

**SUPPORTING
INFORMATION****Total Synthesis of Tartrolon B**

Markus Berger and Johann Mulzer*

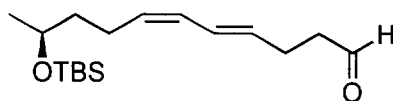
*Institut für Organische Chemie, Universität Wien,
Währingerstraße 38, A-1090 Wien, Austria***Supplementary Material**

General: Fourier transform infrared spectra were recorded on a Perkin Elmer 1600 FT spectrometer, calibrated on an internal standard and are reported in wavenumbers (cm^{-1}). ^1H - and ^{13}C -NMR spectra were taken on a Bruker AMX 250, a Bruker AMX 400 or a Bruker DRX 600. Proton chemical shifts are reported in δ , using the residual CHCl_3 as internal reference (7.26 ppm). Carbon chemical shifts are reported in δ , using CDCl_3 as an internal standard (77.0 ppm). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Mass spectra were obtained under electron impact (EI), field desorption (FD), field ionization and fast atom bombardment (FAB) conditions on a Finnigan MAT 8230, MAT 900 S, Varian CH7 or MAT 711. Fast atom bombardment high resolution spectra were taken on the MAT 900 S and calibrated with CsI. Most FAB samples were doped with CsI and 3-nitrobenzoyl alcohol was used as matrix. A cesium gun was used as ion source with settings of 20 μA and 20 KV. Elemental analyses were performed by Microanalytisches Laboratorium, Institut für Physikalische Chemie der Universität Wien. UV-vis spectra were recorded with a Perkin-Elmer Lambda 7 spectrometer. CD spectra were taken on a CD 6 circular dichrograph (I. S. A. Jobin Yvon) in a thermostated ($20 \pm 0^\circ\text{C}$) quartz cuvette (1 mm length).

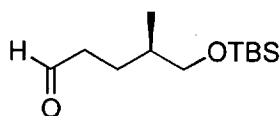
Chemicals were purchased from Aldrich Chemical Company, Fluka and Merck and used without further purification. Where appropriate, reactions were performed in flame-dried glassware under an argon atmosphere.

Ether (Et_2O), tetrahydrofuran (THF) and toluene were freshly distilled from sodium benzophenone ketyl under an argon atmosphere. Dichloromethane (CH_2Cl_2), diisopropylamine (Pr_2NH), triethylamine (Et_3N), Hünig's base ($^i\text{Pr}_2\text{EtN}$) and dimethyl sulfoxide (DMSO) were distilled from calcium hydride. Hexanes and ethyl acetate (EtOAc) were distilled to remove higher boiling fractions.

Silica gel 60 (230–400 mesh ASTM, Merck) was used for chromatography. Precoated aluminium sheets 60 F_{254} (Merck) were used for analytical thin layer chromatography. Compounds were visualised with UV light, p-anisaldehyde stain, or phosphomolybdic acid in EtOH .

(4E, 6Z, 10S)-10-tert-Butyldimethylsilyloxy-undec-4,6-dienal (12)

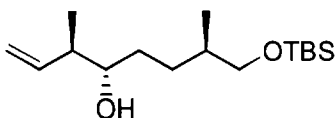
Ethyl (4E, 6Z, 10S)-10-tert-butyldimethylsilyloxy-undec-4,6-dienoate (1.0 g, 2.94 mmol) was dissolved in 15 mL of abs. Et₂O and cooled to -90°C. Over a period of 20 min, a solution of DiBAL-H in toluene (2.8 mL, 1.2 M, 3.36 mmol) was added and the mixture was stirred for a further 3 h. Saturated aqueous tartaric acid (8 mL) was added and the mixture was warmed to ambient temperature under effective stirring. The phases were separated and the organic phase was washed with water (15 mL). The combined aqueous phases were extracted three times with Et₂O, the combined organic layers were washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, filtered and concentrated in vacuo. The residue was purified via column chromatography (40 g of SiO₂, hexane/EtOAc 5 : 1, R_f = 0.43) to provide 0.83 g (93 %) of (4E, 6Z, 10S)-10-tert-butyldimethylsilyloxyundec-4,6-dienal **12** as a colorless oil. Anal. calcd for C₁₇H₃₂O₂Si : C, 68.86; H, 10.88; found: C, 69.13; H, 10.60. ¹H-NMR (400 MHz; CDCl₃): δ [ppm] = 9.88 (t, *J* = 1.5 Hz), 6.36 (dd, *J* = 15.1, 11.0 Hz, 1H), 5.92 (dd, *J* = 11.0, 10.8 Hz, 1H), 5.64 (dt, *J* = 15.1, 6.6 Hz, 1H), 5.35 (dt, *J* = 10.8, 7.4 Hz), 3.82 (tq, *J* = 6.1 Hz, 1H), 2.24 (dt, *J* = 7.2 Hz, 2.6 Hz, 2H), 1.92 (t, *J* = 2.6 Hz, 1H), 1.62 (dt, *J* = 7.2 Hz, 2H), 1.13 (d, *J* = 6.1 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ¹³C-NMR (63 MHz; CDCl₃): δ [ppm] = 201.9, 131.7, 131.2, 128.3, 127.1, 68.3, 43.6, 39.8, 26.1, 25.5, 24.3, 23.9, 18.3, -4.1, -4.5; MS (EI, 70eV, 30°C) *m/z* = 281 [M-15] (1), 239 [M-57] (59), 197 (7), 183 (7), 164 (43), 147 (16), 121 (100), 105 (19), 101 (24), 93 (97), 79 (89), 75 (72); [α]_D²⁰ = +25.5° (c = 2.0; CHCl₃); IR (thin film) 1/λ [cm⁻¹] = 2957, 2930, 2857, 1739, 1463, 1373, 1302, 1255, 1162, 1137, 1095, 1037, 950, 884, 836, 775.

(4R)-5-tert-Butyldimethylsilyloxy-4-methyl-pentanal (4)

Ethyl (4R)-5-tert-butyldimethylsilyloxy-4-methyl-pentanoate **3** (15.7 g, 66.7 mmol) was dissolved in 200 mL abs. Et₂O and cooled to -90°C. Over a period of 90 min, a solution of DiBAL-H in toluene (43 mL, 1.5 M, 69 mmol) was added and the mixture was stirred for a further 2 h. Saturated aqueous tartaric acid (40 mL) was added and the mixture was warmed to ambient temperature under effective stirring. The phases were separated and the organic phase washed with water (30 mL). The combined aqueous phases were extracted three times with Et₂O, the combined organic layers were washed with saturated aqueous NaHCO₃, brine, dried over MgSO₄, filtered and concentrated in vacuo. Distillation under vacuo yielded 12.3 g (89%) of (4R)-5-tert-butyldimethylsilyloxy-4-methyl-pentanal **4** (68°C, 0.5 mm Hg). ¹H-NMR (400 MHz; CDCl₃): δ [ppm] = 9.98 (t, *J* = 2.0 Hz, 1H), 3.43 (d, 5.7 Hz, 1H), 3.42 (d, *J* = 5.9 Hz, 1H), 2.47 (dddd, *J* = 6.9, 4.8, 2.5, 2.0 Hz, 1H), 2.43 (dddd, *J* = 6.9, 5.0, 3.2, 2.0 Hz, 1H), 1.75 (m, 1H), 1.61 (m, 1H), 1.47 (m, 1H), 0.89 (s, 9H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.04 (s;

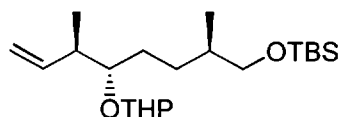
6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 202.8, 67.8, 41.6, 35.2, 25.8, 25.5, 18.3, 16.5, -5.5; MS: (EI, 70 eV, 90°C) m/z = 215 [M-15] (2), 189 (4), 173 [M-57] (36), 171 (14), 155 (8), 131 (10), 105 (9), 99 (11), 81 (13), 75 (100); HRMS (EI) calcd for $\text{C}_8\text{H}_{17}\text{O}_2\text{Si}$ [M- C_4H_9]: 173.0998 found: 173.1003; $[\alpha]_D^{20}$ = +10.0° (c = 2.0; CH_2Cl_2); IR (thin film) $1/\lambda$ [cm^{-1}] = 2957, 2930, 2886, 2858, 1728, 1472, 1255, 1006, 837, 776.

(2R, 5S, 6R)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyloct-7-en-5-ol (5)



Crotylmagnesium chloride (5 mL, 5 mmol, 1 M in ether) was added dropwise at 0°C to a solution of (4S,5S) cyclopentadienyl[(4,5 *trans*)-2,2-dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanolato-O,O']titanium chloride (3.68g, 6 mmol) in 50 mL of ether over 10 min. After stirring for 1 h at 0°C, the orange suspension was cooled to -78°C and (4R)-5-*tert*-butyldimethylsilyloxy-4-methyl-pentanal **7** (1.15 g, 5 mmol) in 10 mL Et_2O was added over 15 min. Stirring at -78°C was continued for 3 h. The reaction mixture was then treated with 10 mL of aqueous 45% NH_4F solution, vigorously stirred for 12 h, filtered through Celite and extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with brine, dried over MgSO_4 and concentrated. The residue was stirred with 30 mL of pentane. Subsequent filtration furnished 1.1 g of recovered ligand. Chromatography (SiO_2 , 200 g, hexane/ EtOAc 5 : 1, R_f = 0.48) of the residue finally afforded 1.11 g (81%) of (2R, 5S, 6R)-1-*tert*-butyldimethylsilyloxy-2,6-dimethyl-oct-7-en-5-ol **5** as a colorless oil. Anal. calcd for $\text{C}_{16}\text{H}_{34}\text{O}_2\text{Si}$: C 67.07; H, 11.96; found: C, 67.30; H, 11.73; ^1H -NMR (400 MHz; CDCl_3): δ [ppm] = 5.77 (ddd, J = 17.2, 10.4, 8.2 Hz, 1H), 5.13 (ddd, J = 10.4, 1.9, 1.0 Hz, 1H), 5.12 (ddd, J = 17.2, 1.9, 0.8 Hz, 1H), 3.46 (dd, J = 9.8, 5.5 Hz, 1H), 3.40 (m, 1H), 3.39 (dd, J = 9.8, 6.2 Hz, 1H), 2.23 (qtdd, J = 6.9, 6.5, 1.0, 0.8 Hz, 1H), 1.59 (m, 4H), 1.36 (m, 1H), 1.13 (m, 1H), 1.04 (d, J = 6.9 Hz, 1H), 0.9 (s, 9H), 0.89 (d, J = 5.0 Hz, 3H), 0.04 (s, 6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 140.3, 115.2, 75.2, 68.3, 43.9, 36.0, 31.8, 29.0, 26.0, 18.4, 17.0, 16.4, -5.3; MS: (EI, 70eV, 90°C) m/z = 237 [M-59] (4), 207 (14), 183 (21), 137 (15), 105 (50), 99 (41), 95 (39), 81 (100); $[\alpha]_D^{20}$ = +7.4° (c = 2.0; CH_2Cl_2); IR (thin film) $1/\lambda$ [cm^{-1}] = 3422, 3385, 2957, 2932, 2886, 2858, 1462, 1255, 966, 912, 837, 775, 667.

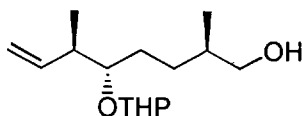
(2R, 5S, 6R)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyl-5-tetrahydropyranyloxyoct-7-ene



(2R, 5S, 6R)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyloct-7-en-5-ol **5** (7.0 g, 24.4 mmol) and camphorsulfonic acid (25 mg, 0.11 mmol) were dissolved in 30 mL of CH_2Cl_2 . 3,4-Dihydro-2H-pyran (2.9 mL, 31.8 mmol) was added dropwise and the solution was stirred for 12 h. The reaction was quenched with 10 mL of saturated aqueous NaHCO_3 and phases were separated.

