 (d, 2H, Ar**H**), 9.73 (m, 1H, C**H**O); **^{13}C-NMR (67.5 MHz, CDCl$_3$)** δ -4.6, 17.9, 25.2, 25.8, 28.0, 30.3, 41.0, 48.6, 48.7, 55.2, 70.9, 72.8, 74.5, 113.7, 129.2, 130.6, 159.1, 202.5; **HRMS [FAB, m-NBA]** calcd for $C_{23}H_{37}O_4Si$ [M-H$^+$]: 405.2461; found: 405.2451.

(1'*R*,2'*R*,5*S*)-5-(*tert*-Butyldimethylsilyloxy)-5-[2'-(4''-methoxybenzyloxymethyl)-cyclopentyl]penta-2*E*-enal (14)



To a solution of **13b** (20.0 mg, 49.2 μmol) in benzene (1.0 ml) was added triphenylphosphoranylidene acetoaldehyde (45.0 mg, 98.5 μmol), and the resulting solution was stirred at 80°C for 2 days. The solvent was then removed in vacuo and the residue was purified by flash chromatography (30:1 hexanes/EtOAc) to afford **14** (15.5 mg, 73%) as a yellow oil.
$[\alpha]_D^{23}$ = +8.3° (*c* = 0.35, $CHCl_3$); **IR (KBr)** 2953, 2857, 1694, 1513, 1249, 1091, 1038 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.04 (s, 3H, C**H**$_3$Si), 0.06 (s, 3H, C**H**$_3$Si), 0.88 (s, 9H, C**H**$_3$CSi), 1.28-1.71 (m, 7H, $C_{3'}$-**H**, $C_{4'}$-**H**, $C_{5'}$-**H** and $C_{1'}$-**H**), 2.08 (m, 1H, $C_{2'}$-**H**), 2.49 (m, 2H, C_4-**H**), 3.22 (t, 1H, *J* = 8.6 Hz, 1/2 C**H**$_2$OPMB), 3.39 (dd, 1H, *J* = 8.6 Hz, 1/2 C**H**$_2$OPMB), 3.78 (m, 1H, C_5-**H**), 3.80 (s, 3H, OC**H**$_3$), 4.39 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.43 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 6.10 (dd, 1H, *J* = 15.5, 7.9 Hz, C_2-**H**), 6.86 (d, 2H, *J* = 8.2 Hz, Ar**H**), 6.88 (m, 1H, C_3-**H**), 7.24 (d, 2H, *J* = 8.2 Hz, Ar**H**), 9.47 (d, 1H, *J* = 7.9 Hz, C**H**O); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -4.6, -4.3, 18.0, 25.2, 25.8, 29.2, 30.3, 38.4, 41.4, 47.7, 55.2, 72.7, 74.5, 74.6, 113.7, 129.2, 130.7, 134.7, 155.2, 159.1, 193.9; **HRMS [EI]** calcd for $C_{25}H_{40}O_4Si$ [M^+]: 432.2696; found: 432.2702.

(1'*R*,2'*R*,7*S*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-[2'-(4''-methoxybenzyloxy-methyl)cyclopentyl]hepta-2*E*,4*Z*-dienenitrile (14a)



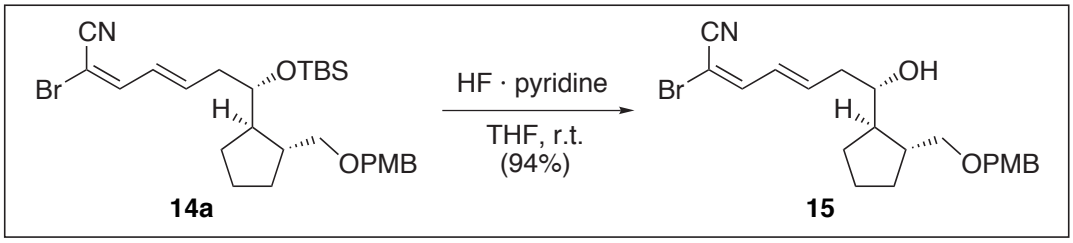
To a solution of **14** (39.8 mg, 92.1 μmol) and diethyl bromo(cyano)methylphosphate (47.0 mg, 184 μmol) in MeCN (1 ml) at 0°C were added DBU (20 μl, 138 μmol) and lithium chloride (6.0

mg, 138 μmol). The solution was stirred for 2 hr, then quenched with sat. aq. $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (60:1 hexanes/EtOAc) afforded **14a** (47.3 mg, 96%) as a colorless oil.

$[\alpha]_D^{22}$ = +31.0° (*c* = 0.47, $CHCl_3$); **IR (KBr)** 2952, 2856, 2217, 1614, 1513, 1248, 1078 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.03 (s, 3H, C**H**$_3$Si), 0.05 (s, 3H, C**H**$_3$Si), 0.88 (s, 9H, C**H**$_3$CSi), 1.25-1.71 (m, 7H, $C_{3'}$-**H**, $C_{4'}$-**H**, $C_{5'}$-**H** and $C_{1'}$-**H**), 2.07 (m, 1H, $C_{2'}$-**H**), 2.36 (m, 2H, C_6-**H**), 3.20 (t, 1H, *J* = 8.6 Hz, 1/2 C**H**$_2$OPMB), 3.39 (dd, 1H, *J* = 8.6, 5.6 Hz, 1/2 C**H**$_2$OPMB), 3.69 (m, 1H, C_7-**H**), 3.80 (s, 3H, OC**H**$_3$), 4.39 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.44 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 6.25 (m, 1H, C_5-**H**), 6.36 (dd, 1H, *J* = 15.2, 10.6 Hz, C_4-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.10 (d, 1H, *J* = 10.6 Hz, C_3-**H**), 7,24 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -4.6, -4.3, 17.9, 25.2, 25.8, 29.3, 30.3, 38.8, 41.3, 47.4, 55.1, 72.6, 74.5, 74.7, 84.1, 113.6, 114.6, 127.6, 129.1, 130.7, 143.5, 149.7, 159.0; **HRMS [FAB, m-NBA]** calcd for $C_{27}H_{40}O_3NBrSiNa$ [M+Na^+]: 556.1858; found: 556.1855.

diethyl bromo(cyano)methylphosphate [$(EtO)_2P(O)CH(Br)CN$] was prepared according to known protocol. (Iorga, B.; Ricard, L.; Savignac, P. *J. Chem. Soc., Perkin Trans. 1*, **2000**, 3311.)

(1'*R*,2'*R*,7*S*)-2-Bromo-7-[2'-(4''-methoxybenzyloxymethyl)-cyclopentyl]-7-hydroxyhept-2*Z*,4*E*-dienenitrile (15)



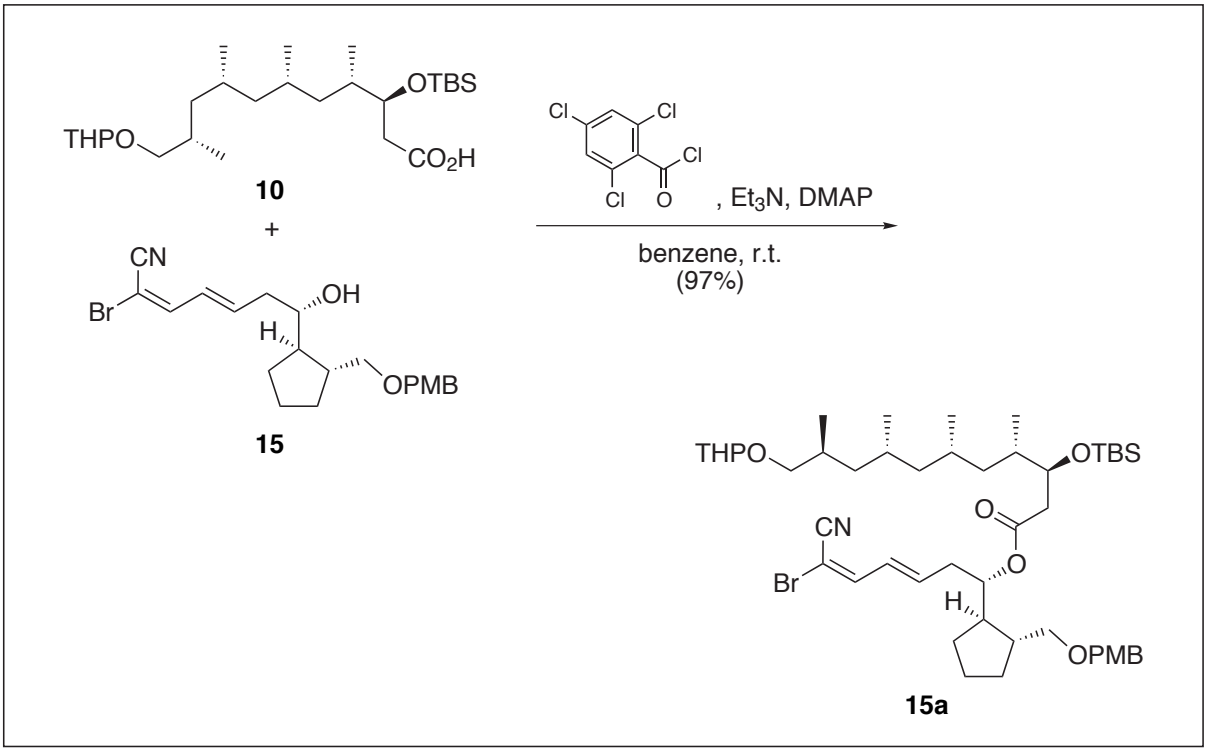
14a **15**

14a (184.0 mg, 345 μmol) was placed in a solution of HF·pyridine (500 μl) in THF (500 μl) and pyridine (500 μl) and stirred at r.t. for 2 days. The resulting solution was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (7:1 hexanes/EtOAc) to afford **15** (135.2 mg, 94%).

$[\alpha]_D^{24}$ = +11.3° (*c* = 0.25, $CHCl_3$); **IR (KBr)** 3406, 2949, 2222, 2216, 1613, 1513, 1248, 1075, 1035 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 1.25 (m, 1H, 1/2 C**H**$_2$), 1.41-1.67 (m, 5H, 1/2 C**H**$_2$ x 2, $C_{1'}$-**H** and $C_{4'}$-**H**), 1.77 (m, 1H, 1/2 C**H**$_2$), 2.04 (m, 1H, $C_{2'}$-**H**), 2.24 (m, 1H, 1/2 C_6-**H**), 2.47 (m,

1H, 1/2 C_6-**H**), 3.14 (dd, 1H, *J* = 10.6, 8.6 Hz, 1/2 C**H**$_2$OPMB), 3.41 (m, 1H, C_7-**H**), 3.56 (dd, 1H, *J* = 8.6, 4.0 Hz, 1/2 C**H**$_2$OPMB), 3.81 (s, 3H, OC**H**$_3$), 4.49 (m, 2H, C**H**$_2$Ph), 6.33-6.48 (m, 2H, C_4-**H** and C_5-**H**), 6.88 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.15 (m, 1H, C_3-**H**), 7.24 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, CDCl$_3$)** δ 24.3, 29.6, 30.9, 39.6, 44.0, 52.2, 55.1, 72.8, 74.0, 74.5, 83.8, 113.7, 114.6, 127.1, 129.1, 129.4, 144.3, 150.0, 159.2; **HRMS [FAB, m-NBA]** calcd for $C_{21}H_{26}O_3NBrNa$ [M+Na$^+$]: 442.0994; found: 442.1002.

(1"*S*,1"'*R*,2"'*R*,3*S*,4*S*,6*S*,8*R*,10*S*)-3-(*tert*-Butyldimethyl-silyloxy)-4,6,8,10-tetramethyl-11-(tetrahydropyran-2'-yloxy)undecanoic acid 6"-bromo-6"-cyano-1-[2"'-(4""-methoxybenzyloxymethyl)cyclopentyl]hexa-3"*E*,5"*E*-dienyl ester (15a)

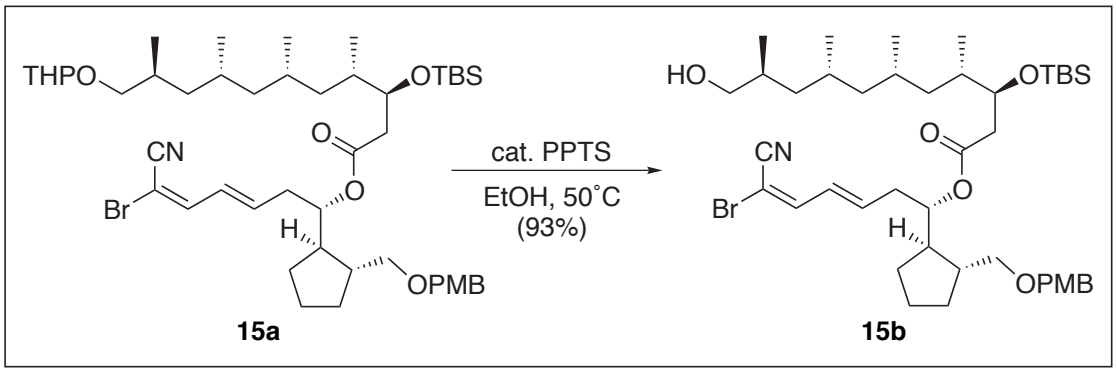


To a stirred solution of **10** (113.0 mg, 0.239 mmol) in benzene (2.4 ml) was added triethylamine (67 μl, 0.479 mmol) followed by 2,4,6-trichlorobenzoyl chloride (41 μl, 0.263 mmol) at r.t.. The resulting solution was stirred for 1 hr, then treated with a solution of **15** (130.4 mg, 0.311 mmol) in benzene (1.4 ml) and DMAP (38.0 mg, 0.311 mmol) in benzene (1.0 ml), and stirred for additional 30 min. The reaction was quenched with sat. aq. $NaHCO_3$ solution and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous

Na_2SO_4 and concentrated in vacuo. Flash chromatography (25:1 hexanes/EtOAc) afforded **15a** (203.5 mg, 97%) as a colorless oil.

$[\alpha]_D^{24}$ = -7.4° (*c* = 0.76, $CHCl_3$); **IR (KBr)** 2957, 2927, 2856, 1732, 1259, 1092, 1034 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.03 (s, 3H, C**H$_3$**Si), 0.07 (s, 3H, C**H$_3$**Si), 0.80-0.92 (m, 23H, C**H$_3$** x 4, 1/2 C**H$_2$** x 2 and C**H$_3$**CSi), 0.99-1.42 (m, 5H, 1/2 C**H$_2$** x 3 and C**H$_2$**), 1.46-1.94 (m, 16H, THP(6H), C**H$_2$** x 2, C**H** x 5 and 1/2 C**H$_2$**), 2.07 (m, 1H, $C_{2'''}$-**H**), 2.31-2.60 (m, 4H, C_2-**H** and $C_{2''}$-**H**), 3.10-3.39 (m, 3H, THP(1H) and C**H$_2$**OPMB), 3.45-3.59 (m, 2H, THP(1H) and 1/2 C_{11}-**H**), 3.80 (s, 3H, OC**H$_3$**), 3.86 (m, 1H, 1/2 C_{11}-**H**), 4.06 (m, 1H, C_3-**H**), 4.41 (d, 1H, *J* = 11.9 Hz, 1/2 C**H$_2$**Ph), 4.44 (d, 1H, *J* = 11.9 Hz, 1/2 C**H$_2$**Ph), 4.57 (m, 1H, THP(1H)), 4.96 (m, 1H, $C_{1''}$-**H**), 6.11 (m, 1H, $C_{3''}$-**H**), 6.37 (dd, 1H, *J* = 15.2, 11.2 Hz, $C_{4''}$-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.07 (d, 1H, *J* = 11.2 Hz, $C_{5''}$-**H**), 7.24 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -4.7, -4.4, 14.5, 16.4, 16.5, 18.0, 19.4, 19.5, 20.4, 20.6, 25.0, 25.5, 25.8, 26.9, 27.0, 27.2, 29.6, 30.1, 30.6, 30.8, 30.9, 35.4, 36.4, 39.6, 39.9, 40.8, 40.9, 41.4, 45.1, 45.7, 55.1, 61.9, 62.0, 71.5, 72.6, 73.7, 73.9, 74.0, 75.6, 85.0, 98.6, 98.9, 113.6, 114.4, 128.0, 128.9, 130.5, 141.5, 149.3, 159.0, 171.5; **HRMS [FAB, m-NBA]** calcd for $C_{47}H_{76}O_7NBrSiNa$ [M+Na^+]: 896.4472; found: 896.4473.

