

Supporting Information:

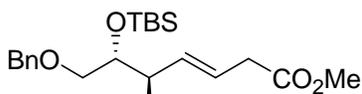
Total Synthesis of Bistramide A

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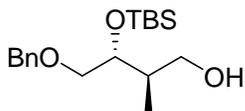
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General Information: All reactions were carried out in oven or flame-dried glassware under argon atmosphere. Triethylamine, diisopropylethylamine, and 2,6-lutidine were distilled and stored over potassium hydroxide. *N,N* Dimethylformamide and dimethylsulfoxide were distilled over calcium hydride and stored over 4 Å molecular sieves. *n*-Butyllithium was purchased from Aldrich and standardized by titration with menthol/1,10-phenanthroline. Oxalyl chloride was freshly distilled immediately before use. All other reagents were used as supplied. Dichloromethane, toluene, diethyl ether, benzene, tetrahydrofuran and acetonitrile were obtained from a dry solvent system (alumina) and used without further drying. Unless otherwise noted, reactions were magnetically stirred and monitored by thin layer chromatography with Macherey Nagel Polygram 0.20 mm silica gel 60 Å plates. Flash chromatography was performed on Sorbent Technologies 32-63 µm 60 Å silica gel. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise noted. ¹H and ¹³C NMR spectra were taken in CDCl₃ at 400 MHz and 75 MHz, respectively. Chemical shifts are reported in parts per million relative to CDCl₃ (¹H, δ 7.24; ¹³C, δ 77.0), benzene-d₆ (¹H, δ 7.15; ¹³C, δ 128.6). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant, integration. Diastereomeric ratios were determined by ¹H NMR (400 MHz) analysis of crude mixtures, operating at signal/noise ratio of 200:1. Infrared resonance spectra were recorded on a Nexus™ 670 FTIR spectrometer. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm and reported as follows: concentration (*c* in g/100mL) and solvent. High resolution mass-spectra were obtained on a Finnigan MAT-90 spectrometer at Boston University Mass Spectrometry Laboratory.

Experimental Procedures



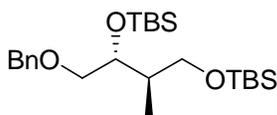
(5R,6R,E)-Methyl-7-(benzyloxy)-6-(tert-butylidimethylsilyloxy)-5-methylhept-3-enoate **10a:** To a solution of (5R,6R,E)-methyl 7-(benzyloxy)-6-hydroxy-5-methylhept-3-enoate¹ **10** (4.30 g, 15.4 mmol) in methylene chloride (150 mL) at 0 °C was added 2,6-lutidine (5.37 mL, 46.3 mmol) followed by *tert*-butyldimethylsilyl trifluoromethanesulfonate (5.32 mL, 23.2 mmol). The reaction mixture was stirred for 1 hour at 0 °C before it was quenched by addition of saturated solution of sodium bicarbonate. The aqueous layer was extracted with dichloromethane (3x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexanes/ethyl acetate: 95/5) to provide ether **10a** as a yellow oil (6.00 g, 98.9%). $[\alpha]_D^{20} + 14.7$ (*c* 1.4, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 7.29 (m, 5H), 5.50 (m, 2H), 4.46 (ABq, *J* = 14.0 Hz, 2H), 3.70 (dt, *J* = 3.4, 6.0 Hz, 1H), 3.65 (s, 3H), 3.34 (m, 2H), 3.01 (d, *J* = 5.6 Hz, 2H), 2.42 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); ¹³C NMR (CDCl₃, 75.0 MHz): δ 172.5, 138.4, 135.8, 128.3, 127.6, 127.5, 122.0, 74.8, 73.3, 73.2, 51.7, 40.3, 38.0, 25.9, 18.2, 17.2, -4.2, -4.9; IR (neat) ν_{\max} : 2955, 2929, 2857, 1743, 1253, 1112, 836, 777 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₂₂H₃₆O₄SiNa 415.2281, found 415.2267.



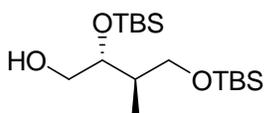
(2R,3R)-4-(Benzyloxy)-3-(tert-butylidimethylsilyloxy)-2-methylbutan-1-ol **10b:** A solution of **10a** (5.80 g, 14.8 mmol), Sudan Red, and two drops of pyridine in methanol (150 mL) was cooled to -78 °C. Ozone was bubbled into the reaction until the color of solution changed from red to clear. The reaction was quenched by addition of sodium tetrahydroborate (0.559 g, 14.8 mmol) and it was allowed to warm up to room temperature over 4 hours. Saturated solution of ammonium chloride was added and the aqueous layer was extracted with ethyl acetate (3x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexanes/ethyl acetate: 90/10) to provide alcohol **10b** as a clear oil (4.40 g, 91.8%). $[\alpha]_D^{20} + 11.4$ (*c* 1.0, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 7.30 (m, 5H), 4.50 (ABq, 14.0 Hz, 2H), 3.85 (m, 1H), 3.72 (dt, *J* = 4.2, 11.2 Hz, 1H), 3.51 (m, 3H), 2.78 (t, *J* = 4.8 Hz, 1H), 1.88 (m, 1H), 1.00 (d, *J* = 7.2 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ¹³C NMR (CDCl₃, 75.0 MHz): δ 138.1, 128.6, 128.0, 76.0, 73.7, 73.1, 65.1, 37.9, 26.1,

¹ Huang, H.; Panek, J. S. *Org. Lett.* **2004**, *6*, 4383.

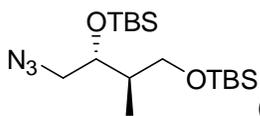
18.3, 14.6, -4.1, -4.8; IR (neat) ν_{\max} : 3426, 2956, 2929, 2857, 1252, 1101, 1029, 836, 777 cm^{-1} ; CIHRMS $[\text{M}+\text{Na}]^+$ m/z calculated for $\text{C}_{18}\text{H}_{32}\text{O}_3\text{SiNa}$ 347.2018, found 347.2014.



[(2R,3R)-2,4-Bis-(tert-butyl-dimethyl-silanyloxy)-3-methylbutoxymethyl]-benzene 11: To a solution of **10b** (4.40 g, 13.6 mmol) in *N,N*-dimethylformamide (90.0 mL) at 0 °C was added 1*H*-imidazole (3.88 g, 56.9 mmol) followed by *tert*-butyldimethylsilyl chloride (4.09 g, 27.1 mmol). Reaction was allowed to warm up to room temperature and was stirred for an additional 16 hours. Reaction was quenched by addition of water and the aqueous layer was extracted with ethyl acetate (3x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexanes/ethyl acetate: 98/2) to yield alcohol **11** as a yellow oil (5.90 g, 99.0%). $[\alpha]_{\text{D}}^{20} + 3.2$ (*c* 1.4, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 7.31 (m, 5H), 4.49 (s, 2H), 3.81 (m, 1H), 3.65 (dd, $J = 6.2, 10$ Hz, 1H), 3.46 (m, 3H), 1.86 (m, 1H), 0.86 (m, 21H), 0.03 (s, 6H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (CDCl_3 , 75.0 MHz): δ 138.6, 128.2, 127.6, 127.4, 73.5, 73.4, 73.3, 64.6, 39.9, 26.0, 25.7, 18.3, 18.2, 13.6, -4.2, -5.0, -5.4, -5.4; IR (neat) ν_{\max} : 2953, 2858, 1466, 1253, 1093, 837, 776 cm^{-1} ; CIHRMS $[\text{M}+\text{Na}]^+$ m/z calculated for $\text{C}_{24}\text{H}_{46}\text{O}_3\text{Si}_2\text{Na}$ 461.2883, found 461.2889.

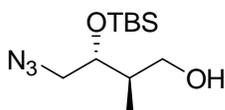


(2R,3R)-2,4-bis(*tert*-Butyldimethylsilyloxy)-3-methylbutan-1-ol 11a: To a degassed solution of **11** (3.00 g, 6.84 mmol) in ethyl acetate (140 mL) was added palladium on carbon (220 mg, 2.0 mmol, 10 wt%). The reaction was allowed to run under an atmosphere of hydrogen for 24 hours. Filtration over Celite[®] provided crude alcohol, which was purified by column chromatography over silica gel (hexanes/ethyl acetate: 95/5) to afford **11a** as a clear oil (2.00 g, 84.0%). $[\alpha]_{\text{D}}^{20} + 3.3$ (*c* 1.0, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz): δ 3.75 (q, $J = 5.2, 10$ Hz, 1H), 3.64 (A of ABX, $J = 6.6, 10$ Hz, 1H), 3.54 (m, 2H), 3.46 (B of ABX, $J = 4.4, 10$ Hz, 1H), 2.56 (dd, $J = 5.6, 7.6$ Hz, 1H), 1.92 (m, 1H), 0.88 (m, 21H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H); ^{13}C NMR (CDCl_3 , 75.0 MHz): δ 74.1, 64.5, 64.1, 38.9, 25.9, 25.8, 18.2, 18.1, 13.0, -4.4, -4.8, -5.5, -5.6; IR (neat) ν_{\max} : 3446, 2953, 2860, 1468, 1254, 1088, 838, 777 cm^{-1} ; CIHRMS $[\text{M}+\text{Na}]^+$ m/z calculated for $\text{C}_{17}\text{H}_{40}\text{O}_3\text{Si}_2\text{Na}$ 371.2414, found 371.2401.



