Synthesis of the ABC substructure of brevenal by sequential *exo*-mode oxacyclizations of acyclic polyene precursors

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SUPPORTING INFORMATION: Experimental details and characterization data

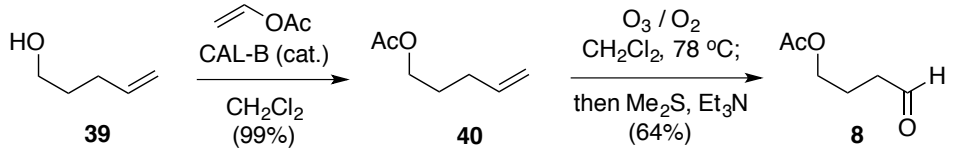
1) General experimental: ^{1}H and ^{13}C NMR spectra were recorded on Varian INOVA 600, INOVA 400, and Bruker AVANCE 600 spectrometers. NMR spectra were generally measured from solutions of deuterated chloroform ($CDCl_3$), with the residual chloroform (7.27 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR) taken as the internal standard, deuterated acetone ($(CD_3)_2CO$) with residual acetone (2.09 ppm for ^{1}H NMR and 30.6 ppm for ^{13}C NMR) taken as the internal standard, or deuterated benzene with residual benzene (7.16 ppm for ^{1}H NMR and 128.23 ppm for ^{13}C NMR) taken as the internal standard, and were reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; ddd, doublet of doublet of doublet; dt, doublet of triplet; m, multiplet.

IR spectra were collected on a Thermo Scientific Nicolet iS10 FT-IR spectrometer as neat films on a plate with diamond screw-down tip. Mass spectra (high resolution ESI and APCI) were recorded on a Thermo LTQ FTMS Mass spectrometer. Optical rotations were measured using a Perkin-Elmer 341 polarimeter (concentration in g/100mL). Thin layer chromatography (TLC) was performed on a precoated glass backed plates purchased from Silicycle (silica gel $60F_{254}$; 0.25mm thickness). Flash column chromatography was carried out with silica gel 60 (230-400 mesh ASTM) from Silicycle.

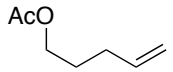
All reactions were carried out with anhydrous solvents in oven dried and argon-charged glassware. All anhydrous solvents were dried with 4Å molecular sieves purchased from Sigma Aldrich and tested for trace water content with Coulometric KF titrator from Denver Instruments. Reactants were used as received from commercial suppliers without prior purification, as were solvents used for extractions and chromatographic separations.

2) Synthesis of acyclic triene-triol 2 (Scheme 1):

4-Hydroxybutanal, acetate ester 8 was prepared in two steps from 4-penten-1-ol (**39**).



Preparation of 4-penten-1-ol, acetate ester 40: 4-Penten-1-ol (**39**, 10.54 g, 122.4 mmol) was dissolved in CH_2Cl_2 (300 mL). Vinyl acetate (16.9 mL, 184 mmol) and CAL-B (500 mg) were added. The reaction mixture was stirred at room temperature for 3 h, then filtered over a pad of Celite (ether eluent) and concentrated under reduced pressure to afford **40** as a clear colorless liquid (15.46 g, 120.6 mmol, 99% yield).



40

Data for 40:

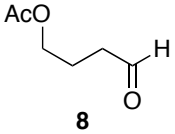
IR (thin film): 2922, 285, 1732, 1456, 1284 cm^{-1}.

HRMS (NSI): *m/z* calcd for $C_7H_{12}O_2Na$ $[M+Na]^+$ 151.0730, found 151.0729.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.05 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.00 (ddt, *J* = 10.2, 1.9, 1.2 Hz, 1H), 4.09 (t, *J* = 6.7 Hz, 2H), 2.18 – 2.10 (m, 2H), 2.06 (s, 3H), 1.81 – 1.68 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 137.4, 115.2, 63.8, 30.1, 27.8, 20.9.

Preparation of aldehyde 8: Alkene **40** (8.19 g, 63.9 mmol) was dissolved in CH_2Cl_2 (400 mL). The solution was cooled to -78 °C. A stream of O_2 was bubbled through the -78 °C solution for 10 min, followed by a stream of O_3 for 45 min, until the saturated solution took on a persistent pale blue color. The reaction was sparged with O_2 at -78 °C for an additional 10 min before the pale blue color faded. Dimethyl sulfide (30 mL) was added. The reaction mixture warmed to room temperature, and after 1 h, NEt_3 (20 mL) was added, and the reaction mixture was stirred for 1 h. The reaction mixture was diluted with water. The aqueous layer was separated and extracted with CH_2Cl_2 (25 mL x 3). The combined organic layer was washed with water (50 mL), washed with brine, and dried over $MgSO_4$ before filtration and concentration under reduced pressure to furnish aldehyde **8** as a yellow oil (5.42 g, 41.7 mmol, 64% yield). The ^{1}H NMR spectrum matched reported spectra from the literature from PCC oxidation.[1]

