Synthesis of a C1–C12 Fragment of Gulmirecin B

Rathikrishnan Rengarasu and Martin E. Maier *

Institut für Organische Chemie, Eberhard Karls Universität Tübingen, Auf der Morgenstelle 18, 72076, Tübingen, Germany

martin.e.maier@uni-tuebingen.de

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**General.** All reactions were performed under nitrogen atmosphere. All solvents used in the reactions were purified before use. The progress of the reactions was followed by using TLC (POLYGRAM SIL G/UV254; petroleum ether/EtOAc). Flash chromatography was performed on silica gel Silica M, 0.04–0.63 mm, from Machery-Nagel GmbH & Co. KG, Germany. Dry diethyl ether (Et2O), tetrahydrofuran, and toluene were distilled from sodium and benzophenone, whereas dry CH2Cl2 and benzene were distilled from CaH2. All commercially available compounds (Acros, Aldrich, Fluka, and Merck) were used without purification. 1H (400.160 MHz) and 13C (100.620 MHz) spectra were recorded on a Bruker Avance 400 III HD spectrometer in CDCl3 as solvent at room temperature. HRMS (ESI-TOF) analysis was performed on Bruker maXis 4G system. The optical rotations were measured with a JASCO polarimeter P-1020, sodium D line (589 nm), c = g/100 mL.

![Image of chemical structure](image)

(S)-Butane-1,2,4-triol1 (14). A mixture of BH3·SMe2 complex (47.2 mL, 0.552 mol) and trimethyl borate (61.6 mL, 0.553 mol) in THF (50 mL) at 0 °C was added dropwise to a solution (S)-malic acid (13) (24.7 g, 0.184 mol) in THF (100 mL) at 0 °C over 20 min. After complete addition, the ice bath was removed and the mixture stirred for 12 h at r.t. Then, the reaction mixture was quenched by dropwise addition of MeOH (150 mL) at r.t. The solvent was removed under reduced pressure. The crude triol 14 (22.0 g) was used for the next reaction without further purification. Rf = 0.42 (CH2Cl2/MeOH, 9:1); HRMS (ESI-TOF): m/z [M + Na]+ calcld for C10H12O3: 129.0522; found: 129.0522.

![Image of chemical structure](image)

(S)-1,2-O-Cyclohexylidene-1,2,4-butanetriol (15). To a solution of triol 14 (22.0 g, 0.207 mol) in cyclohexanone (53 mL, 0.519 mol) was added p-toluenesulfonic acid (pTsOH·H2O) (0.78 g, 4.10 mmol) followed by stirring of the mixture at r.t. for 3 h. Then the reaction mixture was diluted with saturated NaHCO3 solution (55 mL) and H2O (50 mL). The aqueous layer was extracted with CH2Cl2 (3 × 55 mL). The combined organic layers were washed with saturated NaCl solution (45 mL), dried over Na2SO4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give alcohol 15 (20.0 g, 58%, over two steps) as a colorless oil. Rf = 0.72 (petroleum ether/ethyl acetate, 6:4); [α]D18 = -12.7 (c = 0.5, CH2Cl2); [Lit.1 [α]D = -15.4 (c = 2.0, acetone)]; 1H NMR (400 MHz, CDCl3): δ = 1.36–1.37 (m, 2H, CH2), 1.56–1.60 (m, 8H, (CH2)4), 1.78 (q, J = 5.8 Hz, 2H, 3-H), 2.44 (br s, 1H, OH), 3.58 (dd, J = 7.3, 7.3 Hz, 1H, 1-H), 3.78 (t, J = 6.2 Hz, 2H, 4-H), 4.05 (dd, J = 8.0, 5.9 Hz, 1H, 1-H), 4.21–4.27 (m, 1H, 2-H); 13C NMR (100 MHz, CDCl3): δ = 23.8 (CH2), 24.0 (CH2), 25.0 (CH2), 35.1 (CH2), 35.6 (C-3), 36.4 (CH2), 60.6 (C-4), 69.0 (C-1), 74.9 (C-2), 109.7 (acetal C). HRMS (ESI-TOF): m/z [M + Na]+ calcld for C10H16O3: 209.1147; found: 209.1147.

![Image of chemical structure](image)

(S)-2-{1,4-Dioxaspiro[4.5]decan-2-yl}acetaldehyde3 (16). To a solution of oxalyl chloride (6.95 mL, 80.5 mmol) in CH2Cl2 (20 mL) was slowly added DMSO (11.4 mL, 161 mmol) at −78 °C. After being stirred for 15 min at this temperature, a solution of alcohol 15 (10.0 g, 53.7 mmol) in CH2Cl2 (50 mL) was added to the
mixture over a period of 15 min. The reaction mixture was stirred at the same temperature for 1 h. Thereafter, Et₃N (45.3 mL, 322 mmol) was added dropwise. Then, the reaction mixture was brought to r.t. and stirred for 10 min. It was diluted with H₂O (100 mL) and extracted with CH₂Cl₂ (2 × 50 mL). The combined organic layers were washed with saturated NaCl solution (80 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give aldehyde 16 (8.0 g, 81%) as a slightly brown oil. The aldehyde 16 was used for the next reaction without further purification. Rf = 0.87 (petroleum ether/ethyl acetate, 6:4); ¹H NMR (400 MHz, CDCl₃): δ = 1.33–1.40 (m, 2H, CH₂), 1.51–1.58 (m, 8H, (CH₂)₄), 2.57–2.60 (m, 1H, 2-H), 2.81 (dd, J = 17.1, 6.5, 1.8 Hz, 1H, 2-H), 3.55 (dd, J = 8.3, 6.6 Hz, 1H, 3'-H), 4.14 (dd, J = 8.3, 6.0 Hz, 1H, 3'-H), 4.46–4.52 (m, 1H, 2'-H), 9.77 (t, J = 1.6 Hz, 1H, CHO); ¹³C NMR (100 MHz, CDCl₃): δ = 23.7 (CH₂), 23.9 (CH₂), 34.8 (CH₂), 36.4 (CH₂), 47.9 (C-2), 68.7 (C-3'), 70.2 (C-2'), 109.8 (C-5'), 200.1 (C-1).

(S)-2-(3,3-Dibromoallyl)-1,4-dioxaspiro[4.5]decane (17). To a stirred solution of triphenylphosphine (54.1 g, 0.206 mol) in CH₂Cl₂ (70 mL) at 0 °C was added carbon tetrabromide (45.0 g, 0.136 mol) in small portions. After complete addition, the ice bath was removed and the reaction mixture stirred for 30 min at r.t. The reaction mixture was recooled to 0 °C before a solution of aldehyde 16 (10.0 g, 54.3 mmol) in CH₂Cl₂ (85 mL) was added dropwise over 15 min. After addition, the white suspension was stirred at r.t. for 30 min. The reaction mixture was treated with hexane (250 mL) resulting of precipititation of phosphorus compounds. The obtained solid was removed by filtration of the mixture through a pad of celite and the filtrate concentrated under reduced pressure. The same procedure was repeated twice. Finally, the obtained oil was purified by flash chromatography (petroleum ether/ethyl acetate, 90:10) to give dibromide 17 (12.0 g, 65%) as a colorless oil. Rf = 0.72 (petroleum ether/ethyl acetate, 9:1); [α]ᵢ⁺° = –3.91 (c = 0.8, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 1.39–1.40 (m, 2H, CH₂), 1.56–1.62 (m, 8H, (CH₂)₄), 2.35–2.39 (m, 2H, 1'-H), 3.60 (dd, J = 8.2, 6.4 Hz, 1H, 3-H), 4.03 (dd, J = 8.2, 6.1 Hz, 1H, 3-H), 4.15–4.21 (m, 1H, 2-H), 6.49 (t, J = 7.1 Hz, 1H, 2'-H); ¹³C NMR (100 MHz, CDCl₃): δ = 23.8, 23.9, 25.1, 35.0, 36.5 (S × CH₂), 37.3 (C-1'), 62.8 (C-3), 73.3 (C-2), 90.8 (C-3'), 109.9 (C-5'), 134.0 (C-2').

