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Supporting Information

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Total Synthesis of Erythronolide A via Mg(II)-Mediated Nitrile Oxide Cycloaddition[1*]

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Experimental Part

All non-aqueous reactions were carried out using oven-dried or flame-dried glassware under a positive pressure of dry nitrogen or argon unless otherwise noted. Tetrahydrofuran, acetonitrile, toluene, Et_2O, and CH_2Cl_2 were purified by distillation and dried by passage over activated alumina under an argon atmosphere (H_2O content < 30 ppm, Karl-Fischer titration).[i] Triethylamine and pyridine were distilled from KOH. Triethylchlorosilane, 2,4,6-trichlorobenzoyl chloride (*Yamaguchi* reagent), and benzaldehyde dimethylacetal were distilled prior to use.

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4-*N*,*N*-dimethylaminopyridine was recrystallized from toluene. *t*-Butyl lithium was titrated with *s*-BuOH/phenanthroline).[ii] Tetra-*n*-propyl ammonium perruthenate[iii] and zinc borohydride[iv] were prepared according to a literature procedure. Except as indicated otherwise, reactions were magnetically stirred and monitored by thin layer chromatography (TLC) using Merck Silica Gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained using ceric ammonium molybdate or potassium permanganate stain. Chromatographic purification of products was performed on E. Merck Silica Gel 60 (230–400 mesh) using a forced flow of eluant at 0.3–0.5 bar pressure.[v] Concentration under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure. Purified compounds were further dried under high vacuum (0.01–0.05 Torr). Yields refer to purified and spectroscopically pure compounds. Melting points were measured on a Buchi 510 apparatus. All melting points were measured in open capillaries and are uncorrected. Optical rotations were measured on a Jasco DIP-1000 polarimeter operating at the sodium D line with a 100 mm path length cell. NMR spectra were recorded on a Varian Mercury 300 spectrometer operating at 300 MHz and 75 MHz for ^{1}H and ^{13}C acquisitions, respectively, or on a Bruker DRX500 spectrometer operating at 500 MHz and 125 MHz for 1H and 13C acquisitions, respectively. Chemical shifts are reported in ppm with the solvent resonance as the internal standard. Data are reported as follows: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz. IR spectra were recorded on a PerkinElmer Spectrum RXI FT-IR spectrophotometer. Absorptions are given in wavenumbers

(cm^{-1}). Mass spectra were recorded by the MS service at ETH Zurich. EI-MS: VG-TRIBRID spectrometer; spectra were measured at 70 eV. MALDI-MS: IonSpec Ultima Fourier Transform Mass Spectrometer. Peaks are given in percent (m/z). Elemental analyses were performed at the Mikrolabor der ETH Zurich.

Buffers were prepared according to the following procedures:
pH 3.8 citrate phosphate buffer: citric acid (14 g), Na_2HPO_4 (9.9 g), H_2O (1000 ml)
pH 7 phosphate buffer: KH_2PO_4 (6.8 g), NaOH (1.16 g), H_2O (1000 ml)
pH 8.6 carbonate buffer: $NaHCO_3$ (42 g), Na_2CO_3 (0.53 g), H_2O (1000 ml)

[i] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, T. J. Timmers, *Organometallics* **1996**, *15*, 1518–1520.

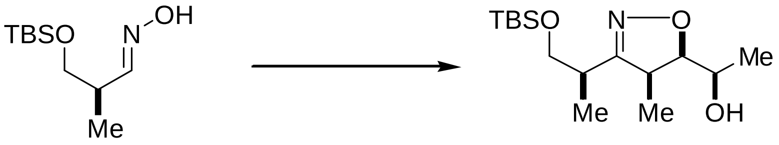
[ii] S.C. Watson, J. F. J. Eastham, *Organomet. Chem.* **1967**, *9*, 165.

[iii] A J. Bailey, W. P. Griffith, S. I. Mostafa, P. A. Sherwood, *Inorg. Chem.* **1993**, *32*, 268.

[iv] W. J. Gensler, F. Johnson, A. D. B. Sloan, *J. Am. Chem. Soc.* **1960**, *82*, 6074.

[v] W. C. Still,M. Kahn,A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925.

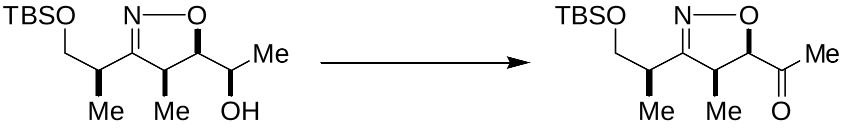
(1*R*)-1-[(4*S*,5*R*)-3-((1*R*)-2-{[*tert*-Butyl-(dimethyl)-silyl]oxy}-1-methylethyl)-4-methyl-4,5-dihydroisoxazol-5-yl]ethanol (4)



To a solution of (*R*)-(*Z*)-3-penten-2-ol (**4**) (0.475 g, 5.52 mmol, 1.20 equiv) and 2-propanol (1.17 ml, 15.2 mmol, 3.30 equiv) in CH_2Cl_2 (250 ml) at 0 ^oC was added EtMgBr (3 M in Et_2O, 4.60 ml, 13.8 mmol, 3.00 equiv). The reaction mixture turns momentarily cloudy, becoming clear and colorless upon stirring at 0 ^oC for 30 min. At this time, the hydroximinoyl chloride, prepared by addition of *t*-butylhypochloride (0.58 ml, 5.06 mmol, 1.10 equiv) to a solution of oxime **2** (1.00 g, 4.60 mmol, 1.00 equiv) in CH_2Cl_2 (46 ml) at -78 ^oC and stirring for 1.5 h, was added dropwise via cannula to the reaction to give a slightly yellow solution. It was allowed to warm to rt and stirred for 16 h. The reaction was quenched by the addition of sat. aq. NH_4Cl (200 ml) and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 ml). The combined organic solutions were washed with brine (50 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (3:1 hexane/EtOAc) provided isoxazoline **4** (1.20 g, 86% yield) as a clear colorless oil.

R_f = 0.21 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{25.0}$ (*c* 1.060, $CHCl_3$) = -13°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 4.16 (dd,1H, *J* = 9.3, 5.3 Hz), 3.98-3.90 (m, 1H), 3.66–3.58 (m, 2H), 3.31–3.23 (m, 1H), 2.67–2.60 (m, 1H), 2.06 (d(br), 1H, *J* = 6.2 Hz), 1.25 (d, 3H, *J* = 6.5 Hz), 1.19 (d, 3H, *J* = 6.9 Hz), 1.17 (d, 3H, *J* = 7.2 Hz), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.6, 85.9, 67.1, 66.1, 45.3, 34.7, 25.9, 20.3, 18.3, 14.6, 10.7, -5.4. IR Spectroscopy (thin film) 3408, 2930, 2857, 1462, 1389, 1255, 1091, 900, 837, 776(cm^{-1}). Mass Spectrometry EI–MS (m/z): 300.3 ([M]$^+$), 244.1(20), 240.1(12), 172.1, (17), 142.0(31), 122.0(13), 115.0(31), 96.0(16), 84.0(23), 75.0(100) 73.0(30). Combustion Analysis: Anal. calcd for $C_{15}H_{31}NO_3Si$: C, 59.76; H, 10.36; found C, 59.69; H, 10.48.

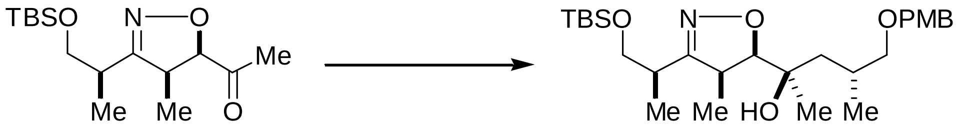
(1*R*)-1-[(4*S*,5*R*)-3-((1*R*)-2-{[*tert*-Butyl-(dimethyl)-silyl]oxy}-1-methylethyl)-4-methyl-4,5-dihydroisoxazol-5-yl]ethanone (5)



To isoxazoline **4** (1.18 g, 3.91 mmol, 1.00 equiv) in CH_2Cl_2 (8 ml) at rt was added NMO (0.69 g, 5.09 mmol, 1.30 equiv) and 4 ? molecular sieves (2 g). Then TPAP (0.041 g, 0.12 mmol, 0.03 equiv) was added as a solid in two portions to give a green mixture. After 10 min, the reaction had become dark red and after 20 min, more TPAP (0.020 g, 0.057 mmol, 0.015 equiv) was added. After stirring for 1.5 h at rt, the dark red mixture was diluted with pentane (8 ml) and filtered over a plug of silica gel, eluting with 3:2 pentane/ether. The solution was concentrated and a green oil was obtained. Purification by flash chromatography (5:1 hexane/EtOAc) provided ketone **5** (0.96 g, 82% yield) as a clear, colorless oil.

R_f = 0.44 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{28.7}$ (*c* 0.950, $CHCl_3$) = +51°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 4.76 (d, 1H, *J* = 10.9 Hz), 3.71-3.58 (m, 3H), 2.72-2.61 (m, 1H), 2.26 (s, 3H), 1.23 (d, 3H, *J* = 7.2 Hz), 1.08 (d, 3Hz, *J* = 7.5 Hz), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 208.2, 165.0, 87.0, 67.0, 47.7, 34.7, 28.4, 25.9, 18.3, 14.5, 12.1, -5.4. IR Spectroscopy (thin film) 2955, 2931, 2858, 1716, 1463, 1359, 1255, 1136, 1095, 1007, 970, 838, 777 (cm^{-1}). Mass Spectrometry EI-MS (m/z): 300.1 ($[M+H]^+$), 243.1(19), 240.1(26), 142.0(67), 115.0(50), 112.0(18). Combustion Analysis: Anal. calcd for $C_{15}H_{29}NO_3Si$: C, 60.16; H, 9.76; found C, 60.10; H, 9.60.

