Synthesis of the Core Structure of Apicularen A by
Transannular Cyclization

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Supporting Information
Experimental Section

**General.** $^1$H and $^{13}$C NMR: Bruker AC 250, Bruker Avance 400, Bruker AMX 600, spectra were recorded in CDCl$_3$, C$_6$D$_6$ and D$_2$O; chemical shifts are calibrated to the residual proton and carbon resonance in CDCl$_3$ (7.25 ppm, 77.00 ppm), C$_6$D$_6$ (7.16 ppm, 128.00 ppm) and D$_2$O (4.80 ppm). Polarimeter: JASCO Polarimeter P-1020. EI-MS; Finnigan Triple-Stage-Quadrupol (TSQ-70). HRMS (EI): modified AMD Intectra MAT 711 A. HRMS (FT-ICR): BRUKER Daltonic APEX 2 with electrospray-ionization (ESI). Flash chromatography: J. T. Baker silica gel 43-60 μm. Thin-layer chromatography Machery-Nagel Polygram Sil G/UV$_{254}$. Solvents were distilled prior to use; petroleum ether with a boiling range of 30-50 °C was used. High vacuum refers to the vacuum of an oil pump. Abbreviations used: DBU = 1,8-Diazabicyclo[5.4.0]undec-7-en, AIBN = 4,4'-Azo-bis-isobutyronitrile, DMAP = 4-Dimethylaminopyridine, TMEDA = N,N',N'-Tetramethylendiamine. For compounds 24 and 25 the apicularen A numbering$^1$ was used.

**2-Hydroxy-6-methoxybenzoic acid (5).** To a solution of the di-protected resorcine 4 (17.5 g, 84.1 mmol) in Et$_2$O (400 ml) was added dropwise (ice-bath) $n$-butyllithium (37.4 ml, 2.7 M in hexane, 101.0 mmol) at 0 °C. After being stirred for 16 h at room temperature, the solution was transferred into a dropping funnel and added dropwise to powdered dry ice (1000 g). After complete addition, the reaction mixture was diluted with Et$_2$O (400 ml) and the excess of the dry ice allowed to evaporate. The mixture was extracted with water (3 × 200 ml), the combined aqueous layers were acidified to pH 1 with conc. HCl, and the resulting white solid was filtered off and washed with cold water to give the pure acid 5 (10.5 g, 74%). TLC (PE/EtOAc, 1:1): $R_f = 0.53$; mp = 136.5 °C; $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta$[ppm] = 4.04 (s, 3H, O-CH$_3$), 6.47 (dd, $J = 8.3$, 0.9 Hz, 1H, C$_5$-H), 6.67 (dd, $J = 8.3$, 0.9 Hz, 1H, C$_3$-H), 7.38 (t, $J = 8.3$ Hz, 1H, C$_4$-H), 11.33 (s, 1H, COOH), 12.13 (s, 1H, OH); $^{13}$C NMR (100 MHz, C$_6$D$_6$): $\delta$[ppm] = 57.0 (O-CH$_3$), 101.3 (C$_6$), 101.4 (C$_5$), 112.2 (C$_3$), 135.6 (C$_4$), 158.4 (C$_2$), 164.1 (C$_1$), 170.1 (C=O).
**Methyl 2-hydroxy-6-methoxybenzoate (6).** To a cooled solution (ice-bath) of the hydroxy acid 5 (8.9 g, 53.0 mmol) in THF (250 ml) was added DBU (7.9 ml, 53 mmol) dropwise within 10 min. Then methyl iodide (3.3 ml, 53.0 mmol) was added and the reaction mixture stirred for 24 h at room temperature. The precipitated ammonium iodide was filtered off, washed with THF (30 ml), and the filtrate concentrated in vacuo. Flash chromatography (PE/EtOAc, 1:1) of the residue gave the methyl benzoate 6 (8.2 g, 85%) as a white solid. TLC (PE/EtOAc, 4:1): $R_f = 0.52$; mp = 51 °C; $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta$[ppm] = 3.83 (s, 3H, COOCH$_3$), 3.93 (s, 3H, OCH$_3$), 6.41 (dd, $J = 8.3$, 0.9 Hz, 1H, C$_5$-H), 6.60 (dd, $J = 8.3$, 0.9 Hz, 1H, C$_3$-H), 7.31 (t, $J = 8.3$ Hz, 1H, C$_4$-H), 12.13 (s, 1H, OH); $^{13}$C NMR (100 MHz, C$_6$D$_6$): $\delta$[ppm] = 52.4 (COOCH$_3$), 56.1 (OCH$_3$), 102.2 (C$_5$), 103.1 (C$_3$), 110.1 (C$_4$), 135.1 (C$_1$), 160.8 (C$_6$), 163.5 (C$_2$), 171.6 (C=O).

**Methyl 2-methoxy-6-[[[(trifluoromethyl)sulfonyl]oxy]benzoate (7).** To a solution of the methyl ester 6 (7.0 g, 38.5 mmol) in pyridine (120 ml) was added triflic acid (7.4 ml, 45.0 mmol) in a dropwise fashion and the reaction mixture stirred for 20 h at room temperature. The reaction was quenched with water (350 ml) and then 2N HCl (400 ml) was added. The mixture was acidified to pH 1 with conc. HCl and extracted with EtOAc (3 × 350 ml). The combined organic layers were washed with satd. NaHCO$_3$ solution (200 ml) and dried with MgSO$_4$. Filtration and evaporation of the solvents gave pure triflate 7 (11.2 g, 93%) as a pale yellow solid. TLC (PE/EtOAc, 4:1): $R_f = 0.33$; mp = 37 °C; $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta$[ppm] = 3.87 (s, 3H, COOCH$_3$), 3.93 (s, 3H, OCH$_3$), 6.93 (d, $J = 8.5$ Hz, 1H, C$_3$-H), 6.96 (d, $J = 8.5$ Hz, 1H, C$_5$-H), 7.44 (t, $J = 8.5$ Hz, 1H, C$_4$-H); $^{13}$C NMR (100 MHz, C$_6$D$_6$): $\delta$[ppm] = 52.7 (COOCH$_3$), 56.5 (OCH$_3$), 111.2 (C$_5$), 113.4 (C$_3$), 117.4 (C$_4$), 118.5 (CF$_3$), 131.9 (C$_1$), 146.8 (C$_6$), 158.3 (C$_2$), 163.5 (C=O).

**2S)-1,2,5-Pentanetriol (8).** To a cooled (0 °C) suspension of LiAlH$_4$ (29.6 g, 0.78 mol) in THF (600 ml) was added dropwise a solution of 5-oxotetrahydrofuran-2-carboxylic acid$^+$ (39.0 g, 0.30 mol) in THF (500 ml). After complete addition, the reaction mixture was refluxed for 20 h, cooled to room temperature and neutralized with 20% H$_2$SO$_4$. The inorganic salts were filtered off and washed with
THF (100 ml). After concentration of the filtrate in vacuo, the remaining water was distilled off in high vacuo ($5 \times 10^{-2}$ mbar, 60 °C) to give the pure pentanetriol 8 (25.5 g, 70%) as a colorless liquid. $^1$H NMR (250 MHz, D$_2$O): $\delta$[ppm] = 1.62-2.05 (m, 4H, C$_4$-H, C$_3$-H), 3.54 (dd, $J = 11.6, 7.1$ Hz, 1H, C$_7$-Ha), 3.63-3.71 (m, 3H, C$_2$-H, C$_5$-H), 3.73-3.82 (m, 1H, C$_1$-Hb), 4.80 (s, 3H, OH); $^{13}$C NMR (63MHz, D$_2$O): $\delta$[ppm] = 30.2 (C$_4$), 31.4 (C$_3$), 64.2 (C$_5$), 68.0 (C$_1$), 74.1 (C$_2$).

(2S)-1,2-O-Isopropylidene-5-O-benzylpentane-1,2,5-triol (9).