(1'*S*,1''*R*,2''*R*,3*S*,4*S*,6*S*,8*R*,10*S*)-3-(*tert*-Butyldimethylsilyloxy)-11-hydroxy-4,6,8,10-tetramethylundecanoic acid 6'-bromo-6'-cyano-1'-[2''-(4'''-methoxybenzyloxymethyl)-cyclopentyl]hexa-3'*E*,5'*E*-dienyl ester (15b)



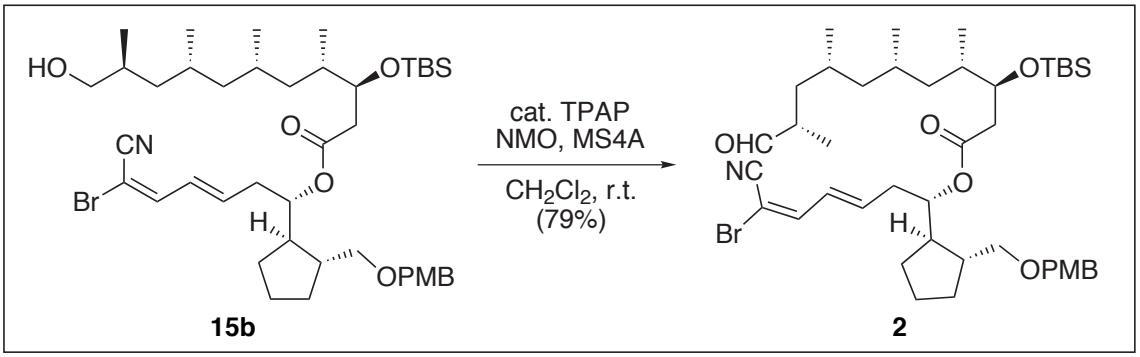
15a **15b**

To a solution of **15a** (195.0 mg, 0.223 mmol) in EtOH (5.0 ml) was added PPTS (28.0 mg, 0.112 mmol), and the resulting solution was stirred at 50°C. After 10 hr, the reaction was diluted with water, and the aqueous phase was extracted with EtOAc. The combined organic extracts were

dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (7:1 hexanes/EtOAc) afforded **15b** (164.3 mg, 93%) as a colorless oil.

$[\alpha]_D^{25}$ = -10.2° (*c* = 0.31, $CHCl_3$); **IR (KBr)** 3500, 2956, 2927, 1733, 1250, 1172, 1084, 1036 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.03 (s, 3H, C**H**$_3$Si), 0.07 (s, 3H, C**H**$_3$Si), 0.80-0.91 (m, 24H, C**H**$_3$ x 4, 1/2 C**H**$_2$ x 3 and C**H**$_3$CSi), 0.94-1.41 (m, 4H, 1/2 C**H**$_2$ x 4), 1.45-1.81 (m, 9H, C**H**$_2$ x 2, C**H** x 4 and 1/2 C**H**$_2$), 1.88 (m, 1H, C**H**), 2.06 (m, 1H, C**H**), 2.31-2.60 (m, 4H, C_2-**H** and $C_{2'}$-**H**), 3.24-3.47 (m, 4H, C_{11}-**H** and C**H**$_2$OPMB), 3.80 (s, 3H, OC**H**$_3$), 4.06 (m, 1H, C_3-**H**), 4.37 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.41 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.93 (m, 1H, $C_{1'}$-**H**), 6.10 (m, 1H, $C_{3'}$-**H**), 6.36 (dd, 1H, *J* = 14.8, 11.2 Hz, $C_{4'}$-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.06 (d, 1H, *J* = 11.2 Hz, $C_{5'}$-**H**), 7.24 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -4.7, -4.4, 14.4, 15.9, 18.0, 20.5, 20.6, 25.0, 25.8, 27.0, 27.2, 29.6, 30.1, 33.1, 35.4, 36.5, 39.5, 39.6, 41.0, 41.5, 45.1, 45.7, 55.1, 69.1, 71.7, 72.7, 73.9, 75.7, 85.0, 113.7, 114.4, 128.0, 129.0, 130.5, 141.5, 149.3, 159.0, 171.6; **HRMS [FAB, m-NBA]** calcd for $C_{42}H_{68}O_6NBrSiNa$ [M+Na^+]: 812.3897; found: 812.3936.

(1'*S*,1"*R*,2"*R*,3*S*,4*S*,6*S*,8*R*,10*S*)-3-(*tert*-Butyldimethylsilyloxy)-4,6,8,10-tetramethy-11-oxoundecanoic acid 6'-bromo-6'-cyano-1'-[2"-(4"'-methoxybenzyloxymethyl)-cyclopentyl]hexa-3'*E*,5'*Z*-dienyl ester (**2**)



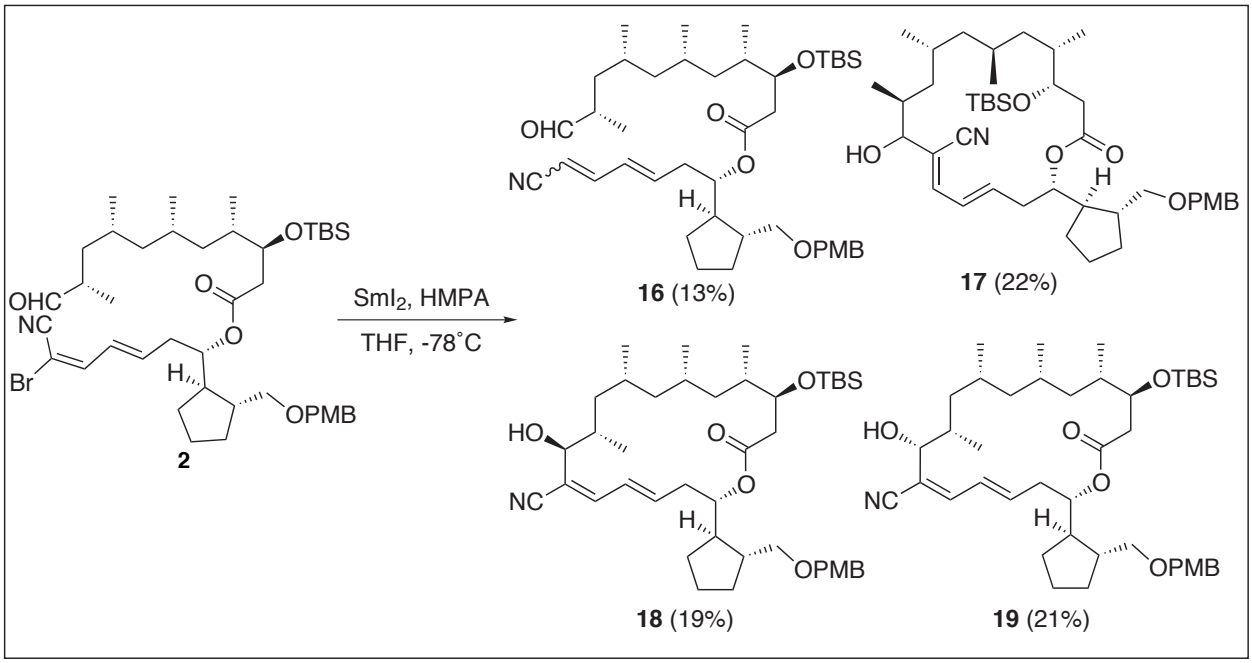
15b **2**

To a solution of **15b** (153.2 mg, 0.194 mmol) in CH_2Cl_2 (4.0 ml) were added dried MS4A (1 g), TPAP (3.4 mg, 9.70 μmol) and NMO (45.6 mg, 0.388 mmol) at r.t.. The resulting solution was stirred for 30 min and filtered through a silica pad. After evaporation of the filtrate, the residue was purified by flash chromatography (15:1 hexanes/EtOAc) to afford **2** (120.3 mg, 79%) as a colorless oil.

$[\alpha]_D^{25}$ = -3.7° (*c* = 0.19, $CHCl_3$); **IR (KBr)** 2955, 2929, 2856, 1731, 1513, 1462, 1249, 1084,

cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.03 (s, 3H, C**H**$_3$Si), 0.07 (s, 3H, C**H**$_3$Si), 0.80-0.91 (m, 21H, C**H**$_3$ x 3, 1/2 C**H**$_2$ x 3 and C**H**$_3$CSi), 0.93-1.10 (m, 2H, 1/2 C**H**$_2$ x 2), 1.07 (d, 3H, *J* = 6.9 Hz, C_{10}-C**H**$_3$), 1.18-1.43 (m, 2H, 1/2 C**H**$_2$ x 2), 1.47-1.76 (m, 9H, C**H**$_2$ x 2, C**H** x 4 and 1/2 C**H**$_2$), 1.86 (m, 1H, C**H**), 2.05 (m, 1H, C**H**), 2.30-2.59 (m, 4H, C_2-**H** and C**H**$_2$OPMB), 3.23-3.38 (m, 2H, $C_{2''}$-**H**), 3.80 (s, 3H, OC**H**$_3$), 4.05 (m, 1H, C_3-**H**), 4.40 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.44 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.96 (m, 1H, $C_{1'}$-**H**), 6.10 (m, 1H, $C_{3'}$-**H**), 6.36 (dd, 1H, *J* = 15.2, 11.2 Hz, $C_{4'}$-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.07 (d, 1H, *J* = 11.2 Hz, $C_{5'}$-**H**), 7.24 (d, 2H, *J* = 8.6 Hz, Ar**H**), 9.61 (d, 1H, *J* = 1.6 Hz, C**H**O); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -4.7, -4.4, 13.0, 14.6, 18.0, 20.4, 20.5, 25.0, 25.8, 27.3, 27.4, 29.7, 30.2, 35.4, 36.3, 36.5, 39.5, 40.7, 41.5, 44.1, 45.1,45.2, 55.2, 71.5, 72.7, 74.0, 75.6, 85.1, 113.6, 114.4, 128.1, 129.0, 130.5, 141.5, 149.3, 159.0, 171.6, 205.1; **HRMS [FAB, m-NBA]** calcd for $C_{42}H_{66}O_6NBrSiNa$ [M+Na^+]: 810.3740; found: 810.3770.

(1'*R*,2*S*,2'*R*,8*R*,9*S*,11*R*,13*S*,15*S*,16*S*)-16-(*tert*-Butyldimethyl-silyloxy)-8-hydroxy-2-[2'-(4''-methoxybenzyloxymethyl)cyclopentyl]-9,11,13,15-tetramethyl-18-oxo-oxaoctadeca-4*E*,6*Z*-diene-7-carbonitrile (19) (Intramolecular Reformatsky reaction)



To a solution of SmI_2 (0.1 M solution in THF, 20 ml, 2.00 mmol) was added HMPA (240 μl, 1.37 mmol) at r.t. The resulting solution was cooled to –78˚C, and **2** (54.2 mg, 68.9 μmol) was added

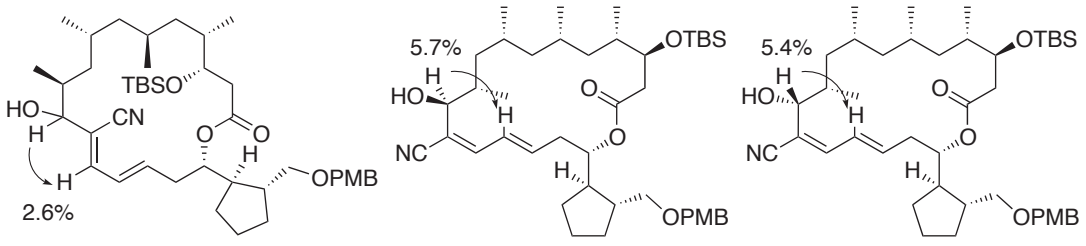
dropwise over 30 min. To the reaction was added hexane (20 ml) and silica gel (20 g), and the resulting mixture was stirred at r.t. for 20 min. The mixture was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (10:1 to 5:1 hexanes/EtOAc) to afford **16** (6.1 mg, 13%), **17** (10.5 mg, 22%), **18** (9.2 mg, 19%), and desired **19** (10.2 mg, 21%).

19 : $[\alpha]_D^{24}$ = -19.0° (*c* = 0.54, $CHCl_3$); **IR (KBr)** 3470, 2956, 2926, 2853, 1737, 1513, 1463, 1249, 1079, 1036 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.10 (s, 3H, C**H**$_3$Si), 0.11 (s, 3H, C**H**$_3$Si), 0.79 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 0.81 (d, 3H, *J* = 5.9 Hz, C**H**$_3$), 0.86 (m, 3H, C**H**$_3$), 0.89 (s, 9H, C**H**$_3$CSi), 1.03 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.76-1.41 (m, 9H, C**H**$_2$ x 4 and 1/2 C**H**$_2$), 1.52-2.20 (m, 7H, 1/2 C**H**$_2$, C**H**$_2$ and C**H** x 4), 2.26-2.25 (m, 6H, C**H**$_2$ x 2 and C**H** x 2), 3.17 (dd, 1H, *J* = 8.9, 7.6 Hz, 1/2 C**H**$_2$OPMB), 3,34 (dd, 1H, *J* = 8.9, 4.9 Hz, 1/2 C**H**$_2$OPMB), 3.80 (s, 3H, OC**H**$_3$), 4.04 (m, 1H, C_{16}-**H**), 4.08 (d, 1H, *J* = 9.9 Hz, C_8-**H**), 4.38 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.43 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 5.02 (m, 1H, C_2-**H**), 6.17 (m, 1H, C_4-**H**), 6.30 (dd, 1H, *J* = 14.8, 10.9 Hz, C_5-**H**), 6.82 (d, 1H, *J* = 10.9 Hz, C_6-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.24 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -5.4, -4.4, 14.9, 17.9, 18.6, 19.8, 20.7, 25.0, 25.9, 26.1, 26.2, 30.0, 30.3, 35.3, 35.6, 36.2, 36.4, 37.6, 42.7, 43.4, 43.6, 48.1, 55.3, 72.6, 72.9, 73.8, 74.0, 75.2, 77.2, 113.8, 115.5, 126.9, 128.9, 130.7, 139.7, 144.2, 159.1, 171.5; **HRMS [FAB, m-NBA]** calcd for $C_{42}H_{67}O_6NSiNa$ [M+Na^+]: 732.4635; found: 732.4639.

18 : $[\alpha]_D^{24}$ = -17.6° (*c* = 1.05, $CHCl_3$); **IR (KBr)** 3454, 2955, 2926, 2854, 1737, 1513, 1463, 1248, 1175, 1078 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.99 (s, 3H, C**H**$_3$Si), 0.11 (s, 3H, C**H**$_3$Si), 0.77 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 0.78 (d, 3H, *J* = 5.9 Hz, C**H**$_3$), 0.86 (s, 9H, C**H**$_3$CSi), 0.88 (m, 3H, C**H**$_3$), 1.05 (d, 3H, *J* = 6.9 Hz, C**H**$_3$), 0.72-1.17 (m, 5H, C**H**$_2$ x 2 and 1/2 C**H**$_2$), 1.21-2.12 (m, 13H, C**H**$_2$ x 3, 1/2 C**H**$_2$ and C**H** x 6), 2.18-2.40 (m, 4H, C_3-**H** and C_{17}-**H**), 3.27 (dd, 1H, *J* = 8.9, 7.3 Hz, 1/2 C**H**$_2$OPMB), 3.36 (dd, 1H, *J* = 8.9, 5.9 Hz, 1/2 C**H**$_2$OPMB), 3.80 (s, 3H, OC**H**$_3$), 4.00 (m, 1H, C_{16}-**H**), 4.40 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.44 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.54 (d, 1H, *J* = 3.3 Hz, C_8-**H**), 5.04 (m, 1H, C_2-**H**), 5.90 (m, 1H, C_4-**H**), 6.38 (dd, 1H, *J* = 14.2, 11.5 Hz, C_5-**H**), 6.74 (d, 1H, *J* = 11.5 Hz, C_6-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.25 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -5.2, -4.3, 12.4, 17.9, 18.5, 19.9, 20.7, 25.0, 25.7, 25.9, 26.0, 29.4, 30.2, 35.7, 35.9, 37.0, 37.4, 37.5, 41.6, 43.8, 46.4, 48.4, 55.2, 72.0, 72.8, 73.2, 74.3, 74.7,

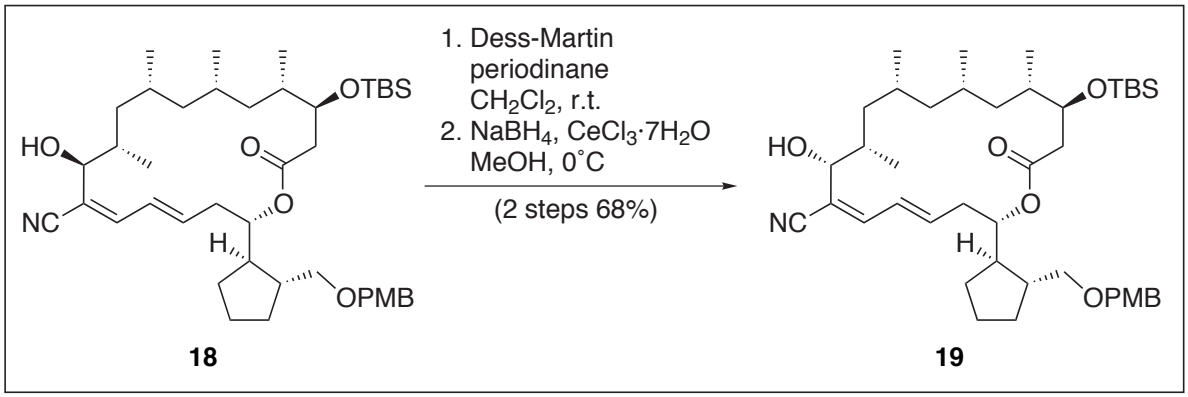
77.2, 112.4, 113.8, 126.7, 129.0, 130.7, 142.2, 145.8, 159.1, 171.3; **HRMS [FAB, m-NBA]** calcd for $C_{42}H_{67}O_6NSiNa$ [M+Na$^+$]: 732.4635; found: 732.4642.

