Synthesis of the C11-C29 Fragment of Amphidinolide F

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Supporting Information
**General Methods:** All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated, all chemicals were used as purchased without further purification.

**Physical Properties and Spectroscopic Measurements:** Proton nuclear magnetic resonance (\(^1\text{H} \) NMR) spectra and carbon-13 (\(^{13}\text{C} \) NMR) spectra were recorded on a Varian Inova-500 spectrometer at 500 MHz and 125 MHz, respectively, or a Varian Inova-400 spectrometer at 400 MHz and 100 MHz, respectively. The proton signal of residual, non-deuterated solvent (7.27 ppm for \(\text{CDCl}_3 \)) was used as an internal reference for \(^1\text{H} \) spectra. For \(^{13}\text{C} \) spectra, chemical shifts are reported relative to the 77.00 ppm resonance of \(\text{CDCl}_3 \). Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as thin films on a Perkin-Elmer Spectrum 1000 FTIR. Mass spectra were recorded on a ZVG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester, UK).

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 \(F_{254} \) glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with \(p\)-anisaldehyde solution (\(p\)-anisaldehyde in ethanolic sulfuric acid). Column chromatography was performed using Kieselgel 60 (230-400 mesh) silica gel.

HPLC purifications were performed using an HPLC system composed of two Rainin HPXL pumps connected to various Dynamax\(^\text{\textcircled{a}} \) axial compression columns packed with Rainin 60 Å irregular silica gel. Samples were loaded into the system with a 2 mL Rheodyne 7125 injector and were detected using a Rainin Dynamax\(^\text{\textcircled{b}} \) UV-C detector. Integration of the various signals was performed using the reprocessing program within the Dynamax\(^\text{\textcircled{b}} \) HPLC Method Manager.

![Chemical Structure](attachment:image.png)

**\((3\text{R},4\text{S})\)-4-(Dimethylphenylsilanyl)-1-(triethylsilanyl)-hex-5-en-1-yn-3-ol (SI-1):** Potassium \(t\)-butoxide (6.05 g, 54.0 mmol, 1.9 eq.) was dissolved in dry THF (90 mL) and cooled to \(-78 \) °C. Phenylimethylallylsilane (8.55 g, 48.6 mmol, 1.7 eq.) was added via syringe in one portion followed by dropwise addition of \(n\)-BuLi (22.5 mL of a 2.41 M solution in hexanes, 54.0 mmol, 1.9 eq.) over 25 min. The resulting orange solution was stirred at \(-78 \) °C for 10 min, then the flask was transferred to a \(-45 \) °C bath and stirred an additional 2 h. The flask was returned to the \(-78 \) °C bath and \((-\)-Ipc\(_2\)BOMe (17.06 g, 1.9 eq.) was added.
54.0 mmol, 1.9 eq.) in THF (110 mL) was added slowly via cannula. The resulting
mixture was stirred for 30 min, then BF$_3$·OEt$_2$ (8.11mL, 64.0 mmol, 2.25 eq.) was added
dropwise followed by slow addition of aldehyde 11 (4.81g, 28.6 mmol, 1 eq.) via cannula
as a solution in THF (50 mL + 20 mL wash). After the solution was stirred at −78 °C for
6 h, the mixture was diluted with 1M KH$_2$PO$_4$·KOH buffer (120 mL, pH = 6) and 30%
H$_2$O$_2$ (50 mL). The cooling bath was removed and the reaction mixture was stirred at
ambient temperature for 1 h, then cooled to 0 °C and aqueous 1M Na$_2$SO$_3$ solution (250
mL) was added portion-wise to destroy excess H$_2$O$_2$. The resulting mixture was extracted
twice with ethyl acetate, dried over sodium sulfate, and concentrated under reduced
pressure. The resulting oil was purified by chromatography on SiO$_2$ (hexanes [O 10%
EtOAc/hexanes) to afford first aldehyde 11 (0.663 mg, 3.95 mmol, 14% yield) followed
by allylsilane SI-1 (6.79g, 19.7 mmol, 69% yield, 91% e.e.) as a clear oil: $[\theta]_D^{27.0}$ +19.1
c (2.01, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.58-7.56 (m, 2H), 7.38-7.55 (m, 3H),
5.80 (ddd, $J = 10, 10, 16$ Hz, 1H), 5.08 (dd, $J = 2, 10$ Hz, 1H), 4.96 (dd, $J = 2, 16$ Hz, 1H), 4.44 (dd, $J = 6, 6$ Hz, 1H), 2.14 (dd, $J = 6, 10, 1$H), 1.77 (d, $J = 5$ Hz, 1H), 0.99 (t, $J$
= 8 Hz, 9H), 0.60 (q, $J = 8$ Hz, 6H), 0.41 (s, 3H), 0.40 (s, 3H); $^{13}$C NMR (100 MHz,
CDCl$_3$) $\delta$ 137.1, 134.8, 134.2, 129.1, 127.7, 115.8, 107.8, 87.7, 63.3, 43.2, 7.4, 4.2, -34;
IR (thin film, NaCl) 3544, 3461, 3069, 3050, 2988, 2935, 2910, 2874, 2165, 1627, 1487,
1457, 1427, 1414, 1377, 1323, 1247, 1158, 1112, 1090, 1019, 973, 955, 900, 835, 814,
796, 778, 730, 701, 653, 585 cm$^{-1}$; mass spectrum, calcd for C$_{20}$H$_{25}$OSi$_2$: 367.1889 m/z
(M+Na); observed, 367.1891 m/z. Anal. Calcd: C, 69.70; H, 9.36. Found: C, 69.36,
H, 9.23.

The enantiomeric excess and absolute configuration of SI-1 were confirmed by
Mosher Ester analysis:

$^{(1S, 2R)}$-$[2-(tert-Butyldimethylsilanyloxy)-4-(triethylsilanyl)-1-vinyl-but-3-
ynyl]-dimethylsilany]-benzene (5). To a solution of propargyl alcohol SI-1 (6.65 g,
19.3 mmol) in dry dimethylformamide (40 mL) was added imidazole (6.9 g, 101 mmol,
5.25 eq.) followed by solid TBSCl (4.8 g, 32 mmol, 1.65 eq.). The resulting solution was
stirred ca 16 h, diluted with hexanes, and washed with saturated aqueous sodium
chloride. The organic layer was dried over sodium sulfate and concentrated in vacuo.
The resulting oil was purified by chromatography on SiO$_2$ (hexanes) to afford allyl silane
5 (7.24 g, 15.8 mmol, 82% yield) as a clear oil: $[\theta]_D^{27.0}$ +5.52 (c 4.15, CHCl$_3$); $^1$H NMR

SI-3
(400 MHz, CDCl$_3$) $\delta$ 7.55-7.52 (m, 2H), 7.36-7.30 (m, 3H), 5.84 (dd, $J = 10$, 10, 17 Hz, 1H), 4.97 (dd, $J = 1.6$, 10 Hz, 1H), 4.83 (dd, $J = 1.6$, 17 Hz, 1H), 4.54 (d, $J = 4.4$ Hz, 1H), 2.11 (dd, $J = 5$, 10 Hz, 1H), 0.98 (t, $J = 8$ Hz, 9H), 0.89 (s, 9H), 0.58 (q, $J = 8$ Hz, 6H), 0.40 (s, 3H), 0.36 (s, 3H), 0.12 (s, 3H), 0.06 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 138.4, 135.7, 134.3, 129.1, 127.7, 114.9, 109.1, 87.7, 64.7, 44.1, 26.1, 18.4, 7.6, 4.4, -2.9, -3.0, -4.1, -4.5; IR (thin film, NaCl) 3071, 3052, 2978, 2929, 1725, 1471, 1427, 1343, 1362, 1253, 1169, 1098, 1070, 1020, 1004, 979, 938, 900, 837, 779, 731, 700, 655 cm$^{-1}$; mass spectrum calcd for C$_{26}$H$_{46}$OSi$_3$ 481.2754 m/z (M+Na)$^+$; observed, 481.2758.