(a) (2S)-1,2-O-Isopropylidenepentane-1,2,5-triol. To a solution of the triol 8 (20.0 g, 166.7 mmol) and 2,2-dimethoxypropane (160.0 ml, 1.3 mol) in acetone (800 ml) was added (±)-camphersulfonic acid (4.0 g, 17.2 mmol) and the reaction mixture stirred for 3 h at 35 °C and for further 12 h at room temperature. The reaction was quenched by addition of triethylamine (24 ml) before the solvent was removed in vacuo. The residue was dissolved in EtOAc (40 ml), the ammonium salt filtered off and washed with EtOAc (100 ml). The filtrate was concentrated in vacuo and the residue redissolved in EtOAc (750 ml). To this solution was added (±)-camphersulfonic acid (4.9 g, 21.1 mmol) and the mixture stirred for 10 min (cleavage of the mixed acetal at the primary OH). The reaction was quenched by addition of a 10% K$_2$CO$_3$ solution (750 ml). The layers were separated and the aqueous layer was extracted with EtOAc (300 ml). The combined organic layers were dried with MgSO$_4$, filtered, and concentrated in high vacuo to give the pure primary alcohol (24.3 g, 136.3 mmol, 91%) as a colorless liquid. TLC (PE/EtOAc, 1:4): $R_f = 0.37$; $^1$H NMR (250 MHz, CDCl$_3$): $\delta$[ppm] = 1.33, 1.38 (2 s, 3H each, CH$_3$), 1.56-1.71 (m, 4H, C$_4$-H, C$_3$-H), 2.44 (s, 1H, OH), 3.50 (t, $J = 7.1$ Hz, 1H, C$_7$-Ha), 3.57-3.68 (m, 2H, C$_2$-H), 4.02 (t, $J = 7.1$ Hz, 1H, C$_1$-Hb), 4.02-4.14 (m, 1H, C$_5$-H); $^{13}$C NMR (63 MHz, CDCl$_3$): $\delta$[ppm] = 25.7 (CH$_3$), 26.8 (CH$_3$), 29.1 (C$_3$), 30.2 (C$_3$), 62.5 (C$_5$), 69.4 (C$_1$), 75.9 (C$_2$), 108.9 (CH$_3$CCH$_3$).

(b) (2S)-1,2-O-Isopropylidene-5-O-benzylpentane-1,2,5-triol (9). To a suspension of NaH (6.9 g, 60% in mineral oil, 171.8 mmol) in THF (400 ml) was added dropwise the primary alcohol (25.0 g, 156.3 mmol) in THF (yy ml). After complete addition, stirring was continued for 45 min. This was
followed by the dropwise addition of benzylbromide (20.4 ml, 171.8 mmol). The solution was stirred for 16 h, then the mixture diluted with Et₂O (1000 ml), washed with a 10% K₂CO₃ solution (370 ml) and brine (200 ml). Drying of the organic layer with MgSO₄, filtration and evaporation of the solvents gave the crude protected triol 9 (40.6 g) which can be used for the next step without further purification. For analytical purposes a small portion was distilled in vacuo to give the pure triol 9 (84%). TLC (PE/EtOAc, 6:1): Rₜ = 0.58; bp = 83°C (75 mm Hg); ¹H NMR (250 MHz, CDCl₃): δ[ppm] = 1.37, 1.40 (2 s, 3H each, CH₃), 1.58-1.80 (m, 4H, C₄-H, C₃-H), 3.50 (m, 3H, C₁-Ha, C₅-H), 3.99-4.14 (m, 2H, C₂-H, C₁-Hb), 4.49 (s, 2H, CH₂C₆H₅), 7.23-7.37 (m, 5H, C₆H₅); ¹³C NMR (63 MHz, CDCl₃): δ[ppm] = 25.8 (CH₃), 26.1 (CH₃), 26.9 (C₄), 30.9 (C₃), 69.4 (C₁), 70.0 (C₁), 72.9 (CH₂Ph), 75.9 (C₂), 108.7 (CH₃CCH₃), 127.6 (C₄[C₆H₅]), 127.7 (C₂[C₆H₅]), 128.5 (C₁[C₆H₅]), 138.6 (C₁[C₆H₅]).

(2S)-1,2-Epoxy-5-benzyloxy-pentane (10).

(2S)-5-O-Benzylpentane-1,2,5-triol. The crude protected triol 9 (40.6 g) was dissolved in 80% acetic acid (180 ml) and stirred for 3 h at room temperature. The reaction was then quenched with a 12 N NaOH solution (180 ml), followed by the addition of a satd. NaHCO₃ solution (180 ml). This mixture was extracted with EtOAc (3 × 700 ml). The combined organic layers were dried with MgSO₄, filtered, concentrated and purified by flash chromatography (PE/EtOAc, 2:1) to provide the pure 1,2-diol (27.3 g, 130.2 mmol, 78% for 2 steps, 93% for this step) as a colorless liquid. TLC (PE/EtOAc, 1:4): Rₜ = 0.28; [α]²⁰D = -4.83° (c = 1.0, CHCl₃); ¹H NMR (400 MHz, C₆D₆): δ[ppm] = 1.36-1.41 (m, 2H, C₃-H), 1.51-1.61 (m, 1H, C₄-Ha), 1.62-1.70 (m, 1H, C₄-Hb), 3.25 (t, J = 6.1 Hz, 2H, C₅-H), 3.30 (s, 1H, C₁-Ha), 3.41 (s, 1H, C₁-Hb), 3.54 (s, 1H, C₂-H), 4.27 (s, 2H, CH₂Ph), 7.10 (d, J = 7.3 Hz, 1H, C₄[C₆H₅]-H), 7.18 (dd, J = 7.3, 7.3 Hz, 2H, C₃[C₆H₅]-H), 7.27 (d, J = 7.3 Hz, 2H, C₂[C₆H₅]-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 26.4 (C₄), 30.7 (C₃), 67.0 (C₁), 70.5 (C₅), 72.2 (C₂), 73.0 (CH₂Ph), 127.8 (C₄[C₆H₅]), 128.0 (C₂[C₆H₅]), 128.6 (C₃[C₆H₅]), 139.0 (C₁[C₆H₅]).

(2S)-1,2-Epoxy-5-benzyloxy-pentane (10). A solution of the 1,2-diol (21.0 g, 100.0 mmol) and trimethylorthoacetate (15.3 ml, 120.0 mmol) in CH₂Cl₂ (150 ml) was treated with PPTS (251 mg, 1.0
mmol) and the reaction mixture stirred for 20 min. The solution was concentrated in vacuo and redissolved in CH₂Cl₂ (150 ml) followed by addition of acetyl bromide (8.9 ml, 120.0 mmol). Stirring was continued for 45 min and then the solvent removed in vacuo. The residue was dissolved in MeOH (350 ml), K₂CO₃ (18 g, 130.0 mmol) was added, and the mixture stirred for 2 h. Then it was poured into a satd. NH₄Cl solution (650 ml) and extracted with CH₂Cl₂ (3 × 500 ml). Drying of the combined organic layers with MgSO₄, filtration, and evaporation of the solvents afforded the pure epoxide 10 (29.1 g, 99.4 mol, 99%) as colorless liquid. TLC (PE/EtOAc, 6:1): Rₛ = 0.50; [α]₂⁰_D = -7.4° (c = 2.08, CHCl₃); ¹H NMR (400 MHz, C₆D₆): δ[ppm] = 1.34-1.48 (m, 2H, C₃-H), 1.49-1.63 (m, 2H, C₄-H), 2.06-2.08 (m, 1H, C₁-Ha), 2.31-2.34 (m, 1H, C₄-Hb), 2.57-2.62 (m, 1H, C₅-H), 3.20-3.29 (m, 2H, C₅-H), 4.28 (s, 2H, CH₂Ph), 7.10 (d, J = 7.3 Hz, 1H, C₄[C₆H₅]-H), 7.19 (dd, J = 7.3, 7.3 Hz, 2H, C₃[C₆H₅]-H), 7.27 (d, J = 7.3 Hz, 2H, C₂[C₆H₅]-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 26.6 (C₄), 29.6 (C₃), 46.3 (C₂), 51.6 (C₁), 69.9 (C₅), 72.9 (CH₂Ph), 127.6 (C₄[C₆H₅]), 127.7 (C₃[C₆H₅]), 128.5 (C₂[C₆H₅]), 139.4 (C₁[C₆H₅]).

1-Triethylsilyloxy-3-(1,3-dithian-2-yl)propane (11).

