Total Synthesis of Marinomycins A–C and of Their Monomeric Counterparts mono-Marinomycin A and iso-mono-Marinomycin A.


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Supporting Information

Experimental Data for Compounds

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, diethyl ether (Et₂O), and methylene chloride (CH₂Cl₂), were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Acetonitrile (CH₃CN), dimethylsulfoxide (DMSO), and ethanol (EtOH) were purchased in anhydrous form and used without further purification. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on
0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of \( p \)-anisaldehyde and heat as a developing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-600, DRX-500 or AMX-400 instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: \( s \) = singlet, \( d \) = doublet, \( t \) = triplet, \( q \) = quartet, \( m \) = multiplet, \( \text{pent} \) = pentet, \( \text{hex} \) = hexet, \( \text{br} \) = broad. IR spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. LC/MS data were recorded on an Agilent 1100 series LC system coupled to an ESI Agilent MSD. Melting points (m.p.) are uncorrected and were recorded on a Thomas Hoover Uni-Melt melting point apparatus. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI TOF (time of flight) mass spectrometer at 4000 V emitter voltage.

**Secondary propargylic alcohol 10**

To a solution of 3-(4-methoxybenzyloxy)propyne 8 (106.0 g, 0.60 mol, 2.0 equiv) in THF (1.5 L) at \(-78^\circ\text{C}\) was added \( n \)-BuLi (240.0 mL, 2.5 M in hexanes, 0.60 mol, 2.0 equiv) and the reaction mixture was stirred at \(-78^\circ\text{C}\) for 45 min. \( \text{BF}_3\cdot\text{OEt}_2 \) (45.7 mL, 0.36 mol, 1.2 equiv) was then added dropwise to the solution, followed by a solution of \((R)\)-1,2-epoxy-4-\text{tert}-butyldimethylsilyl ether 9 (60.9 g, 0.30 mol, 1.0 equiv) in THF (125 mL), and the reaction mixture was stirred at \(-78^\circ\text{C}\) for 4 h. The reaction mixture was then quenched with sat. aqueous \( \text{NH}_4\text{Cl} \) (1 L) and the resulting biphasic mixture was extracted with \( \text{Et}_2\text{O} \) (3 \( \times \) 1 L). The combined organic layers were washed with \( \text{H}_2\text{O} \) (2 \( \times \) 1 L) and brine (1 L), then dried (\( \text{MgSO}_4 \)), and concentrated. Flash column chromatography (silica
gel, hexanes:EtOAc 5:1) afforded secondary propargylic alcohol 10 (101.0 g, 0.53 mol, 89% yield) as a colorless oil. 10: Rf = 0.17 (silica gel, hexanes:EtOAc 17:3); [α]D32 = +16.1 (CHCl₃, c = 1.86); IR (film) νmax 3450, 2921, 2852, 1608, 1514, 1248, 1076, 835 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.27 (d, J = 9.0 Hz, 2 H), 6.87 (d, J = 9.0 Hz, 2 H), 4.51 (s, 2 H), 4.13 (t, J = 2.1 Hz, 2 H), 4.00 (ddt, J = 9.0, 6.5, 2.5 Hz, 1 H), 3.92 (dd, J = 10.0, 5.5, 4.8 Hz, 1 H), 3.83 (dd, J = 10.0, 4.8, 3.8 Hz, 1 H), 3.80 (s, 3 H), 2.50 (ddt, J = 16.6, 5.8, 2.1 Hz, 1 H), 2.43 (ddt, J = 16.6, 6.7, 2.1 Hz, 1 H), 1.87–1.81 (m, 1 H), 1.75 (ddt, J = 14.5, 8.5, 4.5 Hz, 1 H), 0.90 (s, 9 H), 0.08 ppm (s, 6 H); ¹³C NMR (125 MHz, CDCl₃): δ = 159.3, 129.7, 129.6, 113.8, 83.4, 78.0, 71.1, 70.5, 62.3, 57.3, 55.3, 37.2, 27.5, 25.8, 18.1, −5.5, −5.6 ppm; HRMS (ESI-TOF): calcd for C₂₁H₃₄O₄SiCl⁻ [M+Cl⁻]: 413.1920, found 413.1914.

PMB-protected propargylic alcohol 11

To a solution of secondary propargylic alcohol 11 (220.0 g, 0.58 mol, 1.0 equiv) in DMF (500 mL) was added imidazole (119.0 g, 1.74 mol, 3.0 equiv) followed by tert-butylchlorodimethylsilane (105 g, 0.70 mol, 1.2 equiv), and the reaction mixture was stirred at 25 °C for 6 h. The reaction mixture was then quenched with H₂O (1 L), and the aqueous layer was extracted with Et₂O (3 × 1 L). The combined organic layers were washed with H₂O (2 × 1 L) and brine (1 L), then dried (MgSO₄), and concentrated. The resulting oil was azeotroped with toluene (4 × 500 mL) to give PMB-protected propargylic alcohol 11 (266.0 g, 0.56 mol, 96% yield) as a colorless oil, which was used without further purification. 11: Rf = 0.48 (silica gel, hexanes:EtOAc 17:3); [α]D32 = +11.8 (CHCl₃, c = 1.39); IR (film) νmax 2931, 2854, 1250, 1091, 1039, 833 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.28 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 4.51 (s, 2 H), 4.12 (t, J = 2.1 Hz, 2 H), 4.00–3.92
(m, 1 H), 3.81 (s, 3 H), 3.72–3.68 (m, 2 H), 2.41 (dt, \( J = 6.0, 2.1 \text{ Hz}, 2 \text{ H} \)), 1.86 (ddt, \( J = 13.5, 7.0, 4.0 \text{ Hz}, 1 \text{ H} \)), 1.75–1.67 (m, 1 H), 0.89 (s, 18 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.04 ppm (s, 6 H); \(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)): \( \delta = 159.3, 129.8, 129.7, 113.7, 84.1, 77.6, 70.9, 68.0, 59.5, 57.3, 55.3, 39.8, 28.0, 25.9, 25.8, 18.2, 18.0, −4.5, −4.8, −5.3, −5.4 \text{ ppm}; \) HRMS (ESI-TOF): calcd for C\(_{27}\)H\(_{49}\)O\(_4\)Si\(_2\) \([\text{M}+\text{H}]^+\): 493.3164, found 493.3143.

**Primary propargylic alcohol 12**

To a solution of PMB-protected propargylic alcohol 11 (49.0 g, 100 mmol, 1.0 equiv) in CH\(_2\)Cl\(_2\) (1.0 L) at 25 °C was added pH 7 phosphate buffer (100 mL), followed by DDQ (39.0 g, 150 mmol, 1.5 equiv). The reaction mixture was stirred at 25 °C for 3 h, then slowly quenched with sat. aqueous NaHCO\(_3\) (1 L) and the resulting biphasic mixture was extracted with EtOAc (2 x 1.5 L). The combined organic layers were washed with sat. aqueous NaHCO\(_3\) (2 x 1 L), H\(_2\)O (1 L), and brine (1 L), then dried (MgSO\(_4\)), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded primary propargylic alcohol 12 (29.0 g, 79 mmol, 79% yield) as a colorless oil. 12: \( R_f = 0.45 \) (silica gel, hexanes:EtOAc 5:1); \([\alpha]_D^{32} = +18.1 \) (CHCl\(_3\), \( c = 1.24 \)); IR (film) \( \nu_{\text{max}} \) 3379, 2935, 2857, 1459, 1248, 1099, 1022, 833, 772 cm\(^{-1}\); \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)): \( \delta = 4.24 \) (t, \( J = 2.0 \text{ Hz}, 2 \text{ H} \)), 3.99–3.91 (m, 1 H), 3.71–3.67 (m, 2 H), 2.38 (dt, \( J = 6.0, 2.1 \text{ Hz}, 2 \text{ H} \)), 1.83 (ddt, \( J = 14.0, 7.5, 4.5 \text{ Hz}, 1 \text{ H} \)), 1.69 (ddt, \( J = 14.0, 7.0, 6.0 \text{ Hz}, 1 \text{ H} \)), 1.61 (br s, 1 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.04 ppm (s, 6 H); \(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)): \( \delta = 83.6, 80.0, 68.0, 59.5, 51.4, 39.7, 27.9, 25.9, 25.8, 18.3, 18.1, −4.8, −4.5, −5.2, −5.3 \text{ ppm}; \) HRMS (ESI-TOF): calcd for C\(_{19}\)H\(_{41}\)O\(_3\)Si\(_2\) \([\text{M}+\text{H}]^+\): 373.2589, found 373.2587.
Vinyl iodide 13

To a solution of primary propargylic alcohol 12 (50.0 g, 134 mmol, 1.0 equiv) in THF (370 mL) was added Red-Al® (68.5 mL, 3.33 M in toluene, 228 mmol, 1.7 equiv) dropwise and the reaction mixture was stirred at 25 °C for 45 min. The reaction mixture was cooled to –78 °C and a solution of NIS (56.7 g, 242 mmol, 1.8 equiv) in THF (250 mL) was added dropwise, and the reaction mixture was stirred at –78 °C for 30 min. The reaction mixture was allowed to warm to 0 °C, then carefully quenched with sat. aqueous Rochelle’s salt (750 mL) and sat. aqueous NaHCO₃ (250 mL), and then was allowed to warm to 25 °C. The resulting biphasic mixture was extracted with Et₂O (3 × 1 L), and the combined organic layers were washed with 10% aqueous Na₂S₂O₃ (1 L), H₂O (1 L), and brine (1 L), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:Et₂O 10:1) afforded vinyl iodide 13 (44.5 g, 66% yield) as a colorless oil. 13: Rƒ = 0.46 (silica gel, hexanes:EtOAc 5:1); [α]D²⁰ = +15.0 (CHCl₃, c = 1.33); IR (film) νmax 3341, 2929, 2842, 1467, 1255, 1100, 838, 770 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 5.89 (t, J = 5.8 Hz, 1 H), 4.19 (dd, J = 13.5, 5.8 Hz, 1 H), 4.16 (dd, J = 13.5, 6.0 Hz, 1 H), 4.10 (pent, J = 6.3 Hz, 1 H), 3.72–3.64 (m, 2 H), 2.68 (dd, J = 14.0, 6.6 Hz, 1 H), 2.63 (dd, J = 14.0, 6.0 Hz, 1 H), 1.74–1.55 (m, 3 H), 0.90 (s, 9 H), 0.87 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.05 (s, 3 H), 0.04 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 136.1, 106.1, 68.0, 67.3, 59.4, 53.0, 39.5, 26.0, 25.9, 18.2, 18.0, –4.2, –4.5, –5.2, –5.3 ppm; HRMS (ESI-TOF): calcd for C₁₉H₄₂IO₃Si₂ [M+H⁺]: 501.1712, found 501.1710.
**Coupled allylic alcohol 14**

To a 0 °C solution of vinyl iodide 13 (30.0 g, 60 mmol, 1.0 equiv) and Et₃N (45.0 mL, 300 mmol, 5.0 equiv) in THF (500 mL) was added freshly distilled TMSCl (15.0 mL, 120 mmol, 2.0 equiv). The reaction mixture was warmed to 25 °C, stirred for 2 h, and then quenched with H₂O (500 mL). The resulting biphasic reaction mixture was extracted with Et₂O (3 × 500 mL), and the combined organic layers were washed with H₂O (500 mL) and brine (500 mL), then dried (MgSO₄), and concentrated to give the corresponding TMS-ether as a colorless oil. The resulting TMS-ether was dissolved in degassed THF (600 mL) at 25 °C. Pd(dppf)Cl₂ (2.5 g, 3.0 mmol, 0.05 equiv) was added, followed by a solution of Me₂Zn (60.0 mL, 2.0 M in toluene, 120 mmol, 2.0 equiv), and the reaction mixture was heated to 65 °C for 12 h. The reaction mixture was then cooled to 0 °C, quenched slowly with sat. aqueous NH₄Cl (500 mL), and the resulting biphasic mixture was extracted with Et₂O (3 × 500 mL). The combined organic layers were washed with sat. aqueous NH₄Cl (500 mL), H₂O (500 mL) and brine (500 mL), then dried (MgSO₄), and concentrated to give a yellow oil. This was dissolved in MeOH (500 mL), and K₂CO₃ (830.0 mg, 6.0 mmol, 0.1 equiv) was added at 25 °C. The reaction mixture was stirred at 25 °C for 4 h, quenched with H₂O (500 mL), and the aqueous layer was extracted with Et₂O (2 × 500 mL). The combined organic layers were washed with H₂O (500 mL), and brine (500 mL), then dried (MgSO₄), and concentrated to give a yellow oil. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded coupled allylic alcohol 14 (19.2 g, 49 mmol, 81% yield) as a colorless oil. 14: Rₓ = 0.45 (silica gel, hexanes:EtOAc 5:1); [α]D³² = +13.8 (CHCl₃, c = 0.97); IR (film) νmax 3353, 2956, 2847, 1471, 1387, 1254, 1094, 832, 772 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 5.43 (t, J = 6.8 Hz, 1 H), 4.14 (d, J = 6.8 Hz, 2 H), 3.96 (pent, J = 6.6 Hz, 1 H), 3.66 (t, J = 6.6 Hz, 2
Benzyl-protected allylic alcohol 15

To a suspension of NaH (3.0 g, 76 mmol, 1.6 equiv) in THF (500 mL) at 0 °C was added a solution of coupled allylic alcohol 14 (18.5 g, 48 mmol, 1.0 equiv) in THF (100 mL). The reaction mixture was warmed to 25 °C and stirred for 30 min. BnBr (9.6 mL, 80 mmol, 1.7 equiv) was added followed by TBAI (1.8 g, 4.8 mmol, 0.1 equiv), and the reaction mixture was stirred at 25 °C for 6 h. The reaction mixture was then cooled to 0 °C, quenched slowly with sat. aqueous NH₄Cl (500 mL), and the resulting biphasic mixture was extracted with Et₂O (3 × 500 mL). The combined organic layers were washed with H₂O (2 × 500 mL) and brine (500 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:Et₂O 20:1) afforded benzyl-protected allylic alcohol 15 (20.2 g, 42 mmol, 88% yield) as a colorless oil. 15: Rf = 0.42 (silica gel, hexanes:EtOAc 20:1); [α]D³² = +9.3 (CHCl₃, c = 1.19); IR (film) νmax 2943, 2857, 1467, 1248, 1092, 838, 775 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.35–7.10 (m, 5 H), 5.42 (t, J = 6.4 Hz, 1 H), 4.49 (s, 2 H), 4.01 (d, J = 6.4 Hz, 2 H), 4.00–3.93 (m, 1 H), 3.66 (t, J = 6.5 Hz, 2 H), 2.25 (dd, J = 13.3, 5.6 Hz, 1 H), 2.16 (dd, J = 13.3, 6.8 Hz, 1 H), 1.70–1.62 (m, 1 H), 1.64 (s, 3 H), 1.58–1.50 (m, 1 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 6 H), 0.02 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 138.5, 137.2, 128.3, 127.7, 127.5, 123.9, 72.0, 67.7, 66.5, 59.7, 48.1, 39.9, 25.9,
25.8, 18.2, 18.1, 17.0, –4.4, –4.7, –5.2, –5.3 ppm; HRMS (ESI-TOF): calcd for C\textsubscript{27}H\textsubscript{51}O\textsubscript{3}Si\textsubscript{2}\textsuperscript{+} [M+H\textsuperscript{+}]: 479.3371, found 479.3358.