(S)-2-(But-2-yn-1-yl)-1,4-dioxaspiro[4.5]decane (18). To a stirred solution of dibromide 17 (9.5 g, 27.9 mmol) in THF (80 mL) at −78 °C was added a solution of n-BuLi (2.5 M in THF, 27.9 mL, 69.8 mmol) over 15 min. The reaction mixture was stirred at −78 °C for 2 h, before iodomethane (7 mL, 112 mmol) was added dropwise. After addition, the reaction mixture was stirred at r.t. for 30 min. Then the reaction mixture was diluted with saturated NH₄Cl solution, the layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 35 mL). The combined organic layers were washed with saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 9:1) to give alkyne 18 (4.0 g, 74%) as a colorless oil. Rf = 0.75 (petroleum ether/ethyl acetate, 9:1); [α]ᵢ⁺° = +33.01 (c = 0.73, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 1.33–1.40 (m, 2H, CH₂), 1.52–1.63 (m, 8H, (CH₂)₄), 1.75 (t, J = 2.5 Hz, 3H, CH₃), 2.28–2.36 (m, 1H, 1'-H), 2.44–2.50 (m, 1H, 1'-H), 3.73 (dd, J = 8.2, 6.2 Hz, 1H, 3-H), 4.06 (dd, J = 8.3, 6.0 Hz, 1H, 3-H), 4.14–4.20 (m, 1H, 2-H); ¹³C NMR (100 MHz, CDCl₃): δ = 3.4 (4'-H), 23.7 (CH₃), 23.9 (C-1'), 24.1, 25.1, 35.1, 36.5 (4 × CH₂), 68.5 (C-
The resulting mixture was stirred for 2 h at r.t. Thereafter, alkyne 18 (4.57 g, 23.5 mmol) in THF (10 mL) was added dropwise at 0 °C. The resulting mixture was heated for 1 h at 55 °C and then cooled to 0 °C before a solution of NBS (5.20 g, 29.4 mmol) in THF (15 mL) was added. After complete addition, the reaction mixture was stirred for another 30 min at 0 °C. The reaction mixture was carefully quenched with saturated NaHCO₃ solution (15 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give vinyl bromide 19 (6.0 g, 93%; 4:1 mixture of regioisomers). The crude brown oil was used for the next reaction without chromatography. Rf = 0.92 (petroleum ether/ethyl acetate, 8:2); ¹H NMR (400 MHz, CDCl₃): δ = 1.34–1.38 (m, 3H, CH₂), 1.52–1.61 (m, 13H, CH₂), 2.21–2.35 (m, 5H, 3-CH₃, 1'-H), 3.54 (dd, J = 7.9, 6.5 Hz, 1.4H, 3-H), 4.03 (dd, J = 8.1, 6.0 Hz, 1.3H, 3-H), 4.08–4.14 (m, 1.5H, 2-H), 5.85 (td, J = 7.7, 1.2 Hz, 1H, 2'-H, major), 6.00–6.05 (m, 0.2H, 2'-H, minor); ¹³C NMR (100 MHz, CDCl₃): δ = 23.4 (CH₃), 23.8 (CH₃), 24.0 (C-1'), 25.1, 33.9, 35.0, 36.5 (4 × CH₂), 68.3 (C-3), 74.3 (C-2), 109.7 (C-5), 121.7 (C-3'), 127.0 (C-2').

(S,E)-5-Bromohex-4-ene-1,2-diol (20). A solution of acetal 19 (1.24 g, 4.50 mmol) in a mixture of AcOH/H₂O (1:1, 16 mL) was stirred for 12 h at r.t. Thereafter, the reaction mixture was diluted with saturated NaHCO₃ solution (25 mL) and extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with saturated NaCl solution (25 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The regioisomers were separated by flash chromatography (petroleum ether/ethyl acetate, 3:7) to give diol 20 (0.37 g, 42%) and a small amount of minor isomer (68 mg, 8%) as colorless oils. Rf = 0.45 (petroleum ether/ethyl acetate, 2:8); [α]D = –5.44 (c = 0.8, CH₂Cl₂); ¹H NMR (400 MHz, CD₆D₆): δ = 1.83–1.93 (m, 2H, 3-H), 2.00 (s, 3H, 5-CH₃), 2.85 (br s, 2H, OH), 3.20 (dd, J = 11.1, 7.1 Hz, 1H, 1-H), 3.32 (dd, J = 11.1, 2.5 Hz, 1H, 1-H), 3.41–3.46 (m, 1H, 2-H), 5.88 (td, J = 7.8, 1.2 Hz, 1H, 4-H); ¹³C NMR (100 MHz, CD₆D₆): δ = 23.3 (CH₃), 33.5 (C-3), 66.0 (C-1), 71.4 (C-2), 121.7 (C-5), 129.9 (C-4); HRMS (ESI-TOF): m/z [M + Na]+ calcd for C₁₉H₂₇BrO₂: 319.1289; found: 319.1282.

(S,E)-5-Bromo-1-(trityloxy)hex-4-ene-2-ol (21). A solution of diol 20 (0.25 g, 1.28 mmol) in CH₂Cl₂ (10 mL) at r.t. was treated with pyridine (0.2 mL, 2.61 mmol), DMAP (55 mg, 0.45 mmol) and trityl chloride (0.72 g, 2.61 mmol). The resulting mixture was stirred for 2 h at r.t. Thereafter, the reaction mixture was diluted...
with water (20 mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic layers were washed with saturated NaCl solution (15 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 7:3) to give trityl ether 21 (0.34 g, 59%) as a colorless oil. Rf = 0.54 (petroleum ether/ethyl acetate, 8:2); [α]D²⁰ = −2.29 (c = 1.04, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 2.15–2.28 (m, 5H, CH₂); 3.10 (dd, J = 9.5, 6.6 Hz, 1H, 1-H), 3.20 (dd, J = 9.4, 4.0 Hz, 1H, 1-H), 3.47 (br s, 1H, OH), 3.74–3.80 (m, 1H, 1-H), 5.80 (td, J = 7.7, 1.3 Hz, 1H, 4-H), 7.23–7.34 (m, 10H, ArH), 7.41–7.46 (m, 5H, ArH); ¹³C NMR (100 MHz, CDCl₃): δ = 23.3 (CH₃), 33.7 (C-3), 66.8 (C-1), 70.1 (C-2), 86.8 (CPh₃), 121.4 (C-5), 127.2 (Ar C), 127.6 (C-4), 127.9, 128.6, 143.7 (3 × Ar C); HRMS (ESI-TOF): m/z [M + Na]+ calcd for C₂₀H₂₅BrO₂: 459.0933; found: 459.0933.

(S,E)-2-(trityloxy)hex-4-en-2-yl)oxytrisopropylsilane (22). To a solution of alcohol 21 (1.10 g, 2.51 mmol) in CH₂Cl₂ (10 mL) at 0 °C were added 2,6-lutidine (0.58 mL, 5.03 mmol) and TIPSOTf (0.74 mL, 2.76 mmol) dropwise. The resulting mixture was stirred for 1 h at 0 °C before it was diluted with water (15 mL) and the mixture was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic layers were washed with saturated NaHCO₃ solution (15 mL), saturated NaCl solution (15 mL), dried with anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 95:5) to give silyl ether 22 (1.29 g, 86%) as a colorless oil. Rf = 0.77 (petroleum ether/Et₂O, 9:1); [α]D²⁰ = −1.08 (c = 0.55, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 0.79–0.84 (m, 1H, Si(CH(CH₃)₂)₃); 0.92–0.94 (m, 20H, Si(CH(CH₃)₂)₃); 2.15 (s, 3H, CH₃); 2.35–2.47 (m, 2H, 3-H), 2.97 (dd, J = 8.9, 7.3 Hz, 1H, 1-H), 3.03 (dd, J = 9.0, 4.2 Hz, 1H, 1-H); 3.91–3.96 (m, 1H, 1-H), 5.83 (td, J = 7.1, 1.2 Hz, 1H, 4-H), 7.17–7.27 (m, 10H, ArH), 7.36–7.40 (m, 5H, ArH); ¹³C NMR (100 MHz, CDCl₃): δ = 12.3 (Si(CH(CH₃)₂)₃), 18.0 (Si(CH(CH₃)₂)₃), 23.5 (CH₃), 35.2 (C-3), 66.4 (C-1), 70.8 (C-2), 86.5 (CPh₃), 120.5 (C-5), 127.0, 127.7 (2 × Ar C), 128.3 (C-4), 128.7, 144.0 (2 × Ar C); HRMS (ESI-TOF): m/z [M + Na]+ calcd for C₃₄H₄₅BrO₂Si: 615.2272; found: 615.2272.

