Supporting Information for

**Function-Oriented Studies Targeting Pectenotoxin 2: Synthesis of the GH-Ring System and a Structurally Simplified Macrolactone**

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1. Materials and Methods

A. Compound Names
Compound names were generated using Cambridgesoft ChemDraw Professional 15.0 software. For more complex molecules, a synecdochic descriptor has been used.

B. Reagents and Solvents
All reagents and starting materials were purchased from commercial sources and used as received, unless otherwise indicated. Anhydrous dichloromethane (CH$_2$Cl$_2$), diethyl ether (Et$_2$O), dimethylformamide (DMF), tetrahydrofuran (THF) and toluene (PhMe) were obtained by passing HPLC grade solvents through a column of activated alumina using a Glass Contour Solvent Purification System by Pure Process Technology, LLC. Anhydrous methanol (MeOH) and hexanes were purchased in Sure-Seal™ bottles from Sigma-Aldrich. For flash column chromatography, HPLC grade solvents were used without further purification.

Solutions of n-BuLi were purchased from Sigma-Aldrich and titrated against N-benzylbenzamide in accordance with the procedure reported by Chong.$^1$

C. Reaction Set-Up and Purification
All reactions were conducted in flame-dried glassware under an atmosphere of dry nitrogen unless otherwise indicated. Reaction mixtures were magnetically stirred and their progress was monitored by thin layer chromatography (TLC) on EMD TLC silica gel 60 F$_{254}$ glass-backed plates. Compounds were visualized by initial exposure of TLC plates to UV-light (254 nm), followed by staining with p-anisaldehyde.

Purification of crude isolates was achieved by flash column chromatography on a Biotage® Isolera One™ Automated Liquid Chromatography System using Biotage® SNAP Ultra 25 µm HP-Sphere 10–25 g or Biotage® SNAP KP-Sil 10 g silica gel cartridges, or performed using a forced flow of the indicated solvent system on Sorbent Technologies™ silica gel 60 Å (40–63 µm particle size). Concentration of reaction product solutions and chromatography fractions was accomplished by rotary evaporation at 30–35 °C under the appropriate pressure, followed by concentration at room temperature on a vacuum pump (approx. 0–1 mbar). Yields refer to chromatographically purified and spectroscopically pure compounds, unless otherwise indicated.

$^1$ Burchat, A. F.; Chong, J. M.; Nielsen, N., J. Organomet. Chem. 1997, 542, 281–283.
D. Characterization Data for New Compounds

i. Nuclear Magnetic Resonance Spectroscopy

$^1$H-NMR data were recorded on a Bruker Avance III 500 MHz NMR spectrometer (TBI probe) and a Bruker Avance III 600 MHz spectrometer (BBFO probe). $^1$H chemical shifts are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the residual CHCl$_3$ or C$_6$D$_5$H in the deuterated solvent (CDCl$_3$: δ 7.26; C$_6$D$_6$: δ 7.16). NMR coupling constants are measured in Hertz (Hz), and splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. $^{13}$C{($^1$H decoupled)} NMR data were recorded at 125 MHz on a Bruker Avance III 500 MHz spectrometer (TBI probe) and at 150 MHz on a Bruker Avance III 600 MHz spectrometer (BBFO probe). $^{13}$C chemical shifts are reported in parts per million (ppm, δ scale) and are referenced to the central line of the carbon resonances of the solvent (CDCl$_3$: δ 77.16; C$_6$D$_6$: δ 128.06).

Structural assignments for new compounds were supported by two-dimensional NMR experiments (COSY, HSQC, and HMBC) recorded on a Bruker Avance III 600 MHz spectrometer (BBFO probe), while the relative stereochemical assignments were determined by analysis of the data obtained from 1D- or 2D-NOESY experiments, recorded on a Bruker Avance III 500 MHz NMR spectrometer (TBI probe) or a Bruker Avance III 600 MHz spectrometer (BBFO probe), respectively.

ii. Infrared Spectroscopy

Infrared spectra were collected on a JASCO FT/IR-4100 Fourier Transform Infrared Spectrometer. IR absorptions are reported as very strong (vs), strong (s), medium (m), weak (w), or broad (br).

iii. Accurate Mass Determination

HRMS (EI-TOF) analyses were performed at the Mass Spectrometry Laboratory of the University of Illinois at Urbana-Champaign.

iv. Optical Rotation

Optical rotations (α) were obtained on a JASCO P-2000 polarimeter equipped with tungsten-halogen lamp (WI) and interface filter set to 589 nm, using a sample cell with a pathlength of 100 mm. Specific rotations are reported as: $[\alpha]^T_{589}$ (° • c/mL) and are based on the equation $[\alpha]^T_{589} = (100•\alpha)/(l•c)$, where the concentration (c) is reported as g/100 mL and the pathlength (l) in decimeters.
2. Experimental Procedures

A. Synthesis of the GH-Ring System

![Chemical structure](image_url)

**Synthesis of (3R,4R)-4-((tert-butyldimethylsilyl)oxy)-4-(furan-2-yl-3-methylbutan-1-ol (4):** Imidazole (15.14 g, 222.4 mmol), DMAP (1.08 g, 8.84 mmol) and TBSCl (15.58 g, 103.4 mmol) were added sequentially to a mixture of 3 (86.4% wt with S1, 13.56 g, 77.01 mmol) and S1 in anhydrous DMF at 0 °C.2 The cooling bath was removed, and the reaction mixture was stirred at room temperature overnight (~18 h). The next day, the reaction was quenched with a saturated aqueous solution of NH4Cl and then extracted with diethyl ether (× 2). The combined organic layers were washed with dH2O (× 4), dried over anhydrous Na2SO4 and concentrated in vacuo. The crude isolate was passed through a silica gel plug with 99:1 hexanes–CH2Cl2 to afford a mixture of the corresponding silyl ethers 3' (17.95 g, 88%) and S1' (2.81 g), which were used in the subsequent step without additional purification.

A solution of 9-BBN (0.5 M in THF, 162 mL, 81.0 mmol) was added to the aforementioned mixture of 3' (17.95 g, 67.36 mmol) and S1' with stirring at 0 °C. The resulting cloudy, white suspension was warmed gradually to room temperature overnight (~16 h). The flask was cooled to 0 °C, and a solution of NaOH (3.0 M in H2O, 108 mL, 324 mmol) was added, followed by careful dropwise addition of H2O2 (30% wt in H2O, 33.0 mL, 323 mmol). After stirring at 0 °C for 40 minutes, the cold bath was removed and vigorous stirring was maintained at room temperature for 7 h. The reaction mixture was then diluted with dH2O, extracted with EtOAc (× 3), and the combined organic layers were dried over anhydrous Na2SO4. The supernatant was decanted from the drying agent, and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on silica gel with 4:1 hexanes–EtOAc to afford 4 (18.5 g, 96%) as a clear, colorless oil.

**Analytical Data for 4:**

TLC (SiO2) Rf = 0.40 (hexanes–ethyl acetate, 4:1); 1H NMR (600 MHz, CDCl3) δ 7.31 (m, 1H), 6.28 (dd, J = 2.9, 1.8 Hz, 1H), 6.16 (d, J = 2.9 Hz, 1H), 4.49 (d, J = 5.9 Hz, 1H), 3.93 (s, 3H), 3.49 (s, 3H), 3.35–3.25 (m, 4H), 2.97–2.87 (m, 4H), 2.70–2.60 (m, 4H), 2.54–2.44 (m, 4H), 2.38–2.28 (m, 4H), 2.18–2.10 (m, 4H), 2.07–2.00 (m, 4H), 1.96–1.88 (m, 4H), 1.84–1.76 (m, 4H), 1.68–1.60 (m, 4H), 1.59–1.50 (m, 4H), 1.48–1.40 (m, 4H), 1.38–1.30 (m, 4H), 1.28–1.20 (m, 4H), 1.18–1.10 (m, 4H), 1.08–1.00 (m, 4H), 0.98–0.90 (m, 4H), 0.90–0.82 (m, 4H), 0.82–0.74 (m, 4H), 0.74–0.66 (m, 4H), 0.66–0.58 (m, 4H), 0.58–0.50 (m, 4H), 0.50–0.42 (m, 4H), 0.42–0.34 (m, 4H), 0.34–0.26 (m, 4H), 0.26–0.18 (m, 4H), 0.18–0.10 (m, 4H), 0.10–0.02 (m, 4H), 0.02–0.00 (m, 4H).

2 The preparation of 3 was achieved by Brown crotylation of furfural, using (+)-(Ipc)2-(E)-crotylborane. Due to the difficulty associated with chromatographically separating 3 from S1, we opted to carry the mixture through both the silyl-protection (of the secondary alcohol) and subsequent hydroboration/oxidation sequence, after which isolation of spectroscopically pure 4 could be achieved.
3.69 (dt, $J = 10.6, 6.4$ Hz, 1H), 3.59 (dt, $J = 10.6, 7.0$ Hz, 1H), 2.10–1.99 (m, 2H), 1.80 (dt, $J = 14.1, 7.0, 4.6$ Hz, 1H), 1.41 (app ddt, $J = 14.0, 7.6, 6.6$ Hz, 1H), 0.87 (s, 9H), 0.86 (d, $J = 7.0$ Hz, 3H), 0.02 (s, 3H), −0.14 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 156.4 (C), 141.2 (CH), 110.1 (CH), 106.9 (CH), 73.4 (CH), 60.8 (CH$_2$), 36.5 (CH), 35.1 (CH$_2$), 25.9 (CH$_3$), 18.3 (C), 16.1 (CH$_3$), −4.9 (CH$_3$), −5.2 (CH$_3$); IR (neat, cm$^{-1}$) 3404 (br,m), 2956 (s), 2930 (s), 2885 (s), 2857 (s), 1727 (br m), 1501 (w), 1472 (s), 1463 (s), 1406 (w), 1388 (w), 1380 (w), 1360 (w), 1254 (s), 1184 (m), 1151 (m), 1055 (br, s), 1007 (s), 930 (w), 837 (s), 776 (s), 733 (m), 672 (w); HRMS (ES-TOF) $m/z$: [M–H]$^+$ calcd for C$_{15}$H$_{27}$O$_3$Si 283.1729; found 283.1721.

Synthesis of (5S,9R,10R)-10-((tert-butyldimethylsilyl)oxy)-9-methyl-1,6-dioxaspiro[4.5]dec-3-en-2-one (2): $m$-Chloroperoxybenzoic acid (9.08 g, 37.0 mmol, 70.4% wt) was added in one portion to a stirred solution of 4 (9.92 g, 34.9 mmol) in CH$_2$Cl$_2$ (180 mL) at 0 °C. Following the complete consumption of 4 (4 h at 0 °C), a solution consisting of 50% saturated aqueous Na$_2$S$_2$O$_3$ and 50% saturated aqueous NaHCO$_3$ (1:1 v/v; 200 mL) was added to the white slurry. The biphasic mixture was warmed to room temperature, and the phases were separated. The aqueous layer was extracted with EtOAc ($\times$ 2), and the combined organic layers were washed successively with 10% aqueous KOH ($\times$ 5), dH$_2$O, and then brine before drying over anhydrous Na$_2$SO$_4$. The supernatant was decanted from the drying agent, and the solvents were removed in vacuo to afford the intermediate spirocyclic-lactol as a viscous, yellow oil.

The crude spirocyclic-lactol was transferred with anhydrous DMF (134 mL) to a round-bottom flask containing 4 Å molecular sieves (7.04 g), and cooled to 0 °C. PDC (19.74 g, 52.47 mmol) was added in one portion to the reaction flask, and the consumption of the spirocyclic-lactol was monitored by TLC. After 7 hours at 0 °C, the reaction mixture was diluted with EtOAc before being transferred to a separatory funnel. The organic phase was washed with dH$_2$O ($\times$ 3), then brine, dried over anhydrous Na$_2$SO$_4$ and then decanted from the drying agent. The solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on silica gel with 9:1 hexanes–EtOAc to afford 2 (6.83 g, 78% over two steps; yield based on anti-4) as a clear, colorless oil.

**Analytical Data for 2:**

TLC (SiO$_2$) $R_f = 0.31$ (hexanes–ethyl acetate, 9:1); $[\alpha]_{589}^{22.8} = -121.4$ (c 0.812, CHCl$_3$);

$^1$H NMR (600 MHz, CDCl$_3$) δ 7.30 (d, $J = 5.9$ Hz, 1H), 6.10 (d, $J = 5.9$ Hz, 1H), 3.93
(ddd, J = 12.9, 11.4, 2.6 Hz, 1H), 3.90 (ddd, J = 11.4, 5.5, 1.1 Hz, 1H), 3.45 (d, J = 1.8 Hz, 1H), 2.20–2.13 (m, 1H), 1.83 (dt, J = 13.0, 12.8, 5.3 Hz, 1H), 1.26 (app d, J = 13.2 Hz, 1H), 1.05 (s, 3H), –0.02 (s, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) δ 170.5 (C), 154.6 (CH), 122.9 (CH), 108.0 (C), 72.5 (CH), 65.3 (CH\(_2\)), 31.4 (CH), 26.3 (CH\(_2\)), 26.0 (CH\(_3\)), 18.5 (CH\(_3\)), 18.4 (C), –3.6 (CH\(_3\)), –3.8 (CH\(_3\)); IR (neat, cm\(^{-1}\)) 3113 (w), 2955 (s), 2930 (s), 2886 (s), 2857 (s), 1814 (m; overtone 910), 1777 (v s), 1473 (m), 1342 (m), 1298 (s), 1254 (s), 1195 (s), 1125 (s), 1074 (s), 1052 (s), 983 (s), 910 (s), 839 (s), 776 (s), 698 (s);

HRMS (ES-TOF) m/z: [M+H]\(^+\) calcd for C\(_{15}\)H\(_{27}\)O\(_4\)Si 299.1679; found 299.1678.

Scheme S1: Selected nOe interactions for spiro-lactone 2.

Synthesis of (3R,4S,5S,9R,10R)-10-((tert-butyldimethylsilyl)oxy)-3,4-dihydroxy-9-methyl-1,6-dioxaspiro[4.5]decan-2-one (S2): Compound S2 was prepared using a similar procedure to that described by Paquette in his 2004 synthesis of 4’-spiroannulated DNA building blocks.\(^3\) Due to the cross reactivity of S2 with ruthenium tetraoxide, exposure to this reagent had to be brief (i.e., best results were obtained when the reaction was performed on a scale ≤ 230 mg). Sufficient quantities of S2 could readily be accessed by performing a series of smaller experiments, dividing 2 over six reaction flasks (per run) and staggering the addition of reagents to each flask by 30 s intervals. This method, described below, was repeated until a stock solution of 2 had been entirely consumed.

A stock solution of ruthenium tetraoxide sufficient for eleven reactions was prepared by dissolving RuCl\(_3\)•H\(_2\)O (332.2 mg, 1.602 mmol) and NaIO\(_4\) (3.28 g, 15.3 mmol) in deionized water (42.0 mL). To each of ten flasks was added 4.20 mL of a stock solution of 2 (5.194 g in 100.0 mL ethyl acetate–acetonitrile (1:1 v/v)) and 6.2 mL of HPLC grade

\(^3\) Paquette, L. A.; Seekamp, C. K.; Kahane, A. L.; Hilmey, D. G.; Gallucci, J. J. Org. Chem. 2004, 69, 7442–7447.
ethyl acetate–acetonitrile (1:1 v/v). Five reaction flasks at a time were cooled in an ice–water bath to 0 °C and subsequently treated with ruthenium tetraoxide (3.2 mL of stock solution). The resulting slurry was stirred vigorously for 2 min 40 s before being quenched by the addition of a saturated aqueous solution of Na2S2O3 (5.0 mL). The contents of the reaction flasks were transferred into a single separatory funnel containing additional saturated aqueous Na2S2O3 and EtOAc (1:1 v/v; 300 mL). The contents of the flask were shaken together and the aqueous and organic phases were separated. The aqueous layer was extracted with EtOAc (×3), and the combined organic layers were dried over anhydrous Na2SO4. The supernatant was carefully decanted from the drying agent, and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on silica gel with 2:1 hexanes–EtOAc to afford S2 (1.73 g, 66%; 75% brsm) as a viscous, clear, and colorless oil.

Analytical Data for S2:
TLC (SiO2) Rf = 0.27 (hexanes–ethyl acetate, 2:1); [α]22.6°S89 = –46.7 (c 0.788, CHCl3); 1H NMR (600 MHz, CDCl3) δ 4.35 (app br s, 2H), 3.99 (app td, J = 11.4, 3.1 Hz, 1H), 3.96 (ddd, J = 11.4, 6.2, 1.8 Hz, 1H), 3.46 (app d, J = 1.8 Hz, 1H), 3.36 (br s, 1H), 3.15 (br s, 1H), 2.16–2.08 (m, 1H), 1.83 (app dtd, J = 13.2, 12.1, 5.9 Hz, 1H), 1.31 (app dq, J = 13.2, 2.6 Hz, 1H), 0.95 (d, J = 7.0 Hz, 3H), 0.93 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 173.2 (C), 104.5 (C), 71.3 (CH), 70.0 (CH), 69.4 (CH), 64.4 (CH2), 30.3 (CH), 26.6 (CH2), 26.1 (CH3), 18.4 (C), 18.3 (CH3), –3.2 (CH3), –3.9 (CH3); IR (neat, cm−1) 3454 (br, s), 2955 (s), 2930 (s), 2892 (s), 2857 (s), 1793 (vs), 1472 (m), 1436 (m), 1309 (m), 1254 (s), 1129 (s), 1100 (m), 1057 (s), 940 (s), 854 (s), 839 (s), 776 (s), 746 (m); HRMS (ES-TOF) m/z: [M+H]+ calcd for C15H29O6Si 333.1733; found 333.1735.

Synthesis of (4S,5S,9R,10R)-10-((tert-butyldimethylsilyl)oxy)-4-hydroxy-9-methyl-1,6-dioxaspiro[4.5]decan-2-one (5): A solution of S2 (1.931 g, 5.808 mmol) in THF (58.0 mL) was treated with anhydrous ethylene glycol (4.00 mL, 71.7 mmol) and HMPA (8.60 mL, 49.4 mmol). Nitrogen was then bubbled through the reaction mixture for 1 h prior to a relatively quick “dropwise addition” of SmI2 (0.1 M in THF, 216 mL, 21.6 mmol) via an attached addition funnel. The reaction mixture transitioned from a clear, colorless solution to a cream-colored slurry after ~2 h, at which point the reaction was

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4 The eleventh reaction flask contained a smaller aliquot of 2 (3.2 mL). As such, the proportion of reagents added were scaled down accordingly. Outside this alteration, the procedure remained essentially unchanged.
quenched by the addition of a saturated aqueous solution of NaHCO₃. The aqueous phase was extracted with Et₂O (× 2) and the combined organic layers were dried over anhydrous Na₂SO₄. The supernatant was carefully decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 90:10 to 87:13 hexanes–EtOAc gradient elution to afford compound 5 (1.51 g, 82%) as a clear, pale yellow oil.