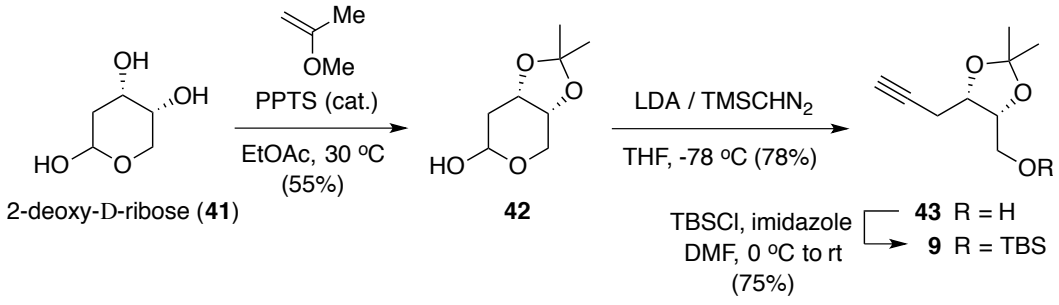


8

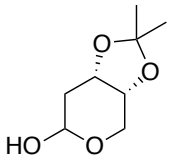
Data for 8:

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (t, *J* = 1.0 Hz, 1H), 4.10 (t, *J* = 6.3 Hz, 2H), 2.55 (dt, *J* = 7.2, 1.3 Hz, 2H), 2.05 (s, 3H), 1.99 (td, *J* = 7.1, 6.4 Hz, 2H).

Terminal alkyne 9 was prepared in three steps from 2-deoxy-D-ribose (**41**).[2,3]



Preparation of acetonide 42: 2-Deoxy-D-ribose (**41**, 25.0 g, 186 mmol) was dissolved in EtOAc (375 mL). 2-Methoxypropane (24.0 mL, 242 mmol) and pyridinium *p*-toluenesulfonate (PPTS, 942 mg, 3.72 mmol) were added, and the resulting suspension was stirred at 30 °C for 18 h. Although **41** was not completely consumed (monitored by TLC), neither extended reaction times, increased heating, nor additional equivalents of 2-methoxypropane or additional PPTS catalyst improved the yield or conversion. Aqueous NH_4Cl (100 mL) was added to the pale yellow, clear reaction mixture and the resulting biphasic mixture was stirred for 1 h. The layers were separated and the aqueous layer was extracted with EtOAc (25 mL x 3). The combined organic extracts were washed with brine and dried over Na_2SO_4 before being filtered and concentrated under reduced pressure to afford a crude yellow oil. The crude oil was purified by silica gel flash column chromatography (30% to 50% EtOAc in hexanes) to afford the acetonide product **42** as a clear, colorless oil (17.9 g, 102 mmol, 55% yield, 3:1 mixture of anomers by ^{1}H NMR). The spectra matched that of the published compound.[2]



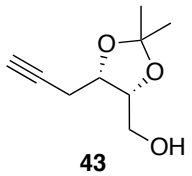
42

Data for 42:

^{1}H NMR (500 MHz, $CDCl_3$) (major anomer) δ 5.26 (dd, *J* = 7.1, 4.3 Hz, 1H), 4.48 (dt, *J* = 6.6, 4.2 Hz, 1H), 4.22 – 4.09 (m, 1H), 3.98 – 3.92 (m, 1H), 3.74 – 3.67 (m, 1H), 3.06 (br s, OH), 2.24 (dt, *J* = 14.8, 4.3 Hz, 1H), 1.78 (ddd, *J* = 14.8, 7.1, 4.2 Hz, 1H), 1.50 (s, 3H), 1.35 (s, 3H).

Preparation of alkynyl alcohol 43: *n*-Butyllithium solution (61.2 mL, 2.45 M in hexanes, 150 mmol) was added dropwise to a stirred solution of diisopropylamine (20.0 mL, 150 mmol) in THF (36 mL) at -78 °C. After stirring for 45 min, $TMSCHN_2$ solution (37.5 mL, 2.0M in ether, 75.0 mmol) was added dropwise. The reaction mixture was stirred at -78 °C for 30 min before slow addition of lactol **42** (8.71 g, 50.0 mmol) in THF (17 mL). The reaction mixture was warmed to room temperature over a period of 4 h, and was stirred overnight before being quenched by addition of saturated aqueous NH_4Cl (40 mL). The aqueous phase was extracted with EtOAc (5 × 30 mL) and the combined organic phase was washed with water (2 x 30 mL), brine, and dried over Na_2SO_4, decanted, and concentrated under reduced pressure to afford an orange residue, which was dissolved in methanol (17 mL) and aqueous K_2CO_3 (10% w/w, 17 mL) and stirred for 30 min. The reaction mixture was then extracted with EtOAc (5 x 25 mL), washed with brine and dried over Na_2SO_4, and decanted before being concentrated under reduced pressure to afford the crude product as an orange syrup. The oil was purified by silica gel flash column chromatography (40% EtOAc in hexanes to 55% EtOAc in hexanes) to afford alkynyl alcohol **43** as a clear orange oil (6.62 g, 38.9 mmol, 78% yield). The spectra matched that of the published compound.[3] This reaction was run with three batches in parallel around 50

mmol scale each, rather than scaling up, due to concerns of rapid nitrogen evolution as the reaction warmed to room temperature.