(2$R$, 4$R$, 5$S$, 1$'R$)-5-[1-(tert-Butyldimethylsilanyloxy)-3'-(triethylsilyl)-prop-2'-ynyl]-4-(dimethylphenylsilyl)-tetrahydrofuran-2-carboxylic acid Ethyl Ester (15). To a solution of allylsilane 5 (0.700 g, 1.52 mmol) and ethyl glyoxylate 13 (0.830 mL, 40% solution in toluene, ca 3.42 mmol, 2.25 eq.) in dichloromethane (10 mL) at −78 °C was added tin (IV) chloride as a 1 M solution in dichloromethane (1.67 mL, 1.10 eq.). The resulting solution was stirred for 45 min, quenched by slow addition of triethylamine (5 mL), and allowed to warm to room temperature. Ethyl acetate, hexanes, and 6 N HCl were added (caution!) and the mixture was vigorously stirred for 2 min. The layers are separated and the organic layer was washed with sodium bicarbonate (until the aqueous layer has pH > 7) and dried over sodium sulfate. Concentration of the solution in vacuo and purification of the crude product by chromatography on SiO$_2$ afforded tetrahydrofuran 15 (0.530 mg, 0.95 mmol, 62% yield) as a clear oil: $[\alpha]_D^{27.0} = -15.8$ (c 2.30, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.52 (m, 2H), 7.36 (m, 3H), 4.63 (d, $J = 3.5$ Hz, 1H), 4.45 (dd, $J = 7.0$, 9.5 Hz, 1H), 4.17 (m, 3 H), 2.31 (ddd, $J = 7.0$, 7.0, 12.5 Hz, 1H), 2.09 (ddd, $J = 8.0$, 8.0, 12.0 Hz, 1H), 1.80 (m, 1H), 1.24 (t, $J = 7$ Hz, 3H), 1.01 (t, $J = 8$ Hz, 9 H), 0.97 (s, 9H), 0.62 (q, $J = 8$ Hz, 6H), 0.38 (s, 3H), 0.36 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 172.5, 137.7, 133.9, 129.1, 127.8, 106.3, 88.8, 85.2, 77.1, 66.3, 60.8, 35.0, 27.1, 25.9, 18.4, 14.1, 7.4, 4.3, -2.7, -4.7, -4.8, -5.0; IR (thin film, NaCl) 3050, 3070, 2956, 2934, 2909, 2858, 1756, 1736, 1471, 1463, 1427, 1413, 1373, 1333, 1252, 1199, 1089, 1019, 1006, 975, 939, 837, 781, 735, 701 cm$^{-1}$; mass spectrum, calcd for C$_{26}$H$_{42}$O$_2$Si$_3$ 583.3071 m/z (M+Na)$^+$; observed, 583.3079 m/z.
(2R, 4R, 5S, 1'R)-[5-[1-(tert-Butyldimethylsilyloxy)-3'-(triethylsilyl)-prop-2'-ynyl]-4-(dimethylphenylsilyl)-tetrahydrofuran-2-yl]-methanol (16). To a solution of ethyl ester 15 (4.20 g, 7.40 mmol) in dry THF (100 mL) at 0 °C was added DIBAL-H as a 1M solution in dichloromethane (26 mL, 3.5 eq.). The resulting solution was stirred for 2.5 h, quenched by slow addition of saturated aq. sodium potassium tartrate (100 mL), and stirred for an additional 6 h. The organic layer was washed with saturated sodium bicarbonate, dried over sodium sulfate, and concentrated in vacuo to afford alcohol 16 as a pale yellow oil (3.82g, 7.40 mmol, 100% yield) of sufficient purity for use in subsequent manipulations: [α]D27.0 26.8 (c 2.40, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.54 (m, 2H), 7.36 (m, 3H), 4.46 (d, J = 4.5 Hz, 1H), 4.09 (m, 1H), 4.01 (dd, J = 4, 7.5 Hz, 1H), 3.67 (ABX, J = 3, 12 Hz, 1H), 3.40 (ABX, J = 6.0, 12.0 Hz, 1H), 2.03 (m, 1H), 1.92 (m, 1H), 1.80 (bs, 1H), 1.56 (m, 1H), 1.02 (t, J = 8 Hz, 9H), 0.93 (s, 9H), 0.63 (q, J = 8 Hz, 6H), 0.38 (s, 3H), 0.37 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 137.8, 133.9, 129.0, 127.8, 106.7, 88.4, 84.4, 79.5, 66.6, 64.3, 31.2, 27.0, 25.9, 18.4, 7.4, 4.3, -2.9, -4.6, -5.0; IR (thin film, NaCl) 3468, 2956, 2933, 2876, 2858, 1472, 1463, 1428, 1414, 1337, 1252, 1080, 1019, 975, 832, 780 cm⁻¹; mass spectrum, calcd for C27H30O3Si3, 541.2966 m/z (M+Na)+; observed, 541.2975 m/z.

The following selected NOEs were observed for 16:

(2R, 4R, 5S, 1’R)-Methanesulfonic acid 5-[1-(tert-butyldimethylsilyloxy)-3-(triethylsilyl)-prop-2'-ynyl]-4-(dimethylphenylsilyl)-tetrahydrofuran-2-yl-methyl Ester (SI-2). To a solution of alcohol 16 (4.17 g, 8.03 mmol), triethylamine (3.4 mL, 24.1 mmol, 3 eq.), and DMAP (20 mg) in dichloromethane (80 mL) at 0 °C was added methanesulfonyl chloride (0.81 mL, 10.4 mmol, 1.3 eq.). The solution was stirred for 45 min and quenched via the addition of saturated sodium bicarbonate. The resulting
organic layer was dried over sodium sulfate, filtered and concentrated to a residue under reduced pressure, and purified by chromatography on SiO₂ (25% EtOAc/hexanes) to afford mesylate SI-2 (4.78 g, 7.99 mmol, 99% yield) as a clear oil: \( \delta^{27.0} _{H} -28.2 \) (c 3.10, CHCl₃); \(^{1}H\) NMR (500 MHz, CDCl₃) \( \delta 7.52 \) (m, 2H), 7.38 (m, 3H), 4.37 (d, \( J = 3.5 \) Hz, 1H), 4.23 (m, 2H), 4.07 (m, 1H), 4.03 (m, 1H), 2.94 (s, 3H), 2.02 (m, 2H), 1.52 (m, 1H), 1.00 (t, \( J = 8 \) Hz, 9H), 0.92 (s, 9H), 0.61 (q, \( J = 8 \) Hz, 6H), 0.38 (s, 3H), 0.37 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H); \(^{13}C\) NMR (125 MHz, CDCl₃) \( \delta 137.2, 133.9, 129.3, 127.9, 106.5, 88.3, 84.7, 76.9, 71.4, 66.3, 37.7, 31.9, 26.7, 25.9, 18.3, 7.4, 4.2, -3.3, -4.5, -4.6, -5.0; IR (thin film, NaCl) 2956, 2935, 2877, 2858, 1463, 1428, 1414, 1361, 1252, 1178, 1113, 1087, 1020, 1004, 961, 795, 780, 736 cm\(^{-1}\); mass spectrum, calcd for C\(_{29}\)H\(_{52}\)O\(_3\)SSi\(_2\) 619.2741 m/z (M+Na); observed, 619.2745 m/z.