The aqueous phase was extracted three times with CH_2Cl_2 , the combined organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated in vacuo. Chromatography (SiO_2 , 400 g, hexane/EtOAc, 10 : 1, R_f = 0.71) of the residue afforded 8.69 g (96%) of (2*R*, 5*S*, 6*R*)-1-*tert*-butyldimethylsilyloxy-2,6-dimethyl-5-tetrahydropyranyloxyoct-7-en as a colorless oil. Anal. calcd for $\text{C}_{21}\text{H}_{42}\text{O}_3\text{Si}$: C, 68.05; H, 11.42. found: C, 67.93; H, 11.17. ^1H -NMR (250 MHz; CDCl_3): δ [ppm] = 5.85 (ddd, J = 14.9, 10.7, 7.3 Hz, 0.5H), 5.78 (ddd, J = 15.1, 10.1, 7.3 Hz, 0.5H), 5.02 (dt, J = 15.1, 1.0 Hz, 0.5H), 5.02 (dt, J = 14.9, 1.0 Hz, 0.5H), 5.01 (dt, J = 10.7, 1.0 Hz, 0.5H), 5.01 (dt, J = 10.1, 1.0 Hz, 0.5H), 4.65 (m, 1H), 3.93 (m, 1H), 3.31-3.53 (m, 4H), 2.48 (m, 1H), 1.83 (m, 1H), 1.39-1.76 (m, 10H), 1.06 (d, J = 6.9 Hz, 1.5H), 0.99 (d, J = 6.9 Hz, 1.5H), 0.89 (s, 9H), 0.87 (d, J = 6.6 Hz, 1.5H), 0.85 (d, J = 6.6 Hz, 1.5H), 0.04 (s, 6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 141.2, 140.8, 114.5, 114.2, 98.3, 98.2, 81.1, 80.9, 68.4, 68.3, 62.6, 62.5, 41.5, 40.0, 36.0, 31.2, 31.0, 29.3, 29.1, 29.0, 27.6, 26.0, 25.6, 19.9, 19.8, 16.8, 16.7, 15.3, 14.8, -5.4; MS: (EI, 70eV, 90°C) m/z = 370 [M] (0.3), 313 [M-57] (4), 269 (35), 231 (80), 201 (14), 173 (83), 159 (97), 137 (35), 115 (21), 101 (16), 95 (63), 85 (100); $[\alpha]_D^{20}$ = +9.9 (c = 2.0; CH_2Cl_2); IR (thin film): $1/\lambda$ [cm^{-1}] = 2954, 2857, 1472, 1463, 1256, 1133, 1115, 1096, 1078, 1032, 1024, 1007, 911, 837, 775.

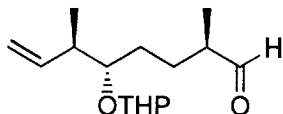
(2*R*, 5*S*, 6*R*)-2,6-Dimethyl-5-tetrahydropyranyloxy-oct-7-en-1-ol (6)



A stock solution of 5 mL HF/pyridine complex, 10 mL pyridine and 15 mL THF was prepared. In a teflon vessel (2*R*, 5*S*, 6*R*)-1-*tert*-butyldimethylsilyloxy-2,6-dimethyl-5-tetrahydropyranyloxy-oct-7-ene (2.35 g, 6.34 mmol) was dissolved in 10 mL THF and 5 mL of the stock solution was added slowly at ambient temperature. The mixture was stirred for 2 h and then diluted with Et_2O (30 mL) and saturated aqueous CuSO_4 (15 mL). The phases were separated and the aqueous layer was extracted three times with Et_2O . The combined organic layers were washed with saturated aqueous NaHCO_3 , dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (SiO_2 , 150 g, EtOAc/hexanes 1 : 1, R_f = 0.51) to provide 1.58 g (97 %) of (2*R*, 5*S*, 6*R*)-2,6-dimethyl-5-tetrahydropyranyloxy-oct-7-en-1-ol **6** as a clear colorless oil. Anal. calcd for $\text{C}_{15}\text{H}_{28}\text{O}_3$: C, 70.27; H, 11.01; found: C, 70.24; H, 10.96; ^1H -NMR (400 MHz; CDCl_3): δ [ppm] = 5.83 (ddd, J = 17.1, 10.5, 7.1 Hz, 0.5H), 5.77 (ddd, J = 17.6, 10.0, 7.5 Hz, 0.5H), 5.02 (d, J = 17.7 Hz, 0.5H), 5.02 (d, J = 17.1 Hz, 0.5H), 5.01 (dt, J = 10.5, 1.0 Hz, 0.5H), 5.01 (dt, J = 10.0, 1.0 Hz, 0.5H), 4.65 (dd, J = 4.5, 2.5 Hz, 0.5H), 4.59 (dd, J = 5.0, 2.5 Hz, 0.5H), 3.93 (m, 1H), 3.31-3.53 (m, 4H), 2.52 (qt, J = 6.5, 6.3 Hz, 0.5H), 2.42 (qt, J = 7.0, 5.9 Hz, 0.5H), 1.81 (m, 1H), 1.39-1.76 (m, 10H), 1.17 (m, 1H), 1.07 (d, J = 7.0 Hz, 1.5H), 0.98 (d, J = 6.5 Hz, 1.5H), 0.90 (d, J = 6.5 Hz, 3H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 141.1, 140.7, 114.6, 114.3, 99.1, 98.3, 81.4, 81.0, 68.2, 67.9, 63.4, 62.7, 41.4, 40.4, 36.0, 35.9, 31.2, 31.1, 29.1, 29.0, 28.8, 28.6, 25.6, 25.5, 20.3, 19.8, 16.7, 16.6, 15.3, 14.8; MS (EI, 70eV, 60°C); m/z = 183 [M-73] (5), 171 (2), 155 (8), 137 (8), 117 (7), 99 (56), 95 (19), 86 (39), 85 (100), 81 (49); $[\alpha]_D^{20}$ = +17.5° (c = 2.0 ; CH_2Cl_2); IR

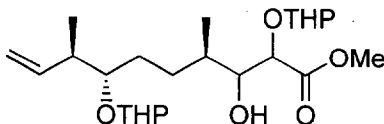
(thin film): $1/\lambda$ [cm^{-1}] = 3420, 2943, 2872, 1455, 1441, 1379, 1352, 1200, 1133, 1115, 1077, 1024, 911.

(2*R*, 5*S*, 6*R*)-2,6-Dimethyl-5-tetrahydropyranyloxy-oct-7-en-1-al (7)



(COCl)₂ (0.95 mL, 11 mmol) was dissolved in 25 mL CH₂Cl₂ and cooled to -78°C. DMSO (1.8 mL, 25 mmol) was added slowly and mixture was stirred for a further 15 min. (2*R*, 5*S*, 6*R*)-2,6-Dimethyl-5-tetrahydropyranyloxy-oct-7-en-1-ol **6** (2.4 g, 9.4 mmol) in 15 mL of CH₂Cl₂ was added over a period of 10 min. After 1 h at -78°C Et₃N (4.2 mL, 30 mmol) was added and mixture was warmed to room temperature. Water (60 mL) was added, the phases were separated and the aqueous layer was extracted three times with Et₂O. The combined organic layers were washed with saturated aqueous NH₄Cl, brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (200 g of SiO₂, hexanes/ EtOAc 3 : 1, R_f = 0.52) to provide 2.3 g (97 %) of (2*R*, 5*S*, 6*R*)-2,6-dimethyl-5-tetrahydropyranyloxy-oct-7-en-1-al **7** as a colorless oil as a mixture of 2 diastereomers: Anal. calcd for C₁₅H₂₆O₃ : C 70.83; H, 10.30; found: C, 70.61; H, 10.09; ¹H-NMR (250 MHz; CDCl₃): δ [ppm] = 9.61 (d, *J* = 2.1 Hz, 0.5H), 9.60 (d, *J* = 2.1 Hz, 0.5H), 5.83 (ddd, *J* = 15.3, 9.9, 7.3 Hz, 0.5H), 5.75 (ddd, *J* = 15.1, 9.9, 7.1 Hz, 0.5H), 5.03 (dt, *J* = 15.3, 1.0 Hz, 0.5H), 5.03 (dt, *J* = 15.1, 1.0 Hz, 0.5H), 5.02 (dt, *J* = 9.9, 1.0 Hz, 0.5H), 5.01 (dt, *J* = 9.9, 1.0 Hz, 0.5H), 4.58-4.66 (m, 1H), 3.93 (m, 1H), 3.41-3.53 (m, 2H), 2.25-2.58 (m, 2H), 1.34-1.95 (m, 10H), 1.08 (d, *J* = 7.1 Hz, 3H), 1.06 (d, *J* = 6.5 Hz, 1.5H), 0.98 (d, *J* = 7.1 Hz, 1.5H); ¹³C-NMR (63 MHz; CDCl₃): δ [ppm] = 205.3, 204.9, 140.9, 140.5, 114.8, 114.5, 98.8, 98.5, 80.7, 80.5, 63.3, 62.7, 46.4, 46.3, 41.3, 31.2, 31.1, 28.8, 27.4, 26.8, 25.5, 25.4, 20.3, 15.0, 14.5, 13.4; MS: (FI, 7kV, 3mA, 20°C) *m/z* = 255 [M+1] (3), 199 (93), 153 (6), 85 (100); [α]_D²⁰ = -9.2° (c = 2.0; CH₂Cl₂), IR (thin film) $1/\lambda$ [cm^{-1}] = 2942, 2871, 1727, 1455, 1442, 1376, 1352, 1200, 1160, 1132, 1115, 1077, 1034, 912, 870.

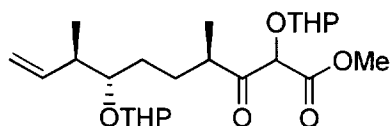
Methyl (2*R*/*S*, 3*R*/*S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3-hydroxy-dec-9-enoate (8)



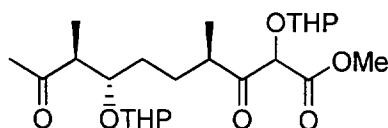
Methyl 2-tetrahydropyranyloxy-acetate (1.4 g, 8.0 mmol) in 16 mL THF was cooled to -90°C. A freshly prepared 1 M LDA-solution (7 mL, 7 mmol) was added and mixture was stirred for a further 20 min. (2*R*, 5*S*, 6*R*) 2,6-Dimethyl-5-tetrahydropyranyloxy-oct-7-en-1-al **8** (1.5 g, 5.9 mmol) in 10 mL THF was added over a period of 15 min and stirring was continued for 30 min at -85°C. The reaction was quenched with 20 mL of a saturated aqueous NH₄Cl and phases were separated. The aqueous phase was extracted three times with Et₂O, the combined organic layers were washed with brine, dried over MgSO₄, filtered and

concentrated in vacuo. The residue was purified by column chromatography (300 g of SiO₂, EtOAc/hexanes 1 : 1, R_f = 0.52) to provide 2.1 g (83 %) of Methyl (2*R*/*S*, 3*R*/*S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3-hydroxy-dec-9-enoate **8** as a mixture of 16 diastereomers: Anal. calcd for C₂₃H₄₀O₇: C, 64.46; H, 9.41; found: C, 64.17; H, 9.12; ¹H-NMR (250 MHz; CDCl₃): δ [ppm] = 5.70-5.96 (m, 1H), 5.02-5.10 (m, 2H), 4.62-4.80 (m, 2H), 3.70-4.16 (m, 4H), 3.80 (s, 3H), 3.42-3.56 (m, 3H), 2.38-2.58 (m, 2H), 1.56-1.94 (m, 17H), 1.07 (d, *J* = 6.9 Hz, 1.5H), 0.99 (d, *J* = 7.1 Hz, 1.5H), 0.95 (d, *J* = 6.9 Hz, 1.5H), 0.90 (d, *J* = 6.5 Hz, 1.5H); MS: (FI, 7kV, 3mA, 155°C) *m/z* = 429 [M+1] (3), 187 (68), 141 (100); IR (thin film) 1/λ [cm⁻¹] = 3450, 2948, 2871, 1748, 1455, 1440, 1383, 1352, 1200, 1184, 1132, 1122, 1077, 1036, 1025, 912, 870.