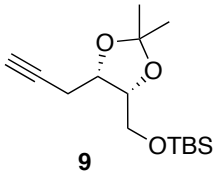
43

Data for 43:

HRMS (NSI): *m/z* calcd for $C_{15}H_{28}O_3NaSi$ $[M+Na]^+$ 307.1700, found 307.1700.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.38 (dt, *J* = 8.0, 6.1 Hz, 1H), 4.29 (td, *J* = 6.3, 4.4 Hz, 1H), 3.84 (dd, *J* = 11.7, 4.4 Hz, 1H), 3.77 (dd, *J* = 11.7, 6.4 Hz, 1H), 2.57 (ddd, *J* = 16.8, 6.1, 2.7 Hz, 1H), 2.51 (ddd, *J* = 16.7, 8.0, 2.7 Hz, 1H), 2.06 (t, *J* = 2.7 Hz, 1H), 1.94 (br s, -OH), 1.49 (s, 3H), 1.39 (s, 3H).

Preparation of silyl ether 9: The alkynyl alcohol **43** (6.62 g, 38.9 mmol) was dissolved in DMF (40 mL), and the solution was cooled to 0 °C. TBSCl (7.02 g, 46.6 mmol) and imidazole (3.32 g, 48.6 mmol) were each added in one portion. The reaction mixture was warmed to room temperature and stirred overnight. Upon completion by TLC, the reaction mixture was diluted with water (300 mL) and ether (50 mL). The aqueous and organic layers were separated and the aqueous layer was extracted with ether (20 mL x 5). The combined organic extracts were washed with H_2O (10 mL x 2) and brine before being dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes to 3% EtOAc in hexanes) to yield silyl ether **9** as a clear orange oil (7.20 g, 29.0 mmol, 75% yield). Although the ^{1}H NMR spectra of the alcohol precursor **43** matched the published compound,[3] the resonances in our spectrum for silyl ether **9** were 0.14 ppm (±0.02 ppm) higher in chemical shift than the reported tabulated data. The image of the published spectra did not have an apparent $CDCl_3$ signal or another obvious reference peak. As the discrepancies in chemical shifts between our spectra and the reported spectra are systematic, we believe the concentrated sample in the literature report was referenced incorrectly, resulting in misreported tabulated data.[3] The discrepancies in coupling constants may be explained by relatively low-resolution spectra in the literature spectra (300 MHz) compared to our spectra (600 MHz).

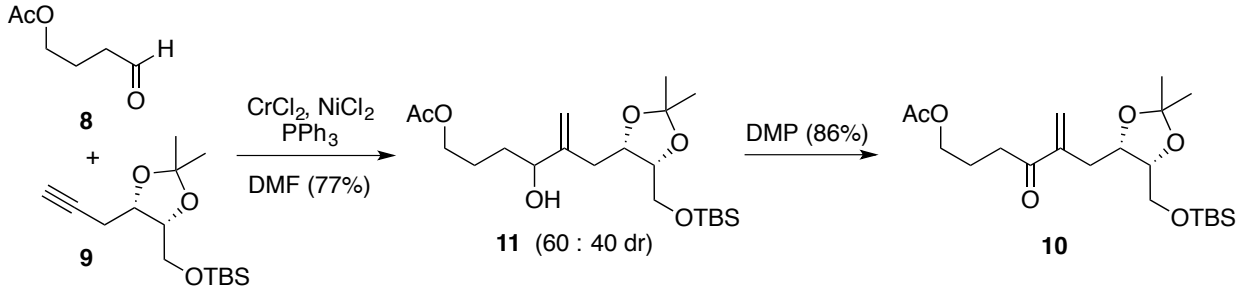


9

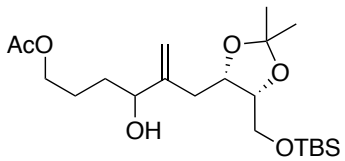
Data for 9:

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.35 (ddd, *J* = 7.9, 6.0, 5.2 Hz, 1H), 4.18 (ddd, *J* = 7.0, 5.9, 5.1 Hz, 1H), 3.79 – 3.66 (m, 2H), 2.60 (ddd, *J* = 16.6, 5.3, 2.6 Hz, 1H), 2.50 (ddd, *J* = 16.9, 7.9, 2.7, 1H), 2.04 (t, *J* = 2.6 Hz, 1H), 1.47 (s, 3H), 1.37 (s, 3H), 0.90 (m, 9H), 0.08 (s, 6H).

Enone 10 was prepared by Cr(II)/Ni(II) mediated reductive coupling of aldehyde **8** and terminal alkyne **9** to form the allylic alcohol **11** as a mixture of diastereomers, followed by oxidation.



