Supporting Information
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Supporting Information

Synthesis of the Spirofungin A Core via a Domino Strategy Consisting of Olefinic Ester Ring-Closing Metathesis and Iodo-Spiroacetalization

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Experimental section

**General.** Unless otherwise noted, all reactions were performed in oven-dried glassware. All solvents used in the reactions were purified before use. Dry diethyl ether, tetrahydrofuran, and toluene were distilled from sodium and benzophenone, whereas dry CH$_2$Cl$_2$, dimethylformamide, methanol, ethyl acetate, benzene, and triethylamine were distilled from CaH$_2$. Petroleum ether with a boiling range of 40–60 °C was used. Reactions were generally run under nitrogen atmosphere. All commercially available compounds (Acros, Aldrich, Fluka, Merck) were used without purification.

$^1$H and $^{13}$C NMR: Bruker Avance 400, spectra were recorded at 295 K in CDCl$_3$ ($\delta$H 7.25, $\delta$C 77.0), benzene-$d_6$ ($\delta$H 7.16, $\delta$C 128.0) or acetone-$d_6$ ($\delta$H 2.04, $\delta$C 29.8); chemical shifts are calibrated to the residual proton and carbon resonance of the solvent. HRMS (FT-ICR): Bruker Daltonic APEX 2 with electron spray ionization (ESI). Analytical LC-MS: HP 1100 Series connected with an ESI MS detector Agilent G1946C, positive mode with fragmentor voltage of 40 eV, column: Nucleosil 100-5, C-18 HD, 5 µm, 70 × 3 mm Machery Nagel, eluent: NaCl solution (5 mM)/acetonitrile, gradient: 0-10-15-17-20 min with 20-80-99-99% acetonitrile, flow: 0.5 mL min$^{-1}$. Flash chromatography: J. T. Baker silica gel 43–60 µm. Thin-layer chromatography Machery-Nagel Polygram Sil G/UV254. Optical rotations: JASCO Polarimeter P-1020, sodium D line (589 nm), $c$ = g per 100 mL. For the spiroacetals 29–30 spirofungin numbering was used. PMP = para-Methoxyphenyl. Chiral GC-MS: Hewlett-Packard HP6890/HP5973, column 25 m × 0.25 mm internal diameter, $d_f$ = 0.25 µm, Chirasil-β-Dex (permethylated β-cyclodextrin), split injection, injection temperature = 200 °C, 50 °C, 3 min isotherm, 3 °C min$^{-1}$ to 160 °C, 5 min isotherm, carrier gas = He, pressure 70 kPa.

3-[(4-Methoxybenzyl)oxy]propane-1,2-diol. Solketal (30.0 g, 0.23 mol) was added dropwise to a suspension of NaH (11.8 g, 60%, 0.3 mol) in THF (400 mL) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and for 1.5 h at room temperature. $^1$PMBCl$_2$ (50.2 g, 0.25 mol) was added at 0 °C and the mixture was stirred for 22 h at 80 °C. The insoluble salts were filtered off and the solvent was evaporated. The residue was dissolved in THF (300 mL) and HCl (1 M, 300 mL) was added. The reaction mixture was stirred for 18 h at room temperature. NaHCO$_3$ was added until the pH reached 8. Most of the organic solvent was removed in vacuo and the mixture extracted with EtOAc (3 × 300 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo evaporated. Purification of the residue by fractional distillation (150 °C, 1.1·10$^{-2}$ mbar) afforded diol 1 (33.1 g, 69%) as a colorless oil. $R_f$ (n-hexane/EtOAc, 4:1) 0.13; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.68 (br. s, 2H, OH), 3.46–3.54 (m, 2H, 3-H), 3.58 (dd, $J$ = 11.5, 5.6 Hz, 1H, 3-H), 3.66 (dd, $J$ = 11.4, 3.8 Hz, 1H, 1-H), 3.79 (s, 3H, OCH$_3$), 3.83–3.88 (m, 1H, 2-H), 4.46 (s, 2H, CH$_2$PMP), 6.87 (d, $J$ = 8.7 Hz, 2H, aryl H), 7.23 (d, $J$ = 8.7 Hz, 2H, aryl H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 55.2 (OCH$_3$), 64.0 (C-1), 70.6 (C-2), 71.4 (C-3), 73.2 (CH$_2$PMP), 113.8 (aryl C), 129.4 (aryl C), 129.7 (aryl C), 159.3 (aryl C).

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(4-Methoxybenzyl)oxy]acetaldehyde (12). NaIO$_4$ (43.04 g, 0.20 mol) and H$_2$O (18 mL, 1.01 mol) were added to a solution of the foregoing diol (32.85 g, 0.15 mol) in CH$_2$Cl$_2$ (300 mL) at 0 °C. The mixture was stirred at room temperature for 22 h and diluted with CH$_2$Cl$_2$ (300 mL). The organic layer was separated, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The aldehyde 12 (28.7 g) was used without further purification. R$_f$ (n-hexane/EtOAc, 1:1) 0.37; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.80 (s, 3H, OCH$_3$), 4.06 (s, 2H, CH$_2$PMP), 4.55 (s, 2H, 2-H), 6.89 (d, $J = 8.7$ Hz, 2H, aryl H), 7.28 (d, $J = 8.7$ Hz, 2H, aryl H), 9.69 (s, 1H, CHO); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 55.3$ (OCH$_3$), 73.3 (CH$_2$PMP), 75.0 (C-2), 114.0 (aryl C), 128.8 (aryl C), 129.8 (aryl C), 159.6 (aryl C), 200.6 (CHO).

(4R)-4-Benzyl-3-{(2R,3R)-3-hydroxy-4-[(4-methoxybenzyl)oxy]-2-methylbutanoyl}-1,3-oxazolidin-2-one (14). Freshly prepared Bu$_2$BOTf$^3$ (23.92 g, 87 mmol) in CH$_2$Cl$_2$ (40 mL) and NEt$_3$ (13.1 mL, 95 mmol) was added successively to a solution of propionyloxazolidinone$^4$ 13 (16.97 g, 72 mmol) in CH$_2$Cl$_2$ (200 mL) at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and cooled to –80 °C. Aldehyde 12 (11.0 g, 61.3 mmol) in CH$_2$Cl$_2$ (1 mL) was added dropwise at –80 °C and the mixture was stirred for 20 min at –80 °C and 1 h at 0 °C. After addition of pH 7 phosphate buffer (15 mL), MeOH (45 mL) and a mixture of H$_2$O$_2$ (30%, 15 mL) and MeOH (30 mL), the solution was stirred at 0 °C for 1 h. Most of the organic solvent was removed in vacuo and the mixture extracted with Et$_2$O (3 × 300 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The aldol product 14 (30.0 g) was used without further purification for the subsequent protection. R$_f$ (n-hexane/EtOAc, 1:1) 0.62.