**Primary alcohol 16**

To a cold (0 °C) solution of benzyl-protected allylic alcohol 15 (7.7 g, 16 mmol) in THF (300 mL) was added HF•py (30 mL) and the reaction mixture was stirred at 0 °C for 3 h. The reaction mixture was added to a solution of sat. aqueous NaHCO\textsubscript{3} (500 mL), stirred at 25 °C for 30 min, and the resulting biphasic mixture was extracted with Et\textsubscript{2}O (3 × 500 mL). The combined organic layers were washed with H\textsubscript{2}O (500 mL), 10% aqueous CuSO\textsubscript{4} (500 mL), H\textsubscript{2}O (500 mL), and brine (500 mL), then dried (MgSO\textsubscript{4}), and concentrated. Flash column chromatography (silica gel, hexanes:Et\textsubscript{2}O 50:1 to 10:1) afforded primary alcohol 16 (4.5 g, 12 mmol, 77% yield) as a colorless oil along with recovered benzyl-protected allylic alcohol 15 (0.68 g, 1.4 mmol, 9% yield). 16: R\textsubscript{f} = 0.56 (silica gel, hexanes:EtOAc 3:1); [\alpha]_{D}\textsuperscript{32} = +7.5 (CHCl\textsubscript{3}, c = 0.78); IR (film) \nu\textsuperscript{max} 3444, 2929, 2856, 1471, 1454, 1360, 1090, 775, 736, 698 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \delta = 7.40–7.25 (m, 5 H), 5.44 (t, J = 6.6 Hz, 1 H), 4.50 (s, 2 H), 4.10–4.02 (m, 1 H), 4.01 (d, J = 6.6 Hz, 2 H), 3.82 (ddd, J = 10.8, 8.4, 4.4 Hz, 1 H), 3.70 (dt, J = 10.8, 5.6 Hz, 1 H), 2.32 (dd, J = 13.3, 5.4 Hz, 1 H), 2.22 (dd, J = 13.3, 8.0 Hz, 1 H), 1.86–1.76 (m, 1 H), 1.65 (s, 3 H), 1.65–1.55 (m, 1 H), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.08 ppm (s, 3 H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \delta = 138.3, 136.5, 128.3, 127.7, 127.5, 124.3, 72.1, 70.0, 66.4, 60.0, 47.3, 37.6, 25.7, 17.9, 17.0, –4.5, –4.8 ppm; HRMS (ESI-TOF): calcd for C\textsubscript{21}H\textsubscript{36}O\textsubscript{3}SiNa\textsuperscript{+} [M+Na\textsuperscript{+}]: 387.2326, found 387.2330.
Aldehyde 17

To a solution of primary alcohol 16 (4.2 g, 12 mmol, 1.0 equiv) in CH₂Cl₂ (60 mL) at 25 °C was added anhydrous NaHCO₃ (480.0 mg, 5.8 mmol, 0.5 equiv) followed by PCC (5.0 g, 23 mmol, 2.0 equiv), and the reaction mixture was stirred at 25 °C for 3 h. The mixture was concentrated to approximately half its original volume and diluted with Et₂O (60 mL). Precipitation of the chromium salts resulted and the salts were removed via filtration through a pad of celite. The remaining solids were then triturated with Et₂O (3 × 100 mL) and the filtrate was concentrated to give a brown oil. Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded aldehyde 17 (3.1 g, 8.8 mmol, 73% yield) as a colorless oil. 17: Rₛ = 0.78 (silica gel, hexanes:EtOAc 3:1); [α]D₃₂ = +5.9 (CHCl₃, c = 1.38); IR (film) νmax 2929, 2856, 1726, 1462, 1360, 1254, 1093, 1028, 1005, 836, 776 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 9.47 (t, J = 1.8 Hz, 1 H), 7.33 (d, J = 7.6 Hz, 2 H), 7.18 (t, J = 7.6 Hz, 2 H), 7.10 (t, J = 7.6 Hz, 1 H), 5.45 (t, J = 6.4 Hz, 1 H), 4.37 (s, 2 H), 4.20–4.12 (m, 1 H), 3.90 (d, J = 6.4 Hz, 2 H), 2.18–2.11 (m, 3 H), 2.08 (dd, J = 13.2, 6.9 Hz, 1 H), 1.45 (s, 3 H), 0.91 (s, 9 H), 0.01 ppm (s, 6 H); ¹³C NMR (100 MHz, CDCl₃): δ = 199.9, 139.3, 135.5, 128.6, 127.7, 125.9, 72.3, 66.9, 66.7, 50.8, 48.4, 25.9, 18.1, 17.1, −4.4, −4.6 ppm; HRMS (ESI-TOF): calcd for C₂₁H₃₄O₃SiNa⁺ [M+Na⁺]: 385.2169, found 385.2172.

Ketophosphonate 18

To a solution of dimethyl methylphosphonate (32.5 mL, 254 mmol, 4.0 equiv) in THF (200 mL) was added a solution of n-BuLi (102.0 mL, 2.5 M in hexanes, 254 mmol, 4.0 equiv) at −78 °C, and the reaction mixture was stirred at −78 °C for 2 h. Then, a solution of aldehyde 17
(23.0 g, 63.4 mmol, 1.0 equiv) in THF (100 mL) was added dropwise and the reaction mixture was stirred at –78 °C for 2 h. The reaction mixture was then quenched with sat. aqueous NaHCO₃ (500 mL), and warmed to 25 °C. The biphasic mixture was extracted with EtOAc (3 × 500 mL), and the combined organic layers were washed with brine (500 mL), dried (MgSO₄), and concentrated to give the crude hydroxy phosphonate. The oily phosphonate was dissolved in DMF (300 mL), 4 Å molecular sieves, and PDC (50.6 g, 134 mmol, 2.1 equiv) were added, and the reaction mixture was stirred at 25 °C for 12 h. The reaction mixture was quenched with H₂O (500 mL), and the resulting biphasic mixture was extracted with EtOAc (3 × 500 mL). The combined organic layers were washed with H₂O (500 mL) and brine (500 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, EtOAc) afforded ketophosphonate 18 (11.1 g, 40.8 mmol, 64% yield over 2 steps) as a colorless oil. 18: R_f = 0.50 (silica gel, EtOAc); [α]_D^{32} = +21.3 (CHCl₃, c = 1.53); IR (film) ν_{max} 2958, 2929, 2854, 1714, 1454, 1359, 1256, 1029, 831, 779 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.36–7.31 (m, 4 H), 7.29–7.25 (m, 1 H), 5.42 (t, J = 6.5 Hz, 1 H), 4.49 (s, 2 H), 4.30 (pent, J = 6.0 Hz, 1 H), 4.00 (d, J = 6.5 Hz, 2 H), 3.77 (s, 3 H), 3.75 (s, 3 H), 3.10 (dd, J = 22.6, 5.2 Hz, 2 H), 2.73 (dd, J = 16.3, 6.7 Hz, 1 H), 2.68 (dd, J = 16.3, 4.9 Hz, 1 H), 2.25 (dd, J = 13.2, 5.5 Hz, 1 H), 2.16 (dd, J = 13.2, 7.2 Hz, 1 H), 1.65 (s, 3 H), 0.85 (s, 9 H), 0.05 (s, 3 H), 0.03 ppm (s, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 200.8 (d, J = 6.5 Hz), 138.4, 136.3, 128.3, 127.7, 127.6, 124.8, 72.2, 67.5, 66.5, 52.9 (d, J = 7.2 Hz), 52.8 (d, J = 7.2 Hz), 50.8, 48.1, 42.6 (d, J = 128 Hz), 25.7, 17.9, 17.0, –4.6, –4.9 ppm; HRMS (ESI-TOF): calcd for C₂₄H₄₂O₆PSi [M+H⁺]: 485.2483, found 485.2492.
**β-Hydroxyketophosphonate 5**

To a cold (0 °C) solution of ketophosphonate 18 (10.0 g, 21 mmol, 1.0 equiv) in CH$_3$CN (570 mL) was added a solution of 48% aqueous HF (2 mL) in CH$_3$CN (20 mL) and the reaction mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was quenched with sat. aqueous NaHCO$_3$ (500 mL) and the resulting biphasic mixture was extracted with EtOAc (3 × 500 mL). The combined organic layers were washed with brine (500 mL), dried (MgSO$_4$), and then concentrated. Flash column chromatography (silica gel, EtOAc) afforded β-hydroxyketophosphonate 5 (7.1 g, 19 mmol, 92% yield) as a colorless oil. 5: $R_f = 0.12$ (silica gel, EtOAc); $[\alpha]_D^{32} = +20.3$ (CHCl$_3$, $c = 1.55$); IR (film) $\nu_{max}$ 3389, 2931, 2848, 1708, 1455, 1249, 1031, 808 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$): $\delta = 7.36–7.32$ (m, 4 H), 7.30–7.26 (m, 1 H), 5.49 (t, $J = 6.6$ Hz, 1 H), 4.50 (s, 2 H), 4.26–4.21 (m, 1 H), 4.04 (d, $J = 6.6$ Hz, 2 H), 3.79 (s, 3 H), 3.77 (s, 3 H), 3.14 (dd, $J = 22.7$, 4.9 Hz, 2 H), 2.76 (dd, $J = 17.1$, 3.7 Hz, 1 H), 2.72 (dd, $J = 17.1$, 8.2 Hz, 1 H), 2.25 (dd, $J = 13.6$, 7.9 Hz, 1 H), 2.18 (dd, $J = 13.6$, 5.4 Hz, 1 H), 1.68 ppm (s, 3 H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta = 202.3$ (d, $J = 6.0$ Hz), 138.3, 136.3, 128.4, 127.8, 127.6, 124.7, 72.3, 66.4, 65.5, 53.1 (d, $J = 6.5$ Hz), 50.5, 46.7, 42.0 (d, $J = 127.8$ Hz), 16.6 ppm; HRMS (ESI-TOF): calcd for C$_{18}$H$_{27}$O$_6$PNa$^+$ [M+Na$^+$]: 393.1437, found 393.1438.

**Aldehyde 22**

To a solution of (–)-$B$-methoxy-diisopinocamphylborane (47.0 g, 149 mmol, 1.7 equiv) in Et$_2$O (500 mL) at −78 °C was added a solution of allyl magnesium bromide (143.0 mL, 1.0 M in Et$_2$O, 143 mmol, 1.7 equiv). The reaction mixture was stirred for 15 min at −78 °C, and then warmed to 25 °C over 2 h. The reaction
mixture was cooled to –78 °C and a solution of known aldehyde 19\(^1\) (17.5 g, 86.5 mmol, 1.0 equiv) in Et\(_2\)O (100 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 4 h and was then warmed to 25 °C over 1 h. A solution of 3 N aqueous NaOH (100 mL) was added followed by a solution of 35% aqueous H\(_2\)O\(_2\) (40 mL), and the reaction mixture was stirred at 25 °C for 12 h. The resulting biphasic mixture was extracted with Et\(_2\)O (3 × 500 mL). The combined organic layers were washed with H\(_2\)O (500 mL) and brine (500 mL), then dried (MgSO\(_4\)), and concentrated. Flash column chromatography (silica gel, hexanes:Et\(_2\)O 20:1) afforded the corresponding allylic alcohol (20, 20.5 g, 82.2 mmol, 95% yield, >40:1 dr) as a colorless oil. The corresponding allylic alcohol was dissolved in DMF (200 mL), and imidazole (22.8 g, 336 mmol, 4.0 equiv) was added, followed by TESCl (24.9 mL, 147 mmol, 1.8 equiv), and the reaction mixture was stirred at 25 °C for 4 h. The reaction mixture was quenched with H\(_2\)O (500 mL), and the resulting biphasic mixture was extracted with Et\(_2\)O (3 × 500 mL). The combined organic layers were washed with H\(_2\)O (4 × 500 mL) and brine (500 mL), dried (MgSO\(_4\)), concentrated, and the obtained residue was azeotroped with toluene (4 × 500 mL) to afford the corresponding TES-protected allylic alcohol (21, 28.3 g, 78.9 mmol) as a colorless oil. The TES-protected allylic alcohol was dissolved in CH\(_2\)Cl\(_2\) (750 mL) and cooled to –78 °C. O\(_3\) was bubbled through the solution until a faint blue color persisted (about 4 h), at which time argon was bubbled through the reaction mixture for 30 min. PPh\(_3\) (29.2 g, 111 mmol, 1.3 equiv) was then added, and the reaction mixture was stirred at –78 °C for 2 h, and then warmed to 25 °C over 1 h. The reaction mixture was then concentrated, the residue triturated and decanted with hexanes (4 × 500 mL), and the resulting solution was concentrated. Flash column chromatography (silica gel, hexanes:Et\(_2\)O 20:1) afforded aldehyde 22 (19.3 g, 64% yield over 2 steps) as a colorless oil. 22: \(R_f = 0.20\) (silica gel, hexanes:EtOAc 10:1); \([\alpha]_D^{32} = -12.4\) (CHCl\(_3\),...
$c = 1.57$; IR (film) $\nu_{\text{max}}$ 2955, 2878, 1726, 1460, 1374, 1254, 1138, 1112, 1091, 1065, 1030, 1005, 833, 777 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.81$ (dd, $J = 3.2, 2.0$ Hz, 1 H), 4.39–4.32 (m, 1 H), 3.90–3.81 (m, 1 H), 2.60 (ddd, $J = 16.0, 4.4, 2.0$ Hz, 1 H), 2.48 (ddd, $J = 16.0, 6.8, 3.2$ Hz, 1 H), 1.79 (ddd, $J = 12.0, 8.4, 5.2$ Hz, 1 H), 1.58 (ddd, $J = 12.0, 8.0, 4.0$ Hz, 1 H), 1.15 (d, $J = 6.0$ Hz, 3 H), 0.95 (t, $J = 8.0$ Hz, 9 H), 0.88 (s, 9 H), 0.60 (q, $J = 8.0$ Hz, 6 H), 0.05 (s, 3 H), 0.03 ppm (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 202.5, 65.7, 65.5, 50.4, 47.7, 25.8, 24.1, 6.8, 4.9, -4.1, -4.8$ ppm; HRMS (ESI-TOF): calcd for C$_{18}$H$_{40}$O$_3$Si$_2$Na$^+$ [M+Na$^+$]: 383.2408, found 383.2403.

Aldehyde 6

To a $-78$ °C solution of (−)-B-methoxy-diisopinocamphylborane (28.4 g, 89.9 mmol, 1.7 equiv) in Et$_2$O (250 mL) was added a solution of allyl magnesium bromide (89.9 mL, 1.0 M in Et$_2$O, 89.9 mmol, 1.7 equiv). The reaction mixture was stirred for 15 min at $-78$ °C, warmed to 25 °C over 2 h, and then cooled to $-78$ °C. A solution of aldehyde 22 (19.3 g, 53.5 mmol, 1.0 equiv) in Et$_2$O (80 mL) was added dropwise, and the reaction mixture was stirred at $-78$ °C for 4 h and then warmed to 25 °C over 1 h. A solution of 3 N aqueous NaOH (60 mL) was added to the reaction mixture, followed by a solution of 35% aqueous H$_2$O$_2$ (25 mL), and the reaction mixture was stirred at 25 °C for 12 h. The resulting biphasic mixture was then extracted with Et$_2$O (3 × 500 mL), the combined organic layers were washed with H$_2$O (500 mL) and brine (500 mL), then dried (MgSO$_4$), and concentrated. Flash column chromatography (silica gel, hexanes:Et$_2$O 20:1) afforded the corresponding allylic alcohol (23, 18.5 g, 45.5 mmol, 85% yield, >40:1 dr) as a colorless oil. The allylic alcohol was dissolved in DMF (100 mL), and imidazole (15.6 g, 230 mmol, 5.0
equiv), and TBSCI (13.8 g, 92 mmol, 2.0 equiv) were added. The reaction mixture was stirred at 25 °C for 4 h, then quenched with H₂O (250 mL), and the resulting biphasic mixture was extracted with Et₂O (3 × 250 mL). The combined organic layers were washed with H₂O (4 × 250 mL) and brine (250 mL), then dried (MgSO₄), and concentrated; and the residue was azeotroped with toluene (4 × 250 mL) to afford the corresponding TBS-protected allylic alcohol (24) as a colorless oil. The TBS protected allylic alcohol was dissolved in CH₂Cl₂ (500 mL) and cooled to –78 °C. O₃ was bubbled through the solution until a faint blue color persisted (about 4 h), at which time argon was bubbled through the reaction mixture for 30 min. PPh₃ (16.0 g, 61 mmol, 1.3 equiv) was then added, the reaction mixture was stirred at –78 °C for 2 h, and then warmed to 25 °C over 1 h. The reaction mixture was then concentrated, the residue triturated and decanted with hexanes (3 × 250 mL), and the resulting solution was concentrated. Flash column chromatography (silica gel, hexanes:Et₂O 20:1) afforded aldehyde 6 (22.3 g, 41 mmol, 91% yield over 2 steps) as a colorless oil. 6: Rᵥ = 0.23 (silica gel, hexanes:EtOAc 10:1); [α]D₃₂ = –15.7 (CHCl₃, c = 1.22); IR (film) νmax 2949, 2892, 2854, 1728, 1464, 1374, 1256, 1110, 1044, 1006, 831, 774 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 9.80 (dd, J = 3.0, 2.0 Hz, 1 H), 4.40–4.32 (m, 1 H), 3.91–3.81 (m, 2 H), 2.60 (ddd, J = 15.0, 4.5, 2.0 Hz, 1 H), 2.46 (ddd, J = 15.0, 7.0, 3.0 Hz, 1 H), 1.73 (t, J = 6.0 Hz, 2 H), 1.69 (ddd, J = 10.0, 7.5, 5.5 Hz, 1 H), 1.53 (ddd, J = 10.0, 7.5, 5.0 Hz, 1 H), 1.14 (d, J = 6.0 Hz, 3 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.88 (s, 9 H), 0.86 (s, 9 H), 0.59 (q, J = 8.0 Hz, 6 H), 0.08 (s, 3 H), 0.06 (s, 6 H), 0.04 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 202.2, 66.7, 65.7, 65.6, 50.7, 48.0, 45.3, 25.8, 25.7, 24.3, 18.0, 17.9, 6.9, 5.1, –4.1, –4.3, –4.6 ppm; HRMS (ESI-TOF): calcd for C₂₆H₅₈O₄Si₃Na⁺ [M+Na⁺]: 541.3535, found 541.3536.
To a solution of ketophosphonate 5 (4.0 g, 10.8 mmol, 1.0 equiv) and aldehyde 6 (6.2 g, 11.9 mmol, 1.0 equiv) in THF (140 mL) and H₂O (7.0 mL) at 25 °C was added Ba(OH)₂•H₂O (1.5 g, 8.1 mmol, 0.75 equiv), and the reaction mixture was stirred at 25 °C for 1 h. The reaction mixture was then diluted with CH₂Cl₂ (250 mL), the organic layers were washed with sat. aqueous NaHCO₃ (100 mL) and brine (100 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded enone 31 (10.5 g, 10.3 mmol, 95% yield) as a colorless oil. 31: Rₐ = 0.52 (silica gel, hexanes:EtOAc 3:1); [α]D₃₂ = +2.9 (CHCl₃, c = 1.31); IR (film) νmax 3448, 2954, 2860, 1666, 1619, 1472, 1367, 1255, 1067, 1002, 831, 773, 732 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.36–7.32 (m, 4 H), 7.30–7.26 (m, 1 H), 6.88 (dt, J = 16.2, 7.2 Hz, 1 H), 6.11 (d, J = 15.9 Hz, 1 H), 5.50 (t, J = 6.5 Hz, 1 H), 4.51 (s, 2 H), 4.29–4.23 (m, 1 H), 4.04 (d, J = 6.5 Hz, 2 H), 3.98–3.92 (m, 1 H), 3.91–3.86 (m, 1 H), 3.85–3.80 (m, 1 H), 2.73 (dd, J = 17.3, 2.2 Hz, 1 H), 2.63 (dd, J = 17.3, 8.6 Hz, 1 H), 2.51–2.44 (m, 1 H), 2.31–2.24 (m, 2 H), 2.19 (dd, J = 13.5, 5.4 Hz, 1 H), 1.70 (s, 3 H), 1.70–1.60 (m, 3 H), 1.51 (dt, J = 13.8, 5.4 Hz, 1 H), 1.12 (d, J = 5.8 Hz, 3 H), 0.95 (t, J = 7.9 Hz, 9 H), 0.88 (s, 18 H), 0.58 (q, J = 7.9 Hz, 6 H), 0.05 (s, 6 H), 0.04 ppm (s, 6 H); ¹³C NMR (150 MHz, CDCl₃): δ = 200.3, 145.5, 138.3, 136.7, 132.5, 128.4, 127.8, 127.6, 124.3, 72.2, 68.3, 66.8, 66.4, 65.7, 48.0, 46.7, 45.6, 45.5, 40.5, 25.9, 25.8, 24.1, 18.0, 17.9, 16.7, 6.9, 5.1, –4.1, –4.3, –4.4, –4.6 ppm; HRMS (ESI-TOF): calcd for C₄₂H₇₈O₆Si₃Na⁺ [M+Na⁺]: 785.4998, found 785.4989.
1,3-syn-Diol 32