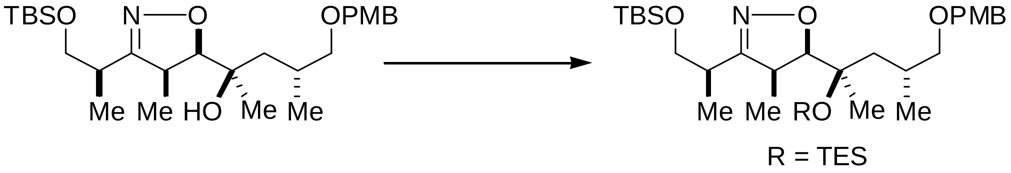
(2*R*,4*R*)-2-[(4*S*,5*R*)-3-((1*R*)-2-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-methylethyl)-4-methyl-4,5-dihydroisoxazol-5-yl]-5-[(4-methoxybenzyl)oxy]-4-methylpentan-2-ol (7)



To a solution of bromide **6** (0.24 g, 0.87 mmol, 1.3 equiv) in Et_2O (4.8 ml) at -78 °C was added *t*BuLi (1.76 M solution in pentane, 1.0 ml, 1.8 mmol, 2.7 equiv). The colorless suspension was stirred for 20 min at -78 °C before $MgBr_2$ (1.0 M solution in ether/benzene(3:1),[vi] 1.00 ml, 1.0 mmol, 1.50 equiv) was added. The colorless reaction mixture was stirred for 10 min and treated with a solution of ketone **5** (0.20 g, 0.67 mmol, 1.0 equiv) in THF (3.4 ml). After stirring for 1 hour at -78 °C, the colorless suspension was quenched with sat. aq. NH_4Cl (5 ml) and extracted with EtOAc (3 x 10 ml). The organic solution was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. NMR analysis of the crude material indicated a 20:1 ratio of diastereomers. Purification by flash chromatography (hexane/EtOAc 5:1 – 3:1) provided pure **7** (0.21 g, 64% yield, > 50:1 dr), accompanied with ketone **5** (0.065 g, 33% recovered starting material).

R_f = 0.33 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{30.0}$ (*c* 2.570, $CHCl_3$) = +3.5°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.26 (d, 2H, *J* = 8.7 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 4.49 (d, 1H, *J* = 11.5 Hz), 4.43 (d, 1H, *J* = 11.5 Hz), 4.03 (d, 1H, *J* = 8.7 Hz), 3.80 (s, 3H), 3.64 (d, 2H, *J* = 6.5 Hz), 3.46 (s(br), 1H), 3.36 (dd, 1H, *J* = 8.7, 5.0 Hz), 3.24-3.14 (m, 2H), 2.68-2.59 (m, 1H), 2.10-2.05 (m, 1H), 1.96 (dd, 1H, *J* = 14.6, 6.9 Hz), 1.44 (dd, 1H, *J* = 14.3, 3.4 Hz), 1.27 (s, 3H), 1.24 (d, 3H, *J* = 5.0 Hz), 1.21 (d, 3H, *J* = 4.4 Hz), 0.95 (d, 3H, *J* = 6.9 Hz), 0.89 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ:167.6, 159.0, 129.9, 129.2, 113.7, 88.5, 76.4, 72.9, 72.2, 67.3, 55.3, 45.5, 34.9, 28.9, 25.9, 23.9, 19.8, 18.3, 14.7, 12.7, -5.3. IR Spectroscopy (thin film) 3436, 2954, 2931, 2857, 1613, 1514, 1361, 1301, 1249, 1174, 1089, 1036, 938, 837, 777 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{27}H_{47}NO_5SiNa]^+$, 516.3121; found, 516.3111. Combustion Analysis: Anal. calcd for $C_{27}H_{47}NO_5Si$: C, 65.68; H, 9.59; found C, 65.78; H, 9.57.

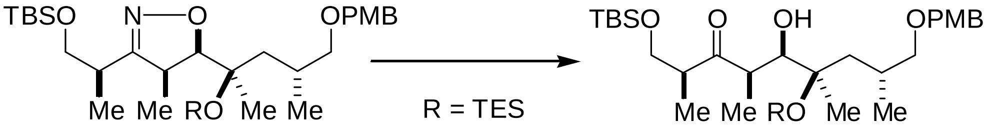
(4*S*,5*R*)-3-((1*R*)-2-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-methylethyl)-5-{(1*R*,3*R*)-4-[(4-methoxybenzyl)oxy]-1,3-dimethyl-1-[(triethylsilyl)oxy]butyl}-4-methyl-4,5-dihydroisoxazole (8)



At 0 °C, triethylsilyl triflate (3.20 ml, 14.0 mmol, 1.30 equiv) was added to a solution of alcohol **7** (5.30 g, 10.7 mmol, 1.00 equiv) and 2,6-lutidine (3.80 ml, 32.2 mmol, 3.00 equiv) in CH_2Cl_2 (30 ml). The yellow solution was stirred for 1 h at 0 °C and quenched with water (30 ml). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2. The organic solution was washed with 1 N HCl (60 ml), brine (30 ml), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography (hexane/EtOAc 6:1) afforded **8** (6.01 g, 93% yield) as a clear, colorless oil.

R_f = 0.67 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{30.0}$ (*c* 1.0450, $CHCl_3$) = -4.8°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.24 (d, 2H, *J* = 8.1 Hz), 6.86 (d, 2H, *J* = 8.4 Hz), 4.41 (s, 2H), 4.12 (d, 1H, *J* = 9.0 Hz), 3.80 (s, 3H), 3.62 (d, 2H, *J* = 6.5 Hz), 3.32 (dd, 1H, *J* = 8.7, 6.2 Hz), 3.21-3.12(m, 2H), 2.63-2.56(m, 1H), 1.95-1.90 (m, 1H), 1.68 (dd, 1H, *J* = 13.9, 4.0 Hz), 1.48 (dd, 1H, *J* = 14.0, 6.5 Hz), 1.34 (s, 3H), 1.20 (d, 3H, *J* = 6.9 Hz), 1.13 (d, 3H, *J* = 7.4 Hz), 1.02 (d, 3H, *J* = 6.7 Hz), 0.94 (t, 9H, *J* = 7.8 Hz), 0.88 (s, 9H), 0.63 (q, 6H, *J* = 7.7 Hz), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.9, 158.9, 130.8, 129.0, 113.6, 88.3, 76.6, 76.5, 76.5, 72.6, 67.3, 55.3, 45.3, 43.6, 34.9, 29.8, 25.9, 19.6, 18.3, 14.7, 12.7, 7.4, 6.9, -5.3. IR Spectroscopy (thin film) 2953, 2875, 1614, 1514, 1463, 1361, 1301, 1249, 1094, 1008, 838, 776, 741 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{33}H_{61}NO_5Si_2Na]^+$, 630.3986; found, 630.3975.

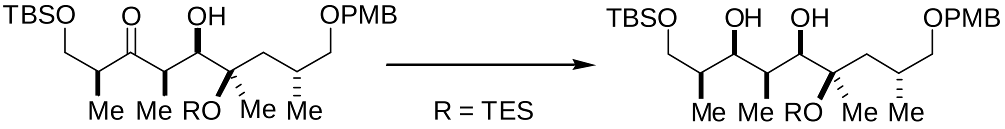
(1-*O*-[*tert*-Butyl(dimethyl)silyl]-2,4,7,8-tetradeoxy-9-*O*-(4-methoxybenzyl)-2,4,8-trimethyl-6-*C*-methyl-6-*O*-(triethylsilyl)-L-*glycero*-D-*gulo*-non-3-ulose (8d)



After addition of boric acid (0.102 g, 1.65 mmol, 5.00 equiv) and Raney-Ni (W2, spatula tip) to an emulsion of **7** (0.202 g, 0.33 mmol, 1.00 equiv) in MeOH/H_2O (5:1, 4.0 ml), the Schlenk flask was purged several times with H_2. The black suspension was stirred rapidly under an atmosphere of H_2 for 2 h. The black reaction mixture was filtered over celite and eluted with CH_2Cl_2. The biphasic mixture was washed with H_2O. The organic solution was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (hexane/EtOAc 7:1) provided β-hydroxyketone **8d** (0.181 g, 89% yield) as a clear, colorless oil.

R_f = 0.54 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{30.1}$ (*c* 1.530, $CHCl_3$) = +12°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.25 (d, 2H, *J* = 8.6 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 4.42 (s, 2H), 3.87-3.83 (m, 1H), 3.81-3.75 (m, 1H), 3.80 (s, 3H), 3.53 (dd, 1H, *J* = 9.7, 5.9 Hz), 3.27-3.16 (m, 2H), 2.99-2.88 (m, 2H), 2.49 (d, 1H *J* = 7.8 Hz), 1.81-1.76 (m, 1H), 1.66-1.50 (m, 2H), 1.18 (s, 3H), 1.16 (d, 3H, *J* = 7.2 Hz), 1.04 (d, 3H *J* = 6.8 Hz), 1.01 (d, 3H, J = 6.5 Hz), 0.95 (t, 9H, J = 8 Hz) 0.87 (s, 9H), 0.61 (q, 6H, J = 8 Hz) 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 216.4, 158.9, 130.7, 129.0, 113.6, 79.2, 76.4, 73.1, 72.6, 65.6, 55.3, 47.1, 47.0, 44.0, 30.0, 26.0, 25.2, 19.4, 18.5, 14.2, 11.2, 7.3, 7.0, -5.3, -5.3. IR Spectroscopy (thin film) 3524, 2954, 2876, 1701, 1613, 1587, 1513, 1463, 1361, 1302, 1249, 1172, 1095, 1005, 837, 775, 741, 724, 666 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{33}H_{62}O_6Si_2Na]^+$, 633.3983; found, 633.3972. Combustion Analysis: Anal. calcd for $C_{33}H_{62}O_6Si_2$: C, 64.87; H, 10.23; found C, 64.69; H, 10.46.

