Efficient Protiodesilylation of Unactivated C(sp^3)-$SiMe_2Ph$ Bonds using Tetrabutylammonium Fluoride

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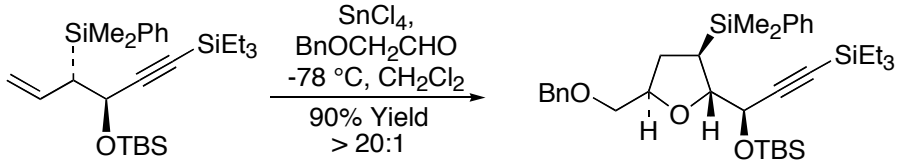
Supporting Information

General Methods: All reaction solvents were purified before use. Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), 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}H NMR) spectra and carbon-13 (^{13}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 for $CHCl_3$) was used as an internal reference for ^{1}H spectra. For ^{13}C spectra, chemical shifts are reported relative to the 77.00 resonance of $CDCl_3$. 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 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 UV-C detector. Integration of the various signals was performed using the reprocessing program within the Dynamax HPLC Method Manager.

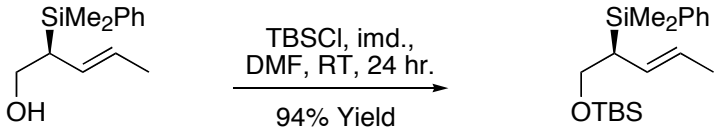


10 **11**

(2S, 3R, 5R, 1'R)-5-Benzyloxymethyl-2-[1'-(*tert*-butyldimethylsilanyloxy)-3'-(triethyl-silanyl)-prop-2'-ynyl]-3-(dimethylphenylsilanyl)-tetrahydrofuran (11). To a –78 °C solution of allylsilane **10** (0.835g, 1.82 mmol) and -benzyloxyacetaldehyde (0.575 mL, 4.10 mmol, 2.25 equiv) in CH_2Cl_2 (10 mL) was slowly added $SnCl_4$ as a 1.0M solution in CH_2Cl_2 (2.0 mL, 1.25 equiv). The resulting solution was stirred for 45 min, quenched by slow addition of Et_3N (2 mL), and allowed to warm to room temperature. Ethyl acetate (EtOAc), 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 aqueous $NaHCO_3$ (until the aqueous layer has pH > 7) and dried over Na_2SO_4. Concentration of the solution *in vacuo* and purification of the crude product by chromatography on SiO_2 afforded tetrahydrofuran **11** (0.999g, 1.64 mmol, 90%) as a clear oil: $[]_D^{27.0}$ –19.5° (*c* 4.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 7.51-7.48 (m, 2H), 7.32-7.21 (m, 8H), 4.53 (AB, *J* = 16 Hz, 1H), 4.51 (bs, 1H), 4.46 (AB, *J* – 16 Hz, 1H), 4.16 (, 1H), 4.00 (dd, *J* = 7.2, 3.6 Hz, 1H), 3.37 (d, *J* = 4.8 Hz, 2H), 2.04-1.92 (m, 2H), 1.49-1.41 (m, 1H), 0.97 (t, *J* = 7.6 Hz, 9H), 0.88 (s, 9H), 0.58 (q, *J* = 8.4 Hz, 6H), 0.33 (s, 3H), 0.30 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.4, 138.1, 133.9, 128.9, 128.2, 127.7, 127.6, 127.4, 106.9, 88.4, 84.4, 78.2, 73.2, 72.4, 66.8, 33.0, 26.7, 25.9, 18.4, 7.4, 4.3, -2.7, -4.6, -4.7, -5.0; IR (thin film, NaCl)

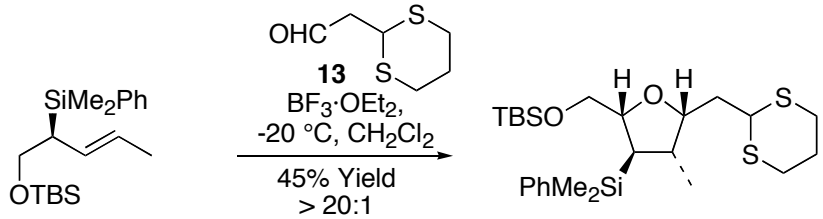
3068, 3029, 2931, 2867, 2956, 2171, 1496, 1462, 1428, 1413, 1362, 1252, 1188, 1081, 1020, 838, 780, 734, 700 cm^{-1}; mass spectrum, calcd for $C_{35}H_{56}O_3Si_3$ 631.3435 *m/z* $(M+Na)^+$; observed, 631.3447 *m/z*. *Anal.* Calcd: C, 69.02; H, 9.27. Found: C, 68.85, H, 9.05.

Note on Stereochemical Proof for 11: Reduction and benzylation of **SI-2** ((1) DIBALH, THF, 23 °C; (2) BnCl, NaH, THF, 12 h) furnishes **11**, thus correlating the relative configuration of **11** with **SI-2** (NOE data for **SI-2** are provided subsequently, *vida infra*).



SI-1 **12**

(S)-{[1-(*tert*-Butyldimethylsilanyloxymethyl)-(*E*)-but-2-enyl]-dimethylsilanyl}-benzene (12). The starting alcohol **SI-1** was prepared in the manner of Davies[1] and Landais[2], its % ee was judged 91% via Mosher ester analysis. To a solution of alcohol **SI-1** (0.570g, 2.62 mmol) in DMF (5 mL) was added imidazole (0.530 g, 7.86 mmol, 3.0 equiv) and *t*-butyldimethylsilylchloride (0.531 g, 3.54 mmol, 1.35 equiv). The resultant solution was stirred for 1 h, diluted with hexanes, and washed twice with aqueous brine. The organic layer was dried over Na_2SO_4, then concentrated to a residue under reduced pressure. Purification of the crude product by chromatography on SiO_2 afforded crotylsilane **12** (0.820g, 2.46 mmol, 94% yield) as a clear oil: $[\alpha]_D^{27.0}$ +1.3° (*c* 0.65, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.35 (m, 3H), 5.36 (m, 1H), 5.26 (m, 1H), 3.69 (m, 2H), 1.94 (ddd, *J* = 5, 7, 9 Hz, 1H), 1.65 (dd, *J* = 1, 6.5 Hz, 3H), 0.86 (s, 9H), 0.30 (s, 3H), 0.28 (s, 3H), -0.02 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 134.0, 129.8, 127.5, 124.1, 64.2, 36.9, 26.0, 18.4, 18.2, -3.6, -4.1, -5.3, -5.4; IR (thin film, NaCl) 3070, 3051, 3015, 2957, 2930, 2887, 2856, 1472, 1463, 1428, 1378, 1362, 1252, 1112, 1090, 1000, 967, 940, 833, 814, 774, 734, 700, 666 cm^{-1}; mass spectrum, calcd for $C_{19}H_{34}OSi_2$ 357.2046 *m/z* $(M+Na)^+$; observed, 357.2048 *m/z*.

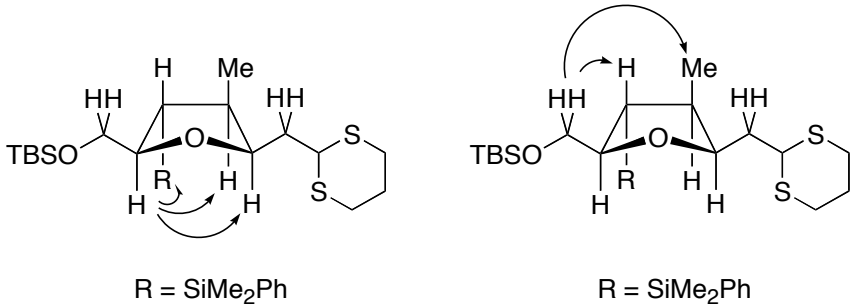


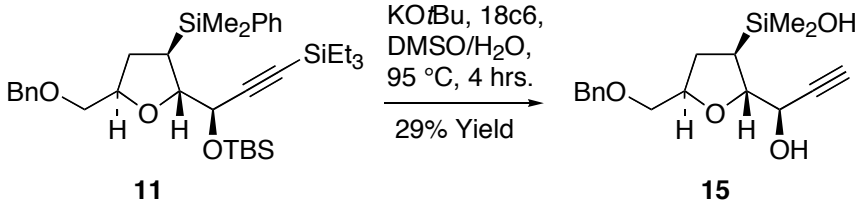
12 **14**

(2S, 3R, 4S, 5R)-2-(*tert*-Butyl-dimethylsilanyloxymethyl)-3-(dimethylphenylsilanyl)-5-[1,3]dithian-2-ylmethyl-4-methyltetrahydrofuran (14): To a –78 °C solution of crotylsilane **12** (0.096 g, 0.29 mmol, 1.0 equiv) and known dithiane **13**[3] (0.095 g, 0.58 mmol, 2.0 equiv) in CH_2Cl_2 (1.5 mL) was added freshly distilled $BF_3{\cdot}OEt_2$ (0.075 mL, 0.58 mmol, 2.0 equiv) dropwise over 5 min. After 45 min the solution was warmed to –45 °C (cryocooler), stirred an addition 45 min, and then quenched with Et_3N (0.300 mL). The solution was diluted with hexanes and EtOAc, washed with saturated aqueous $NaHCO_3$, and the resulting organic layer was dried over Na_2SO_4. Removal of the solvents under reduced pressure and purification of the crude product via chromatography on