Enone 31 (1.0 g, 1.3 mmol, 1.0 equiv) was dissolved in THF:MeOH (4:1, 13 mL), cooled to –78 °C, and a solution of Et₂BOMe (1.4 mL, 1.0 M in THF, 1.4 mmol, 1.1 equiv) was added. The reaction mixture was stirred at –78 °C for 15 min, at which time NaBH₄ (55 mg, 60% w/w in mineral oil, 1.4 mmol, 1.1 equiv) was added, and the reaction mixture was then stirred at –78 °C for an additional 3 h. The reaction mixture was warmed to 0 °C, and 3 N aqueous NaOH (2.0 mL) was added, followed by a solution of 35% aqueous H₂O₂ (0.8 mL), and the reaction mixture was stirred at 25 °C for 12 h. The reaction was quenched with H₂O (30 mL), and the resulting biphasic mixture was extracted with Et₂O (3 × 30 mL). The combined organic layers were washed with H₂O (30 mL) and brine (30 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) afforded 1,3-syn-diol 32 (0.9 g, 1.2 mmol, 89% yield) as a single observable diastereoisomer.

32: Rf = 0.26 (silica gel, hexanes:EtOAc 3:1); [α]D₃₂ = –1.1 (CHCl₃, c = 1.28); IR (film) νmax 3422, 2930, 1649, 1461, 1377, 1250, 1108, 1068, 1008, 831, 772 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.36–7.27 (m, 5 H), 5.68 (dt, J = 15.0, 7.2 Hz, 1 H), 5.54–5.47 (m, 2 H), 4.51 (s, 2 H), 4.35–4.31 (m, 1 H), 4.04 (d, J = 6.6 Hz, 2 H), 4.03–3.97 (m, 1 H), 3.95–3.90 (m, 1 H), 3.85–3.75 (m, 2 H), 2.38–2.17 (m, 4 H), 1.69 (s, 3 H), 1.66–1.56 (m, 5 H), 1.53 (dt, J = 12.6, 6.0 Hz, 1 H), 1.13 (d, J = 6.0 Hz, 3 H), 0.95 (t, J = 7.8 Hz, 9 H), 0.88 (s, 18 H), 0.58 (q, J = 7.8 Hz, 6 H), 0.05 (s, 3 H), 0.04 ppm (9 H); ¹³C NMR (150 MHz, CDCl₃): δ = 139.2, 137.5, 135.7, 129.3, 128.9, 128.7, 128.5, 125.5, 74.4, 73.2, 70.5, 70.1, 67.9, 67.3, 66.7, 49.1, 48.8, 46.5, 44.1, 41.3, 26.8, 24.8, 19.0, 18.9, 17.6, 7.9, 6.0, –3.3, –3.4, –3.5, –3.7 ppm; HRMS (ESI-TOF): calcd for C₄₂H₈₀O₆Si₃Na⁺ [M+Na⁺]: 787.5155, found 787.5152.
Penta-silylated compound 33

To a solution of 1,3-syn-diol 32 (3.0 g, 3.9 mmol, 1.0 equiv) in DMF (15 mL) was added imidazole (2.2 g, 31.4 mmol, 8.0 equiv) and TBSCl (2.4 g, 15.7 mmol, 4.0 equiv), and the reaction mixture was stirred at 25 °C for 8 h. The reaction was quenched with H₂O (100 mL), and the biphasic mixture was extracted with Et₂O (3 × 100 mL). The combined organic layers were washed with H₂O (4 × 100 mL) and brine (100 mL), then dried (MgSO₄), concentrated, and the residue so obtained was azeotroped with toluene (4 × 100 mL) to afford penta-silylated compound 33 (3.5 g, 89% yield) as a colorless oil. 33: Rf = 0.65 (silica gel, hexanes:Et₂O 10:1); [α]D³² = +3.4 (CDCl₃, c = 1.12); IR (film) νmax 2955, 2929, 2856, 1462, 1384, 1360, 1255, 1089, 1005, 835, 807, 774, 733, 696 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.36–7.31 (m, 4 H), 7.30–7.25 (m, 1 H), 5.54 (dt, J = 15.0, 7.2 Hz, 1 H), 5.46–5.38 (m, 2 H), 4.50 (s, 2 H), 4.16 (q, J = 6.6 Hz, 1 H), 4.06–3.97 (m, 2 H), 3.96–3.92 (m, 1 H), 3.90–3.85 (m, 1 H), 3.83–3.78 (m, 1 H), 3.77–3.73 (m, 1 H), 2.25–2.11 (m, 4 H), 1.70–1.75 (m, 1 H), 1.63 (s, 3 H), 1.62–1.49 (m, 5 H), 1.13 (d, J = 6.0 Hz, 3 H), 0.95 (t, J = 7.8 Hz, 9 H), 0.88 (s, 27 H), 0.87 (s, 9 H), 0.58 (q, J = 7.8 Hz, 6 H), 0.05 (s, 3 H), 0.05 (s, 6 H), 0.04 (s, 6 H), 0.04 (s, 3 H), 0.02 (s, 3 H), 0.01 ppm (s, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 138.5, 137.3, 136.0, 128.3, 127.7, 127.5, 126.3, 124.1, 72.0, 70.8, 69.2, 67.9, 67.1, 66.5, 65.8, 47.7, 47.6, 46.2, 45.7, 40.8, 26.0, 25.9, 25.7, 23.7, 18.2, 18.1, 18.0, 17.9, 17.2, 7.0, 5.2, −3.9, −4.0, −4.2, −4.3, −4.4, −4.6, −4.7 ppm; HRMS (ESI-TOF): calcd for C₅₄H₁₀₈O₆Si₅Na⁺ [M+Na⁺]: 1015.6884, found 1015.6898.
Allylic alcohol 34

To a solution of penta-silylated compound 33 (3.5 g, 3.5 mmol, 1.0 equiv) in THF (50 mL), at –78 °C, was added i-PrOH (17 mL), and liquid NH₃ (35 mL) was condensed inside the flask. Small pieces of calcium (4.2 g, 106 mmol, 30 equiv) were then slowly added, and the reaction mixture was stirred at –78 °C for 1 h. Solid NH₄Cl (23 g, 430 mmol, 125 equiv) was added to the reaction mixture, followed by Fe(NO₃)₃•9H₂O (4.2 g, 10.5 mmol, 3.0 equiv). The reaction mixture was stirred at –78 °C for an additional 1 h and then allowed to warm to 25 °C over 2 h. The reaction mixture was then quenched with H₂O (100 mL), and the biphasic mixture was extracted with Et₂O (3 × 100 mL). The combined organic layers were washed with H₂O (100 mL) and brine (100 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:Et₂O 10:1) afforded allylic alcohol 34 (2.4 g, 2.6 mmol, 75% yield) as a colorless oil. 34: Rₛ = 0.16 (silica gel, hexanes:EtOAc 10:1); [α]D₃² = +2.9 (CHCl₃, c = 1.3); IR (film) νₘₐₓ 3447, 2929, 2857, 1458, 1255, 1095, 1051, 1004, 835, 774 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 5.54 (dt, J = 14.9, 6.9 Hz, 1 H), 5.45–5.38 (m, 2 H), 4.18–4.12 (m, 3 H), 3.98–3.92 (m, 1 H), 3.91–3.86 (m, 1 H), 3.84–3.79 (m, 1 H), 3.77–3.73 (m, 1 H), 2.24–2.12 (m, 4 H), 1.71–1.66 (m, 1 H), 1.66 (s, 3 H), 1.63–1.50 (m, 5 H), 1.12 (d, J = 6.0 Hz, 3 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.88 (s, 9 H), 0.88 (s, 18 H), 0.87 (s, 9 H), 0.58 (q, J = 8.0 Hz, 6 H), 0.05 (s, 6 H), 0.05 (s, 3 H), 0.04 (s, 6 H), 0.04 (s, 3 H), 0.02 (s, 3 H), 0.02 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 136.6, 135.9, 126.5, 126.3, 70.8, 69.2, 67.9, 67.1, 59.4, 47.7, 47.5, 46.3, 45.7, 40.8, 25.9, 25.8, 23.7, 18.2, 18.0, 17.9, 17.0, 7.0, 5.2, –3.9, –4.0, –4.3, –4.4, –4.7 ppm; HRMS (ESI-TOF): calcd for C₄₇H₁₀₂O₆Si₅Na⁺ [M+Na⁺]: 925.6415, found 925.6405.
α,β-Unsaturated aldehyde 35

To a 25 °C solution of allylic alcohol 34 (2.4 g, 2.5 mmol, 1.0 equiv) in CH₂Cl₂ (50 mL) was added NaHCO₃ (2.1 g, 25 mmol, 10 equiv) followed by Dess–Martin periodinane (1.6 g, 3.8 mmol, 1.6 equiv), and the reaction mixture was stirred at 25 °C for 30 min. The reaction was then quenched with sat. aqueous NaHCO₃ (100 mL), and the resulting biphasic mixture was extracted with Et₂O (3 × 100 mL). The combined organic layers were washed with H₂O (100 mL) and brine (100 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:Et₂O 10:1) afforded α,β-unsaturated aldehyde 35 (2.0 g, 2.2 mmol, 87% yield) as a colorless oil. 35: Rₛ = 0.40 (silica gel, hexanes:EtOAc 10:1); [α]₃₂° = −4.8 (CDCl₃, c = 0.74); IR (film) ν_max 2955, 2857, 1678, 1472, 1376, 1255, 1086, 1005, 836, 774 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 9.98 (d, J = 8.0 Hz, 1 H), 5.89 (d, J = 8.8 Hz, 1 H), 5.56 (dt, J = 15.5, 7.0 Hz, 1 H), 5.41 (dd, J = 15.4, 6.8 Hz, 1 H), 4.15 (dt, J = 7.0, 6.5 Hz, 1 H), 4.08–4.00 (m, 1 H), 3.98–3.90 (m, 1 H), 3.85–3.73 (m, 2 H), 2.45 (dd, J = 13.0, 4.2 Hz, 1 H), 2.28 (dd, J = 13.0, 7.7 Hz, 1 H), 2.25–2.11 (m, 2 H), 2.18 (s, 3 H), 1.77 (ddd, J = 8.2, 4.8, 1.3 Hz, 1 H), 1.65–1.49 (m, 5 H), 1.13 (d, J = 6.0 Hz, 3 H), 0.97 (t, J = 8.0 Hz, 9 H), 0.89 (s, 9 H), 0.88 (s, 18 H), 0.86 (s, 9 H), 0.59 (q, J = 8.0 Hz, 6 H), 0.05 (m, 15 H), 0.05 (s, 3 H), 0.03 (s, 3 H), 0.00 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 190.8, 161.2, 135.7, 129.9, 126.7, 70.7, 69.2, 68.0, 67.1, 65.8, 48.1, 47.8, 46.6, 45.7, 40.7, 25.9, 25.8, 23.7, 18.4, 18.1, 18.0, 6.9, 5.2, −3.7, −4.0, −4.3, −4.4, −4.5, −4.6 ppm; HRMS (ESI-TOF): calcd for C₄₇H₁₀₁O₆Si₅⁺ [M+H⁺]: 901.6439, found 901.6435.
To a −78 °C solution of diisopropylamine (540.0 μL, 3.9 mmol, 1.8 equiv) in THF (15 mL) was added a solution of n-BuLi (1.3 mL, 2.5 M in hexanes, 3.3 mmol, 1.5 equiv). The reaction mixture was warmed to 0 °C and stirred for 30 min, at which time the reaction mixture was cooled to −78 °C, and a solution of TMS-diazomethane (1.7 mL, 2.0 M in toluene, 3.3 mmol, 1.5 equiv) was added. The reaction mixture was stirred at −78 °C for 30 min, and a solution of α,β-unsaturated aldehyde 35 (2.0 g, 2.2 mmol, 1.0 equiv) in THF (5 mL) was added and the reaction mixture was stirred at −78 °C for an additional 1 h and then warmed to 25 °C over 2 h, before quenching with sat. aqueous NH₄Cl (50 mL) and extraction with Et₂O (3 × 50 mL). The combined organic layers were washed with H₂O (50 mL) and brine (50 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes: Et₂O 50:1) afforded enyne 36 (1.7 g, 1.9 mmol, 85% yield) as a colorless oil. 36: R₆ = 0.67 (silica gel, hexanes:EtOAc 10:1); [α]D³² = −6.6 (CHCl₃, c = 0.96); IR (film) νmax 3315, 2955, 2929, 2856, 1472, 1463, 1374, 1361, 1256, 1085, 836, 774 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 5.55 (dt, J = 15.6, 6.6 Hz, 1 H), 5.42 (dd, J = 15.5, 6.9 Hz, 1 H), 5.28 (s, 1 H), 4.14 (q, J = 7.2 Hz, 1 H), 3.95 (hex, J = 6.6 Hz, 1 H), 3.91 (pent, J = 6.0 Hz, 1 H), 3.82 (pent, J = 6.0 Hz, 1 H), 3.76 (pent, J = 6.0 Hz, 1 H), 3.01 (d, J = 1.9 Hz, 1 H), 2.29 (dd, J = 13.3, 4.9 Hz, 1 H), 2.24–2.12 (m, 3 H), 1.90 (s, 3 H), 1.71 (ddd, J = 13.4, 7.6, 5.5 Hz, 1 H), 1.64–1.49 (m, 5 H), 1.13 (d, J = 6.0 Hz, 3 H), 0.97 (t, J = 8.0 Hz, 9 H), 0.89 (s, 9 H), 0.88 (s, 18 H), 0.87 (s, 9 H), 0.58 (q, J = 8.0 Hz, 6 H), 0.06–0.04 (m, 18 H), 0.03 (s, 3 H), 0.02 ppm (s, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 151.0, 135.9, 126.5, 106.8, 81.7, 79.7, 70.8, 69.2, 67.8, 67.1, 65.8, 47.8, 46.4, 45.7,
40.8, 25.9, 25.8, 23.8, 20.1, 18.1, 18.0, 7.0, 5.2, –3.8, –4.0, –4.3, –4.4, –4.4, –4.5, –4.6, –4.7 ppm; HRMS (ESI-TOF): calcd for C_{48}H_{106}O_{5}Si_{5}Na^{+} [M+Na^{+}]: 919.6309, found 919.6299.