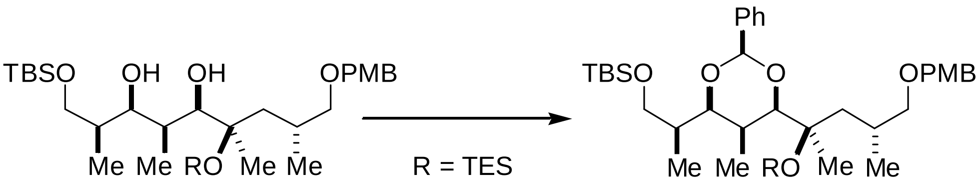
9-*O*-[*tert*-Butyl(dimethyl)silyl]-2,3,6,8-tetradeoxy-1-*O*-(4-methoxybenzyl)-2,6,8-trimethyl-4-*C*-methyl-4-*O*-(triethylsilyl)-L-*threo*-L-ido-nonitol (8e)



At -78 °C, $Zn(BH_4)_2$ (0.145 M solution in Et_2O, 12.0 ml, 1.73 mmol, 2.5 equiv) was added to a solution of ß-hydroxyketone **8d** (0.424 g, 0.694 mmol, 1.00 equiv) in CH_2Cl_2 (35 ml). The clear, colorless solution was stirred at -30 °C for 2 h before more $Zn(BH_4)_2$ (0.145 M solution in Et_2O, 2.4 ml, 0.345 mmol, 0.5 equiv) was added. The solution was stirred for another 30 min before it was quenched with MeOH/H_2O (1:1, 10 ml). The biphasic mixture was stirred for 1 hour at rt and then 1 N HCl (5 ml) was added. The aqueous layer was separated and extracted with CH_2Cl_2 (3 x 10 ml). The combined organics were washed with brine (10 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 10:1 – 7:1) afforded pure 1,3-diol **8e** (0.260 g, 60% yield) as a clear, colorless oil.

R_f = 0.48 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{27.6}$ (*c* 1.035, $CHCl_3$) = +10°. NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.25 (d, 2H, *J* = 7.8 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 4.42 (s, 2H), 3.81 (s, 3H), 3.74 (s, 1H), 3.67-3.63 (m, 1H), 3.62 (dd, 1H, *J* = 10.0, 4.1 Hz) 3.56-3.49 (m, 2H), 3.25-3.16 (m, 2H) 2.72 (d, 1H, *J* = 9.3 Hz), 1.93-1.87 (m, 1H), 1.81-1.73 (m, 1H), 1.71-1.45 (m, 3H), 1.23 (s, 3H), 1.02-0.97 (m, 9H), 0.95 (t, 9H, *J* = 7.8 Hz), 0.88 (s, 9H), 0.62 (q, 6H, *J* = 7.8 Hz), 0.038 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 158.9, 130.6, 129.0, 113.6, 79.6, 79.2, 77.5, 76.3, 72.6, 67.0, 55.3, 44.6, 37.4, 35.8, 30.3, 26.0, 24.7, 19.4, 18.3, 13.0, 7.5, 7.3, 7.0, -5.4, -5.4. IR Spectroscopy (thin film) 3502, 2955, 2876, 1613, 1587, 1514, 1463, 1415, 1389, 1361, 1302, 1249, 1172, 1097, 1004, 972, 837, 776, 742, 668(cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{33}H_{64}O_6Si_2Na]^+$, 635.4139; found, 635.4127. Combustion Analysis: Anal. calcd for $C_{33}H_{64}O_6Si_2$: C, 64.66; H, 10.52; found C, 64.40; H, 10.66.

3,5-*O*-Benzylidene-1-*O*-[*tert*-Butyl(dimethyl)silyl]-2,4,7,8-tetradeoxy-9-*O*-(4-methoxybenzyl)-2,4,8-trimethyl-6-*C*-methyl-6-*O*-(triethylsilyl)-L-*threo*-L-*ido*-nonitol (9)

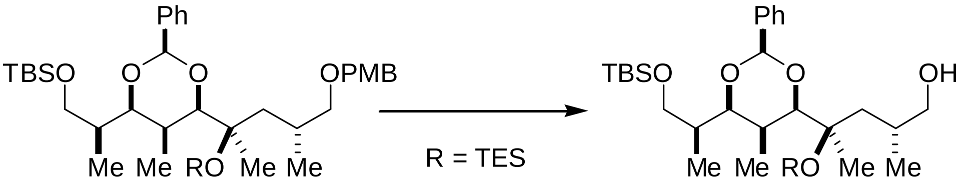


To a solution of **8e** (0.58 g, 0.95 mmol, 1.0 equiv) in toluene (10 ml) was added benzaldehyde dimethyl acetal (0.22 g, 1.5 mmol, 1.5 equiv) and CSA (0.023 g, 0.099

mmol, 0.10 equiv). The solution was stirred at rt and 70 mbar for 1.5 h, then saturated aqueous $NaHCO_3$ (10 ml) and EtOAc (10 ml) were added. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 10 ml). The combined organic phases were washed with brine (10 ml), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (hexane/EtOAc 15:1) to provide **9** (0.58 g, 87% yield) as a clear, colorless oil.

R_f = 0.64 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{23.6}$ (*c* 1.225, $CHCl_3$) = -1.5°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.53-7.50 (m, 2H), 7.38-7.31 (m, 3H), 7.27-7.23 (m, 2H), 6.90-6.85 (m, 2H), 5.50 (s, 1H), 4.43 (s, 2H), 3.81 (s, 3H), 3.60 (d, 1H, *J* = 1.9 Hz), 3.55-3.50 (m, 3H), 3.36 (dd, 1H, *J* = 8.71, 5.6 Hz), 3.15 (dd, 1H, *J* = 8.7, 7.5 Hz), 1.96-1.86 (m, 3H), 1.55 (dd, 1H, *J* = 13.7, 4.4 Hz), 1.42 (dd, 1H, *J* = 13.7, 5.9 Hz), 1.29 (s, 3H), 1.05 (d, 3H, *J* = 6.5 Hz), 1.05 (d, 3H, *J* = 6.5 Hz), 1.02 (d, 3H, *J* = 6.9 Hz), 0.90 (s, 9H), 0.86 (t, 9H, *J* = 8.1 Hz) 0.51 (q, 6H, *J* = 8.1 Hz), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 158.8, 139.1, 130.9, 128.9, 128.3, 127.8, 126.2, 113.6, 102.1, 87.1, 85.0, 78.0, 76.7, 72.5, 64.1, 55.3, 43.2, 36.3, 31.4, 29.4, 26.0, 24.9, 19.9, 18.3, 14.6, 8.4, 7.3, 6.8, -5.3, -5.4. IR Spectroscopy (thin film) 2953, 2874, 1612, 1587, 1514, 1406, 1360, 1302, 1249, 1141, 1101, 1305, 1010, 972, 836, 776, 741, 698 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{40}H_{68}O_6Si_2Na]^+$, 723.4452; found, 723.4439. Combustion Analysis: Anal. calcd for $C_{40}H_{68}O_6Si_2$: C, 68.52; H, 9.78; found C, 68.44; H, 9.79.

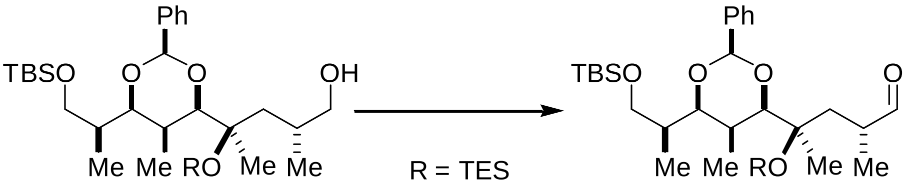
3,5-*O*-Benzylidene-1-*O*-[*tert*-butyl(dimethyl)silyl]-2,4,7,8-tetradeoxy-2,4,8-trimethyl-6-*C*-methyl-6-*O*-(triethylsilyl)-L-*threo*-L-*ido*-nonitol (9g)



At 0 °C, a solution of benzylidene acetal **9** (0.65 g, 0.93 mmol, 1.0 equiv) in CH_2Cl_2 (18 ml) was treated with DDQ (0.25 g, 1.1 mmol, 1.2 equiv) and pH-7 buffer (0.030 ml). The green suspension slowly turned light brown. After stirring for 2 h at 0 °C, the reaction was quenched with sat. aq. $Na_2S_2O_3$ (5 ml) and sat. aq. $NaHCO_3$ (60 ml). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 ml). The organic solution was washed with brine (20 ml), dried over anhydrous Na_2SO_4, filtered over Na_2SO_4, and concentrated under reduced pressure. The light yellow residue was purified by flash chromatography (hexane/EtOAc 7:1) to afford primary alcohol **9g** (0.46 g, 85% yield) as clear, colorless oil.

R_f = 0.51 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{31.4}$ (*c* 1.055, $CHCl_3$) = +8.1°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.53-7.50 (m, 2H), 7.40-7.33 (m, 3H), 5.51 (s, 1H), 3.67 (d, 1H, *J* = 1.9 Hz), 3.58-3.48 (m, 4H), 3.38-3.30 (m, 1H), 2.44 (t, 1H, *J* = 5.5 Hz), 2.00-1.87 (m, 3H), 1.66 (dd, 1H, *J* = 14.3, 5.91 Hz), 1.41 (dd, 1H, *J* = 14.0, 4.1 Hz), 1.34 (s, 3H), 1.06 (d, 3H, *J* = 6.5 Hz), 1.03 (d, 3H, *J* = 6.5 Hz), 0.98 (d, 3H, *J* = 6.9 Hz), 0.90 (s, 9H), 0.86 (t, 9H, *J* = 7.5 Hz), 0.59-0.51 (m, 6H), 0.05 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 139.2, 128.8, 128.3, 126.7, 102.6, 88.2, 85.5, 78.8, 69.3, 64.5, 43.5, 36.5, 31.7, 31.2, 26.1, 24.4, 20.0, 18.5, 14.7, 8.5, 7.3, 6.6, -5.3, -5.3. IR Spectroscopy (thin film) 3436, 2954, 2875, 1947, 1458, 1406, 1376, 1349, 1311, 1253, 1213, 1111, 1065, 1033, 1010, 915, 837, 776, 742, 698, 674 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{32}H_{60}O_5Si_2Na]^+$, 603.3877; found, 603.3870. Combustion Analysis: Anal. calcd for $C_{32}H_{60}O_5Si_2$: C, 66.15; H, 10.41; found C, 66.27; H, 10.58.

