Supporting Information

A Multifaceted Phophate Tether: Application to the C1-C14 Subunit of Dolabelide A-D.

Joshua D. Waetzig and Paul R. Hanson* Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive, Lawrence, KS 66045-7582 phanson@KU.edu

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General Experimental Methods

All air and moisture sensitive reactions were carried out in flame- or oven-dried glassware under argon atmosphere using standard gastight syringes, cannulaes, and septa. Stirring was achieved with oven-dried magnetic stir bars. Et₂O, toluene, THF and CH₂Cl₂ were purified by passage through the Solv-Tek purification system employing activated Al₂O₃ (Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Organometallics 1996, 15, 1518-1520). Et₃N was purified by passage over basic alumina and stored over KOH. Butyl Lithium was purchased from Aldrich and titrated prior to use. Grubbs first and second-generation, as well as the Hoveyda-Grubbs olefin metathesis catalysts, were acquired from Materia and used without further purification. Glycidol ether was acquired from Daiso Co., Ltd., Fine Chemical Department and used without further purification. Flash column chromatography was performed with Sorbent Technologies (30930M-25, Silica Gel 60A, 40-63 um). Thin layer chromatography was performed on silica gel 60F254 plates (EM-5717, Merck). Deuterated solvents were purchased from Cambridge Isotope Isotope laboratories. ¹H, ¹³C and ³¹P NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400 MHz, 100 MHz, and 162 MHz respectively; or a Bruker Avance operating at 500 MHz and 125 MHz respectively. High-resolution mass spectrometry (HRMS) and FAB spectra were obtained on a VG Instrument ZAB double-focusing mass spectrometer.

Experimental Data

TBS-PMB Protected Phosphate (13)



To a stirring solution of olefin 12 (3.22g, 8.51 mmol) and degassed DCE (85 ml) were added bicylcic phosphate 5 (870 mg, 4.26 mmol) and Hoveyda-Grubbs II catalyst (213 mg, 0.27 mmol). The solution was equipped with a reflux condenser and placed into an oil bath at 90 °C, at which time a stream of Ar was bubbled through the solution for 1.5 h (until disappearance of phosphate 5 by TLC). The solution was allowed to cool to room temperature before being concentrated under vacuum pressure. Purification via flash chromatography (2:1 EtOAc/Hexane) supplied 1.71 g (72% yield) of 13 as a viscous oil. $[\alpha]_{\rm p}$ -57.50 (c = 0.80, CH₂Cl₂);

FTIR (neat) 2954, 2927, 2883, 1514, 1463, 1249 cm⁻¹;

¹**H NMR** (500 MHz, CHCl₃-*d*) δ ppm 7.23 (d, *J* = 8.6 Hz, 2 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 6.04 (dddd, *J* = 11.8, 6.5, 2.9, 2.8 Hz, 1 H), 5.90 (dd, *J* = 15.5, 7.5 Hz, 1 H), 5.59 (ddd, *J* = 11.8, 3.7, 2.6 Hz, 1 H), 5.53 (dd, *J* = 15.5, 6.5 Hz, 1 H), 5.11-5.20 (m, 1 H), 4.97 (m, 1 H), 4.95 (dd, *J* = 12.9, 7.8 Hz, 1 H), 4.49 (d, *J* = 11.0 Hz, 1 H), 4.41 (d, *J* = 11.0 Hz, 1 H), 4.37 (ddd, *J*_{HP} = 27.7, *J*_{HH} = 14.8, 6.7 Hz, 1 H), 3.80 (s, 3 H), 3.59-3.67 (m, 1 H), 3.63 (dd, *J* = 8.1, 5.5 Hz, 1 H), 3.29 (dd, *J* = 7.7, 4.0 Hz, 1 H), 2.43-2.50 (m, 1 H), 2.17 (ddd, *J* = 14.7, 12.1, 6.2 Hz, 1 H), 1.78-1.86 (m, 1 H), 1.63 (d, *J* = 13.8 Hz, 1 H), 1.01 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.9 Hz, 3 H), 0.90 (s, 9 H), 0.04 (s, 6 H);