(S,E)-5-Bromo-2-((trisopropylsilyloxy)hex-4-en-1-ol (23). To a solution of trityl ether 22 (1.29 g, 2.17 mmol) in CH₂Cl₂ (15 mL) at 0 °C were added Et₃SiH (1.04 mL, 6.51 mmol) and BF₃·OEt₂ (0.54 mL, 4.34 mmol) dropwise. The resulting mixture was stirred for 1 h at the same temperature before it was diluted with saturated NaHCO₃ solution (10 mL). The layers were separated and the organic layer was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with saturated NaCl solution (10 mL), dried with Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 7:3) to give alcohol 23 (0.57 g, 75%) as a colorless oil. Rf = 0.37 (petroleum ether/ethyl acetate, 8:2); [α]D²⁰ = −3.02 (c = 0.21, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 1.06–1.08 (m, 21H, Si(CH(CH₃)₂)₃), 1.76 (br s, 1H, OH), 2.20–2.27 (m, 4H, CH₂, 3-H), 2.34–2.42 (m, 1H, 1-H), 3.50 (dd, J = 11.1, 3.8 Hz, 1H, 1-H), 3.60 (dd, J = 11.0, 3.8 Hz, 1H, 1-H), 3.87–3.92 (m, 1H, 2-H), 5.82–5.86 (m, 1H, 4-H); ¹³C NMR (100 MHz, CDCl₃): δ = 12.4 (Si(CH(CH₃)₂)₃), 18.0 (Si(CH(CH₃)₂)₃), 23.3 (CH₃), 34.1 (C-3), 65.2 (C-1), 71.7 (C-2), 121.5 (C-5), 127.6 (C-4); HRMS (ESI-TOF): m/z [M + Na]+ calcd for C₁₅H₁₅BrO₂Si: 373.1166; found: 373.1166.
(5,6)-5-Bromo-2-((triisopropylsilyl)oxy)hex-4-enal (24). To a mixture of IBX (1.37 g, 4.90 mmol) in DMSO (8 mL) was added alcohol 23 (0.53 g, 1.50 mmol) in CH$_2$Cl$_2$ (10 mL) at 0 °C. After complete addition, the ice bath was removed and the mixture stirred for 5 h at r.t. The suspension was diluted with CH$_2$Cl$_2$ (20 mL) and filtered through a pad of celite. The filtrate was washed with saturated NaHCO$_3$ solution (10 mL), saturated NaCl solution (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give aldehyde 24 (0.40 g, 76%) as yellow oil that was used for the next reaction without further purification. $R_f = 0.69$ (petroleum ether/ethyl acetate, 7:3); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.05$–1.11 (m, 21H, Si(CH(CH$_3$)$_2$)$_3$), 2.21 (s, 3H, 5-CH$_3$), 2.34–2.47 (m, 2H, 3-H), 4.12 (dt, $J = 5.7$, 1.8 Hz, 1H, 2-H), 5.90 (t, $J = 7.2$ Hz, 1H, 4-H), 9.64 (d, $J = 1.8$ Hz, 1H, CHO); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 12.1$ (Si(CH(CH$_3$)$_2$)$_3$), 17.8 (Si(CH$_2$)$_3$)$_3$), 23.4 (CH$_3$), 33.7 (C-3), 125.9 (C-2), 128.2 (C-5), 129.4 (C-4), 204.0 (C-1); HRMS (ESI-TOF): $m/z$ [M + Na]$^+$ calcld for C$_{15}$H$_{29}$BrO$_2$Si: 403.1278; found: 403.1278.

(35,6)-6-Bromo-3-((triisopropylsilyl)oxy)hept-5-en-2-ol (25). To a solution of aldehyde 24 (0.5 g, 1.43 mmol) in THF (10 mL) at 0 °C was added CH$_3$MgBr (3 M in Et$_2$O, 0.71 mL, 2.14 mmol) dropwise. After addition, the white suspension was stirred for 30 min at 0 °C. Then, the reaction was quenched with saturated NH$_4$Cl solution (5 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with staturated NaCl solution (15 mL), dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/Et$_2$O, 6:4) to give of alcohol 25 (0.40 g, 76%) as a colorless oil. $R_f = 0.41$ (petroleum ether/Et$_2$O, 7:3); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.04$ (s, Si(CH(CH$_3$)$_2$)$_3$, major), 1.07–1.08 (m, Si(CH(CH$_3$)$_2$)$_3$, minor), 1.12 (d, $J = 6.3$ Hz, 1-H, major), 1.18 (d, $J = 6.2$ Hz, 1-H, minor), 2.15–2.27 (m, 7-H, 4-H, minor), 2.40–2.47 (m, 4-H, major), 3.61–3.70 (m, 2-H, 3-H minor), 3.80–3.86 (m, 3-H, major), 5.84–5.90 (m, 1H, 5-H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 12.3$ (Si(CH(CH$_3$)$_2$)$_3$), 12.7 (C-1, minor) 12.8 (C-1, major), 17.7 (Si(CH(CH$_3$)$_2$)$_3$), major), 18.1 (Si(CH$_2$)$_3$)$_3$, minor), 23.4 (C-7, minor and major), 31.9 (C-4, minor), 34.1 (C-4, major), 68.7 (C-2, major), 70.3 (C-2, minor), 75.3 (C-3, minor), 75.6 (C-3, major), 120.5 (C-6, minor), 121.3 (C-6, major), 127.6 (C-5, major), 128.7 (C-5, minor); HRMS (ESI-TOF): $m/z$ [M + Na]$^+$ calcld for C$_{16}$H$_{33}$BrO$_2$Si: 387.1331; found: 387.1331.

(5,6)-6-Bromo-3-((triisopropylsilyl)oxy)hept-5-en-2-one (26). To a stirred solution of alcohol 25 (0.40 g, 1.09 mmol) in CH$_2$Cl$_2$ (10 mL) at 0 °C were added DMP (0.92 g, 2.18 mmol) and NaHCO$_3$ (0.27 g, 3.28 mmol). Thereafter, the reaction mixture was stirred for 1 h at r.t. The reaction mixture was treated with saturated NaHCO$_3$ solution (10 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL). The combined organic layers were washed with saturated NaCl solution (10 mL), dried over Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The crude material was purified by flash
chromatography (petroleum ether/ethyl acetate, 8:2) to give methyl ketone 26 (0.30 g, 75%) as a colorless oil. \( R_f = 0.43 \) (petroleum ether/ethyl acetate, 9:1); [\( \alpha \)]\textsubscript{D} \( ^{22} = +1.88 \) (c = 0.25, CH\textsubscript{3}Cl\textsubscript{2}); \(^1\text{H} \text{NMR} (400 \text{ MHz}, \text{CDCl}_3) \): \( \delta = 1.02-1.07 \) (m, 2H, Si(CH\textsubscript{3})\textsubscript{3}), 2.18-2.19 (m, 6H, 1-H, 7-H), 2.27-2.33 (m, 1H, 4-H), 2.40-2.47 (m, 1H, 4-H), 4.17 (t, \( J = 5.6 \text{ Hz} \), 1H, 3-H), 5.88 (t, \( J = 7.1 \text{ Hz} \), 1H, 5-H); \(^{13}\text{C} \text{NMR} (100 \text{ MHz}, \text{CDCl}_3) \): \( \delta = 12.2 \) (Si(CH(CH\textsubscript{3})\textsubscript{3})\textsubscript{3}), 17.9 (Si(CH(CH\textsubscript{3})\textsubscript{3})\textsubscript{3}), 23.4 (C-7 or C-1), 25.5 (C-1 or C-7), 35.4 (C-4), 78.1 (C-3), 122.0 (C-6), 126.1 (C-5), 211.8 (C-2); HRMS (ESI-TOF): \( m/z \) [M + Na]\textsuperscript{+} calcd for C\textsubscript{18}H\textsubscript{31}BrO\textsubscript{2}Si: 385.1169; found: 385.1169.

