## Supporting Information

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

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## Table of Contents

General Experimental Methods: SI-2
Experimental Section and Characterization Data: SI-3-SI-12
NMR Spectra for New Compounds: SI-13-SI-20

## 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. $\mathrm{Et}_{2} \mathrm{O}$, toluene, THF and $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ were purified by passage through the Solv-Tek purification system employing activated $\mathrm{Al}_{2} \mathrm{O}_{3}$ (Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Organometallics 1996, 15, 1518-1520). $\mathrm{Et}_{3} \mathrm{~N}$ 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 (30930M25 , 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. ${ }^{1} \mathrm{H},{ }^{13} \mathrm{C}$ and ${ }^{31} \mathrm{P}$ NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at $400 \mathrm{MHz}, 100 \mathrm{MHz}$, 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 $12(3.22 \mathrm{~g}, 8.51 \mathrm{mmol})$ and degassed DCE ( 85 ml ) were added bicylcic phosphate $5(870 \mathrm{mg}, 4.26 \mathrm{mmol})$ and Hoveyda-Grubbs II catalyst (213 $\mathrm{mg}, 0.27 \mathrm{mmol})$. The solution was equipped with a reflux condenser and placed into an oil bath at $90^{\circ} \mathrm{C}$, at which time a stream of Ar was bubbled through the solution for 1.5 h (until disappearance of phosphate $\mathbf{5}$ 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 $\mathbf{1 3}$ as a viscous oil. $[\propto]_{\mathbf{D}}-57.50\left(c=0.80, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$;

FTIR (neat) 2954, 2927, 2883, 1514, 1463, $1249 \mathrm{~cm}^{-1}$;
${ }^{1} \mathbf{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CHCl}_{3}-d\right) \delta \mathrm{ppm} 7.23(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H}), 6.83(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H})$, 6.04 (dddd, $J=11.8,6.5,2.9,2.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.90(\mathrm{dd}, J=15.5,7.5 \mathrm{~Hz}, 1 \mathrm{H}), 5.59$ (ddd, $J$ $=11.8,3.7,2.6 \mathrm{~Hz}, 1 \mathrm{H}), 5.53(\mathrm{dd}, J=15.5,6.5 \mathrm{~Hz}, 1 \mathrm{H}), 5.11-5.20(\mathrm{~m}, 1 \mathrm{H}), 4.97(\mathrm{~m}, 1$ H), $4.95(\mathrm{dd}, J=12.9,7.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.49(\mathrm{~d}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.41(\mathrm{~d}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H})$, $4.37\left(\mathrm{ddd}, J_{H P}=27.7, J_{H H}=14.8,6.7 \mathrm{~Hz}, 1 \mathrm{H}\right), 3.80(\mathrm{~s}, 3 \mathrm{H}), 3.59-3.67(\mathrm{~m}, 1 \mathrm{H}), 3.63$ (dd, $J=8.1,5.5 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.29 (dd, $J=7.7,4.0 \mathrm{~Hz}, 1 \mathrm{H}$ ), 2.43-2.50 (m, 1 H ), 2.17 (ddd, $J$ $=14.7,12.1,6.2 \mathrm{~Hz}, 1 \mathrm{H}), 1.78-1.86(\mathrm{~m}, 1 \mathrm{H}), 1.63(\mathrm{~d}, J=13.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.01(\mathrm{~d}, J=6.8$ $\mathrm{Hz}, 3 \mathrm{H}), 0.93(\mathrm{~d}, J=6.9 \mathrm{~Hz}, 3 \mathrm{H}), 0.90(\mathrm{~s}, 9 \mathrm{H}), 0.04(\mathrm{~s}, 6 \mathrm{H})$;
${ }^{13} \mathbf{C}$ NMR ( $126 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm} 159.08,139.30,131.24,129.74,129.19,128.07$, $125.95\left(J_{C P}=10.1 \mathrm{~Hz}\right), 113.72,83.66,76.83\left(J_{C P}=6.4 \mathrm{~Hz}\right), 76.81,74.23,62.93\left(J_{C P}=\right.$ $6.2 \mathrm{~Hz}), 55.28,38.62,38.47,35.27\left(J_{C P}=5.5 \mathrm{~Hz}\right), 29.65,25.97,18.33,14.52,13.78$, 5.33, -5.40;
${ }^{31} \mathbf{P}$ NMR ( $162 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm}-3.57$;
HRMS Exact Mass: calculate for $\mathrm{C}_{28} \mathrm{H}_{49} \mathrm{NO}_{7} \mathrm{PSi}\left(\mathrm{M}+\mathrm{NH}_{4}\right)^{+}$570.3016; found 570.3002 (ESI).