¹³**C NMR** (126 MHz, CHCl₃-*d*) δ ppm 159.08, 139.30, 131.24, 129.74, 129.19, 128.07, 125.95 ($J_{CP} = 10.1$ Hz), 113.72, 83.66, 76.83 ($J_{CP} = 6.4$ Hz), 76.81, 74.23, 62.93 ($J_{CP} = 6.2$ Hz), 55.28, 38.62, 38.47, 35.27 ($J_{CP} = 5.5$ Hz), 29.65, 25.97, 18.33, 14.52, 13.78, -5.33, -5.40;

³¹**P NMR** (162 MHz, CHCl₃-*d*) δ ppm -3.57;

HRMS Exact Mass: calculate for $C_{28}H_{49}NO_7PSi (M+NH_4)^+$ 570.3016; found 570.3002 (ESI).

Partially Hydrogenated TBS-PMB Protected Phosphate (15)



The cross-metathesized phosphate intermediate (14) (1.53 g, 2.76 mmol) was taken up in CH_2Cl_2 (35 mL) followed by the addition of NBSH (6.00 g, 27.60 mmol), and Et_3N (12 mL, ~2 mL/gram of NBS-H). After the reaction was stirred for 12 h, EtOAc (100 mL) was added, and the reaction extracted with NaHCO₃ (saturated aq, 2x). The aq layer was re-extracted with EtOAc (1x). The combined organic layers were dried (anhydrous Na₂SO₄) and concentrated. The material was then re-subjected to the same conditions before being purified. Flash chromatography (2:1 Hex:EtOAc) afforded 15 (1.11 g, 72%) as a clear oil and 150 mg of starting material.

 $[\alpha]_{\mathbf{D}} 20.00 \ (c = 0.46, CH_2Cl_2);$

FTIR (neat) 2954, 2929, 2883, 1514, 1461, 1249 1072 cm⁻¹;

¹**H NMR** (500 MHz, CHCl₃-*d*) δ ppm 7.27 (d, *J* = 7.6 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 6.04 (dddd, *J* = 11.8, 6.5, 2.8, 2.6 Hz, 1 H), 5.59 (ddd, *J* = 11.8, 4.0, 2.5 Hz, 1 H), 5.11 – 5.21 (m, 1 H), 5.01 (dddd, *J* = 11.8, 8.6, 5.2, 2.8 Hz, 1 H), 4.57 (d, *J* = 11.4 Hz, 1 H), 4.44 – 4.51 (m, 1 H), 4.46 (d, *J* = 11.0 Hz, 1 H), 4.37 (ddd, *J_{HP}* = 27.7, *J_{HP}* = 14.8, 6.6 Hz, 1 H), 3.81 (s, 3 H), 3.74 (dd, *J* = 9.8, 5.0 Hz, 1 H), 3.63 (dd, *J* = 9.8, 3.5 Hz, 1 H), 3.26 (dd, *J* = 8.8, 2.5 Hz, 1 H), 2.09 (ddd, *J* = 14.5, 12.0, 6.3 Hz, 1 H), 1.71-1.86 (m, 2 H), 1.55-1.70 (m, 3 H), 1.34 – 1.54 (m, 2 H), 0.92 (s, 9 H), 0.90 (d, *J* = 4.1 Hz, 3 H), 0.88 (d, *J* = 6.6 Hz, 3 H), 0.06 (s, 3 H), 0.06 (s, 3 H);

¹³**C NMR** (126 MHz, CHCl₃-*d*) δ ppm 158.99, 131.50, 129.89, 129.38, 129.16, 127.88, 113.67, 83.01, 77.26, 76.87, 74.14, 64.88, 62.89, 55.28, 38.53, 34.93, 34.60, 33.84, 25.98, 18.34, 14.73, 13.36, -5.32, -5.40;

³¹**P NMR** (162 MHz, CHCl₃-*d*) δ ppm -3.12;

HRMS Exact Mass: calculate for $C_{28}H_{51}NO_7PSi (M+NH_4)^+$ 572.3172; found 572.3163 (ESI).