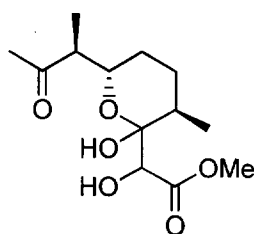
Methyl (2*R*/*S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3-oxo-dec-9-enoate (9)



(COCl)₂ (0.6 mL, 7 mmol) was dissolved in 15 mL CH₂Cl₂ and cooled to -78°C. DMSO (1.2 mL, 17 mmol) was added slowly and the mixture was stirred for a further 15 min. Methyl (2*R*/*S*, 3*R*/*S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3-hydroxy-dec-9-enoate **11** (2.05 g, 4.8 mmol) in 15 mL of CH₂Cl₂ was added over a period of 10 min. After 1 h at -78°C Et₃N (4.0 mL, 28 mmol) was added and mixture was warmed to room temperature. After 30 min 40 mL of water was added. The phases were separated and the aqueous layer was extracted two times with Et₂O and once with EtOAc. The combined organic layers were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (20g of SiO₂, hexane/EtOAc 3 : 1, R_f = 0.39) to provide 1.53 g (75 %) of methyl (2*R*/*S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3-oxo-dec-9-enoate **9** as a colorless oil as a mixture of 8 diastereomers: Anal. calcd for C₂₃H₃₈O₇: C, 64.76; H, 8.98; found: C, 64.91; H, 9.12; ¹H-NMR (250 MHz; CDCl₃): δ [ppm] = 5.68-5.90 (m, 1H), 5.02 (d, *J* = 16.0 Hz, 1H), 5.01 (d, *J* = 11.4 Hz, 1H), 4.93 (s, 0.125H), 4.92 (s, 0.125H), 4.91 (s, 0.125H), 4.89 (s, 0.125H), 4.82 (s, 0.125H), 4.80 (s, 0.125H), 4.76 (s, 0.125H), 4.73 (s, 0.125H), 4.69-4.78 (m, 1H), 4.58-4.66 (m, 0.5H), 4.50-4.56 (m, 0.5 H), 3.78 (s, 3H), 3.70-3.92 (m, 3H), 3.40-3.60 (m, 2H), 2.80-3.10 (m, 2H), 2.20 (s, 1.5H), 2.16 (s, 1.5H), 1.70-1.85 (m, 4H), 1.40-1.70 (m, 9H), 1.20-1.35 (m, 1H), 1.15 (d, *J* = 7.1 Hz, 0.375H), 1.14 (d, *J* = 6.9 Hz, 0.375H), 1.13 (d, *J* = 7.1 Hz, 0.375H), 1.12 (d, *J* = 7.1 Hz, 0.375H), 1.11 (d, *J* = 7.1 Hz, 0.75H), 1.09 (d, *J* = 7.1 Hz, 0.375H), 1.08 (d, *J* = 7.1 Hz, 0.375H), 1.04 (d, *J* = 7.1 Hz, 0.75H), 1.03 (d, *J* = 7.1 Hz, 0.375H), 0.98 (d, *J* = 7.1 Hz, 0.75H), 0.97 (d, *J* = 7.1 Hz, 0.75H), 0.87 (d, *J* = 7.1 Hz, 0.375H); MS: (FI, 7kV, 3mA, 95°C) *m/z* = 426 [M] (12), 325 (17), 253 (16), 173 (27), 113 (100); IR (thin film) 1/λ [cm⁻¹] = 2942, 2873, 1751, 1723, 1455, 1380, 1353, 1261, 1201, 1185, 1132, 1078, 1036, 1024, 965, 911, 870.

Methyl (2*R/S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3,9-dioxodecanoate (10)

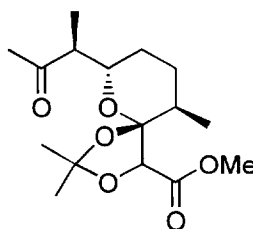
To a solution of methyl (2*R/S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3-oxodec-9-enoate **11** (3.2 g, 7.5 mmol) in 35 mL THF/DMF 5:1 and 14 mL of 1M aqueous Na₂HPO₄ was added PdCl₂ (1.6 g, 9 mmol) and the mixture was stirred vigorously for 24 h. Most of the THF was removed in vacuo, brine (25 mL) was added and the black suspension was extracted three times with Et₂O/hexane 1 : 1. The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (250 g of SiO₂, hexane/EtOAc 3 : 1, *R_f* = 0.20) to provide 2.8 g (84 %) of methyl (2*R/S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3,9-dioxodecanoate **13** as a colorless oil a mixture of 8 diastereomers : Anal. calcd for C₂₃H₃₈O₈: C 62.42; H, 8.65; found: C, 62.66; H, 8.49; ¹H-NMR (250 MHz; CDCl₃): δ [ppm] = 4.93 (s, 0.125H), 4.92 (s, 0.125H), 4.91 (s, 0.125H), 4.89 (s, 0.125H), 4.82 (s, 0.125H), 4.80 (s, 0.125H), 4.76 (s, 0.125H), 4.73 (s, 0.125H), 4.69-4.78 (m, 1H), 4.58-4.66 (m, 0.5H), 4.50-4.56 (m, 0.5H), 3.78 (s, 3H), 3.70-3.92 (m, 3H), 3.40-3.60 (m, 2H), 2.80-3.10 (m, 2H), 2.20 (s, 1.5H), 2.16 (s, 1.5H), 1.70-1.85 (m, 4H), 1.40-1.70 (m, 9H), 1.20 -1.35 (m, 1H), 1.15 (d, *J* = 7.1 Hz, 0.375H), 1.14 (d, *J* = 6.9 Hz, 0.375H), 1.13 (d, *J* = 7.1 Hz, 0.375H), 1.12 (d, *J* = 7.1 Hz, 0.375H), 1.11 (d, *J* = 7.1 Hz, 0.75H), 1.09 (d, *J* = 7.1 Hz, 0.375H), 1.08 (d, *J* = 7.1 Hz, 0.375H), 1.04 (d, *J* = 7.1 Hz, 0.75H), 1.03 (d, *J* = 7.1 Hz, 0.375H), 0.98 (d, *J* = 7.1 Hz, 0.75H), 0.97 (d, *J* = 7.1 Hz, 0.75H), 0.87 (d, *J* = 7.1 Hz, 0.375H); MS: (FI, 7kV, 3mA, 95°C) *m/z* = 442 [M] (4), 341 (5), 269 (4), 173 (27), 101 (13), 85 (100); IR (thin film) 1/λ [cm⁻¹] = 2942, 2870, 1755, 1718, 1458, 1439, 1377, 1356, 1275, 1202, 1183, 1078, 1036, 975, 906, 870, 817, 738.

Methyl (2*R/S*)-2-[(2*R*, 3*R*, 6*S*)-tetrahydro-2-hydroxy-3-methyl-6-[(1*S*)-1-methyl-2-oxoprop-1-yl]-2H-pyran-2-yl]-glycolate

To methyl (2*R/S*, 4*R*, 7*S*, 8*R*)-4,8-dimethyl-2,5-ditetrahydropyranyloxy-3,9-dioxodecanoate **10** (950 mg, 2.15 mmol) in 20 mL of a THF/water 3:1 mixture was added PPTS (15 mg) and the mixture was warmed to 50°C for 12 h. The mixture was diluted with toluene (15 mL) and saturated aqueous NaHCO₃ (15 mL). Most of the THF was removed in vacuo, the layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic

layers were dried over MgSO_4 , filtered and concentrated in vacuo. The residue was purified by column chromatography (40 g of SiO_2 , hexane/EtOAc, 2 : 1, $R_f = 0.21$) to provide 560 mg (96 %) of methyl (2*R/S*)-2-[(2*R*, 3*R*, 6*S*)-tetrahydro-2-hydroxy-3-methyl-6-[(1*S*)-1-methyl-2-oxo-propyl]-2H-pyran-2-yl]-glycolate as a white amorphous solid a mixture of 2 diastereomers. Anal. calcd for $\text{C}_{13}\text{H}_{22}\text{O}_6$: C, 56.92; H, 8.08; found: C, 57.18; H, 8.35. ^1H -NMR (250 MHz; CDCl_3): δ [ppm] = 4.16 (d, $J = 9.1$ Hz, 0.5H), 4.13 (d, $J = 9.0$ Hz, 0.5H), 4.0 (m, 0.5H), 3.93 (m, 0.5H), 3.80 (s, 1.5H), 3.78 (s, 1.5H), 3.20 (d, $J = 9.0$ Hz, 0.5H), 2.98 (d, $J = 9.1$ Hz, 0.5H), 2.48 (m, 1H), 2.03 (s, 1.5H), 2.01 (s, 1.5H), 1.76-1.95 (m, 1H), 1.48-1.75 (m, 3H), 1.20-1.30 (m, 1H), 0.96 (d, $J = 6.7$ Hz, 1.5H), 0.95 (d, $J = 7.1$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 1.5H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 211.9, 173.4, 99.5, 97.7, 73.7, 73.2, 72.2, 52.8, 52.0, 51.8, 33.9, 32.8, 29.9, 29.2, 27.3, 26.5, 16.1, 15.7, 12.8, 12.4; $[\alpha]_D^{20} = +48.9^\circ$ ($c = 2.0$; CH_2Cl_2); MS (EI, 70eV, 25°C) $m/z = 255$ [$\text{M}+1$] (1), 206 (3), 185 (36), 167 (36), 140 (46), 125 (100); IR (thin film): $1/\lambda$ [cm^{-1}] = 3469, 3340, 2951, 2937, 1737, 1703, 1462, 1409, 1377, 1286, 1163, 1089, 1068, 1029, 996.