## Partially Hydrogenated TBS-PMB Protected Phosphate (15)



The cross-metathesized phosphate intermediate (14) ( $1.53 \mathrm{~g}, 2.76 \mathrm{mmol})$ was taken up in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(35 \mathrm{~mL})$ followed by the addition of NBSH ( $6.00 \mathrm{~g}, 27.60 \mathrm{mmol}$ ), and $\mathrm{Et}_{3} \mathrm{~N}$ (12 $\mathrm{mL}, \sim 2 \mathrm{~mL} / \mathrm{gram}$ of NBS-H). After the reaction was stirred for 12 h , EtOAc ( 100 mL ) was added, and the reaction extracted with $\mathrm{NaHCO}_{3}$ (saturated aq, 2 x ). The aq layer was re-extracted with EtOAc (1x). The combined organic layers were dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ) and concentrated. The material was then re-subjected to the same conditions before being purified. Flash chromatography ( $2: 1 \mathrm{Hex}: E t O A c$ ) afforded 15 ( $1.11 \mathrm{~g}, \mathbf{7 2 \%}$ ) as a clear oil and 150 mg of starting material.
$[\propto]_{\mathbf{D}} 20.00\left(c=0.46, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$;
FTIR (neat) 2954, 2929, 2883, 1514, 1461, $12491072 \mathrm{~cm}^{-1}$;
${ }^{1} \mathbf{H}$ NMR ( $\left.500 \mathrm{MHz}, \mathrm{CHCl}_{3}-d\right) \delta \mathrm{ppm} 7.27(\mathrm{~d}, J=7.6 \mathrm{~Hz}, 2 \mathrm{H}), 6.88(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H})$, 6.04 (dddd, $J=11.8,6.5,2.8,2.6 \mathrm{~Hz}, 1 \mathrm{H}), 5.59$ (ddd, $J=11.8,4.0,2.5 \mathrm{~Hz}, 1 \mathrm{H}), 5.11-$ $5.21(\mathrm{~m}, 1 \mathrm{H}), 5.01$ (dddd, $J=11.8,8.6,5.2,2.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.57(\mathrm{~d}, J=11.4 \mathrm{~Hz}, 1 \mathrm{H})$, $4.44-4.51(\mathrm{~m}, 1 \mathrm{H}), 4.46(\mathrm{~d}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.37\left(\mathrm{ddd}, J_{H P}=27.7, J_{H P}=14.8\right.$, 6.6 $\mathrm{Hz}, 1 \mathrm{H}), 3.81(\mathrm{~s}, 3 \mathrm{H}), 3.74(\mathrm{dd}, J=9.8,5.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.63(\mathrm{dd}, J=9.8,3.5 \mathrm{~Hz}, 1 \mathrm{H})$, 3.26 (dd, $J=8.8,2.5 \mathrm{~Hz}, 1 \mathrm{H}$ ), 2.09 (ddd, $J=14.5,12.0,6.3 \mathrm{~Hz}, 1 \mathrm{H}$ ), 1.71-1.86 (m, 2 H), 1.55-1.70 (m, 3 H ), $1.34-1.54(\mathrm{~m}, 2 \mathrm{H}), 0.92(\mathrm{~s}, 9 \mathrm{H}), 0.90(\mathrm{~d}, J=4.1 \mathrm{~Hz}, 3 \mathrm{H})$, 0.88 (d, $J=6.6 \mathrm{~Hz}, 3 \mathrm{H}$ ), 0.06 (s, 3 H ), 0.06 ( $\mathrm{s}, 3 \mathrm{H}$ );
${ }^{13} \mathbf{C}$ NMR ( $126 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm} 158.99,131.50,129.89,129.38,129.16,127.88$, $113.67,83.01,77.26,76.87,74.14,64.88,62.89,55.28,38.53,34.93,34.60,33.84,25.98$, 18.34, 14.73, 13.36, -5.32, -5.40;
${ }^{31} \mathbf{P}$ NMR ( $162 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm}-3.12$;
HRMS Exact Mass: calculate for $\mathrm{C}_{28} \mathrm{H}_{51} \mathrm{NO}_{7} \mathrm{PSi}\left(\mathrm{M}+\mathrm{NH}_{4}\right)^{+}$572.3172; found 572.3163 (ESI).
(4S,6S,9R,10S,11R)-12-(tert-butyldimethylsilyloxy)-10-(4-methoxybenzyloxy)-9,11-dimethyldodec-1-ene-4,6-diol (SI1)