Preparation of allylic alcohol 11 (60 : 40 dr): $CrCl_2$ (3.30 g, 26.8 mmol) and $NiCl_2$ (71 mg, 0.54 mmol) were weighed out in a glovebox. The flask was removed from the glovebox and sparged with argon for 10 min before rapid addition of triphenylphosphine (707 mg, 2.68 mmol). After 10 min under argon, dry, degassed DMF (33 mL) was added. Aldehyde **8** (924 mg, 5.36 mmol) in DMF (21 mL) was added, and the reaction mixture was stirred for 15 min. Alkyne **9** (3.82 g, 13.4 mmol) and water (0.19 mL) in DMF (33 mL) were added via syringe pump over 4 h, and the resulting suspension was stirred at room temperature for 4 h. The reaction mixture was diluted with saturated aqueous NH_4Cl (400 mL) and EtOAc (100 mL) and stirred for 1 h. The layers were separated and the aqueous layer was extracted with EtOAc (50 mL × 6). The combined organic phase was washed with water (50 mL x 2) and brine before being dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (18% EtOAc in hexanes to 25% EtOAc in hexanes) to afford allylic alcohol **11** as a clear pale yellow oil (1.71 g, 4.10 mmol, 77% yield, 60:40 dr favoring the (*S*)-alcohol.



11 (60 : 40 dr)

Data for 11 (60 :40 dr):

$[\alpha]_D^{25}$ -25.6 (c = 1.01, $CHCl_3$)

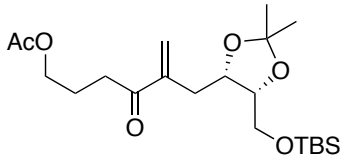
HRMS (NSI): *m/z* calcd. for $C_{21}H_{40}O_6ClSi$ $[M+Cl]^-$ 451.2288, found 451.2290.

IR (neat): 3464, 2930, 2857, 1739, 1471, 1367, 1246, 1163, 1096, 1071, 835, 777, 666 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.13 (s, 0.4H), 5.11 (d, *J* = 1.3 Hz, 0.6H), 5.02 (t, *J* = 1.3 Hz, 0.4H), 5.00 (t, *J* = 1.2 Hz, 0.6H), 4.40 (ddd, *J* = 9.6, 5.9, 3.5 Hz, 0.4H), 4.30 (ddd, *J* = 9.7, 6.1, 3.7 Hz, 0.6H), 4.21 – 4.15 (m, 1H), 4.15 – 4.05 (m, 3H), 3.71 (ddd, *J* = 10.5, 7.9, 1.7 Hz, 1H), 3.65 (ddd, *J* = 15.0, 10.5, 4.6 Hz, 1H), 3.19 (d, *J* = 4.4 Hz, 1H), 2.58 – 2.49 (m, 1H), 2.45 – 2.37 (m, 1H), 2.05 (s, 3H), 1.85 – 1.71 (m, 1H), 1.71 – 1.62 (m, 2H), 1.62 – 1.53 (m, 1H), 1.45 (s, 2H), 1.44 (s, 1H), 1.35 (s, 1H), 1.34 (s, 2H), 0.90 (s, 9H), 0.08 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 148.8, 148.7, 114.3, 112.6, 108.4, 108.2, 78.3, 77.9, 77.9, 77.2, 75.2, 75.2, 75.0, 75.0, 64.6, 64.6, 62.1, 61.9, 32.5, 32.2, 31.6, 30.9, 28.3, 28.0, 26.0, 25.6, 25.5, 25.3, 25.2, 21.2, 18.42, 18.37, -5.3.

Allylic alcohol **11** (2.86 g, 6.86 mmol, arising from multiple batches) was dissolved in CH_2Cl_2 (135 mL), followed by addition of $NaHCO_3$ (1.78 g, 21.0 mmol) and Dess-Martin periodinane (DMP, 4.37 g, 10.3 mmol). The reaction mixture was stirred at room temperature for 3 h. Aqueous $Na_2S_2O_3$ (80 mL) and aqueous $NaHCO_3$ (80 mL) were added and the biphasic mixture was stirred for 1 h, at which point the layers became clear upon standing. The aqueous phase was separated and extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to afford enone **10** as a light yellow clear oil (2.44 g, 5.87 mmol, 86% yield).



10

Data for 10:

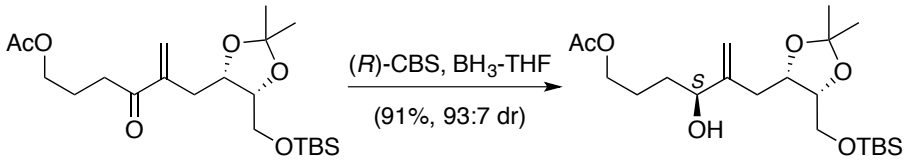
$[\alpha]_D^{25}$ -25.1 (c = 1.00, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{21}H_{38}O_6NaSi$ $[M+Na]^+$ 437.2330, found 437.2327.