NOE experiments were employed to verify the stereochemical assignment for the olefin isomers.



NOE experiments of **17**, **18** and **19**

(1'*R*,2*S*,2'*R*,8*R*,9*S*,11*R*,13*S*,15*S*,16*S*)-16-(*tert*-Butyldimethyl-silyloxy)-8-hydroxy-2-[2'-(4''-methoxybenzyloxymethyl)cyclopentyl]-9,11,13,15-tetramethyl-18-oxo-oxaoctadeca-4*E*,6*Z*-diene-7-carbonitrile (19) (Oxidation/Reduction)

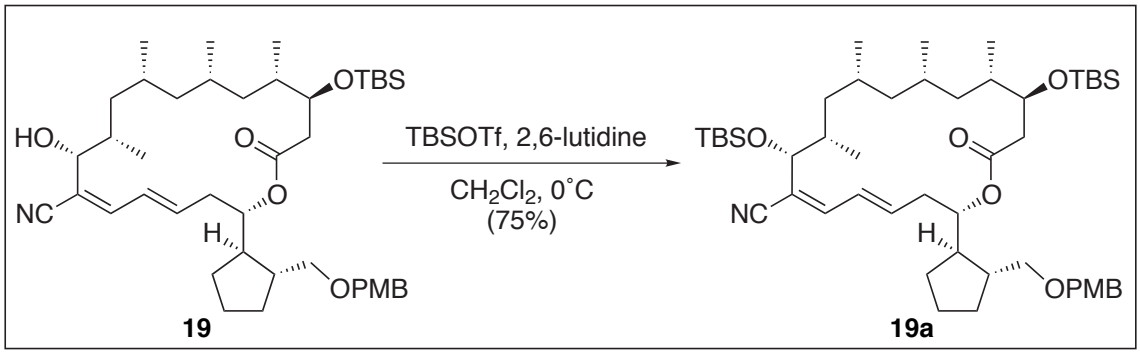


To a solution of **18** (13.2 mg, 18.6 μmol) in CH_2Cl_2 (1 ml) was added Dess-Martin periodinane (22.6 mg, 55.9 μmol). After stirred for 30 min, the reaction was quenched by sat. aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ solutions, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was subjected to the next reaction.

To a solution of the crude ketone in MeOH (1 ml) at 0˚C was added cerium chloride (14.0 mg, 37.2 μmol) followed by sodium borohydride (1.4 mg, 37.2 μmol). The reaction was stirred for 10 min, and then poured into water. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash

chromatography (8:1 hexanes/EtOAc) afforded **19** (8.5 mg, 2 steps 66%) and **18** (0.7 mg, 2 steps 5.3%) as a yellow oil.

(1'*R*,2*S*,2'*R*,8*R*,9*S*,11*R*,13*S*,15*S*,16*S*)-9,16-Bis(*tert*-butyldimethylsilyloxy)-2-[2'-(4''-methoxybenzyloxymethyl)cyclopentyl]-9,11,13,15-tetramethyl-18-oxo-oxaoctadeca-4*E*,6*Z*-diene-7-carbonitrile (**19a**)

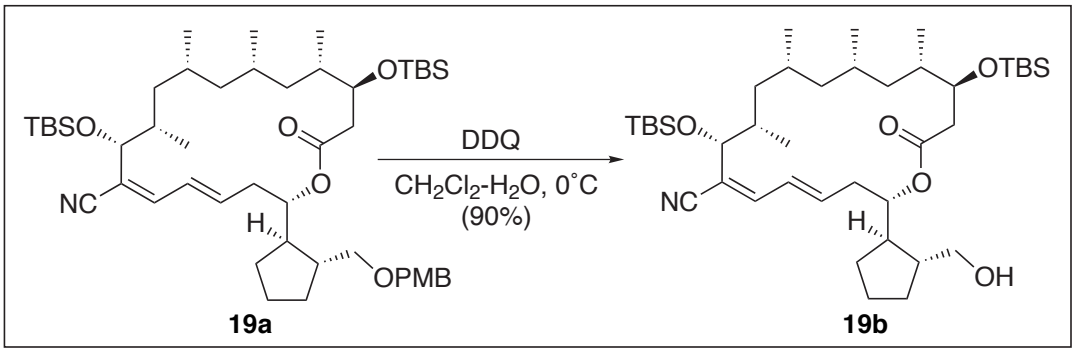


To a 0˚C cooled solution of **19** (13.1 mg, 18.4 μmol) in CH_2Cl_2 (200 μl) was added 2,6-lutidine (4 μl, 31.4 μmol) followed by TBSOTf (6 μl, 24.0 μmol). The resulting solution was then stirred at 0˚C for 1 hr. The reaction was poured into water and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (25:1 hexanes/EtOAc) afforded **19a** (11.4 mg, 75%) as a colorless oil.

$[\alpha]_D^{25}$ = -37.8˚ (*c* = 0.69, $CHCl_3$); **IR (KBr)** 2956, 2928, 2856, 1738, 1612, 1513, 1250, 1084 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.00 (s, 3H, C**H**$_3$Si), 0.05 (s, 3H, C**H**$_3$Si), 0.10 (s, 3H, C**H**$_3$Si), 0.12 (s, 3H, C**H**$_3$Si), 0.78-1.20 (m, 17H, C**H**$_3$ x 4, C**H**$_2$ x 2 and 1/2 C**H**$_2$), 0.90 (s, 9H, C**H**$_3$CSi), 0.91 (s, 9H, C**H**$_3$CSi), 1.23-2.09 (m, 11H, C**H**$_2$ x 3, 1/2 C**H**$_2$ and C**H** x 4), 2.16-2.33 (m, 5H, C_{17}-**H**, 1/2 C_3-**H** and C**H** x 2), 2.52 (m, 1H, 1/2 C_3-**H**), 3.17 (dd, 1H, *J* = 8.6, 8.3 Hz, 1/2 C**H**$_2$OPMB), 3.35 (dd, 1H, *J* = 8.9, 4.9 Hz, 1/2 C**H**$_2$OPMB), 3.80 (s, 3H, OC**H**$_3$), 3.98-4.10 (m, 2H, C_8-**H** and C_{16}-**H**), 4.39 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 4.43 (d, 1H, *J* = 11.9 Hz, 1/2 C**H**$_2$Ph), 5.02 (m, 1H, C_2-**H**), 6.09-6.32 (m, 2H, C_4-**H** and C_5-**H**), 6.75 (d, 1H, *J* = 10.6 Hz, C_6-**H**), 6.87 (d, 2H, *J* = 8.6 Hz, Ar**H**), 7.23 (d, 2H, *J* = 8.6 Hz, Ar**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -5.6, -4.9, -4.6, -3.5, 15.3, 17.9, 18.1, 18.5, 20.0, 20.7, 22.6, 25.0, 25.6, 25.7, 26.1, 26.2, 29.7, 30.0, 30.2, 35.6, 35.9, 36.3, 37.1, 42.9, 43.5, 48.1, 55.2, 72.6, 73.3, 73.9, 74.0, 75.3, 77.2, 113.8, 118.8, 127.1, 129.0, 130.7, 139.0, 142.9, 159.1, 171.5; **HRMS [FAB, m-NBA]** calcd for $C_{48}H_{81}O_6NSi_2Na$ [M+Na^+]:

846.5500; found: 846.5494.

(1'*R*,2*S*,2'*R*,8*R*,9*S*,11*R*,13*S*,15*S*,16*S*)-9,16-Bis(*tert*-butyldimethyl-silyloxy)-2-(2'-hydorxymethylcyclopentyl)-9,11,13,15-tetramethyl-18-oxo-oxaoctadeca-4*E*,6*Z*-diene-7-carbonitrile (19b)

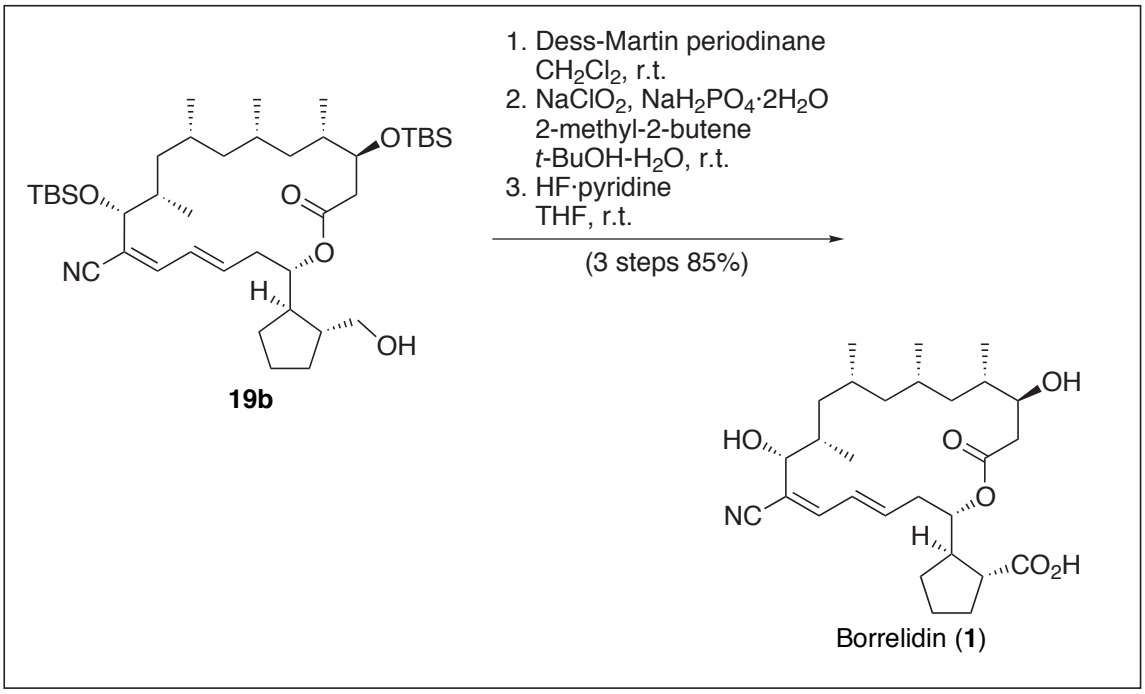


19a **19b**

To a solution of **19a** (11.4 mg, 13.9 μmol) in CH_2Cl_2 (250 μl) and H_2O (50 μl) was added DDQ (3.7 mg, 16.6 μmol) at 0˚C. The reaction mixture was stirred for 15 min, and then poured into water. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (8:1 hexanes/EtOAc) afforded **19b** (8.8 mg, 90%) as a colorless oil.

$[\alpha]_D^{25}$ = -37.2˚ (*c* = 0.36, $CHCl_3$); **IR (KBr)** 3447, 2956, 2927, 2856, 1740, 1464, 1386, 1292, 1253, 1081 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ -0.01 (s, 3H, C**H**$_3$Si), 0.05 (s, 3H, C**H**$_3$Si), 0.11 (s, 3H, C**H**$_3$Si), 0.13 (s, 3H, C**H**$_3$Si), 0.80 (d, 3H, *J* = 5.9 Hz, C**H**$_3$), 0.81 (d, 3H, *J* = 7.3 Hz, C**H**$_3$), 0.85 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.90 (s, 9H, C**H**$_3$CSi), 0.91 (s, 9H, C**H**$_3$CSi), 0.94 (d, 3H, *J* = 6.3 Hz, C**H**$_3$), 0.67-1.18 (m, 5H, C**H**$_2$ x 2 and 1/2 C**H**$_2$), 1.23-2.09 (m, 13H, C**H**$_2$ x 3, 1/2 C**H**$_2$ and C**H** x 6), 2.21-2.39 (m, 3H, C_{17}-**H** and 1/2 C_3-**H**), 2.54 (m, 1H, 1/2 C_3-**H**), 3.42 (dd, 1H, *J* = 10.6, 6.6 Hz, 1/2 C**H**$_2$OH), 3.51 (dd, 1H, *J* = 10.6, 5.9 Hz, 1/2 C**H**$_2$OH), 3.99 (d, 1H, *J* = 9.9 Hz, C_8-**H**), 4.08 (m, 1H, C_{16}-**H**), 5.02 (m, 1H, C_2-**H**), 6.15 (m, 1H, C_4-**H**), 6.28 (dd, 1H, *J* = 15.2, 10.6 Hz, C_5-**H**), 6.75 (d, 1H, *J* = 10.6 Hz, C_6-**H**);**^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ -5.6, -4.9, -4.6, -3.4, 15.3, 17.9, 18.1, 18.4, 20.0, 20.7, 22.7, 25.1, 25.7, 26.1, 26.2, 29.5, 29.7, 30.5, 35.6, 35.9, 36.2, 37.1, 43.4, 43.5, 45.5, 48.0, 66.7, 73.3, 73.9, 75.4, 77.2, 118.7, 127.2, 138.6, 142.8, 171.4; **HRMS [FAB, m-NBA]** calcd for $C_{40}H_{73}O_5NSi_2Na$ [M+Na^+]: 726.4925; found: 726.4924.

Borrelidin (1)



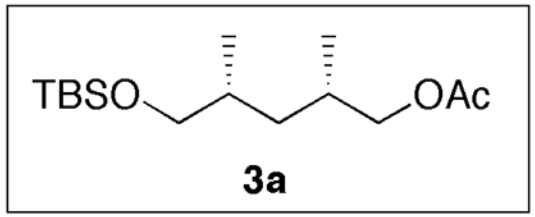
To a solution of **19b** (8.8 mg, 12.5 μmol) at r.t. was added Dess-Martin periodinane (10.6 mg, 25.0 μmol). The mixture was stirred for 30 min. The reaction was quenched with sat. aq. $Na_2S_2O_3$ and sat. aq. $Na_2S_2O_3$ solutions, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude aldehyde was subjected to the next reaction without further purification.

The crude aldehyde was dissolved in *t*-BuOH (250 μl) and H_2O (250 μl) at r.t.. 2-Methyl-2-butene (7 μl, 62.8 μmol), sodium phosphate (5.8 mg, 37.5 μmol) and sodium chlorite (3.3 mg, 37.5 μmol) was added to the solution. After 30 min, the reaction was poured into water and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give the corresponding carboxylic acid.

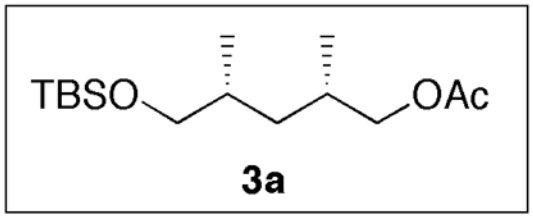
To a solution of the crude acid in THF (1.0 ml) and pyridine (1.0 ml) was added dropwise HF·pyridine (500 μl). The solution was stirred for 2 days. The resulting solution was filtered through a short plug of silica gel and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded borrelidin (**1**) (5.2 mg, 3 steps 85%) as a white solid.

$[\alpha]_D^{27}$ = -26.7° (*c* = 0.10, EtOH); m.p. 140-142°C; **IR (KBr)** 3446, 2924, 2853, 1717, 1465, 1275, 1259 cm^{-1}; **^{1}H-NMR (270 MHz, $CDCl_3$)** δ 0.73 (m, 1H, 1/2 C**H**$_2$), 0.80 (d, 3H, *J* = 6.3 Hz, C**H**$_3$), 0.83 (d, 3H, *J* = 7.2 Hz, C**H**$_3$), 0.84 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 1.05 (d, 3H, *J* = 6.6 Hz, C**H**$_3$), 0.89-

1.44 (m, 6H, C**H**$_2$ x 3), 1.50-1.71 (m, 3H, C**H** x 3), 1.75-2.11 (m, 6H, C**H**$_2$ x 2, 1/2 C**H**$_2$ and C**H**), 2.32 (dd, 1H, *J* = 16.8, 2.3 Hz, 1/2 C**H**$_2$), 2.44 (dd, 1H, *J* = 16.8, 9.9 Hz, 1/2 C**H**$_2$), 2.49-2.78 (m, 4H, C**H**$_2$ and C**H** x 2), 3.87 (dt, 1H, *J* = 9.9, 2.3 Hz, C_{16}-**H**), 4.11 (d, 1H, *J* = 9.6 Hz, C_8-**H**), 4.98 (dt, 1H, *J* = 10.6, 3.3 Hz, C_2-**H**), 6.20 (ddd, 1H, *J* = 14.5, 9.2, 5.3 Hz, C_4-**H**), 6.39 (dd, 1H, *J* = 14.5, 11.2 Hz, C_5-**H**), 6.83 (d, 1H, *J* = 11.2 Hz, C_6-**H**); **^{13}C-NMR (67.5 MHz, $CDCl_3$)** δ 14.9, 16.9, 18.2, 20.1, 25.2, 26.2, 27.1, 29.7, 31.2, 35.2, 35.6, 35.9, 37.4, 39.3, 43.0, 45.8, 47.8, 48.4, 69.8, 73.1, 77.2, 115.9, 118.2, 127.0, 138.5, 144.0, 172.2, 180.6; **HRMS [FAB, m-NBA]** calcd for $C_{28}H_{43}O_6Na$ [M+Na^+]: 512.2988; found: 512.2978.