**Analytical Data for 5:**

TLC (SiO₂) Rₚ = 0.41 (hexanes–ethyl acetate, 4:1); [α]²²/š⁶ = -33.2 (c 0.748, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ 4.27 (app td, J = 7.7, 5.1 Hz, 1H), 3.95–3.91 (m, 2H), 3.55 (app d, J = 1.8 Hz, 1H), 2.77 (ABX, dd, JₐB = 17.5 Hz, Jₓₐ = 7.6 Hz, 1H), 2.71 (d, J = 5.5 Hz, 1H), 2.64 (ABX, dd, JₐB = 17.5 Hz, Jₓₐ = 7.8 Hz, 1H), 2.13–2.05 (m, 1H), 1.81 (app tdd, J = 12.9, 10.1, 8.1 Hz, 1H), 1.25 (app d, J = 13.2 Hz, 1H), 0.95–0.92 (m, 12H), 0.15 (3H), 0.09 (3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.5 (C), 105.0 (C), 72.7 (CH), 70.6 (CH₂), 64.0 (CH₂), 36.9 (CH₂), 31.0 (CH), 26.6 (CH₂), 26.1 (CH₂), 18.5 (CH₃), 18.4 (C), −3.5 (CH₃), −3.7 (CH₃); IR (neat, cm⁻¹) 3488 (br, w), 2954 (s), 2930 (s), 2887 (m), 2857 (m), 1802 (vs), 1472 (w), 1253 (s), 1167 (m), 1131 (s), 1105 (s), 1058 (vs), 1042 (s), 976 (vs), 776 (s); HRMS (ES-TOF) m/z: [M+H]⁺ calcd for C₁₅H₂₉O₅Si 317.1784; found 317.1776.

![Scheme S2](image)

**Scheme S2:** Selected nOe interactions for spiro-lactone 5.

Synthesis of (3R,4R)-3-((tert-butyldimethylsilyl)oxy)-2-((S,E)-1-hydroxy-6-(trimethylsilyl)hex-3-en-5-yn-1-yl)-4-methyltetrahydro-2H-pyran-2-ol (S₄):

Diisobutylaluminum hydride (1.0 M in toluene, 14.7 mL, 14.0 mmol) was added dropwise to a solution of 5 (2.5871 g, 8.1749 mmol) in toluene–dichloromethane (1:1 v/v; 40.0 mL) at −78 °C. After 40 minutes, the reaction flask was moved to a −40 °C bath and the progress of the reaction was monitored by TLC (5: Rₚ = 0.63, S₃: Rₚ = 0.28; hexanes–ethyl acetate, 3:1). After 1.5 h, an additional portion of DIBALH (1.0 M in toluene, 3.3 mL, 3.3 mmol) was added to the reaction mixture and stirring was maintained at −40 °C until 5 was consumed in its entirety (2 h). Excess DIBALH was then quenched at −40 °C.
by dropwise addition of anhydrous MeOH until evolution of gas had ceased. The reaction solution was poured into a vigorously stirred mixture of a saturated aqueous solution of Rochelle’s salt (300 mL), diethyl ether (200 mL) and glycerol (0.2 mL/mmol DIBALH). Vigorous stirring was maintained until the phases became clear, at which point the aqueous and organic layers were separated. The aqueous layer was extracted with diethyl ether (× 2) and the combined organic extracts were dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo to afford S3 (2.53 g, 97%) as a clear, colorless oil. Compound S3 was used directly in the Wittig olefination reaction without purification. HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₁₅H₉O₅SiNa 341.1760; found 341.1748.

To a suspension of 6⁵ (9.02 g, 19.9 mmol) in anhydrous THF (100 mL) at −78 °C was added n-BuLi (2.48 M in hexanes, 7.90 mL, 19.6 mmol) dropwise; the resulting red-orange suspension was stirred at −78 °C for 2 h. A solution of S3 (2.53 g, 7.94 mmol) in anhydrous THF (5.00 mL) was then added dropwise to the slurry, via Teflon® cannula, and the temperature was maintained at −78 °C for 1 h. The reaction flask was moved to an ice-water bath and vigorous stirring was maintained at 0 °C for 4 h. The reaction was quenched under nitrogen by addition of a saturated aqueous solution of NH₄Cl. After warming to room temperature, the mixture was extracted with diethyl ether (× 3) and the combined organic extracts were washed with brine, and then dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent, and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on silica gel with 7:1 hexanes–EtOAc to afford S4 (2.48 g, 76%) as a colorless solid (α:β ≈ 3:1).

**Note:** While the mixture of geometric isomers for the Wittig olefination reaction (to afford S4) consistently afforded E:Z ≥ 12:1, the distribution of products that differ in configuration at the anomic carbon are highly variable (i.e., poor batch-to-batch reproducibility). For this reason, the ¹H- and ¹³C-NMR spectra reported for S4 have been obtained from a batch of material in which one anomer was found to predominate in order to assist with compound characterization.

**Analytical data for S4:**

| TLC (SiO₂) Rf | 0.22 (hexanes–ethyl acetate, 7:1) | ¹H NMR (600 MHz, C₆D₆) δ | 6.59 (dt, J = 16.1, 7.0 Hz, 1H), 5.82 (dt, J = 16.1, 1.5 Hz, 1H), 3.91 (app dt, J = 10.6, 2.2 Hz, 1H), 3.80 (ddd, J = 13.2, 10.6, 2.6 Hz, 1H), 3.51 (dd, J = 11.0, 5.1 Hz, 1H), 3.41 (d, J = 1.5 Hz, 1H), 3.03 (s, 1H), 2.48 (app t, J = 1.8 Hz, 1H), 2.25–2.12 (m, 3H), 1.72 (app qd, J = 12.8, 5.1 Hz, 1H), 0.93 (s, 9H), 0.87 (app dt, J = 13.2, 3.2 Hz, 1H), 0.80 (d, J = 7.3 Hz, 3H), 0.21 (s, 9H), −0.05 (s, 3H), −0.10 (s, 3H) | ¹³C NMR (150 MHz, C₆D₆) δ | 142.3 (CH), 132.3 (CH), 121.0 (CH) |

⁵ Compound 6 was prepared in three steps, from commercially available propargyl alcohol, according to known literature procedures: (a) Kolundžić, F.; Murali, A.; Pérez-Galán, P.; Bauer, J.; Strohmann, C.; Kumar, K.; Walkmann, H. Angew. Chem. Int. Ed. 2014, 53, 8122–8126; (b) M. Zürcher, F. Hof, L. Barandun, A. Schütz, W. B. Schweizer, S. Meyer, D. Bur, F. Diedrich, Eur. J. Org. Chem. 2009, 1707–1719.
112.8 (CH), 104.9 (C), 97.6 (C), 93.4 (C), 72.0 (CH), 71.7 (CH), 97.6 (C), 93.4 (C), 72.0 (CH), 71.7 (CH), 61.1 (CH), 33.5 (CH), 30.3 (CH), 27.7 (CH), 19.0 (C), 18.97 (CH), 0.12 (CH), –2.9 (CH), –3.3 (CH); IR (neat, cm⁻¹) 3389 (br, s), 3027 (w), 2956 (s), 2931 (s), 2895 (s), 2858 (s), 2173 (m), 2133 (m), 1472 (m), 1463 (m), 1251 (s), 1217 (m), 1174 (m), 1133 (m), 1087 (m), 1054 (m), 1006 (m), 987 (m), 954 (m), 852 (s), 772 (s), 661 (m);

HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₂₁H₄₀O₄Si₂Na 435.2363; found 435.2357.

Synthesis of (S,E)-1-((3R,4R)-3-(tert-butyldimethylsilyloxy)-2-methoxy-4-methyltetrahydro-2H-pyran-2-yl)-6-(trimethylsilyl)hex-3-en-5-yn-1-ol (7):
Pyridinium p-toluenesulfonate (304.4 mg, 1.211 mmol) was added, in one portion, to a stirred solution of S₄ (2.4835 g, 6.017 mmol) in anhydrous MeOH (60.2 mL) at 0 °C and then gradually warmed to room temperature overnight (23 h). The following morning, the reaction was quenched by the addition of a saturated aqueous solution of NaHCO₃. The contents of the reaction flask were transferred to a separatory funnel, extracted with CH₂Cl₂ (× 3), and the combined organic layers were dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 98:2 to 78:22 hexanes–EtOAc gradient elution to afford recovered S₄ (786.7 mg) and enyne 7 (1.555 g), in addition to small quantities of S₅ and S₆.

Recovered S₄ (786.7 mg, 1.906 mmol) was dissolved in anhydrous MeOH (19.1 mL), cooled to 0 °C and reacted with PPTS (98.5 mg, 392 μmol) according to the above outlined procedure. After chromatographic purification, an additional 474.9 mg of enyne 7 was obtained, providing a combined 79% yield over two steps.

Note: Enyne 7 was isolated as an inseparable mixture of geometric isomers (E:Z = 15:1), and as a mixture of epimers at the anomeric carbon (α:β = 4:1). A representative ¹H- and ¹³C-NMR for 7 has been annotated later in the Supporting Information (page S53), while analytical data has been provided below for both the α- and β-anomers of (E)-7.

Analytical data for 7:
Physical Appearance: Viscous, clear, yellow oil; TLC (SiO₂) Rf = 0.37 (hexanes–ethyl acetate, 8:1); IR (neat, cm⁻¹) 3581 (m), 3495 (br, m), 2955 (s), 2930 (s), 2885 (s), 2857 (s), 2738 (w), 2174 (m), 2132 (m), 1472 (m), 1463 (m), 1251 (s), 1172 (m), 1127 (s), 1082 (s), 1053 (s), 842 (s), 774 (s), 661 (s); HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₂₂H₄₂O₄Si₂Na 449.2519; found 449.2539.
Analytical data for (E)-7α:

^1^H NMR (600 MHz, C_6D_6) δ 6.73 (app dt, J = 16.1, 7.0 Hz, 1H), 5.87 (dt, J = 16.1, 1.5 Hz, 1H), 4.16 (app dd, J = 11.0, 2.2 Hz, 1H), 3.50 (app dd, J = 11.0, 4.8 Hz, 1H), 3.33 (dd, J = 13.2, 11.0, 2.9 Hz, 1H), 3.29–3.27 (m, 1H), 3.26 (s, 3H), 2.49 (br s, 1H), 2.41 (ddd, J = 15.8, 7.0, 3.7, 2.2 Hz, 1H), 2.19 (ddddd, J = 15.8, 7.0, 3.7, 2.2 Hz, 1H), 2.13–2.08 (m, 1H), 1.72 (app qd, J = 12.8, 5.1 Hz, 1H), 0.92 (s, 9H), 0.83–0.79 (m, 1H), 0.79 (d, J = 7.1 Hz, 3H), 0.19 (s, 9H), –0.07 (s, 3H), –0.09 (s, 3H); ^1^C NMR (150 MHz, C_6D_6) δ 143.1 (CH), 112.5 (CH), 105.1 (C), 98.9 (C), 93.2 (C), 71.75 (CH), 71.68 (CH), 62.2 (CH_2), 50.5 (CH_3), 33.9 (CH_2), 30.2 (CH), 27.3 (CH_2), 26.5 (CH_3), 19.3 (CH_3), 18.8 (C), 0.1 (CH_3), –2.96 (CH_3), –3.03 (CH_3).

Analytical data for (E)-7β:

'^1^H NMR (600 MHz, C_6D_6) δ 6.57 (dt, J = 16.1, 7.3 Hz, 1H), 5.77 (dt, J = 16.1, 1.5 Hz, 1H), 3.89 (d, J = 4.7 Hz, 1H), 3.71 (ddd, J = 10.3, 4.8, 2.9 Hz, 1H), 3.57 (app td, J = 11.7, 2.9 Hz, 1H), 3.20 (ddd, J = 11.4, 5.5, 2.6 Hz, 1H), 3.09 (s, 3H), 2.56–2.51 (m, 1H), 2.46–2.40 (m 1H), 1.89–1.83 (m, 1H), 1.52 (app ddt, J = 13.4, 11.6, 5.5 Hz, 1H), 1.16–1.12 (m, 1H), 1.13 (d, J = 7.0 Hz, 3H), 0.95 (s, 9H), 0.21 (s, 9H), –0.07 (s, 3H), –0.00 (s, 3H); ^1^C NMR (150 MHz, C_6D_6) δ 144.3 (CH), 111.9 (CH), 105.1 (C), 100.3 (C), 93.1 (C), 73.7 (CH), 72.5 (CH), 57.3 (CH_2), 49.2 (CH_3), 36.1 (CH_2), 32.3 (CH), 30.4 (CH_2), 26.3 (CH_3), 18.4 (C), 14.4 (CH_3), 0.1 (CH_3), –3.6 (CH_3), –4.5 (CH_3).

Synthesis of alkynyl oxirane 9: All glassware utilized for the Shi-epoxidation was placed in a base-bath consisting of an aqueous mixture of i-PrOH–KOH overnight, and rinsed thoroughly with deionized water prior to use. Teflon tubing (0.51 mm I.D.) was used in place of metal needles for transfer of the K_2CO_3 and Oxone® solutions.

To a vigorously stirred solution of enyne 7 (1.663 g, 3.897 mmol) and Shi-epoxidation diketal catalyst 8 (605.2 mg, 2.343 mmol), in HPLC grade acetonitrile (56.0 mL) and buffer (39.0 mL; 0.05 M Na_2B_4O_7•10H_2O in 4 × 10^{-4} M aqueous Na_2EDTA), was added n-Bu_4HSO_4 (53.4 mg, 157 μmol) at room temperature. After 3 minutes, the suspension was sequentially treated with a drop of a prepared solution of K_2CO_3 (9.36 g, 67.7 mmol)

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6 The procedure for the Shi-epoxidation reaction was adapted from: Smith, A. B. III; Fox, R. J. Org. Lett. 2004, 6, 1477–1480.
in dH₂O (52.0 mL) followed by a drop of a prepared solution of Oxone® (9.89 g, 32.2 mmol) in aqueous Na₂EDTA (52.0 mL, 4 × 10⁻⁴ M). This process was repeated until the entirety of both the K₂CO₃ solution and Oxone® solution had been added to the reaction flask (2.5 h). The resulting white suspension was diluted with CH₂Cl₂ (200 mL) and dH₂O (200 mL) and transferred to a separatory funnel. The two phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 100 mL). The combined organic extracts were washed with brine and then dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge (pretreated with 1% Et₃N) with 4:1 hexanes–EtOAc to afford compound 9 (1.27 g, 74%) as a viscous, clear and colorless oil. Note: This material was isolated as a mixture of diastereomers (dr ≈ 9.3:2.6:1.0) that was used directly in the subsequent 5-endo-cyclization without characterization.

Synthesis of (2R,3R,5S)-5-(((3R,4R)-3-((tert-butyldimethylsilyl)oxy)-2-methoxy-4-methyltetrahydro-2H-pyran-2-yl)-2-((trimethylsilyl)ethynyl)tetrahydrofuran-3-yl)-1,1-dimethoxypropane (S7 and S8): A prepared stock solution of cobalt carbonyl (0.74 M in CH₂Cl₂, 4.65 mL, 3.44 mmol) was added to a stirred solution of 9 (1.270 g, 2.869 mmol) in CH₂Cl₂ (72.0 mL) at ambient temperature. After 1.5 h the reaction flask was cooled to −78 °C and the dark, red reaction mixture was treated with a stock solution of BF₃•OEt₂ (0.21 M in CH₂Cl₂, 1.5 mL, 0.32 mmol). After 16 minutes had elapsed, a solution of CAN (9.93 g, 18.1 mmol) in anhydrous MeOH (52.0 mL) was quickly transferred (via cannula) to the reaction flask resulting in the formation of a cloudy, orange suspension. Vigorous stirring was maintained at −78 °C for 10 minutes before dH₂O (64.0 mL) was added. The reaction flask was removed from the cooling bath and warmed to room temperature. The contents of the flask were diluted with CH₂Cl₂ (150 mL) and dH₂O (150 mL), and transferred to a separatory funnel. The two phases were separated, the aqueous layer was extracted with CH₂Cl₂ (3 × 100 mL), and the combined organic extracts were dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 97:3 to 77:23 hexanes–EtOAc gradient elution to afford compound S7 (750 mg, 59%), S8 (165 mg, 13%) and S9 (68.9 mg, 5%) as clear, colorless oils. Note: Also isolated from this reaction
was a complex mixture of products that we believe are derived from epoxide-ring opening without the 5-endo-cyclization having taken place. Additional experimentation found that prolonged exposure of the Co–alkyne complex to BF$_3$·OEt$_2$ failed to increase the reported yield for this reaction, leading only to the production of undesired by-products (data not included).

**Analytical data for S7:**

**TLC (SiO$_2$)** $R_f$ = 0.24 (hexanes–ethyl acetate, 85:15); [α]$_{589}^{22.2}$ = −33.1 (c 0.802, CHCl$_3$);

**$^1$H NMR** (600 MHz, C$_6$D$_6$) δ 4.93 (dd, $J = 10.3, 5.9$ Hz, 1H), 4.60 (d, $J = 4.0$ Hz, 1H), 4.14–4.10 (m, 1H), 3.71 (app dd, $J = 11.0, 4.8$ Hz, 1H), 3.47 (ddd, $J = 12.8, 11.0, 2.6$ Hz, 1H), 3.35 (s, 3H), 3.26 (app br s, 1H), 2.19–2.12 (m, 1H), 2.10 (ddd, $J = 12.8, 5.9, 1.8$ Hz, 1H), 1.88 (ddd, $J = 12.8, 10.3, 5.5$ Hz, 1H), 1.80 (app qd, $J = 12.7, 5.1$ Hz, 1H), 0.97 (s, 9H), 0.88–0.84 (m, 1H), 0.81 (d, $J = 7.0$ Hz, 3H), 0.21 (s, 3H), 0.08 (s, 9H), 0.00 (s, 3H); **$^{13}$C NMR** (150 MHz, C$_6$D$_6$) δ 101.6 (C), 99.3 (C), 94.3 (C), 81.5 (CH), 74.4 (CH), 73.3 (CH), 72.9 (CH), 62.3 (CH$_2$), 50.3 (CH$_3$), 34.9 (CH$_2$), 30.2 (CH), 27.3 (CH$_2$), 26.8 (CH$_3$), 19.2 (C), 19.1 (CH$_3$), −0.3 (CH$_3$), −2.7 (CH$_3$), −3.3 (CH$_3$); **IR** (thin film, cm$^{-1}$) 3479 (br, m), 2956 (vs), 2938 (vs), 2876 (s), 2857 (s), 2173 (m), 1725 (m), 1462 (m), 1406 (m), 1347 (m), 1257 (s), 1220 (m), 1173 (s), 1128 (s), 1054 (vs), 994 (m) 846 (vs), 774 (s), 670 (m);

**HRMS (ES-TOF)** $m/z$: [M+Na]$^+$ calcd for C$_{22}$H$_{42}$O$_5$Si$_2$Na 465.2469; found 465.2472.

**Scheme S3:** Selected nOe interactions for S7.

**Analytical data for S8:**

**TLC (SiO$_2$)** $R_f$ = 0.31 (hexanes–ethyl acetate, 85:15); [α]$_{589}^{21.3}$ = −2.85 (c 0.920, CHCl$_3$);

**$^1$H NMR** (600 MHz, C$_6$D$_6$) δ 4.88 (dd, $J = 8.1, 7.3$ Hz, 1H), 4.79 (d, $J = 3.7$ Hz, 1H), 4.12–4.09 (m, 1H), 3.68 (d, $J = 4.8$ Hz, 1H), 3.67 (app td, $J = 11.4, 2.9$ Hz, 1H), 3.47 (s, 3H), 3.29 (ddd, $J = 11.4, 5.1, 2.9$ Hz, 1H), 2.17–2.13 (m, 2H), 1.89–1.83 (m, 1H), 1.52 (ddd, $J = 13.6, 11.0, 5.5, 5.1$ Hz, 1H), 1.21 (ddd, $J = 13.6, 4.8, 3.3, 2.9$ Hz, 1H), 1.00 (d, $J = 7.0$ Hz, 3H), 0.96 (s, 9H), 0.07 (app s, 12H), 0.01 (s, 3H); **$^{13}$C NMR** (150 MHz, C$_6$D$_6$) δ 101.8 (C), 100.5 (C), 93.7 (C), 80.8 (CH), 75.8 (CH), 73.1 (CH), 72.8 (CH), 57.5 (CH$_2$), 51.1 (CH$_3$), 36.4 (CH$_2$), 32.4 (CH), 30.4 (CH$_2$), 26.2 (CH$_3$), 18.4 (C), 14.6 (CH$_3$), −0.2 (CH$_3$), −3.8 (CH$_3$), −4.6 (CH$_3$); **IR** (thin film, cm$^{-1}$) 3468 (br, m), 2956 (vs), 2930 (vs), 2893 (s), 2857 (s), 2171 (w), 1721 (m), 1472 (m), 1252 (vs), 1094 (vs), 1032 (vs), 842 (vs), 774 (s), 671 (m); **HRMS (ES-TOF)** $m/z$: [M+Na]$^+$ calcd for C$_{22}$H$_{42}$O$_5$Si$_2$Na 465.2469; found 465.2468.
Scheme S4: Selected nOe interactions for S8.