Phosphate $15(1.84 \mathrm{~g}, 3.30 \mathrm{mmol})$ was taken up in 90 ml of DCE and stirred at room temperature. In a different reaction vessel $5 \mathrm{~mol} \% \mathrm{Pd}(\mathrm{OAc})_{2}(47 \mathrm{mg}, 0.21 \mathrm{mmol})$ and $\left[\mathrm{HBu}_{3} \mathrm{P}^{+} \mathrm{BF}_{4}^{-}(60 \mathrm{mg}, 0.21 \mathrm{mmol})\right.$ and were taken up in 7 ml of DCE. At this time, $\mathrm{Et}_{3} \mathrm{~N}$ $(2.068 \mathrm{ml}, 14.87 \mathrm{mmol})$ and $\mathrm{CO}_{2} \mathrm{H}_{2}(0.280 \mathrm{ml}, 7.40 \mathrm{mmol})$ were added to the reaction vessel containing phosphate $\mathbf{1 5}$ and the $1: 1$ mixture of $\mathrm{Pd}(\mathrm{OAc})_{2}$ and $\left[\mathrm{HBu}_{3} \mathrm{P}\right]^{+} \mathrm{BF}_{4}{ }^{-}$was also quickly cannulated into the reaction containing phosphate 15 . The reaction was heated to $40{ }^{\circ} \mathrm{C}$. The reaction was stirred at this temperature until the color of the reaction turned black $(\sim 1 \mathrm{~h})$ as well as disappearance of starting material by TLC analysis. The reaction was cooled to room temperature, diluted with $50 \mathrm{ml} \mathrm{CH}_{2} \mathrm{Cl}_{2}$ and 40 ml of 10 $\%$ aqueous HCl was added. The layers separated and the aqueous layer was re-extracted (2x) with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$. The organic layer was then concentrated to $\sim 50 \mathrm{ml}$ under reduced pressure. $\mathrm{MeOH}(2 \mathrm{ml})$ followed by $\mathrm{TMSCHN}_{2}(2 \mathrm{ml}, 2.0 \mathrm{M}$ 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 $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ and a saturated solution of $\mathrm{NaHCO}_{3}$. The aqueous layer was re-extracted ( 2 x ) with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, dried $\left(\mathrm{Na}_{2} \mathrm{SO}_{4}\right)$, filtered, and concentrated under reduced pressure. Flash chromatography (2:1 Hexane:EtOAC) provided 1.67 g of 17 ( $\sim 1: 1$ diastereomeric mixture at phosphate) in $87 \%$ yield as a clear oil.

The $1: 1$ diastereomeric phosphate mixture $(1.67 \mathrm{~g}, 2.91 \mathrm{mmol})$ was taken up in $\mathrm{Et}_{2} \mathrm{O}(103 \mathrm{~mL})$ and cooled to $0{ }^{\circ} \mathrm{C} . \mathrm{LiAlH}_{4}(0.222 \mathrm{~g}, 5.83 \mathrm{mmol})$ was slowly added in $\sim 0.1 \mathrm{~g}$ increments. Upon completion of the addition, the reaction was stirred at $0^{\circ} \mathrm{C}$ for 1 h , and quenched via slow sequential addition of $\mathrm{H}_{2} \mathrm{O}(222 \mu \mathrm{l}), 10 \% \mathrm{NaOH}(222 \mu \mathrm{l})$,
and $\mathrm{H}_{2} \mathrm{O}(666 \mu \mathrm{~L})$, and removal from the bath. After stirring for 1 h , white salts had formed and were filtered through a pad of celite washing $\mathrm{Et}_{2} \mathrm{O}$ 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.
$[\propto]_{\mathbf{D}} 2.00\left(c=0.35, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$;
FTIR (neat) 3344, 3074, 2954, 2929, 2856, 1247, $1082 \mathrm{~cm}^{-1}$;
${ }^{1} \mathbf{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CHCl}_{3}-d\right) \delta \mathrm{ppm} 7.28(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H}), 6.88(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H})$, 5.78-5.88 (m, 1 H$), 5.16-5.19(\mathrm{~m}, 1 \mathrm{H}), 5.13-5.15(\mathrm{~m}, 1 \mathrm{H}), 4.56(\mathrm{~d}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H})$, $4.49(\mathrm{~d}, J=11.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.94(\mathrm{ddd}, J=12.5,7.1,5.4 \mathrm{~Hz}, 1 \mathrm{H}), 3.86-3.92(\mathrm{~m}, 1 \mathrm{H}), 3.81$ (s, 3 H ), 3.72 (dd, $J=9.6,5.2 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.65 (dd, $J=9.7,3.4 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.29 (dd, $J=8.6$, $2.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.23-2.33(\mathrm{~m}, 3 \mathrm{H}), 1.79-1.89(\mathrm{~m}, 1 \mathrm{H}), 1.57-1.66(\mathrm{~m}, 5 \mathrm{H}), 1.38-1.48(\mathrm{~m}, 3$ H), $0.92(\mathrm{~s}, 9 \mathrm{H}), 0.91(\mathrm{~d}, J=0.16 \mathrm{~Hz}, 3 \mathrm{H}), 0.90(\mathrm{~d}, J=4.49 \mathrm{~Hz}, 3 \mathrm{H}), 0.06(\mathrm{~s}, 3 \mathrm{H}), 0.06$ (s, 3 H );
${ }^{13} \mathbf{C}$ NMR ( $126 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm}$ 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 $\mathrm{C}_{28} \mathrm{H}_{50} \mathrm{NaO}_{5} \mathrm{Si}(\mathrm{M}+\mathrm{Na})^{+}$517.3325; found 517.3315 (ESI).
( $(2 R, 3 S, 4 R)-6-((4 S, 6 S)-6-a l l y l-2,2-d i m e t h y l-1,3-d i o x a n-4-y l)-3-(4-$ methoxybenzyloxy)-2,4-dimethylhexyloxy)(tert-butyl)dimethylsilane (18)