\( (2R, 4R, 3S, 1'R)-2-[1-(\text{tert-Butyldimethylsilanyloxy})-3'-(\text{triethylsilanyl})-prop-2'-ynyl]-3-(\text{dimethylphenylsilanyl})-5-iodomethyl-tetrahydrofuran (17) \). A solution of mesylate SI-2 (2.29 g, 3.83 mmol) and sodium iodide (2.9g, 19.1 mmol, 5 eq.) in acetone (50 mL) was placed in a 75 °C oil bath for 48 h. The acetone was removed under reduced pressure, and the resulting solid was suspended in ethyl acetate/hexanes and washed successively with sodium sulfate, saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was dried over sodium sulfate, the solvents were removed under reduced pressure, and the resulting oil was purified by chromatography on SiO₂ to afford iodide 17 (2.26g, 3.6 mmol, 94% yield) as a clear oil: \( \delta^{27.0} _{H} -9.90 \) (c 2.95, CHCl₃); \(^{1}H\) NMR (500 MHz, CDCl₃) \( \delta 7.53 \) (m, 2H), 7.37 (m, 3H), 4.46 (d, \( J = 3.5 \) Hz, 1H), 4.10 (dd, \( J = 3.5, 8.0 \) Hz, 1H), 4.04 (m, 1H), 3.20 (ABX, \( J = 5.0, 10.0 \) Hz, 1H), 3.05 (ABX, \( J = 7.0, 10.0 \) Hz, 1H), 2.20 (m, 1H), 2.09 (m, 1H), 1.44 (m, 1H), 1.01 (t, \( J = 8 \) Hz, 9H), 0.91 (s, 9H), 0.62 (q, \( J = 8 \) Hz, 6H), 0.37 (s, 3H), 0.37 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H); \(^{13}C\) NMR (125 MHz, CDCl₃) \( \delta 138.0, 134.2, 129.4, 128.1, 106.9, 88.8, 85.3, 78.8, 67.0, 37.2, 27.7, 26.2, 18.7, 9.6, 7.7, 4.6, -2.6, -4.1, -4.3, -4.6; IR (thin film, NaCl) 2956, 2931, 2910, 2858, 2170, 1472, 1463, 1428, 1362, 1336, 1252, 1185, 1169, 1113, 1029, 1020, 1006, 976, 939, 911, 834 cm\(^{-1}\); mass spectrum, calcd for C\(_{29}\)H\(_{49}\)IO\(_2\)SSi\(_3\) 651.1983 m/z (M+Na); observed, 651.1978 m/z.

![Diagram](image-url)
(S)-2-[3-(4-Methoxybenzylxylo)-2-methyl-propyl]-[1,3]-dithiane (20). To a solution of 1,3-dithiane (3.77 g, 31.4 mmol, 2 eq.) in THF/HMPA (75 mL/15 mL) at –20 °C was added n-BuLi as a 2.45M solution in hexanes (12.2 mL, 1.9 eq.). The resulting orange solution was stirred for 1 h, and then known primary iodide 18 (5.02g, 15.68 mmol, 1 eq.) was added slowly via cannula (15 mL THF, 5 mL wash). The solution was stirred for 2 h, quenched via slow addition of saturated ammonium chloride, and diluted with diethyl ether. The resulting organic phase was washed four times with small portions of saturated sodium chloride, dried over sodium sulfate, concentrated to a residue and purified via chromatography on SiO (20% EtOAc/hexanes) to afford dithiane 20 (4.34g, 13.89 mmol, 89% yield) as a pale yellow oil: [ ] B 27° +2.04 (c 0.54, CHCl); 1H NMR (400 MHz, CDCl) 7.22 (d, J = 8.5 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 4.39 (app s, 2H), 4.03 (dd, J = 6.8, 8.4 Hz, 1H), 3.76 (s, 3H), 3.26 (app d, J = 6.0 Hz, 2H), 2.84-2.73 (m, 4H), 2.06 (m, 2H), 1.84 (m, 2H), 1.51 (m, 1H), 0.93 (d, J = 8 Hz, 3H); 13C NMR (100 MHz, CDCl) 159.0, 130.7, 113.7, 74.7, 72.4, 55.2, 45.4, 39.3, 30.4, 30.3, 30.2, 26.0, 17.0; IR (thin film, NaCl) 2852, 2848, 1611, 1585, 1511, 1462, 1421, 1361, 1301, 1241, 1171, 1089, 1033, 907 cm⁻¹; mass spectrum, calcd for C₁₆H₁₆O₂S 335.1115 m/z (M+Na); observed, 335.1117 m/z. Anal. Calcd: C, 61.50; H, 7.74. Found: C, 61.40, H, 7.73.

(2S, 3R, 5R, 1′R, 2′′S)-2-[(tert-Butyldimethylsilyloxy)-3′-(triethylsilanyloxy)-prop-2′ynyl]-3-(dimethylphenylsilanyl)-5-(2-[3-(4-methoxy-benzylxylo)-2′′-methyl propyl]-[1,3]-dithian-2-ylmethyl)-tetrahydrofuran (21, R = TES) and (2S, 3R, 5R, 1′R, 2′′S)-2-[(tert-Butyldimethylsilyloxy)-prop-2′-ynyl]-3-(dimethylphenylsilanyl)-5-((S)-2-[3-(4-methoxybenzylxylo)-2′′-methylpropyl]-[1,3]-dithian-2-ylmethyl)-tetrahydrofuran (21, R = H). To a solution of dithiane 20 (2.80g, 8.94 mmol, 2.5 eq.) in dry THF/HMPA (75 mL/10 mL) at –78 °C was added freshly standardized 1.4M t-BuLi (6.4 mL, 2.5 eq.). The resulting dark brown/orange solution was stirred for 45 min, and iodide 17 (2.25g, 3.58 mmol, 1 eq.) was added via cannula as a solution in THF (8 mL and 5 mL wash). After 45 min the resulting solution was quenched with saturated ammonium chloride and warmed to room temperature. The mixture was diluted with ethyl acetate/hexanes and the organic layer was washed three
times with saturated sodium chloride, dried over sodium sulfate, and concentrated *in vacuo* to afford a crude reaction mixture consisting of a roughly 4:1 mixture of 21 (R = TES : R = H). Analytical samples of both compounds could be obtained by chromatography on SiO₂ (30% EtOAc/hexanes), but generally the reaction mixture was advanced without purification:

Data for 21, R = SiEt₃: [α]D²⁷₀ = −5.90 (c 2.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.53 (m, 2H), 7.36 (m, 3H), 7.27 (d, J = 9 Hz, 2H), 6.88 (d, J = 9 Hz, 2H), 4.45 (app d, J = 4 Hz, 2H), 4.35 (d, J = 4 Hz, 1H), 4.22 (m, 1H), 4.00 (dd, J = 4.0, 8.0 Hz, 1H), 3.81 (s, 3H), 3.39 (ABX, J = 5.5, 9.5 Hz, 1H), 3.26 (ABX, J = 7.5, 9.5 Hz, 1H), 2.75 (m, 4 H), 2.22-1.83 (m, 8H), 1.70 (ABX, J = 5.5, 15.0 Hz, 1H), 1.39 (m, 1H), 1.06 (d, J = 7 Hz, 3H), 1.00 (t, J = 8.0 Hz, 9H), 0.91 (s, 9H), 0.61 (q, J = 8 Hz, 6H), 0.36 (s, 3H), 0.34 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.0, 138.0, 133.9, 131.0, 129.1, 129.0, 127.7, 113.6, 107.1, 88.0, 83.5, 76.3, 76.0, 72.4, 66.9, 55.2, 52.7, 44.6, 42.3, 37.8, 30.1, 27.0, 26.2, 25.9, 25.0, 19.8, 18.4, 7.5, 4.3, -3.0, -4.4, -4.5, -4.9; IR (thin film, NaCl) 2953, 2931, 1611, 1585, 1512, 1462, 1426, 1361, 1301, 1171, 1111, 1081, 836 cm⁻¹; mass spectrum, calcd for C₄₄H₃₅O₄Si₂S₂ 835.4078 m/z (M+Na)⁺; observed, 835.4099 m/z.

Data for 21, R = H: [α]D²⁷₀ = −9.41 (c 1.85, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.52 (m, 2H), 7.36 (m, 3H), 7.27 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 4.46 (ABX, J = 12.0, 15.0 Hz, 1H), 4.43 (ABX, J = 12.0, 15.0 Hz, 1H), 4.20 (m, 1H), 4.16 (dd, J = 2.0, 3.5 Hz, 1H), 4.00 (dd, J = 3.5, 8.0 Hz, 1H), 3.81 (s, 3H), 3.39 (ABX, J = 5.0, 9.0 Hz, 1H), 3.27 (ABX, J = 6.5, 9.0 Hz, 1H), 2.76 (m, 4H), 2.33 (d, J = 2.5 Hz, 1H), 2.26-2.07 (m, 5H), 1.91-1.83 (m, 3H), 1.69 (m, 1H), 1.40 (m, 1H), 1.07 (d, J = 6.5 Hz, 3H), 0.91 (s, 9H), 0.35 (s, 3H), 0.34 (s, 3H), 0.12 (s, 3H), 0.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 138.0, 134.1, 131.2, 129.4, 129.4, 128.1, 113.9, 84.3, 83.6, 76.9, 76.2, 73.8, 72.6, 66.2, 55.5, 52.9, 44.6, 42.6, 38.0, 30.4, 27.3, 26.5, 26.2, 25.3, 20.1, 18.6, -3.5, -4.0, -4.3, -4.8; IR (thin film, NaCl) 3305 (d), 2927, 2854, 1612, 1512, 1462, 1360, 1301, 1248, 1171, 1111, 1083, 1036, 920, 836, 777, 734, 700, 654 cm⁻¹; mass spectrum, calcd for C₃₈H₃₅O₄Si₂S₂ 721.3213 m/z (M+Na)⁺; observed, 721.3211 m/z.

(2S, 3R, 5R, 2’S, J’R)-1-(3-(Dimethylphenylsilanyl)-5-[(S)-2-[3’-(4-methoxybenzyl oxy)-2’-methylpropyl]-1,3-dithian-2’ylmethyl]-tetrahydrofuran-2-yl)-prop-2’y-yn-1-ol (22). The crude reaction mixture described above was dissolved in THF (50 mL), cooled to 0 °C, and treated with a 1.0 M TBAF solution in THF (11 mL, ca 3 eq.). The resulting black mixture was slowly warmed to room temperature, stirred for 1 h,
diluted with ethyl acetate/hexanes, and washed successively with 1.0 N HCl, saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was dried over sodium sulfate, concentrated in vacuo, and purified by chromatography on SiO$_2$ (20% EtOAc/hexanes) to afford first recovered dithiane 20 (1.47 g, 4.70 mmol, 53% recovery) and propargyl alcohol 22 (2.03g, 3.48 mmol, 97% yield): $^{1}$H NMR (400 MHz, CDCl$_3$) 7.46 (m, 2H), 7.33 (m, 3H), 7.21 (d, $J$ = 8.5 Hz, 2H), 6.83 (d, $J$ = 8.5 Hz, 2H), 4.38 (app s, 2H), 4.04-3.95 (m, 3H), 3.76 (s, 3H), 3.24 (app d, $J$ = 6.4 Hz, 2H), 2.73 (m, 4H), 2.24 (d, $J$ = 2 Hz, 1H), 2.13 (m, 2H), 2.03 (m, 3H), 1.86 (m, 2H), 1.67 (ABX, $J$ = 6.0, 15.0 Hz, 1H), 1.51 (m, 1H), 1.36 (m, 1H), 1.00 (d, $J$ = 6.5 Hz, 3H), 0.31 (s, 3H), 0.29 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) 159.0, 137.1, 133.8, 130.7, 129.3, 129.2, 127.9, 113.7, 83.4, 82.7, 76.2, 75.8, 73.4, 72.5, 64.3, 55.2, 52.8, 43.4, 42.7, 36.7, 30.2, 27.4, 26.3, 26.3, 25.0, 19.7, -4.2, -4.4; IR (thin film, NaCl) 3468, 3268, 2953, 2909, 1612, 1586, 1513, 1427, 1302, 1248, 1173, 1089, 1034, 943, 908, 822, 773, 736, 702 cm$^{-1}$; mass spectrum, calcd for C$_{32}$H$_{48}$O$_4$Si$_2$ 607.2348 m/z (M+Na)$^+$; observed, 607.2347 m/z.