3a


TBSO
OAc

3a

PPM
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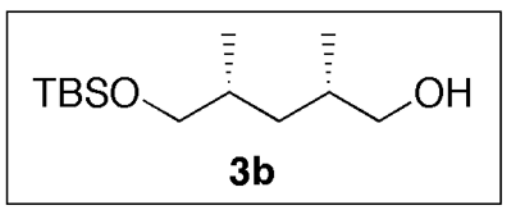

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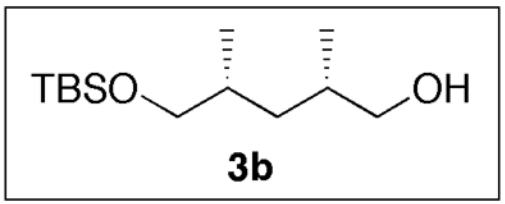

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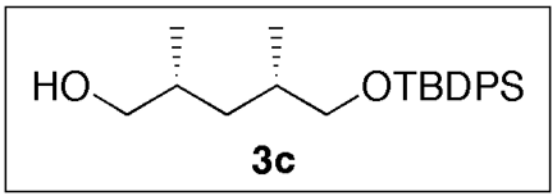

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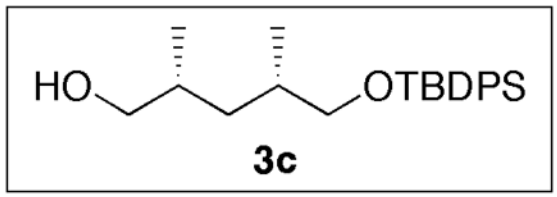
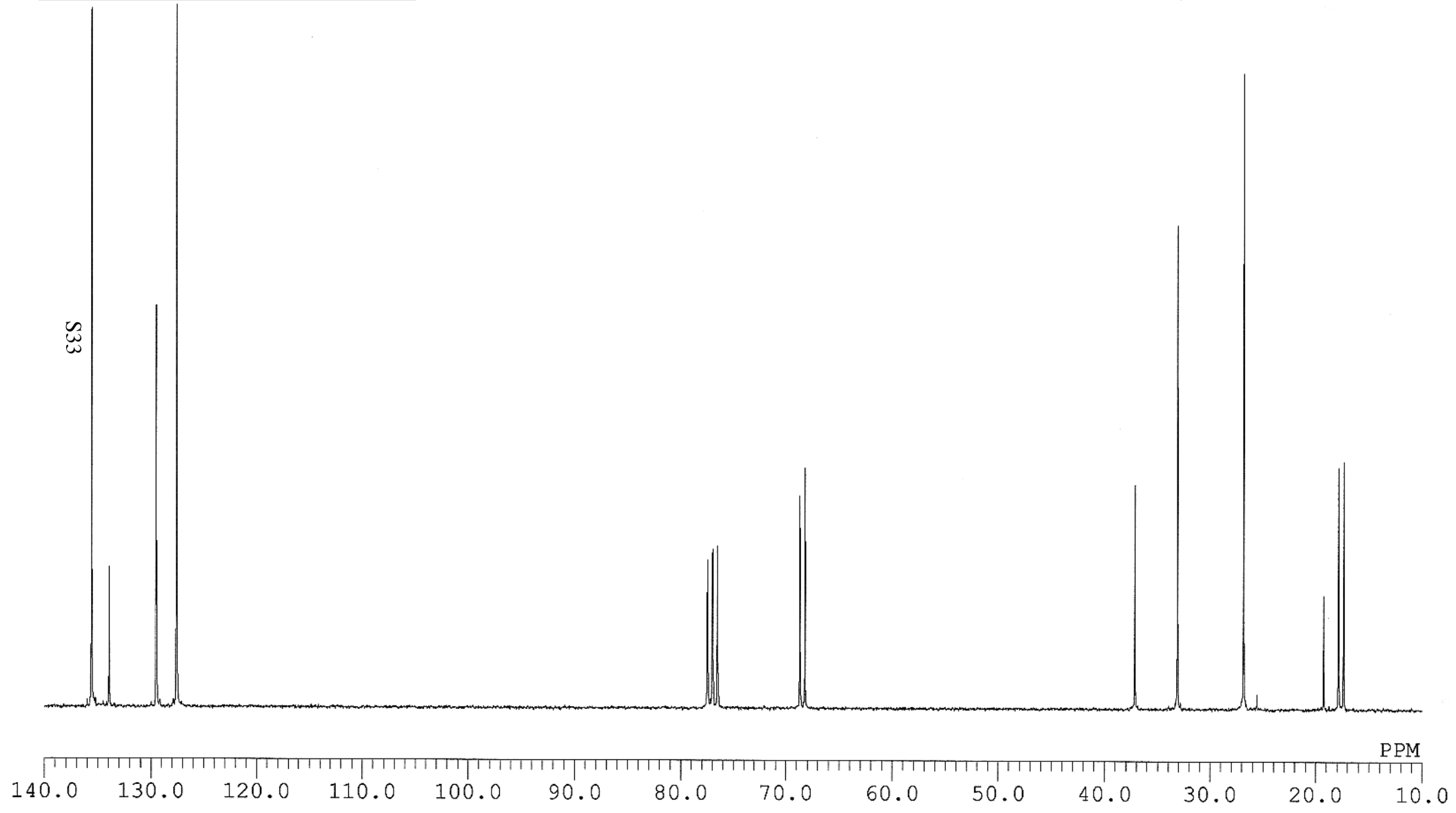

HO
OTBDPS

3c


PPM
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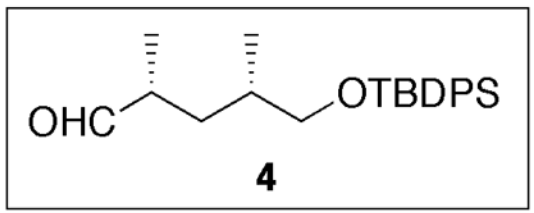
10.0


OHC
OTBDPS
4

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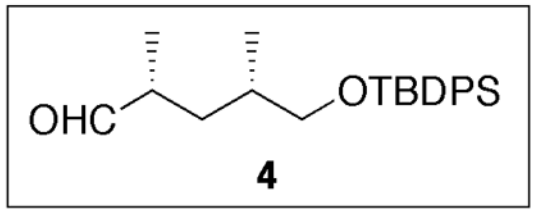
1.0


OHC
OTBDPS

4

PPM
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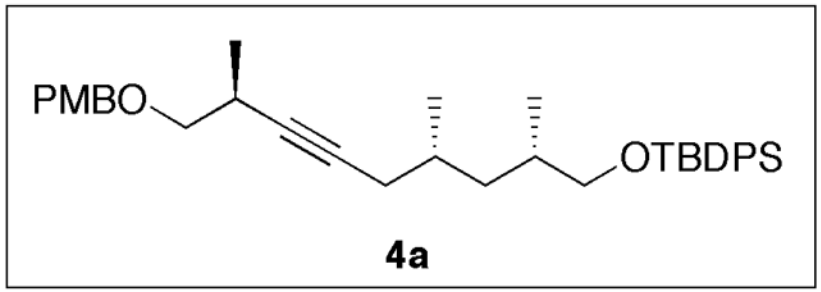

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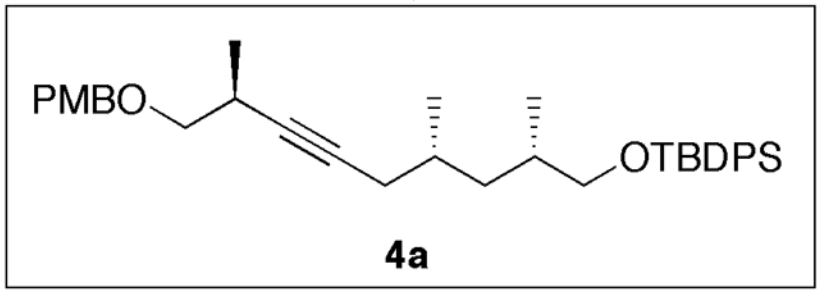
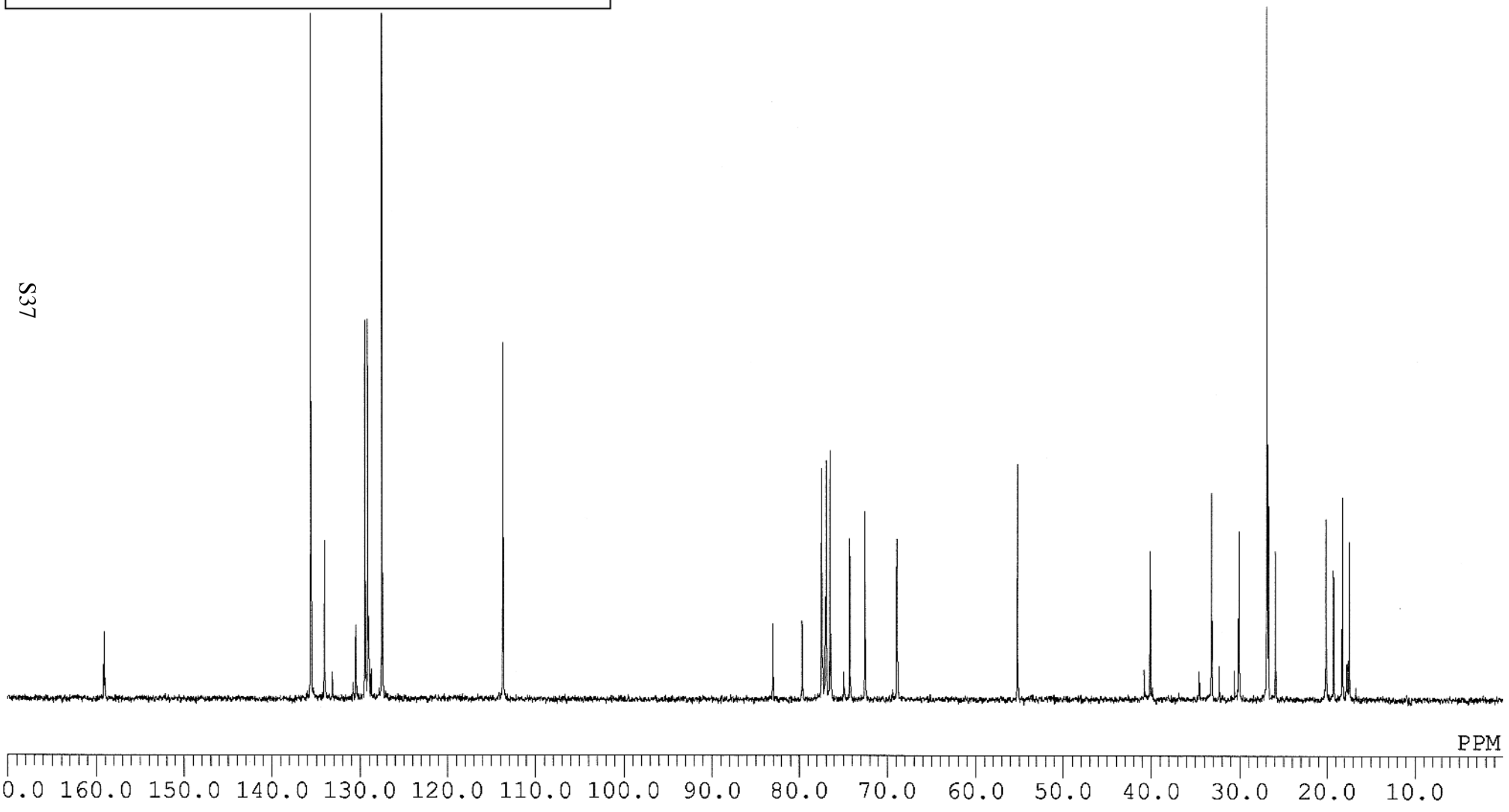

PMBO
OTBDPS

4a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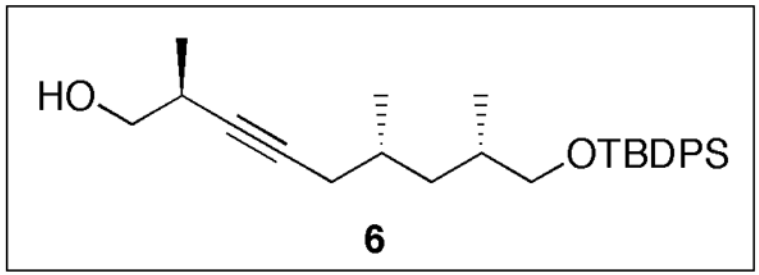

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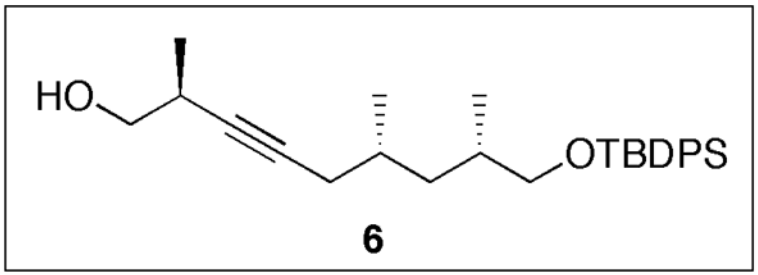
HO
OTBDPS

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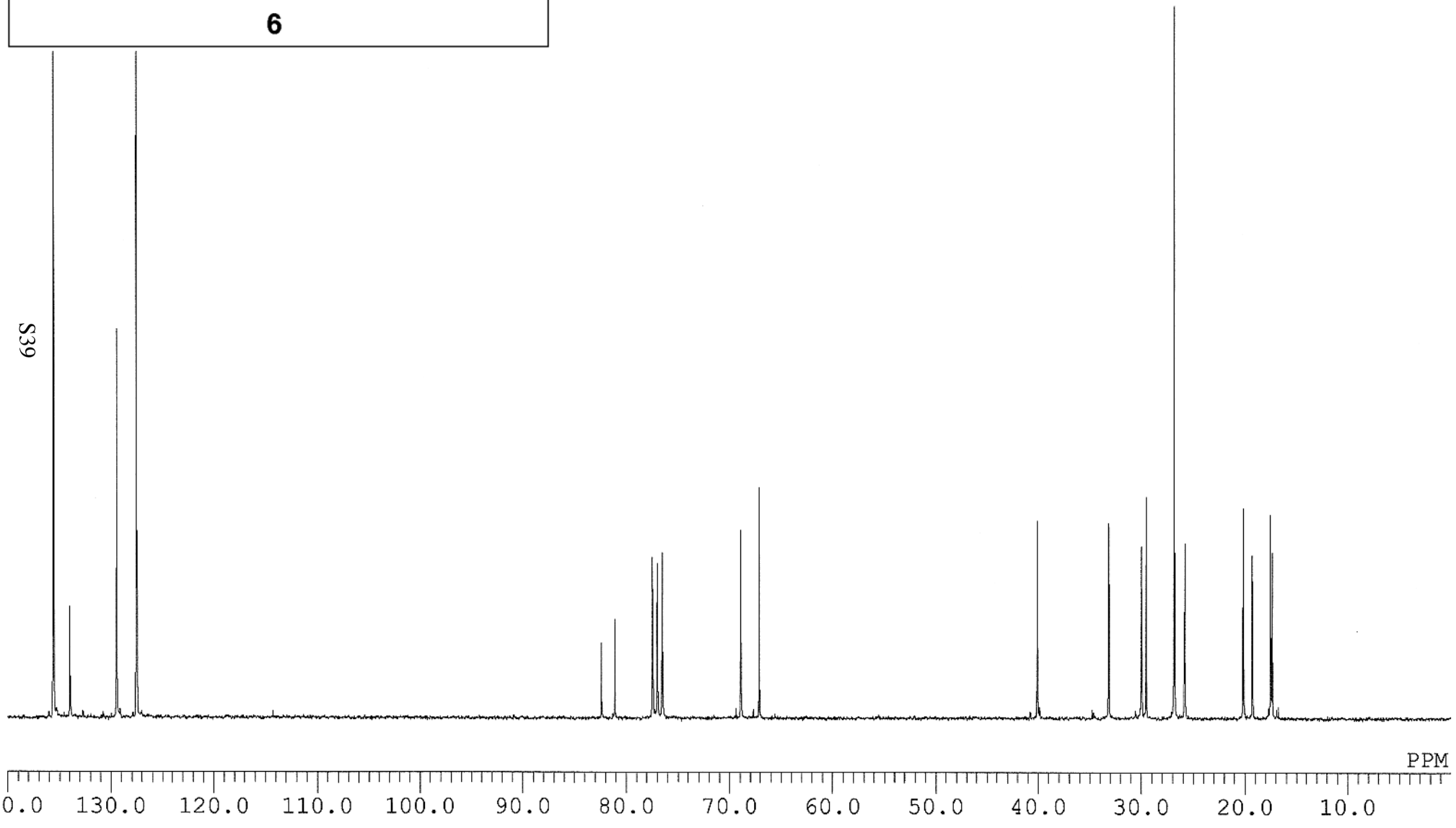
PPM
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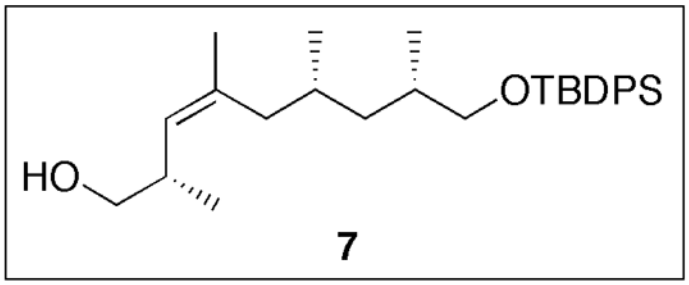
10.0