The diol ( $1.07 \mathrm{~g}, 2.16 \mathrm{mmol}$ ) was dissolved in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(4 \mathrm{~mL})$ followed by the addition of 2,2-DMP ( 4 mL ), and PPTS ( $54 \mathrm{mg}, 0 . .216 \mathrm{mmol}$ ). Upon completion ( $\sim 15 \mathrm{~min}$, monitored by TLC) the reaction was diluted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ and quenched with $\mathrm{NaHCO}_{3}$ (saturated aq., 2 mL ), dried $\left(\mathrm{Na}_{2} \mathrm{SO}_{4}\right)$ and filtered. Flash chromatograph (10:1 Hexane:EtOAc) provided acetonide $\mathbf{1 8}(1.10 \mathrm{~g}, 96 \%)$.
$[\propto]_{\mathbf{D}}-4.33\left(c=0.30, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$;
FTIR (neat) 3074, 2954, 2929, 2856, 1514, 1247, $1039 \mathrm{~cm}^{-1}$;
${ }^{1} \mathbf{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm} 7.27(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}), 6.87(\mathrm{~d}, J=8.7 \mathrm{~Hz}, 2 \mathrm{H})$, 5.82 (dddd, $J=13.7,10.6,10.2,7.1 \mathrm{~Hz}, 1 \mathrm{H}), 5.08(\mathrm{dd}, J=17.2,1.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.04-5.08$ $(\mathrm{m}, 1 \mathrm{H}), 4.55(\mathrm{~d}, J=10.9 \mathrm{~Hz}, 1 \mathrm{H}), 4.48(\mathrm{~d}, J=10.9 \mathrm{~Hz}, 1 \mathrm{H}), 3.82-3.90(\mathrm{~m}, 1 \mathrm{H}), 3.81$ (s, 3 H ), $3.75-3.78$ (m, 2 H), $3.65(\mathrm{dd}, ~ J=9.6,3.4 \mathrm{~Hz}, 1 \mathrm{H}), 3.26(\mathrm{dd}, J=8.4,2.6 \mathrm{~Hz}, 1$ H), 2.27-2.36 (m, 1 H$), 2.16-2.22(\mathrm{~m}, 1 \mathrm{H}), 1.79-1.87(\mathrm{~m}, 1 \mathrm{H}), 1.52-1.61(\mathrm{~m}, 4 \mathrm{H})$, $1.38-1.45(\mathrm{~m}, 3 \mathrm{H}), 1.36(\mathrm{~s}, 3 \mathrm{H}), 1.35(\mathrm{~s}, 3 \mathrm{H}), 0.92(\mathrm{~s}, 9 \mathrm{H}), 0.90(\mathrm{~d}, J=3.6 \mathrm{~Hz}, 3 \mathrm{H})$, 0.89 (d, $J=5.4 \mathrm{~Hz}, 3 \mathrm{H}), 0.06(\mathrm{~s}, 3 \mathrm{H}), 0.05$ (s, 3 H );
${ }^{13} \mathbf{C}$ NMR ( $126 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm} 158.97,134.54,131.56,129.19,116.78,113.65$, $100.22,83.22,74.44,66.71,66.22,64.98,55.26,40.17,38.58,38.22,34.99,33.92,30.37$, 25.98, 24.82, 24.76, 18.34, 14.74, 13.53, -5.30, -5.39;

HRMS Exact Mass: calculate for $\mathrm{C}_{31} \mathrm{H}_{54} \mathrm{O}_{5} \mathrm{Si}(\mathrm{M}+\mathrm{H})^{+} 535.3819$; found 535.3817 (ESI).