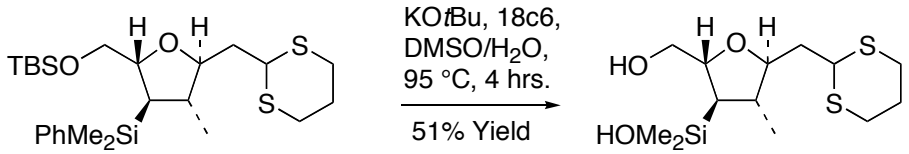
SiO_2 afforded tetrahydrofuran **14** (0.064 g, 0.129 mmol, 45% yield) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) 7.51-7.49 (m, 2H), 7.38-7.33 (m, 3H), 4.22 (dd, *J* = 4.5, 10.5 Hz, 1H), 3.99 (ddd, *J* = 3.5, 7, 11 Hz, 1H), 3.88 (ddd, *J* = 2.5, 5, 7.5 Hz, 1H), 3.56 (dd, *J* = 2.5, 11 Hz, 1H), 3.30 (dd, *J* = 4.5, 11 Hz, 1H), 2.91-2.78 (m, 4H), 2.26-2.19 (m, 1H), 2.14-2.08 (m, 1H), 1.91-1.83 (m, 2H), 1.69-1.63 (m, 1H), 1.20-1.15 (m, 1H), 0.90 (s, 9H), 0.85 (d, *J* = 7 Hz, 3H), 0.35 (s, 3H), 0.33 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 137.6, 133.8, 129.2, 127.9, 82.1, 77.3, 65.9, 44.6, 36.7, 35.1, 33.6, 20.5, 26.2, 26.1, 18.5, 16.3, -4.0, -4.1, -5.2, -5.3; IR (thin film, NaCl) 2952, 2927, 2897, 2854, 1470, 1461, 1426, 1374, 1359, 1274, 1249, 1111, 937, 907, 776 cm^{-1}; mass spectrum, calcd for $C_{25}H_{44}O_2S_2Si_2$ 519.2219 *m/z* $(M+Na)^+$; observed, 519.2215 *m/z*.

The stereochemistry of **14** was assigned via NOE analysis**:**



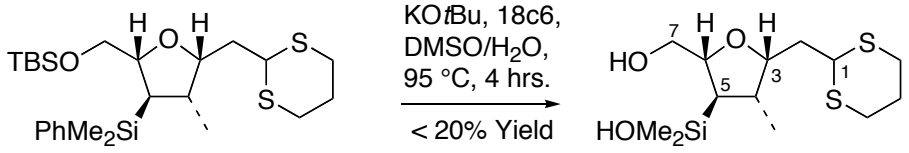


(1R, 2'S, 3'R, 5'R)-1-[5'-Benzyloxymethyl-3'-(hydroxydimethylsilanyl)-tetrahydrofuran-2'-yl]-prop-2-yn-1-ol (15). To a flame dried pressure tube was added **11** (0.150 g, 0.25 mmol, 1.0 equiv), potassium *tert*-butoxide (100 mg), DMSO (1.90 mL), 18-crown-6 (0.065 g, 0.25 mmol, 1.0 equiv), deionized water (100 L), and TBAF as a 1.0 M solution in THF (750 L, 0.25 mmol, 3 equiv). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and stirred at 95 °C for 1.5 h. The resulting dark brown solution was diluted with EtOAc/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on SiO_2 to afford sensitive **15** as a pale yellow oil (0.023g, 0.072 mmol, 29% yield) as a yellow oil: $[]_D^{27.0}$ +18.3° (*c* 0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 7.36 (m, 5H), 4.59 (app d, *J* = 1.2 Hz, 2H), 4.57 (m, 1H), 4.20 (mm, 1H), 4.14 (dd, *J* = 4.8, 8.8, 1H), 3.54 (m, 2H), 3.36 (d, *J* = 5.6, 1H), 3.00 (bs, 1H), 2.50 (d, *J* = 2Hz, 1H), 2.15 (m, 1H), 1.74 (m, 1H), 1.60 (m, 1H), 0.22 (s, 3H), 0.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.0, 128.4, 127.8, 127.7, 83.0, 82.6, 78.7, 74.6, 73.5, 72.1, 64.6, 31.4, 29.3, -0.7, -2.6; IR (thin film, NaCl) 3601, 3581, 3365, 3293, 2956, 2867, 1254, 1061, 1027, 867 cm^{-1}; mass spectrum, calcd for $C_{17}H_{24}O_4Si$ 343.1342 *m/z* $(M+Na)^+$; observed, 343.1342 *m/z*.



14 **17**

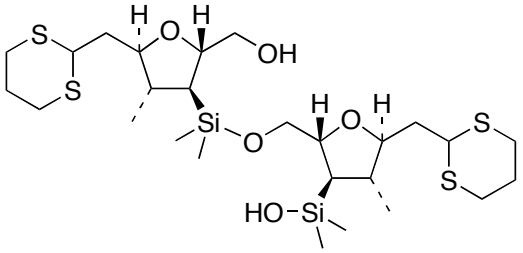
(2S, 3R, 4S, 5S)-[5-[1,3]Dithian-2-ylmethyl-3-(hydroxydimethylsilanyl)-4-methyl-tetrahydrofuran-2-yl]-methanol (17). To a flame dried pressure tube was added **14** (0.040 g, 0.104 mmol, 1.0 equiv), potassium *tert*-butoxide (50 mg), DMSO (0.950 mL), 18-crown-6 (0.030 g, 0.10 mmol, 1.0 equiv) and deionized water (50 L). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and stirred at 95 °C for 4.5 h. The resulting dark brown solution was diluted with EtOAc/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on SiO_2 to afford sensitive **17** as a pale yellow oil (0.017 g, 0.053 mmol, 51% yield) as a yellow oil. Silanol **17** is stable for roughly 45 min at room temperature (mode of decomposition discussed below), and was characterized as efficiently as possible following chromatography: $[\alpha]_D^{27.0}$ -31.0 (*c* 0.67, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) 4.27 (dd, *J* = 3.5, 10 Hz, 1H), 4.08 (m, 1H), 3.67-3.59 (m, 3H), 2.97-2.80 (m, 4H), 2.58 (bs, 2H), 2.14 (m, 1H), 1.96-1.74 (m, 4H), 1.05 (d, *J* = 6 Hz, 3H), 1.00 (dd, *J* = 10.0, 10.0 Hz, 11H). 0.21 (s, 3H), 0.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 82.0, 81.0, 66.2, 45.0, 42.9. 40.1, 39.5, 20.8, 20.3, 26.2, 17.2, -0.2, -1.4; IR (thin film, NaCl) 3400, 2941, 2921, 2897, 1455, 1420, 1383, 1332, 1273, 1251, 1175, 1108, 1045, 885, 870, 836, 796, 762, 664 cm^{-1}; mass spectrum (by the time MS data could be obtained all monomer was consumed): calcd for $C_{26}H_{50}O_5S_4Si_2$ 649.1977 *m/z* $(2M+Na-H_2O)^+$; observed, 649.1978 *m/z*; calcd for $C_{39}H_{74}O_7S_6Si_3$ 953.2964 *m/z* $(3M+Na-2H_2O)^+$; observed, 953.2952 *m/z*.



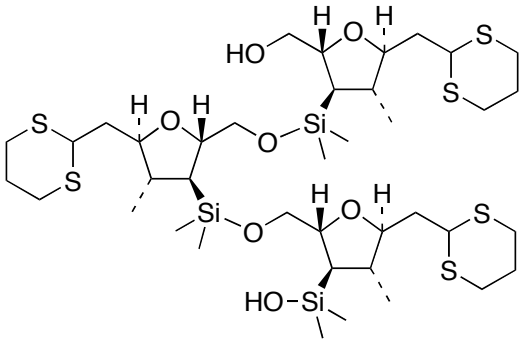
14 **17**

(2S, 3R, 4S, 5R)-[5-[1,3]Dithian-2-ylmethyl-3-(hydroxydimethylsilanyl)-4-methyl-tetrahydrofuran-2-yl]-methanol. Silanol **17** is extremely sensitive to oligomerization and could not be cleanly isolated/characterized following brief exposure to the Hudrlik conditions. ^{1}H NMR/LRMS data of crude mixtures following aqueous workup indicated the presence of silanol monomers, dimers, and trimers. Re-exposure of these mixtures to the reaction conditions gave cleanly **18**, but the individual components of the "silanol mixture" proved too sensitive for chromatographic purification.

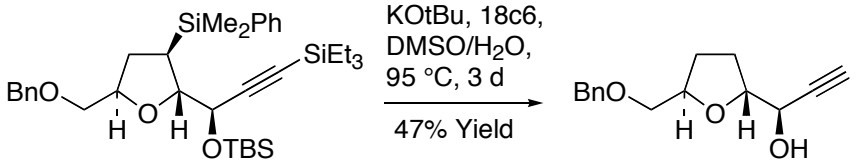
Note on the characterization/attempted isolation of 17/: The oligomerization of **17**/ is envisioned to take place between the Si-OH and C(7)-OH (illustrated below) as the silanols corresponding to **20** and **21** (i.e. **SI-6** and **SI-7**) possessing no free C(7)-OH are completely stable (*vida infra*). This is further consistent with the slower oligomerization/decomposition of **15** (the secondary alcohol is less nucleophilic and less able to react with a silanols).