3-(1,3-Dithian-2-yl)-1-propanol. To a solution of 2,3-dihydrofuran (35.0 g, 0.50 mol) in CH₂Cl₂ and methanol (40.5 ml, 1.00 mol) was added BF₃•Et₂O (19.0 ml, 0.15 mol) dropwise at room temperature. Stirring of the mixture was continued for 20 min, followed by the addition of 1,3-propanethiol (50.2 ml, 0.50 mol). After additional 2 h of stirring at room temperature, the reaction mixture was diluted with CH₂Cl₂ (400 ml), washed with water (150 ml), 20% NaHCO₃ solution, and water (3 × 75 ml). Drying of the organic layer with MgSO₄, filtration, evaporation of the solvent and distillation of the residue in high vacuo provided the dithianylalcohol (78.7 g, 0.44 mol, 88%) as a colourless liquid. TLC (PE/EtOAc, 1:1): Rₛ = 0.47; bp = 110 °C (0.5 mm Hg); ¹H NMR (400 MHz, C₆D₆): δ[ppm] = 1.41-1.48 (m, 1H, C₅-Ha), 1.53-1.63 (m, 1H, C₅-Hb), 1.66 (tt, J = 7.9, 6.3 Hz, 2H, C₂-H), 1.83 (dt, J = 7.9, 6.9 Hz, 2H, C₁-H), 2.31-2.42 (m, 4H, C₄-H), 3.29 (t, J = 6.3 Hz, 2H, C₅-H), 3.87 (t, J = 6.9 Hz,
1H, C₂-H); \(^{13}C\) NMR (100 MHz, \(\text{C}_6\text{D}_6\)): \(\delta\,[\text{ppm}] = 26.1\ (C_5), 30.1\ (C_2), 30.2\ (C_4), 32.3\ (C_3), 47.7\ (C_1), 62.0\,(C_6).\)

1-Triethylsilyloxy-3-(1,3-dithian-2-yl)propane (11). To a solution of the forgoing alcohol (49.2 g, 276.5 mmol) and DMAP (6.8 g, 55.7 mmol) in pyridine (350 ml), chlorotriethylsilane (55.7 ml, 331.7 mmol) was added dropwise and stirring was continued for 20 h at room temperature. The reaction mixture was diluted with \(\text{CH}_2\text{Cl}_2\) (700 ml) and washed with satd. NaHCO₃ solution. The aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) (2 × 350 ml). Drying of the combined organic layers with \(\text{MgSO}_4\), filtration and evaporation of the solvent afforded the pure protected dithianylalcohol 11 (80.7 g, 276.5 mmol, 100%) as a colourless liquid. TLC (PE/EtOAc, 1:1): \(R_f = 0.78\); \(^1\)H NMR (400 MHz, \(\text{C}_6\text{D}_6\)): \(\delta\,[\text{ppm}] = 0.57\ (q, \ J = 8.1\ Hz, 6\text{H}, \text{CH}_3\text{C}_2\text{H}_2), 0.99\ (t, \ J = 8.1\ Hz, 9\text{H}, \text{CH}_3), 1.40\text{-}1.48\ (m, 1\text{H}, C_5\text{-Ha}), 1.53\text{-}1.65\ (m, 1\text{H}, C_5\text{-Hb}), 1.81\ (tt, \ J = 7.6, 6.1\ Hz, 2\text{H}, C_2\text{-H}), 1.96\ (dt, \ J = 6.9, 7.6\ Hz, 2\text{H}, C_3\text{-H}), 2.31\text{-}2.42\ (m, 4\text{H}, C_4\text{-H}), 3.48\ (t, \ J = 6.1\ Hz, 2\text{H}, C_4\text{-H}), 3.92\ (t, \ J = 6.9\ Hz, 1\text{H}, C_2\text{-H}); \(^{13}C\) NMR (100 MHz, \(\text{C}_6\text{D}_6\)): \(\delta\,[\text{ppm}] = 4.8\ (\text{CH}_3\text{CH}_2), 7.1\ (\text{CH}_3), 26.1\ (C_5), 30.29\ (C_2), 30.34\ (C_4), 32.4\ (C_3), 47.8\ (C_2), 62.3\ (C_1);\) MS (EI, 70 eV), \(m/z\) (%): 292 (18), 263 (35), 217 (20), 132 (60), 103 (45), 71 (100), 57 (50); HRMS (EI): calcd for \([\text{C}_{13}\text{H}_{28}\text{OS}_2\text{Si}]\): 292.135083, found 292.133756.

(6S)-1-Triethylsilyloxy-4,4-S-S-propylidene-6-hydroxy-9-benzyloxy-nonane (12). To a solution of the dithiane 11 (28.8 g, 98.6 mmol) in THF (340 ml) and TMEDA (29.8 ml, 197.2 mmol) was added t-BuLi (65.7 ml, 1.5 M in pentane, 98.6 mmol) at \(-20\ ^{\circ}\)C. The mixture was stirred for 3 h \(-20\ ^{\circ}\)C, before the epoxide 10 (9.5 g, 49.3 mmol) was added, followed by further 2 h stirring at \(-20\ ^{\circ}\)C. The reaction mixture was allowed to reach \(-5\ ^{\circ}\)C, then quenched with water (100 ml) and diluted with \(\text{Et}_2\text{O}\) (600 ml). The layers were separated and the aqueous layer was extracted with \(\text{Et}_2\text{O}\) (2 × 300 ml). The combined organic layers were washed with water (200 ml), brine (200 ml) and dried with \(\text{MgSO}_4\). Filtration, evaporation of the solvents and flash chromatography (PE/EtOAc, 5:1) recycled the dithiane 11 (11.5 g, 39.4 mmol, 40%) and provided the title compound 12 (21.2 g, 89%) as a colorless liquid. TLC (PE/EtOAc, 4:1): \(R_f = 0.51\); \([\alpha]_D^{20} = +10.1^\circ\ (c = 2.16, \text{CHCl}_3);\) \(^1\)H NMR (400 MHz, \(\text{C}_8\text{D}_8\)):
δ[ppm] = 0.60 (q, J = 8.1 Hz, 6H, CH₂CH₃), 1.01 (t, J = 8.1 Hz, 9H, CH₃), 1.37-1.49 (m, 2H, SCH₂CH₂CH₂S), 1.51-1.60 (m, 1H, C₇-Ha), 1.61-1.70 (m, 1H, C₇-Hb), 1.72-1.85 (m, 2H, C₈-Ha, C₂-Ha), 1.86-1.97 (m, 3H, C₉-Hb, C₇-H, C₂-Hb), 2.07-2.15 (m, 1H, C₇-Ha), 2.17-2.21 (m, 1H, C₇-Hb), 2.24-2.45 (m, 4H, SCH₃CH₂CH₂S, C₅-Hb), 2.51-2.57 (m, 1H, CH₃CH₂CH₂S), 3.36-3.40 (m, 2H, CH₂Ph), 3.41 (d, J = 2.3 Hz, 1H, OH), 3.53 (t, J = 6.1 Hz, 2H, C₇-H), 4.11-4.18 (m, 1H, C₆-H), 4.34 (s, 2H, CH₂Ph), 7.10 (d, J = 7.3 Hz, 1H, C₄[C₆H₅]-H), 7.18 (dd, J = 7.3, 7.3 Hz, 2H, C₃[C₆H₅]-H), 7.31 (d, J = 7.3 Hz, 2H, C₃[C₆H₅]-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 4.9 (CH₃CH₂), 7.1 (CH₃), 25.2 (SCH₂CH₂CH₂S), 26.0 (SCH₂CH₂CH₂S), 26.3 (SCH₂CH₂CH₂S), 26.4 (C₂), 28.1 (C₂), 35.6 (C₇), 36.4 (C₈), 45.7 (C₉), 52.6 (C₉), 62.8 (C₉), 68.2 (C₉), 70.6 (C₉), 73.0 (CH₂Ph), 127.5 (C₁[C₆H₅]), 127.8 (C₁[C₆H₅]), 128.5 (C₁[C₆H₅]), 139.4 (C₁[C₆H₅]); MS (EI, 70eV), m/z (%): 484 (10), 377 (10), 291 (10), 277 (10), 179 (25), 91 (100), 71 (55); HRMS (EI): calcd for [C₂₅H₄₄O₃S₂Si] 484.250103, found 484.251379.