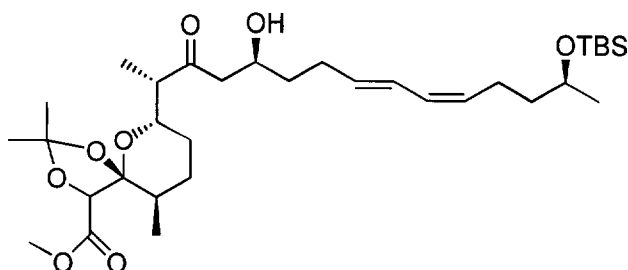
Methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*S*)-1-methyl-2-oxo-prop-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate (11)



Methyl (2*R/S*)-2-[(2*R*, 3*R*, 6*S*)-tetrahydro-2-hydroxy-3-methyl-6-[(1*S*)-1-methyl-2-oxo-prop-1-yl]-2H-pyran-2-yl]-glycolate (0.77 g, 2.8 mmol) was dissolved in acetone (30 mL) (previously dried over potassium carbonate and distilled) and a small amount of phosphorus pentoxide was added. The reaction mixture was stirred at room temperature for 12 h. A second portion of phosphorus pentoxide was added and stirring was continued for an additional 10 h. The mixture was diluted with toluene (15 mL) and saturated aqueous NaHCO_3 (15 mL). Most of the acetone was removed in vacuo, the layers were separated and the aqueous layer was extracted three times with Et_2O . The combined organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated in vacuo. The residue was purified by column chromatography (60 g of SiO_2 , hexane/EtOAc, 2 : 1, $R_f = 0.41$) to provide 0.61 g (69 %) of methyl (4*R/S*, 7*S*, 10*R*, 1'*S*)-2,2,10-trimethyl-7-(1-methyl-2-oxo-prop-1-yl)-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **11** as a colorless oil a mixture of 2 diastereomers: Anal. calcd for $\text{C}_{16}\text{H}_{26}\text{O}_6$: C 61.13; H, 8.34; found: C, 61.32; H, 8.35; ^1H -NMR (400 MHz; CDCl_3): δ [ppm] = 4.59 (s, 0.5H), 4.53 (s, 0.5H), 3.98 (ddd, $J = 11.2, 8.7, 2.3$ Hz, 0.5H), 3.91 (ddd, $J = 10.3, 8.0, 2.1$ Hz, 0.5H), 3.83 (s, 1.5H), 3.80 (s, 1.5H), 2.69 (dq, $J = 8.4, 7.0$ Hz, 0.5H), 2.58 (dq, $J = 7.9, 7.0$ Hz, 0.5H), 2.21 (s, 1.5H), 2.16 (s, 1.5H), 2.03 (ddq, $J = 10.9, 6.7, 4.3$ Hz, 0.5H), 1.91 (ddq, $J = 10.7, 6.6, 4.2$ Hz, 0.5H), 1.75-1.50 (m, 3H), 1.53 (s, 3H), 1.44 (s, 1.5H), 1.41 (s, 1.5H), 1.35-1.25 (m, 1H), 1.03 (d, $J = 7.0$ Hz, 1.5H), 0.99 (d, $J = 7.0$ Hz, 1.5H), 0.98 (d, $J = 6.7$ Hz, 1.5H), 0.75 (d, $J = 6.6$ Hz, 1.5H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 212.0, 211.8, 169.3, 168.5, 112.5, 111.1, 107.7, 107.1, 84.1, 80.1, 74.7, 73.7, 52.2,

51.9, 51.6, 51.3, 31.1, 30.7, 28.7, 28.5, 28.2, 28.1, 27.8, 26.9, 26.7, 25.5, 16.1, 15.8, 12.6, 12.4; MS: (FI, 7kV, 3mA, 40°C) $m/z = 314$ [M] (10), 299 [M-15] (100); $[\alpha]_D^{20} = +75.0^\circ$ ($c = 2$; CH_2Cl_2); IR (thin film) $1/\lambda$ [cm^{-1}] = 2944, 2882, 1765, 1738, 1715, 1456, 1440, 1381, 1287, 1207, 1189, 1118, 1072, 1033, 991, 963.

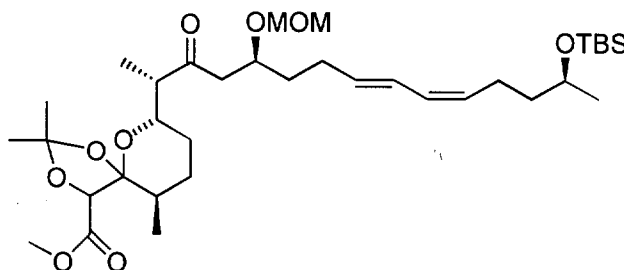
Methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-4-hydroxy-1-methyl-2-oxo-13-*tert*-butyldimethylsilyloxy-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate (13)



(–)-Chlorodiisopinocampheylborane (560 mg, 1.74 mmol) was dissolved in 5 mL of THF. Et_3N (0.26 mL, 1.83 mmol) was added and the mixture was cooled to -78°C . Over a period of 15 min, methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*S*)-1-methyl-2-oxo-prop-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **11** (520 mg, 1.66 mmol) in 5 mL THF was added and the mixture was stirred for further 4 h at -40°C . After this time, a white precipitate had formed and the mixture was cooled to -78°C . Then (4*E*, 6*Z*, 10*S*)-10-*tert*-butyldimethylsilyloxyundek-4,6-dienal **12** (540 mg, 1.83 mmol) in 5 mL of THF was added and the mixture was stored for 60 h at -78°C in a freezer. Saturated aqueous NH_4Cl (15 mL) was added and the mixture was warmed to room temperature. The layers were separated and aqueous layer extracted three times with ether. The combined organic layers were concentrated in vacuo, the residue was dissolved in 30 mL of ice cold pentane and shaken for 10 min with H_2O_2 (0.8 mL, 30%, 7 mmol) in 10 mL of 0.5 M aqueous NaOH . The layers were separated and aqueous layer extracted three times with ether. The combined organic layers were washed with saturated aqueous NH_4Cl , brine, dried over MgSO_4 , filtered and concentrated in vacuo. The residue was purified by column chromatography (40 g of SiO_2 , hexane/ EtOAc 3 : 1, $R_f = 0.39$) to provide 730 mg (72%) of **13** as 4 diastereomers in a 4 : 1 ratio with respect to the C11 center, which could not be separated. Data given for the two main diastereomers: Anal. calcd for $\text{C}_{33}\text{H}_{58}\text{O}_8\text{Si}$: C 64.88; H, 9.57. Found: C, 65.17; H, 9.39. $^1\text{H-NMR}$ (400 MHz; CDCl_3): δ [ppm] = 6.33 (dd, $J = 15.2, 10.9$ Hz, 0.5H), 6.32 (dd, $J = 15.2, 10.9$ Hz, 0.5H), 5.93 (dd, $J = 10.9, 10.7$ Hz, 0.5H), 5.91 (dd, $J = 10.9, 10.7$ Hz, 0.5H), 5.68 (dt, $J = 15.2, 6.9$ Hz, 0.5H), 5.63 (dt, $J = 15.2, 6.9$ Hz, 0.5H), 5.30 (dt, $J = 10.7, 7.4$ Hz), 5.28 (dt, $J = 10.7, 7.4$ Hz), 4.53 (s, 0.5 H), 4.42 (s, 0.5H), 3.97-4.07 (m, 1H), 3.82-3.95 (m, 2H), 3.79 (s, 1.5 H), 3.75 (s, 1.5 H), 2.43-2.64 (m, 3 H), 2.08-2.35 (m, 4 H), 1.97 (dq, $J = 10.5, 7.0, 5.7$ Hz, 0.5 H), 1.86 (dq, $J = 11.0, 6.5, 3.7$ Hz, 0.5 H), 1.60-1.72 (m, 3 H), 1.50 (s, 1.5H), 1.45 (s, 1.5H), 1.38 (s, 1.5 H), 1.36 (s, 1.5 H), 1.35-1.58 (m, 4H), 1.20-1.33 (m, 1H), 1.13 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 7.0$ Hz, 1.5H), 0.95 (d, $J = 7.0$ Hz, 1.5H), 0.92 (d, $J = 7.0$ Hz, 1.5H), 0.71 (d, $J = 6.5$ Hz, 1.5H), 0.04 (s, 6H); $^{13}\text{C-NMR}$ (63 MHz; CDCl_3): δ [ppm] = 215.2, 215.1, 169.2, 168.2, 112.5

134.1, 133.5, 130.1, 129.8, 128.6, 128.5, 126.1, 125.9, 112.5, 111.0, 107.7, 106.9, 84.0, 79.8, 74.9, 73.8, 68.2, 66.9, 66.8, 52.2, 52.0, 51.9, 51.3, 51.0, 50.6, 31.1, 30.7, 28.7, 28.5, 28.3, 28.1, 27.8, 26.9, 26.7, 25.5, 16.1, 15.7, 12.6, 12.4, -4.4, -4.7; MS: (FI, 7 kV, 3 mA, 170°C) m/z = 610 (100), 611 (28), 374 (45); IR (thin film): $1/\lambda$ [cm^{-1}] = 3544, 2931, 2857, 1768, 1739, 1710, 1459, 1375, 1255, 1217, 1120, 1074, 1008, 836, 774.

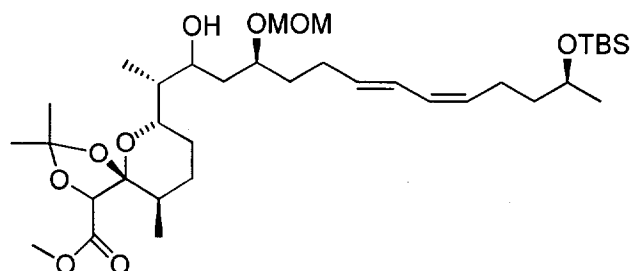
Methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-13-*tert*-butyldimethylsilyloxy-4-methoxymethyloxy-1-methyl-2-oxo-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate (14)



To a stirred solution of methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-4-hydroxy-1-methyl-2-oxo-13-*tert*-butyldimethylsilyloxy-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **13** (100 mg, 0.16 mmol) in 6 mL of CH_2Cl_2 and Hünig's base (130 mg, 1 mmol) was added MOMCl (54 mg, 0.65 mmol). The reaction mixture was stirred for 30 h and saturated aqueous NH_4Cl (8 mL) was added. The layers were separated and the aqueous layer extracted three times with ether. The combined organic layers were washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography (40 g of SiO_2 , hexanes/ EtOAc 5 : 1 R_f = 0.30) to provide 95 mg (90 %) of **14** as a mixture of 2 main diastereomers : Anal. calcd for $\text{C}_{35}\text{H}_{62}\text{O}_9\text{Si}$: C 64.18; H, 9.54; found: C, 63.98; H, 9.40. ^1H -NMR (400 MHz; CDCl_3): δ [ppm] = 6.31 (dd, J = 15.0, 11.1 Hz, 0.5H), 6.30 (dd, J = 15.0, 11.1 Hz, 0.5H), 5.91 (dd, J = 11.1, 11.0 Hz, 0.5H), 5.89 (dd, J = 11.1, 11.0 Hz, 0.5H), 5.65 (dt, J = 15.0, 6.9 Hz, 0.5H), 5.60 (dt, J = 15.0, 6.9 Hz, 0.5H), 5.29 (dt, J = 11.0, 7.5 Hz, 0.5H), 5.25 (dt, J = 11.0, 7.5 Hz, 0.5H), 4.67 (d, J = 2.0 Hz, 0.5H), 4.65 (d, J = 2.0 Hz, 0.5H), 4.59 (d, J = 4.5 Hz, 0.5H), 4.57 (d, J = 4.5 Hz, 0.5H), 4.52 (s, 0.5H), 4.43 (s, 0.5H), 3.97-4.07 (m, 1H), 3.95 (ddd, J = 11.5, 8.7, 2.0 Hz, 0.5H), 3.86 (ddd, J = 11.5, 8.7, 2.0 Hz, 0.5H), 3.76- 3.84 (m, 1H), 3.79 (s, 1.5H), 3.75 (s, 1.5H), 3.33 (s, 1.5H), 3.32 (s, 1.5H), 2.82 (dd, J = 17.0, 7.0 Hz, 0.5H), 2.75 (dd, J = 17.0, 7.5 Hz, 0.5H), 2.65 (dq, J = 8.5, 7.0 Hz, 0.5H), 2.48-2.60 (m, 1.5H), 2.08-2.28 (m, 4 H), 1.98 (dq, J = 10.4, 6.5, 5.8 Hz, 0.5H), 1.85 (dq, J = 11.1, 6.5, 3.6 Hz, 0.5H), 1.60 -1.72 (m, 3 H), 1.49 (s, 1.5H), 1.44 (s, 1.5H), 1.38 (s, 1.5 H), 1.35 (s, 1.5 H), 1.35-1.58 (m, 4H), 1.20 -1.33 (m, 1H), 1.12 (d, J = 6.0 Hz, 3H), 0.96 (d, J = 7.0Hz, 1.5H), 0.94 (d, J = 6.5Hz, 1.5H), 0.91 (d, J = 6.5Hz, 1.5H), 0.88 (s, 9H), 0.70 (d, J = 6.5 Hz, 1.5H), 0.04 (s, 6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 212.3, 211.8, 169.6, 168.6, 134.2, 133.8, 130.4, 130.1, 128.9, 128.8, 126.3, 126.2, 112.7, 111.4, 108.1, 107.3, 96.6, 84.4, 80.2, 74.9, 74.0, 73.8, 68.5, 55.9, 52.5, 52.1, 51.8, 51.7, 50.5, 51.0, 40.0, 35.1, 35.0, 34.1, 34.0, 29.4, 29.0, 28.7, 28.1, 28.0, 27.9,