**Mitsunobu alcohol coupling partner 37**

To a 25 °C solution of enyne 36 (1.5 g, 1.7 mmol, 1.0 equiv) in EtOH (17 mL) was added PPTS (42.0 mg, 0.17 mmol, 0.1 equiv), and the reaction mixture was stirred at 25 °C for 3 h. The reaction mixture was then quenched with sat. aqueous NaHCO₃ (50 mL), and the aqueous layer was extracted with Et₂O (3 × 50 mL). The combined organic layers were washed with sat. aqueous NaHCO₃ (50 mL), H₂O (50 mL), brine (50 mL), dried (MgSO₄), and then concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 50:1) afforded Mitsunobu alcohol coupling partner 37 (1.0 g, 1.3 mmol, 77% yield) as a colorless oil. **37**: R⁰ = 0.48 (silica gel, hexanes:EtOAc 10:1); [α]D⁰ = –6.7 (CHCl₃, c = 0.57); IR (film) νmax 3528, 3314, 2954, 2929, 2857, 1472, 1375, 1362, 1255, 1085, 836, 775 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 5.57 (dt, J = 15.6, 7.2 Hz, 1 H), 5.42 (dd, J = 15.4, 7.0 Hz, 1 H), 5.27 (s, 1 H), 4.16 (q, J = 6.7 Hz, 1 H), 4.05–3.99 (m, 1 H), 3.95–3.82 (m, 3 H), 3.58 (br s, 1 H), 3.01 (s, 1 H), 2.30–2.18 (m, 4 H), 1.89 (s, 3 H), 1.69 (dt, J = 13.2, 6.6 Hz, 1 H), 1.63–1.56 (m, 2 H), 1.55–1.50 (m, 2 H), 1.47 (dt, J = 13.8, 3.6 Hz, 1 H), 1.16 (d, J = 5.8 Hz, 3 H), 0.89 (s, 18 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H), 0.01 ppm (s, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 150.9, 136.2, 126.1, 106.7, 81.6, 79.8, 70.9, 70.8, 68.8, 68.6, 67.7, 46.6, 46.4, 46.2, 43.4, 40.2, 25.9, 25.8, 24.2, 20.0, 18.1, 18.0, 17.9, –3.9, –4.0, –4.1, –4.3, –4.4, –4.6, –4.7, –4.8 ppm; HRMS (ESI-TOF): calcd for C_{42}H_{86}O_{5}Si_{4}Na^{+} [M+Na^{+}]: 805.5444, found 805.5467.
**Pinacol borate 26**

To a 0 °C solution of 2,5-dimethylhexa-2,4-diene (50.7 mL, 341 mmol, 5.5 equiv) in THF (400 mL) was added a solution of BH$_3$•THF (142.0 mL, 1.0 M in THF, 142 mmol, 2.5 equiv) and the reaction mixture was stirred at 0 °C for 3 h. A solution of acetylene $^{25}$ (11.5 g, 57 mmol, 1.0 equiv) in THF (100 mL) was added and the reaction mixture was stirred at 0 °C for an additional 1.5 h. H$_2$O (19 mL) was added carefully and the reaction mixture was warmed to 25 °C and stirred for 1 h. Then, a solution of 37% aqueous formaldehyde (43 mL) was added and the reaction mixture was stirred at 25 °C for 12 h. The reaction was then quenched with H$_2$O (500 mL), and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 500 mL). The combined organic layers were washed with H$_2$O (500 mL) and brine (500 mL), then dried (MgSO$_4$), and concentrated. Flash column chromatography (silica gel, EtOAc) afforded the boronic acid as a yellow solid, which was used in the subsequent cross coupling reaction. For the purpose of characterization, the pinacol ester was prepared and could also be used in the subsequent cross coupling reaction, resulting in the same yield as for the boronic acid. To this end, the boronic acid (0.5 g, 2.0 mmol, 1.0 equiv) was dissolved in CH$_2$Cl$_2$ at 25 °C (10 mL), MgSO$_4$ (excess) and pinacol (0.26 g, 2.2 mmol, 1.1 equiv) were added and the reaction mixture stirred for 12 h. The reaction mixture was then filtered to remove the MgSO$_4$ and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) afforded pinacol borate $^{26}$ (0.58 g, 1.7 mmol, 87% yield) as a colorless viscous oil. $^{26}$: R$_f$ = 0.20 (silica gel, hexanes:Et$_2$O 5:1); IR (film) $\nu_{\text{max}}$ 2978, 1737, 1619, 1572, 1472, 1384, 1349, 1326, 1267, 1208, 1143, 1044, 967, 850 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.21 (d, $J$ = 18.4 Hz, 1 H), 7.35 (t, $J$ = 8.0 Hz, 1 H), 7.18 (d, $J$ = 8.0 Hz, 1 H), 6.78 (d, $J$ = 8.0 Hz, 1 H), 5.99 (d, $J$ = 18.4 Hz, 1 H), 1.56 (s, 6 H), 1.17 ppm (s, 12
H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 159.5$, 156.3, 146.9, 141.8, 135.0, 121.4, 116.9, 110.8, 104.9, 83.0, 25.2, 24.5 ppm; HRMS (ESI-TOF): calcd for C$_{18}$H$_{24}$BO$_5^+$ [M+H$^+$]: 331.1711, found 331.1707.

**TMS-protected diene 28**

To a 25 °C solution of vinyl boronic acid 26 (7.0 g, 28.0 mmol, 1.0 equiv) and (trans-2-bromovinyl)trimethylsilane (27, 5.6 mL, 36.4 mmol, 1.3 equiv) in degassed THF (500 mL) was added Pd(PPh$_3$)$_4$ (3.0 g, 2.6 mmol, 0.1 equiv), followed by a solution of aqueous Cs$_2$CO$_3$ (100.0 mL, 1.4 M, 10 equiv). The reaction mixture was heated to 55 °C and stirred for 1 h. The reaction was quenched with H$_2$O (500 mL), and the aqueous layer was extracted with Et$_2$O (3 × 500 mL). The combined organic layers were washed with H$_2$O (2 × 500 mL) and brine (500 mL), then dried (MgSO$_4$), and concentrated. Flash column chromatography (silica gel, hexanes:Et$_2$O 10:1) afforded TMS-protected diene 28 (7.5 g, 24.9 mmol, 89% yield) as a colorless oil. 28: $R_f = 0.34$ (silica gel, hexanes:Et$_2$O 10:1); IR (film) $\nu_{\text{max}}$ 2954, 1732, 1577, 1469, 1385, 1315, 1268, 1208, 1188, 1075, 1043, 1000, 865, 836, 733 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 7.71$ (d, $J = 15.0$ Hz, 1 H), 7.43 (t, $J = 8.0$ Hz, 1 H), 7.30 (d, $J = 8.0$ Hz, 1 H), 6.84 (d, $J = 8.0$ Hz, 1 H), 6.82–6.73 (m, 2 H), 6.06 (d, $J = 17.5$ Hz, 1 H), 1.70 (s, 6 H), 0.11 ppm (s, 9 H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 160.3$, 156.9, 144.2, 141.6, 137.1, 135.7, 135.0, 130.4, 120.9, 116.1, 110.8, 105.2, 25.6, −1.36 ppm; HRMS (ESI-TOF): calcd for C$_{17}$H$_{23}$O$_3$Si$^+$ [M+H$^+$]: 303.1411, found 303.1411.
Bromo-diene 29

To a solution of TMS-protected diene 28 (5.0 g, 16.5 mmol, 1.0 equiv) in CH$_3$CN (100 mL) at 25 °C was added NBS (3.5 g, 19.8 mmol, 1.2 equiv) and the reaction mixture was stirred at 25 °C for 15 min. The reaction mixture was then quenched with H$_2$O (100 mL), and the aqueous layer was extracted with Et$_2$O (3 × 100 mL). The combined organic layers were washed with H$_2$O (100 mL), 5% aqueous Na$_2$SO$_3$ (3 × 100 mL), H$_2$O (3 × 100 mL), and brine (100 mL), then dried (MgSO$_4$), and concentrated to give bromo-diene 29 (4.5 g, 14.5 mmol, 88% yield) as a yellow solid after recrystallization (hexanes:EtOAc). 29: $R_f$ = 0.26 (silica gel, hexanes:EtO 10:1); mp = 102–104 °C; IR (film) $\nu_{\text{max}}$ 3068, 2997, 1728, 1585, 1568, 1474, 1389, 1379, 1318, 1258, 1209, 1081, 1047, 977, 926 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 7.70 (d, $J = 15.6$ Hz, 1 H), 7.44 (t, $J = 8.2$ Hz, 1 H), 7.26 (d, $J = 8.2$ Hz, 1 H), 6.97 (dd, $J = 13.2$, 10.8 Hz, 1 H), 6.87 (d, $J = 8.2$ Hz, 1 H), 6.64 (dd, $J = 15.6$, 13.2 Hz, 1 H), 6.49 (d, $J = 13.2$ Hz, 1 H), 1.70 ppm (s, 6 H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 160.3, 156.9, 140.8, 137.8, 135.2, 131.1, 129.9, 120.8, 116.6, 110.8, 110.7, 105.3, 25.6 ppm; HRMS (ESI-TOF): calcd for C$_{14}$H$_{13}$BrO$_3$Na$^+$ [M+Na$^+$]: 330.9940, found 330.9935.

Salicylic acid 30

To a solution of bromo-diene 29 (4.2 g, 13.6 mmol, 1.0 equiv) in THF (13.6 mL) at 25 °C was added 5 N aqueous KOH (13.6 mL, 68.0 mmol, 5.0 equiv), and the reaction mixture was heated to 55 °C and stirred for 18 h. The reaction mixture was then cooled, acidified to pH 1 with dilute aqueous HCl, and the resulting biphasic mixture was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with 5% aqueous Na$_2$SO$_3$ (50 mL), H$_2$O (50 mL), and brine (50 mL), then dried
(MgSO₄), and concentrated to give salicylic acid 30 (3.2 g, 11.8 mmol, 87% yield) as a yellow solid after recrystallization (hexanes:EtOAc). 30: R_f = 0.32 (silica gel, EtOAc); mp = 199–200 °C; IR (film) ν_max 2967, 2831, 1646, 1594, 1435, 1209, 974 cm⁻¹; ¹H NMR (400 MHz, THF-d₈): δ = 11.70 (br s, 1 H), 7.56 (d, J = 15.6 Hz, 1 H), 7.46 (t, J = 7.6 Hz, 1 H), 7.14 (d, J = 7.6 Hz, 1 H), 7.07 (ddd, J = 13.2, 10.8, 1.2 Hz, 1 H), 6.96 (dd, J = 7.6, 1.2 Hz, 1 H), 6.71 (d, J = 13.2 Hz, 1 H), 6.69 ppm (dd, J = 15.6, 10.8 Hz, 1 H); ¹³C NMR (100 MHz, THF-d₈): δ = 173.9, 164.3, 141.5, 139.4, 135.3, 135.0, 129.4, 119.5, 118.2, 112.3, 110.5 ppm; HRMS (ESI-TOF): calcd for C₁₁H₈BrO₃⁻ [M–H⁻]: 266.9662, found 266.9661.

**Mitsunobu acid coupling partner 7**

Anhydrous Mg(ClO₄)₂ (25.0 mg, 0.37 mmol, 0.03 equiv), ground into a fine powder, was thoroughly mixed with salicylic acid 30 (1.0 g, 3.7 mmol, 1.0 equiv) at 25 °C. To this mixture was added acetic anhydride (370.0 μL, 4.0 mmol, 1.1 equiv) and the reaction mixture was kept at 25 °C in the dark, with periodic mixing, for 48 h. The resulting brown paste was dissolved into a mixture of EtOAc (50 mL) and H₂O (50 mL), and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with H₂O (6 × 100 mL) and brine (100 mL), then dried (MgSO₄), and concentrated to give Mitsunobu acid coupling partner 7 (1.1 g, 3.6 mmol, 96% yield) as a yellow solid after recrystallization (hexanes:EtOAc). 7: R_f = 0.38 (silica gel, EtOAc); mp = 115–117 °C (dec.); IR (film) ν_max 2923, 1766, 1710, 1252, 1197, 976 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 10.90 (br s, 1 H), 7.47 (dd, J = 7.4, 1.8 Hz, 1 H), 7.45 (t, J = 7.4 Hz, 1 H), 7.08 (dd, J = 7.4, 1.8 Hz, 1 H), 6.95 (d, J = 15.5 Hz, 1 H), 6.91 (dd, J = 13.4, 10.8 Hz, 1 H), 6.65 (dd, J = 15.5, 10.8 Hz, 1 H), 6.51 (d, J = 13.4 Hz, 1 H), 2.31 ppm (s, 3 H); ¹³C NMR (100 MHz,
Mitsunobu coupled product 38

To a 25 °C solution of Mitsunobu alcohol coupling partner 37 (560.0 mg, 0.72 mmol, 1.0 equiv) in THF (6.0 mL) was added DEAD (750.0 μL, 4.3 mmol, 6.0 equiv), followed by the slow addition of PPh₃ (1.1 g, 4.3 mmol, 6.0 equiv), and finally Mitsunobu acid coupling partner 7 (1.3 g, 4.3 mmol, 6.0 equiv). The reaction mixture was stirred at 25 °C for 1 h in the dark, then concentrated and purified by flash column chromatography (silica gel, hexane:EtOAc 25:1) to afford Mitsunobu coupled product 38 (715.0 mg, 0.67 mmol, 93% yield) as a colorless oil. 38: Rₛ = 0.30 (silica gel, hexane:EtOAc 8:1); [α]ₑ³² = −12.6 (CHCl₃, c = 1.0); IR (film) νₘₐₓ 2954, 2929, 2856, 1774, 1719, 1463, 1363, 1255, 1197, 1086, 975, 836, 775 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.42 (d, J = 7.0 Hz, 1 H), 7.38 (t, J = 7.9 Hz, 1 H), 7.04 (d, J = 7.0 Hz, 1 H), 6.83–6.79 (m, 2 H), 6.62–6.57 (m, 1 H), 6.49 (d, J = 13.7 Hz, 1 H), 5.55 (dt, J = 15.0, 6.9 Hz, 1 H), 5.43 (dd, J = 15.5, 6.9 Hz, 1 H), 5.26 (s, 1 H), 5.17–5.12 (m, 1 H), 4.16–4.08 (m, 1 H), 3.94–3.84 (m, 2 H), 3.83–3.76 (m, 1 H), 3.01 (d, J = 2.1 Hz, 1 H), 2.29–2.21 (m, 2 H), 2.26 (s, 3 H), 2.15 (dd, J = 13.4, 7.3 Hz, 1 H), 1.89 (s, 3 H), 1.87–1.66 (m, 6 H), 1.54–1.47 (m, 1 H), 1.19 (d, J = 6.1 Hz, 3 H), 0.91 (s, 9 H), 0.90 (s, 9 H), 0.86 (s, 9 H), 0.85 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 6 H), 0.07 (s, 3 H), 0.01 (s, 6 H), 0.01 (s, 3 H), −0.04 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 168.8, 165.2, 151.1, 148.6, 137.3, 136.9, 136.4, 130.6, 129.7, 129.3, 125.7, 125.7, 123.1, 122.4, 110.8, 106.7, 81.7, 79.7, 72.2, 70.8, 68.7, 67.8, 65.5, 46.4, 46.3, 44.9, 41.9, 40.5, 25.9, 24.1, 21.0,