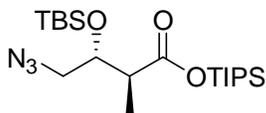
(2R,3R)-1-Azido-2,4-bis-(tert-butyl-dimethyl-silanyloxy)-3-methyl-butane 11b: To a solution of **11a** (0.160 g, 0.459 mmol) in benzene (9.20 mL) at room temperature was added sequentially triphenylphosphine (0.241 g, 0.918 mmol),

diisopropyl azodicarboxylate (0.181 mL, 0.918 mmol), and diphenylphosphonic azide (0.198 mL, 0.918 mmol). Reaction stirred for 4 hours before the volatiles were concentrated *in vacuo*. The residue was purified by column chromatography over silica gel (hexanes/ethyl acetate: 98/2) to afford azide **11b** as a yellow oil (0.160 g, 93.3%). $[\alpha]_D^{20} + 8.4$ (*c* 1.2, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 3.81 (m, 1H), 3.52 (m, 2H), 3.37 (A of ABX, *J* = 3.4, 12.4 Hz, 1H), 3.17 (B of ABX, *J* = 6.4, 12.4 Hz, 1H), 1.89 (m, 1H), 0.90 (s, 9H), 0.87 (s, 9H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.10 (s, 3H), 0.06 (s, 3H), 0.02 (s, 6H); ¹³C NMR (CDCl₃, 75.0 MHz): δ 72.9, 64.6, 54.6, 40.0, 25.9, 25.8, 18.2, 18.0, 12.5, -4.4, -4.9, -5.4, -5.5; IR (neat) ν_{\max} : 2954, 2860, 2100, 1467, 1256, 1096, 838, 776 cm⁻¹; CIHRMS [M+H]⁺ *m/z* calculated for C₁₇H₄₁N₃O₂Si₂ 374.2659, found 374.2660.



(2R,3R)-4-Azido-3-(tert-butyldimethylsilyloxy)-2-methylbutan-1-ol

12: To a solution of **11b** (0.510 g, 1.36 mmol) in a mixture of methylene chloride (13.6 mL) and methanol (13.6 mL) at 0 °C was added 10-camphorsulfonic acid (0.095 g, 0.41 mmol). Reaction was allowed to stir at 0 °C for 2 hours before it was quenched with saturated solution of sodium bicarbonate. The aqueous layer was extracted with dichloromethane (3x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexanes/ethyl acetate: 95/5) to afford alcohol **12** as a clear oil (0.320 g, 90.4%). $[\alpha]_D^{20} + 11.7^\circ$ (*c* 1.6, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): 3.76 (q, *J* = 5.4, 10.2, Hz, 1H), 3.63 (m, 2H), 3.42 (A of ABX, *J* = 4.4, 12.8 Hz, 1H), 3.27 (B of ABX, *J* = 5.4, 12.8 Hz, 1H), 2.07 (t, *J* = 4.8 Hz, 1H), 1.94 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ¹³C NMR (CDCl₃, 75.0 MHz): δ 74.8, 64.7, 54.9, 38.4, 25.7, 17.9, 13.8, -4.4, -4.9; IR (neat) ν_{\max} : 3378, 2943, 2877, 2105, 1461, 1267, 1092, 834, 784 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₁₁H₂₅N₃O₂NaSi 282.1614, found 282.1609.



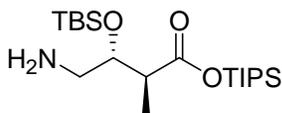
(2S,3R)-4-Azido-3-(tert-butyl-dimethyl-silanyloxy)-2-methyl-

(triisopropylsilyl)-butyric acid 12a: To a solution of **11b** (480 mg, 1.85 mmol) in acetonitrile (10.0 mL) and aqueous K₂HPO₄/KH₂PO₄ pH 7.2 buffer² (7.20 mL) was added TEMPO (21 mg, 0.13 mmol). Reaction mixture was allowed to warm to 35 °C. A solution of sodium chlorite (440 mg, 3.86 mmol, in 1.93 ml water) and sodium hypochlorite (51 uL, 5.25% NaOCl in 1 ml water) was added simultaneously over 1 hour. Reaction stirred at 35 °C until TLC showed no starting material left. Mixture was cooled to room temperature and diluted with water (15ml). The pH was adjusted to 9 with 2.00 N NaOH and the reaction was quenched by pouring into 0 °C Na₂SO₃ solution

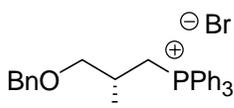
² Commercially available from VWR, catalog number 34170-115.

(590mg/10ml). Mixture was stirred for 1/2 hour at room temperature and extracted once with diethyl ether. The aqueous layer was acidified with 4M HCl to pH 3 and extracted with diethyl ether (2x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The crude acid was used directly in the next step (460 mg, 1.68 mmol, 91%).³

To a solution of (2*S*,3*R*)-4-azido-3-(*tert*-butyl-dimethyl-silyloxy)-2-methylbutyric acid (460 mg, 1.68 mmol) in *N,N*-dimethylformamide (9mL) and tetrahydrofuran (9.0 mL) at 0 °C was added triethylamine (0.352 mL, 2.52 mmol) followed by triisopropylsilyl chloride (436 μ L, 1.85 mmol) dropwise. Reaction stirred for 15 minutes at 0 °C and was diluted with diethyl ether and water. The aqueous layer was extracted with diethyl ether (3x). The combined organic layers were washed with sodium bicarbonate and brine. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexanes/ethyl acetate: 99/1) to afford **12a** as a clear oil (670 mg, 92.7%).⁴ $[\alpha]_D^{20} + 23.9$ (*c* 0.33, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 4.14 (apt. dt, *J* = 7.2, 4.0 Hz, 1H), 3.30 (dd, *J* = 12.4, 4.0 Hz, 1H), 3.27 (dd, *J* = 12.4, 7.2 Hz, 1H), 2.73 (m, 1H), 1.29 (sept., *J* = 7.2 Hz, 3H), 1.15 (d, *J* = 7.2 Hz, 3H), 1.06 (s, 9H), 1.02 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); δ^{13} C NMR (CDCl₃, 75.0 MHz): δ 173.2, 72.5, 54.2, 45.5, 25.7, 18.0, 17.8, 11.9, 11.3, -4.74, -4.94; IR (neat) ν_{\max} : 2945, 2873, 2102, 1717, 1463, 1264, 1197 cm⁻¹; HRMS (CI, NH₃) *m/z* calculated for C₂₀H₄₄N₃O₃Si₂ [M+H]⁺ 430.2921, found 430.2917.



(2*S*,3*R*)-4-Amino-3-(*tert*-butyl-dimethyl-silyloxy)-2-methyl-(triisopropylsilyl)-butyric acid **3**: To a solution of **12a** (0.043 g, 0.10 mmol) in tetrahydrofuran (4.00 mL) was added palladium on carbon (10% wt., 0.008 g) and the mixture was stirred under an atmosphere of hydrogen for approximately 2 hours. The heterogeneous solution was filtered through Celite[®] and concentrated to obtain a clear oil. The resulting oil was coupled with pyran **2** without further purification.



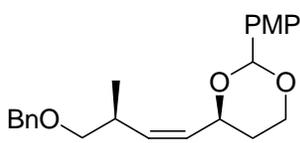
14: A flask was charged with ((*R*)-3-Bromo-2-methylpropoxymethyl)-benzene⁵ (31.50 g,

³ Modified from previously reported: Crimmins, M T.; DeBaillie, A. C. *J. Am. Chem. Soc.* **2006**, *128*, 4936

⁴ Procedure slightly modified from previously reported: Wipf, P.; Uto Y.; Yoshimura, S. *Chem. Eur. J.* **2002**, *8*, 1670.

⁵ Boons, G.-J.; Clase, J. A.; Lennon, I. C.; Ley, S. V.; Staunton, J. *Tetrahedron* **1995**, *51*, 5417.

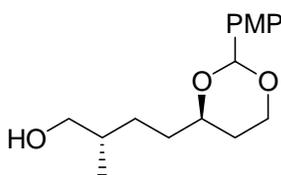
129.6 mmol) and triphenylphosphine (37.4 g, 142.0 mmol) under an atmosphere of argon was stirred and heated to 90 °C for 48 hours. During this time the solution forms a thick precipitate. The reaction mixture is cooled to 60 °C and methylene chloride (~75 mL) is added till the solid is completely dissolved. At this point, the reaction is allowed to cool to room temperature and diethyl ether is slowly added (~300 mL). The resulting precipitate is filtered and rinsed with copious amounts of diethyl ether under a stream of nitrogen. The resulting solid is dried under vacuum to obtain a white solid (62.1 g, 95 %). The spectral data of compound **14** was in agreement with those previously reported.⁶ $[\alpha]_D^{20} +27.3$ (c 0.42, CHCl₃).