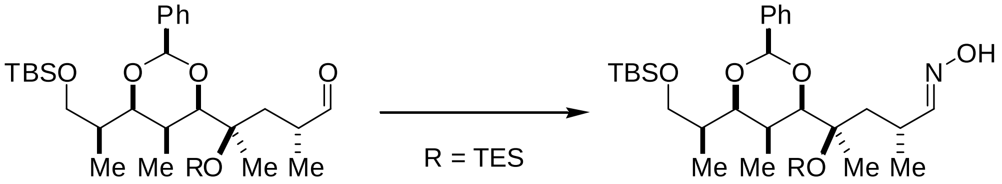
5,7-*O*-Benzylidene-9-*O*-[*tert*-butyl(dimethyl)silyl]-2,3,6,8-tetradeoxy-2,6,8-trimethyl-4-*C*-methyl-4-*O*-(triethylsilyl)-L-*threo*-L-*ido*-nonose (9h)



To a biphasic solution of **9g** (0.46 g, 0.79 mmol, 1.0 equiv), TEMPO (0.019 g, 0.12 mmol, 0.15 equiv), and KBr (0.0092 g, 0.079 mmol, 0.10 equiv) in CH_2Cl_2 (8.0 ml) and pH-8.6 buffer (8.0 ml) was slowly added NaOCl (0.5 M in H_2O, 6.3 ml, 3.2 mmol, 4,0 equiv) at 0 °C. After 10 min, H_2O (5 ml) and CH_2Cl_2 (10 ml) were added. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 ml). The organic solution was washed with brine (10 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The light orange oil was used without further purification.

R_f = 0.65 (3:1 hexane/EtOAc). NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.48 (d, 1H, *J* = 3.1 Hz), 7.52-7.49 (m, 2H), 7.40-7.33 (m, 3H), 5.46 (s, 1H), 3.62 (d, 1H, *J* = 1.9 Hz), 3.58-3.48 (m, 3H), 2.67-2.61 (m, 1H), 2.15 (dd, 1H, J = 14.0, 9.3 Hz), 1.96-1.87 (m, 2H), 1.45 (dd, 1H, J = 14.3, 3.11 Hz), 1.32, (s, 3H), 1.08 (d, 3H, J = 5.3 Hz), 1.06 (d, 3H, J = 7.16 Hz), 1.04 (d, 3H, J = 7.2 Hz), 0.91 (s, 9H), 0.87 (t, 9H, J = 7.5 Hz), 0.53 (q, 6H, J = 7.5 Hz), 0.05 (s, 3H), 0.05 (s, 3H).

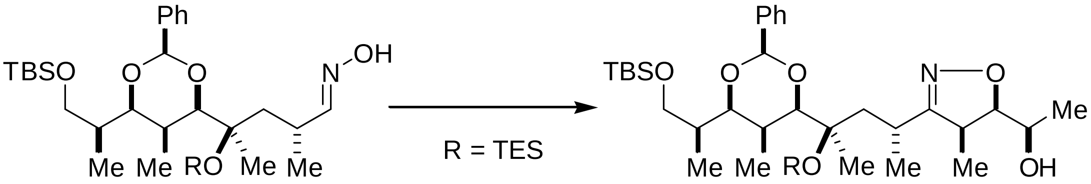
5,7-*O*-Benzylidene-9-*O*-[*tert*-butyl(dimethyl)silyl]-2,3,6,8-tetradeoxy-2,6,8-trimethyl-4-*C*-methyl-4-*O*-(triethylsilyl)-L-*threo*-L-*ido*-nonose oxime (10)



A solution of hydroxylamine hydrochloride (0.11 g, 1.6 mmol, 2.0 equiv) in pyridine (1.6 ml) was added to a solution of aldehyde **9g** (0.46 g, 0.79 mmol, 1.0 equiv) in EtOH (8.0 ml) and stirred for 20 min at rt. The light green solution was quenched with 1 N HCl (20 ml) and the aqueous layer was extracted with EtOAC (3 x 10 ml). The combined organic solutions were washed with brine (10 ml), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 7:1) provided oxime **10** (0.40 g, 85% yield over two steps) as a mixture of *E/Z* isomers (~ 1.5:1).

R_f = 0.56, 0.51* (3:1 hexane/EtOAc, *denotes minor isomer). Specific Rotation $[\alpha]_D^{24.0}$ (c 1.185, $CHCl_3$) = -5.9°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$, *denotes minor isomer) δ: 7.53-7.50 (m, 2H), 7.39-7.29 (m, 3H), 6.75* (s(br), 1H), 6.63 (d, 1H, 7.8 Hz), 5.53* (s, 1H), 5.51 (s, 1H), 3.68* (d, 1H, J = 1.9 Hz), 3.63 (d, 1H, J = 1.9 Hz), 3.60-3.49 (m, 3H), 3.34-3.30* (m, 1H), 2.70-2.61 (m, 1H), 1.94-1.87 (m, 1H), 1.77-1.71 (m, 1H), 1.68-1.60* (m, 1H), 1.29 (s, 3H), 1.29* (s, 3H), 1.11 (d, 3H, *J* = 6.9 Hz), 1.07 (d, 3H, *J* = 6.54 Hz), 1.06* (d, 3H, *J* = 6.54 Hz), 1.04 (d, 3H, *J* = 6.5 Hz), 0.91* (s, 9H), 0.91 (s, 9H), 0.88 (t, 9H, *J* = 7.5 Hz), 0.55 (q, 6H, *J* = 7.8 Hz), 0.06* (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, *denotes minor isomer) δ: 158.5*, 157.6, 139.4*, 139.4, 128.7*, 128.2, 126.5, 102.4, 87.2, 87.1*, 85.4, 64.4, 45.2*, 44.7, 36.6, 36.5*, 31.6, 30.6, 26.1, 26.0, 25.5, 25.2*, 20.9, 19.5, 18.5, 14.6, 8.6, 7.4, 6.9, 6.8*, -5.2, -5.3. IR Spectroscopy (thin film) 3255, 3036, 2955, 2875, 1948, 1805, 1662, 1457, 1407, 1377, 1348, 1311, 1252, 1212, 1111, 1068, 1030, 971, 911, 837, 811, 776, 741, 698, 672 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{32}H_{59}NO_5Si_2Na]^+$, 616.3829; found, 616.3823. Combustion Analysis: Anal. calcd for $C_{32}H_{59}NO_5Si_2$: C, 64.71; H, 10.01; found C, 64.48; H, 9.93.

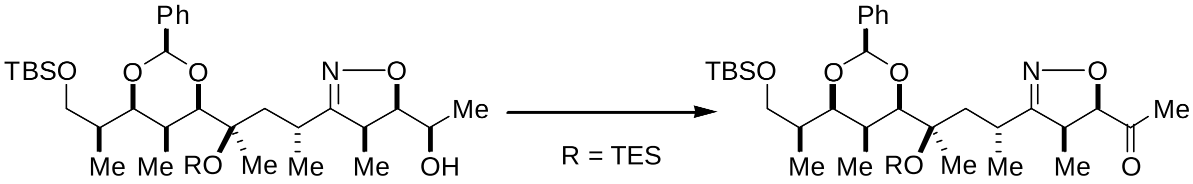
3,5-*O*-Benzylidene-7-*O*-[*tert*-butyl(dimethyl)silyl]-1,4,6-trideoxy-2-*C*-((2*R*)-2-{(4*S*,5*R*)-5-[(1*R*)-1-hydroxyethyl]-4-methyl-4,5-dihydroisoxazol-3-yl}propyl)-4,6-dimethyl-2-*O*-(triethylsilyl)-L-*glycero*-D-*gulo*-heptitol (11)



To a solution of (*R*)-(*Z*)-3-penten-2-ol (**3**) (0.091 g, 1.1 mmol, 1.3 equiv) and 2-propanol (0.21 ml, 2.7 mmol, 3.3 equiv) in CH_2Cl_2 (40 ml) at 0 °C was added EtMgBr (3 M in Et_2O, 0.81 ml, 2.4 mmol, 3.0 equiv). The reaction mixture turns momentarily cloudy, becoming clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride, prepared by addition of *t*-butylhypochlorite (0.10 ml, 0.89 mmol, 1.1 equiv) to a solution of oxime **10** (0.48 g, 0.81 mmol, 1.0 equiv) in CH_2Cl_2 (8.0 ml) at -78 ^oC and stirring for 1.5 h, was added dropwise via cannula to the reaction to give a slightly yellow solution. It was allowed to warm to rt and stirred for 2 h. The reaction was quenched by the addition of sat. aq. NH_4Cl (20 ml) and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 ml). The combined organic solutions were washed with brine (20 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (4:1 hexane/EtOAc) provided isoxazoline **11** (0.52 g, 86% yield) as a clear, colorless oil and as a single diastereomer by ^1H NMR and ^{13}C NMR analysis.