IR (neat): 2984, 2930, 2857, 1740, 1679, 1471, 1138, 1245, 1165, 1045, 836, 777, 667 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (s, 1H), 5.93 (d, *J* = 1.3 Hz, 1H), 4.29 (ddd, *J* = 10.6, 6.0, 2.6 Hz, 1H), 4.16 (dt, *J* = 7.1, 5.6 Hz, 1H), 4.10 (t, *J* = 6.4 Hz, 2H), 3.73 (dd, *J* = 10.5, 7.1 Hz, 1H), 3.68 (dd, *J* = 10.5, 5.2 Hz, 1H), 2.82 (td, *J* = 7.1, 1.0 Hz, 2H), 2.74 (ddd, *J* = 14.7, 2.6, 1.2 Hz, 1H), 2.37 (dd, *J* = 14.8, 10.7 Hz, 1H), 2.05 (s, 3H), 1.97 (p, *J* = 7.0 Hz, 2H), 1.43 (s, 3H), 1.32 (s, 3H), 0.91 (s, 9H), 0.09 (s, 6H).

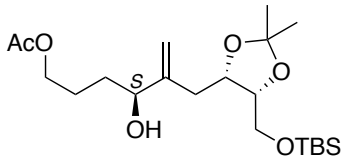
^{13}C NMR (126 MHz, $CDCl_3$) δ 200.2, 170.9, 145.2, 125.9, 107.9, 77.6, 75.4, 63.6, 61.7, 33.8, 30.9, 28.0, 25.8, 25.4, 23.1, 20.8, -5.6.



10 **11** (93 : 7 dr)

Preparation of allylic alcohol 11 (93 : 7 dr): (*R*)-2-Methyl-CBS-oxazaborolidine in toluene (1.0 M, 2.90 mL, 2.90 mmol) and $BH_3 \cdot THF$ (1.0 M, 4.34 mL, 4.34 mmol) were added to THF (14 mL) at room temperature and stirred for 50 min before being cooled to -40 °C, where a solution of enone **10** (1.12 g, 2.89 mmol) in THF (57 mL) was slowly added. The resulting reaction mixture was stirred at -25 °C for 2 h. The reaction mixture was quenched with methanol

(5 mL), warmed to room temperature, and concentrated under reduced pressure. The resulting oil was dissolved in EtOAc, washed with saturated aqueous NH_4Cl (20 mL), and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated in under reduced pressure. The residue was purified by flash column chromatography (15% to 25% EtOAc in hexanes) to furnish compound **11** as a light yellow clear oil (1.10 g, 2.64 mmol, 91% yield, 93 : 7 dr, determined by Mosher ester analysis).



11 (93 : 7 dr)

Data for 11 (93 : 7 dr):

$[\alpha]_D^{25}$ -32.8 (c = 1.10, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{21}H_{40}O_6SiNa$ $[M+Na]^+$ 439.2486, found 43902483.

FT-IR (neat): 3485, 2953, 2930, 2857, 1738, 1649, 1471, 1367, 1245, 1094, 1045, 834, 776, 736, 703, 667, 607 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.11 (s, 1H), 5.01 (t, *J* = 1.2 Hz, 1H), 4.31 (ddd, *J* = 9.7, 6.1, 3.7 Hz, 1H), 4.18 (ddd, *J* = 7.8, 6.1, 4.7 Hz, 1H), 4.16 – 4.12 (m, 1H), 4.10 (tt, *J* = 6.4, 3.3 Hz, 2H), 3.71 (dd, *J* = 10.4, 7.8 Hz, 1H), 3.67 (dd, *J* = 10.4, 4.7 Hz, 1H), 3.19 (d, *J* = 4.5 Hz, -OH), 2.45 – 2.36 (m, 2H), 2.06 (s, 3H), 1.80 – 1.71 (m, 1H), 1.71 – 1.55 (m, 3H), 1.46 (s, 3H), 1.35 (s, 3H), 0.90 (s, 9H), 0.05 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 148.7, 114.2, 108.4, 78.3, 77.9, 75.2, 64.6, 61.9, 32.5, 30.9, 28.0, 26.0, 25.4, 25.2, 21.2, 18.4, -5.3, -5.3.

The Mosher esters were prepared by the following protocol:[4] In an NMR tube, the alcohol (ca. 10 mg) and pyridine-d_5 (2 - 3 drops) were dissolved in $CDCl_3$ (ca. 0.5 mL), and 2 – 3 drops of (*S*)- or (*R*)-methoxy(trifluoromethyl)-phenylacetyl chloride (MTPA-Cl) were added. The tube was gently shaken and then allowed to stand overnight, to afford a solution of the (*R*)- or (*S*)-MTPA ester, respectively. Partial ^{1}H NMR data are provided, absent phenyl and methoxy signals obscured by the excess MTPA reagent:

Data for (*S*)-MTPA ester: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.41 (m, 1H), 5.16 (s, 1H), 5.12 (s, 1H), 4.31 (ddd, *J* = 10.0, 5.9, 2.9 Hz, 1H), 4.04 (dt, *J* = 7.6, 5.3 Hz, 1H), 3.93 (ddt, *J* = 11.1, 6.7, 4.6 Hz, 2H), 3.55 (qd, *J* = 10.4, 6.3 Hz, 2H), 2.40 (dd, *J* = 16.3, 2.7 Hz, 1H), 2.27 (dd, *J* = 16.1, 10.0 Hz, 1H), 1.96 (s, 3H), 1.70 (m, 2H), 1.47 (m, 2H), 1.35 (s, 3H), 1.26 (s, 3H), 0.81 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H).