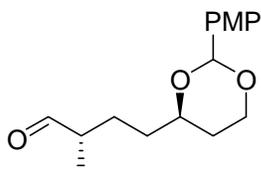
(S)-4-((Z)-(S)-4-benzyloxy-3-methyl-but-1-enyl)-2-(4-methoxyphenyl)-[1,3]dioxane 15: A solution of phosphonium salt **14** (57 g, 110 mmol) in tetrahydrofuran (400 mL) was cooled to 0 °C and *n*-butyllithium (2.5M in hexanes, 45 mL, 110 mmol) was added over a 30 minute period. Freshly prepared aldehyde **13**⁷ (16.4 g, 62.7 mmol, ~85% purity) was dissolved in tetrahydrofuran (700 mL) and added over 30 minutes. The reaction mixture was stirred for an additional 30 minutes, quenched with wet diethyl ether and diluted with water. The aqueous layer was extracted with diethyl ether (3x). The combined organic layers were dried over magnesium sulfate, filtered and concentrated *in vacuo* to obtain an orange oil. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 98/2) to afford **15** as a light yellow oil (16.24 g, 70% 10:1 (*Z:E*)). $[\alpha]_D^{20} +85.4$ (c 0.33, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.37 (d, J = 8.4 Hz, 2H), 7.34-7.25 (m, 5H), 6.83 (d, J = 8.8 Hz, 2H), 5.49 (obsc. dd, J = 11.2, 8.4 Hz, 1H) 5.48 (s, 1H), 5.30 (t, J = 10.8 Hz, 1H), 4.62 (t, J = 8.4 Hz, 1H), 4.47 (s, 2H), 4.14 (dd, J = 11.5, 4.0 Hz, 1H), 3.88 (td, J = 12.4, 2.8 Hz, 1H), 3.75 (s, 3H), 3.26 (ddd, J = 29.2, 8.8, 6 Hz, 2H), 2.84 (m, 1H), 1.85 (ddd, J = 24.8, 12.8, 4.8 Hz, 1H), 1.42 (d apt. q, J = 13.2, 1.2 Hz, 1H), 0.99 (d, J = 6.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 159.8, 138.4, 135.4, 131.2, 130.0, 128.3, 127.5, 127.3, 113.5, 100.98, 100.95, 75.1, 73.8, 73.0, 66.8, 55.2, 33.4, 31.5, 17.6; IR (neat) ν_{\max} 2959, 2852, 1614, 1516, 1457, 1379, 1247, 1103, 1031 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₂₃H₂₈NaO₄: 391.1885, found 391.1865.

⁶ Gaeta, F. C. A.; Lehman de Gaeta, L. S.; Kogan, T. P.; Or, Y. S.; Foster, C.; Czarniecki M. *J. Med. Chem.* **1990**, *33*, 964.

⁷ Blakemore, P. R.; Kim, S. K.; Schulze, V. K.; White, J. D.; Yokochi, A. F. T. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1831.



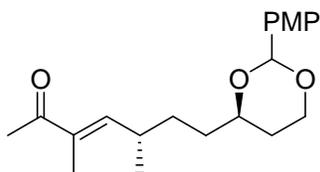
(S)-4-[(R)-2-(4-Methoxy-phenyl)-[1,3]dioxan-4-yl]-2-methylbutan-1-ol 15a: Benzyl ether **15** (6.00 g, 16.3 mmol) was dissolved in ethanol (30 mL) at which time 5 pipettes of Raney nickel (*ca.* 3 g) in an ethanol slurry were added.⁸ The reaction mixture was stirred at room temperature for 5 days under a hydrogen atmosphere. The suspension was filtered through Celite® with ethyl acetate and concentrated *in vacuo* to obtain a colorless oil. The residue was purified by chromatography over silica gel (hexane/ethyl acetate: 90/10 to 70/30) to afford **15a** as a colorless oil (3.55 g, 78%). $[\alpha]_D^{20} +9.8$ (*c* 1.60, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.38 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.43 (s, 1H), 4.22 (ddd, *J* = 11.6, 5.2, 1.2 Hz, 1H), 3.91 (td, *J* = 11.6, 2.8 Hz, 1H), 3.78 (obsc. m, 1H), 3.77 (s, 3H), 1.76 (m, 1H), 1.61 (m, 4H), 1.49 (d apt. q, *J* = 11.6, 1.6 Hz, 1H), 1.37 (br. s, 1H), 1.85 (m, 1H), 1.10 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 159.8, 131.4, 127.3, 113.6, 101.1, 77.5, 68.1, 67.0, 55.3, 35.7, 33.4, 31.3, 28.4, 16.6; IR (neat) ν_{\max} 3425, 2927, 2851, 2745, 1614, 1516, 1368, 1247, 1107, 1032 cm⁻¹; CIHRMS $[M+Na]^+$ *m/z* calculated for C₁₆H₂₄NaO₄: 303.1572, found 303.1557.



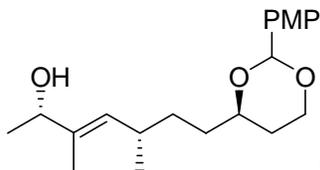
(S)-4-[(R)-2-(4-Methoxy-phenyl)-[1,3]dioxan-4-yl]-2-methylbutyraldehyde 15b: To oxalyl chloride (0.996 mL, 11.8 mmol) in methylene chloride (63 mL) at -78 °C was added dimethyl sulfoxide (1.67 mL, 23.5 mmol) over 15 minutes. The reaction stirred for an additional 15 minutes before **15a** (1.10 g, 3.92 mmol) dissolved in methylene chloride (35 mL) was added *via* a cannula. The mixture stirred for 30 minutes before triethylamine (4.92 mL, 35.3 mmol) was added dropwise. The reaction was allowed to warm up to room temperature for 30 minutes and water (75 mL) was added and the aqueous phase was extracted with methylene chloride. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated. The oil was taken up in hexanes and filtered through a small plug of Celite®. The resulting oil obtained after concentration was used without further purification. $[\alpha]_D^{20} +28.6$ (*c* 0.80, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 9.60 (d, *J* = 1.6 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 5.43 (s, 1H), 4.22 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.91 (td, *J* = 12, 2 Hz, 1H), 3.81 (obsc. m, 1H), 3.78 (s, 3H), 2.36 (m,

⁸ Evans, D. A.; Trenkle, W. C.; Zhang, J.; Burch, J. D. *Org. Lett.* **2005**, *7*, 3335.

1H), 1.93 (m, 1H), 1.77(m, 1H), 1.60 (m, 2H), 1.46 (m, 2H), 1.10 (d, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 204.9, 159.9, 131.3, 127.3, 113.6, 101.1, 76.8, 66.9, 55.3, 46.1, 33.2, 31.2, 25.8, 13.3; IR (neat) ν_{max} 2927, 2851, 2745, 1723, 1247, 1108, 828 cm⁻¹; CIHRMS [M+H]⁺ m/z calculated for C₁₆H₂₃O₄: 279.1596, found 279.1606.



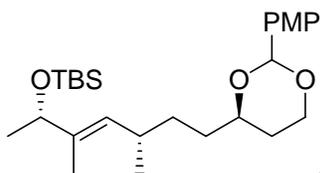
(E)-(S)-7-[(R)-2-(4-Methoxy-phenyl)-[1,3]dioxan-4-yl]-3,5-dimethyl-hept-3-en-2-one 16: To a solution of Ba(OH)₂ (3.08 g, 18.0 mmol) in tetrahydrofuran (14 mL) was added MeCOCH(Me)P(O)(OEt)₂⁹ (1.50 g, 7.18 mmol) at room temperature. Aldehyde **15b** (ca. 1.00 g, 3.59 mmol) dissolved in a mixture of tetrahydrofuran (14 mL) and water (0.85 mL) was added dropwise to the above solution. After stirring for 30 minutes, the reaction was diluted with methylene chloride and washed with a saturated solution of sodium bicarbonate. The aqueous layer was extracted with methylene chloride (3x). The combined organics were washed with brine, dried over magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 90/10) to afford a colorless oil (0.750 g, 63% over 2 steps). [α]_D²⁰ +12.4 (c 0.58, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.38 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.35 (dd, J = 10, 1.2 Hz, 1H), 5.42 (s, 1H), 4.22 (dd, J = 10.4, 4.8 Hz, 1H), 3.91 (td, J = 12.4, 2.8 Hz, 1H), 3.77 (s, 3H), 3.75 (obsc. m, 1H), 2.56 (m, 1H), 2.28 (s, 3H), 1.81-1.68 (qd, J = 12.8, 4.8 Hz, 1H), 1.74 (d, J = 1.2 Hz, 3H), 1.58 (m, 1H), 1.52-1.44 (m, 4H), 1.03 (d, J = 6.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 200.1, 159.8, 148.9, 136.3, 131.3, 127.2, 113.5, 101.0, 76.98, 66.9, 55.2, 33.8, 33.5, 32.1, 31.2, 25.4, 20.0, 11.3; IR (neat) ν_{max} 2928, 1851, 1665, 1616, 1367, 1248 cm⁻¹; CIHRMS [M+Na]⁺ m/z calculated for C₂₀H₂₈NaO₄: 355.1885, found 355.1880.