(2S, 3R, 5R, 2'S, 1''R)-1-(3-(Hydroxymethylsilyl)-5-(2-3''-(4-methoxybenzylxoy)-2''-methylpropyl)-1,3-dithian-2''-ylmethyl)-tetrahydrofuran-2-yl-prop-2''-yn-1''-ol (23). To a flame dried pressure tube was added 21 (20 mg, 0.025 mmol), potassium tert-butoxide (25 mg), DMSO (475 $\mu$L), deionized water (25 $\mu$L), and TBAF as a 1.0M solution in tetrahydrofuran (125 $\mu$L, 0.125 mmol, 5 eq.). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and set to stir at 95 °C for 16 h. The resulting dark brown solution was diluted with ethyl acetate/hexanes (ca 1:1) and washed successively with 1.0 N HCl, saturated potassium bicarbonate, and brine. The organic layer was dried over sodium sulfate, concentrated, and purified by chromatography on SiO$_2$ (20% EtOAc/hexanes to afford 23 as a pale yellow oil (12 mg, 0.023 mmol, 92% yield): $^{1}$H NMR (400 MHz, CHCl$_3$) 7.23 (d, $J$ = 8 Hz, 2H), 6.84 (d, $J$ = 8 Hz, 2H), 4.44 (ap. s, 2H), 4.38 (dd, $J$ = 2, 6Hz, 1H), 4.12 (m, 1H), 4.06 (m, 1H), 3.82 (s, 3H), 3.32 (m, 2H), 2.80 (m, 4H), 2.47 (d, $J$ = 2 Hz, 1H), 2.28-2.08 (m, 5H), 1.92 (m, 2H), 1.75 (ABX, $J$ = 6, 15 Hz, 1H), 1.52 (m, 1H), 1.41 (m, 1H), 1.07 (d, $J$ = 6Hz, 3H), 0.21 (s, 3H), 0.19 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) 159.0, 130.8, 129.3, 113.7, 82.8, 82.4, 76.3, 75.9, 74.4, 72.6, 65.0, 55.3, 52.7, 43.7, 42.6, 36.4, 30.3, 29.7, 26.3, 26.3, 25.0, 19.8, -0.8, -2.4; IR (thin film, NaCl) 3401, 3306, 2953, 2928, 1612, 1512, 1421, 1301, 1249, 1085, 1035 cm$^{-1}$; mass spectrum, calcd for C$_{26}$H$_{40}$O$_5$Si$_2$ 547.1984 m/z (M+Na)$^+$; observed, 547.1984 m/z. Anal. Calcd: C, 59.50; H, 7.68. Found: C, 59.36, H, 7.73.
(2S, 3R, 2’S, 1’’R)-1-(5-{2-[3’-(4-Methoxybenzylxylo)-2’-methylpropyl]-[1,3]-dithian-2’-ylmethyl}-tetrahydrofuran-2-yl)-prop-2’’-yn-1’’-ol (24). To a solution of 22 (0.503 g, 0.863 mmol) in DMF (10 mL) was added TBAF as a 1.0 M solution in tetrahydrofuran (3.45 mL, 4 eq.). The resulting dark brown solution was stirred at 80 °C for 16 h, after which TLC analysis showed ca a 1:1 mixture of protodesilylated 24 and intermediate silanol 23. An additional aliquot of TBAF/THF (1.75 mL, 2 eq.) was added and the resulting solution was stirred for 6 h, cooled to room temperature, diluted with ethyl acetate/hexanes and washed successively with 1.0 N HCl, saturated potassium bicarbonate, and brine. The resulting organic layer was dried over sodium sulfate, concentrated, and purified by chromatography on SiO₂ (40% EtOAc/hexanes to afford 24 as a pale yellow oil (349 mg, 0.776 mmol, 90% yield): [α]_D²⁷0 -1.7 (c 2.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.21 (d, J = 9 Hz, 2H), 6.83 (d, J = 9 Hz, 2H), 4.39 (ap. s, 2H), 4.14 (m, 1H), 4.11 (dd, J = 2, 7 Hz, 1H), 4.01 (q, J = 7 Hz, 1H), 3.75 (s, 3H), 3.24 (m, 2H), 2.74 (m, 4H), 2.36 (d, J = 2 Hz, 1H), 2.20 (ABX, J = 7, 15 Hz, 1H), 2.15 (ABX, J = 4, 15 Hz, 1H), 2.04 (m, 4H), 1.86 (m, 2H), 1.70 (dd, J = 6, 15 Hz, 1H), 1.66 (m, 1H), 1.53 (m, 1H), 1.02 (d, J = 7Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.0, 130.7, 129.2, 113.6, 81.9, 81.4, 76.2, 75.8, 73.5, 72.5, 65.0, 55.2, 52.7, 44.2, 42.6, 33.5, 30.3, 27.8, 26.3, 26.3, 24.9, 19.7; IR (thin film, NaCl) 3436, 3285, 2931, 1612, 1512, 1442, 1421, 1361, 1301, 1247, 1173, 1083, 1036 cm⁻¹; mass spectrum, calcd for C₂₄H₂₃O₄S₂ 473.1796 m/z (M+Na)⁺; observed, 473.1806 m/z.
To a solution of 22 (0.044 g, 0.075 mmol) in DMF (2 mL) was added TBAF as a 1.0 M solution in tetrahydrofuran (400 µL, 5 eq.). The resulting dark brown solution was stirred at 80 °C for 5 h, after which TLC analysis showed a mixture of protodesilylated 24 and intermediate 23. The solution was cooled to room temperature, diluted with ethyl acetate/hexanes, and washed successively with 1.0 N HCl, saturated potassium bicarbonate, and brine. The resulting organic layer was dried over sodium sulfate, concentrated, and purified by chromatography on SiO$_2$ (30% EtOAc/hexanes to afford first 24 as a yellow oil (12 mg, 0.027 mmol, 35% yield) followed by 23 as a yellow oil (22 mg, 0.042 mmol, 56% yield). Resubjecting purified silanol 23 to the reaction conditions lead rapidly to the generation of protodesilylated product 24.

(1R, 2’R, 5’R, 2’’R)-tert-Butyl-[1-(5’-(2’’-[3’’-(4-methoxybenzyloxy)-2’’-methylpropyl]-[1,3]-dithian-2-ylmethyl)-tetrahydrofuran-2-yl)-prop-2-ynyloxy]-dimethylsilane (SI-3). To a solution of propargyl alcohol 24 (0.330 g, 0.733 mmol) and 2,6-lutidine (255 µL, 2.20 mmol, 3 eq.) in dichloromethane (10 mL) at –78 °C was added TBSOTf (210 µL, 0.92 mmol, 1.25 eq.). The resulting solution was allowed to slowly warm to room temperature. After 45 min the reaction was diluted with EtOAc/hexanes and sodium bicarbonate. The layers are separated, and the organic layer was dried over sodium sulfate, concentrated in vacuo, and purified by chromatography on SiO$_2$ to afford silyl ether SI-3 (0.402 g, 0.713 mmol, 97% yield): [α]$_D^{27.0}$ = –1.10 (c 3.84, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) [0] 7.29 (d, $J$ = 8.5 Hz, 2H), 6.89 (d, $J$ = 8.5 Hz, 2H), 4.46 (app s, 2H), 4.37 (dd, $J$ = 2.0, 5.6 Hz, 1H), 4.30 (m, 1H), 4.04 (m, 1H), 3.81 (s, 3H), 3.39 (ABX, $J$ = 5.2, 9.2 Hz, 1H), 3.30 (ABX, $J$ = 6.8, 9.2 Hz, 1H), 2.79 (m, 4H), 2.34 (d, $J$ = 2 Hz, 1H), 2.29 (ABX, $J$ = 5.6, 16.0 Hz, 1H), 2.23–2.02 (m, 5H), 1.94 (m, 3H), 1.73 (m, 1H), 1.56 (m, 1H), 1.09 (d, $J$ = 6.8 Hz, 3H), 0.91 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.0, 130.9, 129.1, 113.6, 83.4, 81.0, 76.8, 75.9, 73.1, 72.4, 66.1, 55.2, 52.7, 44.8, 42.3, 33.9, 30.2, 27.9, 26.3, 26.2, 25.8, 25.0, 19.9, 18.2, –4.7, –5.0; IR (thin film, NaCl) 3595 (d), 3291, 2953, 2930, 2904, 1612, 1513, 1463, 1442, 1361, 1301, 1248, 1172, 1088, 1038, 1006, 963, 938, 908, 838, 779, 666 cm$^{-1}$; mass spectrum, calcd for C$_{36}$H$_{48}$O$_4$S$_2$Si 587.2661 m/z (M+Na)$^+$; observed, 587.2668 m/z.
(2R, 5R, 1’R, 2’’S)-3-(2-(5-[1’-(tert-Butyldimethylsilanyloxy)-prop-2’-ynyl]-tetrahydrofuran-2-ylmethyl)-[1,3]-dithian-2-yl)-2’’-methylpropan-1’’-ol (SI-4). To a solution of PMB-ether SI-3 (0.110 g, 0.195 mmol) in dichloromethane (8 mL) at 0 °C was added pH = 7 phosphate buffer (200 μL) and DDQ (0.090 g, 0.390 mmol, 2 eq.). The resultant slurry was slowly warmed to room temperature, stirred for 1 h, and diluted with additional dichloromethane and saturated sodium bicarbonate. The organic layer was washed three times with sodium bicarbonate, dried over sodium sulfate, concentrated and purified by chromatography on SiO₂ (20% EtOAc/hexanes to afford alcohol SI-4 (0.084 g, 0.189 mmol, 97% yield) as a clear oil: [ŋ]D²⁷⁰-8.10 (c 0.54, CHCl₃); HNMR (400 MHz, CDCl₃) δ 4.36 (dd, J = 1.6, 5.6 Hz, 1H), 4.31 (m, 1H), 4.05 (m, 1H), 3.51 (app d, J = 6.4 Hz, 2H), 2.90-2.75 (m, 4H), 2.36 (d, J = 2.4 Hz, 1H), 2.28-2.13 (m, 4H), 2.09-2.02 (m, 2H), 1.98-1.88 (m, 3H), 1.80 (bs, 1H), 1.76 (ABX, J = 5.2, 15, 1H), 1.57 (m, 1H), 1.05 (d, J = 6.8 Hz, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 83.4, 81.1, 76.8, 73.1, 68.6, 66.1, 52.6, 45.0, 42.7, 33.9, 32.6, 27.8, 26.3, 26.2, 25.7, 25.0, 19.5, 18.2, -4.7, -5.0; IR (thin film, NaCl) 3596 (d), 3463, 3308, 2952, 2857, 1471, 1462, 1442, 1423, 1388, 1361, 1276, 1084, 1006, 938, 908, 838, 778, 666 cm⁻¹; mass spectrum, calcd for C₂₂H₄₀O₅S₂Si 467.2086 m/z (M+Na)⁺; observed, 467.2088 m/z.