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


The olefin ( $0.913 \mathrm{~g}, 1.71 \mathrm{mmol}$ ) was taken up in $\mathrm{CH}_{2} \mathrm{Cl}_{2}: \mathrm{MeOH} 1: 1(29 \mathrm{~mL})$ followed by the addition of pyridine ( $1.352 \mathrm{~g}, 17.10 \mathrm{mmol}$ ) and SUDAN III (indicator, $\sim 1 \mathrm{mg}$ ) at rt under argon. The solution was cooled to $-78^{\circ} \mathrm{C}$, and a stream of $\mathrm{O}_{3}$ was lightly bubbled through the solution until a light yellow color persisted. The stream of $\mathrm{O}_{3}$ was removed when the SM was consumed (monitored by TLC). The flask was flushed with Ar, and $\mathrm{Me}_{2} \mathrm{~S}(5.1 \mathrm{~mL})$ was slowly added. The reaction was slowly warmed to rt over a 4 h period. After stirring for 1 h . at $\mathrm{rt}, \mathrm{Et}_{2} \mathrm{O}(50 \mathrm{~mL})$ was added and extracted with saturated
$\mathrm{CuSO}_{4}$ ( 2 x 15 mL ), and brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), filtered, and concentrated (rotary evaporator). Flash chromatography (9:1 Hexane: EtOAc) afforded the aldehyde $(0.657 \mathrm{~g}, 72 \%)$ as an oil.

To a solution of iodide $(1.6 \mathrm{~g}, 8.0 \mathrm{mmol})$ in $\mathrm{Et}_{2} \mathrm{O}$, with a cold finger condenser (dry ice, acetone), ( $8.9 \mathrm{~mL}, 0.9 \mathrm{M}$ solution) at rt was added freshly prepared magnesium chips ( $150 \mathrm{mg}, 6.24 \mathrm{mmol}$ ). 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 ( $641 \mathrm{mg}, 1.20 \mathrm{mmol}$ ) in $\mathrm{Et}_{2} \mathrm{O}(6 \mathrm{~mL})$ was cooled to $-78{ }^{\circ} \mathrm{C}$, 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 $\mathrm{NH}_{4} \mathrm{Cl}$ (saturated aq) after the disappearance of starting material. The layers were separated and aqueous layer was extracted with $\mathrm{Et}_{2} \mathrm{O}(2 \mathrm{x})$, and the combined organic layers washed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), and concentrated (rotary evaporator). Flash chromatography (10:1 Hex:EtOAc) afforded a $1: 1$ mixture of $\mathbf{1 9}$ (ratio determined by ${ }^{1} \mathrm{H}$ NMR analysis of crude reaction mixture, 700 mg , combine yield of diastereomers 96\%).