Analytical data for S9:
TLC (SiO₂)  
R<sub>f</sub> = 0.13 (hexanes–ethyl acetate, 85:15); [α]<sup>21.5°</sup><sup>589</sup> = +4.63 (c 1.05, CHCl₃);
<sup>1</sup>H NMR (600 MHz, C<sub>6</sub>D<sub>6</sub>) δ 4.73 (app t, J = 7.9 Hz, 1H), 4.67 (app s, 1H), 4.35 (app br s, 1H), 3.67 (ddd, J = 11.0, 5.1, 1.5 Hz, 1H), 3.50 (s, 3H), 3.48 (ddd, J = 12.5, 11.0, 2.9 Hz, 1H), 3.36 (d, J = 1.8 Hz, 1H), 2.37 (ddd, J = 13.2, 7.7, 6.6 Hz, 1H), 2.15–2.07 (m, 2H), 1.94 (ddd, J = 13.2, 7.7, 3.7 Hz, 1H), 1.76 (app qd, J = 12.6, 5.1 Hz, 1H), 1.02 (s, 9H), 0.86–0.83 (m, 1H), 0.83 (d, J = 7.3 Hz, 3H), 0.15 (s, 9H), 0.12 (s, 3H), 0.02 (s, 3H);
<sup>13</sup>C NMR (150 MHz, C<sub>6</sub>D<sub>6</sub>) δ 104.4 (C), 99.3 (C), 90.7 (C), 81.1 (CH), 77.7 (CH), 76.9 (CH), 73.3 (CH), 62.5 (CH₂), 50.7 (CH), 35.5 (CH₂), 30.2 (CH), 27.2 (CH₂), 26.8 (CH), 19.1 (C), 18.9 (CH), 0.0 (CH₃), –3.1 (CH₃), –3.3 (CH₃); IR (thin film, cm<sup>-1</sup>) 3458 (br, m), 2955 (vs), 2929 (vs), 2880 (s), 2857 (s), 2170 (w), 1719 (w), 1463 (w), 1252 (vs), 1224 (m), 1175 (m), 1127 (vs), 1055 (vs), 970 (m), 844 (vs), 773 (s), 670 (m); HRMS (ES-TOF) <i>m/z</i>: [M+Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>42</sub>O<sub>5</sub>S<sub>2</sub>Na 465.2469; found 465.2468.

Scheme S5: Selected nOe interactions for S9.

Note: Chromatographic separation of S7 from S8 becomes increasingly difficult on larger scale. As such, we found it to be advantageous to carry this mixture of anomers through the next two steps of our reaction sequence (i.e., desilylation of the terminal alkyne, followed by protection of the secondary alcohol as a TES ether), at which stage separation of compounds 1 and S12 is readily achieved (see page S17). In order to
unambiguously characterize S10 and S11, the alkyne-deprotection has also been described (below) for reactions of S7 and S8 as a single anomer.

**Synthesis of homopropargylic alcohols S10 and S11:**

Potassium carbonate (220.7 mg, 1.597 mmol) was added, in one portion, to a stirred solution of S7 and S8 (S7:S8 = 5:1; 490.6 mg, 1.108 mmol) in anhydrous methanol (8.9 mL) at room temperature; progress of the reaction was monitored by TLC. After 3 h, the reaction was quenched with dH2O. The contents of the reaction flask were transferred to a separatory funnel and extracted with EtOAc (×3). The combined organic phases were washed with brine and then dried over anhydrous Na2SO4. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 93:7 to 50:50 hexanes–EtOAc gradient elution to afford homopropargylic alcohols S10 and S11 (S10:S11 = 6:1; 370.3 mg, 90%) as a clear, viscous, yellow oil.

Synthesis of (2R,3R,5S)-5-((2R,3R,4R)-3-((tert-butyldimethylsilyl)oxy)-2-methoxy-4-methyltetrahydro-2H-pyran-2-yl)-2-ethynyltetrahydrofuran-3-ol (S10):

Potassium carbonate (240.9 mg, 1.743 mmol) was added, in one portion, to a stirred solution of S7 (546.0 mg, 1.233 mmol) in anhydrous methanol (10.0 mL) at room temperature; progress of the reaction was monitored by TLC. After 40 minutes, the reaction was quenched with dH2O. The contents of the reaction flask were transferred to a separatory funnel and extracted with EtOAc (×3). The combined organic phases were washed with brine and then dried over anhydrous Na2SO4. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 93:7 to 50:50 hexanes–EtOAc gradient elution to afford homopropargylic alcohol S10 (401 mg, 88%) as a clear, viscous, yellow oil.

**Analytical data for S10:**

| Method | Value |
|--------|-------|
| TLC (SiO2) | Rf = 0.24 (hexanes–ethyl acetate, 7:3); [α]221"""" = −42.6 (c 0.406, CHCl3); | |
| 1H NMR (600 MHz, C6D6) | δ 4.93 (dd, $J = 10.3, 5.9$ Hz, 1H), 4.45 (dd, $J = 4.0, 2.2$ Hz, 1H), 4.01–3.98 (m, 1H), 3.72 (ddd, $J = 11.0, 5.5, 1.1$ Hz, 1H), 3.47 (ddd, $J = 12.8, 11.0, 2.9$ Hz, 1H), 3.34 (s, 3H), 3.26 (d, $J = 1.5$ Hz, 1H), 2.20–2.12 (m, 1H), 2.07 (ddd, $J = 12.8, 5.9, 2.2$ Hz, 1H), 2.00 (broad d, $J = 3.3$ Hz, 1H), 1.98 (d, $J = 2.2$ Hz, 1H), 1.88–1.78 (m, 2H), 0.99 (s, 9H), 0.86 (app d, $J = 12.8, 3.3$ Hz, 1H), 0.82 (d, $J = 7.0$ Hz, 3H), 0.21 (s, 3H), 0.01 (s, 3H); |
| 13C NMR (150 MHz, C6D6) | δ 99.3 (C), 81.5 (CH), 79.6 (C), 77.0 (CH), 73.6 (CH), 73.3 (CH), 73.0 (CH), 62.3 (CH2), 50.2 (CH3), 34.8 (CH2), 30.2 (CH), 27.3 |
(CH$_2$), 26.8 (CH$_3$), 19.14 (C), 19.07 (CH$_3$), –2.7 (CH$_3$), –3.2 (CH$_3$); IR (thin film, cm$^{-1}$) 3467 (br, m), 3310 (m), 3244 (m), 2953 (s), 2883 (s), 2857 (s), 2112 (w), 1472 (m), 1463 (m), 1254 (m), 1221 (m), 1173 (m), 1129 (s), 1054 (s), 994 (m), 852 (s), 836 (s), 774 (s), 665 (m); HRMS (ES-TOF) m/z: [M+Na]$^+$ calcd for C$_{19}$H$_{34}$O$_5$SiNa 393.2073; found 393.2078.

Scheme S6: Selected nOe interactions for S10.

Synthesis of (2R,3R,5S)-5-((2S,3R,4R)-3-((tert-butyldimethylsilyl)oxy)-2-methoxy-4-methyltetrahydro-2H-pyran-2-yl)-2-ethynyltetrahydrofuran-3-ol (S11): Potassium carbonate (20.8 mg, 151 μmol) was added, in one portion, to a stirred solution of S8 (45.0 mg, 102 μmol) in anhydrous methanol (800 μL) at room temperature; progress of the reaction was monitored by TLC. After 40 minutes, the reaction was quenched with dH$_2$O. The contents of the reaction flask were transferred to a separatory funnel and extracted with EtOAc ($\times$ 3). The combined organic phases were washed with brine and then dried over anhydrous Na$_2$SO$_4$. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 97:3 to 70:30 hexanes–EtOAc gradient elution to afford homopropargylic alcohol S11 (32.8 mg, 87%) as a clear, viscous, yellow oil.

Analytical data for S11:
TLC (SiO$_2$) R$_f$ = 0.37 (hexanes–ethyl acetate, 7:3); $[\alpha]_{D}^{217}$ = +3.44 (c 0.616, CHCl$_3$); $^1$H NMR (600 MHz, C$_6$D$_6$) δ 4.83 (dd, J = 8.8, 7.0 Hz, 1H), 4.65 (dd, J = 3.3, 2.2 Hz, 1H), 4.03–4.00 (m, 1H), 3.66 (app td, J = 11.4, 3.3 Hz, 1H), 3.65 (d, J = 4.8 Hz, 1H), 3.47 (s, 3H), 3.29 (ddd, J = 11.4, 5.5, 3.0 Hz, 1H), 2.12 (ddd, J = 12.8, 8.8, 5.1 Hz, 1H), 2.07 (ddd, J = 12.8, 7.0, 1.8 Hz, 1H), 2.02 (d, J = 2.2 Hz, 1H), 2.01 (br s, 1H), 1.90–1.82 (m, 1H), 1.52 (ddd, J = 13.2, 11.0, 5.5 Hz, 1H), 1.21 (ddd, J = 13.2, 4.4, 3.3 Hz, 1H) 1.15 (d, J = 7.0 Hz, 3H), 0.96 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H); $^{13}$C NMR (150 MHz, C$_6$D$_6$) δ
100.4 (C), 80.7 (CH), 79.7 (C), 74.9 (CH), 73.1 (CH), 72.8 (CH), 57.5 (CH), 51.1 (CH), 36.2 (CH), 30.4 (CH), 26.2 (CH), 18.4 (C), 14.6 (CH), –3.8 (CH), –4.6 (CH)

IR (thin film in CH₂Cl₂, cm⁻¹) 3459 (br, m), 3310 (m), 3260 (br, m), 2953 (s), 2930 (s), 2892 (s), 2857 (s), 2123 (w), 1472 (m), 1463 (m), 1254 (s), 1187 (s), 1174 (s), 1094 (s), 1076 (s), 1038 (s), 836 (s), 774 (s), 668 (m)

HRMS (ES-TOF) m/z: [M+Na]+ calcd for C₁₉H₃₄O₅SiNa 393.2073; found 393.2079.

Scheme S7: Selected nOe interactions for S11.

Synthesis of homopropargylic TES ethers 1 and S12: Imidazole (388.4 mg, 5.705 mmol) and chlorotriethylsilane (420 μL, 2.50 mmol) were added sequentially to a stirred solution of homopropargyl alcohols S10 and S11 (442.0 mg, 1.193 mmol, S10:S11 = 4.3:1.0) in anhydrous THF (6.0 mL) at room temperature. The resulting white suspension was reacted at room temperature for 2 h, and then quenched by the addition of a saturated aqueous solution of NaHCO₃. The mixture was diluted with Et₂O, and transferred to a separatory funnel. The two phases were separated, and the aqueous layer was extracted with diethyl ether (× 2). The combined organic extracts were washed with brine, and then dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 85:15 pentane–ethyl ether to afford compounds 1 (425 mg, 74%) and S12 (98.5 mg, 17%) as clear, light yellow oils (combined yield: 91%).

Analytical data for 1:

TLC (SiO₂) Rf = 0.27 (pentane–ethyl ether, 85:15); [α]²⁰.⁹° = –15.8 (c 1.01, CHCl₃); H NMR (600 MHz, C₆D₆) δ 4.94 (app t, J = 8.1 Hz, 1H), 4.57 (dd, J = 4.8, 2.2 Hz, 1H), 4.24 (app td, J = 4.8, 4.4 Hz, 1H), 3.74 (ddd, J = 11.0, 5.1, 1.1 Hz, 1H), 3.48 (ddd, J = 12.8, 11.0, 2.9 Hz, 1H), 3.42 (s, 3H), 3.31 (d, J = 1.5 Hz, 1H), 2.23–2.15 (m, 1H), 2.10
(d, J = 2.2 Hz, 1H), 2.03 (app dd, J = 7.7, 4.8 Hz, 2H), 1.82 (app qd, J = 12.7, 5.1 Hz, 1H), 1.05 (t, J = 8.1 Hz, 9H), 0.99 (s, 9H), 0.91–0.86 (m, 1H), 0.84 (d, J = 7.0 Hz, 3H), 0.67 (q, J = 8.1 Hz, 6H), 0.17 (s, 3H), 0.02 (s, 3H); $^{13}$C NMR (150 MHz, CD$_6$D) δ 99.4 (C), 80.9 (C), 80.6 (CH), 75.6 (CH), 73.8 (CH), 73.4 (CH), 73.3 (CH), 73.0 (CH), 52.3 (CH), 50.5 (CH$_3$), 36.0 (CH$_2$), 30.2 (CH), 27.4 (CH$_2$), 26.8 (CH$_3$), 19.13 (CH$_3$), 19.11 (C), 7.2 (CH$_3$), 5.3 (CH$_2$), −2.6 (CH$_3$), −3.2 (CH$_3$); IR (neat, cm$^{-1}$) 3313 (m), 3248 (br, m), 2954 (s), 2916 (s), 2878 (s), 2857 (s), 2742 (w), 2121 (w), 1731 (w), 1462 (m), 1371 (m), 1253 (m), 1132 (s), 1056 (m), 836 (s), 774 (s), 743 (s), 668 (m); HRMS (ES-TOF) m/z: [M+Na]$^+$ calcd for C$_{25}$H$_{48}$O$_5$Si$_2$Na 507.2938; found 507.2944.

Analytical data for S12:

TLC (SiO$_2$) $R_f$ = 0.60 (pentane–ethyl ether, 85:15); $[\alpha]^{20.7}_{D89} = +7.66$ (c 1.97, CHCl$_3$); $^1$H NMR (600 MHz, CD$_6$D) δ 4.88 (dd, J = 8.1, 7.3 Hz, 1H), 4.71 (dd, J = 4.0, 2.2 Hz, 1H), 4.23 (ddd, J = 5.5, 4.0, 2.9 Hz, 1H), 3.72 (app d, J = 4.8 Hz, 1H), 3.70 (app td, J = 11.6, 3.3 Hz, 1H), 3.52 (s, 3H), 3.35 (ddd, J = 11.4, 5.1, 2.9 Hz, 1H), 2.24 (ddd, J = 12.6, 8.3, 5.4 Hz, 1H), 2.10 (d, J = 2.2 Hz, 1H), 2.04 (ddd, J = 12.5, 7.3, 2.9 Hz, 1H), 1.93–1.86 (m, 1H), 1.56 (ddd, J = 13.2, 11.0, 5.5, 5.1 Hz, 1H), 1.25 (ddd, J = 13.5, 4.8, 3.3, 2.9 Hz, 1H), 1.17 (d, J = 7.0 Hz, 3H), 1.04 (t, J = 8.1 Hz, 9H), 0.99 (s, 9H), 0.65 (app qd, J = 8.1, 1.4 Hz, 6H), 0.11 (s, 3H), 0.05 (s, 3H); $^{13}$C NMR (150 MHz, CD$_6$D) δ 100.4 (C), 80.9 (C), 80.1 (CH), 75.2 (CH), 74.5 (CH), 73.8 (CH), 73.0 (CH), 57.6 (CH$_2$), 51.2 (CH$_3$), 37.6 (CH$_2$), 32.4 (CH), 30.4 (CH$_2$), 26.2 (CH$_3$), 18.5 (C), 14.7 (CH$_3$), 7.2 (CH$_3$), 5.3 (CH$_2$), −3.7 (CH$_3$), −4.6 (CH$_3$); IR (thin film, cm$^{-1}$) 3313 (m), 3269 (br, m), 2954 (vs), 2935 (vs), 2879 (s), 2857 (s), 2118 (w), 1726 (w), 1461 (m), 1253 (s), 1187 (m), 1138 (vs), 1094 (vs), 1080 (vs), 1036 (vs), 836 (vs), 774 (s), 743 (s), 667 (m); HRMS (ES-TOF) m/z: [M+Na]$^+$ calcd for C$_{25}$H$_{48}$O$_5$Si$_2$Na 507.2938; found 507.2944.

![Scheme S8](image_url): Selected nOe interactions for S12.
B. Synthesis of the Triaryl-Fragment

Synthesis of benzyl alcohol 15: Potassium carbonate (4.63 g, 33.5 mmol), 14 (7.86 g, 33.0 mmol), S13 (7.32 g, 23.8 mmol)\(^8,9\) and acetone (50.0 mL) were added to a 500 mL round bottom flask equipped with a condenser and large magnetic stir bar. The system was kept under nitrogen, and the resulting mixture was heated to reflux and reacted overnight (17 h). The following morning, the reaction flask was cooled to room temperature, and the acetone was removed by rotary evaporation. The resulting, white residue was transferred to a separatory funnel with a mixture of dichloromethane (200 mL) and dH\(_2\)O (200 mL). The layers were separated, and the aqueous phase was extracted with CH\(_2\)Cl\(_2\) (x 2). The combined organic extracts were washed with aqueous 1M NaOH (90.0 mL), then brine, and dried over anhydrous Na\(_2\)SO\(_4\). The supernatant was carefully decanted from the drying agent and the solvent was removed in vacuo. The remaining solid was scraped from the sides of the flask and then re-suspended in hexanes (500 mL). The resulting white slurry was stirred vigorously for 30 minutes at room temperature, and then filtered through a glass-fritted funnel with medium porosity. The solid obtained from filtration was dried under vacuum, providing compound 15 (6.63 g, 58%) as a white powder, which was used in the subsequent oxidation reaction without additional purification.