\[ \text{Br} \equiv \text{OTIPS} \quad \text{Ph}_3\text{P} (\text{Et}) \text{Br}, \text{THF} \quad \text{Kn(SiMe}_3\text{)z}_2, -78 \degree \text{C} (66\%) \]

\((S,2Z,6E)-7\text{-Bromo-3-methylocta-2,6-dien-4-yloxy}tripropylsilane (27)\). To a solution of ethyltriphenylphosphonium bromide (0.61 g, 1.65 mmol) in THF (5 mL) was added KHMDS (1M in THF, 1.66 mL, 1.65 mmol) dropwise at \(-78 \degree \text{C}\). The resulting yellow suspension was stirred for 45 min at the same temperature. Thereafter, a solution of ketone 26 (0.27 g, 0.74 mmol) in THF (2 mL) was added dropwise at \(-78 \degree \text{C}\). After complete addition, the resulting yellow mixture was stirred for 1 h at \(-78 \degree \text{C}\) and then brought to r.t. The reaction mixture was diluted with water (10 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 \times 10 mL). The combined organic layers were washed with saturated NaCl solution (8 mL), dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 9:1) to give vinyl bromide 27 (0.185 g, 66%) as a colorless oil. \( R_f = 0.88 \) (petroleum ether/ethyl acetate, 95:5); [\( \alpha \)]\textsubscript{D} \( ^{19} = +15.07 \) (c = 1.44, CH\textsubscript{3}Cl\textsubscript{2}); \(^1\text{H} \text{NMR} (400 \text{ MHz}, \text{CDCl}_3) \): \( \delta = 1.03–1.05 \) (m, 21H, Si(CH\textsubscript{3})\textsubscript{3}), 1.55 (dd, \( J = 6.9, 1.4 \text{ Hz}, 3\text{H}, 1\text{-H} \), 1.67 (t, \( J = 1.4 \text{ Hz}, 3\text{H}, 3\text{-CH}_3 \)), 2.19–2.35 (m, 5H, 8-H, 5-H), 4.66 (dd, \( J = 8.0, 6.1 \text{ Hz}, 1\text{H}, 4\text{-H} \)), 5.22–5.28 (m, 1H, 2-H), 5.75 (dt, \( J = 8.3, 1.3 \text{ Hz}, 1\text{H}, 6\text{-H} \)); \(^{13}\text{C} \text{NMR} (100 \text{ MHz}, \text{CDCl}_3) \): \( \delta = 12.3 \) (Si(CH(CH\textsubscript{3})\textsubscript{3})\textsubscript{3}), 13.2 (C-1), 17.5 (3-CH\textsubscript{3}), 17.9 (Si(CH(CH\textsubscript{3})\textsubscript{3})\textsubscript{3}), 18.0 (Si(CH(CH\textsubscript{3})\textsubscript{3})\textsubscript{3}), 23.3 (C-8), 36.5 (C-5), 69.0 (C-4), 120.3 (C-2), 120.6 (C-7), 128.5 (C-6), 137.3 (C-3).

\[ \text{OH} \quad \text{CrO}_3, \text{H}_2\text{SO}_4 \quad \text{acetone, } -5 \degree \text{C} (54\%) \quad \text{CO}_2\text{H} \]

Hex-5-enoic acid\textsuperscript{3} (28). To a stirred solution of chromium trioxide (11.23 g, 112 mmol) in aqueous sulfuric acid (2M, 134 mL, 270 mmol) at \(-5 \degree \text{C}\) was added 5-hexen-1-ol (3.0 g, 29.5 mmol) in acetone (100 mL) over 30 min. The resulting black suspension was stirred for 12 h at \(-5 \degree \text{C}\). Thereafter, the reaction mixture was diluted with diethyl ether (100 mL) and the layers were separated. The organic layer was washed with aqueous NaOH solution (1M, 2 \times 35 mL) and again the layers were separated. The combined aqueous layers were acidified with sulfuric acid (6M, 20 mL), and then extracted with diethyl ether (3 \times 25 mL). The combined organic layers were washed with saturated NaCl solution (15 mL), dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. The crude acid was purified by flash chromatography (petroleum ether/ethyl acetate, 7:3) to give acid 28 (1.85 g, 54%) as a colorless liquid. \( R_f = 0.26 \) (petroleum ether/ethyl acetate, 8:2); \(^1\text{H} \text{NMR} (400 \text{ MHz}, \text{CDCl}_3) \): \( \delta = 1.73 \) (tt, apparent q, \( J = 7.5 \text{ Hz} \), 2H, 3-H), 2.12 (m, 2H, 4-H), 2.38 (t, \( J = 7.5 \text{ Hz} \), 2H, 2-H), 5.01–5.08 (m, 2H, 6-H), 5.77 (ddt, \( J = 17.0, 10.2, 6.7 \text{ Hz} \), 1H, 5-H); \(^{13}\text{C} \text{NMR} (100 \text{ MHz}, \text{CDCl}_3) \): \( \delta = 23.7 \) (C-3), 32.9 (C-4), 33.1 (C-2), 115.2 (C-6), 137.5 (C-5), 179.3 (C-1).
(4S)-Benzyl-3-(hex-5-enoyl)-2-oxazolidinone\(^{4,5}\) (29). To a slurry of 5-hexenoic acid 28 (15.0 g, 131 mmol) in THF (80 mL) was added Et\(_3\)N (25.6 mL, 184 mmol) at 0 °C and the mixture was stirred for 30 min. Then, pivaloyl chloride (17.8 mL, 145 mmol) was added dropwise over 5 min at 0 °C. The resulting white suspension was stirred for 1 h at r.t. To a second flask, charged with (S)-4-benzylxazolidin-2-one (13.9 g, 118 mmol) in THF (125 mL) was added n-ButLi (2.5 M in hexane, 57.8 mL, 145 mmol) at −78 °C over 20 min. The resulting orange suspension was stirred at −78 °C for 1 h before the solution of the mixed anhydride in THF was added in a dropwise fashion. Thereafter, the reaction mixture was stirred for 1 h at −78 °C and then brought to r.t. The reaction mixture was treated with a saturated NH\(_4\)Cl solution (85 mL). Then, the layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 75 mL). The combined organic layers were washed with saturated NaCl solution (50 mL), dried over Na\(_2\)SO\(_4\), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 8:2) to give acylated oxazolidinone 29 (19.5 g, 54%) as a colorless oil. R\(_f\) = 0.56 (petroleum ether/ethyl acetate, 1:1); [α]\(_D\)\(^{20}\) = +68.0 (c = 2, CH\(_2\)Cl\(_2\)); [lit.\(^4\) [α]\(_D\)\(^{23}\) = +56.7 (c = 1.2, CHCl\(_3\))]; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 1.76–1.84\) (m, 2H, 2'-H), 2.16 (dd, \(J = 7.3\) Hz, 2H, 4'-H), 2.76 (dd, \(J = 13.4, 9.6\) Hz, 1H, 5'-H), 2.87–3.02 (m, 2H, 2'-H), 3.10 (dd, \(J = 3.8, 6.0\) Hz, 1H, 5'-H), 4.10–4.21 (m, 2H, 2'H, Ph), 4.63–4.68 (m, 1H, 4-H), 4.98 (d, \(J = 10.1\) Hz, 1H, 6'-H), 5.05 (d, \(J = 17.1\) Hz, 1H, 6'-H), 5.82 (ddt, \(J = 17.0, 10.2, 6.7\) Hz, 1H, 5'-H), 7.21–7.35 (m, 5H, ArH); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta = 23.3\) (C-3'), 32.9 (C-4'), 34.8 (C-2'), 37.9 (C-5), 55.1 (C-4), 66.1 (CH\(_2\), Ph), 115.3 (C-6'), 127.3, 128.9, 129.4, 135.2 (4 × Ar CH), 135.8 (C-5'), 153.4 (C-2), 173.1 (C-1'); HRMS (ESI-TOF): \(m/z\) [M + Na]\(^+\) calcd for \(\text{C}_{16}\text{H}_{17}\text{NO}_3\): 296.1257; found: 296.1257.