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(4R)-4-Benzyl-3-\{(2R,3R)-3-\{\textit{tert}-butyl(dimethyl)silyl\}oxy\}-4-\{(4-methoxybenzyl)oxy\}-2-methylbutanoyl\}-1,3-oxazolidin-2-one (15). To a solution of alcohol 14 (30.0 g, 0.070 mol) and 2,6-lutidine (25.5 mL, 0.22 mol) in CH$_2$Cl$_2$ (250 mL) was added TBSOTf (25 mL, 0.11 mmol) at 0 °C. After stirring for 72 h at room temperature, the reaction mixture was diluted with CH$_2$Cl$_2$ (200 mL) and washed with water (200 mL), HCl (1 M, 200 mL), saturated NaHCO$_3$ solution (100 mL) and saturated NaCl solution (200 mL). The organic layer was dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/EtOAc, 15:1) afforded the silyl ether 15 (16.9 g, 44%, over 3 steps) as a colorless oil. R$_f$ (n-hexane/EtOAc, 1:1) 0.82; [α]$_D$ -42.0 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): δ = 0.07, 0.08 (2s, 3H each, Si(CH$_3$)$_2$), 0.88 (s, 9H, SiC(CH$_3$)$_3$), 1.23 (d, J = 6.9 Hz, 3H, CH$_3$), 2.66 (dd, J = 13.2, 9.7 Hz, 1H, CH$_2$Ph), 3.17 (dd, J = 13.4, 3.2 Hz, 1H, CH$_2$Ph), 3.43 (dd, J = 9.7, 7.1 Hz, 1H, 4'-H), 3.54–3.59 (m, 2H, 4'-H, 5-H), 3.71 (s, 3H, OCH$_3$), 3.91 (dd, J = 8.9, 2.5 Hz, 1H, 5-H), 4.01 (dq, J = 7.1, 6.9 Hz 1H, 2'-H), 4.18 (ddd, J = 7.3, 5.5 Hz 1H, 3'-H), 4.22–4.28 (m, 1H, 4-H), 4.31–4.41 (m, 2H, CH$_2$PMP), 6.80 (d, J = 8.7 Hz, 2H, aryl H), 7.12 (d, J = 6.9 Hz, 2H, aryl H), 7.26 (m, 5H, aryl H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = –5.0 (Si(CH$_3$)$_2$), –4.4 (Si(CH$_3$)$_2$), 14.0 (CH$_3$), 18.0 (SiC(CH$_3$)$_3$), 25.7 (SiC(CH$_3$)$_3$), 37.8 (CH$_2$Ph), 41.9 (C-2'), 55.1 (OCH$_3$), 55.2 (C-4), 65.6 (C-5), 71.9 (C-3'), 72.8 (CH$_2$PMP), 74.0 (C-4'), 113.5 (aryl C), 127.1 (aryl C), 128.7 (aryl C), 129.1 (aryl C), 129.3 (aryl C), 130.3 (aryl C), 135.4 (aryl C), 153.2 (C-2'), 159.0 (aryl C), 175.4 (C-1'); HRMS: [M+H]$^+$ calcd for C$_{29}$H$_{41}$NO$_6$Si 528.27759, found 528.277227.

(2S,3R)-3-\{\textit{tert}-Butyl(dimethyl)silyl\}oxy\}-4-\{(4-methoxybenzyl)oxy\}-2-methylbutan-1-ol (16). LiBH$_4$ (2.35 g, 0.11 mol) was added at 0 °C to a solution of acylated oxazolidinone 15 (15.8 g, 0.03 mol) in THF (500 mL) and MeOH (7.3 mL, 0.18 mol). The solution was stirred for 1 h at 0 °C and for 18 h at room temperature. The reaction mixture was quenched with pH 7 phosphate buffer (100 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/EtOAc, 8:1) afforded alcohol 16 (7.5 g, 77%) as a colorless oil. R$_f$ (n-hexane/EtOAc, 1:1) 0.7; [α]$_D$ +12.2 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): δ = –0.02, 0.00 (2s, 3H each, Si(CH$_3$)$_2$), 0.80 (d, J = 7.0 Hz, CH$_3$), 0.81 (s, 9H, SiC(CH$_3$)$_3$), 1.85–1.90 (m, 1H, 2-H), 2.34 (br. s, 1H, OH), 3.39 (d, J = 5.6 Hz, 2H, 4-H), 3.50–3.51 (m, 2H, 1H, 1-H), 3.74 (s, 3H, OCH$_3$), 3.84–3.88 (m, 1H, 3-H), 4.35–4.42 (m, 2H, CH$_2$PMP), 6.81 (d, J = 8.6 Hz, 2H, aryl H), 7.18 (d, J = 8.8 Hz, 2H, aryl H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = –5.1 (Si(CH$_3$)$_2$), –4.3 (Si(CH$_3$)$_2$), 11.7 (CH$_3$), 18.1 (SiC(CH$_3$)$_3$), 25.8 (SiC(CH$_3$)$_3$), 39.2 (C-2'), 55.2 (OCH$_3$), 65.5 (C-1), 72.0 (C-4'), 73.1 (CH$_2$PMP), 73.4 (C-3), 113.7 (aryl C), 129.3 (aryl C), 130.1 (aryl C), 159.2 (aryl C); HRMS: [M+Na]$^+$ calcd for C$_{19}$H$_{34}$O$_4$Si 377.21186, found 377.212016.
(2R,3R)-4-(Benzyloxy)-3-[(tert-butyl(dimethyl)silyl)oxy]-2-methylbutanal (17). To a solution of alcohol 16 (7.2 g, 20.31 mmol) in CH₂Cl₂ (300 mL) was added Dess-Martin periodinane (11.2 g, 26.4 mmol) at 0 °C and the mixture was stirred for 1 h at 0 °C and for 2 h at room temperature. The reaction mixture was quenched with Na₂O₃ (25 g in 100 mL of saturated NaHCO₃ sol.) and stirred for 15 min. The mixture was extracted with Et₂O (3 × 400 mL). The combined organic layers were washed with saturated NaCl solution (200 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo. The obtained aldehyde 17 was used without further purification. Rf (n-hexane/EtOAc, 1:1) 0.82; [α]D²⁰ = −14.7 (c 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = −0.01, 0.00 (2s, 3H each, Si(CH₃)₂), 0.80 (s, 9H, SiC(CH₃)₃), 1.00 (d, J = 7.1 Hz, 3H, CH₃), 2.50–2.57 (m, 1H, 2-H), 3.32–3.42 (m, 2H, 4-H), 3.75 (s, 3H, OCH₃), 4.25 (ddd, J = 6.5, 5.2, 3.9 Hz, 1H, 1-H), 4.35–4.39 (m, 2H, CH₂PMP), 6.83 (d, J = 8.6 Hz, 2H, aryl H), 7.19 (d, J = 8.6 Hz, 2H, aryl H), 9.68 (s, 1H, 1-H); ¹³C NMR (100 MHz, CDCl₃): δ = −5.1 (Si(CH₃)₃), −4.3 (Si(CH₃)₂), 7.3 (CH₃), 18.0 (SiC(CH₃)₃), 25.7 (SiC(CH₃)₃), 50.0 (C-2), 55.2 (OCH₃), 70.4 (C-3), 71.4 (C-4), 73.0 (CH₂PMP), 113.7 (aryl C), 129.3 (aryl C), 129.9 (aryl C), 159.2 (aryl C), 204.2 (C-1); HRMS: [M+Na⁺CH₃OH]⁺ calcd for C₁₉H₃₄O₅Si 407.22242, found 407.222199.