Analytical data for 15:

\(^1\)H NMR (500 MHz, CDCl\(_3\)) 7.45 (app br s, 4H), 7.29 (app d, J = 8.5 Hz, 2H), 7.25 (app d, J = 8.5 Hz, 2H), 6.97 (app d, J = 8.5 Hz, 2H), 6.94 (app d, J = 8.5 Hz, 2H), 5.08 (s, 2H), 5.07 (s, 2H), 4.68 (s, 2H), 4.62 (d, J = 4.6 Hz, 2H), 1.61 (t, J = 4.6 Hz, 1H), 0.94 (s, 9H), 0.10 (s, 6H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) 158.5 (C), 157.9 (C), 137.1 (C), 136.8 (C), 134.1 (C), 133.6 (C), 128.8 (CH), 127.81 (CH), 127.77 (CH), 127.7 (CH), 115.1

\(^7\) Phenol 14 was prepared according to the procedure of Fasan: Smith, J. M.; Vitali, F.; Archer, S. A.; Fasan, R. Angew. Chem. Int. Ed. 2011, 50, 5075–5080.

\(^8\) The sparingly soluble nature of S13 (and 15) in most organic solvents negated its purification by flash column chromatography or recrystallization when prepared on scales >5g. Consequently S13, for the above-described reaction, was contaminated with ca. 3.42 mmol of xylyl dibromide (determined by quantitative \(^1\)H-NMR analysis). Similarly, full characterization of compound 15 has been reported only after the benzylic oxidation reaction to the corresponding aldehyde (S14) had been accomplished, at which point the increased solubility of S14 enabled the isolation of spectroscopically pure materials.

\(^9\) Smet, M.; Metten, K.; Dehaen, W. Collect. Czech. Chem. Commun. 2004, 69, 1097–1108.
(CH), 114.7 (CH), 69.89 (CH₂), 69.87 (CH₂), 65.2 (CH₂), 64.8 (CH₂), 26.1 (CH₃), 18.6 (C), −5.0 (CH₃).

**Synthesis of benzaldehyde S14:** Benzyl alcohol 15 (6.63 g, 14.3 mmol), activated manganese dioxide (6.25 g, 71.9 mmol), and reagent grade benzene (71.0 mL) were added to an un-dried, round bottom flask equipped with a magnetic stir bar and Dean-Stark apparatus. The resulting black slurry was heated to reflux, with azeotropic removal of H₂O, for 22 h. After this time, the reaction flask was cooled to room temperature and its contents were filtered through a pad of Celite® with diethyl ether. The filtrate was concentrated under reduced pressure and the crude isolate was purified by flash column chromatography on silica gel with 4:1 to 2:1 hexanes–EtOAc gradient elution to afford aldehyde S14 (4.83 g, 73%) as a shiny, white solid.

**Analytical data for S14:**

**TLC (SiO₂)** Rₑ = 0.11 (hexanes–ethyl acetate, 9:1); **¹H NMR** (500 MHz, CDCl₃) δ 9.89 (s, 1H), 7.84 (app d, J = 8.8 Hz, 2H), 7.48 (app d, J = 8.4 Hz, 2H), 7.45 (app d, J = 8.4 Hz, 2H), 7.25 (app d, J = 8.8 Hz, 2H), 7.08 (app d, J = 8.8 Hz, 2H), 6.93 (app d, J = 8.8 Hz, 2H), 5.16 (s, 2H), 5.08 (s, 2H), 4.68 (s, 2H), 0.94 (s, 9H), 0.09 (s, 6H); **¹³C NMR** (150 MHz, CDCl₃) δ 190.9 (CH), 163.8 (C), 157.9 (C), 137.5 (C), 135.8 (C), 134.2 (C), 132.1 (CH), 130.3 (C), 127.9 (CH), 127.8 (CH), 127.7 (CH), 115.3 (CH), 114.7 (CH), 70.1 (CH₂), 69.8 (CH₂), 64.8 (CH₂), 26.1 (CH₃), 18.6 (C), −5.1 (CH₃); **IR** (KBr, cm⁻¹) 2953 (m), 2926 (m), 2857 (m), 2738 (w), 1692 (vs), 1602 (s), 1575 (s), 1508 (s), 1462 (m), 1421 (m), 1382 (m), 1254 (vs), 1230 (s), 1164 (s), 1110 (s), 1092 (s), 1012 (m), 836 (vs), 811 (s), 777 (m); **HRMS** (ES-TOF) m/z: [M+Na]⁺ calcd for C₂₈H₃₄O₄SiNa 485.2124; found 485.2119.
Synthesis of homopropargylic alcohol S15: Toluene (50.0 mL) was added to a nitrogen-purged flask containing S14 (4.64 g, 10.0 mmol), (S)-TRIP (740 mg, 983 μmol), and powdered 4 Å MS (4.98 g). The resulting cream-colored slurry was stirred vigorously at room temperature for 20 minutes before being placed in a −50 °C cold-bath. After the reaction flask had equilibrated to −50 °C, (rac)-16 (5.80 g, 29.9 mmol) was added dropwise by Teflon® cannula and the reaction was stirred at −45 °C overnight (17.5 h). The next day, the reaction was warmed to room temperature, and the contents of the reaction flask were filtered through a pad of Celite® with EtOAc. A saturated aqueous solution of NaHCO3 (145.0 mL) was added to the filtrate and the resulting biphasic mixture was stirred vigorously at room temperature for 1.5 h. The two phases were separated, and the aqueous layer was extracted with EtOAc (× 2). The combined organic layers were dried over anhydrous Na2SO4. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on silica gel with 7:2:1 hexanes–EtOAc–dichloromethane to afford S15 (5.08 g, 96%) as a white solid.

Analytical data for anti-S15:
TLC (SiO2) Rf = 0.45 (hexanes–ethyl acetate–dichloromethane, 7:2:1); 1H NMR (600 MHz, CDCl3) δ 7.39 (app s, 4H), 7.22 (app d, J = 8.6 Hz, 2H), 7.19 (app d, J = 8.5 Hz, 2H), 6.90 (app d, J = 8.5 Hz, 2H), 6.89 (app d, J = 8.5 Hz, 2H), 5.01 (s, 4H), 4.63 (s, 2H), 4.31 (dd, J = 7.3, 3.0 Hz, 1H), 2.68–2.61 (m, 1H), 2.55 (d, J = 3.2 Hz, 1H), 1.80 (d, J = 2.3 Hz, 3H), 0.97 (d, J = 7.0 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); 13C NMR (150 MHz, CDCl3) δ 158.5 (C), 157.9 (C), 137.0 (C), 136.8 (C), 134.3 (C), 134.0 (C), 128.0 (CH), 127.8 (CH), 127.6 (CH), 114.7 (CH), 80.4 (C), 79.3 (C), 77.6 (CH), 69.85 (CH2), 69.84 (CH2), 64.8 (CH2), 35.7 (CH), 26.1 (CH3), 18.5 (C), 17.9 (CH3), 3.7 (CH3), −5.1 (CH3); IR (KBr, cm−1) 3422 (br, m), 3068 (w), 3036 (w), 2953 (s), 2928 (s), 2855 (s), 2735 (w), 1611 (s), 1585 (m), 1510 (vs), 1466 (s), 1307 (s), 1304 (s), 1213 (vs), 1170 (s), 1093 (s), 1017 (vs), 840 (vs), 671 (m); HRMS (ES-TOF) m/z: [M+Na]+ calcd for C33H42O4SiNa 553.2750; found 553.2754.

10 Chiral Brønsted acid catalyzed allenylboration of aldehyde S15 was accomplished following an adaptation of the literature procedure described by Roush: Tsai, A. S.; Chen, M.; Roush, W. R. Org. Lett. 2013, 15, 1568–1571.
11 Preparation of rac-16 was achieved in two steps from 3-pentyn-2-ol following a known literature procedure: Chen, M.; Roush, W. R. J. Am. Chem. Soc. 2012, 134, 10947–10952.
Analytical data for syn-S15:

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.40 (s, 4H), 7.25–7.19 (m, 4H), 6.91–6.87 (m, 4H), 5.01 (s, 4H), 4.63 (s, 2H), 4.59 (dd, $J = 4.8$, 3.7 Hz, 1H), 2.78–2.71 (m, 1H), 2.18 (d, $J = 3.7$ Hz, 1H), 1.74 (d, $J = 2.4$ Hz, 3H), 1.00 (d, $J = 7.0$ Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H).

Synthesis of homopropargylic silyl ether 17: Imidazole (1.27 g, 18.7 mmol) and DMAP (228.3 mg, 1.869 mmol) were sequentially added to a stirred solution of alcohol S15 (4.94 g, 9.31 mmol) in anhydrous CH$_2$Cl$_2$ (62.0 mL) at room temperature. The reaction flask was cooled to 0 °C in an ice–water bath, and TBSCI (2.12 g, 14.1 mmol) was added in one portion. The cooling bath was removed and the resulting white slurry was reacted at ambient temperature for 2 days. After this period, the reaction was quenched by addition of a saturated aqueous solution of NH$_4$Cl. The two phases were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ ($\times$ 3). The combined organic phases were dried over anhydrous Na$_2$SO$_4$. The supernatant was decanted from the drying agent and the solvent was removed in vacuo to afford the crude isolate which was purified by flash column chromatography on silica gel with 95:5 hexanes–EtOAc to afford 17 (5.16 g, 86%) as a viscous, clear and colorless oil. Unreacted alcohol (S15, 732 mg, ca. 14%) was also recovered from the reaction, enriched in syn-S15.

Analytical data for 17:

TLC (SiO$_2$) $R_f$ = 0.44 (hexanes–ethyl acetate, 95:5); $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.47 (app s, 4H), 7.27 (app d, $J = 8.6$ Hz, 4H), 6.96 (app d, $J = 8.6$ Hz, 2H), 6.93 (app d, $J = 8.6$ Hz, 2H), 5.09 (s, 2H), 5.07 (s, 2H), 4.70 (s, 2H), 4.54 (d, $J = 6.5$ Hz, 1H), 2.69–2.62 (m, 1H), 1.81 (d, $J = 2.5$ Hz, 3H), 0.96 (s, 9H), 0.94 (d, $J = 7.0$ Hz, 3H), 0.90 (s, 9H), 0.12 (s, 6H), 0.07 (s, 3H), –0.10 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 158.1 (C), 157.9 (C), 137.02 (C), 136.99 (C), 135.3 (C), 134.1 (C), 128.2 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 114.8 (CH), 114.0 (CH), 82.1 (C), 78.0 (CH), 77.3 (C), 69.9 (CH$_2$), 69.8 (CH$_2$), 64.8 (CH$_2$), 35.6 (CH), 26.1 (CH$_3$), 25.9 (CH$_3$), 18.6 (C), 18.4 (C), 16.7 (CH$_3$), 3.7 (CH$_3$), –4.6 (CH$_3$), –4.9 (CH$_3$), –5.1 (2 × CH$_3$); IR (thin film, cm$^{-1}$) 3065 (w), 3036 (w), 2954 (s), 2928 (s), 2885 (m), 2856 (s), 2856 (s), 1611 (m), 1585 (m), 1510 (s), 1462 (m), 1375 (m), 1249 (s), 1171 (m), 1084 (s), 1039 (m), 1016 (m), 938 (w), 837 (s), 776 (s), 668 (w); HRMS (ES-TOF) $m/z$: [M+Na]$^+$ calcd for C$_{39}$H$_{56}$O$_4$Si$_2$Na 667.3615; found 667.3610.
Synthesis of vinyl stannane S16: Tricyclohexylphosphine (46.2 mg, 165 μmol) was added to a stirred solution of Pd(OAc)$_2$ (19.4 mg, 86.4 μmol) in anhydrous hexanes (17.3 mL). After solubilization, a solution of 17 (1.04 g, 1.61 mmol) in anhydrous hexanes (2.0 mL) was transferred to the reaction flask, via Teflon® cannula, followed by the addition of n-Bu$_3$SnH (1.75 mL, 6.51 mmol) over a 10 min 10 s period. The resulting brown reaction mixture was stirred at room temperature for 4 h, after which the solvents were removed under reduced pressure and the crude isolate was purified by flash column chromatography on silica gel (pretreated with 1% Et$_3$N) with 98:2 hexanes–EtOAc to afford compound S16 (1.46 g, 97%) as a clear, pale yellow oil. Note: $^1$H- and $^{13}$C-NMR spectra found later in the Supplementary Information (page S65) correspond to a different batch of material where rs $\geq$ 25:1 and dr = 7:1.

Analytical data for S16: TLC (SiO$_2$) $R_f$ = 0.38 (hexanes–ethyl acetate, 95:5); $^1$H NMR (600 MHz, CDCl$_3$) δ 7.45 (app s, 4H), 7.25 (app d, $J$ = 8.6 Hz, 2H), 7.17 (app d, $J$ = 8.6 Hz, 2H), 6.94 (app d, $J$ = 8.6 Hz, 2H), 6.87 (app d, $J$ = 8.6 Hz, 2H), 5.37 (dq, $J$ = 9.2, 1.8 Hz, 1H; $J$)$_{^{119}}$Sn = 73.5 Hz), 5.07 (s, 2H), 5.04 (s, 2H), 4.68 (s, 2H), 4.47 (d, $J$ = 5.0 Hz, 1H), 2.86–2.78 (m, 1H), 1.64 (app d, $J$ = 1.8 Hz, 3H; $J$)$_{^{117}}$Sn = 45.8 Hz, $J$)$_{^{119}}$Sn = 48.1 Hz), 1.53–1.42 (m, 6H), 1.34–1.28 (m, 6H), 0.93 (s, 9H), 0.92–0.83 (m, 27H), 0.10 (s, 6H), 0.03 (s, 3H), −0.21 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 158.0 (C), 157.7 (C), 143.5 (CH, $J$)$_{^{13}}$C–$^{117}$Sn = $J$)$_{^{13}}$C–$^{119}$Sn = 26.2 Hz), 137.6 (C), 137.1 (C), 137.0 (C), 136.9 (C), 134.1 (C), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 114.8 (CH), 113.9 (CH), 78.5 (CH), 69.94 (CH$_2$), 69.86 (CH$_2$), 64.8 (CH$_2$), 40.8 (CH, $J$)$_{^{13}}$C–$^{117}$Sn = $J$)$_{^{13}}$C–$^{119}$Sn = 54.8 Hz), 29.4 (CH$_2$), $J$)$_{^{13}}$C–$^{117}$Sn = $J$)$_{^{13}}$C–$^{119}$Sn = 19.6 Hz), 27.6 (CH$_2$), $J$)$_{^{13}}$C–$^{117}$Sn = $J$)$_{^{13}}$C–$^{119}$Sn = 55.6 Hz), 26.1 (CH$_3$), 26.0 (CH$_3$), 19.4 (CH$_3$), 18.6 (C), 18.3 (C), 17.4 (CH$_3$), 13.9 (CH$_3$), 9.2 (CH$_2$), $J$)$_{^{13}}$C–$^{117}$Sn = $J$)$_{^{13}}$C–$^{119}$Sn = 310.6 Hz), $J$)$_{^{13}}$C–$^{119}$Sn = 324.8 Hz), −4.4 (CH$_3$), −4.9 (CH$_3$), −5.0 (CH$_3$); IR (neat, cm$^{-1}$) 3060 (s), 3033 (w), 2955 (s), 2927 (s), 2899 (s), 2856 (s), 2735 (w), 1611 (m), 1509 (s), 1063 (s), 1375 (m), 1248 (s), 1171 (m), 1079 (s), 1019 (s), 836 (s), 775 (s); HRMS (ES-TOF) $m/z$: [M+Na]$^+$ calcld for C$_5$H$_{34}$O$_4$Si$_2$SnNa 959.4828; found 959.4799.

$^{12}$ Semmelhack, M. F.; Hooley, R. J. Tetrahedron Lett. 2003, 44, 5737–5739.
Synthesis of vinyl iodide 18: A solution of I₂ (238.2 mg, 0.9385 mmol) in CH₂Cl₂ was added dropwise, via Teflon® cannula, to a solution of S16 (509.3 mg, 0.5441 mmol; kept in the dark) in CH₂Cl₂ (6.0 mL) kept at 0 °C. After 50 minutes, the reaction was quenched at 0 °C by the addition of a saturated aqueous solution of Na₂S₂O₃ until the color of the organic phase had disappeared. The two phases were separated and the aqueous layer was extracted with CH₂Cl₂ (×2). The combined organic extracts were dried over anhydrous Na₂SO₄, decanted, and the solvents removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 100:0 to 95:5 hexanes–EtOAc gradient elution to afford compound 18 (405.1 mg, 96%) as a clear, orange oil.

Analytical data for 18:

TLC (SiO₂) Rf = 0.51 (hexanes–ethyl acetate, 9:1); ¹H NMR (600 MHz, CDCl₃) δ 7.46 (app s, 4H), 7.24 (app d, J = 8.6 Hz, 2H), 7.15 (app d, J = 8.6 Hz, 2H), 6.94 (app d, J = 8.6 Hz, 2H), 6.91 (app d, J = 8.6 Hz, 2H), 6.01 (dq, J = 9.9, 1.5 Hz, 1H), 5.07 (s, 2H), 5.06 (s, 2H), 4.68 (s, 2H), 4.34 (d, J = 6.2 Hz, 1H), 2.55 (dq, J = 10.0, 6.6 Hz, 1H), 2.18 (d, J = 1.4 Hz, 3H), 0.94 (s, 9H), 0.86 (s, 9H), 0.84 (d, J = 6.8 Hz, 3H), 0.09 (s, 6H), 0.03 (s, 3H), −0.20 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 158.0 (C), 157.9 (C), 144.0 (CH), 137.1 (C), 136.8 (C), 136.2 (C), 134.1 (C), 127.92 (CH), 127.91 (CH), 127.8 (CH), 127.7 (CH), 114.8 (CH), 114.3 (CH), 94.5 (C), 78.5 (CH), 69.92 (CH₂), 69.89 (CH₂), 64.8 (CH₂), 44.7 (CH), 27.9 (CH₃), 26.1 (CH₃), 26.0 (CH₃), 18.6 (C), 18.2 (C), 16.9 (CH₃), −4.5 (CH₃), −4.8 (CH₃), −5.0 (CH₃); IR (thin film, cm⁻¹) 3061 (w), 3030 (w), 2954 (s), 2928 (s), 2884 (m), 2856 (s), 2735 (w), 2710 (w), 1611 (s), 1585 (m), 1510 (vs), 1462 (m), 1376 (m), 1249 (vs), 1171 (m), 1081 (vs), 1044 (m), 1019 (m), 836 (vs), 776 (vs), 669 (m); HRMS (ES-TOF) m/z: [M+Na]+ calcd for C₃₀H₆₇O₄Si₂Na 795.2738; found 795.2715.