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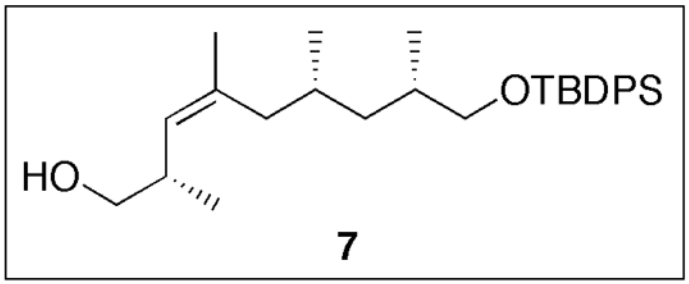
OTBDPS
HO

7

PPM
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90.0
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50.0
40.0
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20.0
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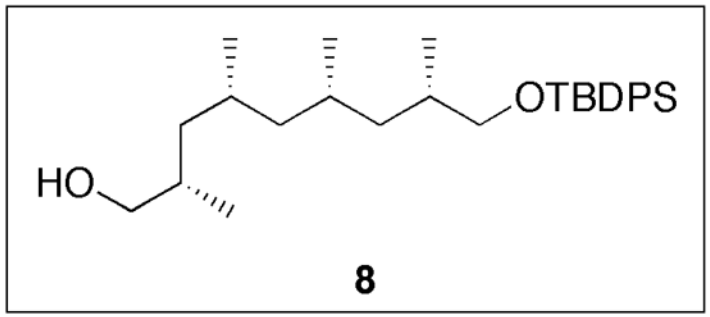

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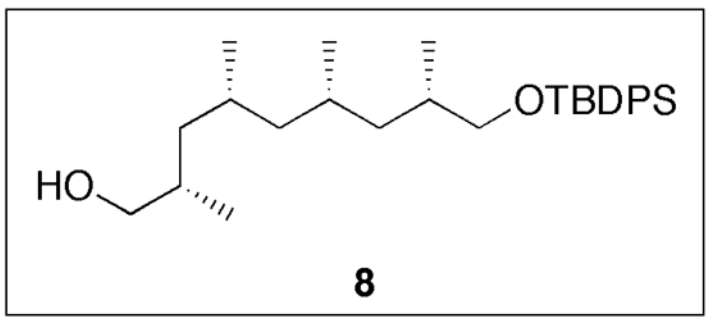
OTBDPS
HO

8

PPM
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80.0
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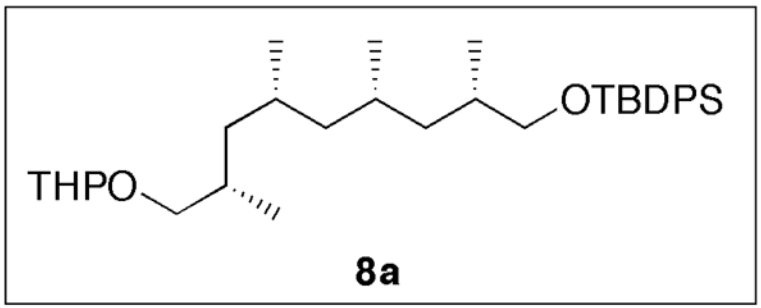
10.0



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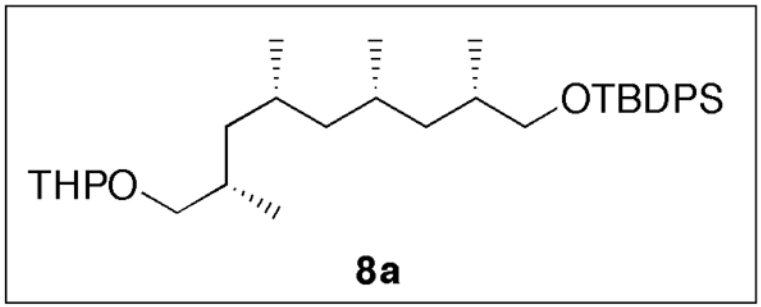
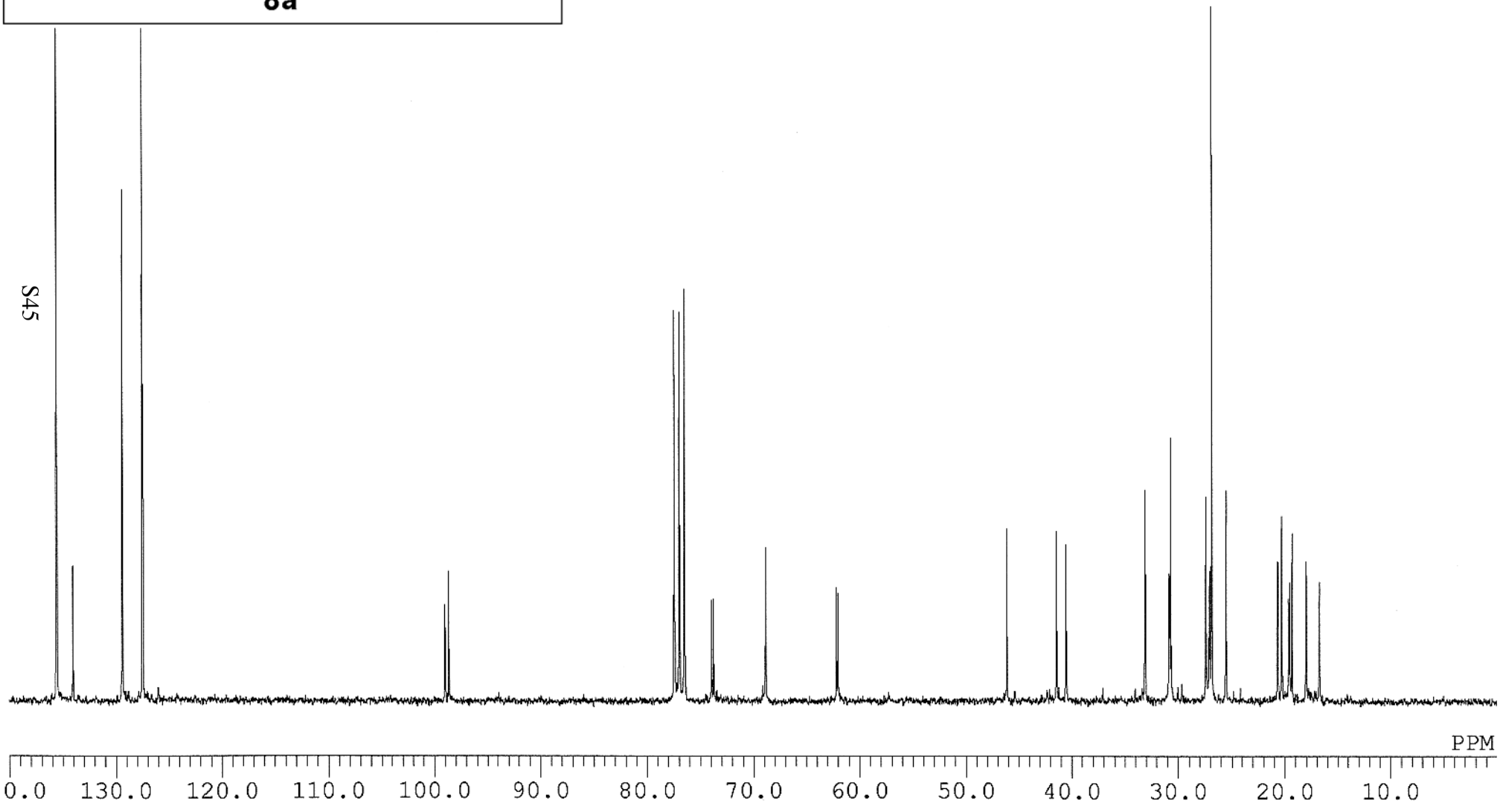

OTBDPS
THPO

8a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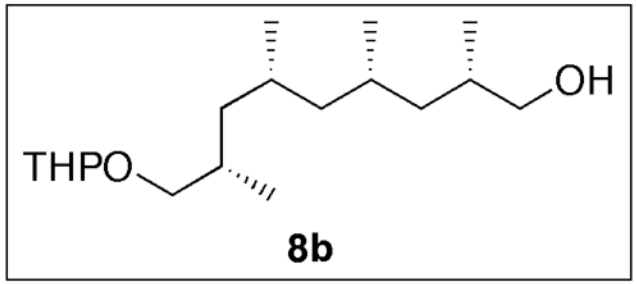
10.0



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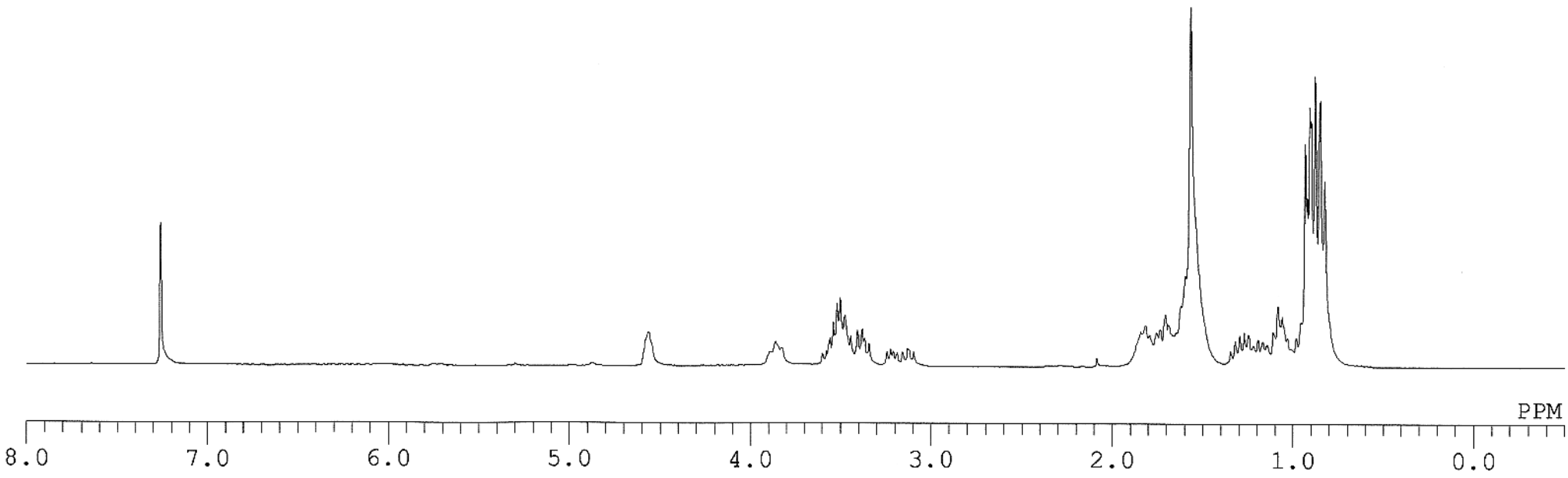

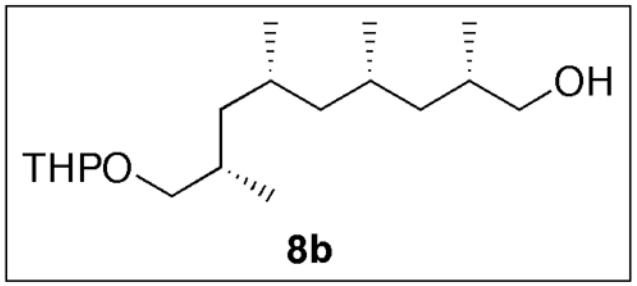

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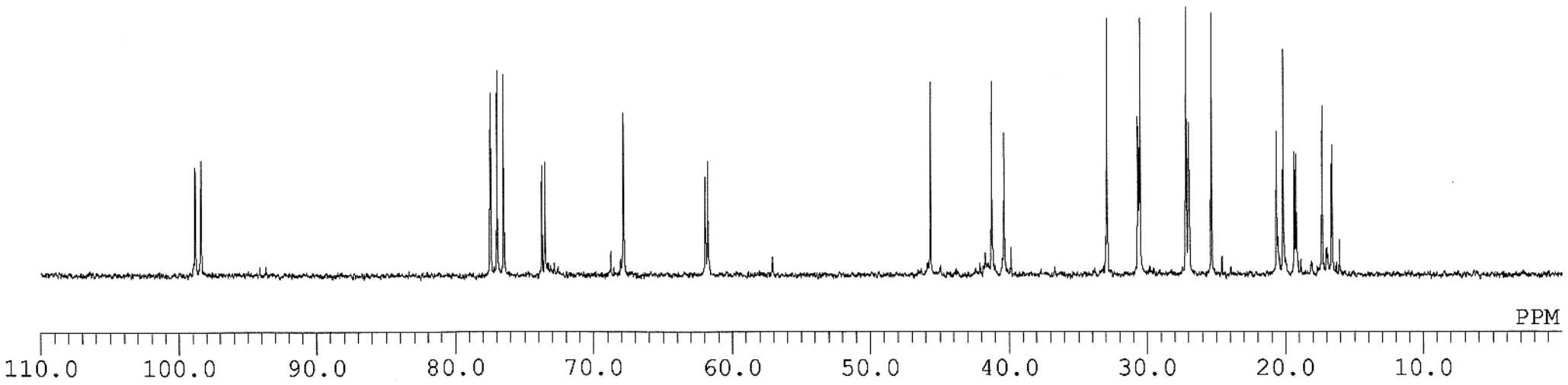