Ethyl (2E,4S,5R)-5-[(tert-butyl(dimethyl)silyl)oxy]-6-[(4-methoxybenzyl)oxy]-4-methylhex-2-enoate (18). To a suspension of LiCl (1.26 g, 29.66 mmol) in MeCN (100 mL) was added successively DBU (3.80 mL, 25.43 mmol) and triethylphosphonoacetate (6.18 g, 27.55 mmol) at 0 °C and the mixture was stirred for 1 h at 0 °C. Aldehyde 17 (1.10 g, 3.41 mL) in MeCN (40 mL) was added at 0 °C and the mixture was stirred for 18 h at room temperature. The reaction mixture was quenched with saturated NaHCO₃ solution (100 mL) and H₂O (200 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/EtOAc 12:1) afforded unsaturated ester 18 (6.42 g, 75% over 2 steps) as a yellowish oil. Rf (n-hexane/EtOAc, 3:1) 0.51; [α]D²⁰ = −10.5 (c 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 0.01 (s, 6H, Si(CH₃)₂), 0.86 (s, 9H, SiC(CH₃)₃), 1.01 (d, J = 6.9 Hz, 3H, CH₃), 1.27 (t, J = 7.1 Hz, 3H, CH₂CH₃), 2.57 (m, 1H, 4-H), 3.35 (m, 2H, 6-H), 3.77–3.81 (m, 4H, OCH₃, 5-H), 4.14–4.20 (m, 2H, CH₂CH₃), 4.37–4.44 (m, 2H, CH₂PMP), 5.79 (d, J = 15.8 Hz, 1H, 2-H), 6.86 (d, J = 8.7 Hz, 2H, aryl H), 6.96 (dd, J = 15.8, 7.6 Hz, 1H, 3-H), 7.23 (d, J = 8.4 Hz, 2H, aryl H); ¹³C NMR (100 MHz, CDCl₃): δ = −4.9 (Si(CH₃)₂), −4.3 (Si(CH₃)₂), 13.1 (CH₃), 14.3 (CH₂CH₃), 18.1 (SiC(CH₃)₃), 25.8 (SiC(CH₃)₃), 39.8 (C-4), 55.2 (OCH₃), 60.1 (CH₂CH₃), 72.3 (C-6), 73.0 (CH₂PMP), 73.8 (C-5), 113.7 (aryl C), 120.9 (C-2), 129.3 (aryl C), 130.2 (aryl C), 152.0 (aryl C), 159.2 (C-3), 166.7 (C-1); HRMS: [M+Na⁺]⁺ calcd for C₂₃H₃₄O₅Si 445.23807, found 445.237974.

Ethyl (4S,5R)-5-[(tert-butyl(dimethyl)silyl)oxy]-6-[(4-methoxybenzyl)oxy]-4-methylhexanoate (19). Pd/C (ca. 300 mg) was added to a solution of ester 18 (3.96 g, 9.37 mmol) in EtOAc (100 mL). The reaction mixture was stirred over an H₂-atmosphere for 18 h at room temperature, filtered through celite and concentrated in vacuo to afford ester 19 (3.9 g, 98%) as a colorless oil. Rf (n-
The reaction mixture was stirred for 18 h at room temperature, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo, resulting in a slightly yellow oil. The acid 20 (3.52 g, 98%) was used without further purification. R$_f$ (n-hexane/EtOAc, 3:1) 0.20–0.27; [α]$^D_{19}$ +3.7 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): δ = 0.02, 0.03 (2s, 3H each, Si(CH$_3$)$_2$), 0.83 (d, J = 6.8 Hz, 3H, CH$_3$), 0.86 (s, 9H, Si(CH$_3$)$_3$), 1.43–1.53 (m, 1H, 3-H), 1.62–1.70 (m, 1H, 4-H), 1.74–1.81 (m, 1H, 3-H), 2.26–2.43 (m, 2H, 2-H), 3.32–3.40 (m, 2H, 6-H), 3.74 (dd, J = 5.8, 5.8, 2.9 Hz, 1H, 5-H), 3.80 (s, 3H, OCH$_3$), 4.33–4.46 (m, 2H, CH$_2$PMP), 6.86 (d, J = 8.6 Hz, 2H, aryl H), 7.23 (d, J = 8.6 Hz, 2H, aryl H), 10.77 (br. s, 1H, CO$_2$H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = –5.0 (Si(CH$_3$)$_2$), –4.1 (Si(CH$_3$)$_3$), 13.4 (CH$_3$), 18.2 (Si(CH$_3$)$_3$), 25.9 (Si(CH$_3$)$_3$), 28.4 (C-3), 32.1 (C-2), 35.8 (C-4), 55.2 (OCH$_3$), 72.6 (C-6), 73.9 (C-5), 113.7 (aryl C), 129.2 (aryl C), 130.5 (aryl C), 159.1 (aryl C), 173.9 (aryl C); HRMS: [M+NH$_4$]$^+$ calcd for C$_{23}$H$_{40}$O$_5$Si 442.29833, found 442.298110.