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¹³ Cornil, J.; Echeverria, P.-G.; Reymond, S.; Phansavath, P.; Ratovelomanana-Vidal, V.; Guérinot, A.; Cossy, J. *Org. Lett.* 2016, *18*, 4534–4537.
Synthesis of benzyl alcohol S17: Camphorsulfonic acid (58.0 mg, 0.250 mmol) was added in one portion to a stirred solution of 18 (963.9 mg, 1.247 mmol) in CH$_2$Cl$_2$–MeOH (1:1 v/v, 25.0 mL) at 0 °C; progress of the reaction was monitored by TLC. After 3 h at 0 °C, the reaction was quenched by the addition of a saturated aqueous solution of NaHCO$_3$. The phases were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (× 3). The combined organic layers were washed with a saturated aqueous solution of NaHCO$_3$, then brine, and dried over anhydrous Na$_2$SO$_4$. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 92:8 to 34:66 hexanes–EtOAc gradient elution to afford compound S17 (766 mg, 93%) as a viscous, clear, yellow oil.

**Analytical data for S17:**

TLC (SiO$_2$) $R_f$ = 0.36 (hexanes–ethyl acetate, 2:1); $^1$H NMR (600 MHz, CDCl$_3$) δ 7.46, 7.46 (ABq, $J = 9.0$ Hz, 4H), 7.29 (app d, $J = 8.6$ Hz, 2H), 7.15 (app d, $J = 8.6$ Hz, 2H), 6.97 (app d, $J = 9.0$ Hz, 2H), 6.90 (app d, $J = 8.6$ Hz, 2H), 6.01 (dq, $J = 10.3$, 1.5 Hz, 1H), 5.08 (s, 2H), 5.06 (s, 2H), 4.62 (d, $J = 5.3$ Hz, 2H), 4.34 (d, $J = 6.1$ Hz, 1H), 2.56 (dqd, $J = 10.3$, 6.8, 6.1 Hz, 1H), 2.18 (d, $J = 1.5$ Hz, 3H), 1.55 (t, $J = 5.5$ Hz, 1H), 0.86 (s, 9H), 0.83 (d, $J = 6.8$ Hz, 3H), 0.03 (s, 3H), −0.21 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 158.5 (C), 158.0 (C), 144.0 (CH), 137.0 (C), 136.8 (C), 136.2 (C), 133.6 (C), 128.0 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 115.1 (CH), 114.3 (CH), 94.5 (C), 78.5 (CH), 69.92 (CH$_2$), 69.86 (CH$_2$), 65.2 (CH$_2$), 44.7 (CH), 27.9 (CH$_3$), 26.0 (CH$_3$), 18.2 (C), 16.9 (CH$_3$), −4.5 (CH$_3$), −4.8 (CH$_3$); IR (thin film, cm$^{-1}$) 3348 (br, m), 3058 (w), 3038 (w), 2954 (s),
2927 (s), 2880 (m), 2856 (s), 1610 (s), 1585 (m), 1510 (vs), 1462 (m), 1377 (m), 1246 (vs), 1173 (s), 1079 (s), 1019 (s), 835 (s), 775 (s), 732 (w), 670 (w); **HRMS (ES-TOF)** m/z: [M+Na]⁺ calcd for C₃₃H₄₃IO₄SiNa 681.1873; found 681.1873.

Synthesis benzaldehyde S18: Manganese oxide (4.80 g, 55.2 mmol) was added to a vigorously stirred solution of alcohol S17 (2.333 g, 3.542 mmol) in CH₂Cl₂ (25.3 mL) and reacted at room temperature overnight (22 h). The charcoal colored slurry was filtered through a pad of silica gel with CH₂Cl₂, and the filtrate was concentrated in vacuo. The crude isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 99:5 to 60:40 hexanes–EtOAc gradient elution to afford compound S18 (2.04 g, 88%) as a viscous, clear, yellow oil. **Note:** Analytical data for this compound is reported for the batch of material prepared by the above procedure. Spectral data for this compound, found later in the Supplementary Information, has been reported for a batch of material from benzyl alcohol S17 where rr ≥ 25:1 and dr = 7:1.

**Analytical data for S18:**
TLC (SiO₂) Rf = 0.66 (hexanes–ethyl acetate, 2:1); **¹H NMR** (600 MHz, CDCl₃) δ 9.89 (s, 1H), 7.84 (app d, J = 8.7 Hz, 2H), 7.46, 7.48 (ABq, J = 8.2 Hz, 4H), 7.15 (app d, J = 8.6 Hz, 2H), 7.08 (app d, J = 8.7 Hz, 2H), 6.91 (app d, J = 8.7 Hz, 2H), 6.01 (dq, J = 10.3, 1.5 Hz, 1H), 5.17 (s, 2H), 5.07 (s, 2H), 4.34 (d, J = 6.1 Hz, 1H), 2.65 (dqd, J = 10.3, 6.7, 6.1 Hz, 1H), 2.17 (d, J = 1.5 Hz, 3H), 0.86 (s, 9H), 0.84 (d, J = 6.7 Hz, 3H), 0.03 (s, 3H), −0.21 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 190.9 (CH), 163.8 (C), 158.0 (C), 143.9 (CH), 137.5 (C), 136.3 (C), 135.8 (C), 132.1 (CH), 130.3 (C), 128.1 (CH), 127.9 (CH), 127.8 (CH), 115.3 (CH), 114.3 (CH), 94.5 (C), 78.4 (CH), 70.2 (CH₂), 69.8 (CH₂), 44.7 (CH), 27.9 (CH₃), 25.9 (CH₃), 18.2 (C), 16.9 (CH₃), −4.5 (CH₃), −4.8 (CH₃); **IR** (thin film, cm⁻¹) 3061 (w), 3030 (w), 2954 (s), 2927 (s), 2880 (m), 2855 (s), 2736 (w), 1694 (vs), 1600 (vs), 1578 (s), 1508 (vs), 1462 (m), 1424 (m), 1377 (m), 1309 (m), 1250 (vs), 1159 (vs), 1079 (s), 1018 (s), 853 (s), 834 (vs), 776 (s), 732 (w); **HRMS (ES-TOF)** m/z: [M+Na]⁺ calcd for C₃₃H₄₁IO₄SiNa 679.1717; found 679.1719.
Synthesis of oxazolidinone 20: A solution of 19 (73.5 mg, 0.315 mmol) and S18 (243.8 mg, 0.3713 mmol) in EtOAc (670 μL) was treated with MgCl₂ (6.7 mg, 0.070 mmol), Et₃N (92.5 μL, 0.664 mmol) and chlorotrimethylsilane (65.0 μL, 0.512 mmol). The resulting mixture was reacted at room temperature for 69 h, over which period a yellow suspension was formed. The solids were removed by filtration through a plug of silica gel with Et₂O (~80.0 mL) and the solvents were removed in vacuo. The crude, yellow isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 97:3 to 80:20 hexanes–EtOAc gradient elution to afford compound 20 (240 mg, 79%) as a brittle, iridescent foam.

Note: Analytical data for this compound is reported for the batch of material prepared by the above procedure. Spectral data for this compound, found later in the Supplementary Information, has been reported for an enriched sample of material from S18 (rr ≥ 45:1, dr = 9:1) where the reaction was performed on multi-gram scale to afford sample of 20 in 73% yield.

Analytical data for 20:
TLC (SiO₂) Rₜ = 0.17 (hexanes–ethyl acetate, 6:1); ¹H NMR (600 MHz, CDCl₃) δ 7.47 (app s, 4H), 7.38–7.34 (m, 2H), 7.33–7.28 (m, 5H), 7.15 (app d, J = 8.8 Hz, 2H), 6.95 (app d, J = 8.8 Hz, 2H), 6.91 (app d, J = 8.8 Hz, 2H), 6.01 (dq, J = 9.9, 1.5 Hz, 1H), 5.07 (s, 2H), 5.06 (s, 2H), 4.84 (d, J = 9.4 Hz, 1H), 4.78–4.72 (m, 1H), 4.33 (d, J = 6.2 Hz, 1H), 4.25 (dq, J = 9.5, 7.0 Hz, 1H), 4.19 (dd, J = 8.8, 8.1 Hz, 1H), 4.14 (dd, J = 8.8, 3.3 Hz, 1H), 3.37 (dd, J = 13.6, 3.3 Hz, 1H), 2.77 (dd, J = 13.6, 9.5 Hz, 1H), 2.59–2.52 (m, 1H), 2.18 (d, J = 1.5 Hz, 3H), 0.90–0.81 (m, 15 H), 0.02 (s, 3H), −0.08 (s, 9H), −0.21 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 176.5 (C), 158.6 (C), 158.0 (C), 153.4 (C), 144.0 (CH), 137.0 (C), 136.9 (C), 136.2 (C), 135.7 (C), 134.9 (C), 129.7 (CH), 129.1 (CH), 128.9 (CH), 127.93 (CH), 127.91 (CH), 127.5 (CH), 114.6 (CH), 114.3 (CH), 94.5 (C), 78.5 (CH), 77.9 (CH), 69.92 (CH₂), 69.90 (CH₂), 65.8 (CH₂), 55.3 (CH), 46.3 (CH), 44.7 (CH), 38.2 (CH₂), 27.9 (CH₃), 26.0 (CH₃), 18.2 (C), 16.9 (CH₃), 14.4 (CH₃), 0.3 (CH₃), −4.5 (CH₃), −4.8 (CH₃); IR (thin film, cm⁻¹) 3061 (w), 3026 (w), 2956 (s), 2928 (s), 2888 (m), 2857 (s), 1791 (vs), 1699 (s), 1610 (s), 1583 (m), 1509 (vs), 1456 (m), 1384 (vs), 1384 (vs).

¹⁴ Evans, D. A.; Tedrow, J. S.; Shaw, J. T.; Downey, C. W. J. Am. Chem. Soc. 2002, 124, 392–393.
1250 (vs), 1212 (vs), 1173 (s), 1077 (vs), 1043 (s), 878 (vs), 834 (vs), 776 (m); **HRMS (ES-TOF) m/z**: [M+Na]⁺ calcd for C_{49}H_{64}INO_{7}Si_{2}Na 984.3164; found 984.3181.

**Synthesis of hydroxy oxazolidinone S19**: Citric acid (1.64 g, 8.54 mmol) was added in one portion to a stirred solution of 20 (1.827 g, 1.899 mmol) in anhydrous MeOH (29.8 mL) at room temperature. After 1 h, the reaction mixture was diluted with dH₂O, and extracted with Et₂O (× 3). The combined organic layers were washed with a saturated aqueous solution of NaHCO₃, then brine, and dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo.

The crude isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 95:5 to 60:40 hexanes–EtOAc gradient elution to afford compounds S19 (1.49 g, 88%) as a brittle, iridescent foam.

**Analytical data for S19:**

TLC (SiO₂) Rᵣ = 0.08 (hexanes–ethyl acetate, 4:1); **¹H NMR** (600 MHz, CDCl₃) δ 7.44 (app s, 4H), 7.36 (app d, J = 8.8 Hz, 2H), 7.34–7.30 (m, 2H), 7.29–7.26 (m, 1H), 7.18 (app d, J = 7.3 Hz, 2H), 7.15 (app d, J = 8.8 Hz, 2H), 6.98 (app d, J = 8.8 Hz, 2H), 6.90 (app d, J = 8.8 Hz, 2H), 6.00 (dq, J = 9.9, 1.5 Hz, 1H), 5.07, 5.08 (ABq, J = 12.1 Hz, 2H), 5.05 (s, 2H), 4.78 (app t, J = 7.7 Hz, 1H), 4.73–4.68 (m, 1H), 4.34 (d, J = 6.2 Hz, 1H), 4.33–4.28 (m, 1H), 4.20 (dd, J = 9.2, 7.7 Hz, 1H), 4.16 (dd, J = 9.2, 2.6 Hz, 1H), 3.24 (dd, J = 13.6, 3.3 Hz, 1H), 2.93 (d, J = 7.0 Hz, 1H), 2.71 (dd, J = 13.6, 9.5 Hz, 1H), 2.59–2.52 (m, 1H), 2.18 (d, J = 1.5 Hz, 3H), 1.08 (d, J = 7.0 Hz, 3H), 0.86 (s, 9H), 0.84 (d, J = 7.0 Hz, 3H), 0.02 (s, 3H), −0.21 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 176.8 (C), 158.7 (C), 158.0 (C), 153.7 (C), 144.0 (CH), 137.0 (C), 136.8 (C), 136.2 (C), 135.4 (C), 134.7 (C), 129.6 (CH), 129.1 (CH), 128.1 (CH), 127.93 (CH), 127.90 (CH), 127.8 (CH), 127.4 (CH), 115.0 (CH), 114.3 (CH), 94.5 (C), 78.5 (CH), 77.3 (CH), 69.90 (CH₂), 69.85 (CH₂), 66.1 (CH₂), 55.6 (CH), 44.7 (CH), 44.6 (CH), 37.8 (CH₂), 27.9 (CH₃), 26.0 (CH₃), 18.2 (C), 16.9 (CH₃), 15.0 (CH₃), −4.5 (CH₃), −4.8 (CH₃); **IR** (thin film, cm⁻¹)

15 Compound 20 is sparingly soluble in MeOH at 0.063 M. The material that fails to go into solution becomes a viscous residue on the bottom of the flask, and may require periodic sonication to assure that stirring is maintained. After the addition of citric acid there is an initial formation of a cloudy suspension, followed by dissolution of the sticky residue to gradually afford a clear and colorless reaction mixture.
Synthesis of oxazolidinone S20: Imidazole (340.7 mg, 5.004 mmol) and TBSCI (502.5 mg, 3.334 mmol) were added sequentially to a stirred solution of S19 (1.4677 g, 1.649 mmol) in DMF (8.8 mL) at 0 °C. The cooling bath was removed and the contents of the flask were stirred at room temperature for 31 h, after which point the reaction was quenched by the addition of a saturated aqueous solution of NaHCO3. The contents of the flask were partitioned between dH2O and EtOAc and the two phases were separated. The aqueous layer was extracted with EtOAc (× 3) and the combined organic phases were dried over anhydrous Na2SO4. The supernatant was decanted from the drying agent and the solvents were removed in vacuo. The crude isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP-25 g cartridge with 95:5 to 60:40 hexanes–EtOAc gradient elution to afford compound S20 (1.576 g, 95%) as a brittle, iridescent foam.

Analytical data for S20:
TLC (SiO2) Rf = 0.45 (hexanes–ethyl acetate, 4:1); 1H NMR (600 MHz, CDCl3) δ 7.46 (app s, 4H), 7.38–7.34 (m, 2H), 7.31–7.26 (m, 5H), 7.15 (app d, J = 8.8 Hz, 2H), 6.94 (app d, J = 8.8 Hz, 2H), 6.91 (app d, J = 8.8 Hz, 2H), 6.01 (dq, J = 9.9, 1.5 Hz, 1H), 5.07 (s, 2H), 5.06 (s, 2H), 4.90 (d, J = 9.5 Hz, 1H), 4.69 (dddd, J = 10.3, 7.3, 3.7, 3.3 Hz, 1H), 4.34 (d, J = 6.2 Hz, 1H), 4.23 (dq, J = 9.2, 7.1 Hz, 1H), 4.17 (dd, J = 9.2, 7.3 Hz, 1H), 4.14 (dd, J = 9.2, 3.7 Hz, 1H), 3.47 (dd, J = 13.6, 3.3 Hz, 1H), 2.70 (dd, J = 13.6, 10.3 Hz, 1H), 2.60–2.52 (m, 1H), 2.18 (d, J = 1.5 Hz, 3H), 0.86 (s, 9H), 0.86–0.82 (m, 6H), 0.79 (s, 9H), 0.02 (s, 3H), −0.01 (s, 3H), −0.21 (s, 3H), −0.27 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 176.2 (C), 158.6 (C), 158.0 (C), 153.3 (C), 144.0 (CH), 137.0 (C), 136.9 (C), 136.2 (C), 135.9 (C), 135.1 (C), 129.6 (CH), 129.1 (CH), 128.9 (CH), 127.9 (CH), 127.4 (CH), 114.6 (CH), 114.3 (CH), 94.5 (C), 78.5 (CH), 77.4 (CH), 69.9 (CH2), 66.0 (CH2), 55.7 (CH), 46.5 (CH), 44.7 (CH), 38.6 (CH2), 27.9 (CH3), 25.98 (CH3), 25.96
(CH₃), 18.3 (C), 18.2 (C), 16.9 (CH₃), 14.9 (CH₃), −4.4 (CH₃), −4.5 (CH₃), −4.76 (CH₃), −4.81 (CH₃); IR (thin film, cm⁻¹) 3059 (w), 3028 (w), 2954 (s), 2928 (s), 2881 (m), 2856 (s), 1783 (vs), 1700 (s), 1610 (m), 1509 (s), 1382 (s), 1249 (vs), 1214 (vs), 1173 (s), 1076 (s), 854 (s), 836 (s), 776 (s); HRMS (ES-TOF) m/z: [M+Na]^+ calcld for C₅₂H₇₀INO₇Si₂Na 1026.3633; found 1026.3652.

Synthesis of alkoxy vinyl iodide 12: To a solution of oxazolidinone S20 (186.1 mg, 0.1853 mmol), MeOH (15.0 µL, 0.370 mmol) and THF (20.0 µL) in anhydrous ethyl ether (1.55 mL) at 0 °C was added LiBH₄ (8.4 mg, 0.39 mmol). The cooling bath was removed and the mixture was stirred at room temperature overnight (25 h). The flask was re-cooled to 0 °C, and MeOH (300.0 µL) and aqueous 1M NaOH (300.0 µL) were added dropwise to the reaction mixture. The contents of the reaction flask were transferred to a separatory funnel and then extracted with EtOAc (× 2). The combined organic layers were dried over anhydrous Na₂SO₄, the supernatant was decanted from the drying agent and the solvents were removed in vacuo. The crude isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP Sphere 25 g cartridge with 95:5 to 60:40 hexanes–EtOAc gradient elution to afford alcohol 12 (132.6 mg, 86%) as a viscous, clear, pale yellow oil. Note: Spectral data for this compound, found later in the Supplementary Information, has been reported for a batch of material from oxazolidinone S20 where rr ≥ 25:1 and dr = 9:1.