SI-2

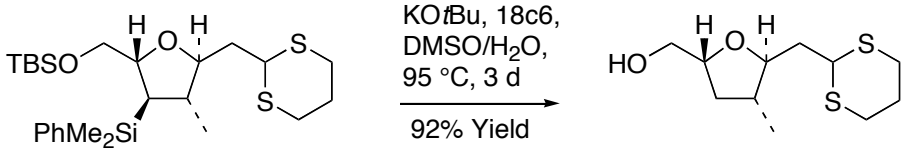


SI-3



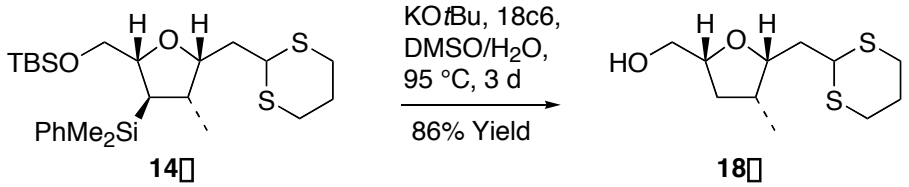
11 **16**

(1R, 2'R, 5'R)-1-(5'-Benzyloxymethyl-tetrahydro-furan-2'-yl)-prop-2-yn-1-ol (16). To a flame dried pressure tube was added **11** (0.195 g, 0.320 mmol, 1.0 equiv), potassium *tert*-butoxide (50 mg), DMSO (0.950 mL), 18-crown-6 (0.085 g, 0.32 mmol, 1.0 equiv), deionized water (50 μL), and TBAF as a 1.0M solution in THF (1.0 mL, 1.0 mmol, 3 equiv). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and stirred at 95 °C for 24 h. The resulting dark brown solution was diluted with EtOAc/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The organic layer was dried over Na_2SO_4, concentrated, and purified by chromatography on SiO_2 to afford **16** as a pale yellow oil (0.037 g, 0.150 mmol, 47% yield) as a yellow oil: $[\alpha]_D^{27.0}$ +0.3° (*c* 3.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 4.61 (AB, *J* = 12 Hz, 1H), 4.57 (AB, *J* = 12 H, 1H), 4.28-4.22 (m, 2H), 4.14 (app q, *J* = 7 Hz, 1H), 3.51 (d, *J* = 5.2 Hz, 2H), 2.51 (bs, 1H), 2.45 (d, *J* = 2 Hz, 1H), 2.12 (m, 1H), 2.06 (m, 1H), 1.85 (m, 1H), 1.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 128.3, 127.6, 82.1, 81.2, 78.8, 73.7, 73.3, 72.4, 65.0, 28.4, 27.7; IR (thin film, NaCl) 3395, 3290, 3059, 3027, 2869, 1496, 1454, 1365, 1308, 1251, 1199, 1072, 1027, 945 cm^{-1}; mass spectrum, calcd for $C_{15}H_{18}O_3$ 269.1154 *m/z* $(M+Na)^+$; observed, 269.1150 *m/z*.



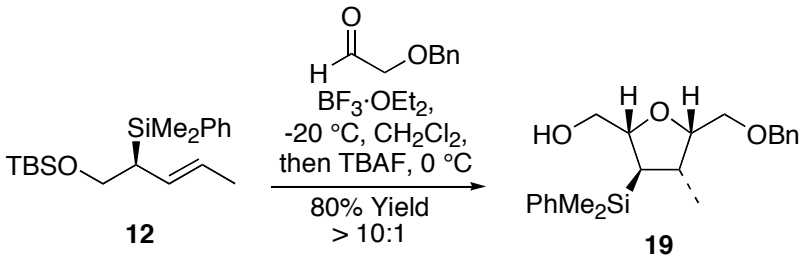
14β **18β**

(2R, 4R, 5S)-(5-[1,3]Dithian-2-ylmethyl-4-methyl-tetrahydrofuran-2-yl)-methanol (18α). To a flame dried pressure tube was added **14α** (0.170 g, 0.341 mmol, 1.0 equiv), potassium *tert*-butoxide (150 mg), DMSO (2.85 mL), 18-crown-6 (0.090 g, 0.34 mmol, 1.0 equiv), deionized water (150 μL), and TBAF as a 1.0M solution in THF (1.2 mL, 1.2 mmol, 3.5 equiv). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and allowed to stir at 95 °C for 24 h. The resulting dark brown solution was diluted with EtOAc/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated aqueous $KHCO_3$, and brine. The organic layer was dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by chromatography on SiO_2 afforded **18α** as a pale yellow oil (0.078 g, 0.315 mmol, 92% yield): $[\alpha]_D^{27.0}$ –29.1° (*c* 2.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.29 (dd, *J* = 4.5, 10.5, 1H), 4.11 (m, 1H), 3.73 (dt, *J* = 3, 9.5 Hz, 1H), 3.68 (ABX, *J* = 3.5, 11.5 Hz, 1H), 3.51 (ABX, *J* = 6. 11.5, 1H), 2.97-2.80 (m, 4H), 2.16-2.07 (m, 2H), 1.96-1.83 (m, 4H), 1.39 (m, 1H), 1.05 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.2, 78.5, 64.9, 44.5, 40.1, 40.1, 36.3, 30.5, 30.0, 25.9, 16.3; IR (thin film, NaCl) 3431, 2952, 1457, 1422, 1378, 1275, 1243, 1188, 1114, 1046, 909, 868, 800, 763 cm^{-1}; mass spectrum, calcd for $C_{11}H_{20}O_2S_2$ 271.0802 *m/z* $(M+Na)^+$; observed, 271.0795 *m/z*.

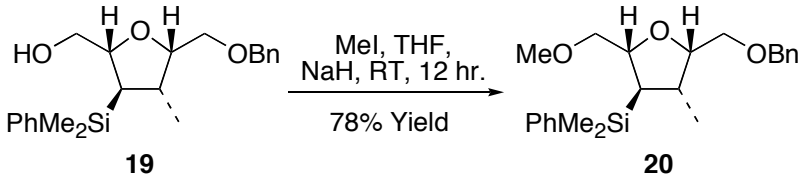


14α **18α**

(2R, 4R, 5R)-(5-[1,3]Dithian-2-ylmethyl-4-methyl-tetrahydrofuran-2-yl)-methanol (18β). To a flame dried pressure tube was added **14β** (0.040 g, 0.080 mmol, 1.0 equiv), potassium *tert*-butoxide (50 mg), DMSO (0.950 mL), 18-crown-6 (0.022 g, 0.080 mmol, 1.0 equiv) deionized water (50 μL), and TBAF as a 1.0 M solution in THF (0.200 mL, .2 mmol, 2.5 equiv). The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and allowed to stir at 95 °C for 24 h. The resulting dark brown solution was diluted with EtOAc/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The organic layer was dried over Na_2SO_4, concentrated, and the crude product was purified by chromatography on SiO_2 to afford **18β** as a pale yellow oil (0.017 g, 0.069 mmol, 86% yield) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.26 (dd, *J* = 5, 8 Hz, 1H), 4.20 (ddd, *J* = 3.5, 7, 10, Hz, 1H), 4.02 (m, 1H), 3.75 (ddd, *J* = 3.5, 6. 9.5 Hz, 1H), 3.51 (m, 1H), 2.98-2.80 (m, 4H), 2.41 (m, 1H), 2.14 (m, 1H), 2.08-2.01 (m, 2H), 1.92-1.87 (m, 1H), 1.80-1.73 (m, 2H), 1.40 (mm, 1H), 0.96 (d, *J* = 7, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.1, 77.7, 65.1, 44.4, 37.4, 36.1, 34.8, 30.7, 30.2, 26.0, 14.7; IR (thin film, NaCl) 3432, 2933, 1454, 1423, 1380, 1276, 1243, 1185, 1032, 908, 868, 796, 757, 663 cm^{-1}; mass spectrum, calcd for $C_{11}H_{20}O_2S_2$ 271.0802 *m/z* $(M+Na)^+$; observed, 271.0794 *m/z*.

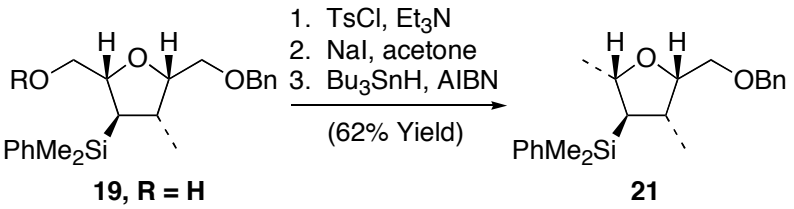


(2S, 3R, 4S, 5S)-[5-Benzyloxymethyl-3-(dimethylphenylsilanyl)-4-methyl-tetrahydrofuran-2-yl]-methanol (19). To a –78 °C solution of crotylsilane **12** (1.36 g, 4.06 mmol, 1.0 equiv), 4 Å molecular sieves (1.22 g), and □-benzyloxyacetaldehyde (1.14 mL, 8.13 mmol, 2.0 equiv) in CH_2Cl_2 (23 mL) was added freshly distilled $BF_3{\cdot}OEt_2$ (1.02 mL, 8.13 mmol, 2.0 equiv) dropwise over 5 min. The solution was maintained at –78 °C for an additional 45 min, quenched with Et_3N (1.50 mL) and warmed to 0 °C. The solution was diluted with hexanes and EtOAc, washed with saturated aqueous $NaHCO_3$, and the resulting organic layer was dried over Na_2SO_4. The solvents were removed under reduced pressure. The residue was taken up in THF (40 mL), cooled to 0 °C, and TBAF as a 1.0M solution in THF (12.1 mL, 12.1 mmol, 3 equiv) was added. After 45 min the THF was removed under reduced pressure and the residue was purified via chromatography on SiO_2 to afford tetrahydrofuran **19** (1.20 g, 3.25 mmol, 80% yield) as a pale yellow oil: $[\alpha]_D^{27.0}$ +13.0 (*c* 1.64, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.47-7.45 (m, 2H), 7.33-7.25 (m, 8H), 4.45 (app d, *J* = 3 Hz, 2H), 3.91 (m, 1H), 3.86 (m, 1H), 3.61 (ABX, *J* = 2, 12 Hz, 1H), 3.48 (ABX, *J* = 4, 10.5 Hz, 1H), 3.41 (ABX, *J* = 6, 10.5 Hz, 1H), 3.17 (ABX, *J* = 4.5, 12.5 Hz, 1H), 2.48 (bs, 1), 2.28 (mm, 1H), 1.27 (m, 1H), 0.85 (d, *J* = 7 Hz, 3H), 0.32 (s, 3H), 0.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 133.8, 129.3, 128.4, 128.0, 127.9, 127.8, 82.3, 80.1, 73.5, 70.5, 64.6, 39.0, 33.8, 15.8, -4.0, -4.2; IR (thin film, NaCl) 3446, 3068, 2957, 2904, 2972, 1721, 1454, 1428, 1251, 1114, 1070, 1028, 903, 839, 812, 735, 700, 653 cm^{-1}; mass spectrum, calcd for $C_{22}H_{30}O_3Si$ 393.1862 *m/z* $(M+Na)^+$; observed, 393.1858 *m/z*.