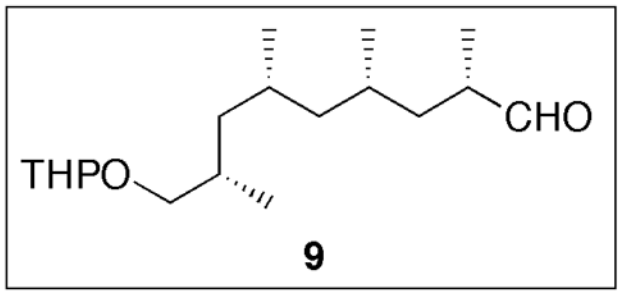

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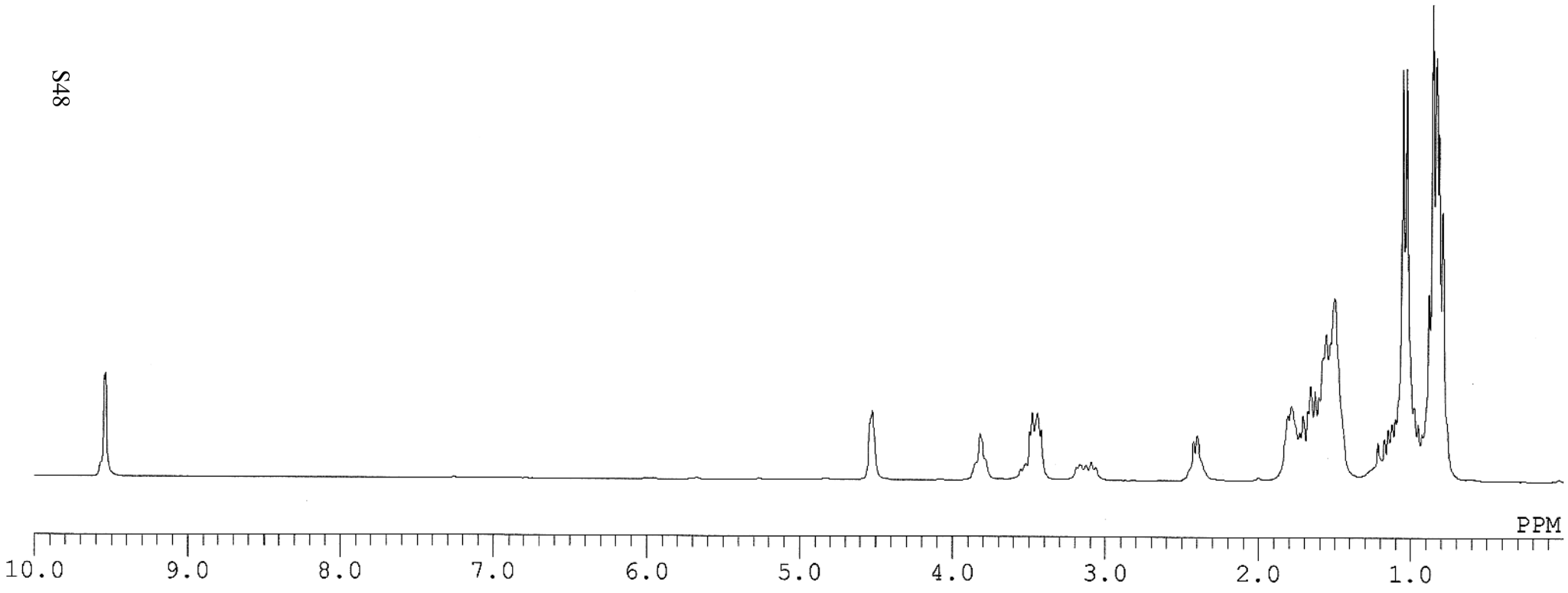
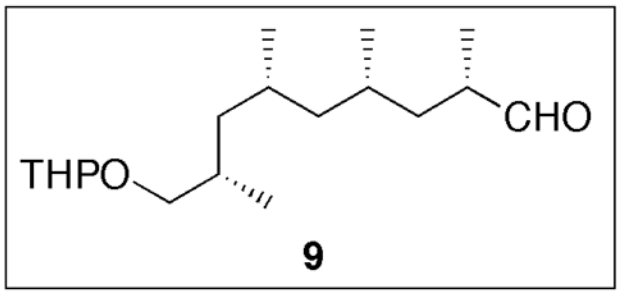
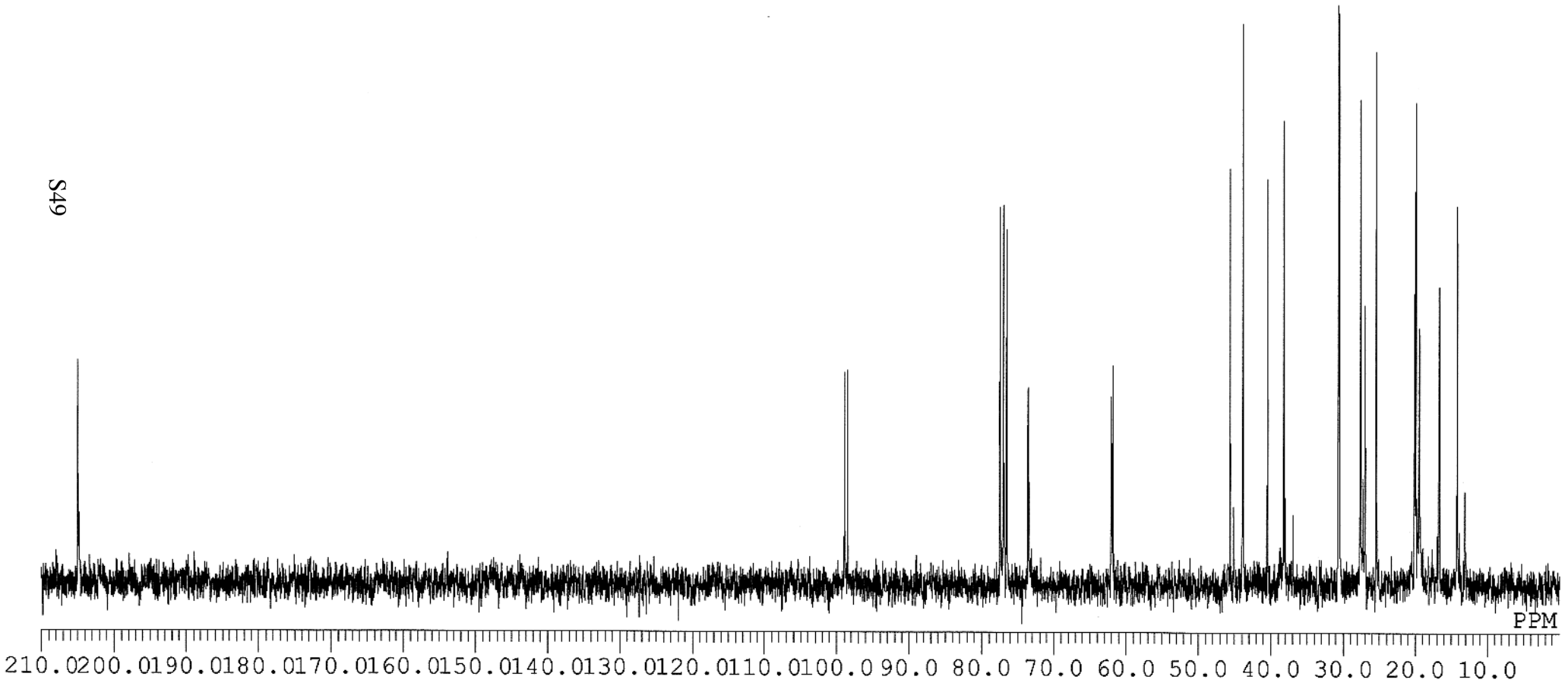



THPO
CHO

9


PPM
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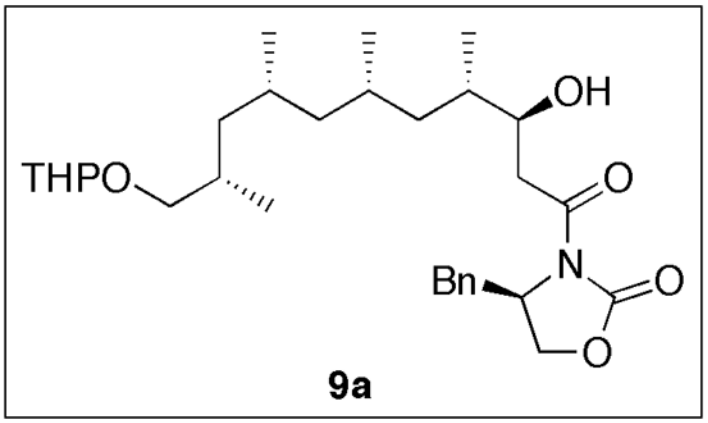

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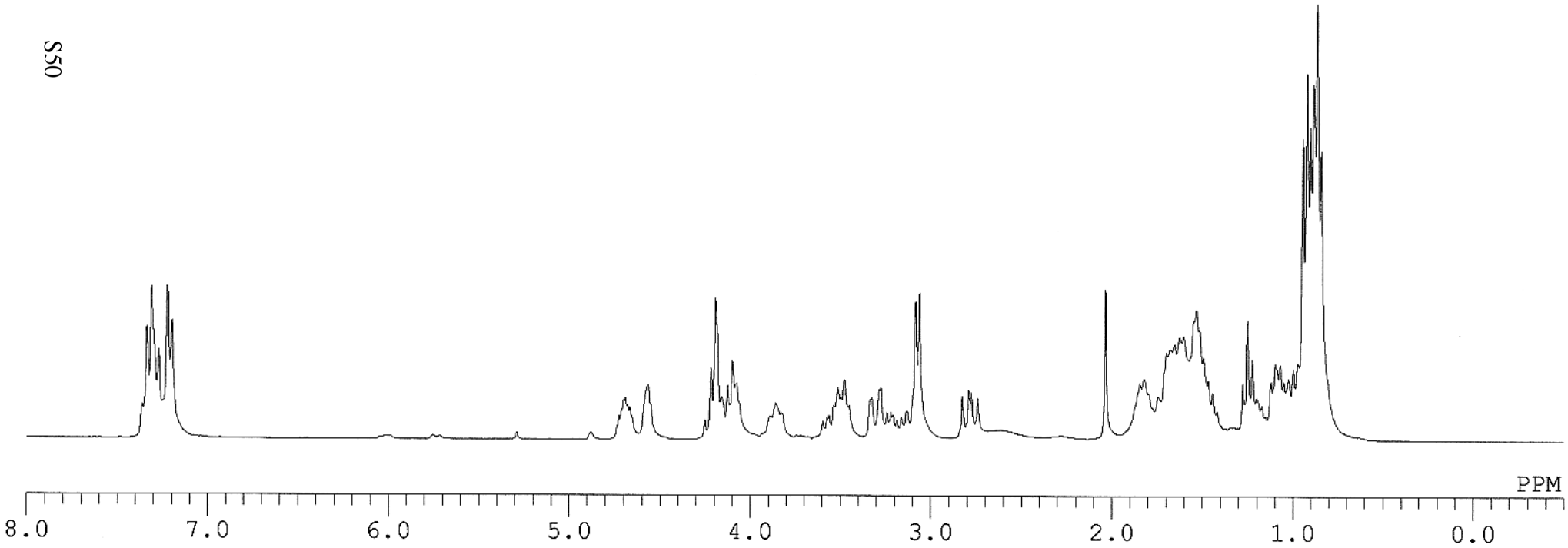
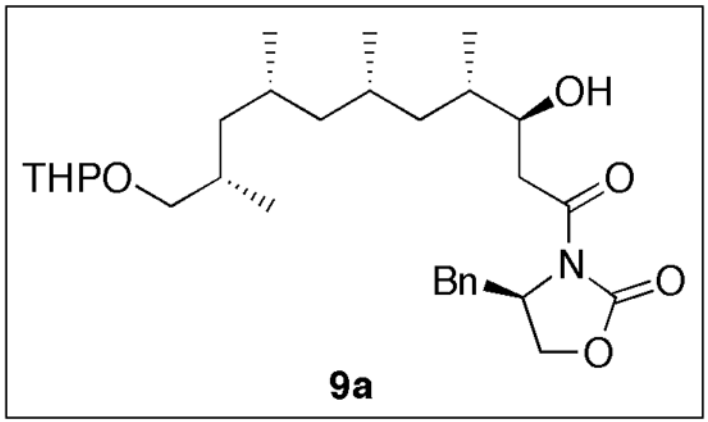
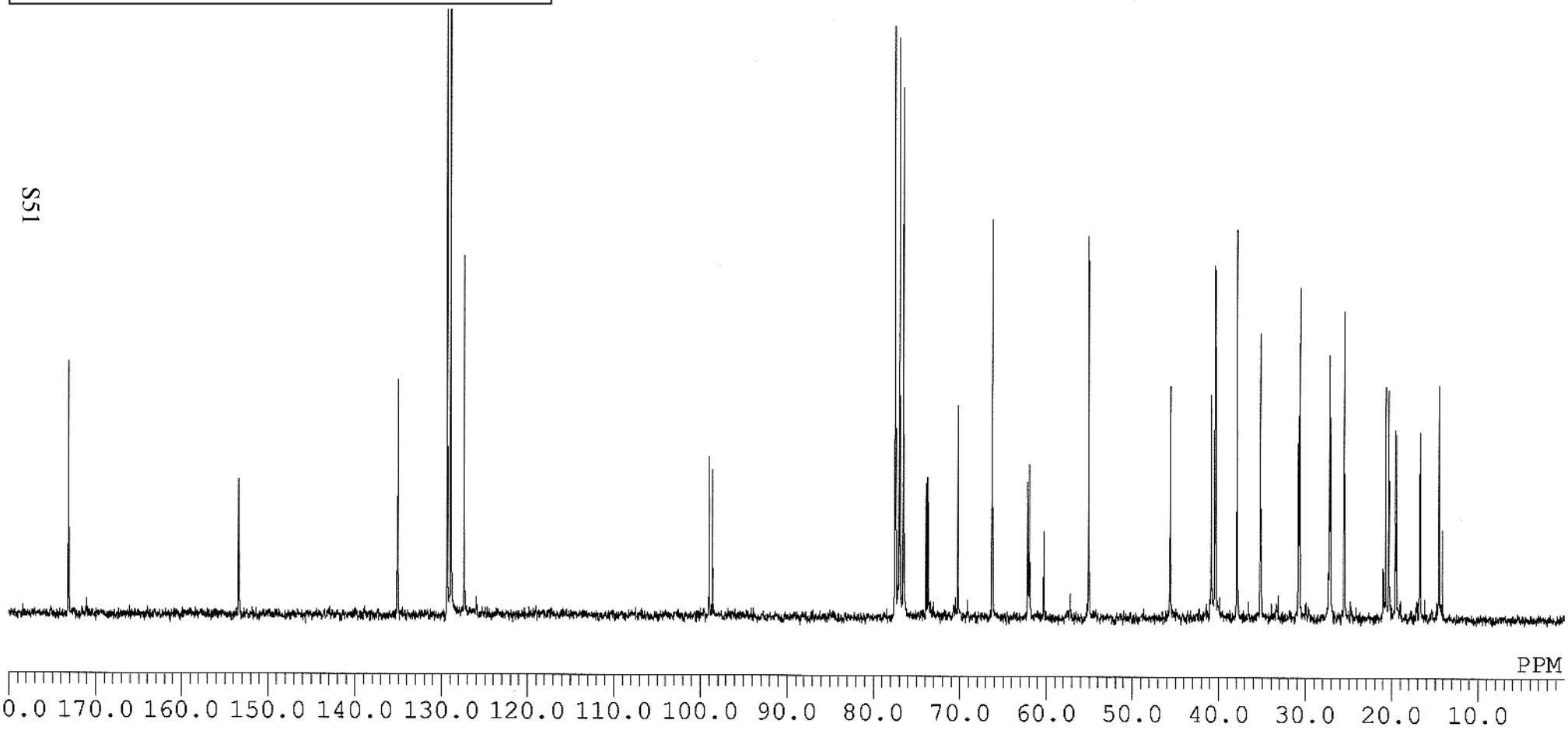



OH
THPO
O
N
Bn
O
O

9a


PPM
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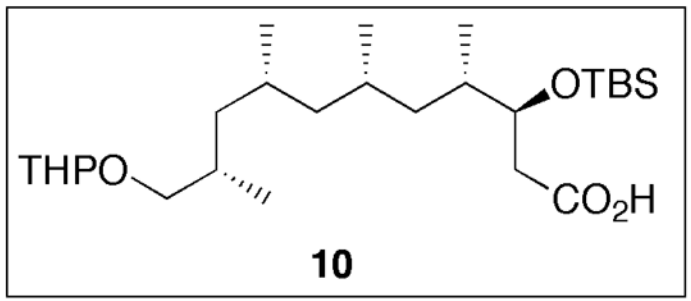

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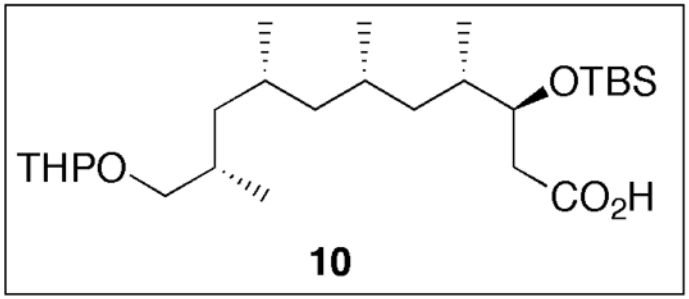
OTBS
THPO
CO_2H

10

PPM
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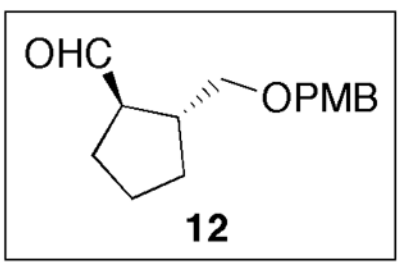
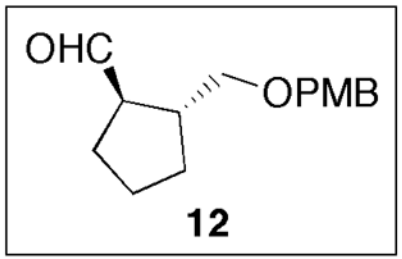


12



12

S55

PPM

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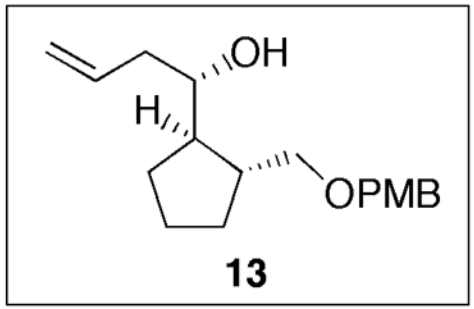