R_f = 0.31 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{28.0}$ (*c* 1.080, $CHCl_3$) = -13°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.60-7.50 (m, 2H), 7.39-7.32 (m, 3H), 5.50 (s, 1H), 4.19 (dd, 1H, *J* = 9.7, 5.0 Hz), 3.97-3.89 (m, 1H), 3.6 (d, 1H, *J* = 1.9 Hz), 3.56-3.46 (m, 3H), 3.33-3.23 (m, 1H), 2.82-2.77 (m, 1H), 2.20 (dd, 1H, *J* = 14.0, 5.3 Hz), 1.98 (d, 1H, *J* = 6.5 Hz), 1.95-1.88 (m, 2H), 1.77 (dd, 1H, *J* = 13.7, 5.3 Hz), 1.30 (s, 3H), 1.27 (d, 3H, *J* = 6.5 Hz), 1.23 (d, 3H, *J* = 6.2 Hz), 1.18 (d, 3H, *J* = 7.5 Hz), 1.08 (d, 3H, *J* = 6.9 Hz), 1.05 (d, 3H, *J* = 6.5 Hz), 0.90 (s, 9H), 0.88 (t, 9H, *J* = 7.5 Hz), 0.55 (q, 6H, *J* = 7.8 Hz), 0.05 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 168.2, 139.0, 128.4, 127.9, 126.2, 102.2, 87.0, 86.0, 85.1, 77.6, 66.2, 64.1, 44.2, 42.3, 36.5, 31.4, 27.8, 26.0, 25.3, 21.8, 20.4, 18.4, 14.6, 10.9, 8.5, 7.3, 6.8, -5.3. IR Spectroscopy (thin film) 3458, 2955, 2933, 2876, 1616, 1458, 1406, 1377, 1348, 1253, 1212, 1134, 1110, 1031, 1007, 975, 901, 837, 776, 743, 698, 671 (cm^{-1}). HRMS-MALDI (m/z): Calcd for [$C_{37}H_{67}NO_6Si_2Na$]$^+$, 700.4405; found, 700.4408.

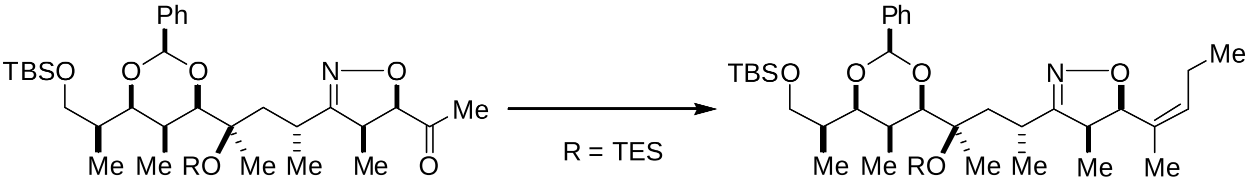
2-*C*-{(2*R*)-2-[(4*S*,5*R*)-5-Acetyl-4-methyl-4,5-dihydroisoxazol-3-yl]propyl}-3,5-*O*-benzylidene-7-*O*-[*tert*-butyl(dimethyl)silyl]-1,4,6-trideoxy-4,6-dimethyl-2-*O*-(triethylsilyl)-L-*glycero*-D-*gulo*-heptitol (11b)



To a biphasic solution of isoxazoline **11** (0.52 g, 0.77 mmol, 1.0 equiv), TEMPO (0.018 g, 0.12 mmol, 0.15 equiv), and KBr (0.0090 g, 0.077 mmol, 0.10 equiv) in CH_2Cl_2 (8.0 ml) and pH-8.6 buffer (8.0 ml) was slowly added NaOCl (0.5 M in H_2O, 6.1 ml, 3.1 mmol, 4.0 equiv) at 0 °C. After stirring for 1 h at 0 °C, the two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 ml). The organic solution was washed with brine (10 ml), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography (hexane/EtOAc 6:1) to afford ketone **11b** (0.48 g, 93% yield) as colorless oil.

R_f = 0.50 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{23.2}$ (*c* 1.205, $CHCl_3$) = +13°. NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.52-7.49 (m, 2H), 7.40-7.33 (m, 3H), 5.50 (s, 1H), 4.75 (d, 1H, *J* = 10.9 Hz), 3.60 (m, 4H), 3.52 (d, 1H, *J* = 4.1 Hz), 2.90-2.85 (m, 1H), 2.25 (s, 3H), 2.21 (dd, 1H, *J* = 14.0, 5.3 Hz), 1.93-1.88 (m, 2H), 1.76 (dd, 1H, J = 14.0, 5.3 Hz), 1.33 (s, 3H), 1.23 (d, 3H, J = 7.2 Hz), 1.08 (d, 3H, J = 6.2 Hz), 1.06 (d, 3H, J = 7.2 Hz), 1.05 (d, 3H, J = 6.5 Hz), 0.90 (s, 9H), 0.86 (t, 9H, J = 7.8 Hz), 0.55 (q, 6H, J = 7.8 Hz), 0.06 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 208.4, 166.7, 138.9, 128.5, 128.0, 126.2, 102.3, 87.5, 87.2, 85.1, 77.5, 64.1, 46.7, 42.3, 36.5, 31.4, 28.4, 27.6, 26.0, 25.2, 21.7, 18.4, 14.6, 12.1, 8.5, 7.3, 6.8, -5.3. IR Spectroscopy (thin film) 2955, 2876, 1716, 1458, 1407, 1377, 1356, 1252, 1135, 1111, 0131, 1007, 973, 914, 837, 811, 837, 776, 742, 698, 674 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{37}H_{65}NO_6Si_2Na]^+$, 698.4248; found, 698.4234.

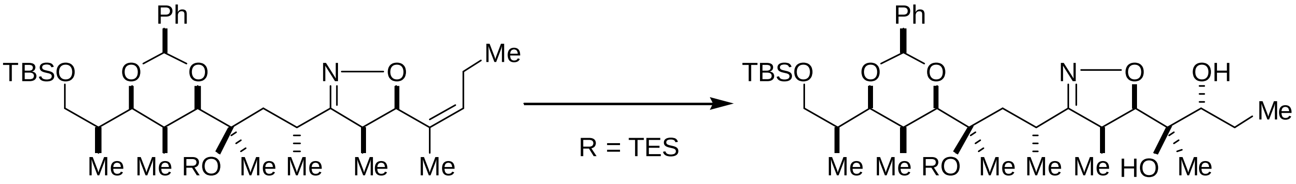
3,5-*O*-Benzylidene-7-*O*-[*tert*-butyl(dimethyl)silyl]-1,4,6-trideoxy-4,6-dimethyl-2-*C*-((2*R*)-2-{(4*S*,5*R*)-4-methyl-5-[(1*Z*)-1-methylbut-1-en-1-yl]-4,5-dihydroisoxazol-3-yl}propyl-2-*O*-(triethylsilyl)-L-*glycero*-D-*gulo*-heptitol (11c)



At -78 °C, *t*BuLi (1.7 M in pentane, 1.9 ml, 3.2 mmol, 5.0 equiv) was added to a suspension of propyltriphenylphosphonium bromide (1.5 g, 3.8 mmol, 6.0 equiv) in THF (60 ml). The reaction mixture slowly turned red, was allowed to warm to rt, and stirred for 2 h. The dark red suspension was cooled to -78 °C before a solution of ketone **11b** (0.43 g, 0.64 mmol, 1.0 equiv) in THF (6.0 ml) was added dropwise via cannula. The red mixture was slowly warmed to rt and stirred for 15 h. To the orange suspension was added H_2O (50 ml) and Et_2O (50 ml) and the two layers were separated. The aqueous phase was extracted with Et_2O (3 x 20 ml). The combined organics were washed with H_2O_2 (3% in H_2O, 50 ml) and brine (20 ml), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 15:1) provided olefine **11c** (0.35 g, 78% yield) as clear, colorless oil and 33:1 mixture of *Z/E* diastereomers, accompanied with 0.020 g of recovered ketone **11b** (5%).

R_f = 0.65 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{25.4}$ (*c* 1.190, $CHCl_3$) = +13°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.53-7.49 (m, 2H), 7.39-7.30 (m, 3H), 5.51 (s, 1H), 5.35 (t, 1H, *J* = 7.3 Hz), 5.30 (d, 1H, *J* = 10.6 Hz), 3.61 (d, 1H, *J* = 1.9 Hz), 3.57-3.46 (m, 3H), 3.40-3.29 (m, 1H), 2.86-2.78 (m, 1H), 2.20 (dd, 1H, *J* = 14.0, 5.0 Hz), 2.10-1.96 (m, 1H), 1.93-1.84 (m, 3H), 1.77 (dd, 1H, *J* = 14.0, 5.6 Hz), 1.68 (d, 3H, *J* = 1.6 Hz), 1.32 (s, 3H), 1.23 (d, 3H, *J* = 7.2 Hz), 1.08 (d, 3H, *J* = 7.8 Hz), 1.05 (d, 3H, *J* = 6.5 Hz), 1.00 (t, 3H, *J* = 7.5 Hz), 0.96 (d, 3H, *J* = 7.5 Hz), 0.90 (s, 9H), 0.87 (t, 9H, *J* = 7.8 Hz), 0.55 (q, 6H, *J* = 7.8 Hz), 0.52 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.5, 139.0, 131.1, 130.8, 128.4, 127.9, 126.2, 102.2, 87.1, 85.1, 82.1, 77.6, 64.0, 45.5, 42.5, 36.5, 31.4, 28.0, 26.0, 25.2, 21.7, 21.2, 20.4, 18.4, 14.6, 14.4, 11.9, 8.4, 7.3, 6.8, -5.3. IR Spectroscopy (thin film) 2956, 2932, 2875, 1616, 1457, 1406, 1378, 1348, 1252, 1211, 1111, 1092, 1031, 1007, 973, 924, 837, 776, 742, 698, 671 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{40}H_{71}NO_5Si_2Na]^+$, 724.4768; found, 724.4755.