(4*S*,6*S*,9*R*,10*S*,11*R*)-12-(*tert*-butyldimethylsilyloxy)-10-(4-methoxybenzyloxy)-9,11dimethyldodec-1-ene-4,6-diol (SI1)



Phosphate 15 (1.84 g, 3.30 mmol) was taken up in 90 ml of DCE and stirred at room temperature. In a different reaction vessel 5 mol % Pd(OAc)₂ (47mg, 0.21 mmol) and $[HBu_3P]^+BF_4^-$ (60mg, 0.21 mmol) and were taken up in 7 ml of DCE. At this time, Et₃N (2.068ml, 14.87 mmol) and CO₂H₂ (0.280 ml, 7.40 mmol) were added to the reaction vessel containing phosphate 15 and the 1:1 mixture of $Pd(OAc)_2$ and $[HBu_3P]^+BF_4^-$ was also quickly cannulated into the reaction containing phosphate 15. The reaction was heated to 40 °C. The reaction was stirred at this temperature until the color of the reaction turned black (~1h) as well as disappearance of starting material by TLC analysis. The reaction was cooled to room temperature, diluted with 50 ml CH₂Cl₂ and 40 ml of 10 % aqueous HCl was added. The layers separated and the aqueous layer was re-extracted (2x) with CH₂Cl₂. The organic layer was then concentrated to \sim 50 ml under reduced pressure. MeOH (2 ml) followed by TMSCHN₂ (2 ml, 2.0M in diethyl ether) were added to the stirring solution that caused the reaction to bubble vigorously. The reaction was allowed to stir for 5 min. and was monitored for disappearance of the phosphate acid. Upon completion of the reaction a drop of glacial acetic acid was added and the mixture was extracted with CH₂Cl₂ and a saturated solution of NaHCO₃. The aqueous layer was re-extracted (2x) with CH₂Cl₂, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. Flash chromatography (2:1 Hexane:EtOAC) provided 1.67 g of 17 (~1:1 diastereomeric mixture at phosphate) in 87% yield as a clear oil.

The 1:1 diastereomeric phosphate mixture (1.67 g, 2.91 mmol) was taken up in Et₂O (103 mL) and cooled to 0 °C. LiAlH₄ (0.222 g, 5.83 mmol) was slowly added in ~ 0.1 g increments. Upon completion of the addition, the reaction was stirred at 0 °C for 1 h, and quenched via slow sequential addition of H₂O (222 µl), 10% NaOH (222 µl),

and H_2O (666 µL), and removal from the bath. After stirring for 1h, white salts had formed and were filtered through a pad of celite washing Et₂O and was concentrated under reduced pressure. The resulting clear oil was pushed through a short plug of silica (2:1 Hexane:EtOAc) to afford 1.09 g of **SI1** (76% yield) as a clear oil.

 $[\alpha]_{D} 2.00 (c = 0.35, CH_2Cl_2);$

FTIR (neat) 3344, 3074, 2954, 2929, 2856, 1247, 1082 cm⁻¹;

¹**H NMR** (500 MHz, CHCl₃-*d*) δ ppm 7.28 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 5.78-5.88 (m, 1 H), 5.16-5.19 (m, 1 H), 5.13-5.15 (m, 1 H), 4.56 (d, *J* = 11.0 Hz, 1 H), 4.49 (d, *J* = 11.0 Hz, 1 H), 3.94 (ddd, *J* = 12.5, 7.1, 5.4 Hz, 1 H), 3.86-3.92 (m, 1 H), 3.81 (s, 3 H), 3.72 (dd, *J* = 9.6, 5.2 Hz, 1 H), 3.65 (dd, *J* = 9.7, 3.4 Hz, 1 H), 3.29 (dd, *J* = 8.6, 2.8 Hz, 1 H), 2.23-2.33 (m, 3 H), 1.79-1.89 (m, 1 H), 1.57-1.66 (m, 5 H), 1.38-1.48 (m, 3 H), 0.92 (s, 9 H), 0.91 (d, *J* = 0.16 Hz, 3 H), 0.90 (d, *J* = 4.49 Hz, 3 H), 0.06 (s, 3 H), 0.06 (s, 3 H);

¹³C NMR (126 MHz, CHCl₃-*d*) δ ppm 158.96, 134.63, 131.56, 129.20, 118.30, 113.67, 83.34, 74.31, 69.46, 68.21, 64.98, 55.28, 42.01, 41.91, 38.58, 35.60, 35.21, 30.88, 25.97, 18.34, 14.76, 13.55, -5.31, -5.40;

HRMS Exact Mass: calculate for $C_{28}H_{50}NaO_5Si$ (M+Na)⁺ 517.3325; found 517.3315 (ESI).