Analytical data for 12:
TLC (SiO₂) Rf = 0.33 (hexanes–ethyl acetate, 4:1); ¹H NMR (600 MHz, CDCl₃) δ 7.46 (app s, 4H), 7.21 (app d, J = 8.8 Hz, 2H), 7.15 (app d, J = 8.8 Hz, 2H), 6.93 (app d, J = 8.8 Hz, 2H), 6.91 (app d, J = 8.4 Hz, 2H), 6.01 (dq, J = 9.9, 1.5 Hz, 1H), 5.07 (s, 4H), 4.51 (d, J = 7.3 Hz, 1H), 4.34 (d, J = 6.2 Hz, 1H), 3.67 (ddd, J = 11.0, 6.2, 3.3 Hz, 1H), 3.60 (ddd, J = 11.0, 6.2, 4.4 Hz, 1H), 2.97 (dd, J = 6.2, 4.4 Hz, 1H), 2.60–2.52 (m, 1H), 2.18 (d, J = 1.5 Hz, 3H), 1.94–1.87 (m, 1H), 0.88 (s, 9H), 0.86 (s, 9H), 0.84 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 7.0 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H), −0.21 (s, 3H), −0.25 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 158.2 (C), 158.0 (C), 143.9 (CH), 137.0 (C), 136.9 (C), 136.3 (C), 136.2 (C), 128.0 (CH), 127.92 (CH), 127.89 (CH), 127.87 (CH), 114.5 (CH), 114.3 (CH), 94.5 (C), 80.9 (CH), 78.5 (CH), 69.89 (CH₂), 69.86 (CH₂), 66.6 (CH₂), 44.6 (CH), 43.3 (CH), 27.9 (CH₃), 25.96 (CH₃), 25.95 (CH₃), 18.21 (C), 18.16 (C), 16.9
(CH$_3$), 14.4 (CH$_3$), –4.3 (CH$_3$), –4.5 (CH$_3$), –4.8 (CH$_3$), –5.0 (CH$_3$); IR (thin film, cm$^{-1}$) 3425 (br, w), 3060 (w), 3033 (w), 2955 (s), 2928 (s), 2889 (m), 2856 (s), 1610 (m), 1509 (vs), 1471 (m), 1458 (m), 1249 (vs), 1171 (m), 1077 (s), 1042 (s), 856 (s), 836 (vs), 776 (s); HRMS (ES-TOF) m/z: [M+Na]$^+$ calcd for C$_{42}$H$_{63}$IO$_5$Si$_2$Na 853.3157; found 853.3132.

C. Sonogashira Cross-Coupling

Synthesis of the GH-ring containing enyne S21. Terminal alkyne 1 (425.4 mg, 0.8774 mmol) and vinyl iodide 12 (726.8 mg, 0.8746 mmol) were dissolved in benzene (4.0 mL), and concentrated under reduced pressure to azeotrope residual water. This process was repeated two additional times before the reaction flask was sealed with a rubber septum, and the atmosphere was exchanged with nitrogen gas. Dry diisopropylamine (4.4 mL) was added to the flask and nitrogen gas was bubbled through the reaction mixture for 40 minutes. Tetrakis(triphenylphosphine)palladium(0) (101.5 mg, 87.4 µmol) and copper(I) iodide (33.4 mg, 20.1 µmol) were added, sequentially, to the stirred mixture and the progress of the reaction was monitored by TLC. After 7 h, the reaction was quenched by the addition of a saturated aqueous solution of NH$_4$Cl. The contents of the reaction flask were transferred to a separatory funnel and extracted with EtOAc (× 3). The combined organic layers were washed with brine, and dried over anhydrous Na$_2$SO$_4$. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude isolate which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 95:5 to 60:40 hexanes–EtOAc gradient elution to afford enyne S21 (926 mg, 89%) as a colorless foam.

Analytical data for S21:

TLC (SiO$_2$) $R_f$ = 0.28 (hexanes–ethyl acetate, 5:1); $^1$H NMR (600 MHz, CDCl$_3$) δ 7.47, 7.47 (ABq, $J$ = 9.1 Hz, 4H), 7.20 (app d, $J$ = 8.6 Hz, 2H), 7.14 (app d, $J$ = 8.6 Hz, 2H), 6.93 (app d, $J$ = 8.6 Hz, 2H), 6.88 (app d, $J$ = 8.6 Hz, 2H), 5.66 (app dd, $J$ = 10.0, 1.4 Hz, 1H), 5.07 (s, 2H), 5.05 (s, 2H), 4.75 (d, $J$ = 4.7 Hz, 1H), 4.67 (dd, $J$ = 9.0, 7.0 Hz, 1H),

(a) Sonogashira, K.; Tohda, Y.; Hagihara, N. Tetrahedron Lett. 1975, 50, 4467–4470; (b) Nishioka, Y.; Yano, Y.; Kinashi, N.; Oku, N.; Toriyama, Y.; Katsumura, S.; Shinada, T.; Sakaguchi, K. Synlett, 2017, 28, 327–332.
4.51 (d, $J = 7.0$ Hz, 1H), 4.44 (d, $J = 4.9$ Hz, 1H), 4.41 (ddd, $J = 5.9$, $4.4$, $4.0$ Hz, 1H), 3.85 (app dd, $J = 11.0$, $4.6$ Hz, 1H), 3.67 (ddd, $J = 10.8$, $6.4$, $3.3$ Hz, 1H), 3.63–3.55 (m, 2H), 3.42 (s, 3H), 3.27 (d, $J = 1.1$ Hz, 1H), 2.98 (dd, $J = 6.2$, $4.8$ Hz, 1H), 2.66–2.58 (m, 1H), 2.19–2.11 (m, 1H), 2.02 (ddd, $J = 12.3$, $9.0$, $6.2$ Hz, 1H), 1.96–1.87 (m, 2H), 1.79 (app qd, $J = 12.7$, $5.1$ Hz, 1H), 1.55 (d, $J = 1.4$ Hz, 3H), 1.13–1.08 (m, 1H), 0.98 (t, $J = 8.1$ Hz, 9H), 0.93 (s, 9H), 0.90 (d, $J = 7.0$ Hz, 3H), 0.88 (s, 9H), 0.87–0.85 (m, 12H), 0.81 (d, $J = 7.0$ Hz, 3H), 0.64 (q, $J = 8.0$ Hz, 6H), 0.14 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), 0.01 (3H), −0.20 (s, 3H), −0.25 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 158.2 (C), 157.8 (C), 139.7 (CH), 137.1 (C), 136.8 (C), 136.4 (C), 136.3 (C), 128.0 (CH), 127.94 (CH), 127.86 (CH), 127.85 (CH), 127.8 (CH), 118.1 (C), 114.5 (CH), 114.1 (CH), 99.2 (C), 90.4 (C), 82.2 (C), 81.0 (CH), 79.8 (CH), 78.4 (CH), 73.7 (CH), 73.6 (CH), 72.7 (CH), 69.9 (CH2), 69.8 (CH2), 66.7 (CH2), 62.6 (CH2), 50.6 (CH3), 43.3 (CH), 42.0 (CH), 35.3 (CH2), 30.0 (CH), 26.9 (CH2), 26.7 (CH3), 25.99 (CH3), 25.96 (CH3), 19.0 (CH3, C), 18.3 (C), 18.2 (C), 17.4 (CH3), 17.1 (CH3), 14.4 (CH3), 7.0 (CH3), 5.0 (CH2), −2.7 (CH3), −3.3 (CH3), −4.3 (CH3), −4.5 (CH3), −4.9 (CH3), −5.0 (CH3); IR (thin film, cm⁻¹) 3507 (br, w), 2954 (s), 2929 (s), 2879 (s), 2856 (s), 2217 (w), 1610 (m), 1587 (w), 1509 (s), 1462 (m), 1251 (s), 1173 (m), 1131 (m), 1053 (s), 941 (w), 836 (s), 775 (s), 731 (m), 670 (m); HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₆₇H₁₁₀O₁₀Si₄Na 1209.7074; found 1209.7057.

Scheme S10: Selected nOe interactions for S21.

Synthesis of the GH-ring containing enyne S22:¹⁶ Terminal alkyne S12 (97.0 mg, 0.200 mmol) and vinyl iodide 12 (166.5 mg, 0.2004 mmol) were dissolved in benzene (2.0 mL), and concentrated under reduced pressure to azeotrope residual water. This process was repeated two additional times before the reaction flask was sealed with a rubber septum, and the atmosphere was exchanged with nitrogen gas. Dry
diisopropylamine (1.0 mL) was added to the flask and nitrogen gas was bubbled through
the reaction mixture for 15 minutes. Tetrakis(triphenylphosphine) palladium(0) (24.5 mg,
21.2 µmol) and copper(I) iodide (8.2 mg, 43 µmol) were added, sequentially, to the
stirred mixture and the progress of the reaction was monitored by TLC. After 6 h, the
reaction was quenched by the addition of a saturated aqueous solution of NH₄Cl. The
contents of the reaction flask were transferred to a separatory funnel and extracted with
EtOAc (× 3). The combined organic layers were washed with brine, and dried over
anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents
were removed in vacuo to afford the crude isolate which was purified by flash column
chromatography on a Biotage® SNAP Ultra HP-Sphere 25 g cartridge with 95:5 to 60:40
hexanes–EtOAc gradient elution to afford enyne S22 (215.9 mg, 91%) as a colorless
foam.

Analytical data for S22:
TLC (SiO₂) Rf = 0.35 (hexanes–ethyl acetate, 4:1); ¹H NMR (600 MHz, CDCl₃) δ 7.46
(app s, 4H), 7.21 (app d, J = 8.4 Hz, 2H), 7.15 (app d, J = 8.4 Hz, 2H), 6.93 (app d, J =
8.4 Hz, 2H), 6.88 (app d, J = 8.4 Hz, 2H), 5.70 (app d, J = 9.9 Hz, 1H), 5.07 (s, 2H), 5.05
(s, 2H), 4.74 (d, J = 3.7 Hz, 1H), 4.71 (app t, J = 7.7 Hz, 1H), 4.51 (d, J = 7.0 Hz, 1H),
4.44 (d, J = 5.1 Hz, 1H), 4.35–4.32 (m, 1H), 3.89 (app td, J = 11.9, 2.6 Hz, 1H),
3.70–3.65 (m, 2H), 3.60 (ddd, J = 10.8, 6.2, 4.6 Hz, 1H), 3.52 (s, 3H), 3.68 (ddd, J = 11.4, 5.1,
1.8 Hz, 1H), 2.98 (dd, J = 6.6, 4.4 Hz, 1H), 2.66–2.58 (m, 1H), 2.24 (ddd, J = 12.8, 8.4,
5.5 Hz, 1H), 2.07–2.00 (m, 1H), 1.94–1.87 (m, 2H), 1.87–1.80 (m, 1H), 1.56 (app s, 3H),
1.46 (app ddd, J = 13.6, 5.5, 2.9 Hz, 1H), 1.15 (d, J = 7.3 Hz, 3H), 0.99 (t, J = 8.1 Hz,
9H), 0.91 (s, 9H), 0.88 (s, 9H), 0.87–0.86 (m, 3H), 0.86 (s, 9H), 0.81 (d, J = 7.3 Hz, 3H),
0.65 (q, J = 8.0 Hz, 6H), 0.07 (s, 6H), 0.04 (s, 3H), 0.01 (s, 3H), –0.20 (s, 3H), –0.25 (s,
3H); ¹³C NMR (150 MHz, CDCl₃) δ 158.2 (C), 157.9 (C), 157.1 (C), 137.1 (C), 136.8
(C), 136.4 (C), 136.3 (C), 128.0 (CH), 127.95 (CH), 127.87 (CH), 117.9 (C), 114.5 (CH),
114.1 (CH), 100.6 (C), 90.1 (C), 81.9 (C), 81.0 (CH), 78.4 (CH), 78.2 (CH), 75.1 (CH),
73.8 (CH), 72.9 (CH), 69.93 (CH₂), 69.86 (CH₂), 66.7 (CH₂), 57.0 (CH₂), 51.7 (CH₃),
43.3 (CH), 42.0 (CH), 37.2 (CH₂), 32.3 (CH), 30.7 (CH₂), 26.1 (CH₃), 26.00 (CH₃), 25.97
(CH₃), 18.34 (C), 18.29 (C), 18.2 (C), 17.5 (CH₃), 17.1 (CH₃), 14.4 (CH₃), 13.6 (CH₃),
7.1 (CH₃), 5.0 (CH₂), –3.6 (CH₃), –4.3 (CH₃), –4.5 (CH₃), –4.8 (CH₃), –4.9 (CH₃), –5.0
(CH₃); IR (thin film, cm⁻¹) 3583 (w), 3514 (br, m), 3059 (w), 3030 (w), 2955 (s), 2929
(s), 2883 (s), 2857 (s), 2223 (w), 1610 (m), 1585 (w), 1509 (s), 1463 (m), 1377 (m), 1250
(s), 1172 (m), 1070 (s), 1032 (s), 860 (m), 836 (s), 775 (s), 732 (s), 670 (m); HRMS (ES-
TOF) m/z: [M+Na]⁺ calcd for C₆₇H₁₁₀O₁₀Si₄Na 1209.7074; found 1209.7070.
D. Synthesis of the seco-Acid

Synthesis of carboxylic acid S23: TEMPO (19.4 mg, 124 µmol) and BAIB (210.0 mg, 652.0 µmol) were added sequentially to a vigorously stirred solution of S21 (257.8 mg, 217.0 µmol) in CH$_3$CN–H$_2$O (3:1 v/v, 1.80 mL) at room temperature and reacted overnight (23.5 h). The following morning, the reaction was quenched by the addition of a saturated aqueous solution of Na$_2$S$_2$O$_3$, and then extracted with EtOAc ($\times$ 3). The combined organic layers were dried over anhydrous Na$_2$SO$_4$, the supernatant was decanted from the drying agent, and the solvents were removed in vacuo. The crude isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 94:6 to 88:12 hexanes–EtOAc gradient elution to afford carboxylic acid S23 (166 mg, 64%) as a clear, orange film.

Analytical data for S23:
TLC (SiO$_2$) $R_f = 0.33$ (hexanes–ethyl acetate, 3:1); $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.46, 7.47 (ABq, $J = 8.4$ Hz, 4H), 7.22 (app d, $J = 8.6$ Hz, 2H), 7.15 (app d, $J = 8.6$ Hz, 2H), 6.94 (app d, $J = 8.6$ Hz, 2H), 6.88 (app d, $J = 8.6$ Hz, 2H), 5.65 (dq, $J = 10.0$, 1.4 Hz, 1H), 5.06 (s, 2H), 5.05 (s, 2H), 4.75 (d, $J = 4.8$ Hz, 1H), 4.68 (d, $J = 8.1$ Hz, 1H), 4.66 (dd, $J = 8.8$, 7.0 Hz, 1H), 4.44 (d, $J = 5.1$ Hz, 1H), 4.41 (ddd, $J = 5.9$, 4.8, 3.7 Hz, 1H), 3.85 (dd, $J = 11.2$, 4.2 Hz, 1H), 3.58 (ddd, $J = 13.0$, 11.2, 2.9 Hz, 1H), 3.42 (s, 3H), 3.27 (d, $J = 1.8$ Hz, 1H), 2.79 (app quintet, $J = 7.3$ Hz, 1H), 2.65–2.58 (m, 1H), 2.19–2.11 (m, 17

The intermediate aldehyde recovered from this reaction can be readily converted to the carboxylic acid using a modification of the above-described procedure. In such cases, the aldehyde (1 eq) can be reacted at room temperature with BAIB (2 eq) and TEMPO (0.2 eq) in CH$_2$Cl$_2$–H$_2$O (2:1 v/v) to yield the desired carboxylic acid S23.
1H), 2.01 (ddd, J = 12.5, 9.2, 5.9 Hz, 1H), 1.93 (ddd, J = 12.5, 7.0, 3.7 Hz, 1H), 1.79 (app qd, J = 12.7, 5.1 Hz, 1H), 1.54 (d, J = 1.4 Hz, 3H), 1.13–1.08 (m, 1H), 0.98 (t, J = 7.9 Hz, 9H), 0.94 (s, 9H), 0.92 (d, J = 7.3 Hz, 3H), 0.90 (d, J = 7.0 Hz, 3H), 0.87–0.85 (m, 12H), 0.85 (s, 9H), 0.64 (q, J = 7.9 Hz, 6H), 0.14 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H), −0.20 (s, 3H), −0.24 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 181.4 (C), 158.6 (C), 157.8 (C), 139.6 (CH), 137.1 (C), 136.7 (C), 136.4 (C), 134.5 (C), 128.3 (CH), 127.9 (CH), 127.83 (CH), 127.82 (CH), 118.1 (C), 114.6 (CH), 114.1 (CH), 99.2 (C), 90.3 (C), 82.1 (C), 79.8 (CH), 78.4 (CH), 77.2 (CH), 73.7 (CH), 73.6 (CH), 72.7 (CH), 69.9 (CH2), 69.8 (CH2), 62.6 (CH2), 50.6 (CH3), 49.5 (CH), 42.0 (CH), 35.3 (CH2), 29.9 (CH), 26.9 (CH2), 26.6 (CH3), 26.0 (CH3), 25.8 (CH3), 19.0 (CH3), 18.3 (C), 18.1 (C), 17.4 (CH3), 17.1 (CH3), 14.0 (CH3), 7.0 (CH3), 5.0 (CH2), −2.7 (CH3), −3.3 (CH3), −4.5 (CH3), −4.6 (CH3), −4.9 (CH3), −5.3 (CH3); IR (thin film, cm⁻¹) 3164 (w), 3060 (w), 3033 (w), 2955 (s), 2930 (s), 2880 (s), 2857 (s), 2739 (w), 2221 (w), 1712 (s), 1611 (s), 1585 (m), 1509 (s), 1462 (s), 1376 (m), 1294 (m), 1251 (s), 1173 (s), 1132 (s), 1054 (s), 1007 (m), 940 (m), 837 (s), 776 (s), 671 (m); HRMS (ES-TOF) m/z: [M+Na]+ calcd for C67H108O11Si4Na 1223.6866; found 1223.6884.

**Scheme S12:** Selected nOe interactions for S23.

**Synthesis of carboxylic acid S24:** TEMPO (15.5 mg, 99.2 µmol) and BAIB (178.2 mg, 0.5533 mmol) were added sequentially to a vigorously stirred solution of S22 (215.0 mg, 0.181 mmol) in CH3CN–H2O (3:1 v/v, 1.52 mL) at room temperature and reacted overnight (16 h). The following morning, the reaction was quenched by the addition of a saturated aqueous solution of Na2S2O3, and then extracted with EtOAc (× 3). The combined organic layers were dried over anhydrous Na2SO4, the supernatant was decanted from the drying agent, and the solvents were removed *in vacuo*. The crude
isolate was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 94:6 to 50:50 hexanes–EtOAc gradient elution to afford carboxylic acid S24 (157.7 mg, 73%) as a clear, orange film.