(4S,5R)-5-[[(tert-Butyl(dimethyl)silyloxy)-6-[(4-methoxybenzyl)oxy]-4-methylhexanoic acid (20). To a suspension of NaH (7.72 g, 0.19 mmol) in THF (500 mL) was added NaOH (1 M in H$_2$O, 50 mL) at 0 °C and the mixture was stirred for 3 h at room temperature. The solution was adjusted to a pH of 2–4 by addition of HCl (1 M in H$_2$O) and the mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo, resulting in a slightly yellow oil. The acid 20 (3.52 g, 98%) was used without further purification. R$_f$ (n-hexane/EtOAc, 3:1) 0.20–0.27; [α]$^D_{19}$ +3.7 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): δ = 0.02, 0.03 (2s, 3H each, Si(CH$_3$)$_2$), 0.83 (d, J = 6.8 Hz, 3H, CH$_3$), 0.86 (s, 9H, Si(Ch$_3$)$_3$), 1.43–1.53 (m, 1H, 3-H), 1.62–1.70 (m, 1H, 4-H), 1.74–1.81 (m, 1H, 3-H), 2.26–2.43 (m, 2H, 2-H), 3.32–3.40 (m, 2H, 6-H), 3.74 (dd, J = 5.8, 5.8, 2.9 Hz, 1H, 5-H), 3.80 (s, 3H, OCH$_3$), 4.37–4.46 (m, 2H, CH$_2$PMP), 6.86 (d, J = 8.6 Hz, 2H, aryl H), 7.23 (d, J = 8.6 Hz, 2H, aryl H), 10.77 (br. s, 1H, CO$_2$H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = –5.0 (Si(CH$_3$)$_2$), –4.1 (Si(CH$_3$)$_3$), 13.4 (CH$_3$), 18.2 (Si(CH$_3$)$_3$), 25.9 (Si(CH$_3$)$_3$), 28.4 (C-3), 32.1 (C-2), 35.8 (C-4), 55.2 (OCH$_3$), 72.6 (C-6), 72.9 (CH$_2$PMP), 73.9 (C-5), 113.7 (aryl C), 129.2 (aryl C), 130.4 (aryl C), 159.1 (aryl C), 179.6 (CO$_2$H); HRMS: [M+NH$_4$]$^+$ calcd for C$_{23}$H$_{40}$O$_5$Si 442.26703, found 414.267084.

3-(Benzyloxy)propan-1-ol.$^5$ To a suspension of NaH (7.72 g, 0.19 mmol) in THF (500 mL) was added propanediol (38 mL, 0.53 mmol) over a period of 1 h at room temperature. The reaction mixture was stirred for 18 h at room temperature, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. Purification of the residue by fractional distillation (104 °C, 1.4 mbar) afforded 3-(benzyloxy)propan-1-ol (16.7 g, 57%) as a colorless oil. R$_f$ (Et$_2$O) 0.63; $^1$H NMR (400 MHz, CDCl$_3$): δ = 1.83–1.89 (m, 2H, 2-H), 2.35 (br. s, 1H, OH), 3.65 (t, J = 5.9 Hz, 2H, 3-H), 3.77 (t, J = 5.6 Hz, 2H, 1-H), 4.52 (s, 2H, CH$_2$Ph), 7.26–7.38 (m, 5H, aryl H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 32.1 (C-2), 61.8 (C-1), 69.3 (C-3), 73.2 (CH$_2$Ph), 127.6 (aryl C), 127.7 (aryl C), 128.4 (aryl C), 138.0 (aryl C).

3-((Benzyloxy)propanal (22). To a solution of oxalyl chloride (9.48 mL, 0.11 mol) in CH$_2$Cl$_2$ (600 mL) was added dropwise DMSO (14.27 mL, 0.2 mol) at –78 °C. After stirring for 30 min at –80 °C, 3-(benzyloxy)propan-1-ol (16.7 g, 0.1 mmol) in CH$_2$Cl$_2$ (100 mL) was added dropwise at –80 °C. The reaction mixture was stirred for 30 min at –80 °C. Thereafter, NEt$_3$ (70 mL, 0.5 mol) was added at this temperature. After stirring for 30 min at –80 °C, the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was washed with saturated NaHCO$_3$ solution (200 mL) and the water layer was extracted with CH$_2$Cl$_2$ (2 × 200 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/Et$_2$O 3:1) afforded aldehyde 22 (12.41 g, 75%) as a yellowish oil. R$_f$ (n-hexane/Et$_2$O, 1:1) 0.43; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.69 (td, $J$ = 6.1, 1.8 Hz, 2H, 2-H), 3.81 (t, $J$ = 6.1 Hz, 2H, 3-H), 4.53 (s, 2H, CH$_2$Ph), 7.33 (m, 5H, aryl H), 9.79 (t, $J$ = 1.8 Hz, 1H, 1-H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 43.8 (C-2), 63.8 (C-3), 73.2 (CH$_2$Ph), 127.7 (aryl C), 127.8 (aryl C), 128.4 (aryl C), 137.8 (aryl C), 201.1 (C-1).

(3R,4S)-1-(Benzyloxy)-4-methylhex-5-yn-3-ol$^6$ (23). To a solution of Pd(OAc)$_2$ (308 mg, 1.37 mmol) in THF (300 mL) was added successively PPh$_3$ (360 mg, 1.37 mmol), aldehyde 22 (4.5 g, 27.41 mmol) and mesylate$^7$ 21 (5.9 g, 39.74 mmol) at –80 °C. Thereafter, diethylzinc (1 M in hexane, 82 mL, 82 mmol) was added slowly at this temperature. The reaction mixture was stirred for 10 min at –80 °C and for 72 h at –20 °C. The mixture was diluted with Et$_2$O (200 mL) and quenched with saturated NH$_4$Cl solution (200 mL). The layers were separated and the water layer was extracted with Et$_2$O (2 × 300 mL). The combined organic layers were washed with saturated NaCl solution (200 mL), dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/EtOAc 8:1) afforded alkynol 23 (4.16 g, 70%) as yellowish oil. R$_f$ (n-hexane/Et$_2$O, 1:1) 0.53; $[\alpha]_D^{20}$ –5.9 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.23 (d, $J$ = 7.1 Hz, 3H, CH$_3$), 1.81–1.91 (m, 2H, 5-H), 2.11 (d, $J$ = 2.3 Hz, 1H, 1-H), 2.53–2.59 (m, 1H, 3-H), 2.75 (d, $J$ = 4.6 Hz, 1H, OH), 3.63–3.68 (m, 1H, 6-H), 3.71–3.77 (m, 2H, 6-H, 4-H), 4.52 (s, 2H, CH$_2$Ph), 7.32 (m, 5H, aryl H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 16.7 (CH$_3$), 32.7 (C-3), 34.1 (C-5), 68.6 (C-6), 70.5 (C-1), 73.0 (C-4), 73.3 (CH$_2$Ph), 85.5 (C-2), 127.7 (aryl C), 127.7 (aryl C), 128.4 (aryl C), 138.0 (aryl C); HRMS: [M+Na]$^+$ calcd for C$_{14}$H$_{18}$O$_2$ 241.11990, found 241.119844.