(2S, 3R, 4S, 5S)-(2,5-Bis-benzyloxymethyl-4-methyl-tetrahydrofuran-3-yl)-dimethyl-phenylsilane (20). To a solution of **19** (0.030 g, 0.081 mmol) in THF (0.75 mL) is added sodium hydride (0.017 g, 0.41 mmol, 5 equiv), and MeI (0.025 mL, 0.41 mmol, 5 equiv). The resultant slurry is stirred overnight, quenched with saturated ammonium chloride (1 mL), diluted with hexanes, and the organic layer is dried over Na_2SO_4. The solvents are removed under reduced pressure and the resulting residue is purified by chromatography on SiO_2 to afford methyl ether **20** as a yellow oil (0.25 g, 0.055 mmol, 78% yield): ^{1}H NMR (500 MHz, $CDCl_3$) □ 7.52-7.47 (m, 2H), 7.38-7.28 (m, 8H), 4.56 (AB, *J* = 12.5 Hz, 1H), 4.48 (AB, *J* = 12.5, 1H), 3.95 (ddd, *J* = 4, 9, 10 Hz, 1H), 3.83 (app q, *J* = 6 Hz, 1h), 3.56 (ABX, *J* = 5.5, 10 Hz, 1H), 5.50 (ABX, *J* = 5.5, 10 Hz, 1H), 3.26 (s, 3H), 3.19 (app s, 1H), 3.18 (app d, *J* = 1 Hz, 1H), 2.28 (m, 1H), 0.99 (dd, *J* = 6.5, 10 Hz, 1H), 0.90 (d, *J* = 7 Hz, 3H), 0.36 (s, 3H), 0.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 138.5, 137.6, 134.0, 129.5, 128.5, 128.1, 128.0, 127.8, 80.7, 80.6, 75.9, 73.6, 70.2, 59.3, 38.3, 35.9, 16.9, -3.8, -

4.2;IR (thin film, NaCl) 3088, 3068, 3028, 2957, 2874, 1496, 1454, 1428, 1250, 1201, 1176, 1112, 1028, 998, 958, 933, 906, 835, 816, 795, 771, 735, 700, 652 cm^{-1}; mass spectrum, calcd for $C_{23}H_{32}O_3Si$ 407.2018 *m/z* $(M+Na)^+$; observed, 407.2026 *m/z*.

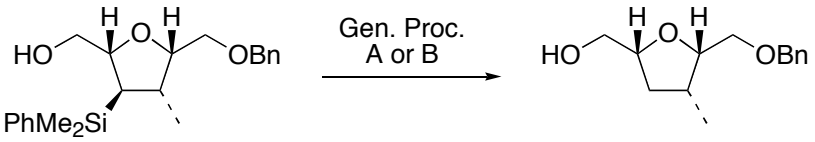


(2S, 3R, 4S, 5S)-(5-Benzyloxymethyl-2,4-dimethyl-tetrahydrofuran-3-yl)-dimethyl-phenylsilane (21). To a solution of alcohol **19** (1.19g, 3.21 mmol) in pyridine (20 mL) was added *p*-toluenesulfonyl chloride (1.22g, 6.42 mmol, 2.0 equiv). The resulting solution was stirred overnight, diluted with ether, and washed successively with 1.0 M $HCl_{(aq)}$ and saturated aqueous $NaHCO_3$. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography on SiO_2 to afford intermediate tosylate **SI-4** (R = Ts) as a white crystalline solid (1.08g, 2.06 mmol, 64% yield). Tosylate **SI-4** (1.00g, 1.90 mmol) was dissolved in acetone (20 mL) and sodium iodide (3.83 g, 25.6 mmol, 10 equiv) was added. The resultant slurry was refluxed (*ca* 75 °C) for 36 h and then the acetone was removed under reduced pressure. The resulting solid was suspended in EtOAc and washed sequentially with sodium sulfite and saturated aqueous $NaHCO_3$. The resulting organic layer was dried over Na_2SO_4, taken to a residue, and the crude product purified by chromatography on silica gel to afford intermediate iodide **SI-5** (R = I, not characterized) as a pale yellow oil (0.910 g, 1.89 mmol, 99% yield). An aliquot of iodide **SI-5** (0.250 g, 0.520 mmol) was dissolved in dry diethyl ether (20 mL) and lithium aluminum hydride was added as a 1.0 M solution in THF (2.6 mL, 2.6 mmol, 5.0 equiv). The resulting solution was stirred for 36 h., cooled to 0 °C, and cautiously quenched by the slow addition of 1.0 M HCl. The resulting slurry was diluted with ether, and the ether layer was washed sequentially with saturated aqueous $NaHCO_3$ and saturated aqueous Rochelle's salt. The resulting organic layer is dried over Na_2SO_4, taken to a residue under reduced pressure, and purified by chromatography on SiO_2 to afford tetrahydrofuran **21** as a pale yellow oil (0.184 g, 0.519 mmol, 99% yield): ^1H NMR (400 MHz, $CDCl_3$) 7.52-7.49 (m, 2H), 7.38-7.27 (m, 8H), 4.61 (AB, *J* = 12 Hz, 1H), 4.49 (AB, *J* = 12 Hz, 1H), 3.88-3.75 (m, 2H), 3.54-3.47 (mm, 2H), 2.25 (m, 1H), 1.50 (d, *J* = 6.4 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.80 (dd, *J* = 6.4, 9.6 Hz, 1H), 0.34 (s, 3H), 0.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 138.2, 137.6, 133.8, 129.2, 128.3, 127.8, 127.8, 127.5, 79.9, 77.4, 73.4, 70.2, 42.5, 38.9, 22.3, 17.3, -4.2, -4.2 IR (thin film, NaCl) 3068, 2964, 2867, 1496, 1454, 1428, 1376, 1250, 1194, 1113, 1070, 1028, 998, 936, 908, 832, 808, 790, 770, 734, 699, 648 cm^{-1}; mass spectrum, calcd for $C_{22}H_{30}O_2Si$ 377.1913 *m/z* $(M+Na)^+$; observed, 377.1920 *m/z*.

General Procedure A (Modified Hudrlik Protocol) for Protiodesilylation of 19-21 (Table 1). A flame dried pressure tube was charged with the dimethylphenylsilyl-substituted tetrahydrofuran, potassium *tert*-butoxide, DMSO, 18-crown-6, deionized water, and with or without added TBAF as a 1.0M solution in THF. The resulting solution was degassed four times using the freeze-pump-thaw method, backfilled with argon, sealed, and stirred at 95 °C for 1-4 d. The resulting dark brown solution was diluted with EtOAc/hexanes (*ca* 1:1) and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The organic layer was dried over Na_2SO_4,

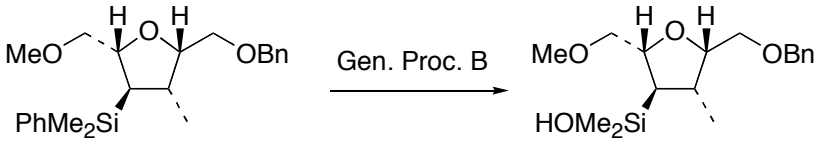
concentrated, and the residue purified by chromatography on SiO_2 to afford the protiodesilylated tetrahydrofurans as yellow oils.

General Procedure B (TBAF-DMF) for Protiodesilylation of 19-21 (Table 1): To a solution of dimethylphenylsilyl-substituted tetrahydrofuran in DMF was added TBAF as a 1.0 M solution in THF. The resulting dark brown solution was stirred at 80 °C for 12 h, cooled to room temperature, diluted with EtOAc/hexanes, and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The resulting organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by chromatography on SiO_2 to afford the protiodesilylated tetrahydrofuran products as yellow oils.



19 **22**

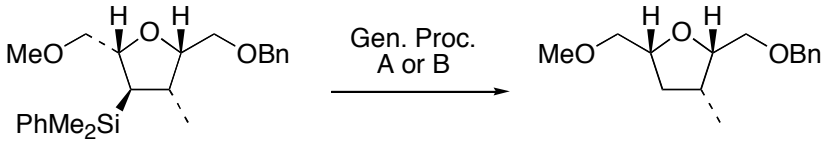
(2S, 3R, 4S, 5S)-(5-Benzyloxymethyl-2-methoxymethyl-4-methyl-tetrahydro-furan-3-yl)-dimethyl-phenyl-silane (22). General Procedure A: 19 (0.025 g, 0.070 mmol, 1.0 equiv), KO*t*Bu (0.050 g), 18-crown-6 (0.019 g, 0.070 mmol, 1.0 equiv), DMSO (0.950 mL), H_2O (50 μL), TBAF soln. (none added) affords **22** (0.015 g, 0.907 mmol, 91% yield). **General Procedure B: 19** (0.050 g, 0.135 mmol, 1.0 equiv), TBAF soln. (0.680 mL, 0.680 mmol, 5 equiv), DMF (1 mL) affords **22** (0.027 g, 0.112 mmol, 83% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 4.55 (app s, 2H), 4.10-4.05 (m, 2H), 3.84 (ddd, *J* = 2.5, 4, 11.5 Hz, 1H), 3.60 (ABX, *J* = 4, 10.5 Hz, 1H), 3.53 (ddd, *J* = 4, 7.5, 11.5 Hz, 1H), 3.47 (ABX, *J* = 4.5, 10 Hz, 1H), 2.59 (dd, *J* = 4, 7.5 Hz, 1H), 2.49 (m, 1H), 1.96 (m, 1H), 1.70 (m, 1H), 1.04 (d, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 128.4, 127.9, 127.8, 80.0, 79.4, 73.5, 70.9, 64.2, 36.1, 34.7, 14.2; IR (thin film, NaCl) 3436, 3088, 3064, 3031, 2962, 2875, 1496, 1454, 1409, 1380, 1367, 1250, 1207, 1168, 1096, 1068, 1029, 927, 879, 819, 737, 699 cm^{-1}; mass spectrum, calcd for $C_{14}H_{20}O_3$ 259.1310 *m/z* $(M+Na)^+$; observed, 259.1319 *m/z*.