3,5-*O*-Benzylidene-7-*O*-[*tert*-butyl(dimethyl)silyl]-1,4,6-trideoxy-2-*C*-((2*R*)-2-{(4*S*,5*R*)-5-[(2*R*)-2-hydroxy-1,1-dimethylbutyl]-4-methyl-4,5-dihydroisoxazol-3-yl}propyl)-4,6-dimethyl-2-*O*-(triethylsilyl)-L-*glycero*-D-*gulo*-heptitol (12)



To a solution of olefine **11c** (380 mg, 0.54 mmol, 1.0 equiv) in *t*BuOH (5.0 ml) and H_2O (5.0 ml) was added $(DHQD)_2PHAL$ (84 mg, 0.11 mmol, 0.20 equiv), $K_3Fe(CN)_6$ (530 mg, 1.6 mmol, 3.0 equiv), K_2CO_3 (220 mg, 1.6 mmol, 3.0 equiv), and methanesulfonylamide (160 mg, 1.6 mmol, 3.0 equiv). The biphasic mixture was cooled to 0 ^{o}C before $K_2OsO_4 \cdot H_2O$ (8.0 mg, 0.020 mmol, 0.04 equiv) was added. The suspension slowly turned brown and was stirred for 3.5 h at 0 ^{o}C. Then it was quenched with sat. aq. $Na_2S_2O_3$ (10 ml) and extracted with EtOAc (4 x 10 ml). The organic solution was washed with brine (10 ml), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography (hexane/EtOAc 6:1 – 3:1) provided diol **12** (320 mg, 81% yield) as a clear, colorless oil and as a single diastereomer by ^{1}H-NMR and ^{13}C-NMR analysis.

R_f = 0.30 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{24.0}$ (*c* 0.590, $CHCl_3$) = +9.9°. NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.53-7.49 (m, 2H), 7.39-7.32 (m, 3H), 5.50 (s, 1H), 4.25 (d, 1H, *J* = 8.4 Hz), 3.61 (d, 1H, *J* = 1.6 Hz), 3.55-3.46 (m, 3H), 3.28 (s, 1H), 3.24-3.12 (m, 2H), 2.82-2.76 (m, 1H), 2.26-2.19 (m, 2H), 1.92-1.88 (m, 2H), 1.78 (dd, 1H, *J* = 14.0, 5.6 Hz), 1.71-1.65 (m, 1H), 1.46-1.33

(m, 1H), 1.31 (s, 3H), 1.29 (d, 3H, J = 8.4 Hz), 1.23 (d, 3H, J = 7.2 Hz), 1.23 (s, 3H), 1.09 (t, 3H, J = 7.2 Hz), 1.08 (d, 3H, J = 6.9 Hz), 1.05 (d, 3H, J = 6.5 Hz), 0.90 (s, 9H), 0.88 (t, 9H, J = 7.8 Hz), 0.55 (q, 6H, J = 7.8 Hz), 0.05 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.5, 139.3, 128.7, 128.2, 126.5, 102.5, 87.2, 86.0, 85.3, 82.4, 77.8, 73.7, 64.2, 45.7, 42.6, 36.6, 31.6, 28.0, 26.1, 25.5, 25.5, 22.4, 21.1, 18.4, 14.7, 13.3, 11.8, 8.5, 7.4, 6.9, -5.2. IR Spectroscopy (thin film) 3531, 2956, 1610, 1457, 1406, 1379, 1347, 1252, 1110, 1035, 1008, 975, 910, 837, 776, 735, 698, 672 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{40}H_{73}NO_7Si_2Na]^+$, 758.4823; found, 758.4810.

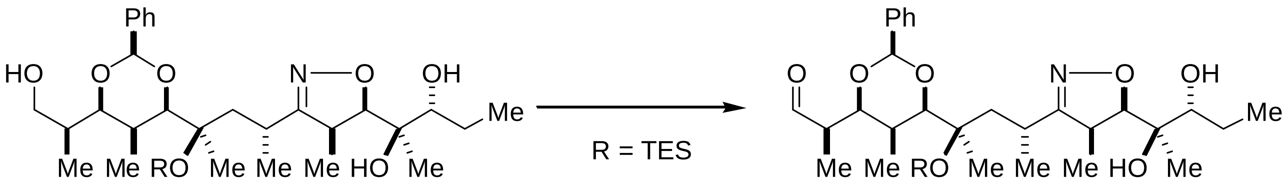
3,5-*O*-Benzylidene-1,4,6-trideoxy-2-*C*-((2*R*)-2-{(4*S*,5*R*)-5-[(1*R*,2*R*)-1,2-dihydroxy-1-methylbutyl]-4-methyl-4,5-dihydroisoxazol-3-yl}propyl)-4,6-dimethyl-2-*O*-(triethylsilyl)-L-*glycero*-D-*gulo*-heptitol (12e)

At 0 °C, HF·pyridine (1.0 ml) was added to a solution of diol **12** (320 mg, 0.44 mmol, 1.0 equiv) in pyridine (3.0 ml). The solution was stirred for 3 h at 0 °C and then quenched with H_2O (2 ml) and solid $NaHCO_3$ (2.5 g) (careful!). The biphasic mixture was extracted with EtOAc (5 x 5 ml). The combined organic solutions were washed with 1 N HCl (50 ml) and brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 1:1 –

1:3) afforded triol **12e** (220 mg, 80% yield) as a colorless foam.

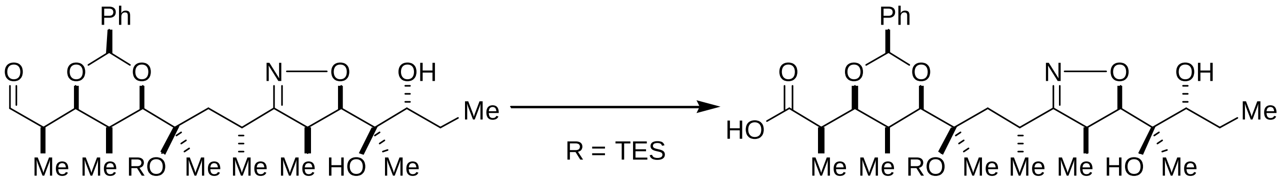
R_f = 0.18 (1:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{24.5}$ (*c* 2.650, $CHCl_3$) = -14°. NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.53-7.49 (m, 2H), 7.39-7.32 (m, 3H), 5.50 (s, 1H), 4.34 (d, 1H, *J* = 8.7 Hz), 3.70 (d, 1H, *J* = 1.0 Hz), 3.68-3.53 (m, 4H), 3.32-3.18 (m, 2H), 2.92-2.86 (m, 1H), 2.43-2.22 (m, 3H), 2.06-2.00 (m, 1H), 1.90-1.83 (m, 1H), 1.74-1.67 (m, 1H), 1.62 (dd, 1H, *J* = 14.5, 4.9 Hz), 1.45-1.40 (m, 1H), 1.36 (d, 3H, *J* = 7.6 Hz), 1.34 (s, 3H), 1.24 (d, 3H, *J* = 8.9 Hz), 1.23 (s, 3H), 1.08 (t, 3H, *J* = 7.1 Hz), 1.09 (d, 3H, *J* = 6.5 Hz), 1.02 (d, 3H, *J* = 6.7 Hz), 0.85 (t, 9H, *J* = 7.8 Hz), 0.51 (q, 6H, *J* = 7.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.1, 138.8, 128.5, 127.9, 126.3, 102.5, 86.8, 85.7, 84.3, 81.4, 78.0, 73.9, 63.3, 45.3, 42.6, 36.0, 31.2, 27.0, 26.0, 25.1, 22.5, 20.5, 14.1, 13.1, 11.7, 8.1, 7.3, 6.7. IR Spectroscopy (thin film) 3414, 2957, 2875, 1457, 1406, 1376, 1350, 1311, 1238, 1215, 1132, 1105, 1050, 1029, 1013, 974, 743, 698 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{34}H_{59}NO_7SiNa]^+$, 644.3958; found, 644.3945.

3,5-*O*-Benzylidene-2,4,7-trideoxy-6-*C*-((2*R*)-2-{(4*S*,5*R*)-5-[(2*R*)-2-hydroxy-1,1-dimethylbutyl]-4-methyl-4,5-dihydroisoxazol-3-yl}propyl)-2,4-dimethyl-3,5-*O*-(1-methylethylidene)-6-*O*-(triethylsilyl)-L-*glycero*-L-*ido*-heptanal(12f)



To a biphasic solution of triol **12e** (220 mg, 0.35 mmol, 1.0 equiv), TEMPO (8.3 mg, 0.053 mmol, 0.15 equiv), and KBr (4.1 mg, 0.035 mmol, 0.10 equiv) in CH_2Cl_2 (4.0 ml) and pH-8.6 buffer (4.0 ml) was slowly added NaOCl (0.5 M in H_2O, 2.8 ml, 1.4 mmol, 4.0 equiv) at 0 °C. After stirring for 30 min at 0 °C, the two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 ml). The organic solution was washed with brine (10 ml), dried over Na_2SO_4, and concentrated *in vacuo*. Crude aldehyde **12f** (0.48 g, 93% yield) was used without further purification.