**TIPS-protected dimerization precursor 39**

To a solution of Mitsunobu coupled product 38 (580.0 mg, 0.54 mmol, 1.0 equiv) in THF (6.0 mL) and MeOH (6.0 mL) at 25 °C was added K_{2}CO_{3} (3.7 mg, 0.027 mmol, 0.05 equiv), and the reaction mixture was stirred at 25 °C in the dark for 15 min. The reaction mixture was then quenched with H_{2}O (25 mL), and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with H_{2}O (50 mL), and brine (50 mL), then dried (MgSO_{4}), and concentrated. The resulting oil was then dissolved in CH_{2}Cl_{2} (12 mL) at 25 °C, and 2,6-lutidine (2.7 mL, 23.2 mmol, 60 equiv) and TIPSOTf (3.1 mL, 11.6 mmol, 30 equiv) were added. The reaction mixture was stirred at 25 °C for 18 h in the dark, then quenched with H_{2}O (25 mL), and extracted with EtOAc (3 × 50 mL). The combined organic layers were then washed with H_{2}O (50 mL) and brine (50 mL), then dried (MgSO_{4}), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 20:1) afforded TIPS-protected dimerization precursor 39 (595.0 mg, 0.50 mmol, 92% yield over two steps) as a colorless oil. 39: R_{f} = 0.66 (silica gel, hexanes:EtOAc 8:1); [\alpha]_{D}^{37} = –13.3 (CH_{2}Cl_{2}, c = 0.23); IR (film) \nu_{\text{max}} 2952, 2929, 2891, 2858, 1730, 1570, 1465, 1257, 1085, 1064, 835, 775 cm\(^{-1}\); \(^{1}\)H NMR (600 MHz, C_{6}D_{6}, mixture of two rotamers around the aryl-carbonyl bond, ca 1:1 ratio): \delta = 6.96 (t, J = 7.2 Hz, 1 H), 6.93–6.87 (m, 3 H), 6.75 (dd, J = 7.8, 5.4 Hz, 1 H), 6.30 (ddd, J = 15.0, 10.8, 3.6 Hz, 1 H), 6.02 (d, J = 13.2 Hz, 1 H), 5.81 (dt, J = 15.0, 7.2 Hz, 1 H), 5.60 (dd, J = 15.0, 6.6 Hz, 1 H), 5.48–
5.43 (m, 1 H), 5.45 (s, 1 H), 4.31–4.25 (m, 1 H), 4.11–4.04 (m, 3 H), 2.82 (d, J = 1.8 Hz, 1 H),
2.48–2.40 (m, 2 H), 2.26 (dd, J = 13.2, 4.2 Hz, 1 H), 2.20–2.11 (m, 3 H), 2.05–1.92 (m, 2 H),
2.03 (s, 3 H), 1.70 (ddd, J = 12.6, 6.6, 6.0 Hz, 1 H), 1.52–1.46 (m, 1 H), 1.35–1.30 (m, 3 H), 1.31
(d, J = 6.0 Hz, 1 H), 1.31 (d, J = 6.0 Hz, 1 H), 1.16 (d, J = 7.2 Hz, 9 H), 1.16 (d, J = 7.2 Hz, 9
H), 1.04 (s, 18 H), 1.01 (s, 9 H), 1.00 (s, 9 H), 0.25 (s, 1.5 H), 0.25 (s, 1.5 H), 0.23 (s, 1.5 H),
0.22 (s, 1.5 H), 0.19 (s, 1.5 H), 0.18 (s, 1.5 H), 0.15–0.14 (m, 9 H), 0.13 (s, 3 H), 0.12 ppm (s, 3
H); ¹³C NMR (150 MHz, C₆D₆, mixture of two rotamers around the aryl-carbonyl bond, ca 1:1
ratio): 167.1, 153.9 (0.5 C), 153.9 (0.5 C), 150.7, 137.7, 137.1, 136.3 (0.5 C), 136.2 (0.5 C),
130.8 (0.5 C), 130.8 (0.5 C), 130.0, 128.6, 127.0, 126.3, 118.2, 118.1 (0.5 C), 118.0 (0.5 C),
110.6, 107.8, 81.8, 80.7, 72.0 (0.5 C), 71.9 (0.5 C), 71.3, 69.8, 68.2, 66.4, 47.2, 46.7, 45.5, 42.5,
40.9, 26.2 (3 C), 26.2 (3 C), 26.2 (3 C), 26.2 (3 C), 24.4, 20.3, 18.3 (6 C), 17.9, 17.9, 17.9 (2 C),
13.6 (3 C), –3.4, –3.8, –3.9 (2 C), –4.1 (2 C), –4.2, –4.4 ppm; HRMS (ESI-TOF): calcd for
C₆₂H₁₁₄BrO₇Si₅⁺ [M+H⁺]: 1189.6588, found 1189.6570.

Marinomycin A (1), mono-marinomycin A (m-1), and iso-mono-marinomycin A (m-2)

To a 25 °C solution of TIPS-protected dimerization precursor 39 (100.0 mg, 0.084 mmol, 1.0
equiv in degassed THF (0.35 mL) was added a solution of catecholborane (0.25 mL, 1 M in
THF, 0.25 mmol, 3.0 equiv) and the reaction mixture was stirred at 25 °C for 1 h in the dark.
Then, a freshly prepared solution of dicyclohexylborane (170.0 μL, 0.1 M in THF, 0.017 mmol,
0.2 equiv) was added at 25 °C and stirred for an additional 30 min in the dark (until starting
material was consumed by TLC). The reaction mixture was then carefully quenched with
degassed H₂O (0.17 mL) and stirred for 1 h in the dark. The resulting boronic acid in the
THF/H₂O solution was diluted with degassed THF (12 mL) and Pd(PPh₃)₄ (9.7 mg, 0.0084
mmol, 0.1 equiv) was added, followed by TIOEt (600.0 μL, 8.4 mmol, 100 equiv). The reaction mixture was stirred at 25 °C for 4 h in the dark, then quenched with H₂O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (3 × 50 mL), dried (MgSO₄), and concentrated. The resulting oil was dissolved in THF (30 mL) and TBAF (2.5 mL, 2.5 mmol, 30 equiv) was added at 25 °C. The reaction mixture was stirred at 25 °C for 18 h in the dark, at which time the volume of the reaction mixture was reduced to about 10 mL. The resulting solution was subjected to HPLC (C18-Luna 5μ column, 100Å, 250 mm × 10 mm, 45% MeCN in H₂O) in 1 mL increments and provided marinomycin A 1 (1.7 mg, 0.00168 mmol, 2% yield), mono-marinomycin A m-1 (14.6 mg, 0.029 mmol, 35% yield), and iso-mono-marinomycin A m-2 (18.8 mg, 0.038 mmol, 45% yield) as yellow solids.

**Marinomycin A (1):**  
Rf = 0.43 (silica gel, CHCl₃:MeOH:H₂O 40:9:1); [α]D³⁶ = +173 (c = 0.01, Reagent alcohol-HPLC grade); IR (film) νmax = 3359, 2952, 2924, 2851, 1658, 1636, 1580, 1454, 1431, 1331, 1292, 1262, 1221, 1101, 1062, 1032, 997, 857, 829 cm⁻¹; ¹H NMR (600 MHz, CDCl₃ + 2 drops MeOH-d₄):

δ = 7.28 (dd, J = 8.4, 7.8 Hz, 2 H), 7.04 (d, J = 7.8 Hz, 2 H), 6.96 (d, J = 15.6 Hz, 2 H), 6.81 (d, J = 8.4 Hz, 2 H), 6.66 (dd, J = 15.6, 10.2 Hz, 2 H), 6.47 (dd, J = 14.4, 11.4 Hz, 2 H), 6.43 (dd, J = 14.4, 10.2 Hz, 2 H), 6.38 (dd, J = 14.4, 10.2 Hz, 2 H), 6.31 (dd, J = 14.4, 10.2 Hz, 2 H), 5.96 (d, J = 11.4 Hz, 2 H), 5.71–5.66 (m, 2 H), 5.49 (br d, J = 3.0 Hz, 4 H), 4.23–4.17 (m, 2 H), 4.00–
3.95 (m, 2 H), 3.90–3.86 (m, 2 H), 3.66–3.61 (m, 2 H), 2.22–1.37 (m, 20 H), 1.77 (s, 6 H), 1.22 ppm (d, \( J = 6.6 \) Hz, 6 H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\) + MeOH-\(d_4\)): \( \delta = 177.4, 159.5, 140.6, 135.7, 135.5, 134.3, 133.9, 132.0, 131.2, 130.4, 129.2, 129.1, 129.0, 128.5, 127.6, 116.5, 115.9, 72.4, 68.8, 66.6, 63.0, 62.7, 48.6, 43.8, 42.7, 42.3, 40.1, 23.8, 16.0 ppm; HRMS (ESI-TOF): calcd for C\(_{58}\)H\(_{76}\)O\(_{14}\)Na\(^+\) [M+Na\(^+\)]: 1019.5127, found 1019.5113.

mono-Marinomycin A (m-1): \( R_f = 0.54 \) (silica gel, CHCl\(_3\)::MeOH:H\(_2\)O 40:9:1); \([\alpha]_D^{37} = -276.6 \) (c = 0.06, CDCl\(_3\)); IR (film) \( \nu_{\text{max}} = 3352, 2926, 2851, 1709, 1656, 1595, 1449, 1376, 1259, 1218, 1118, 1065, 999 \text{ cm}^{-1} \); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \( \delta = 7.35 \) (t, \( J = 7.8 \) Hz, 1 H), 7.13 (d, \( J = 14.4 \) Hz, 1 H), 6.92 (d, \( J = 7.8 \) Hz, 1 H), 6.77 (d, \( J = 7.8 \) Hz, 1 H), 6.47 (dd, \( J = 14.4, 11.4 \) Hz, 1 H), 6.34 (t, \( J = 11.4 \) Hz, 1 H), 6.16–6.03 (m, 3 H), 5.91 (d, \( J = 10.8 \) Hz, 1 H), 5.38–5.20 (m, 3 H), 4.16 (br s, 1 H), 4.10–4.02 (m, 1 H), 4.00–3.91 (m, 1 H), 3.71 (br t, \( J = 9.0 \) Hz, 1 H), 3.68–3.61 (m, 1 H), 3.58 (br s, 1 H), 3.29 (br s, 1 H), 2.56 (br d, \( J = 10.8 \) Hz, 1 H), 2.19 (br d, \( J = 13.8 \) Hz, 1 H), 2.14 (br t, \( J = 10.8 \) Hz, 1 H), 1.97–1.85 (m, 4 H), 1.88 (s, 3 H), 1.79–1.75 (m, 2 H), 1.70–1.62 (m, 3 H), 1.20 ppm (d, \( J = 6.0 \) Hz, 3 H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \( \delta = 171.9, 162.4, 141.7, 135.8, 135.3, 134.6, 134.5, 133.3, 132.8, 131.9, 131.1, 130.3, 129.7, 128.2, 120.1, 117.0, 73.1, 72.5, 66.4, 65.8, 65.6, 50.4, 48.3, 45.5, 43.8, 42.5, 23.4, 17.8, 14.2 ppm; HRMS (ESI-TOF): calcd for C\(_{29}\)H\(_{38}\)O\(_7\)Na\(^+\) [M+Na\(^+\)]: 521.2510, found 521.2530.
iso-mono-Marinomycin A (m-2): \( R_f = 0.48 \) (silica gel, CHCl₃:MeOH:H₂O 40:9:1); mp = 213 °C (dec., recrystallized from CDCl₃:MeOH-d₄); \([\alpha]_D^{37} = +34.0\)

iso-mono-marinomycin A (m-2) (THF, \( c = 0.05 \)); IR (film) \( \nu_{\text{max}} \) 3359, 3190, 2922, 2852, 1702, 1658, 1632, 1467, 1451, 1257, 1064, 996 cm⁻¹; \(^1\)H NMR (CDCl₃ + 2 drops MeOH-d₄): \( \delta = 7.30 \) (dd, \( J = 8.4, 7.8 \) Hz, 1 H), 7.06 (d, \( J = 15.0 \) Hz, 1 H), 6.93 (d, \( J = 7.8 \) Hz, 1 H), 6.84 (d, \( J = 8.4 \) Hz, 1 H), 6.52 (ddd, \( J = 15.6, 7.2, 3.0 \) Hz, 1 H), 6.43 (dd, \( J = 14.4, 10.8 \) Hz, 1 H), 6.41–6.35 (m, 2 H), 6.22 (ddd, \( J = 15.0, 7.2, 3.0 \) Hz, 1 H), 5.82 (d, \( J = 10.8 \) Hz, 1 H), 5.61 (dd, \( J = 15.0, 6.0 \) Hz, 1 H), 5.50 (dt, \( J = 15.0, 6.6 \) Hz, 1 H), 5.36 (sept, \( J = 6.0 \) Hz, 1 H), 4.15 (m, 1 H), 4.10 (ddt, \( J = 9.6, 6.6, 3.0 \) Hz, 1 H), 3.98 (dddd, \( J = 8.4, 7.8, 4.2, 3.6 \) Hz, 1 H), 3.93–3.90 (m, 1 H), 3.37 (s, 1 H), 2.45–2.40 (m, 1 H), 2.24–2.15 (m, 3 H), 1.83–1.74 (m, 3 H), 1.81 (s, 3 H), 1.61 (ddd, \( J = 14.4, 10.8, 3.6 \) Hz, 1 H), 1.53 (ddd, \( J = 13.8, 9.0, 8.4 \) Hz, 1 H), 1.47 (dd, \( J = 14.4, 6.6, 1.8 \) Hz, 1 H), 1.39 ppm (d, \( J = 6.6 \) Hz, 3 H); \(^{13}\)C NMR (150 MHz, CDCl₃ + 2 drops MeOH-d₄): \( \delta = 170.9, 161.2, 140.2, 136.1, 135.7, 133.7, 133.5, 133.0, 132.8, 131.8, 131.0, 139.2, 128.4, 126.3, 119.0, 116.4, 112.1, 71.6, 71.1, 69.0, 67.6, 65.0, 47.2, 43.4 (2 C), 42.7, 41.0, 20.4, 18.5 ppm; HRMS (ESI-TOF): calcd for C_{29}H_{38}O_{7}Na⁺ [M+Na⁺]: 521.2510, found 521.2511.

Fully silylated monomer 52

To a 25 °C solution of TIPS-protected dimerization precursor 39 (24.0 mg, 0.020 mmol, 1.0 equiv) in degassed THF (0.2 mL) was added a solution of catecholborane (61.0 μL, 1 M in THF, 0.061 mmol, 3.0 equiv) and the reaction mixture was stirred at 25
°C for 1 h in the dark. Then, a freshly prepared solution of dicyclohexylborane (40.0 μL, 0.1 M in THF, 0.0040 mmol, 0.2 equiv) was added at 25 °C and the resulting solution was stirred for an additional 30 min in the dark (until starting material was consumed by TLC). The reaction mixture was then carefully quenched with degassed H₂O (0.4 mL) and stirred for 1 h in the dark. The resulting boronic acid in the THF/H₂O solution was diluted with degassed THF (1.6 mL) and Pd(PPh₃)₄ (2.3 mg, 0.0020 mmol, 0.1 equiv) was added, followed by TlOEt (5.7 μL, 0.081 mmol, 4.0 equiv). The reaction mixture was stirred at 25 °C for 1 h, then quenched with H₂O (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL), dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 50:1) provided fully silylated monomer 52 (16.1 mg, 0.015 mmol, 72% yield over two steps) as a pale yellow oil. 