(E)-(2S,5S)-7-[(R)-2-(4-Methoxy-phenyl)-[1,3]dioxan-4-yl]-3,5-dimethyl-hept-3-en-2-ol 16a: To a solution of **16** (0.500 g, 1.50 mmol) in toluene (25 mL) was added (*R*)-CBS reagent (1.0 M in toluene, 1.80 mL, 1.80 mmol) at -78 °C. Catecholborane in toluene (0.321 mL in 7.00 mL of toluene) was then added dropwise *via* syringe. The reaction was stirred for 12 hours at -78 °C before it was quenched with

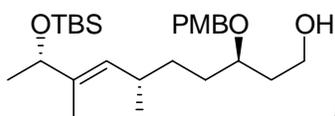
⁹ Diethyl(2-oxopropyl) phosphate and iodomethane was used in place of dimethyl(2-oxopropyl) phosphonate iodomethane-D₃ to give comparable yields: Boons, G.-J.; Clase, J. A.; Lennon, I. C.; Ley, S. V.; Staunton, J. *Tetrahedron* **1995**, *51*, 5417.

methanol (3.00 mL), allowed to warm to room temperature and stir for an additional hour. Ethyl acetate was added followed by a saturated solution of sodium bicarbonate (25 mL). The aqueous layer was extracted with ethyl acetate (3x). The combined organics were dried with magnesium sulfate, filtered and concentrated. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 80/20) to afford **16a** a crude colorless oil (0.441 g, 1.32 mmol, 88%). This impure material was used in the next step without further purification.



tert-Butyl- $\{$ (*E*)- $(1S,4S)$ -6- $\{$ (*R*)-2-(4-methoxy-phenyl)-

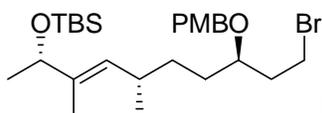
[1,3]dioxan-4-yl-1,2,4-trimethyl-hex-2-enyloxy $\}$ -dimethyl-silane **17**: To a solution of **16a** (0.500 g, 1.49 mmol) in methylene chloride (28 mL) at 0 °C was added 2,6-lutidine (0.277 ml, 2.39 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.446 mL, 1.94 mmol). Reaction was allowed to stir for 2 hours at 0 °C and was quenched by addition of saturated solution of sodium bicarbonate (28 mL). The aqueous layer was extracted with methylene chloride (3x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 98/2 to 95/5) to yield **17** as a yellow oil (0.579 g, 86%). $[\alpha]_D^{20} +13.2$ (*c* 0.37, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.39 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.42 (s, 1H), 5.50 (d, *J* = 10.9 Hz, 1H), 4.21 (dd, *J* = 11.6, 3.6 Hz, 1H), 4.11 (q, *J* = 6.0 Hz, 1H), 3.90 (td, *J* = 12.4, 2.4 Hz, 1H), 3.78 (s, 3H), 3.72 (m, 1H), 2.32 (m, 1H), 1.74 (m, 1H), 1.58 (m, 2H), 1.54 (d, *J* = 1.6 Hz, 3H), 1.52-1.31 (m, 6H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 3H), -0.02 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 159.8, 137.6, 131.5, 130.1, 127.3, 113.5, 101.0, 77.3, 74.1, 67.0, 55.2, 33.9, 32.7, 31.7, 31.3, 25.9, 23.3, 20.9, 18.3, 11.4, -4.75, -4.99; IR (neat) ν_{max} 2953, 2855, 1615, 1516, 1462, 1367, 1248 cm⁻¹; CIHRMS $[M+Na]^+$ *m/z* calculated for C₂₆H₄₄NaO₄Si: 471.2907, found 471.2893.



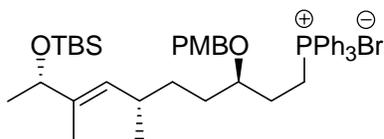
tert-Butyl- $\{$ (*E*)- $(1S,4S)$ -6- $\{$ (*R*)-2-(4-methoxy-phenyl)-

[1,3]dioxan-4-yl-1,2,4-trimethyl-hex-2-enyloxy $\}$ -dimethyl-silane **17a**: A solution of TBS ether **17** (0.500 g, 1.11 mmol) in methylene chloride (50 mL) was cooled to 0 °C. Diisobutylaluminum hydride (1M in hexanes 6.68 mL, 6.68 mmol) was added and stirred for 30 minutes at 0 °C. The reaction mixture was quenched with a saturated solution of Rochelle's salt (50 mL) and the biphasic mixture stirred for 30 minutes at room temperature. The aqueous layer was then extracted with methylene chloride (3x). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 90/10) to provide **17a** as a yellow oil (0.491 g, 98%).

$[\alpha]_D^{20}$ -12.9 (*c* 0.27, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.23 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.04 (d, *J* = 9.6 Hz, 1H), 4.49 (d, *J*_{ab} = 11.2 Hz, 1H), 4.37 (d, *J*_{ab} = 11.2 Hz, 1H), 4.12 (q, *J* = 6 Hz, 1H), 3.78 (s, 3H), 3.75 (m, 1H), 3.70 (m, 1H), 3.56 (m, 1H), 2.40 (t, *J* = 5.6 Hz, 1H), 2.28 (sept., *J* = 6.4 Hz, 1H), 1.71 (m, 1H), 1.58 (m, 1H), 1.54 (s, 3H), 1.42 (m, 1H), 1.32 (m, 2H), 1.20 (obsc. m, 1H), 1.17 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 3H), -0.01 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 137.8, 130.5, 130.0, 129.4, 113.8, 78.3, 74.0, 70.4, 60.9, 55.2, 35.8, 32.8, 31.9, 31.2, 25.8, 23.4, 21.0, 18.3, 11.5, -4.73, -4.99; IR (neat) *v*_{max}: 3425, 2933, 2859, 1612, 1249, 1080 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₂₆H₄₆NaO₄Si: 473.3036, found 473.3095.



[(*E*)-(1*S*,4*S*,7*R*)-9-Bromo-7-(4-methoxy-benzyloxy)-1,2,4-trimethyl-non-2-enyloxy]-tert-butyl-dimethyl-silane **17b:** Alcohol **17a** (0.421 g, 0.934 mmol) in methylene chloride (40 mL) was added into a round bottom flask under an atmosphere of argon at room temperature. Triphenylphosphine (0.735 g, 2.80 mmol) was added followed by carbon tetrabromide (0.697 g, 2.10 mmol). The reaction was allowed to stir at room temperature for 1 hour before water was added. The aqueous phase was extracted with methylene chloride (3x) and the combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5) to afford **17b** as a colorless oil (0.463 g, 97%). $[\alpha]_D^{20}$ -27.2 (*c* 0.43, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.25-7.23 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.03 (d, *J* = 9.6 Hz, 1H), 4.47 (d, *J*_{ab} = 11.2 Hz, 1H), 4.37 (d, *J*_{ab} = 11.2 Hz, 1H), 4.12 (q, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.53 (m, 1H), 3.47 (m, 2H), 2.27 (m, 1H), 2.03 (m, 1H), 1.95 (m, 1H), 1.54 (d, *J* = 1.2 Hz, 3H), 1.50 (m, 1H), 1.45-1.30 (m, 2H), 1.19 (m, 1H), 1.16 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 3H), -0.01 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 137.9, 130.7, 130.0, 129.4, 113.8, 76.58, 74.1, 71.0, 55.3, 37.7, 32.7, 31.8, 31.4, 30.6, 25.9, 23.4, 21.0, 18.3, 11.5, -4.72, -4.96; IR (neat) *v*_{max}: 2953, 2933, 2858, 1612, 1513, 1461, 1249, 1081 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₂₆H₄₅BrNaO₃Si: 535.2219, found 535.2234.



[(*E*)-(3*R*,6*S*,9*S*)-9-(tert-Butyl-dimethyl-silyloxy)-3-(4-methoxy-benzyloxy)-6,8-dimethyl-dec-7-enyl]-triphenyl-phosphonium bromide **8:** To a solution of bromide **17b** (0.463 g, 0.901 mmol) in acetonitrile (7.5 mL) in a 15 ml sealed tube, was added *N,N*-diisopropylethylamine (0.471 mL, 2.70 mmol) and triphenylphosphine (2.13 g, 8.11 mmol). The reaction was heated at 85 °C for 36 hours after which the reaction was concentrated to obtain an oil. The residue was purified by

column chromatography over silica gel (chloroform/methanol: 98/2 to 95/5) to afford **8** as a colorless oil (0.671, 96%). $[\alpha]_D^{20}$ -3.5 (*c* 0.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.80-7.72 (m, 10H), 7.65-7.61 (m, 5H), 7.29 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.97 (d, *J* = 9.6 Hz, 1H), 4.56 (d, *J*_{ab} = 11.2 Hz, 1H), 4.37 (d, *J*_{ab} = 11.2 Hz, 1H), 4.37 (m, 1H), 4.07 (q, *J* = 6.4 Hz, 1H), 3.92 (m, 1H), 3.77 (s, 3H), 3.37 (q, *J* = 13.2 Hz, 1H), 2.20 (sept., *J* = 6.8 Hz, 1H), 1.82 (m, 1H), 1.59 (obsc. m, 1H), 1.49 (d, *J* = 1.6 Hz, 3H), 1.41 (m, 2H), 1.27 (m, 1H), 1.14 (m, 1H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.4 Hz, 3H), 0.83 (s, 9H), -0.02 (s, 3H), -0.06 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ IR (neat) *v*_{max}: 2931, 2858, 1611, 1512, 1439, 1249, 1109, 1080 cm⁻¹; CIHRMS [M]⁺ *m/z* calculated for C₄₄H₆₀PO₃Si: 695.4044, found 695.4082.