20 **SI-6**

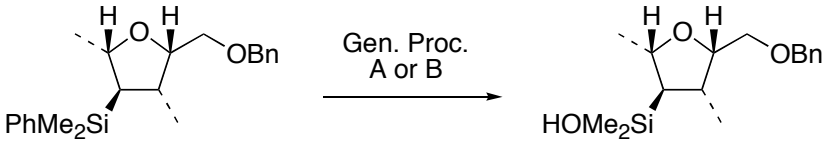
(2S, 3R, 4S, 5S)-(5-Benzyloxymethyl-2-methoxymethyl-4-methyl-tetrahydro-furan-3-yl)-dimethyl-silanol (SI-6). Silanol **SI-6** was isolated (35% Yield, + **20** and **23**) from the protiodesilylation of **22** after exposure to **general procedure B** for 1.5 h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.57 (AB, *J* = 15 Hz, 1H), 4.52 (AB, *J* = 15 Hz, 1H), 4.00 (m, 1H), 3.97 (m, 1H), 3.71 (dd, *J* = 5.5, 11 Hz, 1H), 3.60 (bs, 1H), 3.49 (m, 2H), 3.40 (s, 3H), 3.35 (dd, *J* = 10, 10 Hz, 1H), 2.29 (m, 1H), 1.01 (d, *J* = 9 Hz, 3H), 0.98 (m, 1H), 0.20 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.4, 127.8, 127.6, 80.4, 79.3, 76.9, 73.6, 70.5, 59.4, 40.9, 38.3,

15.8, 0.1, -2.3; IR (thin film, NaCl) 3401, 3030, 2958, 2875, 1496, 1454, 1366, 1252, 1202, 1092, 1028, 882, 837, 795, 738, 698, 654 cm^{-1}; mass spectrum, calcd for $C_{17}H_{28}O_4Si$ 347.1655 *m/z* $(M+Na)^+$; observed, 347.1653 *m/z*.



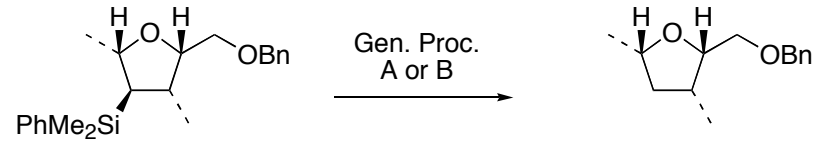
20 **23**

(2S, 3R, 5R)-2-Benzyloxymethyl-5-methoxymethyl-3-methyl-tetrahydrofuran (23). General Procedure A: 20 (0.030 g, 0.078 mmol, 1.0 equiv), KO*t*Bu (0.050 g), 18-crown-6 (0.025 g, 0.095 mmol, 1.2 equiv), DMSO (0.950 mL), H_2O (50 μL), TBAF soln. (none added) affords **23** (0.018 g, 0.072 mmol, 92% yield). **General Procedure B: 20** (0.025 g, 0.073 mmol, 1.0 equiv), TBAF soln. (0.350 mL, 0.350 mmol, 5 equiv), DMF (1 mL) affords **23** (0.015 g, 0.060 mmol, 82% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5H), 4.55 (app q, *J* = 12 Hz, 2H), 4.10-4.04 (m, 2H), 3.53 (app d, *J* = 5 Hz, 2H), 3.48 (ABX, *J* = 6.5, 10 Hz, 1H), 3.42 (ABX, *J* = 4, 10 Hz, 1H), 3.39 (s, 3H), 2.42 (m, 1H), 2.08 (m, 1H), 1.35 (m, 1H), 1.01 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.3, 127.6, 80.3, 77.5, 75.9, 73.4, 70.4, 59.2, 36.6, 35.2, 14.6; IR (thin film, NaCl) 3061, 3031, 2963, 2876, 1497, 1454, 1377, 1365, 1201, 1110, 1097, 1069, 1028, 960, 935, 908, 736, 698 cm^{-1}; mass spectrum, calcd for $C_{15}H_{22}O_3$ 273.1467 *m/z* $(M+Na)^+$; observed, 273.1456 *m/z*.



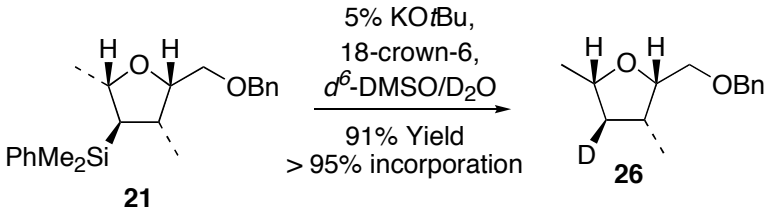
21 **SI-7**

2S, 3R, 4S, 5S)-(5-Benzyloxymethyl-2,4-dimethyl-tetrahydro-furan-3-yl)-dimethyl-silanol (SI-7). Silanol **SI-7** was isolated and characterized (56% Yield + **21** and **24**) after exposure of **20** to general procedure A for 1.5 h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 4.63 (AB, *J* = 12.4 Hz, 1H), 4.52 (AB, *J* = 12.4, 1H), 3.90 (m, 2H), 3.52 (m, 2H), 2.32 (m, 1H), 1.78 (bs, 1H), 1.34 (d, *J* = 5.6 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H), 0.71 (dd, *J* = 8, 10 Hz, 1H), 0.18 (s, 3H), 0.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 128.4, 127.9, 127.6, 80.1, 77.0, 73.5, 70.3, 44.2, 38.3, 22.4, 16.9, -0.7, -1.0; IR (thin film, NaCl) 3400, 2962, 2360, 1454, 1377, 1252, 1098, 875, 736, 697 cm^{-1}; mass spectrum, calcd for $C_{16}H_{26}O_3Si$ 317.1549 *m/z* $(M+Na)^+$; observed, 317.1542 *m/z*.



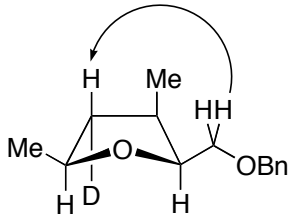
21 **24**

(2S, 3R, 5S)-2-Benzyloxymethyl-3,5-dimethyl-tetrahydrofuran (24). General Procedure A: 21 (0.111 g, 0.313 mmol, 1.0 equiv), KO*t*Bu (0.150 g), 18-crown-6 (0.124 g, 0.470 mmol, 1.50 equiv), DMSO (2.85 mL), H_2O (150 μL), TBAF soln. (none added) affords **24** (0.044 g, 0.200 mmol, 64% yield). **General Procedure B: 21** (0.019 g, 0.054 mmol, 1.0 equiv), TBAF soln. (0.216 mL, 0.216 mmol, 4 equiv), DMF (1 mL) affords **24** (0.010 g, 0.045 mmol, 84% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.62 (AB, *J* = 12 Hz, 1H), 4.52 (AB, *J* = 12 Hz, 1H), 4.03-3.93 (m, 2H), 3.53 (m, 2H), 2.39 (m, 1H), 2.16 (ddd, *J* = 6.4, 7.6, 12 Hz, 1H), 1.28 (d, *J* = 6 Hz, 3H), 1.17 (ddd, *J* = 8, 8.8, 12.4 Hz, 1H), 0.98 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.3, 127.7, 127.5, 80.0, 74.8, 73.4, 70.6, 41.9, 35.7, 21.6, 15.1; IR (thin film, NaCl) 2966, 2927, 2860, 1454, 1380, 1098, 1069, 1028, 735, 697 cm^{-1}; mass spectrum, calcd for $C_{14}H_{20}O_4$ 243.1361 *m/z* $(M+Na)^+$; observed, 243.1362 *m/z*.

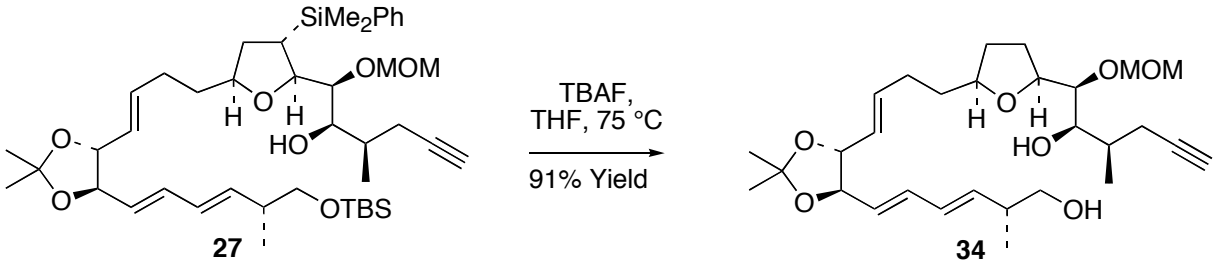


(2S, 3R, 4R, 5S)-2-Benzyloxymethyl-3,5-dimethyl-4-deutero-tetrahydrofuran (26). General Procedure A: 21 (0.030 g, 0.085 mmol, 1.0 equiv), KO*t*Bu (0.050 g), 18-crown-6 (0.040 g, 0.170 mmol, 2.0 equiv), DMSO d^6 (0.950 mL), D_2O (50 μL), TBAF soln. (none added) affords **26** (0.017 g, 0.077 mmol, 91% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.62 (AB, *J* = 12 Hz, 1H), 4.53 (AB, *J* = 12 Hz, 1H), 4.03-3.94 (m, 2H), 3.52 (m, 2H), 2.38 (m, 1H), 1.28 (d, *J* = 6 Hz, 3H), 1.19 (dd, *J* = 8, 8.4 Hz, 1H). 0.98 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.3, 127.7, 80.0, 74.8, 73.4, 70.6, 41.6 (t, *J* = 19.7 Hz), 35.6, 21.6, 15.1; IR (thin film, NaCl) 2968, 2917, 2862, 1727, 1492, 1454, 1381, 1361, 1280, 1199, 1096, 1096, 1022, 736, 697 cm^{-1}; mass spectrum, calcd for $C_{14}H_{19}DO_2$ 244.1424 *m/z* $(M+Na)^+$; observed, 244.1423 *m/z*.