(S)-4-Benzyl-3-((S)-2-methylhex-5-enoyl)oxazolidin-2-one (30). To a solution of N-acyloxazolidinone 29 (13.47 g, 49.28 mmol) in THF (80 mL) at −78 °C was added a solution of NaHMDS (2M in THF, 37.0 mL, 73.9 mmol) over 30 min. The reaction mixture was stirred for 1 h at −78 °C before iodomethane (35 mL, 246 mmol) was added dropwise within 15 min. The resulting yellow mixture was stirred for another 1 h at −78 °C and another 30 min at r.t. Thereafter, the reaction mixture was diluted with AcOH (4 mL) and water (60 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 80 mL). The combined organic layers were washed with saturated NaCl solution, dried over Na\(_2\)SO\(_4\), filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate, 9:1) to give methylated acid derivative 30 (11.82 g, 83%) as a colorless oil. R\(_f\) = 0.38 (petroleum ether/ethyl acetate, 9:1); [α]\(_D\)\(^{20}\) = +91.5 (c = 1.05, CH\(_2\)Cl\(_2\)); [lit.\(^4\) [α]\(_D\)\(^{23}\) = +78.3 (c = 1.7, CHCl\(_3\))]; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta = 1.23\) (d, \(J = 6.8\) Hz, 3H, 2-CH\(_3\)), 1.47–1.55 (m, 1H, 3'-H), 1.83–1.92 (m, 1H, 3'-H), 2.09 (q, \(J = 6.9\) Hz, 2H, 4'-H), 2.77 (dd, \(J = 13.4, 9.6\) Hz, 1H, 5'-H), 3.27 (dd, \(J = 13.4, 3.2\) Hz, 1H, 5'-H), 3.68–3.77 (m, 1H, 2'-H), 4.14–4.21 (m, 2H, 2'H, Ph), 4.63–4.69 (m, 1H, 4'-H), 4.95 (d, \(J = 10.2\) Hz, 1H, 6'-H), 5.03 (d, \(J = 17.1\) Hz, 1H, 6'-H), 5.73–5.83 (m, 3H, 5'-H), 7.20–7.21 (m, 2H, ArH), 7.30–7.34 (m, 3H, ArH); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta = 17.4\) (2-CH\(_3\)), 31.5 (C-4'), 32.4 (C-3'), 37.2 (C-2'), 37.9 (C-5), 55.3 (C-4'), 66.0 (CH\(_2\), Ph), 114.9 (C-6'), 127.3, 128.9, 129.4, 135.3 (4 × Ar CH), 138.1 (C-5'), 153.0 (C-2), 177.1 (C-1'); HRMS (ESI-TOF): \(m/z\) [M + Na]\(^+\) calcd for \(\text{C}_{17}\text{H}_{18}\text{NO}_3\): 310.1413; found: 310.1413.
(S)-2-Methylhex-5-en-1-ol (31). To a stirred solution of N-acyloxazolidinone 30 (11.82 g, 41.13 mmol) in THF (80 mL) and MeOH (1.58 mL, 49.36 mmol) was added a solution of lithium borohydride (4M in THF, 30.9 mL, 75.9 mmol) at 0 °C over 15 min. The resulting mixture was stirred for 2 h at r.t. Thereafter, the reaction mixture was quenched with aqueous NaOH (2M, 40 mL). The aqueous layer was extracted with diethyl ether (2 × 50 mL) and the combined organic layers were washed with a saturated NaCl solution (35 mL), dried over Na2SO4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether: diethyl ether, 9:1) to give primary alcohol 31 (2.92 g, 62%) as a colorless oil. Rf = 0.27 (petroleum ether/ethyl acetate, 9:1); [α]D20 = −11.2 (c = 3.0, CH2Cl2); Lit.6 [α]D20 = −13.3 (c = 1.81, CH2Cl2); 1H NMR (400 MHz, CDCl3): δ = 0.93 (d, J = 6.7 Hz, 3H, 2-CH3), 1.16–1.26 (m, 1H, 3-H), 1.43 (br s, 1H, OH), 1.47–1.55 (m, 1H, 3-H), 1.60–1.68 (m, 1H, 2-H), 2.00–2.17 (m, 2H, 4-H), 3.44 (dd, J = 10.5, 6.5 Hz, 1H, 1-H), 3.50 (dd, J = 10.5, 5.8 Hz, 1H, 1-H), 4.95 (dd, J = 10.1, 1.8 Hz, 1H, 6-H), 5.03 (dd, J = 17.1, 1.8 Hz, 1H, 6-H), 5.81 (ddt, J = 17.0, 10.1, 6.7 Hz, 1H, 5-H); 13C NMR (100 MHz, CDCl3): δ = 16.4 (2-CH3), 31.1 (C-4), 32.3 (C-3), 35.2 (C-2), 68.2 (C-1), 114.4 (C-6), 138.9 (C-5).

Methyl (S,E)-7-[(4-methoxybenzyl)oxy]-6-methylhept-2-enoate (33). A solution of alkene 32 (1.0 g, 4.26 mmol) and methyl acrylate (1.46 mL, 17.1 mmol) in toluene (12 mL) was deoxygenated by bubbling argon through the solution for 2–3 min. Then, Grubbs II catalyst (0.18 g, 0.21 mmol, 5 mol%) in toluene (4 mL) was added dropwise at r.t. The dark red suspension was heated at 85 °C for 8 h. After the reaction mixture had cooled down to r.t., the solvent was removed under reduced pressure. The residue was purified by
flash chromatography (petroleum ether/ethyl acetate, 8:2) to give enoate \(33\) (1.18 g, 95\%) as an off brown oil. \(R_f = 0.33\) (petroleum ether/ethyl acetate, 9:1); \([\alpha]_D^{20} = -1.65\) (c = 1, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.92\) (d, \(J = 6.7\) Hz, 3H, 6-\(CH_3\)), 1.24–1.33 (m, 1H, 5-\(H\)), 1.58–1.67 (m, 1H, 5-\(H\)), 1.75–1.80 (m, 1H, 6-\(H\)), 2.13–2.29 (m, 2H, 4-\(H\)), 3.27 (dd, \(J = 6.3, 1.9\) Hz, 2H, 7-\(H\)), 3.73 (s, 3H, OCH\(_3\)), 3.81 (s, 3H, ArOCH\(_3\)), 4.43 (s, 2H, CH\(_2\)Ar), 5.82 (dt, \(J = 15.7, 1.6\) Hz, 1H, 2-\(H\)), 6.87 (d, \(J = 8.6\) Hz, 2H, ArH), 6.93–7.01 (m, 1H, 2-3), 7.25 (d, \(J = 8.6\) Hz, 2H, ArH); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 16.8\) (6-\(CH_3\)), 29.6 (C-4), 31.8 (C-5), 32.9 (C-6), 51.3 (OCH\(_3\)), 55.2 (OCH\(_3\)), 72.6 (CH\(_2\)Ar), 75.1 (C-7), 113.7 (Ar C), 120.8 (C-3), 129.1 (Ar C), 130.6 (Ar C), 149.6 (C-2), 159.0 (Ar C), 167.1 (C-1); HRMS (ESI-TOF): \(m/z\) [M + Na]\(^+\) calc'd for C\(_{17}\)H\(_{20}\)O\(_5\): 315.1570; found: 315.1570.