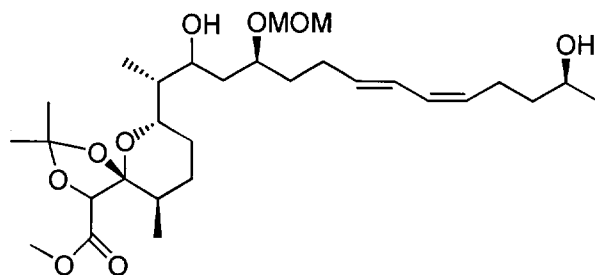
27.1, 27.0, 26.2, 25.8, 24.1, 24.0, 16.4, 16.0, 12.7, 12.2, -3.9, -4.3; MS: (FI, 7kV, 3mA, 170°C) m/z = 654 [M] (100), 597 (18), 391 (13); IR (thin film): $1/\lambda$ [cm^{-1}] = 2932, 2857, 1768, 1739, 1717, 1460, 1438, 1376, 1255, 1216, 1150, 1120, 1093, 1043, 1008, 919, 885, 836, 775.

Methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 2*R/S*, 4*S*, 7*E*, 9*Z*, 13*S*) -13-*tert*-butyldimethylsilyloxy-2-hydroxy-4-methoxymethyloxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate (15)

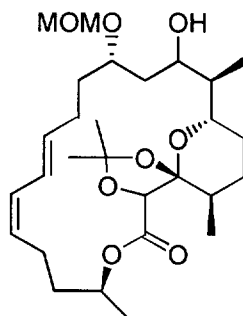


To a stirred solution of methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*) -13-*tert*-butyldimethylsilyloxy-4-methoxymethyloxy-1-methyl-2-oxo-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **14** (405 mg 0.62 mmol) in MeOH (10 mL) and THF (2 mL) at -20°C was added sodium borohydride (36 mg, 0.93 mmol). The reaction mixture was stirred for 2 h allowing the temperature to rise to 0°C and then for 2 h at 0°C. Upon quenching with acetone (1 mL) the reaction mixture was diluted with brine (10 mL) and ether (15 mL). The layers were separated and the aqueous layer extracted three times with ether. The combined organic extracts were dried over MgSO_4 , filtered, and concentrated in vacuo. The crude product was purified by column chromatography (60 g of SiO_2 , hexane/EtOAc, 3 : 1) to provide 102 mg (0.16 mmol) of a minor product (two diastereomers R_f = 0.35) and 263 mg of a main product (two diastereomers R_f = 0.31) (89 % combined yield). HPLC separation delivered all 4 main diastereomers in the analytically pure forms. HPLC data for Merck Supersphere® Si 60 4 μm , 244 mm x 4 mm column, 2 % i-PrOH in hexane, flow: 2 mL/min. Compound 1 **15a**, t_R = 4.4 min; compound 2 **15b**, t_R = 5.4 min; compound 3 **15c**, t_R = 6.5 min; compound 4 **15d**, t_R = 7.5 min. Analytical data given for compound 1 **15a**. Anal. calcd for $\text{C}_{35}\text{H}_{64}\text{O}_9\text{Si}$: C 63.99; H, 9.82; found: C, 63.93; H, 9.58. ^1H -NMR (400 MHz; CDCl_3): δ [ppm] = 6.31 (dd, 15.1, 11.0 Hz, 1H), 5.92 (dd, J = 11.0, 10.5 Hz, 1H), 5.65 (dt, J = 15.1, 6.8 Hz, 1H), 5.30 (dt, J = 10.5, 7.5 Hz, 1H), 4.65 (s, 2H), 4.59 (s, 1H), 4.00 (m, 1H), 3.72-3.86 (m, 2H), 3.79 (s, 3H), 3.38 (s, 3H), 2.08-2.30 (m, 4H), 1.98 (dq, J = 11.0, 6.5, 4.5 Hz, 1H), 1.79 (ddd, J = 14.1, 9.0, 7.0 Hz, 1H), 1.35-1.74 (m, 11H), 1.68 (s, 3H), 1.40 (s, 3H), 1.13 (d, J = 6.5 Hz, 3H), 0.97 (d, J = 6.5 Hz, 3H), 0.89 (s, 9H), 0.89 (d, J = 6.0 Hz, 3H), 0.04 (s, 6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 168.9, 133.9, 130.0, 128.5, 125.9, 112.5, 107.5, 95.4, 80.4, 76.1, 74.5, 68.2, 68.1, 55.7, 52.2, 42.7, 39.9, 39.2, 34.2, 34.0, 29.0, 28.4, 28.3, 27.9, 26.9, 25.9, 23.8, 23.7, 18.1, 16.2, 10.5, -4.4, -4.7; $[\alpha]_D^{20}$ = 31.0° (c = 2.0; CHCl_3); MS: (FI, 7kV, 3mA, 150°C) m/z = 656 [M] (73), 530 (100), 115 (48); IR (thin film): $1/\lambda$ [cm^{-1}] = 3524, 2931, 2858, 1767, 1740, 1460, 1381, 1255, 1217, 1124, 1094, 1035, 919, 886, 837, 775.

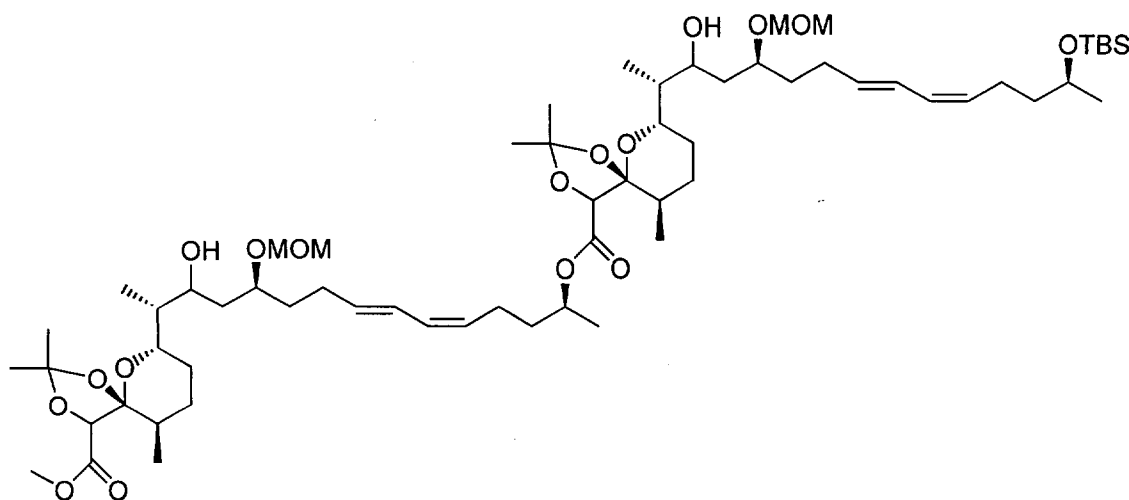
Methyl (5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-2,13-dihydroxy-4-methoxymethyloxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate (16)



A stock solution of 5 mL HF/pyridine complex, 10 mL pyridine and 15 mL THF was prepared. In a Teflon vessel, methyl (5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-13-*tert*-butyldimethylsilyloxy-2-hydroxy-4-methoxymethyloxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **15a** (130 mg, 0.20 mmol) was dissolved in THF (3 mL) and 1.3 mL of the stock solution was added slowly at ambient temperature. The mixture was stirred for 24 h and then diluted with Et₂O (15 mL) and saturated aqueous CuSO₄ (10 mL). The phases were separated and the aqueous layer was extracted three times with EtOAc (3 x 20 mL). The combined organic layers were washed with saturated aqueous NaHCO₃, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (25 g SiO₂, hexane/EtOAc, 1 : 1, R_f = 0.19) to provide 101 mg (94 %) of methyl (5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-2,13-dihydroxy-4-methoxymethyloxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **16** as a clear colorless oil. Anal. calcd for C₂₉H₅₀O₉Si: C 64.18; H, 9.29; found: C, 63.93; H, 9.05. ¹H-NMR (400 MHz; CDCl₃): δ [ppm] = 6.32 (dd, *J* = 14.8, 11.0 Hz, 1H), 5.92 (dd, *J* = 11.0, 11.0 Hz, 1H), 5.64 (dt, *J* = 14.8, 7.0 Hz, 1H), 5.31 (dt, *J* = 11.0, 7.5 Hz, 1H), 4.66 (s, 2H), 3.99 (m, 1H), 3.72-3.86 (m, 3H), 3.75 (s, 3H), 3.37 (s, 3H), 2.59 (m, 1H), 2.12-2.30 (m, 4H), 1.96 (m, 1H), 1.79 (ddd, *J* = 14.5, 9.1, 6.6 Hz, 1H), 1.35 -1.72 (m, 10H), 1.62 (s, 3H), 1.40 (s, 3H), 1.18 (d, *J* = 6.2 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H); ¹³C-NMR (63 MHz; CDCl₃): δ [ppm] = 168.9, 134.3, 129.4, 129.1, 125.8, 112.5, 107.6, 95.5, 80.4, 76.0, 74.5, 68.2, 67.5, 55.7, 52.2, 42.8, 39.3, 39.0, 34.2, 33.8, 29.0, 28.4, 28.3, 27.9, 26.9, 25.9, 24.1, 23.5, 16.2, 10.5; MS: (FI, 7 kV, 3 mA, 100°C) *m/z* = 542 [M] (100); [α]_D²⁰ = +31.0° (*c* = 2.0, CHCl₃); IR (thin film): 1/λ [cm⁻¹] = 3469, 2936, 2858, 1765, 1739, 1439, 1382, 1287, 1217, 1149, 1121, 1033, 989, 919.