(6S)-1,6-Dihydroxy-9-benzyloxy-nonan-4-one (13). To a solution of the dithiane 12 (8.7 g, 18.0 mmol) in THF (435 ml), diisopropylamine (7.2 ml, 51.4 mmol) was added. The reaction mixture was stirred for 20 min and then a solution of HgClO₄·xH₂O (x = 3-5, 18.2 g, 39.6 mmol) in THF (80 ml) was added dropwise over a period of 1 h. The reaction was monitored by TLC (PE/EtOAc, 4:1 and 1:4) and when the starting material was completely consumed, the reaction was immediately diluted with Et₂O (1000 ml) and quenched with a 5% Na₂CO₃ solution (380 ml). The layers were separated and the organic layer was washed with brine (200 ml) and dried with MgSO₄. Filtration, evaporation of the solvent and flash chromatography (PE/EtOAc, 1:6) afforded the dihydroxyketone 13 (4.5 g, 16.1 mmol, 90%) as a colorless liquid. TLC (PE/EtOAc, 1:6): Rf = 0.23; [α]D₂₀ = +13.2° (c = 2.1, CHCl₃);

¹H NMR (400 MHz, C₆D₆): δ[ppm] = 1.39-1.52 (m, 2H, C₇-H), 1.56-1.69 (m, 3H, C₈-Ha, C₇-H), 1.70-1.79 (m, 1H, C₉-Hb), 2.08 (dd, J = 3.3, 16.4 Hz, 1H, C₅-Ha), 2.17 (t, J = 7.1 Hz, 2H, C₇-H), 2.27 (dd, J = 9.4, 16.4 Hz, 1H, C₉-Hb), 3.32 (dt, J = 2.3, 6.1 Hz, 2H, C₅-H), 3.39 (t, J = 5.8 Hz, 2H, C₇-H), 3.97-4.06 (m, 1H, C₉-H), 4.31 (s, 2H, CH₂Ph), 7.10 (d, J = 7.3 Hz, 1H, C₁[C₆H₅]-H), 7.20 (dd, J = 7.3, 7.3
Hz, 2H, C₆H₅-H); 7.30 (d, J = 7.3 Hz, 2H, C₆H₅-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 26.3 (C₈), 26.7 (C₂), 34.2 (C₇), 40.1 (C₃), 49.8 (C₄), 61.7 (C₁), 67.8 (C₅), 70.4 (C₆), 73.0 (CH₂C₆H₅), 127.7 (C₁[C₆H₅]), 127.8 (C₂[C₆H₅]), 128.6 (C₃[C₆H₅]), 139.2 (C₄[C₆H₅]), 211.1 (C₉); HRMS (EI): calcd for [C₆H₂O (M + H⁺ - 2H₂O)] 245.154146, found 245.150701.

(4R,6S)-9-(Benzyloxy)-1,4,6-nonanetriol (14). To a cooled solution (-78 °C) of the dihydroxyketone 13 (4.4 g, 15.7 mmol) in THF/MeOH (4:1, 180 ml) was added diethoxymethylborane (34.6 ml, 1.0 M in THF, 34.6 mmol) dropwise. After being stirred for 30 min at this temperature, NaBH₄ (654.0 mg, 17.3 mmol) was added and the mixture stirred for further 3 h at -78 °C. The reaction was quenched with water (76 ml) and allowed to reach room temperature. The mixture was extracted with EtOAc (3 × 380 ml), the combined organic layers were dried with MgSO₄, filtered and concentrated in vacuo. The residue was dissolved in dry MeOH (50 ml), stirred for 20 min, and then concentrated in vacuo. This procedure was repeated five times to cleave the boronic acid ester intermediate. Flash chromatography (PE/EtOAc, 1:4) afforded the triol 14 (4.1 g, 14.6 mmol, 93%) as a white solid. TLC (PE/EtOAc, 1:4): Rᵣ = 0.20; mp = 39 °C; [α]D⁰ = +1.2° (c = 2.0, CHCl₃); ¹H NMR (400 MHz, C₆D₆): δ[ppm] = 1.22-1.26 (m, 1H, C₅-Ha), 1.41-1.51 (m, 4H, C₃-H₃, C₇-H₇), 1.53-1.61 (m, 3H, C₂-H₂, C₅-Hb), 1.63-1.73 (m, 2H, C₆-H₆), 3.20 (t, J = 5.9 Hz, 2H, C₅-Hb), 3.49-3.59 (m, 2H, C₁-H₁), 3.69-3.81 (m, 2H, C₄-H₄, C₆-H₆), 4.29 (s, 2H, CH₂Ph), 7.10 (d, J = 7.3 Hz, 1H, C₄[C₆H₅]-H), 7.17 (dd, J = 7.3, 7.3 Hz, 2H, C₃[C₆H₅]-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 26.3 (C₈), 29.4 (C₂), 35.7 (C₇), 35.8 (C₃), 43.5 (C₄), 62.8 (C₁), 70.6 (C₅), 72.68 (C₆), 72.69 (C₉), 73.1 (CH₂Ph), 127.6 (C₃[C₆H₅]), 127.7 (C₄[C₆H₅]), 128.6 (C₅[C₆H₅]), 139.2 (C₆[C₆H₅]); MS (EI, 70eV), m/z (%): 283 (0.6), 223 (1), 205 (1.5), 160 (15), 115 (15), 91 (100), 71 (35); HRMS (FT-ICR): calcd for [C₁₆H₂₁O₂ + Na⁺] 305.1723304, found 305.1720.

(4R,6S)-4,6-O-Isopropylidene-9-(benzyloxy)-1,4,6-nonanetriol (15). To a solution of the triol 14 (7.7 g, 27.3 mmol) in 2,2-dimethoxpropane (196.7 ml, 1.6 mol) was added (±)-camphersulfonic acid (158.5 mg, 0.682 mmol). The reaction mixture was stirred for 40 min, quenched with satd. NaHCO₃
solution (110 ml) and stirred for further 20 min. The mixture was diluted with water (130 ml) and extracted with EtOAc (3 × 290 ml). The combined organic layers were washed with brine (130 ml), dried with MgSO₄ and concentrated in vacuo. The residue was redissolved in EtOAc (160 ml) and (±)-camphersulfonic acid (158.5 mg, 0.682 mmol) was added in order to cleave the mixed acetal at the primary hydroxyl group. The reaction was quenched with a 10% K₂CO₃ solution (100 ml) and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 320 ml) and the combined organic layers were washed with brine (120 ml) and dried with MgSO₄. Filtration, evaporation of the solvent and flash chromatography (PE/EtOAc, 1:1) afforded the alcohol 15 (8.5 g, 26.4 mmol, 97%) as a colorless liquid. TLC (PE/EtOAc, 1:1): Rf = 0.41; [α]D₂⁰ = +3.1° (c = 0.96, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ[ppm] = 1.00-1.13 (m, 2H, C₅-H), 1.28 (s, 3H, CH₃), 1.32-1.40 (m, 1H, C₃-Ha), 1.43-1.56 (m, 4H, C₆-Hb, C₇-Ha, C₇-H), 1.50 (s, 3H, CH₃), 1.57-1.63 (m, 1H, C₇-Hb), 1.64-1.70 (m, 1H, C₆-Ha), 1.74-1.84 (m, 1H, C₆-Hb), 3.27-3.39 (m, 2H, C₇-H), 3.45-3.50 (m, 2H, C₈-H), 3.51-3.61 (m, 2H, C₄-H, C₆-H), 4.34 (s, 2H, CH₂Ph), 7.11 (d, J = 7.3 Hz, 1H, C₄-C₆H₅-H), 7.18 (dd, J = 7.3, 7.3 Hz, 2H, C₃-C₆H₅-H), 7.31 (d, J = 7.3 Hz, 2H, C₄-C₆H₅-H); ¹³C NMR (100 MHz, CDCl₃): δ[ppm] = 19.8 (CH₃), 25.9 (C₅), 29.2 (C₆), 30.5 (CH₃), 33.5 (C₇), 33.6 (C₅), 37.4 (C₆), 62.7 (C₇), 68.9 (C₈), 69.2 (C₈), 70.4 (C₆), 73.0 (CH₂Ph), 98.6 ((CH₃)₂C), 127.6 (C₄-C₆H₅), 127.7 (C₃-C₆H₅), 128.5 (C₅-C₆H₅), 139.5 (C₆-C₆H₅); MS (EI, 70eV), m/z (%): 322 (0.5), 307 (1), 265 (1), 247 (6), 205 (10), 155(20), 91 (100), 71 (40); HRMS (EI): calcd for [C₁₈H₂₇O₄] (M - CH₃) 307.190916, found 307.188882.