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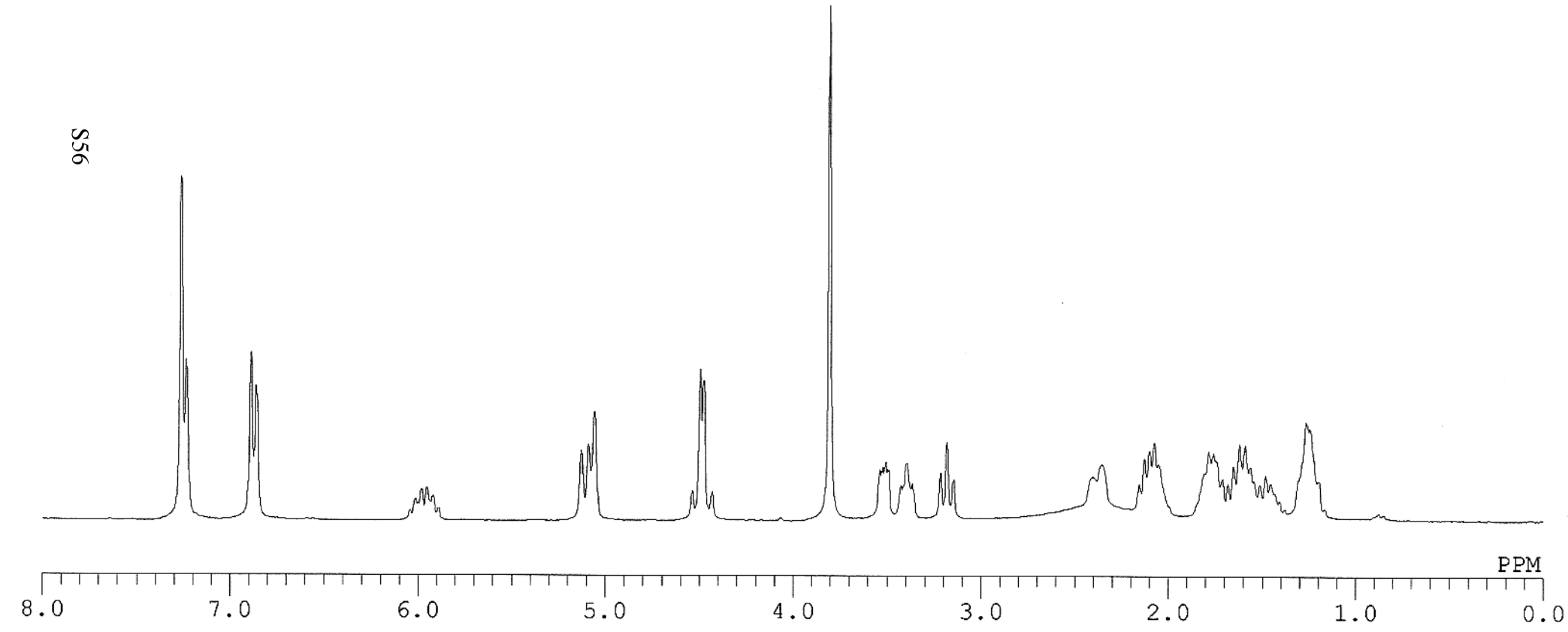
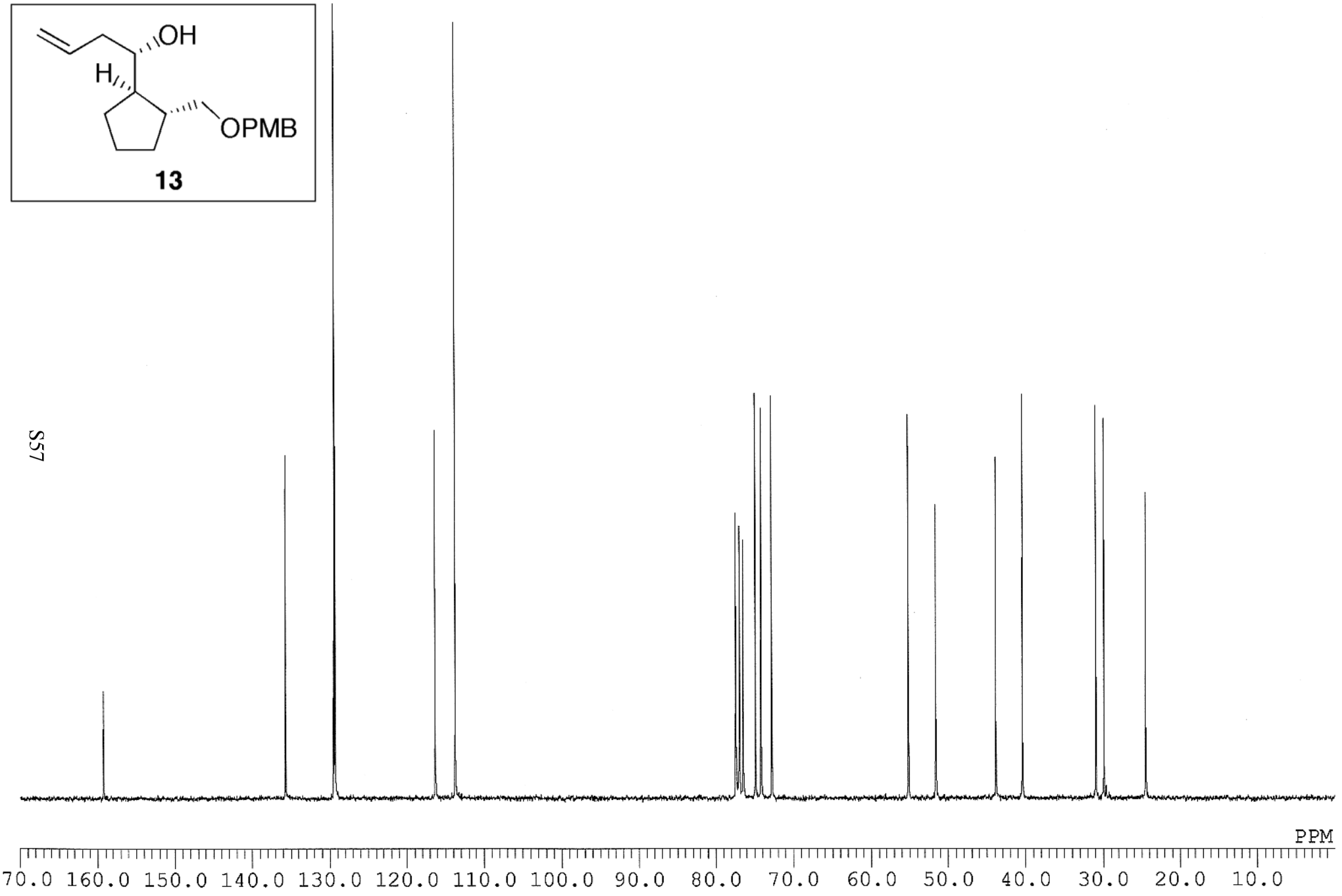
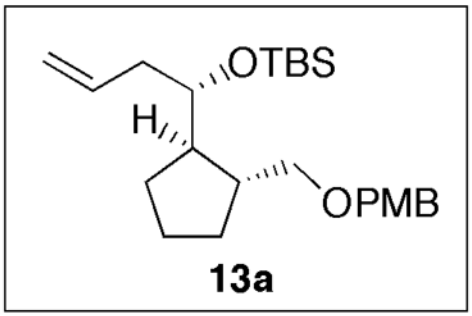



OH
H
OPMB
13
S57
PPM
170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0



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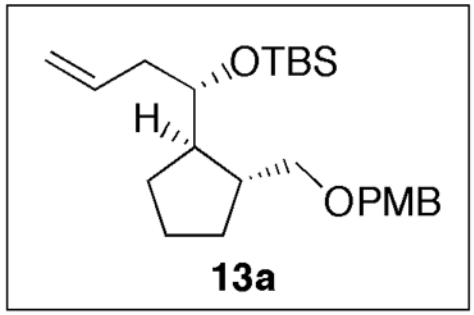
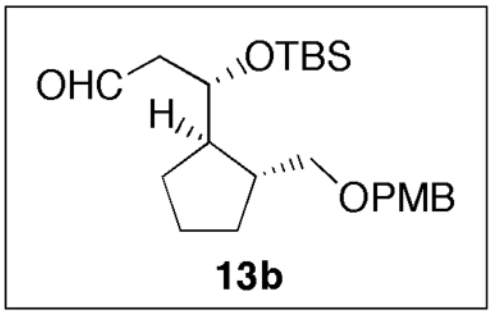


13a

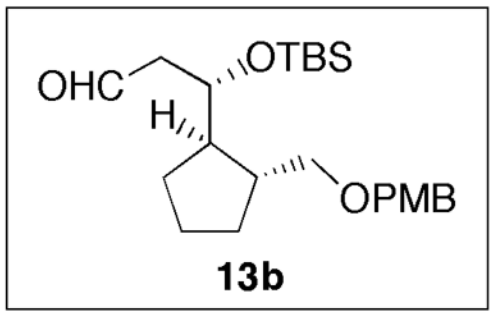
PPM

160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 -10.0



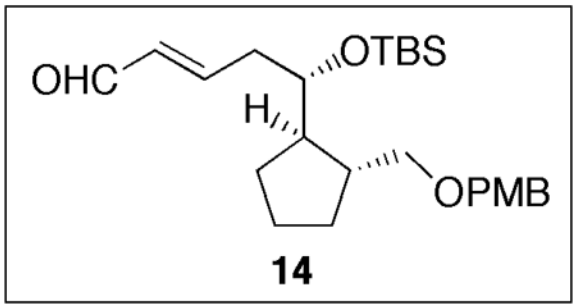
13b

S60


OHC
OTBS
H
OPMB

13b

PPM
210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 -10.0



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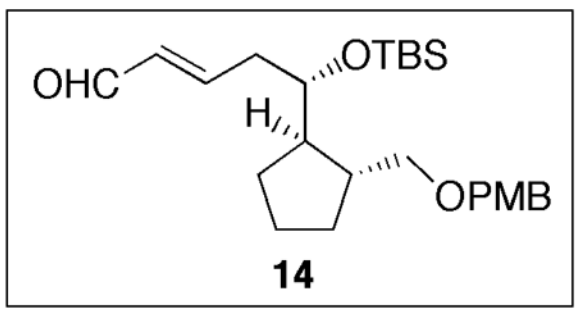
OHC
OTBS
H
OPMB

14

PPM
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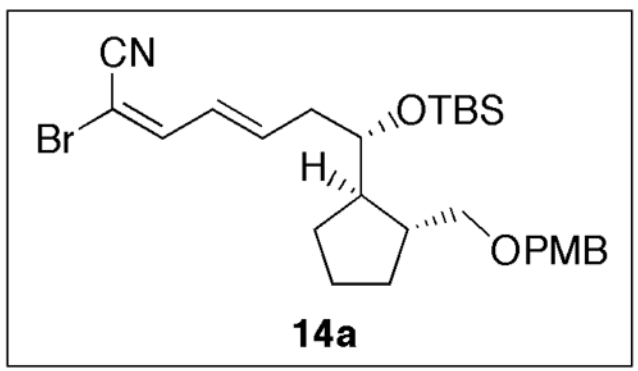
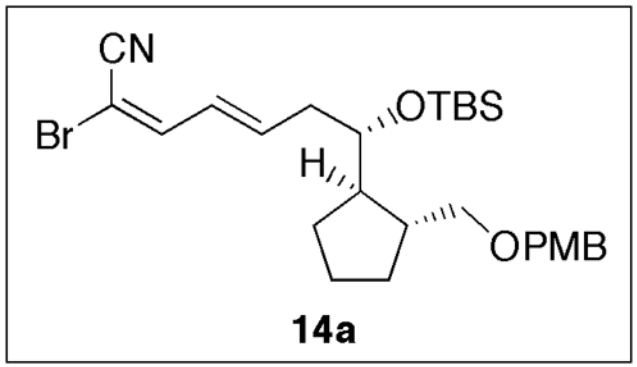


14a


CN
Br
OTBS
H
OPMB

14a

PPM
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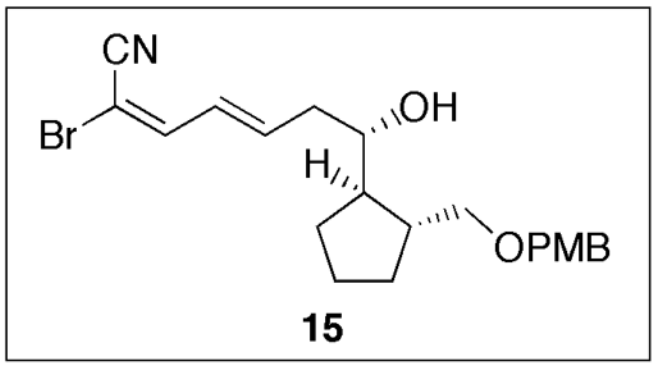

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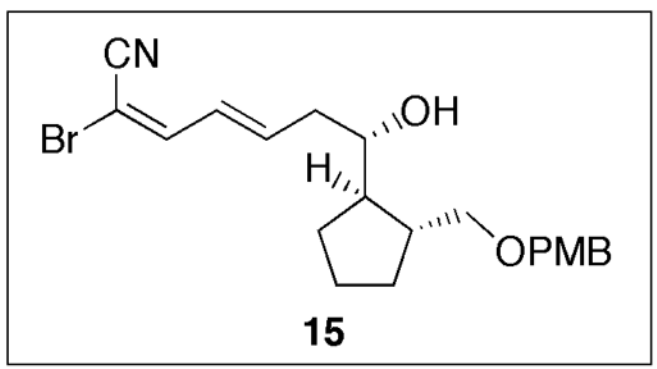
CN
Br
OH
H
OPMB

15

S67
PPM
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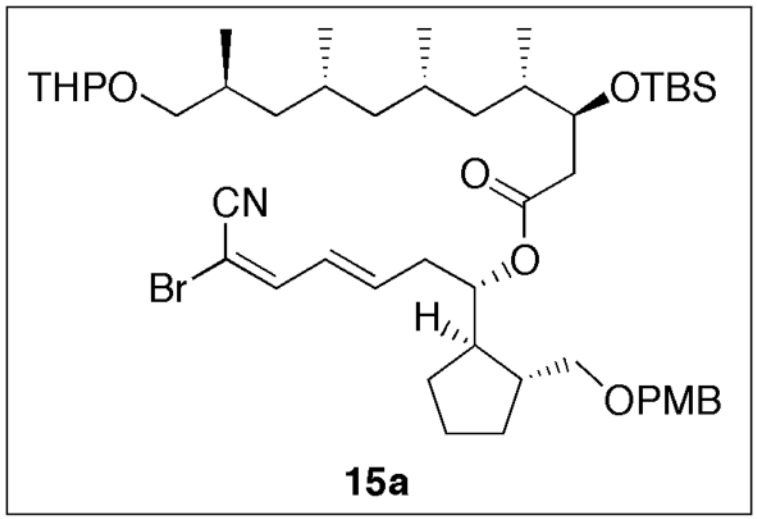
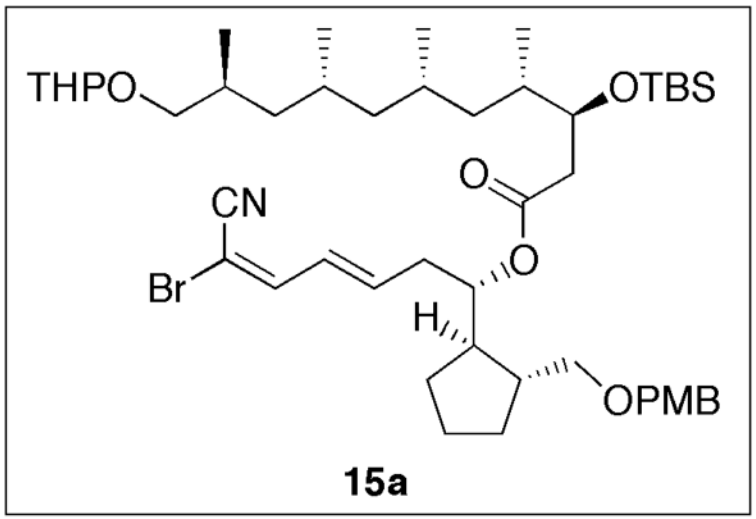


15a



15a

PPM

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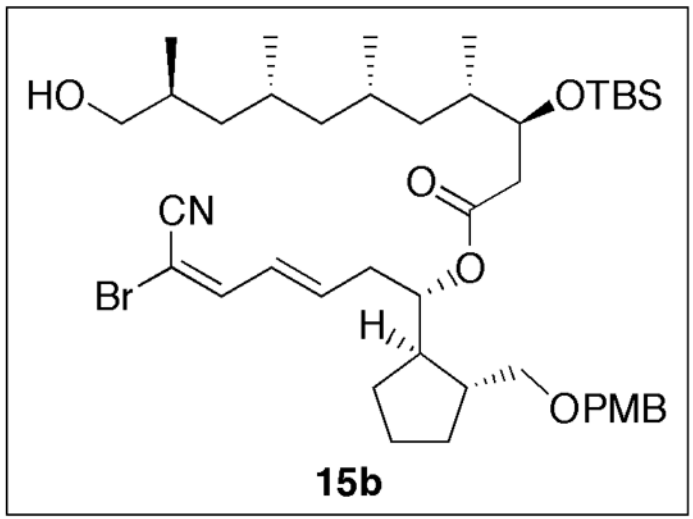