For determination of de and ee, the racemic and the optically active compound 23 were injected separately. Prior to injection they were treated with trifluoroacetic anhydride in CH$_2$Cl$_2$ to produce the corresponding trifluoroacetate derivatives. Retention times in chiral GC-MS (conditions see general section): minor diastereomers: 36.04, 36.13 min; major diastereomers: 36.44, 36.56 min. The retention times of the major isomers are underlined. Diastereomeric excess = 95.1%; enantiomeric excess = 94.6%.

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(4S,5R)-5-[2-(Benzyloxy)ethyl]-4-methyltetrahydrofuran-2-ol (24). BH$_3$·SMc$_2$ (3.22 g, 42.4 mmol) was added dropwise to a solution of 2-methyl-2-butene (6.0 g, 84.7 mmol) in THF (100 mL) at 0 °C and the solution was stirred for 1 h at room temperature. Alkyne 23 (3.08 g, 14.1 mmol) in THF (100 mL) was added dropwise at 0 °C. After stirring for 30 min at room temperature, the reaction mixture was cooled to 0 °C and quenched with NaOH (3 M in H$_2$O, 70 mL) and H$_2$O$_2$ (30%, 24 mL). Stirring was continued for 30 min at room temperature and the mixture was extracted with CH$_2$Cl$_2$ (3 × 100 mL). The combined organic layers were washed with saturated NaCl solution (200 mL), dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The hemiacetal 24 (3.36 g) was used without further purification. R$_f$ (n-hexane/Et$_2$O, 1:1) 0.24; HRMS: [M+Na]$^+$ calcd for C$_{14}$H$_{20}$O$_3$ 259.13047, found 259.130415.

(3R,4S)-1-(Benzyloxy)-4-methylhept-6-en-3-ol (25). To a suspension of PPh$_3$CH$_2$Br (12.7 g, 35.55 mmol) in THF (100 mL) was added t-BuOK (3.51 g, 31.28 mmol) at 0 °C and the mixture was stirred for 30 min at 0 °C. hemiacetal 24 (3.36 g, 14.22 mmol) in THF (50 mL) was added dropwise at 0 °C. After stirring for 18 h at room temperature, the reaction mixture was cooled to 0 °C. The mixture was quenched with saturated NH$_4$Cl solution (50 mL) and extracted with Et$_2$O (3 × 50 mL). The combined organic layers were washed with saturated NaCl solution (200 mL), dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/Et$_2$O, 3:1) afforded alkenol 25 (2.72 g, 82%) as a colorless oil. R$_f$ (n-hexane/Et$_2$O, 1:1) 0.46; [α]$_D^{20}$ = −4.9 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): δ = 0.85 (d, J = 6.9 Hz, 3H, CH$_3$), 1.57–1.63 (m, 1H, 4-H), 1.69–1.73 (m, 2H, 6-H), 1.85–1.93 (m, 1H, 3-H), 2.23–2.29 (m, 1H, 3-H), 2.98 (br. s, 1H, OH), 3.59–3.65 (m, 2H, 5-H, 7-H), 3.69–3.74 (m, 1H, 7-H), 4.49 (s, 2H, CH$_2$Ph), 4.95–5.02 (m, 2H, 1-H), 5.72–5.82 (m, 2H, 1-H), 7.22–7.33 (m, 5H, aryl H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 15.1 (CH$_3$), 32.7 (C-2), 36.9 (C-5), 38.6 (C-4), 69.6 (C-1), 73.3 (CH$_2$Ph), 75.1 (C-3), 115.8 (C-7), 127.6 (aryl C), 127.7 (aryl C), 128.4 (aryl C), 137.5 (C-6), 137.8 (aryl C); HRMS: [M+Na]$^+$ calcd for C$_{15}$H$_{22}$O$_2$ 257.15120, found 257.151149.

(1R,2S)-1-[2-(Benzyloxy)ethyl]-2-methylpent-4-en-1-yl (4S,5R)-5-[[tert-butyl(dimethyl)silyl]oxy]-6-[(4-methoxybenzyl)oxy]-4-methylhexanoate (26). NEt$_3$ (2.05 mL, 14.8 mmol) and
2,4,6-trichlorobenzoyl chloride (0.85 mL, 5.43 mmol) were added successively to a solution of acid 20 (2.15 g, 5.43 mmol) in toluene (100 mL) at room temperature and the reaction mixture was stirred for 30 min. Alkenol 25 (1.16 g, 4.93 mmol) and 4-DMAP (2.41 g, 19.73 mmol) were added and the mixture was stirred for 2 h. The reaction mixture was quenched with saturated NaHCO₃ solution (50 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/EtOAc, 14:1) afforded the ester 26 (2.93 g, 97%) as a colorless oil. Rₜ (n-hexane/EtOAc, 3:1) 0.65; [α]D₂⁰ +9.9 (c 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 0.00, 0.01 (2s, 3H each, Si(CH₃)₃), 0.80 (d, J = 6.6 Hz, 3H, 4-CH₃), 0.83–0.85 (m, 12H, Si(CH₃)₃), 1.41–1.50 (m, 1H, 3-H), 1.58–1.63 (m, 1H, 4-H), 1.68–1.73 (m, 1H, 3-H), 1.75–1.87 (m, 4H, 2''-H, 3''-H, 1''-H), 2.12–2.17 (m, 1H, 3'-H), 2.22–2.27 (m, 2H, 2-H), 3.31–3.38 (m, 2H, 6-H), 3.40–3.48 (m, 2H, 2''-H), 3.71–3.74 (m, 1H, 5-H), 3.76 (3H, OCH₃), 4.34–4.43 (m, 4H, CH₂PMP, CH₂Ph), 4.93–5.00 (m, 3H, 1'-H, 5'-H), 5.66–5.76 (m, 1H, 4'-H), 6.84 (d, J = 8.7 Hz, 2H, aryl H), 7.21 (d, J = 8.7 Hz, 2H, aryl H), 7.24–7.32 (m, 5H, aryl H); ¹³C NMR (100 MHz, CDCl₃): δ = –5.0 (Si(CH₃)₃), –4.1 (Si(CH₃)₃), 13.1 (2''-CH₃), 14.9 (2'-CH₃), 18.2 (Si(C(CH₃)₃)), 25.9 (Si(C(CH₃)₃)), 29.0 (C-3), 30.8 (C-1''), 32.8 (C-2), 35.8 (C-4), 36.3 (C-2''), 36.7 (C-3''), 55.2 (OCH₃), 67.1 (C-2''), 72.8 (CH₂PMP), 72.9 (C-6), 73.1 (CH₂Ph), 73.8 (C-5), 74.4 (C-1''), 113.6 (aryl C), 116.2 (C-5'), 127.5 (aryl C), 127.6 (aryl C), 128.3 (aryl C), 129.2 (aryl C), 130.4 (aryl C), 136.7 (aryl C), 138.3 (aryl C), 159.1 (aryl C), 173.3 (C-1); HRMS: [M+NH₄]⁺ calc for C₃₆H₅₆O₆Si 630.41844, found 630.417985.