(4R,6S)-1-Methylsulfonyloxy-4,6-O-Isopropylidene-9-(benzyloxy)-4,6-nonanediol (16). To a cooled solution (ice-bath) of the alcohol 15 (7.0 g, 21.7 mmol) and diisopropylamine (5.2 ml, 30.4 mmol) in CH₂Cl₂ was added methansulfonylchloride (2.0 ml, 26.1 mmol) dropwise over a period of 5 min. The resulting mixture was allowed to reach room temperature over a period of 20 min. The mixture was diluted with Et₂O (630 ml) and poured into satd NaHCO₃ solution (380 ml). The layers were separated and the aqueous layer extracted with Et₂O (2 × 380 ml). The combined organic layers were washed with brine (250 ml) and dried with MgSO₄. Filtration and evaporation of the solvents
provided the crude mesylate 16 (10.3 g, 93%) which can be used for the next step without further purification. For analytical purposes, a small portion was purified by flash chromatography (PE/EtOAc, 2:1). TLC (PE/EtOAc, 2:1): Rf = 0.40; [α]D20 = +2.1° (c = 1.04, CHCl3); 1H NMR (400 MHz, C6D6): δ[ppm] = 0.95-1.04 (m, 2H, C5-H), 1.19-1.28 (m, 1H, C7-Ha), 1.26 (s, 3H, CH3), 1.29-1.37 (m, 1H, C7-Hb), 1.47 (s, 3H, CH3), 1.48-1.53 (m, 2H, C3-Ha, C7-Ha), 1.56-1.71 (m, 3H, C7-Hb, C8-Ha, C7-Hb, C8-Ha), 1.74-1.84 (m, 1H, C3-Hb), 2.20 (s, 3H, SO2CH3), 3.31-3.39 (m, 2H, C3-H), 3.40-3.47 (m, 1H, C3-H), 3.54-3.60 (m, 1H, C6-H), 3.81-3.87 (m, 1H, C1-Ha), 3.88-3.94 (m, 1H, C1-Hb), 4.34 (s, 2H, CH2Ph), 7.12 (d, J = 7.3 Hz, 1H, C4[6H5]-H), 7.19 (dd, J = 7.3, 7.3 Hz, 2H, C3[6H5]-H), 7.31 (d, J = 7.3 Hz, 2H, C2[6H5]-H); 13C NMR (100 MHz, C6D6): δ[ppm] = 19.8 (CH3), 25.3 (C2), 25.9 (C3), 30.5 (CH2), 32.3 (C4), 33.5 (C5), 36.6 (SO2CH3), 37.2 (C6), 68.3 (C4), 68.8 (C5), 69.6 (C6), 70.4 (C8), 73.0 (CH2Ph), 98.5 (C1[6H5]), 127.6 (C2[6H5]), 127.7 (C2[6H5]), 128.5 (C3[6H5]), 139.4 (C4[6H5]); MS (EI, 70eV), m/z (%): 385 (5), 235 (30), 160 (10), 91 (100), 71 (30); HRMS (EI): calcd for [C19H29O6S](M-CH3): 385.168458, found 385.166300.

(4R,6S)-1-Iodo-4,6-O-isopropylidene-9-(benzyloxy)-4,6-nonanediol (17). To a solution of the crude mesylate 16 (10.3 g) in acetone (210 ml), NaI (13.0 g, 87.0 mmol) was added. After stirring for 48 h the mixture was diluted with EtOAc (350 ml) and diluted with water (175 ml). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 350 ml). The combined organic layers were washed with brine (150 ml) and dried with MgSO4. Filtration and evaporation of the solvents afforded the crude iodide 17 (9.3 g, 86% for 2 steps, 92% for this step), which can be used for the next step without further purification. For analytical purposes, a small portion was purified by flash chromatography (PE/EtOAc, 9:1). TLC (PE/EtOAc, 9:1): Rf = 0.46; [α]D20 = +2.3° (c = 0.90, CHCl3); 1H NMR (400 MHz, C6D6): δ[ppm] = 0.91-1.03 (m, 2H, C5-H), 1.23 (s, 3H, CH3), 1.19-1.28 (m, 1H, C5-Ha), 1.30-1.37 (m, 1H, C5-Hb), 1.47 (s, 3H, CH3), 1.44-1.52 (m, 1H, C7-Ha), 1.53-1.84 (m, 5H, C7-Hb, C8-H, C2-H), 2.72-2.82 (m, 2H, C1-H), 3.30-3.40 (m, 2H, C9-H), 3.38-3.44 (m, 1H, C8-H), 3.50-3.57 (m, 1H, C9-H), 4.35 (s, 2H, CH2Ph), 7.11 (d, J = 7.3 Hz, 1H, C4[6H5]-H), 7.19 (dd, J = 7.3, 7.3 Hz, 2H,
C₃[H₃]-H), 7.31 (d, J = 7.3 Hz, 2H, C₃[H₃]-H); ¹³C NMR (100 MHz, CD₂Cl₂): δ[ppm] = 6.8 (C₁), 19.8 (C₅), 25.9 (C₆), 29.6 (C₇), 30.5 (CH₂-C-CH₃), 33.5 (C₈), 37.3 (C₉), 37.4 (C₁₀), 68.1 (C₁₁), 68.8 (C₄), 70.4 (C₁₂), 73.0 (CH₂Ph), 98.4 ((CH₂)₃), 127.6 (C₄[C₆H₅]), 127.7 (C₅[C₆H₅]), 128.5 (C₆[C₆H₅]), 139.5 (C₇[C₆H₅]); MS (EI, 70eV), m/z (%): 417 (10), 374 (5), 283 (10), 207 (35), 91 (100), 71 (20); HRMS (EI): calcd for [C₁₈H₂₆IO₃] (M - CH₃): 417.092684, found 417.094761.

(4S,6R)-1-Benzyloxy-4,6-O-isopropylidene-10-undecyne-4,6-diol (18). Lithium acetylide-ethylendiamine (4.0 g, 43.5 mmol) was suspended in DMSO (140 ml) and stirred for 30 min. The crude iodide 17 (9.3 g), dissolved in DMSO (110 ml) was added to the suspension and the resulting mixture was stirred at room temperature for 4 d before it was quenched with water (70 ml). The mixture was extracted with Et₂O (3 × 900 ml), the combined organic layers were washed with water (200ml), brine (200 ml), and dried with MgSO₄. Filtration, evaporation of the solvents and flash chromatography of the residue (PE/EtOAc, 9:1) provided the acetylene 18 (4.7 g, 14.3 mmol, 66% for 3 steps, 77% for this step) as a colorless liquid. TLC (PE/EtOAc, 9:1): Rᵣ = 0.52; [α]D²⁰ = +2.1° (c = 2.12, CHCl₃); ¹H NMR (400 MHz, C₆D₆): δ[ppm] = 0.97-1.07 (m, 2H, C₅-H), 1.25 (s, 3H, CH₃), 1.32-1.37 (m, 1H, C₇-Ha), 1.39-1.52 (m, 3H, C₈-Ha, C₃-Ha, C₇-Hb), 1.48 (s, 3H, CH₃), 1.54-1.70 (m, 3H, C₃-Hb, C₈-Hb, C₇-Ha), 1.74-1.82 (m, 1H, C₂-Hb), 1.81 (t, J = 2.6 Hz, 1H, C₁₁-H), 1.97-2.02 (m, 2H, C₉-H), 3.29-3.39 (m, 2H, C₁-H), 3.46-3.52 (m, 1H, C₆-H), 3.52-3.59 (m, 1H, C₄-H), 4.34 (s, 2H, CH₂Ph), 7.11 (d, J = 7.3 Hz, 1H, C₄[C₆H₅]-H), 7.19 (dd, J = 7.3, 7.3 Hz, 2H, C₃[C₆H₅]-H), 7.31 (d, J = 7.3 Hz, 2H, C₂[C₆H₅]-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 18.6 (C₉), 19.8 (CH₃), 24.5 (C₈), 25.9 (C₇), 30.6 (CH₃), 33.5 (C₅), 35.7 (C₆), 37.4 (C₇), 68.5 (C₈), 68.8 (C₉), 69.0 (C₁₀), 70.4 (C₁₁), 72.9 (CH₂Ph), 84.3 (C₁₂), 98.4 ((CH₂)₃), 127.6 (C₄[C₆H₅]), 127.7 (C₅[C₆H₅]), 128.5 (C₆[C₆H₅]), 139.5 (C₇[C₆H₅]); MS (EI, 70eV), m/z (%): 315 (5), 181 (5), 165 (5), 123 (10), 107 (5), 91 (100), 71 (30); HRMS (EI): calcd for [C₂₀H₂₀O₃] (M - CH₃): 315.196006, found 315.197448.