52: R_f = 0.59 (silica gel, hexane:EtOAc 8:1); [α]D³² = +158.2 (CH₂Cl₂, c = 0.17); IR (film) νmax 2946, 2927, 2850, 1726, 1575, 1464, 1380, 1287, 1255, 1105, 1062, 1003, 880, 835, 806, 774 cm⁻¹; ¹H NMR (500 MHz, CD₆D₆): δ = 7.00 (d, J = 7.8 Hz, 1 H), 6.98 (t, J = 7.8 Hz, 1 H), 6.85 (d, J = 15.0 Hz, 1 H), 6.74 (d, J = 7.8 Hz, 1 H), 6.63 (dd, J = 15.0, 10.2 Hz, 1 H), 6.47–6.41 (m, 2 H), 6.31–6.23 (m, 2 H), 6.00 (d, J = 11.4 Hz, 1 H), 5.74 (ddd, J = 15.6, 8.4, 4.8 Hz, 1 H), 5.54–5.48 (m, 1 H), 5.48 (dd, J = 15.6, 7.2 Hz, 1 H), 4.36 (q, J = 6.6 Hz, 1 H), 4.24–4.21 (m, 1 H), 4.07–4.01 (m, 2 H), 2.52 (dd, J = 13.2, 3.6 Hz, 1 H), 2.38–2.33 (m, 1 H), 2.20–1.90 (m, 6 H), 1.79–1.73 (m, 1 H), 1.78 (s, 3 H), 1.68 (dd, J = 14.4, 8.4 Hz, 1 H) 1.46 (d, J = 6.0 Hz, 3 H), 1.35–1.26 (m, 3 H), 1.18 (d, J = 7.8 Hz, 9 H), 1.16 (d, J = 7.8 Hz, 9 H), 1.07 (s, 9 H), 1.05 (s, 9 H), 1.02 (s, 9 H), 0.99 (s, 9 H), 0.28 (s, 6 H), 0.22 (s, 6 H), 0.19 (s, 3 H), 0.16 (s, 3 H), 0.12 (s, 3 H), 0.11 ppm (s, 3 H); ¹³C NMR (125 MHz, CDCl₃): δ = 167.1, 153.7, 137.6, 137.4, 136.2, 133.5, 133.2, 133.0, 132.5, 131.9, 131.4, 130.1, 129.9, 129.1, 126.2, 118.5, 117.8, 71.6, 71.4, 70.6, 69.1, 66.6, 46.9, 46.6, 46.0, 43.3, 43.1, 26.4, 26.2, 26.1, 26.1, 24.2,

**Suzuki coupled mono tetraene 53**

To a 25 °C solution of Mitsunobu alcohol coupling partner 37 (340.0 mg, 0.43 mmol, 1.0 equiv) in degassed THF (0.87 mL) was added a solution of catecholborane (1.3 mL, 1 M in THF, 1.3 mmol, 3.0 equiv) and the reaction mixture was stirred at 25 °C for 1 h. A freshly prepared solution of dicyclohexylborane (870.0 μL, 0.1 M in THF, 0.87 mmol, 0.2 equiv) was then added at 25 °C and the reaction mixture was stirred for an additional 30 min (until starting material was consumed by TLC). The reaction mixture was then carefully quenched with degassed H₂O (1.0 mL) and stirred for 1 h. To the resulting boronic acid in the THF/H₂O solution was added TIPS-protected dimerization precursor 39 (300.0 mg, 0.26 mmol, 0.6 equiv) in degassed THF (18 mL) and the reaction mixture was diluted with degassed H₂O (8 mL). Pd(PPh₃)₄ (50.2 mg, 0.043 mmol, 0.1 equiv) was added, followed by a solution of KOH (510.0 μL, 5 M in H₂O, 2.55 mmol, 10 equiv) at 25 °C. The reaction mixture was stirred at 25 °C for 1 h in the dark (until starting material was consumed by TLC), then quenched with H₂O (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (3 × 50 mL), dried (MgSO₄), and concentrated. Flash column chromatography (Florisil, hexanes:EtOAc 50:1) provided Suzuki coupled mono tetraene 53 as a
yellow oil (310.0 mg, 0.16 mmol, 63% yield based on 39). 53: $R_f = 0.48$ (silica gel, hexanes:EtOAc 8:1); $[\alpha]_D^{37} = -128.7$ (CH$_2$Cl$_2$, $c = 0.04$); IR (film) $\nu_{\text{max}}$ 3524, 2952, 2929, 2857, 1731, 1656, 1578, 1464, 1254, 835 cm$^{-1}$; $^1$H NMR (600 MHz, C$_6$D$_6$, mixture of two rotamers around the aryl-carbonyl bond, ca 1:1 ratio): $\delta = 7.11$ (d, $J = 7.8$ Hz, 1 H), 7.03–6.98 (m, 2 H), 6.88–6.83 (m, 1 H), 6.74–6.70 (m, 1 H), 6.62–6.53 (m, 2 H), 6.45–6.36 (m, 2 H), 6.14 (d, $J = 11.4$ Hz, 1 H), 5.88–5.80 (m, 2 H), 5.63 (dd, $J = 15.0$, 7.2 Hz, 1 H), 5.59 (dd, $J = 15.0$, 6.6 Hz, 1 H), 5.50–5.46 (m, 1 H), 5.46 (s, 1 H), 4.40 (q, $J = 6.6$ Hz, 1 H), 4.29–4.26 (m, 1 H), 4.17–4.04 (m, 6 H), 4.01–3.98 (m, 1 H), 2.83 (d, $J = 1.8$ Hz, 1 H), 2.47–2.15 (m, 8 H), 2.06–1.90 (m, 5 H), 2.03 (s, 3 H), 1.88–1.75 (m, 3 H), 1.84 (s, 3 H), 1.72–1.68 (m, 1 H), 1.65 (ddd, $J = 13.8$, 5.4, 3.0 Hz, 1 H), 1.53–1.49 (m, 2 H), 1.35–1.28 (m, 9 H), 1.19–1.15 (m, 18 H), 1.07–1.05 (m, 36 H), 1.02 (s, 9 H), 1.01 (s, 9 H), 1.00 (s, 9 H), 0.97 (s, 9 H), 0.29 (m, 3 H), 0.25 (m, 3 H), 0.20 (s, 6 H), 0.20 (s, 9 H), 0.16 (s, 6 H), 0.15 (s, 3 H), 0.15 (s, 3 H), 0.14 (m, 3 H), 0.12 (s, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H), 0.07 ppm (s, 3 H); $^{13}$C NMR (150 MHz, C$_6$D$_6$, mixture of two rotamers around the aryl-carbonyl bond, ca 1:1 ratio): $\delta = 167.4$, 153.8 (0.5 C), 153.8 (0.5 C), 150.8, 137.5, 137.3 (0.5 C), 137.2 (0.5 C), 137.0, 136.9, 135.7, 132.4, 132.3, 131.6, 130.9, 130.8, 129.9, 129.3 (0.5 C), 129.2 (0.5 C), 126.8, 126.4, 117.9 (0.5 C), 117.9 (0.5 C), 117.5, 117.5, 107.8 (2 C), 81.9, 80.7, 71.9, 71.6, 71.4, 71.1, 69.9 (0.5 C), 69.8 (0.5 C), 69.1, 68.9, 68.7, 68.2, 66.6 (0.5 C), 66.5 (0.5 C), 48.7, 47.4, 47.2, 46.7, 45.6, 44.5, 42.6, 41.0, 40.3, 39.2, 30.2, 26.3 (3 C), 26.3 (3 C), 26.2 (9 C), 26.2 (3 C), 26.1 (3 C), 26.0 (3 C), 24.5, 24.3, 20.3, 18.3 (14 C), 13.6 (3 C), −3.3, −3.6, −3.8, −3.9, −3.9 (2 C), −3.9, −4.0, −4.1 (3 C), −4.2, −4.3, −4.4, −4.5, −4.6 ppm; HRMS (ESI-TOF): calcd for C$_{104}$H$_{200}$O$_{12}$Si$_9$Na$^+$ [M+Na$^+$]: 1916.2855, found 1916.2858.
Suzuki cyclization precursor 56

To a 25 °C solution of Suzuki coupled mono
tetraene 53 (139.0 mg, 0.073 mmol, 1.0 equiv) in
THF (1.2 mL) was added
DEAD (80.0 μL, 0.44 mmol, 6.0 equiv), followed
by slow addition of PPh₃ (115.0 mg, 0.44 mmol, 6.0 equiv), and finally Mitsunobu acid coupling
partner 7 (137.0 mg, 0.44 mmol, 6.0 equiv). The reaction mixture was stirred at 25 °C for 1 h in
the dark, then concentrated and purified by flash column chromatography (Florisil, hexanes:EtOAc 50:1) to provide the corresponding Mitsunobu coupled product (54). This was
dissolved in THF (1.0 mL) and MeOH (1.0 mL) at 25 °C, and K₂CO₃ (0.5 mg, 0.0037 mmol, 0.05 equiv) was added to the reaction mixture. The reaction mixture was stirred at 25 °C in the
dark for 15 min and then quenched with H₂O (15 mL), and the resulting biphasic mixture was
extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H₂O (20 mL) and brine (20 mL), then dried (MgSO₄), and concentrated. The resulting oil was then
dissolved in CH₂Cl₂ (1.0 mL), and 2,6-lutidine (510.0 μL, 4.4 mmol, 60 equiv) and TIPSOTf
(590.0 μL, 2.2 mmol, 30 equiv) were added. The reaction mixture was stirred at 25 °C for 18 h
in the dark, then quenched with H₂O (15 mL), and the resulting biphasic mixture was extracted
with EtOAc (3 × 25 mL). The combined organic layers were then washed with H₂O (25 mL)
and brine (25 mL), then dried (MgSO₄), and concentrated. Flash column chromatography
(Florisil, hexanes:EtOAc 100:1) afforded Suzuki cyclization precursor 56 (131.0 mg, 0.060
mmol, 78% yield over three steps) as a yellow oil. 56: \( R_f = 0.57 \) (silica gel, hexanes:EtoAc, 8:1); \( [\alpha]_D^{37} = -98.8 \) (c = 0.014, CH\(_2\)Cl\(_2\)); IR (film) \( \nu_{\text{max}} = 2952, 2828, 2856, 1729, 1570, 1465, 1255, 835, 775 \text{ cm}^{-1} \); \(^1\)H NMR (600 MHz, C\(_6\)D\(_6\), mixture of two rotamers around the aryl-carbonyl bond, ca 1:1 ratio): \( \delta = 7.15 \) (d, \( J = 8.4 \text{ Hz}, 1 \text{ H} \)), 7.11 (d, \( J = 8.4 \text{ Hz}, 1 \text{ H} \)), 7.03–6.96 (m, 2 H), 6.94–6.89 (m, 3 H), 6.85 (dd, \( J = 15.6, 10.8 \text{ Hz}, 1 \text{ H} \)), 6.75 (d, \( J = 7.8 \text{ Hz}, 1 \text{ H} \)), 6.72 (d, \( J = 7.8 \text{ Hz}, 1 \text{ H} \)), 6.61 (dd, \( J = 13.2, 11.4 \text{ Hz}, 1 \text{ H} \)), 6.55 (dd, \( J = 13.8, 11.4 \text{ Hz}, 1 \text{ H} \)), 6.49–6.37 (m, 2 H), 6.31 (dd, \( J = 15.6, 10.8 \text{ Hz}, 1 \text{ H} \)), 6.16 (d, \( J = 11.4 \text{ Hz}, 1 \text{ H} \)), 6.03 (d, \( J = 13.8 \text{ Hz}, 1 \text{ H} \)), 5.85 (dt, \( J = 15.0, 7.2 \text{ Hz}, 1 \text{ H} \)), 5.83 (dt, \( J = 15.0, 7.2 \text{ Hz}, 1 \text{ H} \)), 5.66 (dd, \( J = 15.6, 7.2 \text{ Hz}, 1 \text{ H} \)), 5.59 (dd, \( J = 15.6, 7.2 \text{ Hz}, 1 \text{ H} \)), 5.51–5.45 (m, 2 H), 5.46 (s, 1 H), 4.38 (q, \( J = 7.2 \text{ Hz}, 1 \text{ H} \)), 4.28 (q, \( J = 7.2 \text{ Hz}, 1 \text{ H} \)), 4.16–4.05 (m, 6 H), 2.83 (d, \( J = 2.4 \text{ Hz}, 1 \text{ H} \)), 2.49–2.40 (m, 4 H), 2.33–2.25 (m, 2 H), 2.23–2.10 (m, 6 H), 2.05–1.92 (m, 5 H), 2.04 (s, 3 H), 1.86 (s, 3 H), 1.85–1.79 (m, 2 H), 1.70 (ddd, \( J = 13.2, 7.2, 4.8 \text{ Hz}, 1 \text{ H} \)), 1.35–1.28 (m, 12 H), 1.19–1.16 (m, 36 H), 1.07 (s, 9 H), 1.06 (s, 9 H), 1.06 (s, 27 H), 1.05 (s, 9 H), 1.02 (s, 9 H), 1.01 (s, 9 H), 0.28 (s, 3 H), 0.26 (s, 6 H), 0.23 (s, 3 H), 0.21 (s, 3 H), 0.20 (s, 3 H), 0.19 (s, 3 H), 0.19 (s, 3 H), 0.16 (s, 6 H), 0.15 (s, 3 H), 0.15 (s, 3 H), 0.14 (s, 3 H), 0.14 (s, 3 H), 0.12 ppm (s, 3 H); \(^{13}\)C NMR (150 MHz, C\(_6\)D\(_6\), mixture of rotamers around the aryl-carbonyl bond, ca 1:1 ratio): \( \delta = 167.4 \) (0.5 C), 167.4 (0.5 C) 167.1, 153.9, 153.8 (0.5 C), 153.8 (0.5 C), 150.8, 137.8 (3 C), 137.7, 137.2, 137.1, 136.4, 136.2 (0.5 C), 136.2 (0.5 C), 135.7, 132.4 (0.5 C), 132.3 (0.5 C), 131.5 (0.5 C), 130.9 (0.5 C), 130.9, 130.1, 130.1 (0.5 C), 130.0, 129.9 (0.5 C), 129.1, 129.0, 126.5 (0.5 C), 126.4 (0.5 C), 126.3 (0.5 C), 126.2 (0.5 C), 118.1, 117.9, 117.9, 117.4, 110.6, 110.4 (0.5 C), 110.3 (0.5 C), 107.8 (2 C), 81.9, 80.7, 72.0, 71.9 (0.5 C), 71.8 (0.5 C), 71.5, 71.4, 69.8 (0.5 C), 69.7 (0.5 C), 68.7, 68.2, 66.5, 66.4 (2 C), 51.7, 48.6, 47.4, 47.2, 46.7, 45.6, 45.5, 42.6, 42.5, 41.0, 30.2, 26.3 (9 C), 26.2 (9 C), 26.2 (3 C), 26.2 (3 C), 24.5, 24.4, 20.3, 18.3 (8 C), 17.9 (12 C), 12.7
(6 C), −3.4, −3.4, −3.8 (2 C), −3.9 (3 C), −3.9, −4.0, −4.1 (4 C), −4.2, −4.3, −4.4 ppm; HRMS (ESI-TOF): calcd for $\text{C}_{124}\text{H}_{226}\text{BrO}_{14}\text{Si}_{10}$ $\text{[M−H]}^−$: 2298.3853, found 2298.3852.

**Marinomycin A (1)**

To a 25 °C solution of Suzuki cyclization precursor **56** (120.0 mg, 0.052 mmol, 1.0 equiv) in degassed THF (0.10 mL) was added a solution of catecholborane (160.0 μL, 1.0 M in THF, 0.16 mmol, 3.0 equiv) at 25 °C and the reaction mixture was stirred for an additional 30 min in the dark (until starting material was consumed by TLC). The reaction mixture was then carefully quenched with degassed H$_2$O (0.30 mL) and stirred for 1 h in the dark. The resulting boronic acid in the THF/H$_2$O solution was diluted with degassed THF (56 mL) and degassed H$_2$O (5.3 mL), and Pd(PPh$_3$)$_4$ (60.0 mg, 0.052 mmol, 1.0 equiv) was added, followed by TIOEt (1.1 mL, 15.6 mmol, 300 equiv). The reaction mixture was stirred at 25 °C for 4 h in the dark, then quenched with H$_2$O (50 mL) and extracted with EtOAc ($3 \times 100$ mL). The combined organic layers were washed with brine ($3 \times 100$ mL), dried (MgSO$_4$), and concentrated. The resulting oil was dissolved in THF (40 mL) and TBAF (2.6 mL, 2.6 mmol, 50 equiv) was added at 25 °C. The reaction mixture was stirred at 25 °C for 18 h, at which time the volume of the reaction was
reduced to about 5 mL. The solution was purified by HPLC (C8-Luna 5μ column, 100Å, 250 mm × 10 mm, 60% MeCN in H2O) in 1 mL increments and provided marinomycin A (1) (11.9 mg, 0.012 mmol, 23% yield over 3 steps), which exhibited identical physical properties to those recorded for the naturally occurring substance (see above).