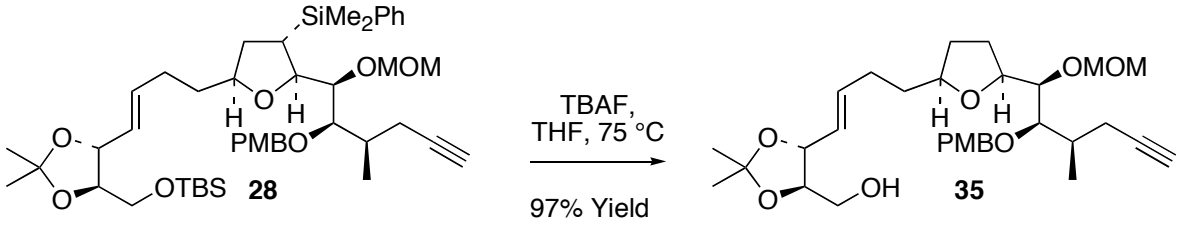
The stereochemistry of **26** was assigned via NOE analysis, selected NOEs for **26** are summarized below:



26

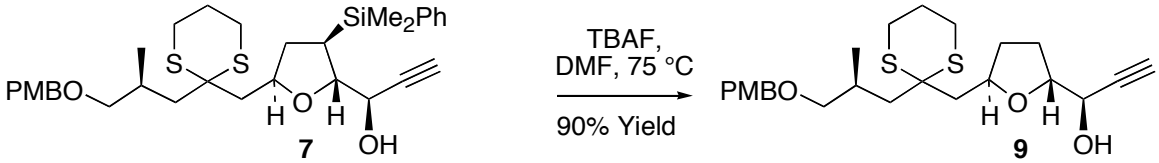


(2R, 4'R, 5'R, 2'''S, 5'''S, 1''''S, 2''''R, 3''''R)-6-(5'-{4''-[5'''-(2''''-Hydroxy-1''''-methoxymethoxy-3''''-methyl-hex-5''''-ynyl)-tetrahydrofuran-2'''-yl]-(*E*)-but-1''-enyl}-2',2'-dimethyl-[1',3']dioxolan-4'-yl)-2-methyl-(*E,E*)-hexa-3,5-dien-1-ol (34). To **27** (5 mg, 0.0066 mmol) in a 1.5 dram vial was added TBAF (0.26 mL of 1.0 M THF solution, 0.26 mmol). The reaction vial was capped, stirred at room temperature for 1 h and placed in a 60 °C oil bath. After 3 h, more TBAF (0.13 mL of 1.0 M THF solution, 0.13 mmol) was added. After 5 h, the reaction was quenched with pH 7 phosphate buffer (10 mL) and ether (10 mL). The layers were separated and the aqueous layer was extracted with ether (3x 10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by preparative TLC to afford **34** as a thin film (3 mg, 91 %): $[\alpha]_D^{27.0}$ -9.0 (*c* 0.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (dd, *J* = 10.5, 15.0 Hz, 1H), 6.13 (dd, *J* = 10.5, 15.0 Hz, 1H), 5.78 (dt, *J* = 6.5, 15.0 Hz, 1H), 5.61 (dd, *J* = 8.0, 15.0 Hz, 1H), 5.54 (dd, *J* = 7.0, 15.5, 1H), 5.42 (dd, *J* = 7.0, 15.5 Hz, 1H), 4.99 (d, *J* = 6.5 Hz, 1H), 4.71 (d, *J* = 6.5 Hz, 1H), 4.01-4.12 (m, 3H), 3.80-3.60 (m, 1H), 3.59 (dd, *J*= 1.0, 7.0 Hz, 1H), 3.53 (dd, *J* = 5.5, 10.5 Hz, 1H), 3.38-3.47 (m, 1H), 3.42 (s, 3H), 3.28-3.35 (m, 1H), 2.60-2.68 (m, 1H), 2.49 (ddd, *J* = 2.5, 3.5, 16.5 Hz, 1H), 2.38-2.45 (m, 1H), 2.32 (ddd, *J* = 2.5, 7.5, 16.5 Hz, 1H), 2.06-2.20 (m, 2H), 1.88-2.00 (m, 3H), 1.96 (t, *J* = 2.5 Hz, 1H), 1.42-1.70 (m, 5H), 1.43 (s, 6H), 1.05 (d, *J* = 6.5 Hz, 3H), 1.02 (d, *J*= 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 136.1, 134.0, 130.2, 127.3, 126.0, 108.8, 97.4, 82.2, 81.8, 81.1, 79.0, 78.8, 75.3, 69.5, 67.3, 56.3, 39.7, 35.2, 35.0, 30.5, 26.7, 29.1, 28.0, 27.1, 27.0, 22.0, 16.3, 15.7; IR (thin film, NaCl) 3453, 3308, 2927, 2874, 1456, 1379, 1237, 1031, 886 cm^{-1}; mass spectrum, calcd for $C_{29}H_{46}O_7$ 529.3141 *m/z* $(M+Na)^+$; observed, 529.3148 *m/z*.

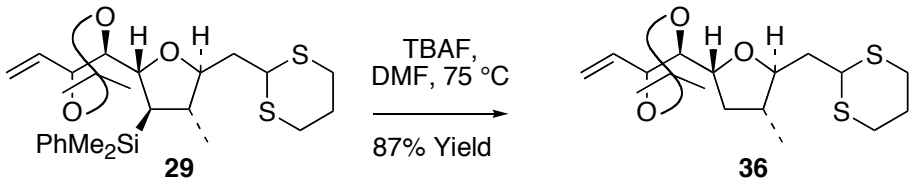


(4R, 5R,2''S, 5''S, 1'''R, 2'''R, 3'''R)-[5-(4'-{5''-[2'''-(4''''-Methoxy-benzyloxy)-1'''-methoxymethoxy-3'''-methyl-hex-5'''-ynyl]-tetrahydrofuran-2''-yl}--(*E*)-but-1'-enyl)-2,2-dimethyl-[1,3]dioxolan-4-yl]-methanol (35). To a room temperature solution of **28** (15 mg, 0.0189 mmol) in THF (190 μL) was added TBAF (0.6 mL of 1.0 M THF solution, 0.6 mmol). The reaction vessel was fitted with a reflux condenser and placed in a 90 °C oil bath. After 4 h, more TBAF (0.2 mL of 1.0 M THF solution, 0.2 mmol) was added. After 11 h, the reaction was quenched with pH 7 phosphate buffer (10 mL) and ether (10 mL). The layers were separated and the aqueous layer was extracted with ether (3x 10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was

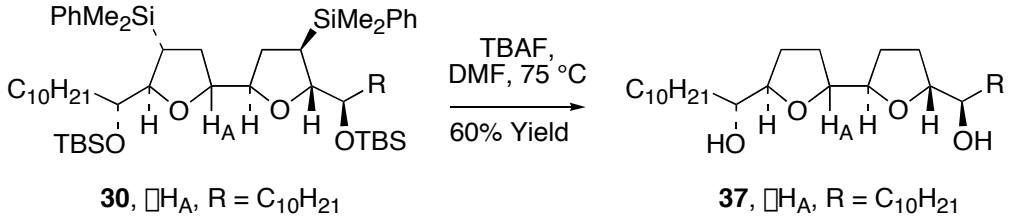
purified by column chromatography to afford (**35**) as a colorless oil (10 mg, 97%): $[\alpha]_D^{27.0}$ +0.4 (*c* 0.56, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.84 (dt, *J* = 6.8, 15.2 Hz, 1H), 5.45 (dd, *J* = 8.0, 15.2 Hz, 1H), 4.92 (d, *J* = 6.4 Hz, 1H), 4.73 (d, *J* = 7.2 Hz, 1H), 4.59 (d, *J* = 10.8 Hz, 1H), 4.53 (d, *J* = 10.4 Hz, 1H), 4.25 (dd, *J* = 8.4, 8.4 Hz, 1H), 4.05 (dd, *J* = 6.8, 14.4 Hz, 1H), 3.53-3.84 (m, 3H), 3.78 (s, 3H), 3.62 (dd, *J* = 3.2, 6.8 Hz, 1H), 3.52-3.60 (m, 1H), 3.38-3.42 (m, 1H), 3.40 (s, 3H), 2.28-2.40 (m, 2H), 2.05-2.24 (m, 4H), 1.97 (t, *J* = 2.8 Hz, 1H), 1.76-1.97 (m, 2H), 1.60-1.76 (m, 2H), 1.40-1.60 (m, 2H), 1.42 (s, 3H), 1.41 (s, 3H), 1.11 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 136.6, 130.6, 129.4, 126.6, 113.6, 108.8, 97.6, 83.2, 82.2, 81.0, 79.7, 79.8, 78.6, 78.2, 73.3, 69.7, 60.7, 56.1, 55.2, 31.1, 33.8, 31.0, 29.1, 28.0, 27.1, 26.9, 21.9, 16.3; IR (thin film, NaCl) 3465, 3293, 2984, 2934, 1613, 1514, 1248, 1035 cm^{-1}; mass spectrum, calcd for $C_{31}H_{46}O_8$ 569.3090 *m/z* $(M+Na)^+$; observed, 569.3082 *m/z*.