Methyl (2R,3S,6S)-2,3-dihydroxy-7-((4-methoxybenzyl)oxy)-6-methylheptanoate (34). To a stirred solution of enoate \(33\) (1.18 g, 4.03 mmol) in t-BuOH/H\(_2\)O (3:1, 40 mL) was added solid of AD-mix \(\alpha\) (5.65 g) and methyl sulfonamide (0.95 g, 10.1 mmol) at 0°C. The yellow suspension was stirred for 36 h at r.t. After that, the reaction mixture was quenched with sodium thiosulfate solution (25 mL) and the aqueous phase was extracted with ethyl acetate (3 × 16 mL). The combined organic layers were washed with saturated NaCl solution (20 mL), dried over Na\(_2\)SO\(_4\), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 6:4) to give dihydroxy ester \(34\) (0.84 g, 64\%) as a colorless oil. \(R_f = 0.34\) (petroleum ether/ethyl acetate, 1:1); \([\alpha]_D^{19} = -19.75\) (c = 2, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.91\) (d, \(J = 6.7\) Hz, 3H, 6-\(CH_3\)), 1.31–1.37 (m, 1H, 5-\(H\)), 1.47–1.58 (m, 2H, 4-\(H\), 5-\(H\)), 1.63–1.70 (m, 1H, 4-\(H\)), 1.75–1.83 (m, 1H, 6-\(H\)), 3.25 (dd, \(J = 6.4, 1.8\) Hz, 2H, 7-\(H\)), 3.79 (s, 3H, OCH\(_3\)), 3.81 (s, 3H, OCH\(_3\)), 3.83–3.87 (m, 1H, 3-\(H\)), 4.07 (d, \(J = 2.1\) Hz, 1H, 1-\(H\)), 4.41 (s, 2H, CH\(_2\)Ar), 6.87 (d, \(J = 8.6\) Hz, 2H, ArH), 7.23 (d, \(J = 7.8\) Hz, 2H, ArH); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 17.1\) (6-\(CH_3\)), 29.9 (C-4), 31.0 (C-5), 33.2 (C-6), 43.4 (C-3), 52.8 (OCH\(_3\)), 55.3 (OCH\(_3\)), 72.7 (CH\(_2\)Ar), 73.2 (C-2), 75.4 (C-7), 113.7, 129.2, 130.6, 159.1 (4 × Ar C), 174.0 (C-1); HRMS (ESI-TOF): \(m/z\) [M + Na]\(^+\) calc'd for C\(_{17}\)H\(_{20}\)O\(_6\): 349.1621; found: 349.1621.

Methyl (4R,5S)-5-((S)-4-((4-methoxybenzyl)oxy)-3-methylbutyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (35). 2,2-Dimethoxypropane (0.38 mL, 3.11 mmol) and \(p\)-toluenesulfonic acid (\(p\)TsOH/H\(_2\)O) (3 mg, 0.02 mmol) were added to a stirred solution of dihydroxy ester \(34\) (0.84 g, 2.57 mmol) in aceton (10 mL) at r.t. followed by stirring of the mixture for 2 h. The reaction mixture was diluted with saturated NaHCO\(_3\) solution (5 mL) and H\(_2\)O (10 mL). The aqueous phase was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with saturated NaCl solution (10 mL), dried over Na\(_2\)SO\(_4\), filtered, and concentrated under reduced pressure. The crude acetal was purified by flash chromatography (petroleum ether/ethyl acetate, 8:2) to give protected dihydroxy ester \(35\) (0.67 g, 71\%) as a colorless oil. \(R_f = 0.55\) (petroleum ether/ethyl acetate, 8:2); \([\alpha]_D^{20} = -13.28\) (c = 0.5, CH\(_2\)Cl\(_2\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.92\) (d, \(J = 6.7\) Hz, 3H, 3'-\(CH_3\)), 1.26–1.36 (m, 1H, 1'-\(H\)), 1.42 (s, 3H, C(\(CH\(_3\))\(_2\)), 1.45 (s, 3H, C(\(CH\(_3\))\(_2\)), 1.50–1.59 (m, 1H, 2'-\(H\)), 1.67–1.81 (m, 3H, 1'-\(H\), 3'-\(H\), 2'-\(H\)), 3.22–3.30 (m, 2H, 4'-\(H\)), 3.76 (s, 3H, OCH\(_3\)), 3.79 (s, 3H, OCH\(_3\)), 4.08–4.12 (m, 2H, 4-\(H\), 5-\(H\)), 4.42 (s, 2H, CH\(_2\)Ar), 6.87 (d, \(J = 8.6\) Hz, 2H, ArH), 7.25 (d, \(J = 8.6\) Hz, 2H, ArH); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 16.9\) (3'-\(CH_3\)), 25.6 (C(\(CH\(_3\))\(_2\)), 27.2 (C(\(CH\(_3\))\(_2\)), 29.5 (C-1' or C-2'), 30.9 (C-2' or C-3'), 33.4 (C-3'), 52.3 (OCH\(_3\)), 55.2 (OCH\(_3\)), 72.6 (CH\(_2\)Ar), 75.4 (C-4'), 79.0 (C-4), 79.2 (C-5), 110.8, 113.7,
129.1, 130.7 (4 × Ar C), 159.1 (C-2), 171.3 (CO₂Me); HRMS (ESI-TOF): \text{m/z } [M + Na]^+ \text{ calcd for } C_{20}H_{30}O_6: 389.1935; \text{ found: } 389.1935.

\[
\begin{aligned}
&\text{CO}_2\text{Me} \quad \text{LiAlH}_4, \text{THF} \\
&0 \ ¹C \ \text{to r.t. (96%)} \quad \text{OPMB}
\end{aligned}
\]

\[\text{35} \quad \text{36} \quad \text{37}\]

\((4R,5S)-5-[(5)-4-((4-\text{Methoxybenzyl})\text{oxo})-3-\text{methylbutyl})-2,2,3,3\text{-dioxolane}-4\text{-yl}]\text{methanol} \ (36) \) To a solution of LiAlH₄ (0.10 g, 2.61 mmol) in THF (3 mL) at 0 °C was added a solution of methyl ester \text{35} (0.64 g, 1.74 mmol) in THF (8 mL). After complete addition, the resulting suspension was stirred at r.t. for 2 h. The reaction mixture was quenched by adding H₂O (5 mL) and 15% aqueous NaOH (2 mL). The white suspension was filtered through a pad of celite, which was rinsed with ethyl acetate (10 mL). The obtained filtrate was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 5:5) to give primary alcohol \text{36} (0.57 g, 96%) as a colorless oil. \(R_f = 0.23 \) (petroleum ether/ethyl acetate, 7:3); \([\alpha]_D^{21} = -14.64 \) (c = 2, CH₂Cl₂); \(^1^H\ NMR (400 MHz, CDCl₃): \( \delta = 0.93 \) (d, \( J = 6.7 \) Hz, 3H, 3'-CH₃), 1.29–1.40 (m, 6H, C(CH₃)₂, 2'-H), 1.46–1.53 (m, 2H, 2'-H, 1'-H), 1.71–1.79 (m, 1H, 1'-H), 1.93–1.96 (m, 1H, 3'-H), 3.26 (dd, \( J = 17.9, 9.0 \) Hz, 2H, 4'-H), 3.54–3.61 (m, 1H, CH₂OH), 3.69–3.79 (m, 5H, 5'-H, 4'-H, OCH₃), 3.81–3.86 (m, 1H, CH₂OH), 4.41 (s, 2H, CH₂Ar), 6.87 (d, \( J = 8.6 \) Hz, 2H, ArH), 7.25 (d, \( J = 8.6 \) Hz, 2H, ArH); \(^{13}C\ NMR (100 MHz, CDCl₃): \delta = 17.0 (3'-CH₃), 27.0 (C(CH₃)₂), 27.3 (C(CH₃)₂), 29.8 (C-2'), 30.5 (C-1'), 33.5 (C-3'), 55.2 (OCH₃), 62.0 (CH₂OH), 72.6 (CH₂Ar), 75.3 (C-4'), 77.0 (C-4 or C-5), 81.7 (C-5 or C-4), 108.5, 113.7, 129.1, 130.7 (4 × Ar C), 159.0 (C-2); HRMS (ESI-TOF): m/z [M + Na]^+ calcd for C₁₉H₂₉O₆: 361.1988; found: 361.1988.

\[\text{36} \quad \text{37}\]