(4S,6R,10E)-1-(Benzyloxy)-4,6-O-isopropylidene-11-(tributylstannyl)-10-undecene-4,6-diol (19). A solution of the acetylene 18 (660.0 mg, 2.0 mmol), tri-n-butyltin hydride (635.4 µl, 2.4 mmol) and
AIBN (50.40 mg, 0.30 mmol) in toluene (10 ml) was refluxed for 16 h. Evaporation of the solvent and flash chromatography (PE/EtOAc, 19:1) of the residue afforded the stannane 19 (1.13 g, 1.82 mmol, 91%) as a colorless liquid. TLC (PE/EtOAc, 19:1): R\textsubscript{f} = 0.43; [\alpha]_{D}^{20} = -0.9° (c = 1.66, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (400 MHz, C\textsubscript{6}D\textsubscript{6}): \delta[ppm] = 0.95 (t, J = 7.3 Hz, 9H, CH\textsubscript{2}CH\textsubscript{3}), 0.94-1.02 (m, 6H, SnCH\textsubscript{2}), 1.02-1.16 (m, 2H, C\textsubscript{3}-H), 1.32 (s, 3H, CH\textsubscript{3}), 1.34-1.44 (m, 7H, C\textsubscript{5}-Ha, CH\textsubscript{2}CH\textsubscript{3}), 1.46-1.57 (m, 2H, C\textsubscript{6}-Ha, C\textsubscript{3}-Ha), 1.52 (s, 3H, CH\textsubscript{3}), 1.57-1.72 (m, 10H, C\textsubscript{7}-Hb, C\textsubscript{5}-Hb, SnCH\textsubscript{2}CH\textsubscript{2}, C\textsubscript{6}-Hb, C\textsubscript{2}-Ha), 1.77-1.87 (m, 1H, C\textsubscript{7}-Hb), 2.15-2.27 (m, 2H, C\textsubscript{9}-H), 3.30-3.40 (m, 2H, C\textsubscript{1}-H), 3.59-3.67 (m, 2H, C\textsubscript{6}-H, C\textsubscript{4}-H), 4.34 (s, 2H, CH\textsubscript{2}Ph), 6.00-6.25 (m, 2H, C\textsubscript{10}-H, C\textsubscript{11}-H), 7.11 (d, J = 7.3 Hz, 1H, C\textsubscript{4}[C\textsubscript{6}H\textsubscript{5}]-H), 7.19 (dd, J = 7.3, 7.3 Hz, 2H, C\textsubscript{3}[C\textsubscript{6}H\textsubscript{5}]-H), 7.31 (d, J = 7.3 Hz, 2H, C\textsubscript{2}[C\textsubscript{6}H\textsubscript{5}]-H); \textsuperscript{13}C NMR (100 MHz, C\textsubscript{6}D\textsubscript{6}): \delta[ppm] = 9.7 (SnCH\textsubscript{2}), 13.9 (CH\textsubscript{2}CH\textsubscript{3}), 19.9(CH\textsubscript{3}), 24.9 (C\textsubscript{5}), 25.9 (C\textsubscript{2}), 27.7 (CH\textsubscript{2}CH\textsubscript{3}), 29.6 (SnCH\textsubscript{2}CH\textsubscript{2}), 30.6 (CH\textsubscript{3}), 33.6 (C\textsubscript{6}), 36.5 (C\textsubscript{3}), 37.6 (C\textsubscript{7}), 38.4 (C\textsubscript{9}), 68.9 (C\textsubscript{4}), 69.0 (C\textsubscript{5}), 70.5 (C\textsubscript{7}), 72.9 (CH\textsubscript{2}Ph), 98.4 (CH\textsubscript{3}), 127.5 (C\textsubscript{10}), 127.6 (C\textsubscript{4}[C\textsubscript{6}H\textsubscript{5}]), 127.7 (C\textsubscript{3}[C\textsubscript{6}H\textsubscript{5}]), 128.5 (C\textsubscript{2}[C\textsubscript{6}H\textsubscript{5}]), 139.5 (C\textsubscript{1}[C\textsubscript{6}H\textsubscript{5}]), 150.0 (C\textsubscript{11}); MS (EI, 70eV), m/z (%): 621 (2), 565 (35), 507 (30), 329 (80), 177 (30), 91 (100), 71 (15); HRMS (EI): calcd for [C\textsubscript{29}H\textsubscript{49}O\textsubscript{3}Sn] (M - C\textsubscript{4}H\textsubscript{9}): 565.270355, found 565.267963.

Methyl 2-[(1\textit{E},6\textit{R},8\textit{S})-11-(benzyloxy)-6,8-dihydroxy-6,8-\textit{O}-isopropylidene-1-undecenyl]-6-methoxybenzoate (20). The triflate 7 (211.0 mg, 0.672 mmol), \textit{tris}-(dibenzylidenacetone)-dipalladium (6.2 mg, 6.7 \textmu mol), \textit{tri}-2-furyl-phoshine (12.5 mg, 53.8 \textmu mol) and LiCl (85.0 mg, 2.0 mmol) were dissolved in \textit{N}-methylpyrrolidine (18 ml) and the mixture was stirred for 10 min, before a solution of the stannane 19 (500 mg, 0.805 mmol) in \textit{N}-methylpyrrolidine (10 ml) was added. The reaction mixture was stirred at 60 °C for 16 h, then it was diluted with PE (280 ml), a satd. KF solution (70 ml), and water (70 ml). The mixture was then stirred for 30 min, filtered and the layers were separated. The aqueous layer was extracted with PE (150 ml) and the combined organic layers were dried with MgSO\textsubscript{4}, filtered and concentrated in vacuo. Flash chromatography (PE/EtOAc, 4:1) of the residue provided the styrene 20 (310.0 mg, 0.625 mmol, 93%) as a colorless liquid. TLC (PE/EtOAc, 4:1): R\textsubscript{f} = 0.50; [\alpha]_{D}^{20} = +1.1° (c = 2.0, CH\textsubscript{2}Cl\textsubscript{2}); \textsuperscript{1}H NMR (400 MHz, C\textsubscript{6}D\textsubscript{6}): \delta[ppm] = 1.03-1.12 (m, 2H, C\textsubscript{7}-H),
1.26-1.36 (m, 1H, C$_5$-Ha), 1.32 (s, 3H, CH$_3$), 1.36-1.44 (m, 1H, C$_4$-H), 1.52 (s, 3H, CH$_3$), 1.47-1.73 (m, 5H, C$_9$-H, C$_5$-Hb, C$_4$-Hb, C$_{10}$-Ha), 1.76-1.87 (m, 1H, C$_{10}$-Hb), 2.04-2.09 (m, 2H, C$_3$-H), 3.23 (s, 3H, OCH$_3$), 3.31-3.41 (m, 2H, C$_{11}$-H), 3.54-3.60 (m, 1H, C$_6$-H), 3.61-3.65 (m, 1H, C$_8$-H), 3.65 (s, 3H, CO$_2$CH$_3$), 4.35 (s, 2H, CH$_2$Ph), 6.17 (dt, J = 15.9, 7.1 Hz, 1H, C$_2$-H), 6.35 (dd, J = 7.8, 1.0 Hz, 1H, C$_3$-H), 6.69 (d, J = 15.9 Hz, 1H, C$_1$-H), 7.03 (t, J = 7.8 Hz, 1H, C$_4$-H), 7.08 (dd, J = 7.8, 1.0 Hz, 1H, C$_5$-H), 7.11 (d, J = 7.3 Hz, 1H, C$_4$[C$_6$H$_5$]-H), 7.19 (dd, J = 7.3, 7.3 Hz, 2H, C$_3$[C$_6$H$_5$]-H), 7.27 (d, J = 7.3 Hz, 2H, C$_2$[C$_6$H$_5$]-H); $^{13}$C NMR (100 MHz, C$_6$D$_6$): $\delta_{[ppm]}$ = 19.9 (CH$_3$), 25.0 (C$_4$), 25.9 (C$_{10}$), 30.7 (CH$_3$), 33.4 (C$_y$), 33.6 (C$_y$), 36.3 (C$_y$), 37.5 (C$_y$), 51.7 (CO$_2$CH$_3$), 55.4 (OCH$_3$), 68.90 (C$_6$), 68.91 (C$_6$), 70.5 (C$_{11}$), 72.9 (CH$_2$Ph), 98.4 (C$_{11}$), 109.5 (C$_y$), 109.7 (C$_y$), 118.0 (C$_y$), 127.3 (C$_y$), 127.5 (C$_4$), 127.7 (C$_2$), 128.5 (C$_3$), 130.1 (C$_y$), 134.3 (C$_y$), 137.1 (C$_y$), 139.5 (C$_1$), 157.0 (C$_1$), 168.3 (C=O); MS (EI, 70eV), m/z (%): 497 (0.5), 481 (2), 439 (5), 406 (10), 389 (10), 347 (10), 91 (100), 71 (25); HRMS (EI): calcd for [C$_{29}$H$_{37}$O$_6$] (M - CH$_3$): 481.258987, found 481.255961.