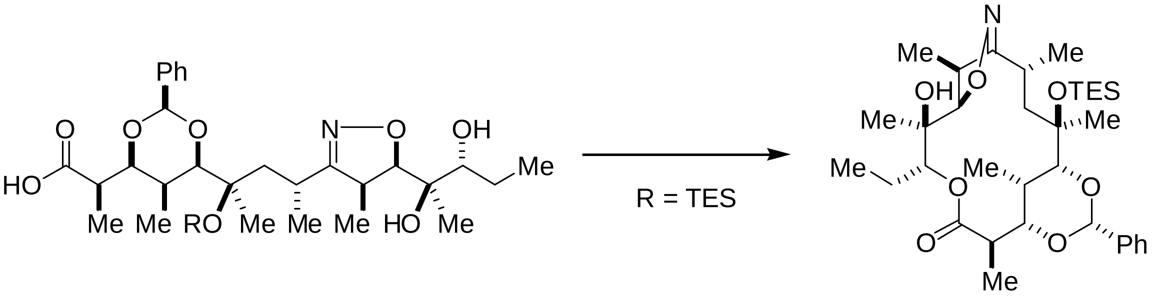
3,5-*O*-Benzylidene-2,4,7-trideoxy-6-*C*-((2*R*)-2-{(4*S*,5*R*)-5-[(2*R*)-2-hydroxy-1,1-dimethylbutyl]-4-methyl-4,5-dihydroisoxazol-3-yl}propyl)-2,4-dimethyl-3,5-*O*-(1-methylethylidene)-6-*O*-(triethylsilyl)-L-*glycero*-L-*ido*-heptonic acid (13)



At 0 °C, a premixed solution of 2-methyl-2-butene (0.19 ml, 1.8 mmol, 5.0 equiv) and $NaClO_2$ (96 mg, 1.1 mmol, 3 equiv) in *t*BuOH (9.0 ml) and pH-3.8 buffer (1.8 ml) was added to aldehyde **12f** (220 mg, 0.35 mmol, 1.0 equiv). After stirring for 30 min at 0 °C, more pH-3.8 buffer (3.0 ml) was added and the solution was extracted with EtOAc (6 x 5 ml). The organic solution was washed with brine (5 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purifiaction by flash chromatography (hexane/EtOAc 2:1 – 2:1+1% HOAc) provided erythronolide A *seco* acid **13** (190 mg, 83% yield over two steps) as a clear, colorless oil.

R_f = 0.38 (1:1 hexane/EtOAc + 1% HOAc). Specific Rotation $[\alpha]_D^{25.4}$ (*c* 2.650, $CHCl_3$) = -32°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$) δ: 7.51-7.46 (m, 2H), 7.40-7.32 (m, 3H), 5.51 (s, 1H), 4.40 (d, 1H, *J* = 9.1 Hz), 3.75 (s, 1H), 3.73 (dd, 1H, *J* = 10.0, 0.8 Hz), 3.39 (d, 1H, *J* = 9.5 Hz), 3.29-3.24 (m, 1H), 2.81-2.74 (m, 2H), 2.45 (dd, 1H, *J* = 14.7, 3.4 Hz), 1.96-1.91 (m, 1H), 1.74-1.68 (m, 1H), 1.55 (dd, 1H, *J* = 14.6, 5.0 Hz), 1.48-1.42 (m, 1H), 1.37 (d, 3H, *J* = 7.4 Hz), 1.33 (s, 3H), 1.27 (d, 3H, *J* = 6.7 Hz), 1.24 (s, 3H), 1.23 (d, 3H, *J* = 5.5 Hz), 1.09 (t, 3H, *J* = 6.1 Hz), 1.08 (d, 3H, *J* = 6.5 Hz), 0.85 (t, 9H, 8.0 Hz), 0.50 (q, 6H, *J* = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.6, 169.3, 138.5, 128.7, 128.0, 126.4, 102.6, 86.7, 85.8, 82.0, 81.8, 78.2, 74.2, 45.2, 42.3, 41.4, 32.1, 26.9, 26.1, 24.9, 22.5, 20.7, 14.8, 12.9, 11.7, 8.1, 7.3, 6.7. IR Spectroscopy (thin film) 3450, 2957, 2876, 1722, 1457, 1407, 1379, 1348, 1312, 1274, 1239, 1215, 1129, 1105, 1065, 1028, 1007, 976, 938, 912, 884, 757, 698, 668 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{34}H_{57}NO_8SiNa]^+$, 658.3751; found, 658.3739.

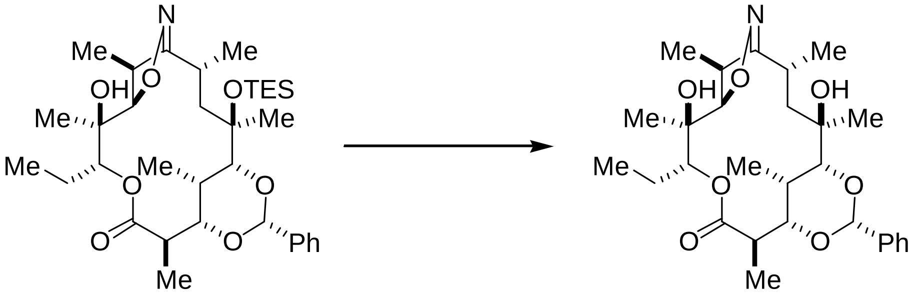
(1*R*,2*R*,4*R*,8*R*,9*R*,10*R*,13*R*,14*S*,18*S*,19*S*)-10-Ethyl-9-hydroxy-2,4,9,13,18,19-hexamethyl-16-phenyl-2-[(triethylsilyl)oxy]-7,11,15,17-tetraoxa-6-azatricyclo[12.3.1.1^{5,8}]nonadec-5-en-12-one (14)



To a solution of acid **13** (136 mg, 0.214 mmol, 1.00 equiv) in THF (4.00 ml) was added triethylamine (179 μl, 1.28 mmol, 6.00 equiv) and 2,4,6-trichlorobenzoylchloride (167 μl, 1.07 mmol, 5.00 equiv) at 0 °C. The solution turned cloudy and was stirred for 30 min. The colorless suspension was allowed to warm to rt and toluene (12.0 ml) was added. This cloudy reaction mixture was added to a 50 °C solution of DMAP (261 mg, 2.14 mmol, 10.0 equiv) in toluene (24.0 ml) via syringe pump over 3 h. After addition, the stirring was maintained for another 45 min at 50 °C before the colorless suspension was filtered over a plaque of silica gel (eluent hexane/EtOAc 1:1). The filtrate was concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 10:1 – 6:1 – 3-1) provided macrolactone **14** (103 mg, 78% yield) as a colorless foam and as a mixture of two atropisomers (4:1).

R_f = 0.37* and 0.28 (3:1 hexane/EtOAc, *denotes minor isomer). Specific Rotation $[\alpha]_D^{22.6}$ (*c* 0.730, $CHCl_3$) = -49°. NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, *denotes minor isomer) δ: 7.53-7.46 (m, 2H), 7.39-7.30 (m, 3H), 5.58 (s, 1H), 5.43* (s, 1H), 5.03 (dd, 1H, *J* = 10.6, 2.5 Hz), 4.83* (dd, 1H, *J* = 9.0, 1.9 Hz), 4.49* (d, 1H, J = 9.5 Hz), 4.15 (d, 1H, *J* = 6.3 Hz), 4.10 (d, 1H, J = 1.4 Hz), 3.95 (dd, 1H, *J* = 8.2, 1.1 Hz), 3.90* (dd, 1H, *J* = 6.3, 1.4 Hz), 3.62* (d, 1H, *J* = 1.3 Hz), 3.60-3.50 (m, 1H), 2.91-2.82 (m, 1H), 2.79-2.69 (m, 1H), 2.17-2.05* (m, 1H), 2.04 (s, 1H), 1.93-1.80 (m, 1H), 1.81 (dd, 1H, *J* = 15.1, 7.9 Hz), 1.72-1.64* (ddd, 1H, *J* = 14.4, 7.5, 2.1 Hz), 1.65-1.45 (m, 3H), 1.41* (dd, 1H, *J* = 15.0, 1.6 Hz), 1.28 (s, 3H), 1.27 (d, 3H, *J* = 6.9 Hz), 1.22 (d, 3H, *J* = 7.0 Hz), 1.18 (s, 3H), 1.17 (d, 3H, *J* = 7.0 Hz), 1.01 (d, 3H, *J* = 6.7 Hz), 0.96 (t, 3H, *J* = 7.4 Hz), 0.85 (t, 9H, *J* = 8.0 Hz), 0.59-0.39 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, *denotes minor isomer) δ: 175.4, 172.3, 165.3*, 138.7, 128.5, 127.8, 126.4, 102.7*, 102.5, 86.9*, 85.4, 84.9*, 84.3, 83.3*, 82.3*, 81.8, 79.1, 78.7*, 78.4, 78.2*, 72.8, 47.4, 45.4*, 43.4*, 42.0, 41.0, 34.4*, 34.2, 27.8, 27.0, 26.4*, 26.1*, 25.6*, 23.0*, 22.6*, 21.4, 21.3, 17.5, 14.0, 12.6*, 11.2*, 11.0, 10.3*, 7.8, 7.3, 6.8. IR Spectroscopy (thin film) 3438, 2954, 2876, 1741, 1456, 1379, 1349, 1236, 1159, 1129, 1080, 1007, 972, 908, 741, 699 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{34}H_{55}NO_7SiNa]^+$, 640.3645; found, 640.3634.

(1*R*,2*R*,4*R*,8*R*,9*R*,10*R*,13*R*,14*S*,16*R,*18*S*,19*S*)-10-Ethyl-2,9-dihydroxy-2,4,9,13,18,19-hexamethyl-16-phenyl-7,11,15,17-tetraoxa-6-azatricyclo[12.3.1.1^{5,8}]nonadec-5-en-12-one (14b)

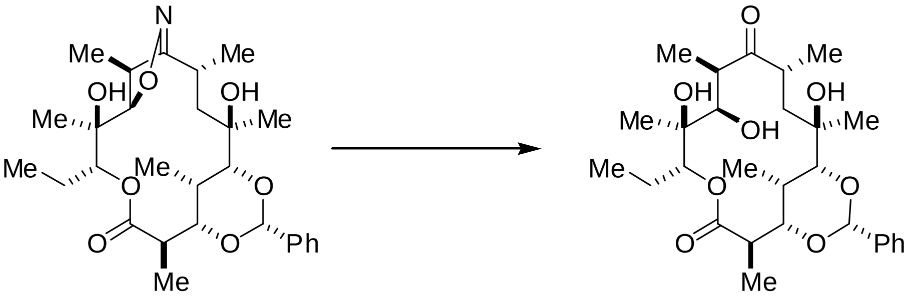


To a solution of macrolactone **14** (39 mg, 0.069 mmol, 1.0 equiv) in CH_3CN (0.50 ml) was added triethylamine (0.050 ml) and HF·NEt_3 (0.50 ml). The clear solution was stirred for 64 h at 30 ^oC. The reaction was slowly quenched with sat. aq. $NaHCO_3$ (5 ml) and extracted with EtOAc (5 x 5 ml). The organic solution was washed with brine (2 ml), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography (hexane/EtOAc 1:1) afforded diol **14b** (32 mg, > 99% yield) as a clear, colorless oil and as a 9:1 mixture of atropisomers.