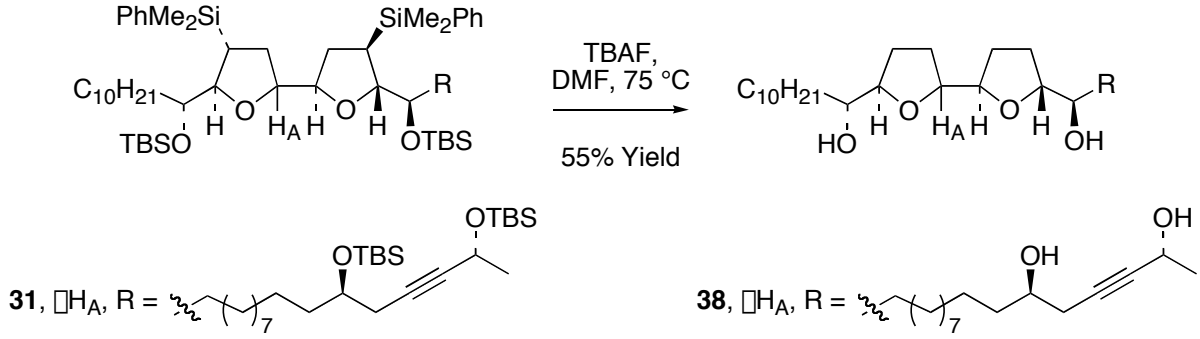
(2*S*, 3*R*, 2'*S*, *1''R*)-1-(5-{2-[3'-(4-Methoxybenzyloxy)-2'-methylpropyl]-[1,3]-dithian-2'-ylmethyl}-tetrahydrofuran-2-yl)-prop-2''-yn-1''-ol (9). To a solution of **7** (0.503 g, 0.863 mmol) in DMF (10 mL) was added TBAF as a 1.0 M solution in THF (3.45 mL, 4 equiv). The resulting dark brown solution was stirred at 80 °C for 16 h, after which TLC analysis showed *ca* a 1:1 mixture of protiodesilylated **9** and intermediate silanol. An additional aliquot of TBAF/THF (1.75 mL, 2 equiv) was added and the resulting solution was stirred for 6 h, cooled to room temperature, diluted with EtOAc/hexanes and washed successively with 1.0 *N* HCl, saturated $KHCO_3$, and brine. The resulting organic layer was dried over Na_2SO_4, concentrated, and the residue purified by chromatography on SiO_2 (40% EtOAc/hexanes to afford **9** as a pale yellow oil (349 mg, 0.776 mmol, 90% yield): $[\alpha]_D^{27.0}$ -1.7° (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 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), 3.25 (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); ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{24}H_{34}O_4S_2$ 473.1796 *m/z* $(M+Na)^+$; observed, 473.1806 *m/z*.



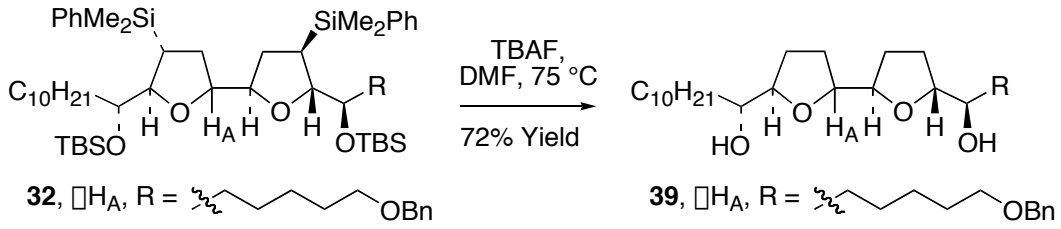
(4S, 5R, 2'R, 4'R, 5'S)-4-(5'-[1,3]Dithian-2''-ylmethyl-4'-methyl-tetrahydrofuran-2'-yl)-2,2-dimethyl-5-vinyl-[1,3]dioxolane (36). Prepared via general procedure B (Table 1); **29** (0.012 g, 0.025 mmol), TBAF soln. (0.150 mL, 0.150 mmol, 6 equiv), DMF (1 mL) affords **36** (0.0075 g, 0.0218 mmol, 87% yield) as a clear oil: $[\alpha]_D^{27.0}$ –5.0° (*c* 0.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.93 (ddd, *J* = 8.5, 10, 17 Hz, 1H), 5.29 (dd, *J* = 1.5, 10 Hz, 1H), 5.27 (dd, *J* = 1.5, 17 Hz, 1H), 4.49 (dd, *J* = 6.5, 8.5 Hz, 1H), 4.31 (dd, *J* = 5.5, 9.5 Hz, 1H), 4.08 (dd, *J* = 6.5, 6.5 Hz, 1H), 3.96 (ddd, *J* = 6, 6, 10 Hz, 1H), 3.50 (m, 1H), 2.96-2.78 (m, 4H), 2.13 (m, 2H), 1.88 (m, 4H), 1.55 (s, 3H), 1.41 (s, 3H), 1.32 (m, 1H), 1.04 (d, *J* = 7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 119.1, 109.4, 81.7, 81.3, 79.2, 76.6, 44.2, 40.3, 39.7, 37.4, 30.4, 29.8, 27.8, 26.0, 25.7, 16.5; IR (thin film, NaCl) 2976, 2951, 2929, 2897, 1457, 1423, 1379, 1250, 1214, 1164, 1095, 1060, 1011, 925, 872, 666 cm^{-1}; mass spectrum, calcd for $C_{17}H_{28}O_3S_2$ 367.1378 *m/z* $(M+Na)^+$; observed, 367.1372 *m/z*.



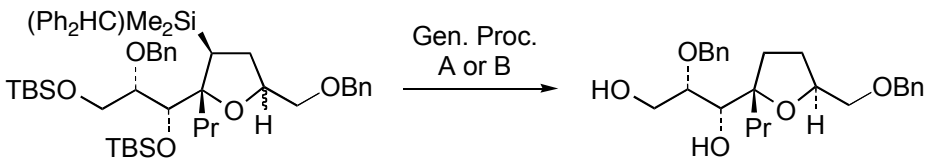
(2R, 2R', 5R, 5R')-5,5'-bis[(1R)-1-hydroxyundecyl] octahydro-2,2'bifuran (37). General Procedure B: 30 (0.044 g, 0.045 mmol), TBAF soln. (0.450 mL, 0.450 mmol, 10 equiv), DMF (0.450 mL), 90 °C, 20 h, affords **37** (0.013 g, 0.027 mmol, 60% yield): $[\alpha]_D^{27.0}$ +9.2° (*c* 01.41, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.92-3.82 (m, 4H), 3.42-3.38 (m, 2H), 2.02-1.96 (m, 4H), 1.80-1.22 (m, 42H), 0.89 (t, *J* = 7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 83.4, 82.0, 74.3, 33.7, 32.2, 30.0, 29.9, 29.9, 29.9, 29.9, 29.2, 28.6, 25.9, 22.9, 14.4; IR (thin film, NaCl) 3437, 2923, 2854, 1782, 1466, 1378, 1303, 1062, 955 cm^{-1}; mass spectrum, calcd for $C_{30}H_{58}O_4$ 505.4223 *m/z* $(M+Na)^+$; observed, 505.4232 *m/z*.



(2R, 2'R, 5R, 5'R)-5-[(1R)-1-hydroxyundecyl]-5'-[(1R, 12R, 16R)-1,12,16-trihydroxyheptadec-14-yne] (38). General Procedure B: **32** (0.026 g, 0.018 mmol, 1.0 equiv), TBAF soln. (0.180 mL, 0.180 mmol, 10 equiv), DMF (0.180 mL) affords **40** (0.006 g, 0.010 mmol, 55% yield): $[\alpha]_D^{27.0}$ +17° (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.54 (tq, *J* = 2, 6.5 Hz, 1H), 3.92-3.82 (m, 4H), 3.77-3.71 (m, 1H), 3.41-3.37 (m, 2H), 2.72-2.28 (bs, 4H), 2.46 (A of ABxx', J_{AB} = 16.5 Hz, J_{ax} = 4.5 Hz, $J_{ax'}$ = 2.0 Hz, 1H), 2.33 (B of ABxx', J_{AB} = 16.5 Hz, J_{Bx} = 6.5 Hz, $J_{Bx'}$ = 2.0 Hz, 1H), 2.02-1.92 (m, 4H), 1.72-1.60 (m, 4H), 1.56-1.23 (m, 41H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 85.1, 83.5, 83.4, 82.1, 82.1, 81.1, 74.3, 70.1, 58.6, 36.4, 33.7, 33.7, 32.2, 30.0, 29.9, 29.9, 29.9, 29.7, 29.6, 29.5, 29.5, 29.5, 29.4, 29.3, 28.6, 27.9, 25.9, 25.7, 25.7, 24.9, 22.9, 14.4; IR (thin film, NaCl) 3435, 2915, 2850, 1466, 1316, 1069, 959, 860 cm^{-1}; mass spectrum, calcd for $C_{36}H_{66}O_6$ 617.4757 *m/z* $(M+Na)^+$; observed, 617.4760 *m/z*.