The alcohol ( $0.171 \mathrm{~g}, 0.281 \mathrm{mmol}$ ) was taken up in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(9.3 \mathrm{~mL})$ followed by the addition of $\mathrm{NaHCO}_{3}(0.236 \mathrm{~g}, 2.81 \mathrm{mmol})$ and Dess-Martin periodinane $(0.261 \mathrm{~g}$, 0.618 mmol ) at rt under argon. Upon completion (monitored by TLC ), $\mathrm{Et}_{2} \mathrm{O}(15 \mathrm{~mL})$ was added, and the solution extracted with $\mathrm{NaHCO}_{3}$ (saturated aq., 2x). The combined organic layers were rinsed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica (10:1 Hex:EtOAc) to give the SI2 ( $0.154 \mathrm{~g}, 90 \%$ ) as a clear oil.
$[\propto]_{\mathbf{D}} 17.70\left(c=1.65, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$;
FTIR (neat) 2954, 2933, 2856, 1718, 1458, 1247, $1037 \mathrm{~cm}^{-1}$;
${ }^{1} \mathbf{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CHCl}_{3}-d\right) \delta \mathrm{ppm} 7.28(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}), 6.88(\mathrm{~d}, J=8.8 \mathrm{~Hz}, 2 \mathrm{H})$, $4.75(\mathrm{~s}, 1 \mathrm{H}), 4.67(\mathrm{~s}, 1 \mathrm{H}), 4.58(\mathrm{~d}, J=10.7 \mathrm{~Hz}, 1 \mathrm{H}), 4.49(\mathrm{~d}, J=10.7 \mathrm{~Hz}, 1 \mathrm{H}), 4.30$ (ddd, $J=14.4,9.3,5.4 \mathrm{~Hz}, 1 \mathrm{H}$ ), $3.82(\mathrm{~s}, 3 \mathrm{H}), 3.73(\mathrm{dd}, J=9.9,5.3 \mathrm{~Hz}, 2 \mathrm{H}), 3.64(\mathrm{dd}, J$ $=9.9,3.3 \mathrm{~Hz}, 1 \mathrm{H}$ ), $3.28(\mathrm{dd}, J=9.1,2.88 \mathrm{~Hz}, 1 \mathrm{H}), 2.68(\mathrm{dd}, J=15.9,8.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.62$ (dd, $J=7.3,1.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.60(\mathrm{~d}, J=6.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.48(\mathrm{dd}, J=15.9,4.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.29$
(dd, $J=8.1,7.3 \mathrm{~Hz}, 2 \mathrm{H}), 1.78-1.87(\mathrm{~m}, 1 \mathrm{H}), 1.75(\mathrm{~s}, 3 \mathrm{H}), 1.48-1.73(\mathrm{~m}, 7 \mathrm{H}), 1.36(\mathrm{~s}, 3$ H), $1.33(\mathrm{~s}, 3 \mathrm{H}), 0.93(\mathrm{~s}, 9 \mathrm{H}), 0.92(\mathrm{~d}, J=4.8 \mathrm{~Hz}, 3 \mathrm{H}), 0.90(\mathrm{~d}, J=4.6 \mathrm{~Hz}, 3 \mathrm{H}), 0.07$ (d, $J=2.0 \mathrm{~Hz}, 6 \mathrm{H}$ );
${ }^{13} \mathbf{C}$ NMR ( $\left.126 \mathrm{MHz}, \mathrm{CHCl}_{3}-d\right) \delta \mathrm{ppm} 208.25,158.94,144.46,131.59,129.16,113.64$, 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 $\mathrm{C}_{35} \mathrm{H}_{60} \mathrm{NaO}_{6} \mathrm{Si}(\mathrm{M}+\mathrm{H})^{+}$627.4057; found 627.4038 (ESI).

## (5S,7R,9S,12R,13S,14R)-15-(tert-butyldimethylsilyloxy)-13-(4-methoxybenzyloxy)-

## 2,12,14-trimethylpentadec-1-ene-5,7,9-triol (21)




A solution of ketone SI2 $(0.050 \mathrm{~g}, 0.083 \mathrm{mmol})$ in $\mathrm{CH}_{3} \mathrm{CN}(1.38 \mathrm{ml})$ was added $\mathrm{H}_{2} \mathrm{O}$ $(198 \mu \mathrm{l})$ followed by $\mathrm{CeCl}_{3} \cdot 7 \mathrm{H}_{2} \mathrm{O}(93 \mathrm{mg}, 0.250 \mathrm{mmol})$. The reaction was stirred until the disappearance of starting material $(\sim 5 \mathrm{~h})$. The reaction was diluted with $\mathrm{Et}_{2} \mathrm{O}$, quenched with $\mathrm{NaHCO}_{3}$ (saturated aq.), and the aqueous layer was re-extracted with $\mathrm{Et}_{2} \mathrm{O}$ (2x). The organic layer was dried $\left(\mathrm{Na}_{2} \mathrm{SO}_{4}\right)$, 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 $\mathbf{E t}_{\mathbf{2}} \mathbf{B O M e}, \mathbf{N a B H}_{4}$ : To a solution of $20(0.090 \mathrm{~g}, 0.159 \mathrm{mmol})$ in $4: 1$ THF: $\mathrm{MeOH}\left(0.353 \mathrm{~mL}\right.$ ) was added $\mathrm{Et}_{2} \mathrm{BOMe}\left(1 \mathrm{M}\right.$ in $\mathrm{THF}, 0.043 \mathrm{~mL}$ ) at $-78{ }^{\circ} \mathrm{C}$ and stirred for 15 minutes. $\mathrm{NaBH}_{4}(0.014 \mathrm{~g}, 0.368 \mathrm{mmol})$ was added and stirred at $-78^{\circ} \mathrm{C}$ for