R_f = 0.24 (3:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{29.7}$ (*c* 0.190, $CHCl_3$) = -32°. NMR Spectroscopy: ^1H NMR (300 MHz, $CDCl_3$, *denotes minor isomer) δ: 7.50-7.46 (m, 2H), 7.40-7.35 (m, 3H), 5.64 (s, 1H), 5.46* (s, 1H), 4.97 (dd, 1H, *J* = 10.4, 2.7 Hz), 4.84* (dd, 1H, *J* = 11.0, 1.8 Hz), 4.51* (d, 1H, *J* = 10.2 Hz), 4.30 (s, 1H), 4.19 (d, 1H, *J* = 6.3 Hz), 4.15* (d, 1H, *J* = 6.3 Hz), 3.96 (dd, 1H, *J* = 7.3, 1.1 Hz), 3.64* (s, 1H), 3.59-3.49 (m, 1H), 2.95-2.84 (m, 1H), 2.80 (d, 1H, J = 1.8 Hz), 2.78-2.69 (m, 1H), 2.15-2.07* (m, 1H), 2.02 (s, 1H), 1.92-1.83 (m, 1H), 1.77 (dd, 1H, *J*

= 15.6, 8.6 Hz), 1.66-1.45 (m, 3H), 1.27 (d, 3H, *J* = 6.6 Hz), 1.26 (s, 3H), 1.24 (d, 3H, *J* = 7.2 Hz), 1.2 (s, 3H), 1.19 (d, 3H, *J* = 7.2 Hz), 1.04 (d, 3H, *J* = 6.7 Hz), 0.97 (t, 3H, *J* = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, *denotes minor isomer) δ: 175.9, 172.6, 139.0*, 138.8, 129.1, 128.4, 126.5, 102.9, 85.6, 85.0*, 83.7, 83.1*, 82.2*, 81.9, 79.8, 79.4*, 75.0, 74.7*, 73.2, 73.0*, 45.5*, 44.3, 42.3, 41.0, 34.5*, 34.3, 28.0, 27.0, 26.5*, 26.1*, 25.7*, 23.1*, 22.2*, 21.8, 21.2, 17.8, 13.4, 12.8, 11.9*, 11.2, 10.7*, 10.4*, 7.8, 7.7*. IR Spectroscopy (thin film) 3437, 2975, 2936, 2878, 1740, 1455, 1378, 1352, 1161, 1124, 1091, 1071, 1049, 1014, 980, 954, 894, 756, 700, 668 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{28}H_{41}NO_7Na]^+$, 526.2781; found, 526.2769.

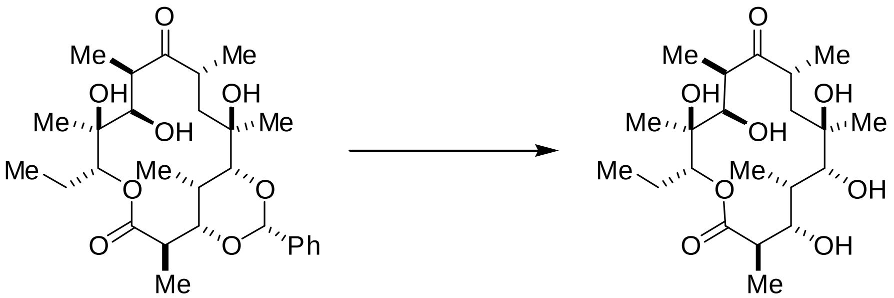
3,5-*O*-Benzylidene erythronolide A 15



To a solution of the diol **14b** (15 mg, 0.030 mmol, 1.0 equiv) in EtOH (0.38 ml) was added acetic acid (8.5 μl, 0.15 mmol, 5.0 equiv) and Raney-Ni (W2, spatula tip). The Schlenk flask was purged several times with H_2. The black suspension was stirred rapidly under an atmosphere of H_2 for 20 min. The black reaction mixture was filtered over celite and eluted with CH_2Cl_2. The filtrate was concentrated *in vacuo*. Purification by flash chromatography (hexane/EtOAc 2:1) provided **15** (14 mg, 93% yield) as a clear, colorless oil.

R$_f$ = 0.35 (1:1 hexane/EtOAc). Specific Rotation $[\alpha]_D^{29.7}$ (*c* 0.107, CHCl$_3$) = -36°. NMR Spectroscopy: ^{1}H NMR (300 MHz, CDCl$_3$) δ: 7.53-7.49 (m, 2H), 7.43-7.38 (m, 3H), 5.68 (s, 1H),4.87 (dd, 1H, *J* = 10.7, 1.8 Hz), 4.01 (d, 1H, *J* = 1.1 Hz), 3.83 (dd, 1H, *J* = 10.0, 0.8 Hz), 3.77-3.74 (m, 1H), 3.23 (d, 1H, *J* = 5.4 Hz), 3.07-3.02 (m, 1H), 2.97 (dd, 1H, *J* = 10.8, 6.5 Hz), 2.95-2.85 (m, 1H), 2.57 (s, 1H), 2.29 (s, 1H), 2.05-1.93 (m, 1H), 1.79-1.75 (m, 1H), 1.72-1.70 (m, 2H), 1.63-1.52 (m, 1H), 1.35 (d, 3H, *J* = 6.3 Hz), 1.34 (s, 3H), 1.29 (d, 3H, *J* = 6.6 Hz), 1.21 (d, 3H, *J* = 7.1 Hz), 1.18 (d, 3H, *J* = 6.6 Hz), 1.10 (s, 3H), 0.91 (t, 3H, *J* = 7.3 Hz). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 215.3, 176.4, 137.7, 129.1, 128.2, 126.1, 103.3, 86.4, 84.3, 79.0, 75.3, 74.5, 70.3, 46.0, 41.7, 40.9, 38.3, 32.8, 26.8, 21.2, 18.4, 16.2, 13.6, 11.6, 11.0, 7.9. IR Spectroscopy (thin film) 3488, 2978, 2938, 2879, 1707, 1456, 1374, 1282, 1175, 1104, 1074, 1047, 1028, 1005, 975, 907, 835, 758, 700, 667 (cm^{-1}). HRMS-MALDI (m/z): Calcd for [C$_{28}$H$_{42}$O$_8$SiNa]$^+$, 529.2777; found, 529.2765.

Erythronolide A (1)



To a solution of ketone **15** (12 mg, 0.024 mmol, 1.0 equiv) in MeOH (0.40 ml) was added Pd(OAc)$_2$ (20 mg, 0.089 mmol, 3.8 equiv) and H$_2$O (0.030 ml). The brown solution was purged several times with H$_2$ and a black precipitate appeared. After 2 and after 4 h of stirring, more $Pd(OAc)_2$ (55 mg, 0.24 mmol, 10 equiv (x2)) were added. Formation of side products can be observed by TLC analysis. The black suspension was filtered over celite with MeOH as eluent. The filtrate was concentrated under reduced pressure. Purification by flash chromatography (hexane/acetone 2:1 – 3:2) provided erythronolide A (**1**) (4.0 mg, 40% yield) as a clear, colorless solid.

R_f = 0.20 (1:3 hexane/EtOAc). Mp = 171-172 ^oC. Specific Rotation $[\alpha]_D^{23.5}$ (*c* 0.54, CH_3OH) = -36°. NMR Spectroscopy: ^1H NMR (300 MHz, CD_3OD) δ: 5.19 (dd, 1H, *J* = 11.0, 2.3 Hz), 3.86 (d, *J* = 1H, 1.5 Hz), 3.55 (d, 1H, *J* = 10.5 Hz), 3.50 (d, 1H, *J* = 3.2 Hz), 3.18-3.11 (m, 1H), 2.74-2.63 (m, 2H), 2.05-2.00 (m, 1H), 1.94-1.85 (m, 2H), 1.55-1.45 (m, 1H), 1.39 (dd, 1H, *J* = 14.7, 4.2 Hz), 1.29 (s, 3H), 1.18 (d, 3H, *J* = 7.6 Hz), 1.17 (s, 3H), 1.15 (d, 3H, *J* = 6.5 Hz), 1.12 (d, 3H, *J* = 6.6 Hz), 0.98 (d, 3H, *J* = 7.3 Hz), 0.85 (t, 3H, *J* = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 220.1, 176.1, 81.1, 78.7, 77.0, 75.1, 74.3, 69.5, 44.0, 43.9, 39.8, 38.1, 36.3, 25.1, 21.3, 17.1, 16.2, 14.5, 10.9, 9.5, 6.9. IR Spectroscopy (thin film) 3466, 2973, 2937, 2879, 1712, 1456, 1376, 1348, 1267, 1181, 1083, 1035, 980, 957, 912, 737, 704 (cm^{-1}). HRMS-MALDI (m/z): Calcd for $[C_{21}H_{38}O_8SiNa]^+$, 441.2464; found, 441.2452.

[vi] For the preparation of the $MgBr_2$ solution, see: M. Nakatsuka, J. A. Ragan, T. Sammakia, D. B. Smith, D. E. Uehling, S. L. Schreiber *J. Am. Chem. Soc.* **1990**, *112*, 5583-5601.