((2*R*,3*S*,4*R*)-6-((4*S*,6*S*)-6-allyl-2,2-dimethyl-1,3-dioxan-4-yl)-3-(4methoxybenzyloxy)-2,4-dimethylhexyloxy)(*tert*-butyl)dimethylsilane (18)



The diol (1.07 g, 2.16 mmol) was dissolved in CH_2Cl_2 (4 mL) followed by the addition of 2,2-DMP (4 mL), and PPTS (54 mg, 0..216 mmol). Upon completion (~15 min, monitored by TLC) the reaction was diluted with CH_2Cl_2 and quenched with NaHCO₃ (saturated aq., 2 mL), dried (Na₂SO₄) and filtered. Flash chromatograph (10:1 Hexane:EtOAc) provided acetonide **18** (1.10 g, 96%).

 $[\alpha]_{\mathbf{D}}$ -4.33 (c = 0.30, CH₂Cl₂);

FTIR (neat) 3074, 2954, 2929, 2856, 1514, 1247, 1039 cm⁻¹;

¹**H NMR** (400 MHz, CHCl₃-*d*) δ ppm 7.27 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.82 (dddd, *J* = 13.7, 10.6, 10.2, 7.1 Hz, 1 H), 5.08 (dd, *J* = 17.2, 1.8 Hz, 1 H), 5.04-5.08 (m, 1 H), 4.55 (d, *J* = 10.9 Hz, 1 H), 4.48 (d, *J* = 10.9 Hz, 1 H), 3.82-3.90 (m, 1 H), 3.81 (s, 3 H), 3.75 – 3.78 (m, 2 H), 3.65 (dd, *J* = 9.6, 3.4 Hz, 1 H), 3.26 (dd, *J* = 8.4, 2.6 Hz, 1 H), 2.27-2.36 (m, 1 H), 2.16 – 2.22 (m, 1 H), 1.79-1.87 (m, 1 H), 1.52-1.61 (m, 4 H), 1.38-1.45 (m, 3 H), 1.36 (s, 3 H), 1.35 (s, 3 H), 0.92 (s, 9 H), 0.90 (d, *J* = 3.6 Hz, 3 H), 0.89 (d, *J* = 5.4 Hz, 3 H), 0.06 (s, 3 H), 0.05 (s, 3 H);

¹³C NMR (126 MHz, CHCl₃-*d*) δ ppm 158.97, 134.54, 131.56, 129.19, 116.78, 113.65, 100.22, 83.22, 74.44, 66.71, 66.22, 64.98, 55.26, 40.17, 38.58, 38.22, 34.99, 33.92, 30.37, 25.98, 24.82, 24.76, 18.34, 14.74, 13.53, -5.30, -5.39;

HRMS Exact Mass: calculate for $C_{31}H_{54}O_5Si(M+H)^+$ 535.3819; found 535.3817 (ESI).

1-((4*R*,6*S*)-6-((3*R*,4*S*,5*R*)-6-(*tert*-butyldimethylsilyloxy)-4-(4-methoxybenzyloxy)-3,5dimethylhexyl)-2,2-dimethyl-1,3-dioxan-4-yl)-5-methylhex-5-en-2-one (SI2)



The olefin (0.913 g, 1.71 mmol) was taken up in CH_2Cl_2 :MeOH 1:1 (29 mL) followed by the addition of pyridine (1.352 g, 17.10 mmol) and SUDAN III (indicator, ~1 mg) at rt under argon. The solution was cooled to -78 °C, and a stream of O₃ was lightly bubbled through the solution until a light yellow color persisted. The stream of O₃ was removed when the SM was consumed (monitored by TLC). The flask was flushed with Ar, and Me₂S (5.1 mL) was slowly added. The reaction was slowly warmed to rt over a 4 h period. After stirring for 1 h. at rt, Et₂O (50 mL) was added and extracted with saturated CuSO₄ (2x 15 mL), and brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). Flash chromatography (9:1 Hexane: EtOAc) afforded the aldehyde (0.657 g, 72 %) as an oil.