1 h . Then the reaction flask was warmed to rt and stirred for an additional hour. The reaction was quenched at $-20^{\circ} \mathrm{C}$ with $10 \%$ aqueous $\mathrm{NaOH}, 35 \% \mathrm{H}_{2} \mathrm{O}_{2}$, and stirred for 12 h at rt . The layers were separated, and the aq. layer extracted with $\mathrm{Et}_{2} \mathrm{O}(2 \mathrm{x})$. The combined organic layers were rinsed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), 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 ${ }^{1} \mathrm{H}$ NMR of crude reaction) of $\mathbf{2 0}(0.054 \mathrm{~g}, 60 \%, 95 \% \mathrm{brsm})$ as a clear oil as well as 32 mg of starting ketone.

Reduction with DIBAL-H: To a solution of the ketone ( $0.010 \mathrm{~g}, 0.0176 \mathrm{mmol}$ ) in toluene $(0.200 \mathrm{~mL})$ was slowly added DIBAL-H ( 1.0 M in toluene, 0.040 mL ) at $-78{ }^{\circ} \mathrm{C}$. After two hours of stirring at $-78^{\circ} \mathrm{C}$, the reaction was quenched with $\mathrm{NH}_{4} \mathrm{Cl}$ (saturated, aq.$)$, and the reaction warmed to rt while stirring. The layers were separated, and the aq. layer extracted with $\mathrm{Et}_{2} \mathrm{O}(2 \mathrm{x})$. The combined organic layers were rinsed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica ( $2: 1 \mathrm{Hex}: \mathrm{EtOAc}$ ) to afford the title compound as a $1: 1$ mixture (determined by ${ }^{1} \mathrm{H}$ NMR of crude reaction) of $21(0.0075 \mathrm{~g}$, $75 \%$ ) as a clear oil.

Reduction with $\mathrm{LiAlH}_{4} / \mathrm{LiI}:$ To a solution of the ketone $\left(0.020 \mathrm{~g}, 0.035 \mathrm{mmol}^{2}\right)$ in $\mathrm{Et}_{2} \mathrm{O}$ $(0.440 \mathrm{~mL})$ was added $\mathrm{LiI}(0.047 \mathrm{~g}, 0.350 \mathrm{mmol})$ at $0{ }^{\circ} \mathrm{C}$ (solution turns reddish-brown color). Once the LiI is completely dissolved ( $<5 \mathrm{~min}$ ), the reaction was cooled to $-78{ }^{\circ} \mathrm{C}$ and a solution of $\mathrm{LiAl}_{4} \mathrm{H}\left(2.0 \mathrm{M}\right.$ in $\left.\mathrm{Et}_{2} \mathrm{O}, 0.175 \mathrm{~mL}\right)$ 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 $\mathrm{Et}_{2} \mathrm{O}(2 \mathrm{x})$. The combined organic layers were rinsed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica ( $2: 1 \mathrm{Hex}: \mathrm{EtOAc}$ ) to afford the title compound as a $1.6: 1$ mixture (determined by ${ }^{1} \mathrm{H}$ NMR of crude reaction) of $21(0.018 \mathrm{~g}, 90 \%)$ as a clear oil.

Reduction with $\mathbf{E t}_{3} \mathbf{B}, \mathbf{N a B H}_{4}$ : To a solution of the ketone ( $0.020 \mathrm{~g}, 0.035 \mathrm{mmol}$ ) in $4: 1$ THF: MeOH ( 0.353 mL ) was added $\mathrm{Et}_{3} \mathrm{~B}$ ( 1.0 M in THF 0.056 ml ) at rt stirred for 15 minutes. The reaction was then cooled to $-78^{\circ} \mathrm{C}$ and $\mathrm{NaBH}_{4}(0.003 \mathrm{~g}, 0.071 \mathrm{mmol})$ was
added and stirred at that temperature for 3 h . The reaction was quenched at $-78{ }^{\circ} \mathrm{C}$ with $10 \%$ aqueous $\mathrm{NaOH}, 35 \% \mathrm{H}_{2} \mathrm{O}_{2}$, and the reaction was stirred for 12 h at rt . The layers were separated, and the aq. layer extracted with $\mathrm{Et}_{2} \mathrm{O}(2 \mathrm{x})$. The combined organic layers were rinsed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), 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 ${ }^{1} \mathrm{H}$ NMR of crude reaction) of $21(0.014 \mathrm{~g}, 70 \%)$ as a clear oil.