Monolide (18)

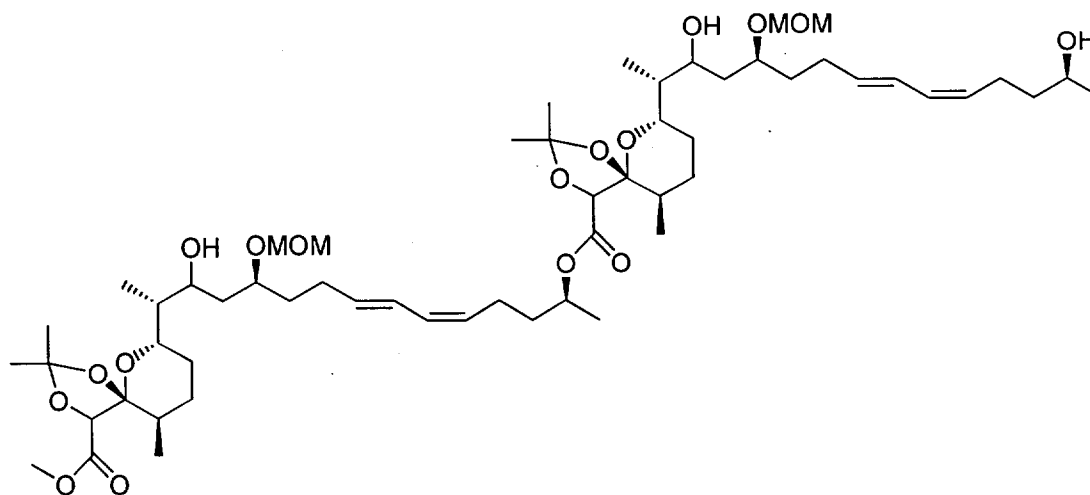
Methyl (5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-2,13-dihydroxy-4-methoxymethyloxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **18** (12 mg, 22 μ mol) was dissolved in MeOH (1 mL) and powdered Ba(OH)₂·8H₂O (200 mg, 0.63 mmol) was added. The white suspension was vigorously stirred for 1 h, then diluted with 5 mL Et₂O and 5 mL brine and acidified to pH 3 with 1M HCl (1.4 mL). The two clear phases were separated and aqueous layer was extracted four times with EtOAc. The combined organic extracts were washed with brine, dried over MgSO₄ and concentrated in vacuo. The crude seco acid **17** was used for macrolactonization without any further purification. A stock solution was prepared by dissolving 2,4,6-trichlorobenzoyl chloride (96 mg, 400 μ mol) and triethylamine (44 mg, 440 μ mol) in 2 mL toluene. A portion of the stock solution (0.1 mL) was added to the seco acid in 0.5 mL toluene. After stirring for 2 h the mixture was diluted with 0.4 mL toluene and added over 1 h via syringe pump to a solution of DMAP (24 mg, 200 μ mol) in 2 mL toluene at room temperature. The suspension was stirred for an additional 0.5 h, diluted with EtOAc (10 mL) and saturated aqueous NaHCO₃ (5 mL). The phases were separated and aqueous layer was extracted three times with EtOAc. Combined organic extracts were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (8 g of SiO₂, hexane/EtOAc, 3 : 1 to 1 : 1) to provide 9 mg (80 %, R_f = 0.25 hexane/EtOAc 3 : 1) of the monolide **18** and 1 mg (9 %, R_f = 0.25 hexane/EtOAc 3 : 1) of the diolide as clear colorless oils. Analytical data given for the monolide **18**: ¹H-NMR (400 MHz; CDCl₃): δ [ppm] = 6.31 (dd, J = 15.4, 11.1 Hz, 1H), 6.06 (dd, J = 11.1, 10.2 Hz, 1H), 5.67 (ddd, J = 15.4, 8.2, 5.7 Hz, 1H), 5.40 (dt, J = 10.2, 7.8 Hz, 1H), 4.86 (dq, J = 9.6, 6.4, 3.8 Hz, 1H), 4.67 (d, J = 6.6 Hz, 1H), 4.64 (d, J = 6.6 Hz, 1H), 4.52 (s, 1H), 4.07 (dq, J = 10.1, 1.8 Hz, 1H), 3.76–3.88 (m, 2H), 3.38 (s, 3H), 2.92 (d, J = 2.5 Hz, 1H), 2.27–2.38 (m, 1H), 1.90–2.25 (m, 5H), 1.54–1.80 (m, 1H), 1.61 (s, 3H), 1.40 (s, 3H), 1.25–1.58 (m, 4H), 1.13 (d, J = 7.0 Hz, 3H), 0.97 (d, J = 6.5 Hz, 1.5H), 0.84 (d, J = 7.0 Hz, 1.5H), 0.76 (d, J = 7.0 Hz, 1.5H), 0.74 (d, J = 6.5 Hz, 1.5H); ¹³C-NMR (63 MHz; CDCl₃): δ [ppm] = 168.1, 133.3, 130.0, 128.5, 126.7, 112.2, 107.4, 95.2, 80.4, 76.6, 72.7, 71.8, 68.5, 55.8, 44.3, 39.6, 36.2, 34.6, 33.1, 29.6, 28.5, 28.4, 27.8, 27.0, 23.7, 19.8, 16.2, 9.5; MS: (FAB, NBA, CsI) m/z = 643 (100); HRMS (FAB) calcd for C₂₈H₄₆O₈Cs, [M+Cs] : 643.2247 found: 643.2244; IR (thin film): $1/\lambda$ [cm⁻¹] = 3545, 2937, 1761, 1729, 1459, 1380, 1280, 1219, 1153, 1119, 1092, 1036, 1003, 954, 923, 737.

Protected dimer (19)

Methyl (4*R/S*, 5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 2*R/S*, 4*S*, 7*E*, 9*Z*, 13*S*)-13-*tert*-butyldimethylsilyloxy-2-hydroxy-4-methoxymethoxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **15** (42 mg, 64 μ mol) was dissolved in MeOH (2 mL) and fine powdered barium hydroxide octahydrate (400 mg, 1.27 mmol) was added. The mixture was vigorously stirred for 1 h at room temperature. The white suspension was diluted with brine (4 mL) and acidified with 1M HCl to pH 3 resulting in a clear solution which was four times extracted with EtOAc. Combined organic layers were washed with brine and dried over MgSO₄. The crude acid was judged pure by TLC (R_f = 0.23 hexane/ EtOAc/MeOH 4:4:1) and used for esterification without further purification. A stock solution was prepared by dissolving 2,4,6-trichlorobenzoylchloride (96 mg, 400 μ mol) and triethylamine (44 mg, 440 μ mol) in 2 mL toluene. The acid was azeotroped with toluene (2 x 0.5 mL) and a portion of the stock solution (0.48 mL) was added to the acid in toluene (0.5 mL). After stirring for 1 h, the mixture was diluted with toluene (0.6 mL) and added over 1 h via syringe pump to a solution of methyl (5*S*, 7*S*, 10*R*)-2,2,10-trimethyl-7-[(1*R*, 4*S*, 7*E*, 9*Z*, 13*S*)-2,13-dihydroxy-4-methoxymethoxy-1-methyl-tetradeca-7,9-dien-1-yl]-1,3,6-trioxaspiro[4.5]decan-4-carboxylate **16b** (38 mg, 70 μ mol) and DMAP (12 mg, 100 μ mol) in 3 mL toluene at room temperature. The suspension was stirred for an additional 0.5 h, diluted with EtOAc (10 mL) and saturated aqueous NaHCO₃ (5 mL) were added. The phases were separated and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (25 g of SiO₂, hexanes/ EtOAc 2 : 1, R_f = 0.26) to provide 55 mg (74%) of the protected dimer **19** as a clear colorless oil and 7 mg (13 μ mol) of recovered alcohol **16b**. Anal. calcd for C₆₃H₁₁₀O₁₇Si : C 64.80; H, 9.50; found: C, 64.65; H, 9.20. ¹H-NMR (400 MHz; CDCl₃): δ [ppm] = 6.31 (dd, J = 15.1, 11.3 Hz, 1H), 6.27 (dd, J = 15.1, 11.3 Hz, 1H), 5.95 (dd, J = 11.3, 11.0 Hz, 1H), 5.92 (dd, J = 11.3, 11.0 Hz, 1H), 5.67 (dt, J = 15.1, 7.1 Hz, 1H), 5.63 (dt, J = 15.1, 7.1 Hz, 1H), 5.30 (dt, J = 11.0, 7.4 Hz, 1H), 5.26 (dt, J = 11.0, 7.4 Hz, 1H), 5.02 (qt, J = 6.4, 6.2 Hz, 1H), 4.66 (d, J = 6.7 Hz, 1H), 4.64 (s, 2H), 4.63 (d, J = 6.7 Hz, 1H), 4.58 (s, 1H), 4.49 (s, 1H), 4.15 (m, 1H), 3.99 (m, 1H), 3.97-4.07 (m, 1H), 3.76-3.91 (m, 5H), 3.75 (s, 3H), 3.37 (s, 6H), 2.08-2.34 (m, 8H), 1.91-2.01 (m, 2H), 1.73-1.90 (m, 4H), 1.40-1.72 (m, 18H), 1.62 (s, 3H), 1.52 (s, 3H), 1.51 (s, 3H), 1.40 (s, 3H), 4H), 1.27 (d, J

= 6.4 Hz, 3H), 1.12 (d, J = 6.0 Hz, 3H), 0.96 (d, J = 6.4 Hz, 3H), 0.92 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.78 (d, J = 6.4 Hz, 1.5H), 0.04 (s, 6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 168.9, 168.2, 134.8, 133.8, 130.1, 129.3, 128.5, 128.3, 125.9, 125.5, 112.5, 110.7, 107.6, 107.5, 95.4, 95.3, 84.3, 80.4, 76.2, 76.1, 75.4, 74.5, 72.3, 68.5, 68.2, 68.1, 55.7, 52.2, 42.8, 42.3, 39.7, 39.3, 35.6, 34.2, 34.1, 34.0, 29.0, 28.8, 28.5, 28.4, 28.0, 26.6, 25.9, 25.5, 24.0, 23.7, 19.6, 18.1, 16.2, 16.1, 10.5, 10.1, -4.4, -4.7; $[\alpha]_D^{20}$ = +46.0° (c = 1.0; CHCl_3); MS: (FI, 7 kV, 3 mA, 270°C) m/z = 1167 [M] (100), 1022 (6), 846 (18); IR (thin film): $1/\lambda$ [cm^{-1}] = 3524, 2933, 1765, 1455, 1381, 1216, 1121, 1035, 919, 836, 774.

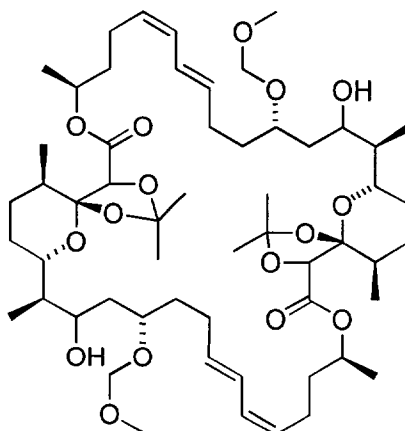
Dimeric triole (20)



A stock solution of 5 mL HF/pyridine complex, 10 mL pyridine and 15 mL THF was prepared. In a Teflon vessel the protected dimer **19** (51 mg, 43.7 μmol) was dissolved in 3 mL THF and 0.5 mL of the stock solution was added slowly at ambient temperature. The mixture was stirred for 24 h and then diluted with Et_2O (15 mL) and saturated aqueous CuSO_4 (10 mL). The phases were separated and aqueous layer was extracted three times with EtOAc . The combined organic layers were washed with saturated aqueous NaHCO_3 , dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (25 g SiO_2 , 50% EtOAc /hexanes, (R_f = 0.14) to provide 44 mg (96 %) of dimeric triole **20** as a clear colorless oil. ^1H -NMR (600 MHz; CDCl_3): δ [ppm] = 6.34 (dd, J = 15.1, 11.0 Hz, 1H), 6.26 (dd, J = 15.1, 10.9 Hz, 1H), 5.95 (dd, J = 11.0, 10.8 Hz, 1H), 5.94 (dd, J = 10.9, 10.6 Hz, 1H), 5.66 (dt, J = 15.1, 7.0 Hz, 1H), 5.65 (dt, J = 15.1, 6.9 Hz, 1H), 5.30 (dt, J = 10.8, 7.6 Hz, 1H), 5.26 (dt, J = 10.6, 7.6 Hz, 1H), 5.02 (qt, J = 6.4, 6.2 Hz, 1H), 4.66 (d, J = 6.8 Hz, 1H), 4.64 (s, 2H), 4.63 (d, J = 6.8 Hz, 1H), 4.58 (s, 1H), 4.49 (s, 1H), 4.14 (ddd, J = 9.0, 3.7, 2.2 Hz, 1H), 3.99 (m, 1H), 3.87 (ddd, J = 11.3, 6.1, 2.1 Hz, 1H), 3.82 (ddd, J = 11.5, 5.5, 2.2 Hz, 1H), 3.73–3.82 (m, 3H), 3.74 (s, 3H), 3.36 (s, 6H), 2.12–2.28 (m, 8H), 1.97 (dq, J = 10.9, 6.5, 4.1 Hz, 1H), 1.85 (dq, J = 10.9, 6.4, 4.2 Hz, 1H), 1.73–1.83 (m, 4H), 1.40–1.72 (m, 18H), 1.62 (s, 3H), 1.52 (s, 3H), 1.51 (s, 3H), 1.40 (s, 3H), 1.27 (d, J = 6.3 Hz, 3H), 1.18 (d, J = 6.3 Hz, 3H), 0.96 (d, J = 6.5 Hz, 3H), 0.92 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H), 0.77 (d, J = 6.4 Hz, 3H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 168.9, 168.2, 134.8, 134.2, 129.5, 129.3, 129.0, 128.2, 125.8, 125.5, 112.5, 110.7, 107.6, 107.5, 95.4, 84.3, 80.4, 76.1, 75.4,