A solution of 4-benzyloxybutyraldehyde **18**¹⁰ (2.00 g, 11.2 mmol) and organosilane **9**¹¹ (3.00 g, 8.56 mmol) in methylene chloride (200 mL) was cooled to -50 °C. Trimethylsilyl trifluoromethanesulfonate (1.55 mL, 8.56 mmol) was added and the solution was allowed to stir overnight at -50 °C. A saturated solution of sodium bicarbonate was added and the aqueous phase was extracted with methylene chloride (3x). The combined organics were dried over magnesium sulfate, filtered and concentrated *in vacuo* to give an oil. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 90/10) to afford **19** as a colorless oil (2.53 g, 97%). $[\alpha]_D^{20}$ +123.6 (*c* 0.94, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31 (m, 4H), 7.25 (m, 1H), 5.73 (apt. qt, *J* = 10, 2.4 Hz, 2H), 4.69 (m, 1H), 4.49 (d, *J* = 2.0 Hz, 2H), 3.75 (s, 3H), 3.50 (m, 2H), 3.11 (td, *J* = 8.0, 3.2 Hz, 1H), 2.19 (m, 1H), 1.98-1.88 (m, 1H), 1.87-1.79 (m, 1H), 1.73-1.66 (m, 2H), 1.60-1.52 (m, 1H), 0.91 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 138.4, 133.8, 128.1, 127.4, 127.2, 123.1, 80.0, 74.6, 72.6, 70.0, 52.0, 33.7, 29.3, 25.6, 17.0; IR (neat) *v*_{max}: 2955, 2856, 1763, 1736, 1111 cm⁻¹; CIHRMS [M+H]⁺ *m/z* calculated for C₁₈H₂₅O₄: 305.1753, found 305.1759.

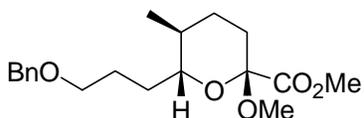


To a solution of **19** (2.53 g, 8.31 mmol) in tetrahydrofuran (39 mL) was added tetra-*n*-butylammonium hydroxide (1M in methanol, 24.9 mL) at room temperature. After stirring for 1 hour, water was added and the aqueous

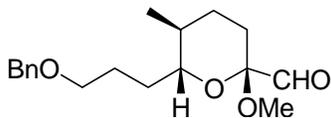
¹⁰ Sharma, G. V. M.; Cherukupalli, G. R. *Tetrahedron: Asymmetry* **2006**, *17*, 1081.

¹¹ For the preparation of α -substituted (*E*)-crotylsilanes, see: (a) Sparks, M. A.; Panek, J. S. *J. Org. Chem.* **1991**, *56*, 3431. (b) Panek, J. S.; Yang, M.; Solomon, J. S. *J. Org. Chem.* **1993**, *58*, 1003.

layer was extracted with diethyl ether (3x). The combined organics were dried over magnesium sulfate, filtered and concentrated *in vacuo* to give an oil. The residue was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 90/10) to provide **20** as a colorless oil (2.43 g, 96%). $[\alpha]_D^{20} +50.8$ (*c* 0.88, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31 (m, 4H), 7.25 (m, 1H), 5.99 (apt. dd, *J* = 4.8, 3.6 Hz, 1H), 4.49 (d, *J* = 1.2 Hz, 2H), 3.75 (s, 3H), 3.61 (td, *J* = 8.0, 3.2 Hz, 1H), 3.51 (m, 2H), 2.22 (dt, *J* = 18.4, 5.2 Hz, 1H), 1.93-1.57 (m, 7H), 0.95 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 163.3, 143.0, 138.4, 128.1, 127.4, 127.3, 110.1, 80.5, 72.6, 69.9, 51.7, 29.7, 28.6, 28.3, 25.1, 17.5; IR (neat) ν_{\max} : 2952, 2926, 2855, 1734, 1651, 1248 1108 cm⁻¹; CIHRMS [M+H]⁺ *m/z* calculated for C₁₈H₂₅O₄: 305.1729, found 305.1727.

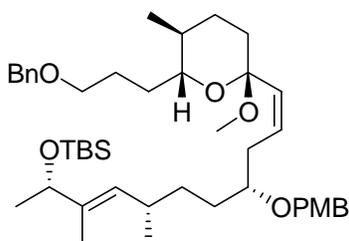


(2R,5S,6R)-6-(3-Benzyloxy-propyl)-2-methoxy-5-methyl-tetrahydro-pyran-2-carboxylic acid methyl ester 20a: To a solution of **20** (1.50 g, 4.93 mmol) in methanol (15 mL) was added 10-camphorsulfonic acid (1.14 g, 4.93 mmol). The solution was heated to 60 °C for 5 days and upon completion, the reaction was concentrated *in vacuo* to provide an oil. The residue was purified by careful (slow) column chromatography over silica gel (hexane/ethyl acetate: 99/1 to 90/10) to afford **20a** as a colorless oil (1.66 g, 81% [95% BORSM, 0.209 g of starting material was isolated from the reaction]). $[\alpha]_D^{20} +102.7$ (*c* 0.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31 (m, 4H), 7.25 (m, 1H), 4.50 (s, 2H), 3.75 (s, 3H), 3.49 (m, 2H), 3.24 (td, *J* = 9.6, 2.4 Hz, 1H), 3.19 (s, 3H), 2.03-1.88 (m, 2H), 1.82-1.74 (m, 1H), 1.70-1.60 (m, 2H), 1.58-1.55, (m, 2H), 1.51-1.38 (m, 2H), 0.83 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 138.7, 128.3, 127.7, 127.5, 98.3, 76.48, 72.9, 70.5, 52.3, 50.6, 34.0, 32.6, 29.2, 27.5, 25.8, 17.7; IR (neat) ν_{\max} : 2953, 2931, 2859, 1747, 1454, 1275, 1068, 1049 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₁₉H₂₈NaO₅: 359.1834, found 359.1822.



(2R,5S,6R)-6-(3-Benzyloxy-propyl)-2-methoxy-5-methyl-tetrahydro-pyran-2-carbaldehyde 7: To a solution of ester **20a** (0.220 g, 0.654 mmol) in diethyl ether (10 mL) under an atmosphere of argon at -78 °C was added diisobutylaluminum hydride (1.0 M in hexane, 2.62 mL) dropwise over 30 minutes. The reaction mixture was stirred for an additional 4 hours at -78 °C. Methanol (0.106 mL, 2.62 mmol) was added followed by a saturated solution of Rochelle's salt (*ca.* 15 mL). The biphasic solution was stirred for an additional 1 hour at room temperature. The aqueous phase was extracted with diethyl ether (3x) and the combined organics were dried over magnesium sulfate. After filtration the solution was concentrated *in vacuo* to provide an oil. The residue was purified by column chromatography over silica gel

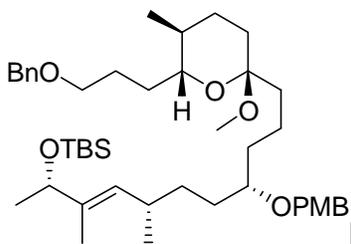
(hexane/ethyl acetate: 95/5 to 80/20) to afford **7** as a colorless oil (0.189 g, 94%). $[\alpha]_D^{20} +46.4$ (*c* 0.45, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 9.40 (s, 1H), 7.31 (m, 4H), 7.25 (m, 1H), 4.45 (s, 2H), 4.49 (d, *J* = 1.2 Hz, 2H), 3.48 (m, 2H), 3.29 (td, *J* = 9.6, 2.4 Hz, 1H), 3.20 (s, 3H), 1.98-1.88 (m, 1H), 1.84-1.76 (m, 1H), 1.68-1.57 (m, 4H), 1.49 (m, 1H), 1.41 (m, 1H), 0.85 (d, *J* = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 199.6, 138.6, 128.3, 127.6, 127.5, 99.7, 76.2, 72.9, 70.4, 50.3, 34.0, 29.3, 29.0, 26.9, 25.4, 17.8; IR (neat) ν_{max} : 2931, 2862, 1745, 1455, 1097, 1046 cm^{-1} ; CIHRMS $[\text{M}+\text{H}]^+$ *m/z* calculated for $\text{C}_{18}\text{H}_{27}\text{O}_4$: 307.1885, found 307.1884.



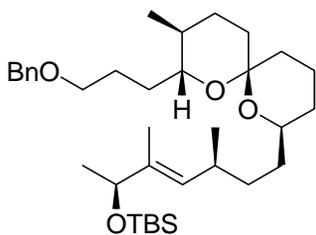
[(2*E*,9*Z*)-(S)-10-[(2*R*,5*S*,6*R*)-6-(3-Benzyloxy-propyl)-2-methoxy-5-methyl-tetrahydro-pyran-2-yl]-7-((*R*)-4-methoxy-benzyloxy)-1,4-dimethyl-2-(S)-methyl-deca-2,9-dienyloxy]-tert-butyl-dimethyl-silane **21**:
Phosphonium salt **8** (0.354 g, 0.457 mmol) was azeotropically dried with toluene (3x) under vacuum (rotovaporator at 70 °C) each time being back-filled with argon. The compound was allowed to cool to room temperature under vacuum. The resulting glass was dissolved in tetrahydrofuran (2.2 mL) and cooled to 0 °C. A solution of *n*-butyllithium (2.5 M in hexane, 0.189 mL) was added drop-wise to the solution and stirred for 30 minutes at this temperature. Aldehyde **7** (0.100 g, 0.326 mmol) was dried at 50 °C for 30 minutes under vacuum, back filled with argon and dissolved in tetrahydrofuran (2.2 mL) at room temperature. The aldehyde was then added to the phosphonium salt (a dark orange solution) *via* cannula and stirred at 0 °C for 30 minutes. Wet diethyl ether was added followed by water and the aqueous layer was extracted with diethyl ether (3x). After drying over magnesium sulfate the solution was filtered and concentrated under vacuum to obtain an oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 99/1 to 95/5) to afford **21** as a colorless oil¹² (0.202 g, 86%). $[\alpha]_D^{20} +54.1$ (*c* 0.12, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.32-7.24 (m, 5H), 7.24-7.21 (obsc. d, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 5.51 (m, 1H), 5.27 (d, *J* = 12 Hz, 1H), 5.01 (d, *J* = 9.6 Hz, 1H), 4.48 (s, 2H), 4.44 (d, *J*_{ab} = 11.2 Hz, 1H), 4.37 (d, *J*_{ab} = 11.2 Hz, 1H), 4.11 (q, *J* = 6.4 Hz, 1H), 3.77 (s, 3H), 3.47 (q, *J* = 6.8 Hz, 2H), 3.33 (quint., *J* = 6.0 Hz, 1H), 3.20 (td, *J* = 9.6, 1.6 Hz, 1H), 3.09 (s, 3H), 2.51 (m, 1H), 2.35 (m, 1H), 1.90 (m, 1H), 1.80-1.55 (m, 4H), 1.51 (d, *J* = 1.2 Hz, 3H), 1.51-1.46 (obsc. m, 2H), 1.45-1.20 (m, 7H), 1.14 (d, *J* = 6.4 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.005 (s, 3H), -0.020 (s, 3H); $^{13}\text{C NMR}$ (75 MHz, C_6D_6): δ 159.6, 139.5, 138.0, 133.2, 131.8, 130.9, 129.9, 129.3, 128.5, 127.7, 127.5, 114.0, 99.8, 78.7, 75.5, 74.7, 73.0,