**Methyl 2-[(1E,6R,8S)-11-(benzyloxy)-6,8-dihydroxy-1-undecenyl]-6-methoxybenzoate (21).** A solution of the methyl benzoate 20 (310.0 mg, 0.625 mmol) in 80% AcOH (15 ml) was stirred for 80 min at room temperature. The reaction was quenched with 12 N NaOH (15 ml) and a satd. NaHCO$_3$ solution (17 ml) with ice-cooling. The mixture was extracted with EtOAc (3 × 50 ml) and the combined organic layers were dried with MgSO$_4$. Filtration, evaporation of the solvent and flash chromatography of the residue (PE/EtOAc, 1:1) provided the methyl dihydroxybenzoate 21 (282.0 mg, 0.618 mmol, 99%) as a colorless liquid. TLC (PE/EtOAc, 1:1): $R_f$ = 0.26; $[\alpha]_{D}^{20} = -0.2^\circ$ (c = 2.0, CHCl$_3$); $^1$H NMR (400 MHz, C$_6$D$_6$): $\delta_{[ppm]}$ = 1.23-1.28 (m, 1H, C$_7$-Ha), 1.29-1.36 (m, 1H, C$_5$-Ha), 1.37-1.50 (m, 5H, C$_9$-H, C$_5$-Hb, C$_4$-Ha, C$_7$-Hb), 1.52-1.57 (m, 1H, C$_4$-Hb), 1.59-1.68 (m, 2H, C$_{10}$-H), 2.06-2.11 (m, 2H, C$_3$-H), 3.22 (s, 3H, OCH$_3$), 3.24-3.30 (m, 2H, C$_{11}$-H), 3.65 (s, 3H, CO$_2$CH$_3$), 3.66-3.73 (m, 2H, C$_8$-H, C$_6$-H), 4.27 (s, 2H, CH$_2$Ph), 6.19 (dt, J = 15.7, 7.1 Hz, 1H, C$_2$-H), 6.35 (dd, J = 7.8, 1.0 Hz, 1H, C$_3$-H), 6.70 (d, J = 15.7 Hz, 1H, C$_1$-H), 7.03 (t, J = 7.8 Hz, 1H, C$_4$-H), 7.08 (m, 1H, C$_5$-H), 7.10 (d, J = 7.3 Hz, 1H, C$_4$[C$_6$H$_5$]-H), 7.17 (dd, J = 7.3, 7.3 Hz, 2H, C$_3$[C$_6$H$_5$]-H), 7.27 (d, J = 7.3
1H NMR (400 MHz, C6D6): δ[ppm] = 1.28-1.80 (m, 10H, C4'-H, C5'-H, C7'-H, C9'-H, C10'-H), 2.12-2.27 (m, 2H, C3'-H), 3.28 (s, 3H, OCH3), 3.32-3.35 (m, 2H, C11'-H), 3.83-3.93 (m, 2H, C8'-H, C6'-H), 4.33 (s, 2H, CH2Ph), 6.21 (dt, J = 15.7, 6.8 Hz, 1H, C2'-H), 6.34 (d, J = 8.1 Hz, 1H, C7'-H), 6.86 (d, J = 15.7 Hz, 1H, C1'-H), 7.03 (t, J = 8.1 Hz, 1H, C5'-H), 7.07 (d, J = 8.1 Hz 1H, C5'-H), 7.11 (d, J = 7.3 Hz, 1H, C1[C6H5]-H), 7.20 (dd, J = 7.3, 7.3 Hz, 2H, C3[C6H5]-H), 7.30 (d, J = 7.3 Hz, 2H, C2[C6H5]-H); 13C NMR (100 MHz, C6D6): δ[ppm] = 24.6 (C4'), 26.2 (C10'), 32.8 (C3'), 35.2 (C5'), 37.0 (C9'), 43.1 (C7'), 55.5 (OCH3), 70.6 (C11'), 72.5 (C8'), 72.6 (C6'), 73.0 (CH2Ph), 109.6 (C6), 118.4 (C3), 123.8 (C1), 127.88 (C4[C6H5]), 127.89 (C1'), 128.1 (C2[C6H5]), 128.6 (C3[C6H5]), 130.8 (C13'), 134.3 (C2'), 137.3 (C7), 139.0 (C1[C6H5]), 156.8 (C6), 170.9 (C=O); MS (EI, 70eV), m/z (%): 443 (5), 424 (5), 406 (40), 388 (15), 315 (10), 187 (15), 185 (30), 155 (20), 91 (100), 71 (35); HRMS (EI): calcd for [C28H28O4] (M+ - CH3 - 2H2O): 406.214391, found 406.212753.
(3S,5R)-3-[3-(benzyloxy)propyl]-5-hydroxy-14-methoxy-3,4,5,6,7,8-hexahydro-1H-2-
benzoxacyclododecin-1-one (23). The dihydroxy benzoic acid 22 (427.0 mg, 0.966 mmol) was
dissolved in THF (20 ml) and triethylamine (160.8 µl, 1.16 mmol) was added. The solution was stirred
for 10 min, then 2,4,6-trichlorobenzoylchloride (165.6 µl, 1.06 mmol) was added and stirring was
continued for 2 h. The reaction mixture was then diluted with toluene (200 ml), transferred to a
dropping funnel and added dropwise to a refluxing solution of DMAP (1.2 g, 9.8 mmol) in toluene
(400 ml) over a period of 2 h. Refluxing was continued for 16 h and before the solution was
concentrated in vacuo. The residue was redissolved in EtOAc (200 ml) and washed with 10% citric
acid (40 ml), a satd. NaHCO₃ solution (40 ml) and brine (40 ml). The organic layer was dried with
MgSO₄, filtered and concentrated in vacuo. Flash chromatography (PE/EtOAc, 2:1) of the residue
provided the 12-membered lactone 23 (203.0 mg, 0.479 mmol, 50%) as a colorless liquid. TLC
(PE/EtOAc, 2:1): Rᵣ = 0.36; [α]ᵣ° = +92.5° (c = 1.0, CH₂Cl₂); ¹H NMR (400 MHz, C₆D₆): δ[ppm] =
1.14-1.25 (m, 1H, C₆-Hₐ), 1.34-1.43 (m, 1H, C₇-Hₐ), 1.48-1.54 (m, 1H, C₇-Hₖb), 1.55-1.71 (m, 3H, C₆-
Hₖb, C₄-H), 1.72-1.87 (m, 3H, C₅-Hₐ, C₂-Hₐ), 1.88-1.94 (m, 1H, C₅-Hₖb), 2.03-2.07 (m, 2H, C₈-H), 3.25
(s, 3H, OCH₃), 3.35-3.42 (m, 2H, C₃ₖ-H), 3.90-3.98 (m, 1H, C₅-H), 4.35 (s, 2H, CH₂Ph), 5.33-5.39 (m,
1H, C₉-H), 5.84 (dt, J = 15.7, 7.1 Hz, 1H, C₉-H), 6.35 (d, J = 8.3 Hz, 1H, C₁₃-H), 6.44 (d, J = 15.7 Hz,
1H, C₁₀-H), 6.75 (d, J = 7.6 Hz, 1H, C₁₁-H), 7.00 (dd, J = 7.6, 8.3 Hz, 1H, C₁₂-H), 7.11 (d, J = 7.3 Hz,
1H, C₁₃[H₆]-H), 7.20 (dd, J = 7.3, 7.3 Hz, 2H, C₁₃[H₆]-H), 7.32 (d, J = 7.3 Hz, 2H, C₁₃[H₆]-H); ¹³C
NMR (100 MHz, C₆D₆): δ[ppm] = 22.2 (C₂), 26.2 (C₂), 32.3 (C₁), 32.7 (C₄), 34.8 (C₅), 41.0 (C₆), 55.4
(OCH₃), 66.3 (C₃), 70.3 (C₃), 72.6 (C₃), 72.9 (CH₂Ph), 109.6 (C₁₃), 120.3 (C₁), 124.8 (C₁₆), 127.5
(C₁₃[H₆]), 127.9 (C₂[H₆]), 128.5 (C₃[H₆]), 129.6 (C₁₀), 129.8 (C₁₁), 135.7 (C₅), 138.1 (C₁₄), 139.5
(C₁[H₆]), 156.5 (C₁₄), 167.6 (C=O); MS (EI, 70eV), m/z (%): 425 (2), 406 (30), 388 (10), 333 (15),
315 (75), 297 (35), 263 (30), 245 (35), 231 (40), 227 (55), 201 (40), 185 (75), 91 (100); HRMS (EI):
Macrolactone (24). To a solution of the lactone 23 (123.0 mg, 0.290 mmol) in CH₂Cl₂ (5 ml) were added (±)-camphersulfonic acid (6.7 mg, 29.0 µmol) and N-phenylselenophthalimide (105.2 mg, 348.1 µmol). After being stirred for 2 h at room temperature, the reaction mixture was diluted with Et₂O (10 ml) and diluted with water (2 ml). The layers were separated, the organic layer was washed with water (2 × 2 ml), brine (2 ml), and dried with MgSO₄. Filtration, evaporation of the solvents and flash chromatography (PE/EtOAc = 4:1) of the residue afforded the pyran 24 (101 mg, 0.174 mmol, 60%) as a yellow oil. TLC (PE/EtOAc, 4:1): Rₜ = 0.50; [α]²₀ = +74.1° (c = 2.5, CH₂Cl₂); ¹H NMR (400 MHz, C₆D₆): δ[ppm] = 0.99-1.14 (m, 3H, C₁₂-H, C₁₄-Ha), 1.23-1.29 (m, C₁₁-H), 1.48-1.68 (m, 3H, C₁₄-Hb, C₁₆-H), 1.70-1.86 (m, 3H, C₁₀-H, C₁₇-Ha), 1.88-1.99 (m, 1H, C₁₇-Hb), 3.21 (s, OCH₃), 3.39-3.51 (m, 2H, C₁₈-H), 3.83 (dt, J = 4.8, 9.6 Hz, 1H, C₁₃-H), 4.06 (dt, J = 19.4, 6.8 Hz, 1H, C₉-H), 4.38 (s, 2H, CH₂Ph), 5.56-5.63 (m, 1H, C₁₅-H), 5.60 (d, J = 10.4 Hz, 1H, C₆-H), 6.24 (d, J = 8.1 Hz, 1H, C₆-H), 6.82 (d, J = 7.6 Hz, 1H, C₆-H), 6.95 (t, J = 8.1 Hz, 2H, C₃[SeC₆H₅]-H), 6.97 (dd, J = 8.1, 7.6 Hz, 1H, C₅-H), 7.12 (d, J = 7.3 Hz, 1H, C₅-H), 7.21 (dd, J = 7.3, 7.3 Hz, 2H, C₃[CH₂C₆H₅]-H), 7.34 (d, J = 7.3 Hz, 1H, C₃[CH₂C₆H₅]-H), 7.53 (d, J = 7.8 Hz, 1H, C₃[SeC₆H₅]-H), 7.69 (d, J = 7.8 Hz, 2H, C₃[SeC₆H₅]-H); ¹³C NMR (100 MHz, C₆D₆): δ[ppm] = 19.2 (C₁ᵢ), 26.2 (C₁₇), 27.5 (C₁₀), 30.6 (C₁₂), 31.6 (C₁₆), 41.9(C₁₄), 46.1 (C₉), 55.4 (OCH₃), 68.0 (C₁₃), 69.9 (C₁₈), 72.9 (CH₂C₆H₅), 73.9 (C₁₅), 80.6 (C₆), 109.7 (C₉), 121.8 (C₃[SeC₆H₅]), 126.8 (C₅), 127.6 (C₃[CH₂C₆H₅]), 127.9 (C₃[CH₂C₆H₅]), 128.5 (C₃[CH₂C₆H₅]), 128.6 (C₃[SeC₆H₅]), 129.4 (C₃[SeC₆H₅]), 130.0 (C₅), 131.5 (C₂), 132.3 (C₂[SeC₆H₅]), 139.5 (C₃[CH₂C₆H₅]), 141.5 (C₇), 155.5 (C₉), 170.2 (C₆); MS (EI, 70eV), m/z (%): 314 (10), 234 (3), 157 (15),...
147 (100), 104 (90), 76 (95), 50 (50); HRMS (FT-ICR): calcd for $[C_{32}H_{36}SeO_5 + Na^+]$ 603.16202, found 603.1607.