74.5, 72.3, 68.4, 68.2, 64.4, 55.7, 52.2, 42.8, 42.3, 39.3, 39.2, 39.0, 35.6, 34.2, 33.9, 29.0, 28.8, 28.5, 28.4, 28.0, 26.9, 26.6, 25.5, 24.1, 23.7, 23.6, 19.5, 16.1, 10.5, 10.1; $[\alpha]_D^{20} = +29.8^\circ$ ($c = 0.5$; CHCl_3); MS: (FI, 7kV, 3mA, 255°C) $m/z = 1054$ [M] (39), 1053 [M] (100), 1052 [M] (67); MS (FAB, NBA, CsI, 20kV, 3 μ A) (rel. intensity) calcd for $\text{C}_{57}\text{H}_{96}\text{O}_{17}\text{Cs}$ 1185.6 (100), 1186.6 (66), 1187.6 (25), 1188.6 (7), found : 1185.2 (100), 1186.2 (56), 1187.3 (22), 1156.3 (6); HRMS (FAB) calcd for $\text{C}_{57}\text{H}_{96}\text{O}_{17}\text{Cs}$: [M+Cs] :1185.5702 found: 1185.5695; IR (thin film): $1/\lambda$ [cm^{-1}] = 3502, 2936, 1760, 1456, 1381, 1216, 1120, 1033, 920, 836.

Cyclic dimeric diol (22)

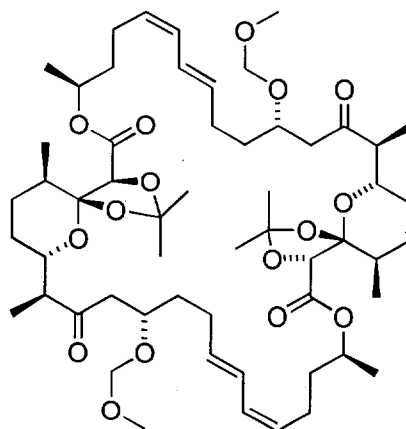


Dimeric triole **20** (10.5 mg, 10 μ mol) was dissolved in MeOH (1.3 mL) and powdered $\text{Ba}(\text{OH})_2 \cdot 8 \text{H}_2\text{O}$ (200 mg, 0.63 mmol) was added. The white suspension was vigorously stirred for 30 min, then diluted with 5 mL Et_2O and 5 mL brine and acidified to pH 3 with 1M HCl (1.4 mL). The two clear phases were separated and the aqueous layer was extracted four times with EtOAc. The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo. The crude dimeric seco acid **21** was used for macrolactonization without any further purification. A stock solution was prepared by dissolving 2,4,6-trichlorobenzoylchloride (96 mg, 400 μ mol) and triethylamine (44 mg, 440 μ mol) in 2 mL toluene. A portion of 0.1 mL was added to the dimeric seco acid in 0.5 mL toluene. After stirring for 2 h the mixture was diluted with 0.6 mL toluene and added over 2 h *via* syringe pump to a solution of DMAP (12 mg, 100 μ mol) in 3 mL toluene at 35°C. The suspension was stirred for an additional 0.5 h diluted with EtOAc (10 mL) and saturated aqueous NaHCO_3 (5 mL). The phases were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (12 g SiO_2 , 50% EtOAc/hexanes; $R_f = 0.41$) to provide 8.4 mg (82 %) of **22** as a clear colorless oil.

$^1\text{H-NMR}$ (600 MHz; CDCl_3): δ [ppm] = 6.30 (dd, $J = 15.4, 11.0$ Hz, 2H), 5.97 (dd, $J = 11.0, 10.8$ Hz, 1H), 5.95 (dd, $J = 11.0, 10.8$ Hz, 1H), 5.71 (dt, $J = 15.4, 6.9$ Hz, 1H), 5.68 (dt, $J = 15.4, 7.0$ Hz, 1H), 5.28 (dt, $J = 10.8, 7.5$ Hz, 2H), 4.96-5.06 (m, 2H), 4.68 (d, $J = 6.7$ Hz, 1H), 4.66 (s, 2H), 4.63 (d, $J = 6.7$ Hz, 1H), 4.54 (s, 1H), 4.50 (s, 1H), 4.16 (m, 1H), 4.07 (m, 1H), 3.86-3.91 (m, 1H), 3.76-3.82 (m, 3H), 3.38 (s, 6H), 2.12-2.29 (m, 8H), 1.94-1.99 (m, 1H), 1.89, (ddd, $J = 14.4, 10.0, 5.1$ Hz, 1H), 1.73-1.84 (m, 4H), 1.50-1.72 (m, 14H), 1.63 (s, 3H), 1.54 (s, 3H), 1.51 (s, 3H), 1.40 (s, 3H), 1.32-1.38 (m, 4H) 1.29 (d, $J = 6.1$ Hz, 3 H), 1.23 (d, J

= 6.2 Hz, 3H), 1.00 (d, J = 7.2 Hz, 3H), 0.97 (d, J = 6.4 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.81 (d, J = 6.7 Hz, 3H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 168.8, 134.8, 134.7, 129.4, 129.2, 128.6, 128.2, 125.5, 112.3, 110.6, 107.3, 107.2, 95.5, 95.4, 84.1, 80.2, 76.6, 75.9, 73.5, 72.3, 71.5, 67.7, 67.6, 64.4, 55.7, 43.8, 42.3, 39.8, 39.6, 35.9, 35.6, 34.6, 34.4, 33.9, 33.8, 29.5, 28.9, 28.5, 28.0, 27.0, 26.4, 25.2, 23.9, 23.7, 19.7, 16.2, 16.0, 10.5, 9.9; MS (FAB, NBA, CsI, 20kV, 3 μ A) (rel. intensity) calcd for $\text{C}_{56}\text{H}_{92}\text{O}_{16}\text{Cs}$ 1153.6 (100), 1154.6 (65), 1155.6 (24), 1156.6 (6), found : 1153.6 (100), 1154.6 (62), 1155.6 (24), 1156.6 (7); HRMS (FAB) calcd for $\text{C}_{56}\text{H}_{92}\text{O}_{16}\text{Cs}$: $[\text{M}+\text{Cs}]$: 1153.5439 found: 1153.5206; $[\alpha]_{\text{D}}^{20}$ = +44.2° (c = 1.0; CHCl_3); IR (thin film): $1/\lambda$ [cm^{-1}] = 3545, 2935, 1757, 1729, 1458, 1381; 1274, 1217, 1119, 1036, 955, 736.

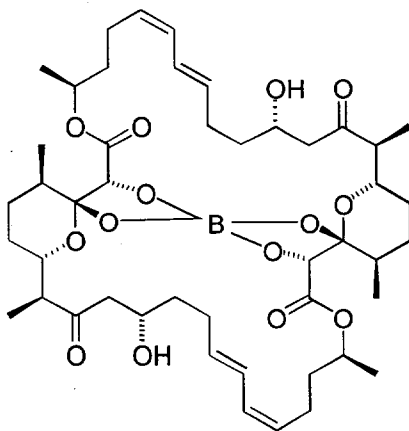
MOM/acetonid protected tartrolon A 2 (23)



(COCl_2)₂ (50 μl , 0.55 mmol) was dissolved in 4 mL CH_2Cl_2 and cooled to -78°C . DMSO (90 μl , 1.25 mmol) was added slowly and the mixture was stirred for further 15 min. Cyclic diole 4 (35 mg, 34 μmol) in CH_2Cl_2 (2 mL) was added over a period of 10 min, after 1 h at -78°C Et_3N (300 μl , 2.1 mmol) was added and the mixture was warmed to room temperature. Saturated aqueous NH_4Cl (8 mL) was added. The phases were separated and the aqueous layer was extracted twice Et_2O and once with EtOAc . The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (15 g of SiO_2 , EtOAc /hexanes 1 : 1, R_f = 0.63) to provide 31 mg (89 %) of MOM/acetonide protected tartrolon A 2 **23** as a colorless foam. ^1H -NMR (400 MHz; CDCl_3): δ [ppm] = 6.46 (dd, J = 15.0, 11.2 Hz, 1H), 6.28 (dd, J = 15.0, 11.2 Hz, 1H), 6.00 (dd, J = 11.2, 11.0 Hz, 1H), 5.96 (dd, J = 11.2, 11.0 Hz, 1H), 5.76 (dt, J = 15.0, 6.5 Hz, 1H), 5.66 (dt, J = 15.0, 7.0 Hz, 0.5H), 5.30 (dt, J = 11.0, 7.4 Hz, 1H), 5.28 (dt, J = 11.0, 7.4 Hz, 1H), 5.04-5.14 (m, 2H), 4.74 (d, J = 7.0 Hz, 1H), 4.71 (d, J = 7.0 Hz, 1H), 4.68 (d, J = 6.0 Hz, 1H), 4.62 (d, J = 6.0 Hz, 1H), 4.49 (s, 1H), 4.39 (s, 1H), 4.05-4.15 (m, 2H), 3.93 (ddd, J = 11.5, 8.7, 2.0 Hz, 1H), 3.86 (ddd, J = 11.5, 8.7, 2.0 Hz, 0.5H), 3.37 (s, 3H), 3.35 (s, 3H), 2.86 (dd, J = 17.5, 7.7 Hz, 1H), 2.62-2.74 (m, 4H), 2.51 (dq, J = 9.5, 7.0 Hz, 1H), 2.12-2.32 (m, 4H), 2.03 (dq, J = 10.5, 7.0, 5.7 Hz, 1H), 1.89 (dq, J = 11.0, 6.5, 3.7 Hz, 1H), 1.58-1.82 (m, 8H), 1.57 (s, 3H), 1.51 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.25-1.45 (m, 8H), 1.34 (d, J = 6.5 Hz, 3H), 1.30 (d, J = 6.4 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.99 (d, J = 7.0 Hz, 3H), 0.94 (d, J = 7.0 Hz,

3H), 0.77 (d, $J = 6.5$ Hz, 3H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 213.0, 212.1, 168.8, 167.4, 135.3, 134.7, 130.0, 129.5, 129.0, 128.4, 126.0, 125.9, 112.7, 111.1, 107.9, 107.1, 96.8, 84.5, 79.9, 75.5, 74.8, 73.9, 73.8, 72.5, 71.5, 56.0, 55.9, 51.9, 51.7, 51.2, 50.4, 36.5, 36.1, 35.0, 34.7, 30.1, 29.5, 29.3, 29.0, 28.8, 28.1, 27.3, 27.1, 25.7, 24.4, 23.9, 20.7, 19.8, 16.6, 16.4, 13.0, 12.7; MS (FAB, NBA, CsI, 20 kV, 3 μA) (rel. intensity) calcd for $\text{C}_{56}\text{H}_{88}\text{O}_{16}\text{Cs}$ 1149.6 (100), 1150.6 (65), 1151.6 (24), 1152.6 (6), found : 1149.6 (100), 1150.6 (61), 1151.6 (36), 1152.6 (14); HRMS (FAB) calcd for $\text{C}_{56}\text{H}_{88}\text{O}_{16}\text{Cs}$: $[\text{M}+\text{Cs}]$: 1149.5127 found : 1149.5058; (EI, 80 eV, 190°C) calcd for $\text{C}_{54}\text{H}_{81}\text{O}_{14}$ $[\text{M}-\text{C}_2\text{H}_7\text{O}_2]$: 953.5626 found : 953.5689; $[\alpha]_D^{20} = +55.0^\circ$ ($c = 0.67$; CHCl_3); IR (thin film): $1/\lambda$ [cm^{-1}] = 2937, 1758, 1719, 1458, 1381, 1215, 1117, 1044.