¹² This material proved to be unstable in CDCl_3 over a short period of time. This material was stored in at -20 °C.

70.8, 70.7, 54.7, 48.8, 36.0, 34.7, 33.7, 32.62, 32.61, 32.2, 30.2, 28.7, 26.4, 26.1, 23.6, 21.3, 18.4, 18.0, 11.4, -4.48, -4.76; IR (neat) ν_{\max} : 2953, 2929, 2856, 1612, 1513, 1463, 1248, 1092 cm^{-1} ; CIHRMS $[\text{M}+\text{Na}]^+$ m/z calculated for $\text{C}_{44}\text{H}_{70}\text{NaO}_6\text{Si}$ 745.4839, found 745.4884.



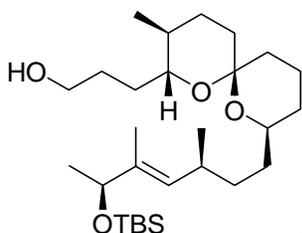
[(E)-(S)-10-[(2S,5S,6R)-6-(3-Benzyloxy-propyl)-2-methoxy-5-methyl-tetrahydro-pyran-2-yl]-7-((S)-4-methoxy-benzyloxy)-1,4-dimethyl-2-(S)-methyl-dec-2-enyloxy]-tert-butyl-dimethyl-silane 21a: Olefin **21** (0.190 g, 0.263 mmol) and tris(triphenylphosphine) rhodium(I) chloride (0.0243 g, 0.0263 mmol) were dissolved in benzene (5.00 mL) and added to a sealed tube. The reaction was stirred at room temperature for 18 hours under 80 psi atmosphere of H_2 . Upon completion of the reaction, the solvent was removed under vacuum to obtain an oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 99/1 to 95/5) to afford **21a** as a colorless oil¹³ (0.143 g, 75 %). $[\alpha]_{\text{D}}^{20} +18.5$ (c 0.70, CHCl_3); ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.24 (m, 5H), 7.24-7.22 (obsc. d, 2H), 6.83 (d, $J = 8.8$ Hz, 2H), 5.03 (d, $J = 9.6$ Hz, 1H), 4.48 (s, 2H), 4.40 (d, $J_{\text{ab}} = 11.2$ Hz, 1H), 4.36 (d, $J_{\text{ab}} = 11.2$ Hz, 1H), 4.12 (q, $J = 6.4$ Hz, 1H), 3.77 (s, 3H), 3.47 (q, $J = 6.8$ Hz, 2H), 3.29 (quint., $J = 5.6$ Hz, 1H), 3.14 (td, $J = 9.6, 2.4$ Hz, 1H), 3.07 (s, 3H), 2.26 (m, 1H), 1.88 (m, 1H), 1.78-1.57 (m, 5H), 1.52 (d, $J = 1.2$ Hz, 3H), 1.51-1.20 (m, 12H), 1.15 (d, $J = 6.4$ Hz, 3H), 0.90 (d, $J = 6.4$ Hz, 3H), 0.86 (s, 9H), 0.81 (d, $J = 6.8$ Hz, 3H), 0.009 (s, 3H), -0.014 (s, 3H); ^{13}C NMR (75 MHz, C_6D_6): δ 159.6, 139.6, 138.0, 132.0, 131.0, 129.3, 128.5, 127.75, 127.5, 114.0, 99.2, 78.6, 75.5, 74.7, 73.0, 70.9, 70.6, 54.7, 47.1, 37.0, 35.0, 34.6, 33.6, 33.5, 32.2, 32.1, 30.1, 28.5, 26.3, 26.1, 23.7, 21.3, 19.7, 18.4, 18.0, 11.4, -4.48, -4.76; IR (neat) ν_{\max} 2952, 2856, 1612, 1513, 1248, 1094 cm^{-1} ; CIHRMS $[\text{M}+\text{Na}]^+$ m/z calculated for $\text{C}_{44}\text{H}_{72}\text{NaO}_6\text{Si}$ 747.4816, found 747.4895.



{(S)-6-[(3S,6S,8R,9S)-8-(3-Benzyloxy-propyl)-9-methyl-1,7-dioxa-spiro[5.5]undec-2-yl]-2,4-dimethyl-1-(S)-methyl-hex-2-enyloxy}-tert-butyl-dimethyl-silane 23: A solution of **21a** (0.093 g, 0.13 mmol) and pyridine (0.066 mL, 0.

¹³ This material proved to be unstable in CDCl_3 over a short period of time. This material was stored in at -20 °C.

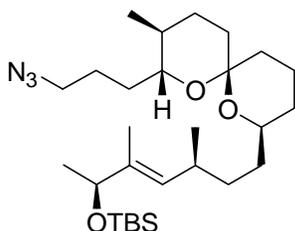
82 mmol) in methylene chloride (10.0 mL) under an atmosphere of argon was cooled to 0 °C. DDQ (0.093 g, 0.41 mmol) was added in portions over 1 hour and the reaction was allowed to stir at 0 °C for 12 hours. An additional amount of DDQ (0.0291 g, 0.128 mmol) was added in portions and the mixture stirred for an additional 12 hours at 0 °C. A final portion of DDQ (0.0291 g, 0.128 mmol) was then added in portions and stirred for 1 hour at which point the mixture was diluted with methylene chloride and water. The aqueous layer was extracted with methylene chloride (3x) and the combined extracts were dried over magnesium sulfate, filtered and concentrated to obtain an oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 99/1 to 95/5) to afford **23** as a colorless oil (0.056 g, 76 %). $[\alpha]_D^{20} +27.2$ (*c* 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31 (apt. d, *J* = 4.4 Hz, 4H), 7.25 (m, 1H), 5.07 (d, *J* = 9.6 Hz, 1H), 4.50 (s, 2H), 4.11 (q, *J* = 6.0 Hz, 1H), 3.48 (obsc. m, 2H), 3.43 (obsc. m, 1H), 3.13 (td, *J* = 10.0, 2.0 Hz, 1H), 2.29 (m, 1H), 1.96 (m, 1H), 1.86-1.70 (m, 2H), 1.62-1.40 (m, 8H), 1.52 (d, *J* = 1.2 Hz, 3H), 1.37-1.20 (m, 8H), 1.15 (d, *J* = 6.4 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.80 (d, *J* = 6.4 Hz, 3H), 0.008 (s, 3H), -0.011 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 138.7, 137.3, 130.4, 128.4, 127.7, 127.5, 95.4, 74.4, 74.1, 73.0, 70.9, 69.0, 36.1, 35.5, 35.2, 34.3, 33.7, 31.8, 31.4, 29.9, 28.0, 26.4, 25.9, 23.4, 20.9, 19.2, 18.3, 18.0, 11.6, -4.68, -5.05; IR (neat) ν_{\max} : 2929, 1455, 1254, 1097 cm⁻¹; CIHRMS $[M+H]^+$ *m/z* calculated for C₃₅H₆₁O₄Si 573.4339, found 573.4365.