Data for (*R*)-MTPA ester: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.33 (t, *J* = 6.5 Hz, 1H), 5.03 (s, 1H), 4.99 (s, 1H), 4.26 (ddd, *J* = 10.0, 6.0, 2.9 Hz, 1H), 3.98 (m, 3H), 3.47 (m, 2H), 2.32 (m, 1H), 2.16 (m, 1H), 1.95 (s, 3H), 1.75 (m, 2H), 1.60 (m, 2H), 1.33 (s, 3H), 1.25 (s, 3H), 0.80 (s, 9H), -0.02 (s, 3H), -0.03 (s, 3H).

Table 1. MTPA-ester data for compound **11**

MTPA-ester resonance	δ *S*-ester (ppm)	δ *R*-ester (ppm)	$\Delta(\delta_S-\delta_R)$ (ppm)	$\Delta(\delta_S-\delta_R)$ (Hz)
b	5.16	5.03	0.13	78
c	5.12	4.99	0.13	78
j	2.27	2.16	0.11	66
g	3.68	3.59	0.09	54
a	5.41	5.33	n/a	n/a
h	3.55	3.47	0.08	48
i	2.40	2.32	0.08	48
d	4.31	4.26	0.05	30
e	4.05	4.01	0.04	24
m_3	1.35	1.33	0.02	12
n_3	1.26	1.25	0.01	6
o_9	0.81	0.80	0.01	6
p_6	-0.02	-0.03	0.01	6
f_2	3.93	3.98	-0.05	-30
k_2	1.70	1.75	-0.05	-30
l_2	1.47	1.6	-0.13	-78

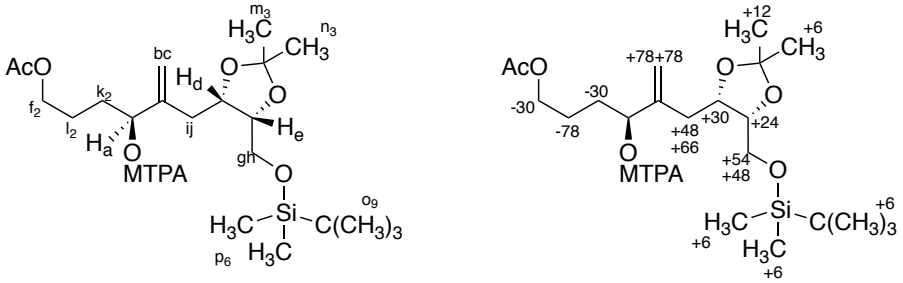
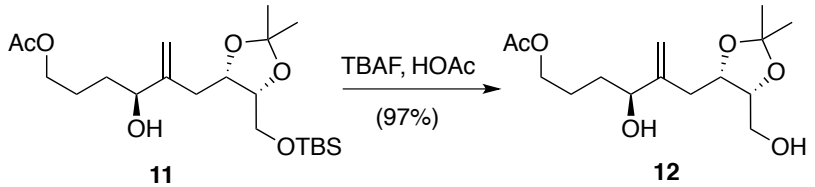
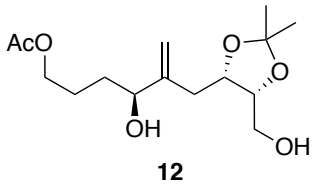


Figure 1. MTPA-ester data for compound **11**



11 **12**

Diol 12: Silyl ether **11** (93 : 7 dr, 1.78 g, 4.27 mmol) was dissolved in THF (40 mL) and cooled to 0 °C. Acetic acid (0.49 mL, 8.53 mmol) and TBAF (1.0 M in THF, 6.40 mL, 6.40 mmol) were added. The resulting solution was gradually warmed to room temperature and stirred for 18 h before removal of solvent under reduced pressure. The resulting oil was purified by silica gel flash column chromatography (75% EtOAc in hexanes) to afford compound **12** as a clear colorless oil (93 : 7 dr, 1.248 g, 4.13 mmol, 97% yield).



12

Data for 12:

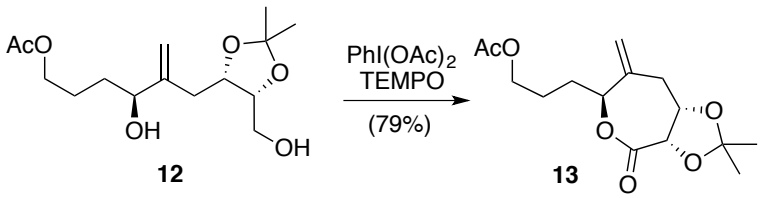
$[\alpha]_D^{25}$ -11.3 (c = 0.981, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{15}H_{26}O_6Na$ $[M+Na]^+$ 325.1622, found 325.1614.

IR (neat): 3425, 2985, 2931, 1734, 1648, 1454, 1368, 1243, 1164, 1037, 981, 899, 837, 734, 702, 607 cm^{-1}.