Tartrolon B (1)



To a stirred solution of the protected tartrolon A 2 **23** (10.3 mg, 10 μmol) in CH_2Cl_2 (2 mL) at -78°C was added a 0.5 M solution of NEt_3 (0.1 mL, 0.05 mmol) and a 1 M solution of dimethylboron bromide (0.3 mL, 0.3 mmol) in CH_2Cl_2 . After 4 h at -78°C , 3 mL water and 5 mL THF were added and the mixture was quickly warmed to ambient temperature. After 10 min of efficient stirring 3 mL brine and 10 mL EtOAc were added. The phases were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over MgSO_4 and concentrated in vacuo. The residue was filtered through a short column (10 g SiO_2 ; 10 % MeOH in CH_2Cl_2) to provide 5.5 mg (65 %) of a crude mixture of all three tartrolon A forms. The unseparated mixture was dissolved in MeOH (2 mL). $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10 \text{H}_2\text{O}$ (5 mg, 12 μmol) was added and the mixture was warmed to 55°C for 12 h. The cold mixture was concentrated under reduced pressure and dissolved in CH_2Cl_2 (2 mL). The solution was passed through a Sephatex[®] LH 20 column (10 g, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 10 : 1). The residue was purified by HPLC (data for Merck Supersphere Si 60 4 μm , 244 mm x 4 mm column, 25 % EtOAc in hexane, flow: 2 mL/min, $t_R = 2.2$ min) to provide 2.3 mg (27 % over two steps) tartrolon B **1** as a colorless foam. ^1H -NMR (600 MHz; CDCl_3): δ [ppm] = 6.07 (dd, $J = 10.8, 10.4$ Hz, 2H), 5.98 (dd, $J = 15.5, 10.8$ Hz, 2H), 5.91 (dt, $J = 15.5, 4.2$ Hz, 2H), 5.26 (ddd, $J = 10.8, 10.8, 6.0$ Hz, 2H), 4.65 (dq, $J =$

10.4, 6.0 Hz, 2H), 4.43 (s, 2H), 4.01 (ddd, $J = 10.8, 10.8, 1.3$ Hz, 2H), 3.98 (m, 2H), 3.33 (s, 2H), 3.22 (dd, $J = 19.0, 10.3$ Hz, 2H), 2.36-2.46 (m, 4H), 2.38 (d, $J = 19.0$ Hz, 2H), 2.21 (dq, $J = 10.8, 7.3$ Hz, 2H), 1.89-2.02 (m, 4H), 1.74-1.86 (m, 6H), 1.50-1.73 (m, 6H), 1.34 (m, 2H), 1.26 (m, 2H), 1.19 (d, $J = 6.5$ Hz, 6H), 1.06 (m, 2H), 1.0 (d, $J = 6.0$ Hz, 6H), 0.99 (d, $J = 6.5$ Hz, 6H); ^{13}C -NMR (63 MHz; CDCl_3): δ [ppm] = 214.8, 174.4, 134.7, 131.0, 127.8, 122.9, 104.4, 78.2, 71.2, 69.4, 67.7, 54.9, 42.5, 35.9, 35.7, 31.6, 28.3, 28.2, 23.0, 20.6, 16.9, 12.8; MS (FAB, NBA): $m/z = 878$ [M], 855[M-Na], UV: $\lambda_{\text{max}} = 235$ nm ($\epsilon = 19400$; MeOH); CD: $\lambda_{\text{max}} = 205$ nm ($\Delta\epsilon = -4.5$; MeOH); natural sample ($\Delta\epsilon = -7.5$); IR: (thin film): $1/\lambda$ [cm^{-1}] = 3545, 2966, 2937, 2894, 1729, 1702, 1459, 1458, 1380, 1274, 1119, 1036.

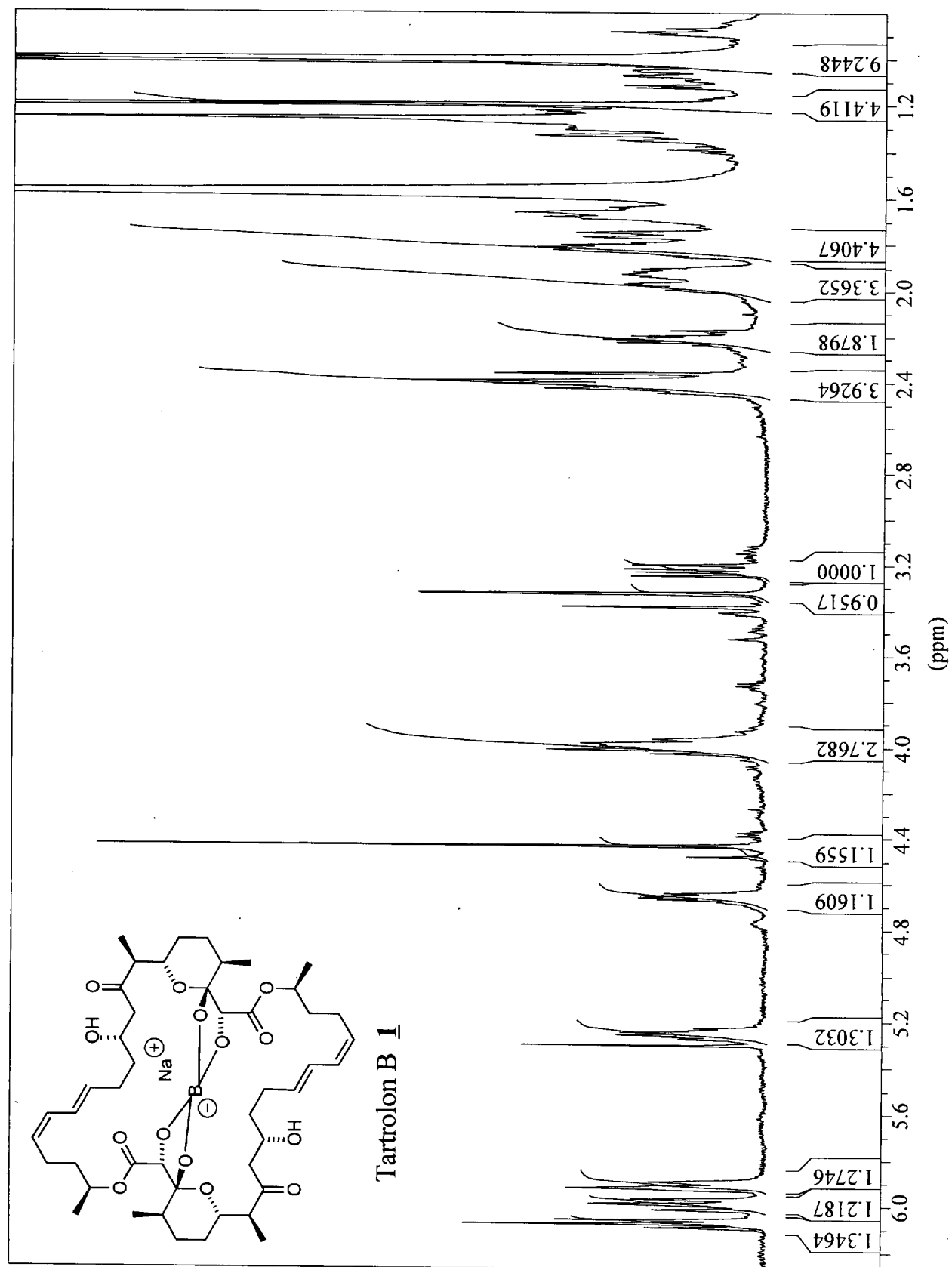
Comparison of ¹H-NMR data

	natural tartrolon B		synthetic tartrolon B	
	δ [ppm]	<i>J</i> [Hz]	δ [ppm]	<i>J</i> [Hz]
H16	6.06	dd, 10.6, 10.6	6.07	dd, 10.8, 10.4
H15	5.98	ddd, 15.5, 10.6	5.98	dd, 15.5, 10.8
H14	5.90	ddd, 15.5, 4.5, 4.3	5.91	ddd, 15.5, 4.2, 4.2
H17	5.26	ddd, 11.0, 10.6, 5.5	5.25	ddd, 10.8, 10.8, 6.0
H20	4.64	dqd, 10.4, 6.2, 1.0	4.65	dq, 10.4, 6.0
H2	4.42	s	4.43	s
H7	4.00	ddd, 11.0, 10.9, 1.8	4.01	ddd, 10.8, 10.8, 1.3
H11	3.97	ddd, 10.5, 10.5, 3.2	3.98	m
11OH	3.30	s	3.33	s
H10a	3.22	dd, 19.0, 10.5	3.22	dd, 19.0, 10.3
H13a	2.41	m	2.41	m
H18a	2.41	m	2.41	m
H10b	2.36	d, 19.0	2.38	19.0
H8	2.20	dq, 10.9, 7.1	2.21	dq, 10.8, 7.3
H13b	1.96	m	1.98	m
H18b	1.91	m	1.93	m
H4	1.80	ddd(dqd), 12.0, 6.4, 4.5	1.81	m
H19a	1.80	m	1.80	m
H6a	1.74	m	1.76	m
H12a	1.68	m	1.68	m
H5a	1.62	m	1.65	m
H5b	1.55	m	(1.55)	m
H19b	1.32	m	1.34	m
H12b	1.26	m	1.26	m
H21	1.16	d, 6.2	1.19	d, 6.5
H6b	1.05	m	1.06	m
H22	1.00	d, 6.4	1.00	d, 6.1
H23	0.99	d, 7.1	0.99	d, 6.7

Comparison of ^{13}C -NMR-data

carbon	natural tartrolon B [ppm]	synthetic tartrolon B [ppm]
9	214.8	214.8
1	174.4	174.4
14	134.7	134.7
17	127.8	127.8
15	122.9	122.9
16	131.0	131.0
3	104.4	104.4
2	78.2	78.2
11	67.8	67.7
7	71.3	71.2
20	69.5	69.4
8	55.0	54.9
10	42.6	42.5
19	35.9	35.9
4	35.7	35.7
12	31.7	31.6
6	30.4	30.3
13	28.3	28.3
5	28.2	28.2
21	20.6	20.6
22	16.9	16.9
18	23.0	23.0
23	13.8	13.8

¹H-NMR spectra of tartrolon B



¹³C-NMR spectra of tartrolon B