![Chemical Structure](image)

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**TES-Protected mono-olefin 64**

To a 25 °C solution of terminal acetylene 25 (7.1 g, 35.1 mmol, 1.0 equiv) in THF (35 mL) was added triethylsilane (6.4 mL, 77.2 mmol, 2.2 equiv) and a solution of freshly prepared Pt(DVDS)/2,8,9-triisobutyl-2,5,8,9-tetraaza-1-phosphabicyclo{3.3.3}undecane (15.4 mL, 1.4 mmol, 0.04 equiv). The reaction mixture was stirred at 25 °C for 18 h and then quenched with H2O (100 mL) and the resulting biphasic mixture was extracted with EtOAc (3 × 100 mL), the combined organic layers were washed with H2O (100 mL) and brine (100 mL), dried (MgSO4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 20:1) gave TES-protected mono olefin 64 as a colorless oil (9.8 g, 30.8 mmol, 88%). 64: Rf = 0.68 (silica gel, hexanes:EtOAc 4:1); IR (film) \( \nu_{\text{max}} \) 2952, 2909, 2874, 1736, 1601, 1571, 1472, 1388, 1377, 1314, 1269, 1200, 1077, 1042, 1015, 984, 965, 923, 805, 782, 772, 713, 686 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \( \delta = 7.93 \) (d, \( J = 19.2 \) Hz, 1 H), 7.43 (dd, \( J = 8.4, 7.8 \) Hz, 1 H), 7.23 (d, \( J = 7.8 \) Hz, 1 H), 6.84 (d, \( J = 8.4 \) Hz, 1 H), 6.39 (d, \( J = 19.2 \) Hz, 1 H), 1.69 (s, 6 H), 1.00 (t, \( J = 7.8 \) Hz, 9 H), 0.68 ppm (q, \( J = 7.8 \) Hz, 6 H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \( \delta = 160.0, 156.5, 143.4, 143.1, 135.0, 131.2, 121.3, 116.2, 110.5, \)
105.0, 25.5, 7.3, 3.4 ppm; HRMS (ESI-TOF): calcd for C$_{18}$H$_{27}$O$_3$Si$^+$ [M+H$^+$]: 318.1724, found 319.1729.

**Bromo-mono olefin 65**

TES-protected mono olefin 64 (9.8 g, 30.8 mmol, 1.0 equiv) was dissolved in MeCN (240 mL) and NBS (11.0 g, 61.5 mmol, 2.0 equiv) was added to the reaction mixture at 25 °C. The reaction mixture was stirred for 18 h at 25 °C, then quenched with H$_2$O (250 mL), and the resulting biphasic mixture was extracted with EtOAc (3 × 250 mL). The combined organic layers were washed with Na$_2$S$_2$O$_3$ (2 × 250 mL) and brine (250 mL), dried (MgSO$_4$), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 16:1) provided bromo-mono olefin 65 (7.9 g, 28.0 mmol, 91% yield) as a colorless oil. 65: R$_f$ = 0.40 (silica gel, hexanes:EtOAc 4:1); IR (film) $\nu_{\max}$ 1720, 1572, 1474, 1433, 1379, 1317, 1269, 1202, 1171, 1080, 1043, 1017, 965, 923, 907, 853, 822, 766, 729, 687, 678, 585 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 8.12 (d, $J$ = 13.8, 1 H), 7.44 (dd, $J$ = 8.4, 7.8 Hz, 1 H), 7.09 (d, $J$ = 7.8 Hz, 1 H), 6.90 (d, $J$ = 8.4 Hz, 1 H), 6.74 (d, $J$ = 13.8 Hz, 1 H), 1.68 ppm (s, 6 H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 159.9, 156.7, 139.4, 135.4, 121.4, 117.2, 110.1, 109.9, 105.4, 25.5 ppm; HRMS (ESI-TOF): calcd for C$_{12}$H$_{12}$BrO$_3^+$ [M+H$^+$]: 282.9964, found 282.9964.

**Vinyl bromide carboxylic acid 66**

To a solution of bromo-mono olefin 65 (1.0 g, 3.53 mmol, 1.0 equiv) in THF (7.1 mL) was added 5 N aqueous KOH (7.1 mL, 35.3 mmol, 10 equiv), and the reaction mixture was heated to 55 °C and stirred for 18 h. The reaction mixture
was then cooled, acidified with dilute aqueous HCl until pH 1, and the resulting biphasic mixture was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with 5% aqueous Na₂SO₃ (50 mL), H₂O (50 mL), and brine (50 mL), then dried (MgSO₄), and concentrated to give the corresponding salicylic acid (730.0 mg, 3.0 mmol, 85% yield) as a yellow solid after recrystallization (hexanes:EtOAc). Anhydrous Mg(ClO₄)₂ (58.0 mg, 0.26 mmol, 0.1 equiv), ground into a fine powder, was thoroughly mixed with the corresponding salicylic acid (1.0 g, 3.7 mmol, 1.0 equiv) at 25 °C. To this mixture was added acetic anhydride (250.0 μL, 2.6 mmol, 1.0 equiv), and the reaction mixture was kept at 25 °C in the dark, with periodic mixing, for 18 h. The resulting brown paste was dissolved into a mixture of EtOAc (50 mL) and H₂O (50 mL), and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with H₂O (6 × 100 mL) and brine (100 mL), then dried (MgSO₄), and concentrated to give vinyl bromide carboxylic acid 66 (700.0 mg, 2.5 mmol, 95% yield) as a yellow viscous oil, which was used in the following step without further purification.

66: Rₐ = 0.41 (silica gel, EtOAc); IR (film) νₚₑ₉₈₈, 3164, 3073, 2923, 2845, 1769, 1734, 1596, 1565, 1465, 1370, 1197, 1121, 1021, 936, 875, 774, 672 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.49 (d, J = 13.8 Hz, 1 H), 7.48 (dd, J = 8.4, 7.8 Hz, 1 H), 7.34 (d, J = 7.8 Hz, 1 H), 7.12 (d, J = 8.4 Hz, 1 H), 6.78 (d, J = 13.8 Hz, 1 H), 2.31 ppm (s, 3 H); ¹³C NMR (150 MHz, CDCl₃): δ = 169.3, 169.2, 149.2, 137.1, 134.3, 132.0, 124.4, 123.2, 123.1, 110.2, 20.9 ppm; HRMS (ESI-TOF): calcd for C₁₁H₈BrO₄Na⁺ [M+Na⁺]: 306.9576, found 306.9679.
Stille dimerization precursor 58

To a 25 °C solution of Mitsunobu alcohol coupling partner 37 (100.0 mg, 0.13 mmol, 1.0 equiv) in THF (2.1 mL) was added DEAD (140.0 μL, 0.77 mmol, 6.0 equiv), followed by slow addition of PPh₃ (201.0 mg, 0.77 mmol, 6.0 equiv), and finally vinyl bromide carboxylic acid 66 (218.0 mg, 0.77 mmol, 6.0 equiv). The reaction mixture was stirred at 25 °C for 1 h, then concentrated and purified by flash column chromatography (silica gel, hexanes:EtoAc 25:1) to afford the corresponding Mitsunobu coupled product as a colorless oil. This was dissolved in THF (1.0 mL) and MeOH (1.0 mL) at 25 °C and K₂CO₃ (1.8 mg, 0.013 mmol, 0.1 equiv) was added. The reaction mixture was stirred at 25 °C in the dark for 15 min, then quenched with H₂O (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H₂O (25 mL) and brine (25 mL), then dried (MgSO₄), and concentrated. The resulting oil was then dissolved in CH₂Cl₂ (1.8 mL), and 2,6-lutidine (900.0 μL, 7.7 mmol, 60 equiv) and TIPSOTf (1.0 mL, 3.8 mmol, 30 equiv) were added. The reaction mixture was stirred at 25 °C for 18 h, then quenched with H₂O (25 mL), and extracted with EtOAc (3 × 50 mL). The combined organic layers were then washed with H₂O (50 mL) and brine (50 mL), then dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtoAc 25:1) afforded Stille dimerization precursor 58 (92.0 mg, 0.079 mmol, 62% yield over three steps) as a colorless oil. 58: Rᵥ = 0.63 (silica gel, hexanes:EtoAc 8:1); IR (film) νmax 2950, 2929, 2886, 2857, 1731, 1573, 1464, 1380, 1361, 1291, 1254, 1105, 1082, 1063, 1027, 975, 937, 883, 834, 807, 774, 689 cm⁻¹, ¹H NMR (600 MHz, C₆D₆): δ = 7.46 (d, J = 13.8 Hz, 1 H), 6.85 (dd, J = 8.4, 7.8 Hz, 1 H), 6.72 (d, J = 8.4 Hz, 1 H), 6.56 (d, J = 7.8 Hz, 1 H), 6.39 (d, J = 13.8 Hz, 1 H), 5.86
(dt, $J = 15.6, 7.2$ Hz, 1 H), 5.61 (dd, $J = 15.6, 7.2$ Hz, 1 H), 5.51 (pent, $J = 6.6$ Hz, 1 H), 5.45 (s, 1 H), 4.32–4.27 (m, 1 H), 4.13–4.03 (m, 3 H), 2.82 (s, 1 H), 2.48 (t, $J = 6.0$ Hz, 1 H), 2.26 (dd, $J = 13.2, 4.8$ Hz, 1 H), 2.19–2.09 (m, 3 H), 2.04–1.92 (m, 3 H), 2.03 (s, 3 H), 1.71 (dt, $J = 13.2, 6.6$ Hz, 1 H), 1.35 (d, $J = 6.0$ Hz, 3 H), 1.31–1.23 (m, 4 H), 1.14 (d, $J = 7.2$ Hz, 9 H), 1.14 (d, $J = 7.2$ Hz, 9 H), 1.04 (s, 9 H), 1.01 (s, 9 H), 1.00 (s, 9 H), 0.28 (s, 3 H), 0.23 (s, 3 H), 0.20 (s, 3 H), 0.16 (s, 3 H), 0.15 (s, 3 H), 0.14 (s, 3 H), 0.14 (s, 3 H), 0.11 ppm (s, 3 H); $^{13}$C NMR (150 MHz, C$_6$D$_6$): $\delta = 166.5, 154.0, 150.7, 137.0, 135.5, 135.2, 130.2, 126.4, 125.4, 118.6, 118.4, 109.4, 107.8, 81.8, 80.7, 71.9, 71.4, 69.6, 68.2, 66.4, 47.2, 46.7, 45.7, 42.5, 41.1, 26.2, 26.2, 24.5, 20.3, 18.4, 18.3, 18.3, 18.2, 13.5, –3.4, –3.8, –3.9, –4.0, –4.1, –4.2, –4.4 ppm; HRMS (ESI-TOF): calcd for C$_{60}$H$_{112}$BrO$_7$Si$_4$ $^+$ [M+H$^+$]: 1163.6432, found 1163.6389.

**Heck cyclization precursor 63**

To a solution of TIPS-protected dimerization precursor 39 (13.0 mg, 0.011 mmol, 1.0 equiv) in THF (0.11 mL) at 25 °C was added ZrCp$_2$HCl (5.6 mg, 0.022 mmol, 2.0 equiv). The reaction mixture was stirred at 25 °C for 30 min, then quenched with H$_2$O (0.11 mL), and stirred an additional 30 min. The biphasic mixture was extracted with EtOAc (3 $\times$ 0.5 mL), and the combined organic layers were washed with H$_2$O (0.5 mL) and brine (0.5 mL), dried (MgSO$_4$), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 50:1) yielded Heck cyclization precursor 63 (8.5 mg, 0.0071 mmol, 65% yield) as a colorless oil.

63: $R_f = 0.39$ (silica gel, hexanes:EtOAc 16:1); $[\alpha]_D^{32} = –7.3$ (CH$_2$Cl$_2$, $c = 0.95$); IR (film) $\nu_{\text{max}}$ 2951, 2929, 2891, 2857, 1730, 1569, 1465, 1287, 1255, 1107, 1084, 1064, 1026, 973, 835, 806, 774 cm$^{-1}$; $^1$H
NMR (600 MHz, C$_6$D$_6$): $\delta = 6.96$ (dd, $J = 8.4$, 7.8 Hz, 1 H), 6.95–6.87 (m, 3 H), 6.74 (d, $J = 8.4$ Hz, 1 H), 6.60 (ddd, $J = 16.8$, 10.8, 10.2 Hz, 1 H), 6.30 (dd, $J = 15.6$, 10.8 Hz, 1 H), 6.04 (d, $J = 10.2$ Hz, 1 H), 6.02 (d, $J = 13.8$ Hz, 1 H), 5.85–5.78 (m, 1 H), 5.64 (dd, $J = 15.6$, 7.2 Hz, 1 H), 5.47–5.43 (m, 1 H), 5.16 (dd, $J = 16.8$, 1.8 Hz, 1 H), 5.02 (dd, $J = 10.8$, 1.8 Hz, 1 H), 4.36–4.33 (m, 1 H), 4.12–4.04 (m, 3 H), 2.50–2.40 (m, 2 H), 2.34 (dd, $J = 13.2$, 4.8 Hz, 1 H), 2.26 (dd, $J = 13.2$, 7.2 Hz, 1 H), 2.19–2.11 (m, 2 H), 2.03–1.93 (m, 3 H), 1.77 (s, 3 H), 1.31 (d, $J = 6.0$ Hz, 3 H), 1.31–1.25 (m, 4 H), 1.16 (d, $J = 7.2$ Hz, 9 H), 1.16 (d, $J = 7.2$ Hz, 9 H), 1.04 (s, 18 H), 1.03 (s, 9 H), 1.02 (s, 9 H), 0.25 (s, 3 H), 0.25 (s, 3 H), 0.18 (s, 3 H), 0.17 (s, 9 H), 0.14 (s, 3 H), 0.11 ppm (s, 3 H); $^{13}$C NMR (150 MHz, C$_6$D$_6$): $\delta = 167.1$, 153.9, 137.7, 137.2, 136.4, 136.0, 133.6, 130.9, 130.0, 129.3, 128.9, 126.5, 126.2, 118.2, 117.9, 115.3, 110.6, 72.0, 71.5, 69.8, 66.5, 48.2, 47.3, 45.6, 42.5, 41.0, 26.2, 26.2, 24.4, 18.4, 18.3, 18.3, 18.2, 17.6, 13.6, –3.4, –3.8, –3.9, –3.9, –4.0, –4.1, –4.1, –4.4 ppm; HRMS (ESI-TOF): calcd for C$_{62}$H$_{115}$BrO$_7$Si$_5$Na$^+$ [M+Na$^+$]: 1213.6564, found 1213.6572.

**General procedure for Heck cyclization**

To a 25 °C solution of Heck cyclization precursor 63 (2.5 mg, 0.0021 mmol, 1.0 equiv) in DMF (0.10 mL) was added Pd(OAc)$_2$ (0.07 mg, 0.11 μmol, 0.05 equiv), KOAc (0.5 mg, 0.0053 mmol, 2.5 equiv), and $n$-Bu$_4$NCl (1.5 mg, 0.0053 mmol, 2.5 equiv). The reaction mixture was stirred at 25 °C for 18 h, then quenched with H$_2$O (0.5 mL), and the biphasic reaction mixture was extracted with EtOAc (3 × 0.5 mL). The combined organic layers were washed with H$_2$O (3 × 1 mL) and brine (2 × 1 mL), then dried (MgSO$_4$), and concentrated. The resulting oil was dissolved in THF (1.0 mL) and a solution of TBAF (110.0 μL, 1 M in THF, 0.11 mmol, 50 equiv) was added to the reaction mixture at 25 °C. The reaction mixture was stirred at 25 °C for
18 h, concentrated to about 0.5 mL, and purified by HPLC (C18-Sunfire 10μ column, 250 × 10 mm, 10 to 100% MeCN in H2O) to yield mono-marinomycin A (m-1) (0.63 mg, 0.0013 mmol, 60% yield), iso-mono-marinomycin A (m-2) (0.21 mg, 0.00042 mmol, 20% yield), and marinomycin A (1) (trace, detectable by HPLC).