^{1}H NMR (600 MHz, Acetone-d_6) δ 5.09 (dt, *J* = 1.9, 1.0 Hz, 1H), 4.97 (q, *J* = 1.6 Hz, 1H), 4.42 (q, *J* = 6.6 Hz, 1H), 4.16 (q, *J* = 5.9 Hz, 1H), 4.10 (br s, 1H), 4.08 – 3.97 (m, 2H), 3.87 (s, 1H), 3.62 (dd, *J* = 11.3, 5.9 Hz, 1H), 3.57 (dd, *J* = 10.9, 6.0 Hz, 1H), 2.85 (d, *J* = 11.6 Hz, 1H), 2.37 (d, *J* = 6.5 Hz, 2H), 1.98 (s, 3H), 1.78 – 1.69 (m, 1H), 1.69 – 1.59 (m, 2H), 1.59 – 1.50 (m, 1H), 1.37 (s, 3H), 1.29 (s, 3H).

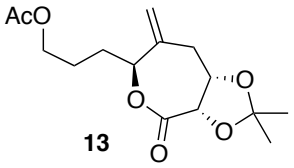
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 148.1, 114.0, 108.5, 78.0, 77.2, 75.1, 64.5, 61.6, 32.3, 30.9, 28.0, 25.4, 25.1, 21.2.



12 **13**

Lactone 13: In a procedure adapted from Forsyth *et al.*,[5] $PhI(OAc)_2$ (1.67 g, 5.17 mmol) and TEMPO (47 mg, 0.30 mmol) were added to CH_2Cl_2 (25 mL), followed by addition in portions of a solution of the diol **12** (93 : 7 dr, 447 mg, 1.47 mmol) in CH_2Cl_2 (5 mL). The resulting mixture was stirred at room temperature for 8 h before being diluted with diethyl ether and quenched with $Na_2S_2O_3$ (10 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with aqueous $NaHCO_3$ (20

mL) and brine before being dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting oil was purified by silica gel flash column chromatography (30% to 45% diethyl ether in pentane) to afford diastereomerically pure lactone **13** as an orange-yellow oil (383 mg, 1.28 mmol, 79% yield).



13

Data for 13:

$[\alpha]_D^{25}$ -93.4 (c = 1.10, $CHCl_3$)

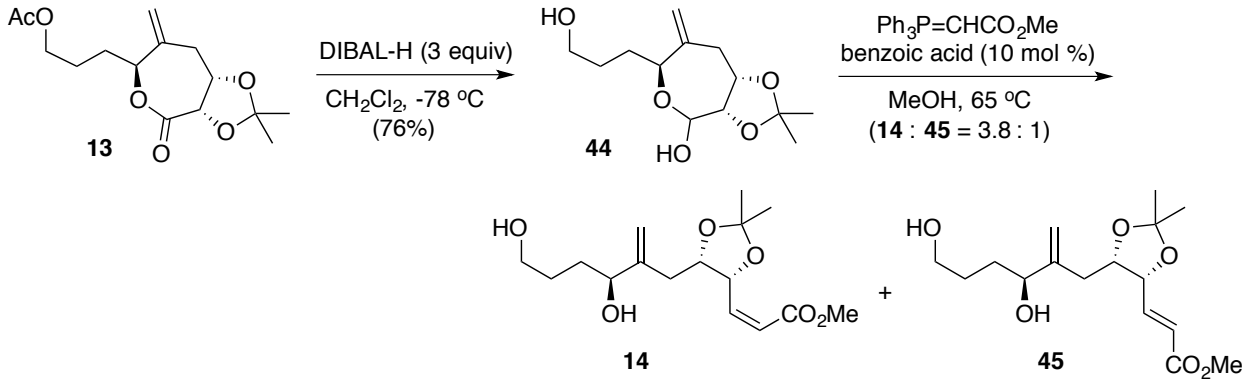
HRMS (APCI): *m/z* calculated for $C_{15}H_{23}O_6$ $[M+H]^+$ 299.1489, found 299.1490.

IR (neat): 3435, 2925, 2855, 1734, 1437, 1370, 1249, 1088, 1042, 980, 908 cm^{-1}.

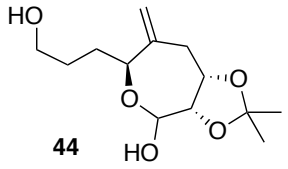
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.41 (d, *J* = 7.9 Hz, 1H), 5.11 (d, *J* = 1.8 Hz, 1H), 5.06 (d, *J* = 1.5 Hz, 1H), 4.83 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.59 (ddd, *J* = 7.7, 5.0, 2.3 Hz, 1H), 4.21 – 4.05 (m, 2H), 2.78 (dd, *J* = 15.7, 5.0 Hz, 1H), 2.61 (d, *J* = 15.7 Hz, 1H), 2.06 (s, 3H), 1.98 – 1.86 (m, 2H), 1.86 – 1.73 (m, 2H), 1.55 (s, 3H), 1.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 170.5, 141.4, 115.6, 111.3, 78.7, 78.2, 73.6, 64.0, 35.2, 29.5, 26.1, 24.6, 24.1, 21.1.

Dienoate-diol 14: This compound was prepared in two steps via the lactol **44**.