(2R, 5R, 1’R, 2’’S)-2-(5-[1’-(tert-Butyldimethylsilanyloxy)-prop-2’-ynyl]-tetrahydrofuran-2-ylmethyl)-[1,3]-dithian-2-yl)-2’’-methylpropionaldehyde (25). To a solution of alcohol SI-4 (0.084 g, 0.19 mmol), diisopropylethylamine (57 μL, 0.94 mmol, 5 eq.) and DMSO (134 μL, 1.89 mmol, 10 eq.) in dichloromethane (2 mL) at 0 °C was added solid SO₃·Pyr (75 mg, 0.47 mmol, 2.5 eq.). The solution was stirred for 15 min, diluted with dichloromethane, and quenched via the addition of saturated sodium bicarbonate. The organic layer was separated and dried over sodium sulfate, concentrated, and purified by chromatography through a short pad of silica gel (10% EtOAc/hexanes) to afford nearly pure aldehyde 25 (84 mg, 0.19 mmol, 99% yield) as a yellow oil. The resulting aldehyde was used immediately in the following transformation.
(2R, 5S, 6S, 2'R, 5'S, 1''R)-7-(-2'-(5''-(tert-Butyldimethylsilanyloxy)-prop-2'-'-ynyl)-tetrahydrofuran-2-ylmethyl)-[1,3]-dithian-2-yl)-5-hydroxy-1-(4-methoxybenzoyloxy)-2,6-dimethylheptan-3-one (27). To a solution of methyl ketone 26 (0.110 g, 0.491 mmol, 2.50 eq.) in dry diethyl ether (2.75 mL) at -78 °C was added dicyclohexylboron chloride as a 1.0 M solution in hexanes (0.470 mL, 2.40 eq.). The resulting solution was stirred for 5 min, during which time a fine white precipitate forms. To the suspension was added freshly distilled triethylamine (0.275 mL, 1.964 mmol, 4 eq.) and the resulting mixture was stirred for 1 h, at which time aldehyde 25 was added via cannula as a solution in diethyl ether (3 mL, 1 mL wash). After 25 min methanol (1.5 mL) was added, the solution was warmed to room temperature, and pH = 7 buffer (0.50 mL) and 30% H₂O₂ (0.70 mL) were slowly added. The resulting mixture was stirred for 2 h, diluted with EtOAc/hexanes, and quenched with 1.0M sodium sulfite. The organic layer was dried over sodium sulfate, concentrated in vacuo, and purified via chromatography on SiO₂ (20% EtOAc/hexanes) to afford [4]-hydroxy ketone 27 (0.121 mg, 0.182 mmol, 93% yield) as a single diastereomer: [□]D 27.0 =-21.03 (c 0.92, CHCl₃); ¹H NMR (400 MHz, CDCl₃) [□]7.22 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 4.44 (ABX, J = 14.5 Hz, 14.5 Hz, 1H), 4.41 (ABX, J = 14.5, 14.5 Hz, 1H), 4.39 (dd, J = 2.4, 6.0 Hz, 1H), 4.31 (m, 1H), 4.20 (m, 1H), 4.05 (m, 1H), 3.81 (s, 3H), 3.59 (ABX, J = 8.0, 9.2 Hz, 1H), 3.46 (ABX, J = 5.2, 9.2 Hz, 1H), 3.10 (bs, 1H), 2.90 (m, 1H), 2.82 (m, 4H), 2.63 (ABX, app bs, 1H), 2.62 (ABX, J = 2 Hz, 1H), 2.37 (d, J = 2.4 Hz, 1H), 2.37 (ABX, J = 4.0, 15.0 Hz, 1H), 2.29 (ABX, J = 5.6, 14.8 Hz, 1H), 2.22 (m, 1H), 2.15 (ABX, J = 5.2, 15.2 Hz, 1H), 2.05 (m, 1H), 1.95 (m, 4H), 1.72 (ABX, J = 5.6, 15.2 Hz, 1H), 1.57 (m, 1H), 1.08 (d, J = 6.8 Hz, 3H), 1.01 (d, J = 7.2 Hz, 3H), 0.91 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); ¹3C NMR (100 MHz, CDCl₃) [□]214.6, 159.2, 129.2, 129.3, 113.8, 83.4, 80.9, 76.7, 73.2, 72.9, 71.8, 70.9, 66.1, 55.2, 52.8, 46.7, 46.0, 45.1, 42.1, 34.7, 34.0, 27.8, 26.3, 26.2, 25.7, 25.0, 18.2, 16.5, 13.3, -4.7, -5.0; IR (thin film, NaCl) 3596 (d), 3463, 3306, 2930, 2857, 1709, 1612, 1514, 1462, 1361, 1302, 1249, 1173, 1088, 1036, 838, 779, 666 cm⁻¹; mass spectrum, calcd for C₃₅H₅₀O₆S₂Si 687.3185 m/z (M+Na)⁺; observed, 683.3193 m/z.