To a solution of iodide (1.6 g, 8.0 mmol) in Et₂O, with a cold finger condenser (dry ice, acetone), (8.9 mL, 0.9M solution) at rt was added freshly prepared magnesium chips (150 mg, 6.24 mmol). At which time the reaction refluxed (metal gray color) and was stirred under Ar until the solution had re-cooled to room temperature. A separate reaction flask of aldehyde (641 mg, 1.20 mmol) in Et₂O (6 mL) was cooled to -78 °C, then 6.64 ml of MgI solution was added dropwise. The bath was removed after 5 min. of stirring and the reaction was warmed to rt. The reaction was quenched with aqueous 5 mL of NH₄Cl (saturated aq) after the disappearance of starting material. The layers were separated and aqueous layer was extracted with Et₂O (2x), and the combined organic layers washed with brine (1x), dried (anhydrous Na₂SO₄), and concentrated (rotary evaporator). Flash chromatography (10:1 Hex:EtOAc) afforded a 1:1 mixture of **19** (ratio determined by ¹H NMR analysis of crude reaction mixture, 700 mg, combine yield of diastereomers 96%).

The alcohol (0.171 g, 0.281 mmol) was taken up in CH_2Cl_2 (9.3 mL) followed by the addition of NaHCO₃ (0.236 g, 2.81 mmol) and Dess-Martin periodinane (0.261 g, 0.618 mmol) at rt under argon. Upon completion (monitored by TLC), Et₂O (15 mL) was added, and the solution extracted with NaHCO₃ (saturated aq., 2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica (10:1 Hex:EtOAc) to give the **SI2** (0.154 g, 90%) as a clear oil.

 $[\alpha]_{\mathbf{D}}$ 17.70 (c = 1.65, CH₂Cl₂);

FTIR (neat) 2954, 2933, 2856, 1718, 1458, 1247, 1037 cm⁻¹;

¹**H NMR** (400 MHz, CHCl₃-*d*) δ ppm 7.28 (d, *J* = 7.8 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 4.75 (s, 1 H), 4.67 (s, 1 H), 4.58 (d, *J* = 10.7 Hz, 1 H), 4.49 (d, *J* = 10.7 Hz, 1 H), 4.30 (ddd, *J* = 14.4, 9.3, 5.4 Hz, 1 H), 3.82 (s, 3 H), 3.73 (dd, *J* = 9.9, 5.3 Hz, 2 H), 3.64 (dd, *J* = 9.9, 3.3 Hz, 1 H), 3.28 (dd, *J* = 9.1, 2.88 Hz, 1 H), 2.68 (dd, *J* = 15.9, 8.3 Hz, 1 H), 2.62 (dd, *J* = 7.3, 1.5 Hz, 1 H), 2.60 (d, *J* = 6.3 Hz, 1 H), 2.48 (dd, *J* = 15.9, 4.8 Hz, 1 H), 2.29

(dd, *J* = 8.1, 7.3 Hz, 2 H), 1.78-1.87 (m, 1 H), 1.75 (s, 3 H), 1.48-1.73 (m, 7 H), 1.36 (s, 3 H), 1.33 (s, 3 H), 0.93 (s, 9 H), 0.92 (d, *J* = 4.8 Hz, 3 H), 0.90 (d, *J* = 4.6 Hz, 3 H), 0.07 (d, *J* = 2.0 Hz, 6 H);

¹³**C NMR** (126 MHz, CHCl₃-*d*) δ ppm 208.25, 158.94, 144.46, 131.59, 129.16, 113.64, 110.04, 100.42, 83.41, 74.53, 66.94, 64.98, 63.18, 55.25, 48.74, 41.73, 38.59, 38.42, 35.17, 34.02, 31.05, 30.62, 25.97, 24.65, 24.53, 22.68, 18.34, 14.70, 13.39, -5.32, -5.40; **HRMS** Exact Mass: calculate for $C_{35}H_{60}NaO_6Si$ (M+H)⁺ 627.4057; found 627.4038 (ESI).