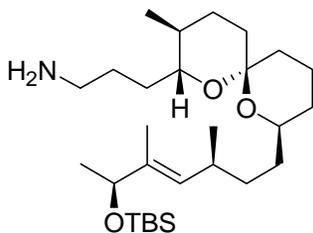
3-{(2*R*,3*S*,6*S*,9*S*)-8-[(4*S*,7*S*)-6-(*tert*-Butyl-dimethyl-silyloxy)-3,5-dimethyl-hept-4-enyl]-3-methyl-1,7-dioxaspiro[5.5]undec-2-yl}-propan-1-ol **23a:**

Ammonia (*ca.* 2.00 mL, 0.0701 mol) was condensed into a round bottom flask at -78 °C. A solution of benzyl ether **23** (0.043 g, 0.075 mmol) in tetrahydrofuran (0.50 mL) was added drop-wise to the condensed liquid ammonia. Sodium metal (0.010 g, 0.430 mmol) was added and the dark blue solution was stirred until TLC showed no starting material present. Wet diethyl ether was added and the reaction was allowed to slowly reach room temperature. The reaction was concentrated *in vacuo* to obtain an oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 90/10) to afford **23a** as a colorless oil (0.033 g, 91 %). $[\alpha]_D^{20} +29.2$ (*c* 0.25, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 5.07 (d, *J* = 9.6 Hz, 1H), 4.11 (q, *J* = 6.4 Hz, 1H), 3.65 (m, 2H), 3.44 (br. m, 1H), 3.13 (apt. t, *J* = 9.2 Hz, 1H), 2.29 (m, 2H), 1.83-1.70 (m, 3H), 1.68-1.41 (m, 10H), 1.54 (s, 3H), 1.40-1.23 (m, 6H), 1.15 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.86 (s, 9H), 0.81 (d, *J* = 6.4 Hz, 3H), 0.009 (s, 3H), -0.010 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 137.4, 130.2, 95.8, 74.5, 74.0, 69.1, 63.3, 36.2, 35.3, 34.4, 34.2, 33.6, 31.7, 31.3, 29.6, 28.6, 27.8, 25.9, 23.4, 20.9, 19.1, 18.3, 18.0, 11.6, -4.68, -5.02; IR (neat) ν_{\max} :

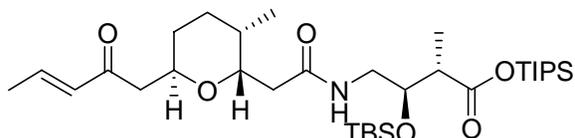
3359, 2933, 2862, 1456, 1380, 1251, 1087 cm^{-1} ; CIHRMS $[\text{M}+\text{Na}]^+$ m/z calculated for $\text{C}_{28}\text{H}_{54}\text{O}_4\text{NaSi}$ 505.3689, found 505.3715.



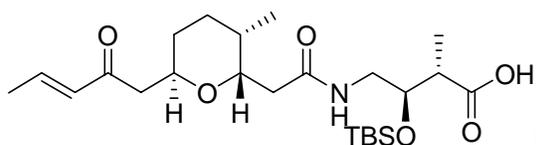
{(S)-6-[(3S,6S,8R,9S)-8-(3-Azido-propyl)-9-methyl-1,7-dioxaspiro[5.5]undec-2-yl]-2,4-dimethyl-1-(S)-methyl-hex-2-enyloxy}-tert-butyl-dimethyl-silane **23b:** To a solution of **23a** (0.032 g, 0.066 mmol) in tetrahydrofuran (0.60 mL) at 0 °C was added triphenylphosphine (0.017 g, 0.0663 mmol), diisopropyl azodicarboxylate (0.013 mL, 0.0663 mmol), and diphenylphosphonic azide (0.014 mL, 0.0663 mmol). After 3 hours, the reaction was quenched with a saturated solution of sodium bicarbonate and the aqueous layer was extracted with diethyl ether (3x). The combined organics were dried over magnesium sulfate, filtered and concentrated *in vacuo* to obtain an oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 90/10) to afford **23b** as a colorless oil (0.029 g, 86 %). $[\alpha]_{\text{D}}^{20} +19.8$ (*c* 0.76, CHCl_3); ^1H NMR (400 MHz, CDCl_3): δ 5.07 (d, *J* = 9.6 Hz, 1H), 4.11 (q, *J* = 6.0 Hz, 1H), 3.40 (br. m, 1H), 3.30 (m, 2H), 3.13 (apt. td, *J* = 9.6, 2.0 Hz, 1H), 2.30 (m, 1H), 1.92 (m, 1H), 1.83-1.66 (m, 2H), 1.68-1.46 (m, 8H), 1.54 (s, 3H), 1.38-1.23 (m, 8H), 1.16 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.010 (s, 3H), -0.009 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 137.4, 130.2, 95.5, 74.1, 74.0, 69.1, 51.9, 36.1, 35.4, 35.0, 34.2, 33.7, 31.8, 31.4, 30.3, 27.9, 25.9, 25.5, 23.4, 20.9, 19.2, 18.3, 17.9, 11.6, -4.70, -5.03; IR (neat) ν_{max} : 2933, 2862, 2095, 1456, 1378, 1253, 1090 cm^{-1} ; CIHRMS $[\text{M}]^+$ m/z calculated for $\text{C}_{28}\text{H}_{53}\text{N}_3\text{O}_3\text{Si}$ 507.3856, found.



3-[(2R,3S,6S,9S)-8-[(4S,7S)-6-(tert-Butyl-dimethyl-silyloxy)-3,5-dimethyl-hept-4-enyl]-3-methyl-1,7-dioxaspiro[5.5]undec-2-yl]-propylamine **4:** To a solution of azide **23b** (0.016 g, 0.032 mmol) in tetrahydrofuran (1.44 mL) and water (0.48 mL) at room temperature was added trimethyl phosphine (1.00 M in THF, 0.158 mL). The solution was stirred for *ca.* 1 hour and a saturated sodium chloride solution was added. The aqueous solution was extracted with diethyl ether (3x) and the combined extracts were dried over magnesium sulfate. The solution was then filtered and concentrated to obtain an yellow oil. This material proved to be unstable on silica column so the resulting amine **4** was taken directly to the next step.



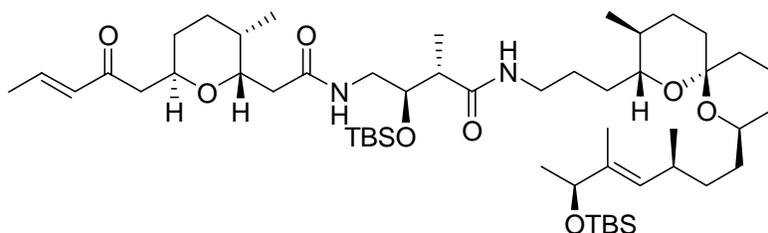
(R)-3-(tert-Butyl-dimethyl-silyloxy)-2-(S)-methyl-4-{2-[(2S,3S,6R)-3-methyl-6-((E)-2-oxo-pent-3-enyl)-tetrahydro-pyran-2-yl]-acetylamino}-(triisopropylsilyl)-butyric acid 2a: Tetrahydropyran **2**¹⁴ (0.020 g, 0.083 mmol) was dissolved in methylene chloride (3.00 mL) under an atmosphere of argon at room temperature. Amine **4** (0.040 g, 0.0999 mmol) in methylene chloride (1.00 mL) was then added followed by (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (0.048 g, 0.0916 mol) and triethylamine (0.015 mL, 0.108 mmol). The reaction was stirred at room temperature for 16 hours and diluted with diethyl ether. This solution was washed with saturated sodium bicarbonate and saturated sodium chloride solutions, dried over magnesium sulfate and filtered. The solution was concentrated *in vacuo* to obtain a clear oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 90/10) to afford **2a** as a colorless oil (0.032 g, 61 %). $[\alpha]_{\text{D}}^{20}$ -12.5 (*c* 0.27, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.81 (q, *J* = 6.8 Hz, 1H), 6.67 (br. t, *J* = 5.6 Hz, 1H), 6.05 (dt, *J* = 15.6, 1.6 Hz, 1H), 4.12 (br. m, 2H), 4.02 (q, *J* = 4.0 Hz, 1H), 3.48 (quint. *J* = 6.8 Hz, 1H), 3.25 (apt dt, *J* = 14.0, 5.6 Hz, 1H), 2.83 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.65 (m, 1H), 2.59-2.53 (m, 2H), 2.12 (dd, *J* = 15.6, 2.8 Hz, 1H), 1.86 (dd, *J* = 7.2, 1.6 Hz, 3H), 1.70 (m, 1H), 1.61 (m, 1H), 1.33-1.22 (m, 7H), 1.14 (d, *J* = 7.2 Hz, 3H), 1.06 (s, 9H), 1.04 (s, 9H), 0.85 (s, 9H), 0.82 (d, *J* = 7.2 Hz, 3H), 0.077 (s, 3H), 0.053 (s, 3H); ¹³C (75 MHz, CDCl₃): δ 197.9, 173.7, 171.6, 143.2, 132.4, 74.1, 72.4, 65.8, 44.95, 44.90, 42.9, 33.8, 33.0, 29.8, 26.5, 25.8, 18.3, 18.0, 17.9, 16.5, 13.2, 11.9, -4.48, -4.79; IR (neat) ν_{max} : 3352, 2925, 1718, 1697, 1672, 1536, 1464, 1253, 1193 cm⁻¹; CIHRMS [M+H]⁺ *m/z* calculated for C₃₃H₆₄NO₆Si₂ 626.4272, found: 626.4233.



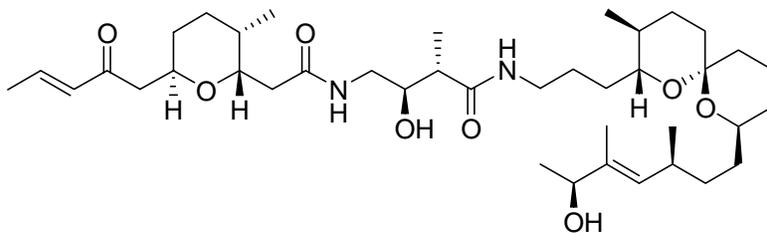
(R)-3-(tert-Butyl-dimethyl-silyloxy)-2-(S)-methyl-4-{2-[(2S,3S,6R)-3-methyl-6-((E)-2-oxo-pent-3-enyl)-tetrahydro-pyran-2-yl]-acetylamino}-butyric acid 24: A solution of TIPS acid **2a** (0.029 g, 0.046 mmol) in tetrahydrofuran (4.0 mL) was cooled to 0 °C under argon. A dilute solution of TBAF (0.10 M in tetrahydrofuran, 0.527 mL) was added to the reaction flask and the reaction was monitored till by TLC (*ca.* 30 minutes). The reaction solution was diluted with diethyl ether and washed with 0.01M HCl and saturated sodium chloride solutions. The organics were then dried over magnesium sulfate, filtered and concentrated to afford **24** as a colorless oil (0.020 g, 92 %). This material was taken to the next step without further purification. $[\alpha]_{\text{D}}^{20}$ -10.7 (*c* 0.13, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.55 (m, 1H), 6.88 (apt. dq, *J* = 16.0, 6.8 Hz, 1H), 6.08 (apt. dd, *J* = 15.6, 1.6 Hz, 1H), 4.15 (br. m,

¹⁴ Lowe, J. T.; Panek, J. S. *Org. Lett.* **2005**, *7*, 3231.