(2R,3S)-2-(2-(Benzyloxy)ethyl)-6-((3S,4R)-4-tert-butyldimethylsilyloxy-5-(4-methoxybenzoyloxy)-3-methylpentyl)-3-methyl-3,4-dihydro-2H-pyran (27). THF (1 mL) was added dropwise to a solution of TiCl₄ (1.26 mL, 11.42 mmol) in CH₂Cl₂ (200 mL) at 0 °C (solution becomes yellow). After stirring for 5 min at 0 °C, TMEDA (9.85 mL, 66 mmol) was added dropwise and the mixture was stirred for 10 min at room temperature (solution becomes red brown). Thereafter, Zn dust (1.71 g, 26.10 mmol) and PbCl₂ (0.45 g, 1.63 mmol) were added and the mixture was stirred for 20 h at room temperature (solution turns into greenish blue-brown). Now, ester 26 (200 mg, 0.33 mmol) in CH₂Cl₂ (20 mL) and CH₂CHBr₂ (2.45 g, 13.05 mmol) were added followed by stirring of the mixture for 2.5 h at 55 °C. The reaction mixture was cooled to 0 °C, quenched with saturated K₂CO₃ solution (3 mL), stirred for 30 min at 0 °C and then filtered through cotton. The solvents were evaporated in vacuum and the residue was filtered through A₁₂O₃ (neutral) and flushed with n-hexane/EtOAc, 10:1. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography (Al₂O₃, neutral, petroleum ether/EtOAc, 15:1) afforded the cyclic enol ether 27 (197 mg, 83%) as a colorless oil. Rₜ (Al₂O₃, n-hexane/EtOAc, 6:1) 0.63; ¹H NMR (400 MHz, C₅D₅): δ = 0.16, 0.17 (2s, 3H each, Si(CH₃)₂), 0.78 (d, J = 6.6 Hz, 3H, 3-CH₃), 0.96 (d, J = 6.9 Hz, 3H, 3''-CH₃), 1.03 (s, 9H, Si(C(CH₃)₃)), 1.49–1.62 (m, 3H, 2''-H, 3-H, 4-H), 1.73–1.87 (m, 3H, 3''-H, 2''-H, 1''-H), 1.90–1.97 (m, 2H, 4-H, 1'-H), 2.12–2.21 (m, 2H, 1''-H), 3.30 (s, 3H, OCH₃), 3.38–3.45 (m, 2H, 5''-H), 3.62–3.75 (m, 2H, 2-H, 2''-H), 3.92–3.95 (m, 1H, 4''-H), 4.26–4.42 (m, 4H, CH₂PMP, CH₂Ph), 4.49–4.52 (m, 1H, 5-H), 6.79–6.82 (m, 2H, aryl H), 7.10 (t, J = 7.4 Hz, 1H, aryl H), 7.17–7.23 (m, 4 H, aryl H), 7.31–7.34 (m, 2H, aryl H); ¹³C NMR (100 MHz, C₅D₅): δ = –4.6 (Si(CH₃)₂), –3.7 (Si(CH₃)₂), 13.9 (3''-CH₃), 17.8 (3-CH₃), 18.6 (Si(C(CH₃)₃)), 26.3 (Si(C(CH₃)₃)), 28.9 (C-4), 31.2 (C-3), 31.7 (C-2''), 32.6 (C-1''), 33.4 (C-1'), 36.3 (C-3''), 54.7 (OCH₃), 67.2 (C-2''), 73.1, 73.2 (CH₂PMP, CH₂Ph), 73.7 (C-5''), 74.9 (C-4''), 77.5
(2R,3S)-5-{(2R,3S)-2-[2-(Benzyloxy)ethyl]-3-methyl-3,4-dihydro-2H-pyran-6-yl}-1-[(4-methoxybenzyl)oxy]-3-methylpentan-2-ol (28). TBAF (237 mg, 0.75 mmol) was added to a solution of enol ether 27 (146 mg, 0.25 mmol) in THF (5 mL) at room temperature and the reaction mixture was stirred for 2 h at 60 °C. The solvent was evaporated and the residue filtered through Al₂O₃ (neutral). The filtrate was concentrated in vacuo and the crude alcohol purified by flash chromatography (Al₂O₃, neutral, petroleum ether/EtOAc, 15:1) to afford alcohol 28 (146 mg, 92%) as a colorless oil. R \(_f\) (Al₂O₃, n-hexane/EtOAc, 6:1) 0.1–0.25; \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)): δ = 0.77 (d, \(J = 6.3\) Hz, 3H, 3'-CH\(_3\)), 0.99 (d, \(J = 6.8\) Hz, 3H, 3-CH\(_3\)), 1.42–1.49 (m, 1H, 4-H), 1.52–1.65 (m, 3H, 3-H, 3'-H, 4'-H), 1.74–1.81 (m, 1H, 1''-H), 1.84–2.00 (m, 3H, 4-H, 4'-H, 7-H), 2.04–2.12 (m, 1H, 5-H), 2.16–2.28 (m, 2H, 5-H, OH), 3.31 (s, 3H, OCH\(_3\)), 3.33–3.36 (m, 2H, 1-H), 3.59–3.64 (m, 1H, 2''-H), 3.68–3.71 (m, 2H, 2'-H, 2''-H), 3.74–3.78 (m, 1H, 2-H), 4.27, 4.40 (2s, 2H each, CH\(_2\)PMP, CH\(_2\)Ph), 4.45–4.47 (m, 1H, 5'-H), 6.79 (d, \(J = 8.6\) Hz, 2H, aryl H), 7.10 (t, \(J = 7.3\) Hz, 1H, aryl H), 7.14–7.20 (m, 4H, aryl H), 7.32 (d, \(J = 7.6\) Hz, 2H, aryl H); \(^13\)C NMR (100 MHz, C\(_6\)D\(_6\)): δ = 4.5 (3-CH\(_3\)), 17.8 (3'-CH\(_3\)), 29.0 (C-4'), 30.9 (C-4), 31.3 (C-3'), 32.2 (C-5), 33.4 (C-1''), 35.4 (C-3), 54.7 (OCH\(_3\)), 67.1 (C-2''), 73.0, 73.1 (CH\(_2\)PMP, CH\(_2\)Ph), 73.2 (C-1), 73.4 (C-2), 77.4 (C-2''), 94.5 (C-5'), 114.1 (aryl C), 127.5 (aryl C), 127.9 (aryl C), 128.5 (aryl C), 129.4 (aryl C), 130.8 (aryl C), 139.5 (aryl C), 153.7 (C-6''), 159.8 (aryl C).