(5*S*,7*R*,9*S*,12*R*,13*S*,14*R*)-15-(*tert*-butyldimethylsilyloxy)-13-(4-methoxybenzyloxy)-2,12,14-trimethylpentadec-1-ene-5,7,9-triol (21)



A solution of ketone **SI2** (0.050 g, 0.083 mmol) in CH₃CN (1.38 ml) was added H₂O (198 μ l) followed by CeCl₃•7H₂O (93 mg, 0.250 mmol). The reaction was stirred until the disappearance of starting material (~5h). The reaction was diluted with Et₂O, quenched with NaHCO₃ (saturated aq.), and the aqueous layer was re-extracted with Et₂O (2x). The organic layer was dried (Na₂SO₄), filtered and concentrated under reduced pressure. Flash chromatography (3:1 Hexane:EtOAc) provided 40 mg of **20** in 87% yield as a clear oil.

Reduction with Et₂BOMe, NaBH₄: To a solution of **20** (0.090 g, 0.159 mmol) in 4:1 THF:MeOH (0.353 mL) was added Et₂BOMe (1M in THF, 0.043 mL) at -78 °C and stirred for 15 minutes. NaBH₄ (0.014 g, 0.368 mmol) was added and stirred at -78 °C for

1 h. Then the reaction flask was warmed to rt and stirred for an additional hour. The reaction was quenched at -20 °C with 10% aqueous NaOH, 35% H₂O₂, and stirred for 12 h at rt. The layers were separated, and the aq. layer extracted with Et₂O (2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). The mixture was pushed through a silica column (2:1 Hex:EtOAc) to afford the title compound as a >20:1 mixture (determined by ¹H NMR of crude reaction) of **20** (0.054 g, 60%, 95% brsm) as a clear oil as well as 32 mg of starting ketone.

Reduction with DIBAL-H: To a solution of the ketone (0.010 g, 0.0176 mmol) in toluene (0.200 mL) was slowly added DIBAL-H (1.0M in toluene, 0.040 mL) at -78 °C. After two hours of stirring at -78 °C, the reaction was quenched with NH₄Cl (saturated, aq.), and the reaction warmed to rt while stirring. The layers were separated, and the aq. layer extracted with Et₂O (2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica (2:1 Hex:EtOAc) to afford the title compound as a 1:1 mixture (determined by ¹H NMR of crude reaction) of **21** (0.0075 g, 75%) as a clear oil.

Reduction with LiAlH₄/LiI: To a solution of the ketone (0.020 g, 0.035 mmol) in Et₂O (0.440 mL) was added LiI (0.047 g, 0.350 mmol) at 0 $^{\circ}$ C (solution turns reddish-brown color). Once the LiI is completely dissolved (< 5 min), the reaction was cooled to -78 $^{\circ}$ C and a solution of LiAl₄H (2.0 M in Et₂O, 0.175 mL) was slowly added. After twenty minutes, the reaction was quenched with sodium-potassium tartrate (saturated, aq.), and the reaction warmed to rt while stirring. The layers were separated, and the aq. layer extracted with Et₂O (2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica (2:1 Hex:EtOAc) to afford the title compound as a 1.6:1 mixture (determined by ¹H NMR of crude reaction) of **21** (0.018 g, 90%) as a clear oil.