\((4R,5S)-5-[(5)-4-((4-\text{Methoxybenzyl})\text{oxo})-3-\text{methylbutyl})-2,2,3,3\text{-dioxolane}-4\text{-carbaldehyde} \ (37) \) To a solution of oxalyl chloride (0.21 mL, 2.48 mmol) in CH₂Cl₂ (5 mL) was slowly added DMSO (0.35 mL, 4.96 mmol) at –78 °C. After being stirred for 15 min at this temperature, a solution of alcohol \text{36} (0.56 g, 1.65 mmol) in CH₂Cl₂ (8 mL) was added over a period of 5 min. The reaction mixture was stirred at the same temperature for 1 h. Thereafter, Et₃N (1.3 mL, 9.92 mmol) was added dropwise. Then the reaction mixture was warmed to r.t. The mixture was diluted with H₂O (10 mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 8 mL). The combined organic layers were washed with saturated NaCl solution (10 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The aldehyde \text{37} (0.53 g, 95%) was used for the next step without chromatography. \(R_f = 0.55 \) (petroleum ether/ethyl acetate, 7:3); \([\alpha]_D^{19} = -3.40 \) (c = 1.5, CH₂Cl₂); \(^1^H\ NMR (400 MHz, CDCl₃): \( \delta = 0.91 \) (d, \( J = 6.7 \) Hz, 3H, 3'-CH₃), 1.25–1.46 (m, 8H, C(CH₃)₂, 2'-H), 1.48–1.77 (m, 3H, 3'-H, 1'-H), 3.21–3.29 (m, 2H, 4'-H), 3.79 (s, 3H, OCH₃), 3.88–3.93 (m, 1H, 4-H), 3.98–4.03 (m, 1H, 5-H), 4.41 (s, 2H, CH₂Ar), 6.86 (d, \( J = 8.6 \) Hz, 2H, ArH), 7.23 (d, \( J = 7.7 \) Hz, 2H, ArH), 9.70 (s, 1H, CHO); \(^{13}C\ NMR (100 MHz, CDCl₃): \delta = 16.9 (3'-CH₃), 26.1 (C(CH₃)₂), 27.0 (C(CH₃)₂), 29.4 (C-2'), 30.8 (C-1'), 33.3 (C-3'), 55.2 (OCH₃), 72.6 (CH₂Ar), 75.2 (C-4'), 77.1 (C-5), 84.8 (C-4), 110.8, 113.7, 129.1, 130.7 (4 × Ar C), 159.0 (C-2), 201.1 (CHO); HRMS (ESI-TOF): m/z [M + CH₂OH + Na]^+ calcd for C₁₉H₂₉O₆: 391.2090; found: 391.2090.
C1-C12 fragment 39. Vinyl bromide 22 (0.15 g, 0.25 mmol) was dried by dissolving it in a mixture of benzene/toluene (3 mL, 1:1) followed by evaporation of the solvents using a rotavapor and placing it under high vacuum for 1 h. Thereafter, THF (1.5 mL) was added under an argon atmosphere and the reaction flask was cooled to −78 °C. Then, s-BuLi (1.4 M in cyclohexane, 0.21 mL, 0.30 mmol) was added dropwise and the reaction mixture stirred for 30 min at −78 °C before aldehyde 37 (0.14 g, 0.43 mmol), dissolved in THF (1.5 mL), was added dropwise. After complete addition, the reaction mixture was stirred for 2 h at −78 °C and at r.t. for 1 h. Finally, the reaction mixture was treated with saturated NH₄Cl solution (5 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 8 mL). The combined organic layers were washed with saturated NaCl solution (5 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude allylic alcohol 39 (86 mg, dr = 10:4) was used for the next reaction without chromatography. HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₃₃H₄₆O₃Si: 873.5094; found: 873.5094.

Enone 40. To a solution of alcohol 39 (70 mg, 0.08 mmol) in CH₂Cl₂ (5 mL) at 0 °C were added DMP (70 mg, 0.16 mmol) and NaHCO₃ (20 mg, 0.24 mmol). After addition, the cooling bath was removed and the mixture stirred for 2 h at r.t. Then the reaction mixture was diluted with saturated NaHCO₃ solution (5 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL). The combined organic layers were washed with saturated NaCl solution (8 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate, 85:15) to give enone 40 (50 mg, 71%) as a colorless oil. Rₜ = 0.48 (petroleum ether/ethyl acetate, 9:1); [α]₂° = −6.85 (c = 0.52, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 0.90 (d, J = 6.7 Hz, 3H, 2-CH₃), 0.94–0.96 (m, 21H, Si(CH(CH₃)₂)₃), 1.25–1.30 (m, 1H, 3-H), 1.30 (s, 3H, C(CH₃)₂), 1.37–1.44 (m, 4H, C(CH₂)₂, 3-H), 1.50–1.53 (m, 1H, 4-H), 1.56–1.60 (m, 1H, 4-H), 1.68–1.73 (m, 1H, 2-H), 1.80 (s, 3H, 8-CH₃), 2.70–2.73 (m, 2H, 10-H), 2.97 (t, J = 8.3 Hz, 1H, 12-H), 3.10–3.20 (m, 2H, 12-H, 1-H), 3.26 (dd, J = 9.0, 5.8 Hz, 1H, 1-H), 3.77 (s, 3H, OCH₃), 4.10–4.18 (m, 1H, 11-H), 4.22–4.26 (m, 1H, 5-H), 4.34 (d, J = 7.4 Hz, 1H, 6-H), 4.48 (d, J = 1.8 Hz, 2H, CH₂Ar), 6.86 (d, J = 8.6 Hz, 2H, ArH), 6.97 (t, J = 6.4 Hz, 1H, 9-H), 7.17–7.27 (m, 12H, ArH), 7.38–7.41 (m, 5H, ArH); ¹³C NMR (100 MHz, CDCl₃): δ = 11.8 (8-CH₃), 12.3 (Si(CH(CH₃)₂)₃), 16.9 (2-CH₃), 18.0 (Si(CH(CH₃)₂)₃), 26.2 (C(CH₃)₂), 27.2 (C(CH₂)₃), 29.7 (C-3), 30.6 (C-4), 33.4 (C-2), 34.8 (C-1), 55.2 (OCH₃), 66.3 (C-12), 70.3 (C-11), 72.6 (CH₂Ar), 75.5 (C-1), 78.0 (C-5 or C-6), 80.3 (C-6 or C-5), 86.6 (CPh₃), 109.8 (C(CH₃)₂), 113.7, 127.0, 127.7, 128.6, 129.0, 130.8 (6 × Ar), 137.7 (C-8), 142.5 (C-9), 143.9 (Ar C), 159.0 (Ar C), 197.5 (C-7); HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₃₃H₄₆O₃Si: 873.4929; found: 871.4929.
Triisopropyl(((S,2Z,6Z)-3-methyl-octa-2,6-dien-4-yloxy)silane (S1). To a stirred solution of vinyl bromide 27 (25 mg, 0.06 mmol) in THF (0.5 mL) at –78 °C was added a solution of s-BuLi (1.4 M in cyclohexane, 0.074 mL, 0.1 mmol) over 5 min. The reaction mixture was stirred at –78 °C for 1 h, before aldehyde 37 (40 mg, 0.1 mmol) in THF (0.3 mL) was added dropwise. After addition, the reaction mixture was stirred at –78 °C for 30 min and 2 h at r.t. The reaction mixture was diluted with saturated NH₄Cl solution (3 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 3 mL). The combined organic layers were washed with saturated NaCl solution (2 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (petroleum ether/diethyl ether, 8:2) to give debrominated diene S1 (10 mg, 51%) as the major compound. Rf = 0.7 (petroleum ether/diethyl ether, 9:1); ¹H NMR (400 MHz, CDCl₃): d = 1.05-1.04 (m, 21H, Si(CH(CH₃)₂)₃), 1.52-1.62 (m, 6H, 2 CH₃), 1.68 (t, J = 1.5 Hz, 3H, 3-CH₃), 2.27-2.41 (m, 2H, 5-H), 4.66 (dd, J = 8.6, 5.5 Hz, 1H, 4-H), 5.20-5.31 (m, 2H, 6-H, 7-H), 5.44-5.50 (m, 1H, 2-H); ¹³C NMR (100 MHz, CDCl₃): d = 12.4 (Si(CH(CH₃)₂)₃), 12.9 (C-8), 13.2 (C-1), 17.4 (3-CH₃), 17.9 (Si(CH(CH₃)₂)₃), 18.0 (Si(CH(CH₃)₂)₃), 34.0 (C-5), 69.5 (C-4), 119.6 (C-2), 125.2 (C-7), 126.2 (C-6), 138.0 (C-3).