Reduction with $\mathbf{Z n C l}_{\mathbf{2}}, \mathbf{N a B H}_{\mathbf{4}}$ : To a solution of the ketone ( $0.010 \mathrm{~g}, 0.0175 \mathrm{mmol}$ ) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(0.175 \mathrm{~mL})$ was added $\mathrm{ZnCl}_{2}(1 \mathrm{M}$ in THF, 0.0175 mL$)$ at rt and stirred for 15 minutes. $\mathrm{NaBH}_{4}(0.0015 \mathrm{mg}, 0.0012 \mathrm{mmol})$ was then added and the reaction was stirred for 12 h . The reaction was quenched with $10 \%$ aqueous $\mathrm{NaOH}, 35 \% \mathrm{H}_{2} \mathrm{O}_{2}$, and the reaction was stirred for 12 h at rt . The layers were separated, and the aq. layer extracted with $\mathrm{Et}_{2} \mathrm{O}(2 \mathrm{x})$. The combined organic layers were rinsed with brine (1x), dried (anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$ ), filtered, and concentrated (rotary evaporator). The mixture was pushed through a short plug of silica ( $2: 1 \mathrm{Hex}: \mathrm{EtOAc}$ ) to afford the title compound as a 3.3:1 mixture (determined by ${ }^{1} \mathrm{H}$ NMR of crude reaction) of $21(0.006 \mathrm{~g}, 64 \%)$ as a clear oil.
$[\propto]_{\mathbf{D}} 7.26\left(c=1.35, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$;
FTIR (neat) $3371,2933,2883,2856,1612,1514,1461 \mathrm{~cm}^{-1}$;
${ }^{1} \mathbf{H}$ NMR ( $\left.400 \mathrm{MHz}, \mathrm{CHCl}_{3}-d\right) \delta \mathrm{ppm} 7.27(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H}), 6.89(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H})$, $4.74(\mathrm{~d}, J=1.3 \mathrm{~Hz}, 1 \mathrm{H}), 4.73(\mathrm{~s}, 1 \mathrm{H}), 4.56(\mathrm{~d}, J=10.9 \mathrm{~Hz}, 1 \mathrm{H}), 4.49(\mathrm{~d}, J=10.9 \mathrm{~Hz}, 1$ H), 4.18-4.26 (m, 1 H$), 3.85-3.97(\mathrm{~m}, 2 \mathrm{H}), 3.80(\mathrm{~s}, 3 \mathrm{H}), 3.73(\mathrm{dd}, J=9.6,5.3 \mathrm{~Hz}, 1 \mathrm{H})$, 3.63 (dd, $J=9.6,3.3 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.30 (dd, $J=8.8,2.5 \mathrm{~Hz}, 1 \mathrm{H}$ ), 2.14 (dddd, 2 H ), 1.78$1.86(\mathrm{~m}, 1 \mathrm{H}), 1.75(\mathrm{~s}, 3 \mathrm{H}), 1.58-1.73(\mathrm{~m}, 8 \mathrm{H}), 1.46-1.57(\mathrm{~m}, 4 \mathrm{H}), 1.27(\mathrm{~m}, 3 \mathrm{H}), 0.92$ (s, 9 H$), 0.91(\mathrm{~d}, J=2.3 \mathrm{~Hz}, 3 \mathrm{H}), 0.89(\mathrm{~d}, J=2.3 \mathrm{~Hz}, 3 \mathrm{H}), 0.06$ (s, 3 H ), 0.05 (s, 3 H );
${ }^{13} \mathbf{C}$ NMR ( $126 \mathrm{MHz}, \mathrm{CHCl}_{3}-d$ ) $\delta \mathrm{ppm} 158.95,145.69,131.61,129.22,113.65,110.31$, $83.30,77.25,74.34,73.17,70.89,69.79,64.95,55.28,42.53,38.58,35.87,35.74,35.33$, $33.75,31.05,25.96,22.40,18.33,14.73,13.39,-5.32,-5.41$;

HRMS Exact Mass: calculate for $\mathrm{C}_{32} \mathrm{H}_{58} \mathrm{NaO}_{6} \mathrm{Si}(\mathrm{M}+\mathrm{Na})^{+} 589.3900$; 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 SI1). In accordance with Rychnovsky-Evans acetonide analysis, ${ }^{1}{ }^{13} \mathrm{C}$ analysis of the SI3 contained acetonide peaks at $30.24 \mathrm{ppm}, 19.68 \mathrm{ppm}$, and 98.68 , indicative of the newly formed 1,3-syn acetonide.

## Scheme SI-1



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[^0]:    (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 propionatederived polyols. Tetrahedron Lett. 1990, 31, 7099-100