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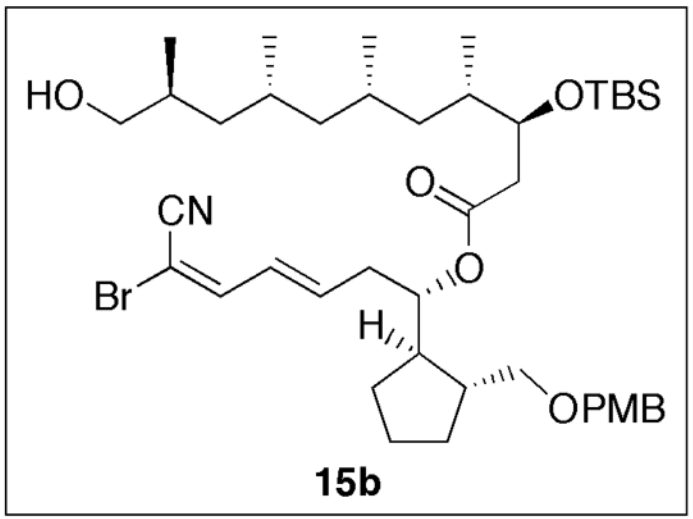
HO
OTBS
O
CN
Br
O
H
OPMB

15b

PPM
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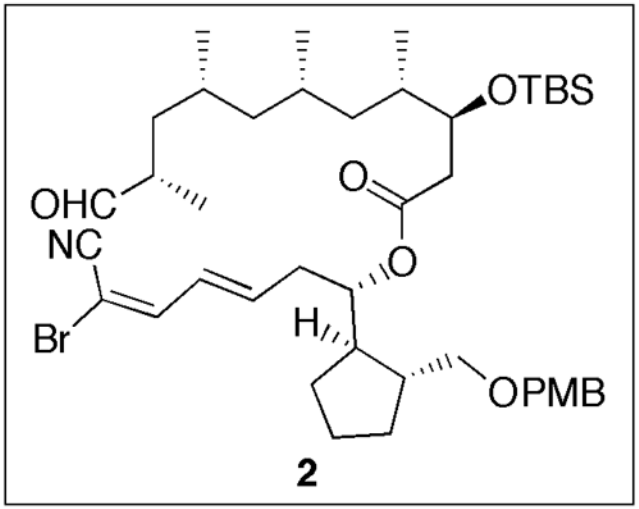
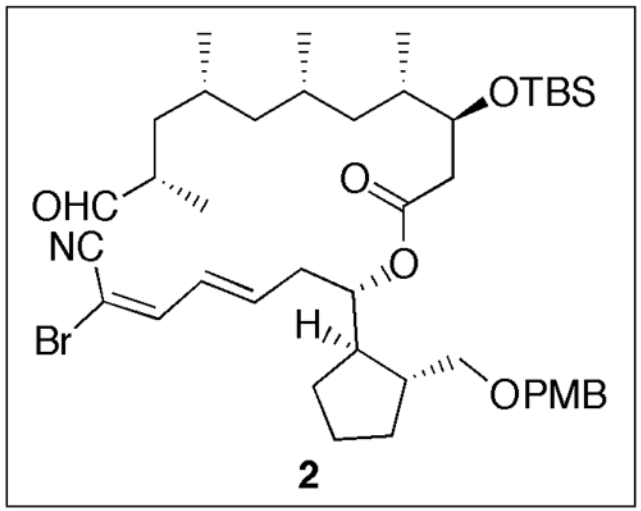
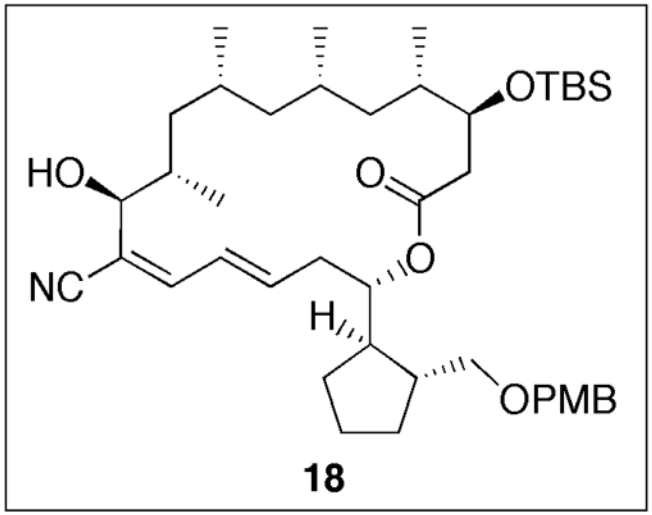


2

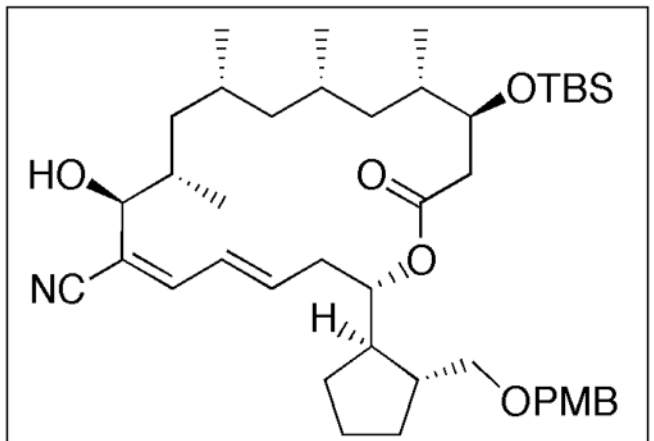

OTBS
O
OHC
NC
O
Br
H
OPMB

2

PPM
210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 -10.0

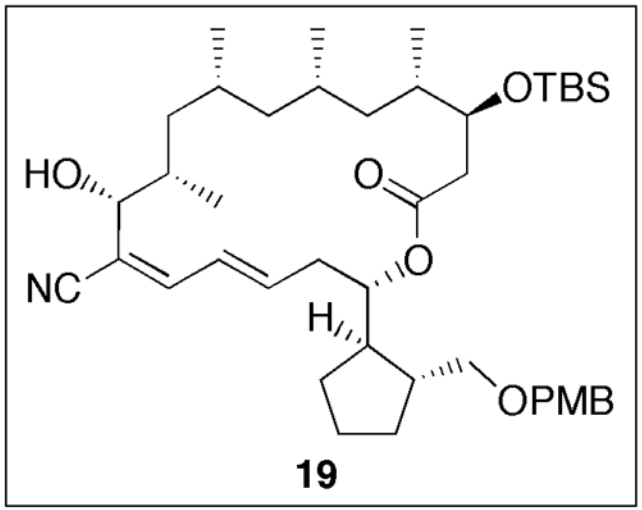


18

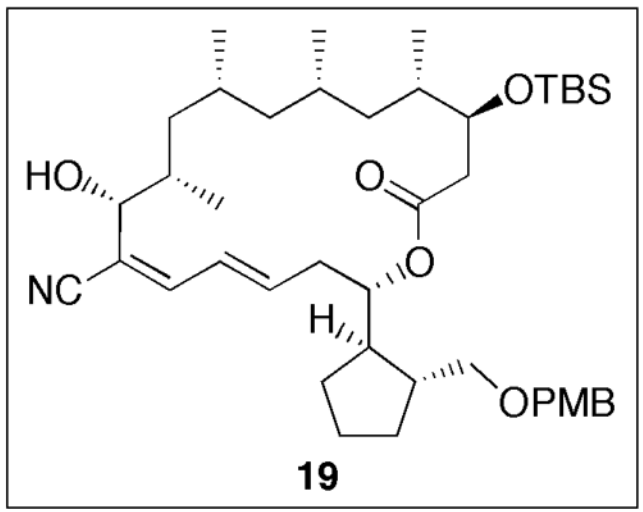

OTBS
HO
O
O
NC
H
OPMB

18

PPM
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 -10.0



19


OTBS
HO
O
O
NC
H
OPMB

19

PPM
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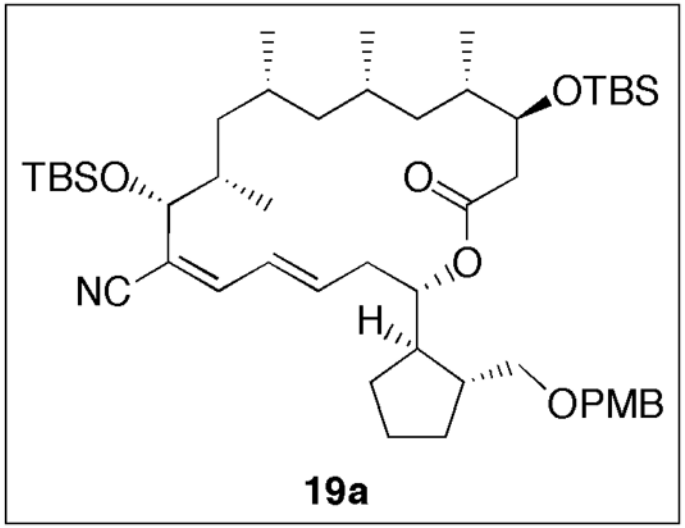
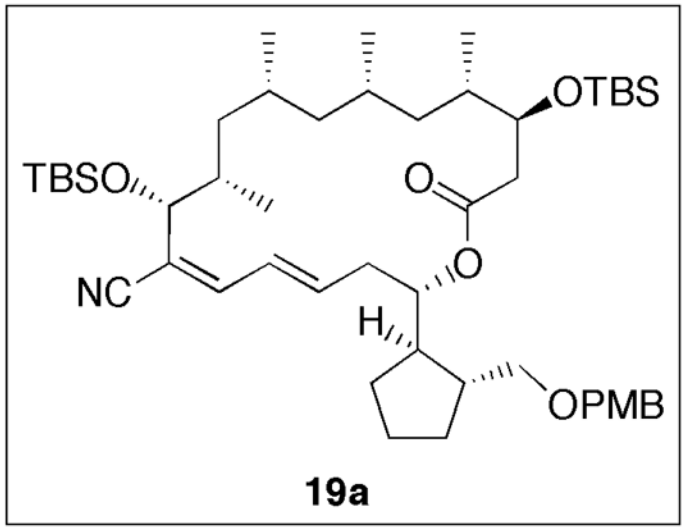


19a


OTBS
TBSO
O
O
NC
H
OPMB

19a

PPM
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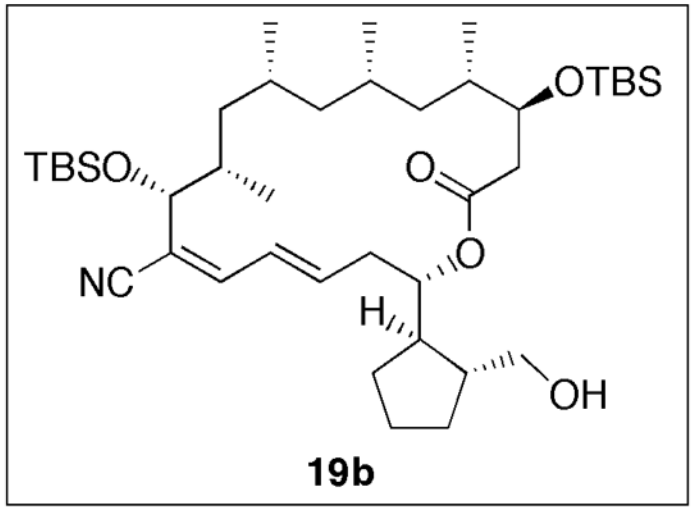
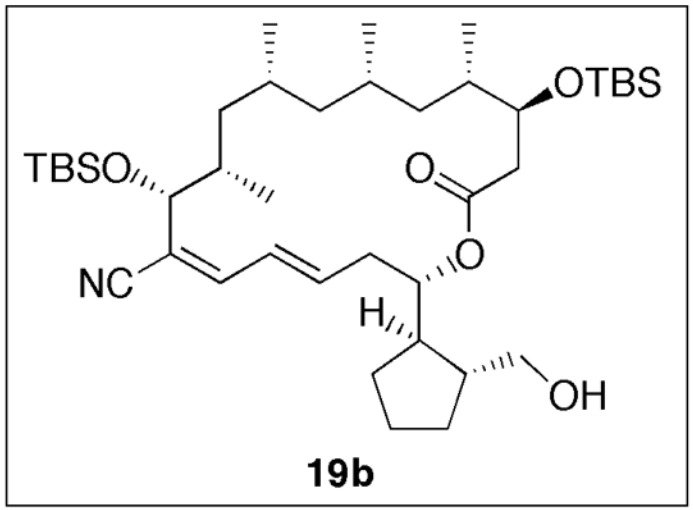
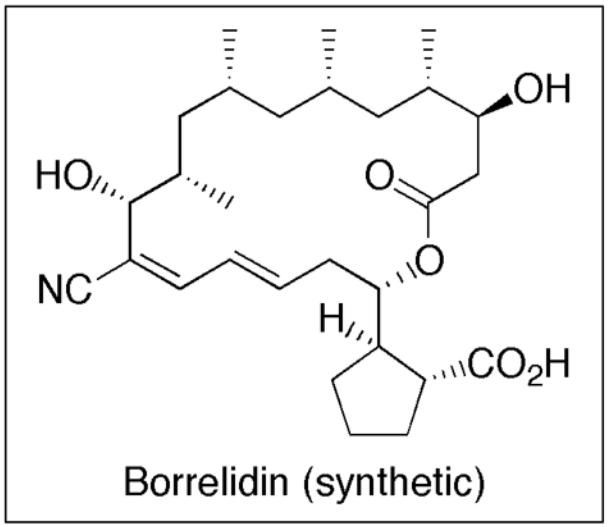


19b

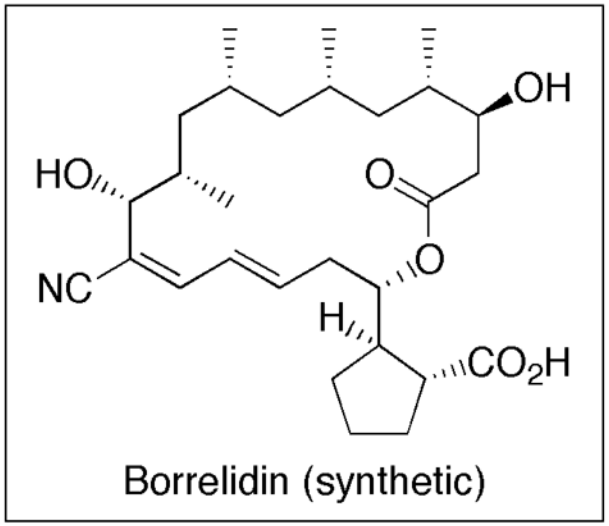

OTBS
TBSO
O
O
NC
H
OH

19b

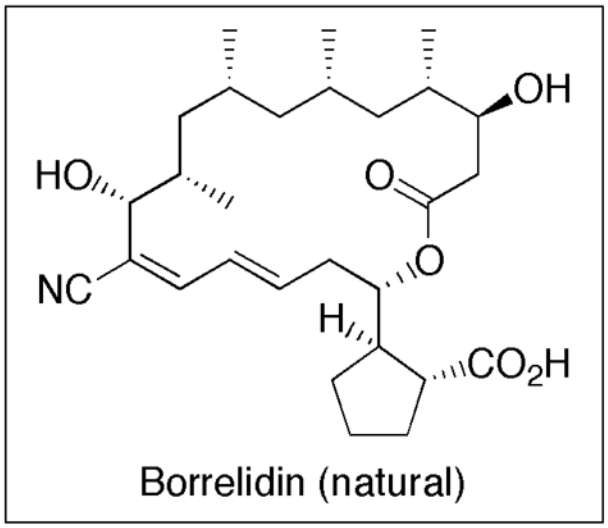
PPM
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 -10.0



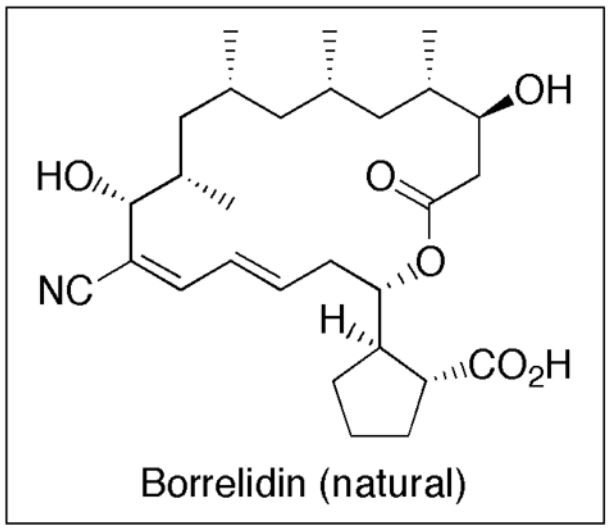
Borrelidin (synthetic)



Borrelidin (synthetic)



Borrelidin (natural)



Borrelidin (natural)

S85