**Analytical data for S24:**

**TLC (SiO₂)** Rf = 0.49 (hexanes–ethyl acetate, 3:1); **¹H NMR** (600 MHz, CDCl₃) δ 7.47, 7.47 (ABq, J = 8.6 Hz, 4H), 7.24 (app d, J = 8.4 Hz, 2H), 7.16 (app d, J = 8.4 Hz, 2H), 6.94 (app d, J = 8.4 Hz, 2H), 6.89 (app d, J = 8.4 Hz, 2H), 5.71 (app d, J = 10.3 Hz, 1H), 5.07 (s, 2H), 5.05 (s, 2H), 4.75 (d, J = 4.0 Hz, 1H), 4.72 (app t, J = 8.1 Hz, 1H), 4.70 (d, J = 9.2 Hz, 1H), 4.45 (d, J = 5.1 Hz, 1H), 4.36–4.32 (m, 1H), 3.89 (app td, J = 11.9, 2.6 Hz, 1H), 3.68 (d, J = 5.1 Hz, 1H), 3.53 (s, 3H), 3.51–3.46 (m, 1H), 2.75 (app dq, J = 8.4, 7.2 Hz, 1H), 2.66–2.59 (m, 1H), 2.26 (ddd, J = 12.8, 8.1, 5.5 Hz, 1H), 2.08–2.00 (m, 1H), 1.92 (ddd, J = 12.5, 7.3, 1.8 Hz, 1H), 1.89–1.80 (m, 1H), 1.57 (app s, 3H), 1.49–1.44 (m, 1H), 1.16 (d, J = 7.0 Hz, 3H), 1.00 (t, J = 7.9 Hz, 9H), 0.94–0.91 (m, 12H), 0.88–0.85 (m, 12H), 0.83 (s, 9H), 0.66 (q, J = 7.9 Hz, 6H), 0.08 (s, 6H), 0.02 (s, 6H), –0.19 (s, 3H), –0.25 (s, 3H); **¹³C NMR** (150 MHz, CDCl₃) δ 181.2 (C), 158.5 (C), 157.8 (C), 140.0 (CH), 137.1 (C), 136.7 (C), 136.3 (C), 134.5 (C), 128.3 (CH), 127.9 (CH), 127.8 (CH), 117.9 (C), 114.6 (CH), 114.1 (CH), 100.6 (C), 90.0 (C), 81.9 (C), 78.4 (CH), 78.2 (CH), 77.2 (CH), 75.0 (CH), 73.7 (CH), 72.8 (CH), 69.9 (CH₂), 69.8 (CH₂), 56.9 (CH₂), 51.6 (CH₃), 49.4 (CH), 42.0 (CH), 37.2 (CH₂), 32.2 (CH), 30.7 (CH₂), 26.1 (CH₃), 25.9 (CH₃), 25.7 (CH₃), 18.3 (C), 18.2 (C), 18.1 (C), 17.4 (CH₃), 17.0 (CH₃), 14.0 (CH₃), 13.5 (CH₃), 7.0 (CH₃), 4.9 (CH₂), –3.7 (CH₃), –4.5 (CH₃), –4.6 (CH₃), –4.9 (CH₃), –5.0 (CH₃), –5.3 (CH₃); **IR** (thin film, cm⁻¹) 3060 (w), 3028 (w), 2955 (s), 2929 (w), 2883 (s), 2857 (s), 2737 (w), 2219 (w), 2184 (w), 1713 (s), 1610 (m), 1509 (s), 1462 (s), 1377 (m), 1303 (m), 1251 (s), 1173 (m), 1079 (s), 1032 (s), 939 (m), 858 (s), 837 (s), 776 (s), 734 (m), 670 (m); **HRMS** (ES-TOF) m/z: [M+Na]⁺ calcd for C₆₇H₁₀₈O₁₁Si₄Na 1223.6866; found 1223.6829.

![Scheme S13: Selected nOe interactions for S24.](image-url)
Synthesis of seco-acid 11: p-Toluenesulfonic acid monohydrate (15.2 mg, 79.9 µmol) was added in one portion to a stirred solution of carboxylic acid S23 (166.0 mg, 138.1 µmol) in CH₂Cl₂–MeOH (1:1 v/v, 23.0 mL) at 0 °C; progress of the reaction was monitored by TLC. After 2 h at 0 °C, the reaction was quenched by the addition of a saturated aqueous solution of NaHCO₃. The phases were separated, and the aqueous layer was extracted with CH₂Cl₂ (× 3). The combined organic layers were washed with brine, and then dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 95:5 to 50:50 hexanes–EtOAc gradient elution to afford compound 11 (151 mg, >99%) as a viscous, clear, pale yellow oil.

Analytical data for 11:
TLC (SiO₂) Rₛ = 0.39 (hexanes–ethyl acetate, 2:1); ¹H NMR (600 MHz, CDCl₃) δ 7.46, 7.47 (ABq, J = 8.3 Hz, 4H), 7.22 (app d, J = 8.6 Hz, 2H), 7.15 (app d, J = 8.6 Hz, 2H), 6.94 (app d, J = 8.6 Hz, 2H), 6.90 (app d, J = 8.6 Hz, 2H), 5.75 (dq, J = 9.9, 1.5 Hz, 1H), 5.06 (app s, 4H), 4.87 (d, J = 4.2 Hz, 1H), 4.70–4.66 (m, 2H), 4.39 (d, J = 5.7 Hz, 1H), 4.37–4.34 (m, 1H), 3.86 (app dd, J = 11.0, 4.4 Hz, 1H), 3.60 (ddd, J = 12.8, 11.0, 2.9 Hz, 1H), 3.43 (s, 3H), 3.28 (d, J = 1.8 Hz, 1H), 2.75 (app quintet, J = 7.3 Hz, 1H), 2.66–2.59 (m, 1H), 2.20–2.12 (m, 1H), 2.07 (ddd, J = 12.8, 6.2, 2.6 Hz, 1H), 2.01 (ddd, J = 12.8, 9.9, 5.1 Hz, 1H), 1.80 (app qd, J = 12.7, 5.5 Hz, 1H), 1.60 (d, J = 1.5 Hz, 3H), 1.14–1.09 (m, 1H), 0.99 (d, J = 7.1 Hz, 3H), 0.94 (s, 9H), 0.90 (d, J = 7.1 Hz, 3H), 0.88–0.82 (m, 21H), 0.16 (s, 3H), 0.08 (s, 3H), 0.03 (s, 3H), 0.00 (s, 3H), −0.21 (s, 3H), −0.24 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 181.0 (C), 158.7 (C), 158.0 (C), 142.2 (CH), 137.1 (C), 136.8 (C), 136.2 (C), 134.6 (C), 128.3 (CH), 127.95 (CH), 127.86 (CH), 117.0 (C), 114.6 (CH), 114.2 (CH), 99.1 (C), 92.9 (C), 80.7 (CH), 79.7 (C), 78.6 (CH), 77.2 (CH), 74.1 (CH), 72.8 (2 × CH), 69.9 (CH₂), 69.8 (CH₂), 62.7 (CH₂), 50.4 (CH₃), 49.4 (CH), 42.2 (CH), 34.4 (CH₂), 30.0 (CH), 26.9 (CH₂), 26.7 (CH₃), 25.9 (CH₃), 25.8 (CH₃), 19.0 (C), 18.9 (CH₃), 18.3 (C), 18.1 (C), 17.4 (CH₃), 16.9 (CH₃), 14.0 (CH₃), −2.8 (CH₃), −3.4 (CH₃), −4.5 (CH₃), −4.9 (CH₃), −5.3 (CH₃); IR (thin film, cm⁻¹) 3545 (br, w), 3061 (w), 3032 (w), 2954 (s), 2929 (s), 2884 (m), 2857 (s), 2215 (w), 1713 (s), 1610 (m), 1509 (s), 1463 (m), 1252 (s), 1173 (m), 1128 (m), 1074 (s), 1053 (s), 938 (w), 836 (s), 776 (s), 737 (m), 670 (m); HRMS (ES-TOF) m/z: [M+Na]⁺ calced for C₆₁H₉₄O₁₁Si₃Na 1109.6002; found 1109.6034.
**Synthesis of seco-acid S25:** $p$-Toluenesulfonic acid monohydrate (14.1 mg, 74.1 µmol) was added in one portion to a stirred solution of carboxylic acid S24 (147.7 mg, 122.9 µmol) in CH$_2$Cl$_2$–MeOH (1:1 v/v, 22.4 mL) at 0 °C; progress of the reaction was monitored by TLC. After 2.5 h at 0 °C, the reaction was quenched by the addition of a saturated aqueous solution of NaHCO$_3$. The phases were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ ($\times$ 3). The combined organic layers were washed with brine, and then dried over anhydrous Na$_2$SO$_4$. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 93:7 to 84:16 hexanes–EtOAc gradient elution to afford compound S25 (83.0 mg, 62%) as a viscous, clear, pale yellow oil.

**Analytical data for S25:**
TLC (SiO$_2$) R$_f$ = 0.20 (hexanes–ethyl acetate, 3:1); $^1$H NMR (600 MHz, CDCl$_3$) δ 7.47, 7.47 (ABq, $J$ = 9.1 Hz, 4H), 7.23 (app d, $J$ = 8.8 Hz, 2H), 7.16 (app d, $J$ = 8.8 Hz, 2H), 6.94 (app d, $J$ = 8.8 Hz, 2H), 6.90 (app d, $J$ = 8.8 Hz, 2H), 5.78 (dq, $J$ = 9.9, 1.1 Hz, 1H), 5.06 (s, 2H), 5.05 (s, 2H), 4.87 (d, $J$ = 4.0 Hz, 1H), 4.71–4.66 (m, 2H), 4.39 (d, $J$ = 5.9 Hz, 1H), 4.32–4.29 (m, 1H), 3.88 (app td, $J$ = 11.7, 2.6 Hz, 1H), 3.72 (d, $J$ = 5.1 Hz, 1H), 3.51 (s, 3H), 3.51–3.47 (m, 1H), 2.74 (dq, $J$ = 9.0, 7.0 Hz, 1H), 2.67–2.60 (m, 1H), 2.30 (ddd, $J$ = 13.0, 8.6, 5.5 Hz, 1H), 2.08–2.01 (m, 2H), 1.90–1.81 (m, 1H), 1.63 (d, $J$ = 1.1 Hz, 3H), 1.49–1.44 (m, 1H), 1.16 (d, $J$ = 7.3 Hz, 3H), 0.94 (d, $J$ = 7.3 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.86 (d, $J$ = 7.0 Hz, 3H), 0.82 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H), 0.02 (s, 3H), 0.00 (s, 3H), –0.21 (s, 3H), –0.25 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$) δ 180.9 (C), 158.6 (C), 158.0 (C), 142.4 (CH), 137.1 (C), 136.8 (C), 136.2 (C), 134.6 (C), 128.3

Scheme S14: Selected nOe interactions for 11.
(CH), 127.94 (CH), 127.89 (CH), 127.86 (CH), 117.0 (C), 114.6 (CH), 114.2 (CH), 100.6 (C), 92.4 (C), 79.8 (C), 79.0 (CH), 78.6 (CH), 77.2 (CH), 75.4 (CH), 73.0 (CH), 72.7 (CH), 69.90 (CH2), 69.85 (CH2), 57.0 (CH2), 51.4 (CH3), 49.4 (CH), 42.2 (CH), 35.7 (CH2), 32.3 (CH), 30.6 (CH2), 26.1 (CH3), 25.9 (CH3), 18.3 (C), 18.2 (C), 18.0 (C), 17.5 (CH3), 16.9 (CH3), 14.0 (CH3), 13.6 (CH3), –3.6 (CH3), –4.5 (CH3), –4.8 (CH3), –4.9 (CH3), –5.3 (CH3); IR (thin film, cm⁻¹) 3557 (w), 3055 (w), 3032 (w), 2954 (s), 2929 (s), 2887 (m), 2857 (s), 2217 (w), 1712 (s), 1610 (m), 1509 (s), 1462 (m), 1377 (w), 1304 (w), 1251 (s), 1136 (m), 1077 (s), 1035 (m), 938 (w), 857 (m), 836 (s), 775 (s), 737 (m), 670 (m); HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₆₁H₉₄O₁₁Si₃Na 1109.6002; found 1109.5978.

E. Yamaguchi Lactonization

Synthesis of macrolactone S26: Triethylamine (230.0 µL, 1.650 mmol) and 2,4,6-trichlorobenzoyl chloride (90.0 µL, 576 µmol) were sequentially added to a stirred solution of seco-acid 11 (97.7 mg, 89.8 µmol; azeotrope with PhH (× 3)) in anhydrous THF (18.0 mL) at 0 °C. After 1 h, the reaction flask was removed from the ice–water bath and stirring was maintained at room temperature for 4 h. The mixed anhydride was diluted with anhydrous toluene (67.4 mL) and THF (4.5 mL) before being taken up in an air tight syringe and added, at a rate of 2.10 mL/h, to a solution of DMAP (331.9 mg, 2.717 mmol) in PhMe (90.0 mL) at 45 °C. Once addition of the mixed anhydride was complete, the syringe was rinsed with 5.0 mL of PhMe, and the rinsing was added to the reaction flask. Stirring was maintained at 45 °C for an additional hour. After this time, the reaction flask was cooled to room temperature, and its contents were poured into a saturated aqueous solution of NaHCO₃. The phases were separated and the organic layer was washed with a saturated aqueous solution of NaHCO₃, and then brine, before drying over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 98:2

18 (a) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. Bull. Chem. Soc. Jpn. 1979, 52, 1989–1993; (b) Baumann, D. O.; McGowan, K. M.; Kedei, N.; Peach, M. L.; Blumberg, P. M.; Keck, G. E. J. Org. Chem. 2016, 81, 7862–7883.
to 78:22 hexanes–EtOAc gradient elution to afford macrolactone S26 (62.5 mg, 65%) as a colorless, iridescent film.

**Analytical data for S26:**

TLC (SiO₂) Rₜ = 0.29 (hexanes–ethyl acetate, 8:1); [α]²⁰°⁸⁹ = −83.7 (c 2.09, CHCl₃), ¹H NMR (600 MHz, CDCl₃) δ 7.17 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 6.67 (d, J = 8.6 Hz, 2H), 6.49 (d, J = 8.6 Hz, 2H), 5.75 (dd, J = 10.3, 1.1 Hz, 1H), 5.24–5.20 (m, 1H), 5.20 (s, 2H), 5.10 (d, J = 5.6 Hz, 1H), 5.05, 4.98 (ABq, J = 13.3 Hz, 2H), 4.67 (app t, J = 8.1 Hz, 1H), 4.62 (d, J = 9.1 Hz, 1H), 4.52 (d, J = 1.6 Hz, 1H), 3.85 (app dd, J = 11.1, 4.8 Hz, 1H), 3.59 (ddd, J = 12.8, 11.4, 2.9 Hz, 1H), 3.42 (s, 3H), 3.28 (d, J = 1.4 Hz, 1H), 2.58 (dq, J = 9.1, 7.0 Hz, 1H), 2.56–2.50 (m, 1H), 2.24 (app dt, J = 13.2, 8.4 Hz, 1H), 2.20–2.15 (m, 1H), 2.24 (ddd, J = 13.2, 7.7, 4.8 Hz, 1H), 1.80 (app qd, J = 12.8, 5.1 Hz, 1H), 1.39 (d, J = 1.1 Hz, 3H), 1.14–1.10 (m, 1H), 0.96–0.93 (m, 12H), 0.90–0.89 (m, 12H), 0.81 (s, 9H), 0.71 (d, J = 7.0 Hz, 3H), 0.17 (s, 3H), 0.09 (s, 3H), 0.02 (s, 3H), −0.03 (s, 3H), −0.24 (s, 3H), −0.28 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 173.9 (C), 157.0 (C), 156.9 (C), 139.0 (CH), 137.2 (C), 136.70 (C), 136.67 (C), 134.9 (C), 128.1 (CH), 128.0 (CH), 127.50 (CH), 127.48 (CH), 117.8 (C), 117.3 (CH), 117.2 (CH), 99.0 (C), 91.0 (C), 80.5 (C), 79.2 (CH), 78.2 (CH), 76.7 (CH), 73.5 (CH), 72.7 (CH), 72.2 (CH₂), 71.2 (CH), 70.6 (CH₂), 62.7 (CH₂), 50.8 (CH₃), 50.5 (CH), 41.6 (CH), 30.6 (CH₂), 29.9 (CH), 26.9 (CH₂), 26.6 (CH₃), 26.1 (CH₃), 25.8 (CH₃), 19.0 (C, CH₃), 18.4 (C), 18.1 (C), 17.9 (CH₂), 17.4 (CH₃), 13.5 (CH₃), −2.7 (CH₃), −3.4 (CH₃), −4.3 (CH₃), −5.0 (CH₃), −5.2 (CH₃); IR (thin film, cm⁻¹) 3058 (w), 3031 (w), 2955 (vs), 2929 (vs), 2883 (s), 2857 (s), 2213 (w), 1741 (s), 1609 (m), 1509 (s), 1462 (m), 1362 (m), 1254 (vs), 1219 (s), 1173 (s), 1128 (s), 1077 (vs), 1053 (vs), 938 (vs), 775 (vs), 735 (m), 669 (m); HRMS (ES-TOF) m/z: [M+Na]+= calcd for C₆₁H₉₂O₁₀Si₃Na 1091.5896; found 1091.5876.

![Scheme S15: Selected nOe interactions for S26.](image-url)
Synthesis of macrolactone S27: Triethylamine (195.0 µL, 1.399 mmol) and 2,4,6-trichlorobenzoyl chloride (75.0 µL, 48.0 µmol) were sequentially added to a stirred solution of seco-acid S25 (82.4 mg, 75.8 µmol; azeotrope with PhH (× 3)) in anhydrous THF (18.9 mL) at 0 °C. After 16 minutes, the reaction flask was removed from the ice–water bath and stirring was maintained at room temperature for 3.5 h. The mixed anhydride was diluted with anhydrous toluene (56.9 mL) before being taken up in an air tight syringe and added, at a rate of 2.10 mL/h, to a solution of DMAP (283.1 mg, 2.317 mmol) in PhMe (76.0 mL) at 45 °C. Once the addition of the mixed anhydride was complete, the syringe was rinsed with 5.0 mL of PhMe and the rinsing was added to the reaction flask. Stirring was maintained at 45 °C for an additional hour. After this time, the reaction flask was cooled to room temperature, and its contents were poured into a saturated aqueous solution of NaHCO₃. The phases were separated and the organic layer was washed with a saturated aqueous solution of NaHCO₃, and then brine, before drying over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 96:4 hexanes–EtOAc to afford macrolactone S27 (39.4 mg, 49%) as a colorless, iridescent film.