Mosher Ester analysis confirms the Felkin diastereomer (shown) was the major product.
(1S, 3S, 4R, 1’S, 2''R, 5''R, 1''''R)-Benzoic acid 1-[2''''-(2''''-[5''''-[(1R)-1''''-(tert-butyldimethylsilylanyloxy)-prop-2''''-ynyl]-tetrahydrofuran-2''''-ylmethyl]-[1,3]-dithian-2''''-yl)-1'-methylthyl]-3-hydroxy-5-(4-methoxybenzylxy)-4-methyl-pentyl Ester (28). To a solution of 1-hydroxy ketone 27 (0.105 mg, 0.158 mmol) and freshly distilled benzaldehyde (0.081 mL, 0.791 mmol, 5 eq.) in THF (2 mL) at -10 °C was added freshly prepared 0.1M samarium (II) iodide in THF (0.400 mL, ca 0.25 eq.). The resulting solution was stirred for 15 min, diluted with EtOAc/hexanes, and washed with saturated sodium bicarbonate. The organic layer was dried over sodium sulfate, concentrated under reduced pressure, and purified by flash column chromatography (30% EtOAc/hexanes) to afford benzoate ester 28 (114 mg, 0.148 mmol, 94% yield) as an inseparable 11:1 mixture of diastereomers: $\delta_{\text{obsd}}^{27.0} -11.90$ (c 1.03, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.08 (d, $J = 7.6$, 2H), 7.58 (app t, $J = 7.6$ Hz, 1H), 7.46 (app t, $J = 8$ Hz, 2H), 7.20 (d, $J = 8.4$ Hz, 2H), 6.82 (d, $J = 8.4$ Hz, 2H), 5.45 (ddd, $J = 3.0$, 3.0, 10.0 Hz, 1H), 4.48 (ABX, $J_x = 11.6$ Hz, 1H), 4.39 (ABX, $J_x = 11.6$ Hz, 1H), 4.34 (dd, $J = 2.0$, 5.6 Hz, 1H), 4.28 (m, 1H), 4.01 (m, 1H), 3.79 (s, 3H), 3.49 (app d, $J = 6.4$ Hz, 2H), 2.81-2.73 (m, 4H), 2.32 (d, $J = 2$ Hz, 1H), 2.26-2.12 (m, 5H), 2.03-1.86 (m, 6H), 1.78 (m, 1H), 1.67 (m, 1H), 1.52 (m, 1H), 1.22 (d, $J = 6.8$ Hz, 3H), 0.94 (d, $J = 7.2$ Hz, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.2, 159.1, 133.0, 130.4, 130.3, 129.8, 129.1, 128.3, 113.7, 83.3, 80.9, 76.6, 76.4, 73.4, 73.2, 72.8, 70.5, 66.0, 55.2, 52.6, 45.0, 42.5, 38.9, 37.0, 34.0, 33.9, 27.7, 26.3, 26.3, 25.7, 24.9, 18.2, 17.2, 14.0, -4.7, -5.0; IR (thin film, NaCl) 3469, 3307, 2955, 2930, 2856, 1713, 1612, 1589, 1514, 1462, 1452, 1423, 1362, 1314, 1255, 1250, 1175, 1096, 1038, 969, 938, 909, 838, 779, 713, 687 cm$^{-1}$; mass spectrum, calcd for C$_{42}$H$_{58}$O$_3$S$_2$Si 793.3604 m/z (M+Na)$^+$; observed, 793.3602 m/z.