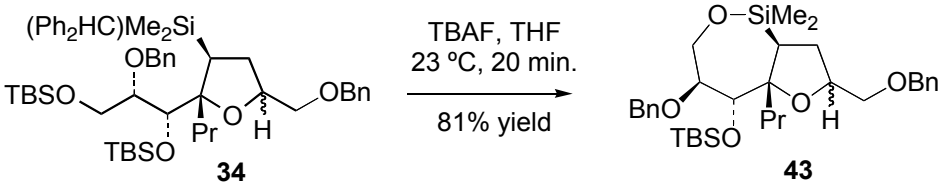
(2S, 2'R, 5R, 5'R)-5-[(1R)-1-(hydroxy)undecyl]-5'-[(1R)-1-(hydroxy)-6-(phenylmethoxy)hexyl]octahydro-2,2'-bifuran (39). To a solution of **32** (0.064 g, 0.063 mmol) in DMF (2.0 mL) was added TBAF (0.20 mL of a 1.0 M solution in THF, 0.20 mmol). The resulting solution was stirred at 75 °C for 16 h. At this time, TLC indicated the presence of intermediate products, and additional TBAF solution (0.20 mL, 0.20 mmol) was added. The reaction mixture was stirred at 75 °C for an additional 56 h with aliquots of TBAF solution (0.20 mL, 0.20 mmol) added three times during this period. The reaction mixture was cooled room temperature and diluted with EtOAc (5 mL). The resulting solution was washed with 15 mL portions of 1.0 M aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated to an amber oil. Purification of the product by silica gel chromatography (40% EtOAc/hexanes) afforded **39** (0.023 g, 72%) as a clear oil: $[\alpha]_D^{25.0}$ +0.9° (*c* 0.58, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (m, 5H), 4.50 (s, 2H), 4.04 (ddd, *J* = 5.0, 5.5, 7.5 Hz, 1H), 3.96 (td, 4.9, 6.8 Hz, 1H), 3.84 (q, *J* = 6.3 Hz, 1H), 3.81 (q, *J* = 6.6 Hz, 1H), 3.48 (t, *J* = 6.6 Hz, 2H), 3.39 (q, *J* = 5.9 Hz, 1H), 3.37 (dt, *J* = 4.9, 8.0 Hz, 1H), 2.33 (bs, 2H), 2.05 (m, 1H), 2.01-1.91 (m, 3H), 1.89-1.83 (m, 1H), 1.81-1.73 (m, 1H), 1.73-1.67 (m, 2H), 1.64 (app quint. *J* = 6.3 Hz, 2H), 1.59-1.33 (m, 9H), 1.26 (bs, 13H), 0.89 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 128.4, 127.6, 127.5, 83.2, 82.7, 81.6, 80.9, 74.6, 73.8, 72.9, 70.4, 34.2, 33.5, 31.9, 29.8, 29.7, 29.6, 29.4, 28.9, 28.2, 28.0, 28.3, 27.1, 26.2, 25.8, 25.5, 22.7, 14.1; IR (thin film, NaCl) 4215, 3019, 2978, 1523, 1477, 1422, 1218, 1046, 929, 859, 772, 667, 623 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{32}H_{54}O_5$ $(M+Na)^+$ 541.3869, observed 541.3884.



34
dr 3.3:1

42

(1*R*, 2*S*, 2'*S*, 5'*S*)-2-Benzyloxy-1-(5'-benzyloxymethyl-2'-*n*-propyl-tetrahydrofuran-2'-yl)-propane-1,3-diol (40). General Procedure A: **33** (0.022 g, 0.026 mmol, 1.0 equiv, dr 3.3:1), KO*t*Bu (0.017 g), 18-crown-6 (0.007 g, 0.026 mmol, 1.0 equiv), DMSO (0.370 mL), H_2O (0.020 mL), TBAF soln. (0.156 mL) affords **40** (0.006 g, 0.016 mmol, 61%) along with a diastereomeric diol (0.002 g, 0.004 mmol, 15%); combined yield 76%. **General Procedure B:** **33** (0.027 g, 0.031 mmol, 1.0 equiv, dr 3.3:1), TBAF soln. (0.218 mL, 0.218 mmol, 7 equiv), DMF (0.5 mL) affords **40** (0.008 g, 0.019 mmol, 61%) along with a diastereomeric diol (0.002 g, 0.005 mmol, 16%); combined yield 77%. Data for **40**: $[\alpha]_D^{26}$ +19° (*c* 0.47, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.5 Hz, 3H), 1.24-1.39 (m, 2H), 1.43 (td, *J* = 14.0, 5.0 Hz, 1H), 1.56-1.66 (m, 2H), 1.87-1.93 (m, 1H), 1.93-1.99 (m, 1H), 2.18 (ddd, *J* = 13.0, 10.0, 8.0 Hz, 1H), 2.81 (d, *J* = 2.0 Hz, OH), 3.43 (br s, OH), 3.46 (ABX, J_{AB} = 10.0 Hz, J_{AX} = 6.7 Hz, 1H), 3.49 (ABX, J_{AB} = 10.0 Hz, J_{BX} = 4.3 Hz, 1H), 3.58-3.64 (m, 2H), 3.82 (br m, 2H), 4.16 (dtd, *J* = 9.5, 6.0, 4.0 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 4.55 (AB, *J* = 12.0 Hz, 1H), 4.57 (AB, *J* = 12.0 Hz, 1H), 4.76 (d, *J* = 12.0 Hz, 1H), 7.26-7.37 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.20, 137.77, 128.54, 128.35, 128.06, 127.99, 127.58, 127.57, 86.89, 79.22, 78.81, 77.12, 73.28, 72.83, 72.00, 62.24, 36.90, 32.66, 28.98, 16.62, 14.69; IR (thin film) 3436, 2957, 2928, 2871, 1454, 1072, 735, 698 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{34}O_5$ 437.2304 *m/z* $(M+Na)^+$; observed, 437.2309 *m*/z.



34
dr 3.3:1

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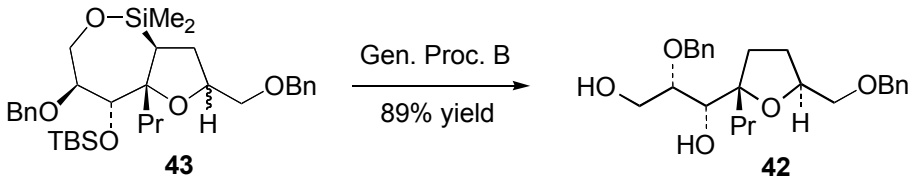
(2*S*, 3a*S*, 7*S*, 8*R*, 8a*R*)-7-Benzyloxy-2-benzyloxymethyl-8-(*t*-butyldimethylsilanyloxy)-4,4-dimethyl-8a-*n*-propyl-octahydro-1,5-dioxa-4-sila-azulene (41): To a solution of **33** (0.102 g, 0.118 mmol, dr 3.3:1) in THF (0.6 mL) was added TBAF (0.236 mL of a 1M soln. in THF) at 23 °C. The mixture was stirred at this temperature for 20 min and was then diluted with water (3 mL) and extracted with Et_2O (5 mL). The ethereal layer was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford a yellow oil. Purification of the crude product by flash column chromatography (5% EtOAc in hexanes) provided siloxane **41** (0.056 g, 0.096 mmol, 81%) as a mixture of diastereomers as a pale yellow oil. The major diastereomer could be isolated after HPLC separation (21 mm column eluting with 3% EtOAc in hexanes) of the diastereomeric mixture: $[\alpha]_D^{26}$ -15 (*c* 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.08 (s, 3H), 0.07 (s, 3H), 0.12 (s, 3H), 0.20 (s, 3H), 0.78 (t, *J* = 7.5 Hz, 3H), 0.83 (s, 9H), 1.29 (ddd, *J* = 12.0, 12.0, 5.0 Hz, 1H), 1.40-1.55 (m, 2H), 1.63 (ddd, *J* = 14.0, 12.0, 10.0 Hz, 1H), 2.00 (quint, *J* = 6.0 Hz, 1H), 2.11 (ddd, *J* = 13.5, 11.5, 5.0 Hz, 1H), 2.17 (dd, *J* = 14.0, 6.5 Hz, 1H), 3.18 (t, *J* = 3.5 Hz, 1H), 3.45 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.52 (dd, *J* = 10.0, 6.0 Hz, 1 H), 3.89 (ABX, J_{AB} = 13.0 Hz, J_{AX} = 3.3 Hz, 1H), 3.93

(A<u>B</u>X, J_{AB} = 13.0 Hz, J_{BX} ~ 0 Hz, 1H), 4.06 (sext, J = 5.5 Hz, 1H), 4.11 (d, J = 4.0 Hz, 1H), 4.53 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.5 Hz, 1H), 4.63 (d, J = 12.5 Hz, 1H), 4.71 (d, J = 12.0 Hz, 1H), 7.25-7.29 (m, 2H), 7.32-7.37 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) 138.73, 138.39, 128.27, 128.24, 127.66, 127.51, 127.38, 90.83, 80.88, 79.21, 74.42, 73.15, 71.60, 70.99, 58.05, 38.71, 31.02, 29.15, 25.91, 17.99, 17.23, 14.68, -1.06, -2.03, -4.41, -5.39; IR (thin film) 2954, 2928, 2857, 1454, 1253, 1076, 878, 866, 836, 778, 735, 697 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{52}O_5Si_2$ 607.3251 *m/z* $(M+Na)^+$; observed, 607.3250 *m*/z.



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General Procedure B: **41** (0.022 g, 0.038 mmol, 1.0 equiv), TBAF soln. (0.264 mL, 0.264 mmol, 7 equiv), DMF (0.6 mL) affords **40** (0.011 g, 0.027 mmol, 71%) along with a diastereomeric diol (0.003 g, 0.007 mmol, 18%).

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[1] Davies, H. M. L.; Hansen, T.; Rutberg, J.; Bruzinski, P. *Tetrahedron Lett*. **1997**, *38*, 1741.

[2] Bulugahapitiya, P.; Landais, Y.; Parra-Rapado, L.; Planchenault, ,D.; Weber, V. *J. Org. Chem*. **1997**, *62*, 1630.

[3] Stossel, D.; Chan, T. H. *J. Org. Chem*. **1988**, *53*, 4901.