References

$^1$H NMR (400 MHz) spectrum of acetal 15 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of acetal 15 in CDCl$_3$ (1.0 – 4.5 ppm)
<table>
<thead>
<tr>
<th>Chemical Shift (ppm)</th>
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<tbody>
<tr>
<td>136</td>
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<tr>
<td>16</td>
</tr>
</tbody>
</table>

\(^{13}\text{C NMR (100 MHz) spectrum of acetal 15 in CDCl}_3 (10 – 140 ppm)\)
H NMR (400 MHz) spectrum of aldehyde 16 in CDCl₃ (0.5 – 10.0 ppm)

H NMR (400 MHz) spectrum of aldehyde 16 in CDCl₃ (1.0 – 4.75 ppm)
$^{13}$C NMR (100 MHz) spectrum of aldehyde 16 in CDCl$_3$ (5 – 205 ppm)
### $^1$H NMR (400 MHz) spectrum of dibromoalkene 17 in CDCl$_3$ (0.5 – 7.5 ppm)

![H NMR spectrum](image)

### $^{13}$C NMR (100 MHz) spectrum of dibromoalkene 17 in CDCl$_3$ (10 – 140 ppm)

![C NMR spectrum](image)
$^1$H NMR (400 MHz) spectrum of alkyne 18 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of alkyne 18 in CDCl$_3$ (1.0 – 4.5 ppm)
$^{13}$C NMR (100 MHz) spectrum of alkyne 18 in CDCl$_3$ (0 – 130 ppm)
$^1$H NMR (400 MHz) spectrum of vinyl bromide 19 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of vinyl bromide 19 in CDCl$_3$ (10 – 140 ppm)
$^1$H NMR (400 MHz) spectrum of vinyl bromide 20 in C$_6$D$_6$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of vinyl bromide 20 in C$_6$D$_6$ (1.5 – 6.0 ppm)
$^1$H NMR (400 MHz) spectrum of vinyl bromide 20 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of vinyl bromide 20 in CDCl$_3$ (1.8 – 4.0 ppm)
$^{13}$C NMR (100 MHz) spectrum of vinyl bromide 20 in CDCl$_3$ (10 – 140 ppm)
$^1$H NMR (400 MHz) spectrum of trityl ether 21 in CDCl$_3$ (0.5 – 8.0 ppm)

$^{13}$C NMR (100 MHz) spectrum of trityl ether 21 in CDCl$_3$ (10 – 150 ppm)
$^1$H NMR (400 MHz) spectrum of silyl ether 22 in CDCl$_3$ (0.5 – 8.0 ppm)

$^{13}$C NMR (100 MHz) spectrum of silyl ether 22 in CDCl$_3$ (10 – 150 ppm)
$^1$H NMR (400 MHz) spectrum of primary alcohol 23 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of alcohol 23 in CDCl$_3$ (10 – 150 ppm)
$^3$H NMR (400 MHz) spectrum of aldehyde 24 in CDCl$_3$ (0.5 – 10.0 ppm)

$^{13}$C NMR (100 MHz) spectrum of aldehyde 24 in CDCl$_3$ (10 – 215 ppm)
$^1$H NMR (400 MHz) spectrum of alcohol 25 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of alcohol 25 in CDCl$_3$ (10 – 140 ppm)
DEPT-135 (100 MHz) spectrum of alcohol 25 in CDCl₃ (10 – 35 ppm)
$^1$H NMR (400 MHz) spectrum of methyl ketone 26 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of methyl ketone 26 in CDCl$_3$ (0.5 – 6.0 ppm)
$^1$C NMR (100 MHz) spectrum of methyl ketone 26 in CDCl$_3$ (5 – 215 ppm)

$^1$C NMR (100 MHz) spectrum of methyl ketone 26 in CDCl$_3$ (10 – 80 ppm)
HSQC spectrum of methyl ketone 26 in CDCl$_3$ (0.5 – 6.0, 5 – 140 ppm)
HMBC spectrum of methyl ketone 26 in CDCl₃ (0.5 – 6.0, 5 – 140 ppm)
\(^1\)H NMR (400 MHz) spectrum of alkene 27 in CDCl\(_3\) (0.5 – 7.5 ppm)
COSY spectrum of alkene 27 in CDCl₃ (0.5 – 6.0 ppm)
NOESY spectrum of alkene 27 in CDCl$_3$ (0.5 – 6.0 ppm)
$^{13}$C NMR (100 MHz) spectrum of alkene 27 in CDCl$_3$ (10 – 140 ppm)
HSQC spectrum of alkene 27 in CDCl$_3$ (0.5 – 6.0, 5 – 140 ppm)
$^1$H NMR (400 MHz) spectrum of hexenoic acid 28 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of hexenoic acid 28 in CDCl$_3$ (10 – 190 ppm)
$^1$H NMR (400 MHz) spectrum of acyloxazolidinone 29 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of acyloxazolidinone 29 in CDCl$_3$ (10 – 180 ppm)
$^3$H NMR (400 MHz) spectrum of 2-methylhexenoic acid derivative 30 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of 2-methylhexenoic acid derivative 30 in CDCl$_3$ (10 – 190 ppm)
$^1$H NMR (400 MHz) spectrum of alkenol 31 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of alkenol 31 in CDCl$_3$ (10 – 150 ppm)
$^1$H NMR (400 MHz) spectrum of PMB ether 32 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of PMB ether 32 in CDCl$_3$ (10 – 170 ppm)
$^3$H NMR (400 MHz) spectrum of enoate 33 in CDCl$_3$ (0.5 – 7.5 ppm)

$^{13}$C NMR (100 MHz) spectrum of enoate 33 in CDCl$_3$ (10 – 180 ppm)
$^1$H NMR (400 MHz) spectrum of diol 34 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of diol 34 in CDCl$_3$ (0.5 – 4.5 ppm)
C NMR (100 MHz) spectrum of diol 34 in CDCl₃ (10 - 180 ppm)
$^1$H NMR (400 MHz) spectrum of acetonide 35 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of acetonide 35 in CDCl$_3$ (0.5 – 4.5 ppm)
$^{13}$C NMR (100 MHz) spectrum of acetonide 35 in CDCl$_3$ (10 – 180 ppm)
$^1$H NMR (400 MHz) spectrum of alcohol 36 in CDCl$_3$ (0.5 – 7.5 ppm)

$^1$H NMR (400 MHz) spectrum of alcohol 36 in CDCl$_3$ (0.5 – 4.5 ppm)
\[13C\text{ NMR (100 MHz) spectrum of alcohol 36 in CDCl}_3 (10 – 170 \text{ ppm})\]
$^1$H NMR (400 MHz) spectrum of aldehyde 37 in CDCl$_3$ (0.5 – 10.0 ppm)

$^1$H NMR (400 MHz) spectrum of aldehyde 37 in CDCl$_3$ (0.5 – 4.5 ppm)
$^{13}$C NMR (100 MHz) spectrum of aldehyde 37 in CDCl$_3$ (10 – 205 ppm)
\[ ^{1}H \text{ NMR (400 MHz) spectrum of allyl alcohol 39 in CDCl}_3 (0.5 \text{ – } 8.0 \text{ ppm}) \]

\[ ^{13}C \text{ NMR (100 MHz) spectrum of allyl alcohol 39 in CDCl}_3 (10 \text{ – } 170 \text{ ppm}) \]
$^1$H NMR (400 MHz) spectrum of enone 40 in CDCl$_3$ (0.5 – 8.0 ppm)

$^1$H NMR (400 MHz) spectrum of enone 40 in CDCl$_3$ (0.5 – 4.5 ppm)
\(^{13}\)C NMR (100 MHz) spectrum of enone 40 in CDCl\(_3\) (10 – 200 ppm)
HSQC spectrum of enone 40 in CDCl₃ (0.5 – 7.5, 5 – 150 ppm)
\textsuperscript{1}H NMR (400 MHz) spectrum of diene S1 in CDCl\textsubscript{3} (0.5 – 7.5 ppm)

\textsuperscript{13}C NMR (100 MHz) spectrum of diene S1 in CDCl\textsubscript{3} (10 – 150 ppm)