**Enone metathesis partner 40b**

To a solution of aldehyde 17 (78.7 mg, 0.22 mmol, 1.0 equiv) in THF (2.2 mL) at −78 °C was added a solution of freshly prepared vinyl Grignard (1.6 mL, 0.42 M in THF, 0.65 mmol, 3.0 equiv) and the reaction mixture was stirred for 45 min. At that time (TLC indicated consumption of starting aldehyde) the reaction mixture was quenched with NH4Cl (5 mL) and allowed to warm to 25 °C. The biphasic mixture was extracted with Et2O (3 × 10 mL), the combined organic layers were washed with H2O (3 × 10 mL) and brine (1 × 10 mL), then dried (MgSO4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded the corresponding allylic alcohol (66.5 mg, 0.17 mmol, 78% yield) as a colorless oil. This alcohol (63.2 mg, 0.16 mmol, 1.0 equiv) was dissolved in DMSO (0.81 mL), and IBX (90 mg, 0.32 mmol, 2.0 equiv) was added at 25 °C. The reaction mixture was stirred for 3 h at 25 °C (consumption of starting material by TLC) and then quenched with H2O (2 mL). The biphasic mixture was extracted with EtOAc (3 × 5 mL), then washed with H2O (5 mL) and brine (5 mL), then dried (MgSO4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 6:1) yielded enone metathesis partner 40b (58.0 mg, 0.15 mmol, 92% yield) as a colorless oil. 40b: Rf = 0.73 (silica gel, hexanes:EtOAc 3:1); [α]D35 = +34.5 (CDCl3, c = 0.99); IR (film) ν max 2956, 2929, 2856, 1696, 1682, 1615, 1471, 1400, 1361, 1254, 1087, 1070, 1026, 1006, 835, 809, 776, 736, 697 cm⁻¹; 1H NMR (600 MHz,
C₆D₆): $\delta = 7.32$ (d, $J = 7.8$ Hz, 2 H), 7.18 (t, $J = 7.8$ Hz, 2 H) 7.09 (t, $J = 7.8$ Hz, 1 H), 6.09 (dd, $J = 17.4$, 10.8 Hz, 1 H), 5.85 (dd, $J = 17.4$, 1.2 Hz, 1 H), 5.52 (dt, $J = 6.6$, 1.2 Hz, 1 H), 5.19 (dd, $J = 10.8$, 1.2 Hz, 1 H), 4.53–4.47 (m, 1 H), 4.36 (s, 2 H), 3.96–3.88 (m, 2 H), 2.60 (dd, $J = 16.2$, 7.2 Hz, 1 H), 2.42 (dd, $J = 16.2$, 5.4 Hz, 1 H), 2.25 (dd, $J = 13.2$, 5.4 Hz, 1 H), 2.15 (dd, $J = 13.2$, 7.2 Hz, 1 H), 1.54 (s, 3 H), 0.95 (s, 9 H), 0.08 (s, 3 H), 0.08 ppm (s, 3 H); $^{13}$C NMR (150 MHz, C₆D₆): $\delta = 198.3, 139.4, 137.6, 136.0, 128.5, 127.8, 127.6, 127.5, 125.7, 72.2, 68.1, 66.8, 48.7, 46.8, 26.1, 18.2, 17.0, −4.5, −4.6 ppm; HRMS (ESI-TOF): calcd for C₂₃H₃₆O₃SiNa⁺ [M+Na⁺]: 411.2326, found 411.2332.

**Homo-allylic alcohol metathesis partner 23**

$^{23}$: $R_f = 0.62$ (silica gel, hexanes:EtOAc 4:1); [$\alpha$]$_D^{35} = −43.1$ (CDCl₃, $c = 0.87$); IR (film) $\nu_{\text{max}}$ 3456, 2955, 2930, 2879, 2857, 1462, 1413, 1375, 1254, 1064, 1004, 941, 914, 835, 807, 773, 743 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl₃): $\delta = 5.82$ (ddt, $J = 17.4$, 10.2, 7.2 Hz, 1 H), 5.10 (d, $J = 17.4$ Hz, 1 H), 5.07 (d, $J = 10.2$ Hz, 1 H), 4.14–4.09 (m, 1 H), 3.85–3.78 (m, 2 H), 3.68 (s, 1 H), 2.26 (dt, $J = 13.8$, 7.2 Hz, 1 H), 2.18 (dt, $J = 13.8$, 7.2 Hz, 1 H), 1.80–1.76 (m, 1 H), 1.72 (ddd, $J = 13.8$, 9.6, 4.2 Hz, 1 H), 1.50 (ddd, $J = 13.2$, 9.6, 3.0 Hz, 1 H), 1.40 (dt, $J = 14.4$, 9.6 Hz, 1 H), 1.13 (d, $J = 6.0$ Hz, 3 H), 0.97 (t, $J = 7.8$ Hz, 9 H), 0.87 (s, 9 H), 0.64 (q, $J = 7.8$ Hz, 6 H), 0.04 (s, 3 H), 0.01 ppm (s, 3 H); $^{13}$C NMR (150 MHz, CDCl₃): $\delta = 135.0, 117.3, 71.3, 70.9, 65.7, 48.5, 42.3, 41.8, 25.8, 24.7, 17.9, 6.8, 5.2, −4.0, −4.8 ppm; HRMS (ESI-TOF): calcd for C₂₁H₄₇O₃Si₂⁺ [M+H⁺]: 403.3058, found 403.3058.
General procedure for metathesis:

Deprotected enone metathesis partner 40a (20.0 mg, 0.073 mmol, 1.0 equiv) and model olefin partner (24, 75.4 mg, 0.15 mmol, 2.0 equiv) were dissolved in CH$_2$Cl$_2$ (1.0 mL) at 25 °C. Grubbs second generation catalyst (43, 6.2 mg, 0.0073 mmol, 0.1 equiv) was added to the reaction mixture and then stirred for 18 h at 25 °C. The reaction mixture was concentrated and purified by flash column chromatography (silica gel, hexanes:EtOAc 6:1) to yield Horner–Wadsworth–Emmons enone 31a (20.0 mg, 0.026 mmol, 36% yield, 72% based on recovered starting material).

Simple metathesis product 42

42: $R_f = 0.19$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{35} = +16.0$ (CDCl$_3$, $c = 0.28$); IR (film) $\nu_{\text{max}}$ 3427, 2951, 2927, 2855, 1666, 1628, 1461, 1380, 1357, 1255, 1096, 976, 835, 777 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$): $\delta = 7.36–7.25$ (m, 5 H), 6.87 (dt, $J = 16.2$, 7.2 Hz, 1 H), 6.14 (dd, $J = 16.2$, 1.2 Hz, 1 H), 5.49 (dt, $J = 6.6$, 1.2 Hz, 1 H), 4.51 (s, 2 H), 4.28–4.23 (m, 1 H), 4.05 (d, $J = 6.6$ Hz, 2 H), 3.73 (t, $J = 6.6$ Hz, 2 H), 2.74 (dd, $J = 17.4$, 3.6 Hz, 1 H), 2.64 (dd, $J = 17.4$, 8.4 Hz, 1 H), 2.45–2.41 (m, 2 H), 2.29 (dd, $J = 13.8$, 7.2 Hz, 1 H), 2.19 (dd, $J = 13.8$, 6.0 Hz, 1 H), 1.69 (s, 3 H), 0.88 (s, 9 H), 0.05 ppm (s, 6 H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta = 200.6$, 145.6, 138.4, 136.7, 132.0, 128.4, 127.8, 127.6, 124.4, 72.2, 66.4, 65.8, 61.4, 46.7, 45.5, 35.9, 29.7, 25.9, 18.3, 16.7, 15.3, –5.4 ppm; HRMS (ESI-TOF): calcd for C$_{25}$H$_{40}$O$_4$SiNa$^+$ [M+Na$^+$]: 455.2588, found 455.2585.
Fully silylated metathesis product 31b

31b: \( R_f = 0.29 \) (silica gel, hexanes:EtOAc 8:1); \( [\alpha]_D^{35} = +13.7 \) (CDCl\( _3 \), \( c = 0.77 \)); IR (film) \( \nu_{\text{max}} \) 2954, 2929, 2857, 1672, 1628, 1469, 1462, 1378, 1361, 1254, 1071, 1005, 835, 809, 774, 737, 697 cm\(^{-1} \); \( ^1\)H NMR (600 MHz, CDCl\( _3 \)) \( \delta \) 7.35–7.25 (m, 5 H), 6.82 (dt, \( J = 16.2, 7.8 \) Hz, 1 H), 6.09 (d, \( J = 16.2 \) Hz, 1 H), 5.43 (t, \( J = 6.6 \) Hz, 1 H), 4.49 (s, 2 H), 4.37 (q, \( J = 6.6 \) Hz, 1 H), 4.01 (d, \( J = 6.6 \) Hz, 2 H), 3.91–3.79 (m, 3 H), 2.72 (dd, \( J = 15.6, 7.2 \) Hz, 1 H), 2.55 (dd, \( J = 15.6, 4.8 \) Hz, 1 H), 2.45–2.40 (m, 1 H), 2.32–2.28 (m, 1 H), 2.25 (dd, \( J = 13.2, 6.0 \) Hz, 1 H), 2.18 (dd, \( J = 13.2, 6.6 \) Hz, 1 H), 1.71–1.47 (m, 4 H), 1.67 (s, 3 H), 1.14 (d, \( J = 4.2 \) Hz, 3 H), 0.95 (t, \( J = 7.8 \) Hz, 9 H), 0.88 (s, 18 H), 0.84 (s, 9 H) 0.59 (q, \( J = 7.8 \) Hz, 6 H), 0.07 (s, 3 H), 0.06 (s, 6 H), 0.05 (s, 3 H), 0.03 (s, 3 H), –0.01 ppm (s, 3 H); \( ^{13} \)C NMR (150 MHz, CDCl\( _3 \)) \( \delta \) = 198.8, 144.2, 138.5, 136.7, 133.4, 128.3, 127.7, 127.5, 124.5, 72.1, 68.9, 67.7, 67.5, 66.5, 65.8, 48.5, 48.4, 46.9, 46.2, 40.5, 25.9, 25.8, 24.4, 18.1, 18.0, 18.0, 17.1, 7.0, 5.6, 5.4, –3.9, –4.3, –4.3, –4.5, –4.6, –4.8 ppm; HRMS (ESI-TOF): calcd for C\( _{48} \)H\( _{92} \)O\( _6 \)Si\( _4 \)Na\(^+ \) [M+Na\(^+ \)]: 899.5863, found 899.5852.

Mitsunobu model alcohol 47

To a 25 °C solution of TES-protected Mitsunobu model alcohol (50.0 mg, 0.097 mmol, 1.0 equiv) in EtOH (1.0 mL) was added PPTS (2.4 mg, 0.0097 mmol, 0.1 equiv) and the reaction mixture was stirred for 1 h. The reaction mixture was then quenched with H\( _2 \)O (3 mL) and the resulting biphasic mixture was extracted with EtOAc (3 × 5 mL), then washed with H\( _2 \)O (5 mL) and brine (5 mL), then dried (MgSO\( _4 \)), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 20:1)
yielded Mitsunobu model alcohol 47 (32.0 mg, 0.080 mmol, 82% yield) as a colorless oil. 47: 

\[ R_f = 0.31 \text{ (silica gel, hexanes:EtOAc 8:1); } [\alpha]_D^{35} = +2.0 \text{ (CDCl}_3, c = 0.48); \] 

IR (film) \( \nu_{\text{max}} \) 3529, 2946, 2930, 2857, 1472, 1378, 1362, 1255, 1076, 1004, 911, 836, 801, 775 cm\(^{-1}\); \( ^1\)H NMR (600 MHz, CDCl\(_3\)): \( \delta = 5.80 \text{ (ddt, } J = 15.8, 10.8, 7.2 \text{ Hz, 1 H}), 5.05 \text{ (d, } J = 15.8 \text{ Hz, 1 H}), 5.05 \text{ (d, } J = 10.8 \text{ Hz, 1 H}), 4.06-4.00 \text{ (m, 1 H), 3.96-3.85 (m, 2 H), 3.58 (s, 1 H), 2.33-2.19 (m, 2 H), 1.64-1.49 (m, 4 H), 1.17 (d, } J = 6.0 \text{ Hz, 3 H), 0.89 (s, 18 H), 0.09 ppm (s, 12 H); }^{13}\text{C NMR (150 MHz, CDCl}_{3}\): \( \delta = 134.6, 117.2, 71.0, 68.8, 68.6, 46.4, 43.6, 42.1, 25.8, 24.2, 18.0, 17.9, -4.0, -4.1, -4.6, -4.8 \text{ ppm}; \] 

HRMS (ESI-TOF): calcd for \( \text{C}_{21}\text{H}_{47}\text{O}_{3}\text{Si}_{2}^{+} [\text{M+H}^+] \): 403.3058, found 403.3060.

**Model Mitsunobu coupled product 51**

To a 25 °C solution of Mitsunobu model alcohol 47 (6.0 mg, 0.015 mmol, 1.0 equiv) in THF (0.25 mL) was added DEAD (16.3 \( \mu\)L, 0.090 mmol, 6.0 equiv), followed by slow addition of PPh\(_3\) (23.4 mg, 0.090 mmol, 6.0 equiv), and the corresponding Mitsunobu TMS-carboxylic acid coupling partner (50, 27.2 mg, 0.090 mmol, 6.0 equiv). The reaction mixture was stirred at 25 °C for 1 h, then concentrated and purified by flash column chromatography (silica gel, hexanes:EtOAc 20:1) to yield model Mitsunobu coupled product 51 (8.3 mg, 0.012 mmol, 81% yield) as a colorless oil. 51: 

\[ R_f = 0.29 \text{ (silica gel, hexanes:EtOAc 8:1); } [\alpha]_D^{35} = -1.5 \text{ (CDCl}_3, c = 0.53); \] 

IR (film) \( \nu_{\text{max}} \) 2956, 2929, 2857, 1776, 1725, 1580, 1463, 1365, 1249, 1196, 1112, 1062, 1000, 863, 836, 775 cm\(^{-1}\); \( ^1\)H NMR (600 MHz, CDCl\(_3\)): \( \delta = 7.47 \text{ (d, } J = 7.8 \text{ Hz, 1 H}), 7.38 \text{ (dd, } J = 8.4, 7.8 \text{ Hz, 1 H}), 7.00 \text{ (d, } J = 8.4 \text{ Hz, 1 H}), 6.79 \text{ (d, } J = 15.6 \text{ Hz, 1 H}), 6.72 \text{ (dd, } J = 15.6, 9.6 \text{ Hz, 1 H}), 6.62 \text{ (dd, } J = 18.0, 9.6 \text{ Hz, 1 H}), 6.05 \text{ (d, } J = 18.0 \text{ Hz, 1 H}), 5.82 \text{ (ddt, } J = 16.8, 10.2, 7.2 \text{ Hz, 1 H}), 5.15 \text{ (pent, } J = 6.6 \text{ Hz, 1 H}), 5.06 \text{ (d, } J = 16.8 \text{ Hz, 1 H}); \]
Acetylsalicylate Mitsunobu coupled product 49c

To a 25 °C solution of Mitsunobu model alcohol 47 (5.2 mg, 0.013 mmol, 1.0 equiv) in THF (0.22 mL) was added DEAD (14.1 μL, 0.078 mmol, 6.0 equiv), followed by slow addition of PPh₃ (20.3 mg, 0.078 mmol, 6.0 equiv) and acetylsalicylic acid (14.0 mg, 0.078 mmol, 6.0 equiv). The reaction mixture was stirred at 25 °C for 1 h, then concentrated and purified by flash column chromatography (silica gel, hexanes:EtOAc 20:1) to yield acetylsalicylate Mitsunobu coupled product 49c (5.3 mg, 0.0094 mmol, 72% yield) as a colorless oil.

49c: \( R_f = 0.26 \) (silica gel, hexanes:EtOAc 8:1); \([\alpha]_{D}^{35} = -2.3 \) (CDCl₃, c = 0.21); IR (film) \( \nu_{\text{max}} \) 2951, 2929, 2860, 1772, 1721, 1605, 1474, 1362, 1292, 1255, 1195, 1112, 1074, 1003, 910, 836, 776, 703 cm⁻¹; \( ^1 \)H NMR (600 MHz, CDCl₃): \( \delta = 7.96 \) (d, \( J = 7.8 \) Hz, 1 H), 7.54 (t, \( J = 7.8 \) Hz, 1 H), 7.30 (t, \( J = 7.8 \) Hz, 1 H), 7.09 (d, \( J = 7.8 \) Hz, 1 H), 5.82 (ddt, \( J = 16.2, 10.2, 7.2 \) Hz, 1 H), 5.18 (pent, \( J = 6.6 \) Hz, 1 H), 5.06 (d, \( J = 16.2 \) Hz, 1 H), 5.05 (d, \( J = 10.2 \) Hz, 1 H), 3.91 (hex, \( J = 6.0 \) Hz, 1 H), 3.85–3.81 (m, 1 H), 2.32 (s, 3 H), 2.30–2.21 (m, 2 H), 1.87–1.70 (m, 4 H), 1.16 (d, \( J = 6.0 \) Hz, 3 H), 0.88 (s, 18 H), 0.03 (s, 6 H), 0.02 ppm (s, 6 H); \( ^{13} \)C NMR (150 MHz, CDCl₃): \( \delta = 169.5, 163.8, 150.6, 134.5, 133.5, 131.5, 125.9, 124.1, 123.8, 117.3, 71.2, 68.6, 65.5, 45.2, \)
42.4, 42.2, 29.7, 25.9, 25.9, 24.4, 21.1, 18.0, 18.0, –4.3, –4.3, –4.6, –4.7 ppm; HRMS (ESI-TOF): calcd for C$_{30}$H$_{53}$O$_6$Si$_2^+$ [M+H$^+$]: 565.3375, found 565.3383.

References


References from Full paper