Reduction with Et₃B, NaBH₄: To a solution of the ketone (0.020 g, 0.035 mmol) in 4:1 THF:MeOH (0.353 mL) was added Et_3B (1.0M in THF 0.056 ml) at rt stirred for 15 minutes. The reaction was then cooled to -78 °C and NaBH₄ (0.003 g, 0.071 mmol) was

added and stirred at that temperature for 3h. The reaction was quenched at -78 °C with 10% aqueous NaOH, 35% H₂O₂, and the reaction was stirred for 12h at rt. The layers were separated, and the aq. layer extracted with Et_2O (2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica (2:1 Hex:EtOAc) to afford the title compound as a 5.3:1 mixture (determined by ¹H NMR of crude reaction) of **21** (0.014 g, 70%) as a clear oil.

Reduction with ZnCl₂, NaBH₄: To a solution of the ketone (0.010 g, 0.0175 mmol) in CH_2Cl_2 (0.175 mL) was added ZnCl₂ (1M in THF, 0.0175 mL) at rt and stirred for 15 minutes. NaBH₄ (0.0015 mg, 0.0012 mmol) was then added and the reaction was stirred for 12h. The reaction was quenched with 10% aqueous NaOH, 35% H₂O₂, and the reaction was stirred for 12h at rt. The layers were separated, and the aq. layer extracted with Et₂O (2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous Na₂SO₄), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica (2:1 Hex:EtOAc) to afford the title compound as a 3.3:1 mixture (determined by ¹H NMR of crude reaction) of **21** (0.006 g, 64%) as a clear oil.

 $[\alpha]_{\mathbf{D}}$ 7.26 (c = 1.35, CH₂Cl₂);

FTIR (neat) 3371, 2933, 2883, 2856, 1612, 1514, 1461 cm⁻¹;

¹**H NMR** (400 MHz, CHCl₃-*d*) δ ppm 7.27 (d, J = 8.6 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 4.74 (d, J = 1.3 Hz, 1 H), 4.73 (s, 1 H), 4.56 (d, J = 10.9 Hz, 1 H), 4.49 (d, J = 10.9 Hz, 1 H), 4.18-4.26 (m, 1 H), 3.85-3.97 (m, 2 H), 3.80 (s, 3 H), 3.73 (dd, J = 9.6, 5.3 Hz, 1 H), 3.63 (dd, J = 9.6, 3.3 Hz, 1 H), 3.30 (dd, J = 8.8, 2.5 Hz, 1 H), 2.14 (dddd, 2 H), 1.78-1.86 (m, 1 H), 1.75 (s, 3 H), 1.58-1.73 (m, 8 H), 1.46-1.57 (m, 4 H), 1.27 (m, 3 H), 0.92 (s, 9 H), 0.91 (d, J = 2.3 Hz, 3 H), 0.89 (d, J = 2.3 Hz, 3 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ¹³**C NMR** (126 MHz, CHCl₃-*d*) δ ppm 158.95, 145.69, 131.61, 129.22, 113.65, 110.31,

83.30, 77.25, 74.34, 73.17, 70.89, 69.79, 64.95, 55.28, 42.53, 38.58, 35.87, 35.74, 35.33, 33.75, 31.05, 25.96, 22.40, 18.33, 14.73, 13.39, -5.32, -5.41;

HRMS Exact Mass: calculate for $C_{32}H_{58}NaO_6Si (M+Na)^+$ 589.3900; found 589.3890 (ESI).

Stereochemical Analysis of the C11 Carbinol Position.

Finally, isolation of the major diastereomer of the reduction, followed by acetonide formation provided a mixture of **19** and regioisomeric acetonide (Scheme SI-1). In accordance with Rychnovsky-Evans acetonide analysis,^{1 13}C analysis of the **SI3** contained acetonide peaks at 30.24 ppm, 19.68 ppm, and 98.68, indicative of the newly formed 1,3-*syn* acetonide.

Scheme SI-1



 ⁽a) Rychnovsky, S. D.; Skalitzky, D. J., Stereochemistry of alternating polyol chains: NMR analysis of 1,3-diol acetonides. *Tetrahedron Lett.* 1990, 31, 945-8. (b) Evans, D. A.; Rieger, D. L.; Gage, J. R., Carbon-13 NMR chemical shift correlations in 1,3-diol acetonides. Implications for the stereochemical assignment of propionate-derived polyols. *Tetrahedron Lett.* 1990, 31, 7099-100