**Analytical data for S27:**

TLC (SiO₂) Rₓ = 0.39 (hexanes–ethyl acetate, 8:1); [α]₂⁰.₈[SG] = −55.9 (c 0.662, CHCl₃);

**¹H NMR** (600 MHz, CDCl₃) δ 7.17, 7.16 (ABq, J = 8.5 Hz, 4H), 7.01 (app d, J = 8.6 Hz, 2H), 6.98 (app d, J = 8.6 Hz, 2H), 6.62 (app d, J = 8.6 Hz, 2H), 6.57 (app d, J = 8.6 Hz, 2H), 6.68 (app dd, J = 10.0, 1.3 Hz, 1H), 5.22–5.18 (m, 1H), 5.20, 5.17 (ABq, J = 13.8 Hz, 2H), 5.07, 5.05 (ABq, J = 13.5 Hz, 2H), 5.03 (d, J = 5.1 Hz, 1H), 4.66–4.61 (m, 2H), 3.84 (app td, J = 11.7, 3.0 Hz, 1H), 3.70 (d, J = 4.8 Hz, 1H), 3.53–3.49 (m, 1H), 3.49 (s, 3H), 2.61 (dq, J = 9.0, 7.0 Hz, 1H), 2.59–2.54 (m, 1H), 2.45 (app dt, J = 13.8, 7.1 Hz, 1H), 2.10 (ddd, J = 13.6, 7.7, 3.3 Hz, 1H), 2.07–2.00 (m, 1H), 1.89–1.81 (m, 1H), 1.49–1.45 (m, 1H), 1.44 (d, J = 1.3 Hz, 3H), 1.14 (d, J = 7.0 Hz, 3H), 0.92–0.88 (m, 21H), 0.80 (s, 9H), 0.75 (d, J = 7.0 Hz, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H), −0.03 (s, 3H), −0.19 (s, 3H), −0.31 (s, 3H);

**¹³C NMR** (150 MHz, CDCl₃) δ 174.1 (C), 157.04 (C), 157.01 (C), 139.5 (CH), 136.9 (C), 136.8 (C), 136.6 (C), 135.0 (C), 127.8 (CH), 127.5 (CH), 117.5 (C), 117.1 (CH), 116.7 (CH), 100.3 (C), 90.7 (C), 80.5 (C), 78.4 (CH), 77.9 (CH), 76.6 (CH), 74.4 (CH), 72.6 (CH), 72.4 (CH), 71.5 (CH₂),
70.9 (CH₂), 57.2 (CH₂), 51.3 (CH₃), 50.2 (CH), 41.7 (CH), 33.22 (CH₂), 32.19 (CH), 30.5 (CH₂), 26.1 (CH₃), 26.0 (CH₃), 25.8 (CH₃), 18.4 (C), 18.1 (C), 17.5 (CH₃), 17.1 (CH₃), 13.7 (CH₃), 13.5 (CH₃), −3.6 (CH₃), −4.3 (CH₃), −4.5 (CH₃), −4.7 (CH₃), −5.0 (CH₃), −5.2 (CH₃); IR (thin film, cm⁻¹) 3060 (w), 3030 (w), 2955 (vs), 2929 (vs), 2885 (s), 2857 (vs), 2219 (w), 1740 (s), 1610 (m), 1509 (s), 1471 (m), 1462 (m), 1253 (vs), 1222 (m), 1171 (m), 1081 (vs), 1035 (s), 837 (vs), 775 (s), 737 (w), 669 (w);

HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₆₁H₉₂O₁₀Si₃Na 1091.5896; found 1091.5872.

Scheme S16: Selected nOe interactions for S27.

F. Deprotection Sequence to a First-Generation PTX2 Analogue

Synthesis of macrolactone S28:¹⁹ A solution of TASF (201.6 mg, 731.8 µmol) in DMF (750 µL) was added to a stirred solution of S26 (62.5 mg, 58.4 µmol) and dH₂O (20.0 µL, 1.10 mmol) in DMF (310 µL) and the resulting clear, yellow mixture was reacted for 23.5 h at room temperature. Following this period, the contents of the reaction flask were diluted with EtOAc, and then washed with pH 7.0 buffer (3 × 8.0 mL). The combined aqueous washings were extracted with EtOAc (× 3), and then the combined organic extracts were washed with brine and dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 92:8 to 44:66 hexanes–EtOAc gradient elution to afford triol S28 (38.3 mg, 90%) as a colorless, iridescent film.

¹⁹ Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. J. Org. Chem. 1998, 63, 6436–6437.
**Analytical data for S28:**

**TLC (SiO$_2$)** $R_f = 0.26$ (hexanes–ethyl acetate, 1:1); $[\alpha]_{589}^{20.8} = -107.4$ (c 0.628, CHCl$_3$);

**$^1$H NMR** (600 MHz, CDCl$_3$) $\delta$ 7.18, 7.13 (ABq, $J = 8.0$ Hz, 2H), 7.05 (app d, $J = 8.6$ Hz, 2H), 6.90 (app d, $J = 8.5$ Hz, 2H), 6.65 (app d, $J = 8.6$ Hz, 2H), 6.50 (app d, $J = 8.5$ Hz, 2H), 5.77 (app dd, $J = 9.9$, 1.1 Hz, 1H), 5.37 (ddd, $J = 5.9$, 4.4, 2.2 Hz, 1H), 5.18, 5.18 (ABq, $J = 14.4$ Hz, 2H), 5.09, 5.04 (ABq, $J = 13.2$ Hz, 2H), 5.00 (d, $J = 4.4$ Hz, 1H), 4.75 (app d, $J = 7.9$ Hz, 1H), 4.57 (dd, $J = 9.5$, 6.7 Hz, 1H), 4.39 (app d, $J = 4.3$ Hz, 1H), 3.77 (app dd, $J = 11.2$, 5.0 Hz, 1H), 3.61 (ddd, $J = 13.2$, 11.4, 2.9 Hz, 1H), 3.59–3.55 (br s, 1H), 3.38 (s, 3H), 3.36 (dd, $J = 7.3$, 1.8 Hz, 1H), 2.76 (dq, $J = 7.7$, 7.2 Hz, 1H), 2.67–2.60 (m, 1H), 2.42 (ddd, $J = 13.6$, 9.5, 5.9 Hz, 1H), 2.30 (d, $J = 7.6$ Hz, 1H), 2.16–2.10 (m, 2H), 2.08–2.03 (br s, 1H), 1.56 (app qd, $J = 13.2$, 5.1 Hz, 1H), 1.48 (d, $J = 1.1$ Hz, 3H), 1.26 (app dt, $J = 13.2$, 2.9 Hz, 1H), 0.94 (d, $J = 7.0$ Hz, 3H), 0.86 (d, $J = 7.1$ Hz, 3H);

**$^{13}$C NMR** (150 MHz, CDCl$_3$) $\delta$ 174.5 (C), 157.01 (C), 157.00 (C), 140.4 (CH), 136.9 (C), 136.6 (C), 136.2 (C), 134.0 (C), 128.5 (CH), 127.6 (CH), 127.3 (CH), 118.4 (C), 118.3 (CH), 116.7 (CH), 98.5 (C), 91.0 (C), 80.54 (C), 80.49 (CH), 78.0 (CH), 75.6 (CH), 75.0 (CH), 72.4 (CH)$_2$, 72.1 (CH), 71.5 (CH), 70.2 (CH)$_2$, 62.0 (CH)$_2$, 50.2 (CH$_3$), 47.6 (CH), 40.4 (CH), 33.3 (CH$_2$), 29.1 (CH), 26.6 (CH$_2$), 17.5 (CH$_3$), 17.12 (CH$_3$), 17.08 (CH$_3$), 13.3 (CH$_3$);

**IR** (thin film, cm$^{-1}$) 3432 (br, vs), 3059 (w), 3031 (w), 2961 (m), 2931 (m), 2874 (m), 2222 (w), 1733 (s), 1644 (s), 1610 (s), 1508 (s), 1456 (m), 1377 (m), 1262 (s), 1219 (s), 1173 (s), 1123 (m), 1046 (s), 934 (m), 837 (m), 812 (m), 735 (m), 702 (m);

**HRMS (ES-TOF)** $m/z$: [M+Na]$^+$ calcd for C$_{43}$H$_{50}$O$_{10}$Na 749.3302; found 749.3304.

**Scheme S17:** Selected nOe interactions for S28.
Synthesis of S29: A solution of TASF (91.4 mg, 332 µmol) in DMF (335 µL) was added to a stirred solution of S27 (33.1 mg, 30.9 µmol) and dH2O (11.0 µL, 610 µmol) in DMF (165 µL) and the resulting clear, yellow mixture was reacted for 2 days at room temperature. Following this period, the contents of the reaction flask were diluted with EtOAc (6.0 mL) and then washed with pH 7.0 buffer (3 × 4.0 mL). The combined aqueous washings were extracted with EtOAc (× 3), and then the combined organic extracts were washed with brine and dried over anhydrous Na2SO4. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP Ultra HP-Sphere 10 g cartridge with 92:8 to 44:66 hexanes–EtOAc gradient elution to afford triol S29 (12.3 mg, 55%) as a colorless, iridescent film. Note: The global desilylation of S27 was found to proceed at a considerably slower rate relative to S26, and mono-silylated products (derived from S27) were isolated from the reaction mixture (8.3 mg, 32%; analytical data not reported).

Analytical data for S29:
TLC (SiO2) Rf = 0.29 (hexanes–ethyl acetate, 1:1); [α]D22.9 = −79.0 (c 0.232, CHCl3); 1H NMR (600 MHz, CDCl3) δ 7.18 (app d, J = 8.0 Hz, 2H), 7.13 (app d, J = 8.0 Hz, 2H), 7.05 (app d, J = 8.6 Hz, 2H), 6.89 (app d, J = 8.6 Hz, 2H), 6.65 (app d, J = 8.6 Hz, 2H), 6.52 (app d, J = 8.6 Hz, 2H), 5.79 (app dd, J = 10.3, 1.5 Hz, 1H), 5.36 (ddd, J = 6.2, 4.4, 2.9 Hz, 1H), 5.18, 5.18 (ABq, J = 14.5 Hz, 2H), 5.11, 5.07 (ABq, J = 13.2 Hz, 2H), 5.02 (d, J = 4.4 Hz, 1H), 4.74 (d, J = 8.2 Hz, 1H), 4.50 (app t, J = 8.1 Hz, 1H), 4.35 (d, J = 4.8 Hz, 1H), 3.74 (dd, J = 9.9, 5.5 Hz, 1H), 3.71 (app td, J = 11.9, 2.9 Hz, 1H), 3.57 (ddd, J = 11.4, 5.5, 2.6 Hz, 1H), 3.43–3.36 (m, 4H), 2.80 (dq, J = 8.1, 7.2 Hz, 1H), 2.68–2.62 (m, 1H), 2.58 (ddd, J = 13.6, 8.4, 6.6 Hz, 1H), 2.21 (d, J = 9.9 Hz, 1H), 2.17–2.11 (m, 2H), 1.93–1.86 (m, 2H), 1.50 (d, J = 1.5 Hz, 3H), 1.48 (app ddd, J = 13.6, 6.2, 2.6 Hz, 1H), 1.10 (d, J = 7.2 Hz, 3H), 0.91 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H); 13C NMR (150 MHz, CDCl3) δ 174.7 (C), 157.2 (C), 157.0 (C), 140.6 (CH), 137.0 (C), 136.5 (C), 136.2 (C), 133.8 (C), 128.7 (CH), 127.8 (CH), 127.4 (CH), 127.3 (CH), 118.6 (CH), 118.5 (C), 116.5 (CH), 99.9 (C), 90.7 (C), 80.7 (C), 80.2 (CH), 78.2 (CH), 75.7 (CH), 75.1 (CH), 72.6 (CH), 72.5 (CH2), 69.9 (CH2), 69.4 (CH), 57.2 (CH2), 49.7 (CH3), 47.5 (CH), 40.5 (CH), 33.8 (CH2), 31.1 (CH), 30.1 (CH2), 17.2 (CH3), 17.1 (CH3), 13.44 (CH3), 13.36 (CH3); IR (thin film, cm⁻¹) 3445 (br, s), 3055 (w), 3030 (w), 2963 (s), 2929 (s), 2882 (s), 2854 (s), 2222 (w), 1734 (s), 1069 (s), 1509 (s), 1457 (m), 1261 (s), 1220
(s), 1173 (s), 1038 (w), 932 (w), 896 (m), 836 (m), 817 (m), 735 (s), 702 (w); HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₄₃H₅₀O₁₀Na 749.3302; found 749.3307.

Scheme S18: Selected nOe interactions for S29.

Note: Substrates S28 and S29 were each subject to the general reaction conditions annotated in the above scheme. We have chosen to provide the experimental procedure for the reaction of substrate S29 (rather than S28), as the accompanying characterization data is specific to that procedure, and the resulting ratio of anomers for compound 10 was found to be similar in either case.

Synthesis of 10:²⁰ An aqueous solution of 2N HCl (2.0 mL) was added to a stirred solution of S29 (11.6 mg, 16.0 µmol) in THF (8.0 mL) at room temperature and reacted overnight (24 h). The following day, the reaction flask was placed in an ice–water bath and cooled to 0 °C before being quenched by the careful addition of a saturated aqueous solution of NaHCO₃. The contents of the reaction flask were transferred to a separatory funnel, extracted with CH₂Cl₂ (× 3), and the combined organic extracts were dried over anhydrous Na₂SO₄. The supernatant was decanted from the drying agent and the solvents were removed in vacuo to afford the crude product, which was purified by flash column chromatography on a Biotage® SNAP KP-Sil 10 g cartridge with 88:12 to 0:100 hexanes–EtOAc gradient elution to afford 10 (dr = 6:1 to 7:1) as a colorless foam.

²⁰ Fujiwara, K.; Suzuki, Y.; Koseki, N.; Aki, Y.; Kikuchi, Y.; Murata, S.; Yamamoto, F.; Kawamura, M.; Norikura, T.; Matsue, H.; Murai, A.; Katoono, R.; Kawai, H.; Suzuki, T. Angew. Chem. Int. Ed. 2014, 53, 780–784.
Analytical data for 10:
TLC (SiO₂) Rf = 0.39 (hexanes–ethyl acetate, 1:2); ¹H NMR (600 MHz, CDCl₃) δ 7.19, 7.14 (ABq, J = 8.0 Hz, 4H), 7.06 (app d, J = 8.6 Hz, 2H), 6.90 (app d, J = 8.5 Hz, 2H), 6.65 (app d, J = 8.6 Hz, 2H), 6.52 (app d, J = 8.6 Hz, 2H), 5.78 (app dd, J = 9.9, 1.5 Hz, 1H), 5.39 (ddd, J = 5.7, 4.2, 1.8 Hz, 1H), 5.19, 5.19 (ABq, J = 14.4 Hz, 2H), 5.10, 5.06 (ABq, J = 13.2 Hz, 2H), 5.03 (d, J = 4.4 Hz, 1H), 4.74 (app d, J = 7.9 Hz, 1H), 4.44 (dd, J = 10.4, 5.8 Hz, 1H), 4.38 (app d, J = 4.4 Hz, 1H), 3.96 (ddd, J = 12.8, 11.4, 2.6 Hz, 1H), 3.7 (app dd, J = 11.3, 1.8 Hz, 1H), 3.46–3.44 (br s, 1H), 3.33 (dd, J = 9.8, 2.1 Hz, 1H), 3.04 (s, 1H), 2.78 (dq, J = 8.1, 7.1 Hz, 1H), 2.67–2.60 (m, 1H), 2.26 (ddd, J = 13.6, 5.9, 1.8 Hz, 1H), 2.18–2.12 (m, 1H), 2.10 (ddd, J = 13.7, 10.4, 5.8 Hz, 1H), 1.92 (br s, 1H), 1.76 (d, J = 9.9 Hz, 1H), 1.54–1.46 (m, 4H), 1.36–1.31 (m, 1H), 0.97 (d, J = 6.9 Hz, 3H), 0.91 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 174.4 (C), 157.11 (C), 157.06 (C), 140.6 (CH), 137.0 (C), 136.6 (C), 136.1 (C), 134.0 (C), 128.6 (CH), 127.7 (CH), 127.6 (CH), 127.3 (CH), 118.7 (C), 118.4 (CH), 116.7 (CH), 96.8 (C), 91.5 (C), 81.3 (CH), 80.1 (C), 78.1 (CH), 75.7 (CH), 74.8 (CH), 73.3 (CH), 72.4 (CH₂), 71.1 (CH), 70.1 (CH₂), 61.0 (CH₂), 47.6 (CH), 40.4 (CH), 32.9 (CH₂), 29.3 (CH), 27.1 (CH₂), 17.4 (CH₃), 17.1 (CH₃), 13.4 (CH₃); IR (thin film, cm⁻¹) 3438 (br, s), 3054 (w), 2961 (s), 2930 (s), 2875 (s), 2222 (w), 1735 (s), 1609 (s), 1509 (s), 1456 (m), 1378 (m), 1306 (m), 1264 (s), 1219 (s), 1173 (s), 1081 (m), 1037 (s), 1008 (s), 835 (m), 819 (m), 737 (s), 702 (w); HRMS (ES-TOF) m/z: [M+Na]⁺ calcd for C₄₂H₄₈O₁₀Na 735.3145; found 735.3133.

Scheme S19: Selected nOe interactions for 10.
4. NMR Spectra
Figure S1: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 4 (with 3% EtOAc).

![NMR spectra of compound 4](image-url)
**Figure S2:** Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 4 (with 3% EtOAc).
Figure S3: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 2.
Figure S4: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 2.
Figure S5: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S2.
**Figure S6:** Expanded region from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S2.
Figure S7: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 5.
Figure S8: Expanded region from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 5.
Figure S9: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S4.
Figure S10: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of S4.
Figure S11: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of 7.
Figure S12: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of 7.
Figure S13: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S7.
Figure S14: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of S7.
Figure S15: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S8.
Figure S16: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of S8.
Figure S17: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S9.
Figure S18: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of S9.
Figure S19: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S10.
Figure S20: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of S10.
Figure S21: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S11.
Figure S22: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of S11.
Figure S23: $^1$H NMR (600 MHz, $\text{C}_6\text{D}_6$) and $^{13}$C NMR (150 MHz, $\text{C}_6\text{D}_6$) of 1.
Figure S24: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) spectrum of 1.
Figure S25: $^1$H NMR (600 MHz, C$_6$D$_6$) and $^{13}$C NMR (150 MHz, C$_6$D$_6$) of S12.
Figure S26: Expanded regions from the $^1$H NMR (600 MHz, C$_6$D$_6$) of S12.
Figure S27: $^1$H NMR (500 MHz, CDCl$_3$) and $^{13}$C NMR (125 MHz, CDCl$_3$) of 15.
Figure S28: Expanded region from the $^1$H NMR (500 MHz, CDCl$_3$) spectrum of 15.
Figure S29: $^1$H NMR (500 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S14.
Figure S30: Expanded region from the $^1$H NMR (500 MHz, CDCl$_3$) spectrum of S14.
Figure S31: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S15.
Figure S32: Expanded region from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S15.
Figure S33: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 17.
Figure S34: Expanded region from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 17.
Figure S35: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S16.
**Figure S36:** Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S16.
Figure S37: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 18.
Figure S38: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 18.
Figure S39: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S17.
Figure S40: Expanded region from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S17.
Figure S41: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S18.
Figure S42: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S18.
Figure S43: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 20.
Figure S44: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 20.
Figure S45: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S19.
Figure S46: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S19.
Figure S47: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S20.
Figure S48: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S20.
Figure S49: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 12.
**Figure S50:** Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 12.
Figure S51: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S21.
Figure S52: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S21.
Figure S53: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S22.
**Figure S54**: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S22.
Figure S55: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S23.
Figure S56: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S23.
Figure S57: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S24.
Figure S58: Expanded regions from the $^1$H NMR (600 MHz, CDCl₃) spectrum of S24.
Figure S59: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 11.
Figure S60: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 11.
Figure S61: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S25.
Figure S62: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S25.
Figure S63: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S26.
Figure S64: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S26.
Figure S65: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S27.
Figure S66: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S27.
Figure S67: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S28.
Figure S68: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S28.
Figure S69: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of S29.
Figure S70: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of S29.
Figure S71: $^1$H NMR (600 MHz, CDCl$_3$) and $^{13}$C NMR (150 MHz, CDCl$_3$) of 10.
Figure S72: Expanded regions from the $^1$H NMR (600 MHz, CDCl$_3$) spectrum of 10.