Hydrolysis and generation of the corresponding acetonide indicates the newly formed 1,3-diol was anti as anticipated, Mosher analysis indicates no Bz migration occurred.
(1S, 3S, 4R, 1’S, 2’’R, 5’’R, 1’’’R)-Benzoic acid 1-[2’’-(2’’-(5’’- [1’’’-(tert-butyldimethylsilyl oxy)-prop-2’’’-nyl]-tetrahydrofuran-2’’’-ylmethyl)-[1,3]-dithian-2-yl)-1’’-methyl-ethyl)-(5-(4-methoxybenzyl oxy)-4-methyl-3-(triisopropyl- butyldimethylsilanyloxy)-prop-2’’-ynyl]-tetrahydrofuran-2’’-ylmethyl}-[1,3]-penta nyloxoy)-pentyl Ester (SI-5). To a solution of benzoate ester 28 (0.010 g, 0.013 mmol) in dichloromethane (0.200 mL) at –78 °C was added 2,6-lutidine (6 mL, 0.066 mmol, 5 eq.) and TIPS-OTf (4.5 mL, 0.017 mmol, 1.25 eq.). The resulting solution was slowly warmed to room temperature, stirred for 6 h, diluted with EtOAc/hexanes and quenched with saturated sodium bicarbonate. The organic layer was dried over sodium sulfate, concentrated under reduced pressure, and the resulting residue purified by chromatography on SiO2 (5% EtOAc/hexanes) to afford TIPS-ether SI-5 (0.013 mg, 0.013 mmol, 99% Yield) as a yellow oil. [θ]D27.0 –13.20 (c 0.94, CHCl3); 1H NMR (400 MHz, CDCl3) δ 8.00 (d, J = 7.2 Hz, 2H), 7.50 (app t, J = 7.2 Hz, 1H), 7.36 (app t, J = 7.2 Hz, 2H), 7.16 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 5.25 (ddd, J = 2.4, 2.4, 10.0 Hz, 1H), 4.38 (app s, 2H), 4.33 (dd, J = 1.6, 5.6 Hz, 1H), 4.23 (m, 1H), 4.13 (m, 1H), 3.98 (m, 1H), 3.79 (s, 3H), 3.42 (ABX, J = 9.6, 10.0 Hz, 1H), 3.33 (ABX, J = 6.8, 9.6 Hz, 1H), 2.74 (m, 1H), 2.62 (m, 1H), 2.35 (m, 2H), 2.30 (d, J = 1.6 Hz, 1H), 2.23 (ABX, J = 5.2, 15.0 Hz, 1H), 2.18-2.08 (m, 2H), 2.02 (ABX, J = 5.2, 15.0 Hz, 1H), 1.96 (m, 1H), 1.84 (m, 4H), 1.74 (ABX, J = 8.0, 15.0 Hz, 1H), 1.65 (m, 1H), 1.45 (m, 1H), 1.18 (d, J = 6.8 Hz, 3H), 1.04-1.01 (m, 21H), 0.96 (d, J = 6.8 Hz, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 166.2, 158.9, 132.5, 130.9, 130.8, 128.7, 128.5, 128.2, 113.6, 83.4, 80.8, 77.0, 76.6, 73.1, 72.6, 72.6, 70.5, 66.0, 55.2, 52.1, 45.0, 41.1, 39.7, 33.9, 33.4, 33.2, 27.7, 26.3, 26.3, 25.7, 24.9, 18.3, 18.3, 18.2, 17.9, 12.9, 11.6, -4.7, -5.0; IR (thin film, NaCl) 3596 (d) 3308, 2936, 2865, 1716, 1612, 1586, 1514, 1463, 1452, 1423, 1363, 1314, 1249, 1173, 1097, 1070, 882, 838, 779, 712, 678 cm⁻¹; mass spectrum, calcd for C51H82O7S2Si2 949.4938 m/z (M+Na)+; observed, 949.4948 m/z.
(1S, 3R, 4R, 1'S, 2''R, 5''R, 1'''S)-Benzoic acid 1-[2-(2''-{5''-[1'''-((tert-butyl-dimethyl-silyl)oxy)-(E)-3'''-iodo-allyl]-tetrahydro-furan-2''-ylmethyl}-[1,3]dithian-2''-yl]-1'-methyl-ethyl]-5-(4-methoxy-benzyloxy)-4-methyl-3-(triisopropyl-silyl)oxy)-pentyl ester (29). To a solution of alkyn SI-5 (0.100 g, 0.108 mmol) in THF (2 mL) at 0 °C was added trans PdCl2(PPh3)2 (0.005 g, 0.005 mmol, 0.05 eq.) and n-Bu3SnH (0.075 mL, 0.270 mmol, 2.5 eq.). The resulting solution was stirred for 2 hours, warmed to room temperature, and the THF was removed under reduced pressure. The resulting yellow oil was dissolved in dichloromethane (2 mL), cooled to −78 °C, and titrated slowly with a 20 mg/mL I2 solution in dichloromethane until a dark brown color persisted (ca 1 mL). The solution was quenched with 1M sodium sulfite, and the organic phase was washed with saturated sodium bicarbonate, dried over sodium sulfate, and the residue was taken to dryness under reduced pressure, and purified by chromatography on SiO2 (2% EtOAc/Hex) to afford vinyl iodide 29 (90 mg, 0.085 mmol, 79% yield) as a clear oil. 1H NMR analysis of the crude hydrostannylation mixture reveals ca 5:1 mixture of [T] substitution: [T]δ270 = 4.83 (c 1.22, CHCl3); 1H NMR (400 MHz, CDCl3) δ 8.02 (d, J = 8.8 Hz, 2H), 7.51 (app t, J = 8.8 Hz, 1H), 7.36 (app t, J = 8.8 Hz, 2H), 7.16 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 6.58 (dd, J = 5.2, 14.8 Hz, 1H), 6.27 (dd, J = 1.2, 14.8 Hz, 1H), 5.26 (ddd, J = 2.0, 2.0, 9.6 Hz, 1H), 4.38 (app d, J = 2 Hz, 2H), 4.16-4.09 (m, 3H), 3.91 (m, 1H), 3.79 (s, 3H), 3.42 (ABX, J = 8.0, 9.2 Hz, 1H), 3.33 (ABX, J = 6.8, 10.0 Hz, 1H), 2.80-2.70 (m, 3H), 2.64-2.35 (m, 1H), 2.35 (m, 2H), 2.17 (m, 2H), 1.96 (m, 2H), 1.90-1.73 (m, 6H), 1.69-1.55 (m, 2H), 1.37 (m, 1H), 1.19 (d, J = 6.8 Hz, 3H), 1.05-1.02 (m, 21H), 0.96 (d, J = 7.2 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 166.1, 158.9, 145.5, 132.6, 130.9, 130.8, 129.5, 129.7, 128.2, 113.6, 80.5, 77.2, 76.5, 76.5, 72.6, 70.5, 55.2, 52.7, 44.9, 41.3, 39.7, 33.8, 33.4, 33.2, 26.5, 26.4, 26.3, 25.8, 18.3, 18.3, 18.2, 17.9, 12.9, 11.6, -4.8, -4.9; IR (thin film, NaCl) 3596, 3401, 2933, 2863, 1717, 1612, 1586, 1513, 1462, 1452, 1423, 1365, 1314, 1272, 1249, 1173, 1098, 1069, 945, 882, 837, 778, 742, 712, 678, 666 cm−1; calced for C53H43O6Si6S2; 1077.4061 m/z (M+Na)+; observed, 1077.4083 m/z.
(1S, 3R, 4R, 1’S, 2''R, 5''R, 1''''S)-Benzoic acid 1-[2''-(1''''-methylhexa-2''''-ylmethyl)-1''''-methylethyl]-5-(4-methoxybenzoyloxy)-4-methyl-3-(triisopropylsilyloxy)-pentyl ester (31). To a solution of vinyl iodide 29 (0.018 g, 0.017 mmol) and vinylstannane 30 (15 μL, 0.051 mmol, 3 eq.) in DMF (200 μL) was added trans-BnPdCl(PPh₃)$_2$ (0.002 g, 0.002 mmol, 0.10 eq.). The resulting solution was degassed via the freeze-pump-thaw method with argon purge, sealed, and warmed to 65 °C for 16 h. The black solution was diluted with EtOAc/hexanes, washed twice with saturated sodium bicarbonate, dried over sodium sulfate, concentrated under reduced pressure, and purified via chromatography on SiO₂ (5% EtOAc/hexanes) to afford tetrahydrofuran 31 (9 mg, 0.009 mmol, 53% yield) as a clear oil: [α]$_{D}^{27.0}$ = 2.87 (c 0.42, CHCl₃); $^1$H NMR (400 MHz, CDCl₃) δ 8.01 (d, $J = 8.0$ Hz, 2H), 7.50 (app t, $J = 7.6$ Hz, 1H), 7.35 (app t, $J = 7.6$ Hz, 2H), 7.15 (d, $J = 8.4$ Hz, 2H), 6.79 (d, $J = 8.4$ Hz, 2H), 4.45 (dd, $J = 11.2$, 14.4 Hz, 1H), 5.83 (d, $J = 10.8$ Hz, 1H), 5.53 (dd, $J = 5.2$, 14.8 Hz, 1H), 5.26 (app d, $J = 10$ Hz, 1H), 4.37 (app s, 2H), 4.19 (app t, $J = 5.2$ Hz, 1H), 4.12 (m, 2H), 3.91 (m, 1H), 3.79 (s, 3H), 3.41 (ABX, $J = 7.6$, 9.6 Hz, 1H), 3.33 (ABX, $J = 6.4$, 9.6 Hz, 1H), 2.80-2.72 (m, 3H), 2.64-2.60 (m, 1H), 2.36-2.33 (m, 2H), 2.01-1.96 (m, 2H), 1.87-1.58 (m, 2H), 1.87-1.58 (m, 8H), 1.79 (s, 3H), 1.75 (s, 3H), 1.40 (m, 1H), 1.19 (d, $J = 6.8$ Hz, 3H), 1.05-1.01 (m, 21 H), 0.96 (d, $J = 6.8$ Hz, 3H), 0.90 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); $^{13}$C NMR (100 MHz, CDCl₃) δ 166.4, 159.1, 134.7, 132.7, 131.1, 131.0, 130.0, 129.7, 128.9, 128.4, 127.4, 125.1, 113.8, 81.7, 76.4, 75.2, 72.8, 70.7, 55.4, 52.9, 45.3, 41.4, 39.9, 34.3, 33.6, 33.5, 29.8, 27.2, 26.5, 26.5, 26.2, 26.1, 25.1, 18.5, 18.5, 18.1, 13.1, 11.8, -4.4, -4.5; IR (thin film, NaCl) 2930, 2862, 1716, 1611, 1513, 1462, 1376, 1271, 1246, 1096, 1069, 836, 712, 666 cm⁻¹; mass spectrum, calcd for C₅₅H₇₀O₇S₂Si₂ 1005.5564 m/z (M+Na)+; observed, 1005.5590 m/z.

SI-17