1H), 4.03 (dd, J = 10.4, 4.4 Hz, 1H), 3.92 (dt, J = 8.0, 4.4 Hz, 1H), 3.48 (m, 1H), 3.27 (m, 1H), 2.87 (dd, J = 17.6, 8.8 Hz, 1H), 2.73 (dd, J = 15.2, 11.6 Hz, 1H), 2.58 (m, 2H), 2.14 (dd, J = 14.8, 2.0 Hz, 1H), 1.90 (dd, J = 6.8, 1.6 Hz, 3H), 1.63 (m, 2H), 1.44-1.22 (m, 4H), 1.19 (d, J = 6.8 Hz, 3H), 0.87 (s, 9H), 0.83 (d, J = 7.2 Hz, 3H), 0.107 (s, 3H), 0.092 (s, 3H); ¹³C (75 MHz, CDCl₃): δ 198.9, 174.5, 173.7, 144.3, 132.0, 74.6, 73.4, 64.6, 45.2, 43.6, 42.7, 33.3, 32.0, 30.6, 29.7, 26.3, 25.7, 18.4, 17.9, 17.0, 14.9, -4.45, -5.02; IR (neat) ν_{max}: 3339, 2929, 2857, 1727, 1662, 1630, 1549, 1103 cm⁻¹; CIHRMS [M+H]⁺ m/z calculated for C₂₄H₄₄NO₆Si₂ 470.2938, found: 470.2932.



3-(tert-Butyl-dimethyl-silyloxy)-N-(3-{8-[6-(tert-butyl-dimethyl-silyloxy)-3,5-dimethyl-hept-4-enyl]-3-methyl-1,7-dioxaspiro[5.5]undec-2-yl}-propyl)-2-methyl-4-{2-[3-methyl-6-(2-oxopent-3-enyl)-tetrahydro-pyran-2-yl]-acetylamino}-butyramide **24a:** Amine **4** (0.0140 g, 0.029 mmol) was added into a round bottom flask under an atmosphere of argon. A solution of acid **24** (0.0136 g, 0.0290 mmol) in *N,N*-dimethylformamide (0.700 mL) was added followed by (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluoro phosphate (0.030 g, 0.058 mmol) and *N,N*-diisopropylethylamine (0.0126 mL, 0.0723 mmol). The mixture was stirred for 4 hours at room temperature before it was diluted with diethyl ether. The reaction was washed successively with 10% citric acid, saturated sodium bicarbonate and sodium chloride solutions. The organics were then dried over magnesium sulfate, filtered and concentrated *in vacuo* to provide an oil. The resulting oil was purified by column chromatography over silica gel (hexane/ethyl acetate: 95/5 to 90/10) to afford **24a** as a colorless oil (0.0195 g, 72 %). [α]_D²⁰ +17.2 (c 0.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.82 (obsc. dq, J = 15.6, 6.8 Hz, 1H), 6.80 (t, J = 7.2 Hz, 1H), 6.76 (t, J = 5.2 Hz, 1H), 6.08 (dd, J = 15.6, 1.2 Hz, 1H), 5.07 (d, J = 9.6 Hz, 1H), 4.14-4.09 (m, 3H), 3.91 (apt. quint., J = 4.4 Hz, 1H), 3.56 (m, 1H), 3.48 (dt, J = 13.9, 5.3 Hz, 1H), 3.39 (m, 1H), 3.32-3.18 (m, 2H), 3.17-3.09 (m, 2H), 2.87 (dd, J = 16.4, 7.6 Hz, 1H), 2.63 (dd, J = 15.2, 11.2 Hz, 1H), 2.53 (dd, J = 16.4, 4.4 Hz, 1H), 2.45-2.38 (m, 1H), 2.28 (m, 1H), 2.13 (dd, J = 15.2, 2.0 Hz, 1H), 1.89 (dd, J = 6.8, 1.6 Hz, 3H), 1.84-1.26 (m, 26H), 1.15 (d, J = 6.0 Hz, 3H), 1.13 (d, J = 7.6 Hz, 3H), 0.91 (obsc. d, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.83 (d, J = 7.6 Hz, 3H), 0.78 (d, J = 6.4 Hz, 3H), 0.13 (s, 3H), 0.08 (s, 3H), 0.01 (s, 3H), -0.02 (s, 3H); ¹³C (75 MHz, CDCl₃): δ 198.7, 173.9, 171.9, 143.8, 137.3, 132.4, 130.3, 95.3, 74.4, 74.2, 74.1, 72.7, 69.0, 65.4, 45.1, 44.0, 43.2, 39.7, 36.1, 35.5, 34.9, 34.4, 33.6, 33.10, 33.07, 32.9, 31.9, 31.4, 30.9, 30.6, 27.9, 27.8, 26.5, 25.90, 25.87, 23.4, 20.9, 19.1, 18.4, 18.3, 18.0, 16.9, 15.8, 11.5, -4.5, -4.7, -4.99, -5.03; IR (neat) ν_{max}: 3335, 2930, 2858, 1662, 1661, 1646, 1547, 1534; 1252 cm⁻¹; CIHRMS [M+Na]⁺ m/z calculated for C₅₂H₉₆N₂NaO₈Si₂ 955.6603, found: 955.6591.



3-(S)-Hydroxy-N-{3-[(2*R*,3*S*,6*S*,9*S*)-8-((4*S*,7*S*)-6-hydroxy-3,5-dimethyl-hept-4-enyl)-3-methyl-1,7-dioxaspiro[5.5]undec-2-yl]-propyl}-2-(*R*)-methyl-4-{2-[(1*R*,3*S*,4*S*)-3-methyl-6-(2-oxopent-3-enyl)-tetrahydro-pyran-2-yl]-acetamino}-butyramide (Bistramide A) 1: To a solution of **24a** (0.0026 g, 0.0028 mmol) in methanol (1.00 mL) was added pyridinium *p*-toluenesulfonate (0.010 g, 0.040 mmol) and the reaction was stirred at room temperature overnight. The reaction mixture was concentrated *in vacuo* to obtain an oil slurry. The resulting material was purified by preparative thin layer chromatography (CHCl₃/MeOH 97/3) to afford **1** as a colorless oil (0.0012 g, 61 %). $[\alpha]_{\text{D}}^{20} +9.1$ (c 0.12, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 7.30 (t, J = 5.8 Hz, 1H), 6.93 (t, J = 5.5 Hz, 1H), 6.88 (dq, J = 15.6, 6.8 Hz, 1H), 6.10 (dd, J = 15.6, 2.0 Hz, 1H), 5.16 (d, J = 9.6 Hz, 1H), 4.60 (br. d, J = 5.2 Hz, 1H), 4.19-4.15 (m, 2H), 4.04 (dd, J = 10.4, 4.4 Hz, 1H), 3.69 (quint., 1H), 3.48 (dt, J = 13.9, 5.3 Hz, 1H), 3.43-3.40 (m, 1H), 3.27 (dt, J = 12.8, 6.5 Hz, 2H), 3.20 (dt, J = 13.6, 5.6 Hz, 1H), 3.12 (dt, J = 9.3, 1.8 Hz, 1H), 2.88 (dd, J = 17.2, 8.8 Hz, 1H), 2.74 (dd, J = 15.6, 12.0 Hz, 1H), 2.50 (dd, J = 17.2, 2.8 Hz, 1H), 2.40-2.28 (m, 2H), 2.11 (dd, J = 14.8, 1.2 Hz, 1H), 1.90 (dd, J = 6.8, 2.0 Hz, 3H), 1.84-1.26 (m, 28H), 1.23 (apt. t, J = 7.2 Hz, 6H), 0.93 (d, J = 6.8, 3H), 0.84 (d, J = 6.8 Hz, 3H), 0.78 (d, J = 6.8 Hz, 3H); ¹³C (75 MHz, CDCl₃): δ 198.9, 175.1, 173.5, 144.5, 137.2, 132.1, 131.4, 95.4, 74.9, 74.3, 73.9, 73.3, 69.1, 64.7, 45.3, 44.7, 43.3, 39.5, 36.1, 35.5, 34.9, 34.1, 33.5, 33.3, 32.3, 31.9, 31.3, 30.8, 30.4, 27.9, 26.5, 25.9, 21.7, 21.0, 19.2, 18.4, 18.0, 17.2, 15.6, 11.8; IR (neat) ν_{max} : 3328, 2928, 2868, 1645, 1549 cm⁻¹; CIHRMS [M+Na]⁺ *m/z* calculated for C₄₀H₆₈N₂NaO₈ 727.4873, found: 727.4865.