Spiroacetals (29a and 29b). To a solution of enol ether 28 (52 mg, 0.11 mmol) in CH₂Cl₂ (3 mL) was added CSA (52 mg, 0.22 mmol) followed by stirring of the mixture for 2 h at room temperature. The reaction mixture was quenched with saturated NaHCO₃ solution (3 mL) and extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. Purification of the residue by preparative TLC (0.25 mm thickness, n-hexane/EtOAc, 6:1) afforded acetal 29a (9 mg, 17%) and 29b (28 mg, 54%) as colorless oils.

29a: R \(_f\) (n-hexane/EtOAc, 3:1) 0.60; [α]\(_D\)\(^{20}\) +16.1 (c 1.0, EtOAc); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)): δ = 0.80 (d, \(J = 6.10\) Hz, 3H, 12-CH\(_3\)), 0.91 (d, \(J = 6.87\) Hz, 3H, 18-CH\(_3\)), 1.15 (ddd, \(J = 13.5, 13.5, 3.7\) Hz, 1H, 14-H), 1.27–1.37 (m, 2H, 12-H, 13-H), 1.38–1.52 (m, 3H, 16-H, 17-H), 1.57–1.70 (m, 2H, 14-H, 18-H), 1.78–1.90 (m, 2H, 12-H, 16-H), 2.03 (ddd, \(J = 13.2, 3.1, 3.1\) Hz, 2H, 10-H, 14-H), 3.30 (s, 3H, OCH\(_3\)), 3.50 (dd, \(J = 9.5, 6.0\) Hz, 1H, 20-H), 3.65 (dd, \(J = 9.7, 6.4\) Hz, 1H, 20-H), 3.73–3.80 (m, 2H, 9-H), 3.88 (ddd, \(J = 6.1, 6.1, 3.6\) Hz, 1H, 19-H), 4.02–4.08 (m, 1H, 11-H), 4.34–4.46 (m, 4H, CH\(_2\)PMP, CH\(_2\)Ph), 6.82 (d, \(J = 8.7\) Hz, 2H, aryl H), 7.09 (t, \(J = 7.4\) Hz, 1H, aryl H), 7.14–7.20 (m, 2H, aryl H), 7.27 (d, \(J = 8.4\) Hz, 2H, aryl H), 7.34 (d, \(J = 7.6\) Hz, 2H, aryl H); \(^13\)C NMR (100 MHz, C\(_6\)D\(_6\)): δ = 13.5 (18-CH\(_3\)), 18.1 (12-CH\(_3\)), 26.7 (C-17), 27.9 (C-13), 30.1 (C-18), 33.0 (3H, OCH\(_3\)), 3.50 (dd, \(J = 9.5, 6.0\) Hz, 1H, 20-H), 3.65 (dd, \(J = 9.7, 6.4\) Hz, 1H, 20-H), 3.73–3.80 (m, 2H, 9-H), 3.88 (ddd, \(J = 6.1, 6.1, 3.6\) Hz, 1H, 19-H), 4.02–4.08 (m, 1H, 11-H), 4.34–4.46 (m, 4H, CH\(_2\)PMP, CH\(_2\)Ph), 6.82 (d, \(J = 8.7\) Hz, 2H, aryl H), 7.09 (t, \(J = 7.4\) Hz, 1H, aryl H), 7.14–7.20 (m, 2H, aryl H), 7.27 (d, \(J = 8.4\) Hz, 2H, aryl H), 7.34 (d, \(J = 7.6\) Hz, 2H, aryl H); \(^13\)C NMR (100 MHz, C\(_6\)D\(_6\)): δ = 13.5 (18-CH\(_3\)), 18.1 (12-CH\(_3\)), 26.7 (C-17), 27.9 (C-13), 30.1 (C-18),
31.5 (C-14), 33.4 (C-16), 34.2 (C-10), 35.4 (C-12), 54.7 (OCH₃), 67.5 (C-9), 71.3 (C-20), 73.0, 73.1 (CH₂PMP and CH₂Ph), 73.4 (C-11), 74.6 (C-19), 96.8 (C-15), 114.0, 127.4, 127.6, 128.4, 129.3, 131.3, 139.8, 159.7 (aryl C); HRMS: [M+H]+ calcd for C₂₉H₄₀O₄ 469.29485, found 469.295039.

29b: R₇ (n-hexane/EtOAc, 3:1) 0.45; [α]D²⁰ +44.2 (c 1.0, EtOAc); ¹H NMR (400 MHz, C₆D₆): δ = 0.64 (d, J = 6.6 Hz, 3H, 12-CH₃), 1.00 (d, J = 6.9 Hz, 3H, 18-CH₃), 1.03–1.11 (m, 1H, 13-H), 1.21–1.28 (m, 3H, 12-H, 16-H, 17-H), 1.37–1.43 (m, 1H, 13-H), 1.59 (ddd, J = 12.8, 3.6, 3.4 Hz, 1H, 14-H), 1.64–1.71 (m, 1H, 10-H), 1.76 (dd, J = 13.2, 13.2, 4.6 Hz, 1H, 14-H), 1.81–1.86 (m, 1H, 17-H), 1.94–2.04 (m, 3H, 10-H, 16-H, 18-H), 3.21 (ddd, J = 9.7, 9.7, 1.3 Hz, 1H, 11-H), 3.29 (s, 3H, OCH₃), 3.46–3.50 (m, 1H, 20-H), 3.55–3.59 (m, 1H, 9-H), 3.62 (dd, J = 9.2, 5.9 Hz, 1H, 20-H), 6.77 (d, J = 8.7 Hz, 2H, aryl H), 7.10 (t, J = 7.4 Hz, 1H, aryl H), 7.15–7.21 (m, 4H, aryl H), 7.33 (d, J = 7.4 Hz, 1H, aryl H); ¹³C NMR (100 MHz, C₆D₆): δ = 11.3 (18-CH₃), 17.5 (12-CH₃), 23.4 (C-17), 26.1 (C-16), 28.3 (C-18), 29.5 (C-13), 34.4 (C-12), 36.8 (C-14), 54.7 (OCH₃), 67.3 (C-9), 70.8 (C-19), 71.1 (C-20), 73.1, 73.2 (CH₂PMP, CH₂Ph), 74.9 (C-11), 97.4 (C-15), 114.0 (aryl C), 127.5 (aryl C), 127.8 (aryl C), 128.5 (aryl C), 129.6 (aryl C), 131.2 (aryl C), 139.5 (aryl C), 159.6 (aryl C).