Macrolactone (25). To a solution of the selenide 24 (30.0 mg, 0.052 mmol) and tri-n-butylinthide (27.4 µl, 103.5 µmol) in toluene (3 ml) was added a solution of AIBN (164.0 µg, 1.0 µmol) in toluene (100 µl). After refluxing of the mixture for 1 h, the solvent was removed in vacuo. Flash chromatography (PE/EtOAc = 4:1) of the residue afforded 25 (21.8 mg, 0.051 mmol, 99%) as a white solid. TLC (PE/EtOAc, 4:1): R$_f$ = 0.35; mp = 111 °C; $[\alpha]_{D}^{20}$ = -1.2 ° (c = 2.5, CH$_2$Cl$_2$); $^1$H NMR (400 MHz, C$_6$D$_6$): δ[ppm] = 1.05-1.14 (m, 2H, C$_{14}$-Ha, C$_{12}$-Ha), 1.17-1.24 (m, 1H, C$_{10}$-Ha), 1.25-1.32 (m, 1H, C$_{12}$-Hb), 1.33-1.46 (m, 3H, C$_{11}$-H, C$_{16}$-Hb), 1.56-1.80 (m, 3H, C$_{16}$-H, C$_{14}$-Hb), 1.82-1.89 (m, 1H, C$_{17}$-Ha), 2.10 (d, $J$ = 14.2 Hz, 1H, C$_{8}$-Ha), 3.29 (s, 3H, OCH$_3$), 3.41-3.53 (m, 2H, C$_{18}$-H), 3.54-3.60 (m, 1H, C$_{8}$-Hb), 3.88-3.93 (m, 1H, C$_{9}$-H), 3.97-4.03 (m, 1H, C$_{13}$-H), 4.39 (s, 2H, CH$_2$Ph), 5.65-5.71 (m, 1H, C$_{15}$-H), 6.39 (d, $J$ = 8.1 Hz, 1H, C$_{5}$-H), 6.60 (d, $J$ = 8.1 Hz, 1H, C$_{6}$-H), 7.08 (dd, $J$ = 8.1, 8.1 Hz, 1H, C$_{5}$-H), 7.12 (d, $J$ = 7.3 Hz, 1H, C$_{4}$[CH$_2$C$_6$H$_5$]-H), 7.21 (dd, $J$ = 7.3, 7.3 Hz, 2H, C$_3$[CH$_2$C$_6$H$_5$]-H), 7.34 (d, $J$ = 7.3 Hz, 2H, C$_2$[CH$_2$C$_6$H$_5$]-H); $^{13}$C NMR (100 MHz, C$_6$D$_6$): δ[ppm] = 20.0 (C$_{11}$), 26.2 (C$_{17}$), 29.9 (C$_{20}$), 30.5 (C$_{12}$), 32.0 (C$_{16}$), 38.3 (C$_{8}$), 40.0 (C$_{14}$), 55.5 (O-CH$_3$), 69.0 (C$_{13}$), 70.0 (C$_{19}$), 72.9 (CH$_2$Ph), 73.3 (C$_{15}$), 74.8 (C$_{9}$), 109.4 (C$_{4}$), 123.0 (C$_{6}$), 127.3 (C$_4$[C$_6$H$_5$]), 127.5 (C$_3$[C$_6$H$_5$]), 128.5 (C$_2$[C$_6$H$_5$]), 129.4 (C$_{3}$), 133.5 (C$_{2}$), 139.5 (C$_1$[C$_6$H$_5$]), 139.7 (C$_{7}$), 156.4 (C$_5$), 169.4 (C$_4$); HRMS (FT-ICR): calcd for [C$_{26}$H$_{32}$O$_5$ + Na$^+$]: 447.21420, found 447.2140.

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