(2R,3S,6S,8R,9S)-2-[2-(Benzyloxy)ethyl]-8-{[(4-methoxybenzyloxy)methyl]-3,9-dimethyl-1,7-dioxaspiro[5.5]undecane (29a). A solution of NIS (242 mg, 1.08 mmol) in a mixture of CH₂Cl₂/MeCN (5:1, 10 mL) was added slowly to a solution of enol ether 28 (336 mg, 0.72 mmol) in CH₂Cl₂ (20 mL) at –90 °C followed by stirring of the mixture for 2 h at this temperature. The reaction mixture was quenched with saturated NaHCO₃ solution (5 mL) at –80 °C and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with saturated NaCl solution (50 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was dissolved in toluene (20 mL), Bu₃SnH (1.18 mL, 4.39 mmol) and BEt₃ (0.73 mL, 0.73 mmol) were added and the reaction mixture was stirred for 18 h at room temperature. The reaction was quenched with saturated NaHCO₃ solution (5 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/EtOAc 20:1) afforded acetal 29a [235 mg, 69%, dr (29a/29b) = 97/3] as a colorless oil.

(4R)-4-[(1S,4)-{(1R,2S)-1-[2-(Benzyloxy)ethyl]-2-methylpent-4-en-1-yl}oxy]-1-methylpent-4-en-1-yl]-2,2-dimethyl-1,3-dioxolane (32). AlMe₃ (72 mL, 0.14 mmol) was added to a solution of
Cp₂TiCl₂ (20 mg, 0.08 mmol) in toluene (1 mL) at room temperature and the reaction mixture was stirred for 72 h. After stirring for 72 h, additional AlMe₃ (20 mL, 0.06 mmol) was added and the reaction mixture was stirred for 18 h. This solution was slowly added to a solution of ester² 31 (7.5 mg, 0.02 mmol) in THF (1 mL) at 0 °C and the mixture was stirred for 1 h at 60 °C for 18 h. The reaction mixture was diluted with Et₂O (2 mL), treated at 0 °C with NaOH solution (15%, 0.2 mL), filtered through celite and concentrated in vacuo. Purification of the residue by flash chromatography (Al₂O₃, petroleum ether/Et₂O, 20:1) afforded the acyclic enol ether (5 mg, 67%) as a colorless oil. R<sub>f</sub> (Al₂O₃, n-hexane/Et₂O, 4:1) 0.61; ¹H NMR (400 MHz, acetone-d₆): δ = 0.88 (d, J = 6.4 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H), 1.26–1.30 (m, 6H), 1.54–1.80 (m, 2H), 1.84–1.98 (m, 3H), 2.13–2.21 (m, 2H), 3.51–3.57 (m, 3H), 3.84–3.89 (m, 2H), 3.93–3.98 (m, 2H), 4.16–4.20 (m, 1H), 4.44–4.51 (m, 2H), 4.96–5.05 (m, 2H), 5.75–5.86 (m, 1H), 7.24–7.27 (m, 1H) 7.30–7.33 (m, 4H); ¹³C NMR (100 MHz, acetone-d₆): δ = 15.0, 15.6, 25.7, 26.9, 31.2, 33.3, 33.7, 35.7, 36.5, 37.8, 67.6, 68.1, 73.3, 76.3, 80.7, 81.8, 116.4, 128.1, 128.2, 129.0, 138.1; due to the low amount carbon signals C₂, C₄', and C₄'' could not be detected.

(2R,3S)-2-[2-(Benzyloxy)ethyl]-6-[(3S)-3-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]butyl]-3-methyl-3,4-dihydro-2H-pyran (33). Cp₂TiMe₂¹⁰ (379 mg, 11.8% in THF, 0.22 mmol) was added to a solution of ester 31 (15 mg, 0.04 mmol) and the reaction mixture was stirred for 16 h at 65 °C. The reaction mixture was diluted with petroleum ether (2 mL), filtered through celite and concentrated in vacuo. Purification of the residue by flash chromatography (Al₂O₃, petroleum ether/Et₂O, 20:1) afforded the acyclic enol ether 32 (1 mg, 8%) and the cyclic enol ether 33 (2 mg, 15%) as colorless oils. R<sub>f</sub> (Al₂O₃, n-hexane/Et₂O, 1:1) 0.80; ¹H NMR (400 MHz, acetone-d₆): δ = 0.81–0.88 (m, 1H), 0.92–0.94 (m, 6H), 1.13–1.22 (m, 1H), 1.25 (s, 3H), 1.29 (s, 3H), 1.46–1.56 (m, 2H), 1.60–1.65 (m, 2H), 1.68–1.76 (m, 1H), 1.91–2.01 (m, 3H), 3.51–3.56 (m, 1H), 3.59–3.67 (m, 3H), 3.80–3.85 (m, 1H), 3.96 (dd, J = 7.8, 6.1 Hz, 1H), 4.42–4.45 (m, 1H), 4.51 (s, 2H), 7.24–7.28 (m, 1H), 7.31–7.36 (m, 4H); ¹³C NMR (100 MHz, acetone-d₆): δ = 15.6, 18.0, 25.7, 26.9, 30.4, 30.9, 31.7, 32.1, 33.6, 36.6, 67.4, 68.4, 73.3, 77.9, 80.8, 95.2, 108.9, 128.1, 128.2, 129.0, 140.0, 153.7.

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⁹ Ester 31 was prepared via a similar route as described for ester 26. The main difference was an initial aldol reaction between benzyloxyacetaldehyde and propionate derivative 13. See also: Arai, N.; Chikaraishi, N.; Omura, S.; Kuwajima, I. Org. Lett. 2004, 6, 2845-2848.