Preparation of lactol 44: Lactone **13** (383 mg, 1.28 mmol) was dissolved in CH_2Cl_2 (25 mL), and the solution was cooled to -78 °C. DIBAL-H (1.0 M in hexanes, 3.85 mL) was added dropwise. The reaction mixture was stirred at -78 °C for 1.5 h before being warmed to 0 °C, and diluted with diethyl ether before quenching with H_2O (0.16 mL), 15% aqueous NaOH (0.16 mL), then more water (0.39 mL). The reaction was then allowed to warm to room temperature where it was stirred for 15 min before addition of $MgSO_4$. The mixture was stirred for 15 min before being filtered through a coarse frit, and concentrated under reduced pressure, to afford crude lactol **44** as a light-yellow oil (248 mg, 0.97 mmol, 76% yield).



44

Data for 44:

$[\alpha]_D^{25}$ -2.1 (c = 0.975, $CHCl_3$)

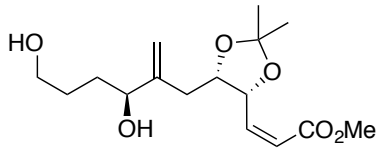
HRMS (NSI): *m/z* calculated for $C_{13}H_{23}O_5$ $[M+H]^+$ 259.1540, found 259.1540.

IR (neat): 3402, 2986, 2931, 2870, 1434, 1381, 1219, 1155, 1061, 909, 789, 733, 701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (d, *J* = 13.8 Hz, 2H), 4.65 (d, *J* = 8.1 Hz, 1H), 4.33 (d, *J* = 5.3 Hz, 1H), 4.23 (d, *J* = 6.1 Hz, 1H), 3.91 – 3.79 (m, 1H), 3.75 – 3.60 (m, 2H), 2.70 – 2.55 (m, 2H), 2.45 (br s, OH), 1.86 – 1.64 (m, 3H), 1.56 (m, 1H), 1.44 (s, 3H), 1.37 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 116.2, 108.6, 95.7, 82.2, 80.9, 74.6, 62.8, 32.2, 31.1, 29.4, 28.4, 25.9.

Preparation of dienoate-diol 14: The lactol **44** (248 mg, 0.97 mmol) was dissolved in methanol (5 mL). The Wittig reagent (388 mg, 1.16 mmol) and benzoic acid (12 mg, 0.10 mmol) were added. The reaction mixture was placed in an oil bath at 65 °C where it was heated for 4 h. The reaction mixture was then cooled to room temperature before the solvent was removed under reduced pressure. The resulting oil was purified by silica gel flash column chromatography (75% EtOAc in hexanes) to afford the products **14** and **45** as a 3.8/1 *Z/E* alkene isomer mixture, with contamination by triphenylphosphine oxide. The impure material was partially separable at this point (enriched to 5.7:1 *Z/E*, still containing ca. 10% $Ph_3P{=}O$ by ^{1}H integration) and was subjected to the next step, at which point the triphenylphosphine oxide and alkene isomers were completely separated.



14

Data for (*Z*)-enoate 14 (5.7 : 1, *Z* : *E* mixture): $[\alpha]_D^{25}$: -96.9 (c = 1.04, $CHCl_3$)

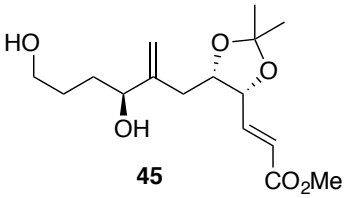
HRMS (NSI): *m/z* calcd. for $C_{16}H_{26}O_6Na$ $[M+Na]^+$ 337.1622, found 337.1617.

IR (neat): 3375, 2987, 2935, 1718, 1648, 1439,1381, 1200, 1051, 902, 850, 826, 724, 542 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$, major isomer reported) δ 6.28 (dd, *J* = 11.6, 7.8 Hz, 1H), 5.98 (dd, *J* = 11.6, 1.5 Hz, 1H), 5.66 (td, *J* = 8.1, 7.5, 1.6 Hz, 1H), 5.10 (s, 1H), 4.98 (d, *J* = 1.2 Hz, 1H), 4.57 (ddd, *J* = 10.2, 6.8, 3.7 Hz, 1H), 4.19 – 4.07 (m, 2H), 3.75 (s, 3H), 3.67 (m, 2H), 2.26 – 2.12 (m, 3H), 1.70 – 1.60 (m, 4H), 1.54 (s, 3H), 1.38 (s, 3H).

$(C_6H_5)_3PO$ impurity (#H relative to **14**): δ 7.68 (ddt, *J* = 10.8, 6.9, 1.4 Hz, 0.5H), 7.56 (td, *J* = 7.3, 1.4 Hz, 0.25H), 7.47 (td, *J* = 7.7, 7.2, 2.9 Hz, 0.5H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 148.1, 146.7, 132.2 (PPh_3O), 128.5 (PPh_3O), 121.5, 114.0, 109.0, 78.8, 75.3, 75.2, 62.8, 51.7, 33.1, 32.3, 29.4, 27.8, 25.0.



45

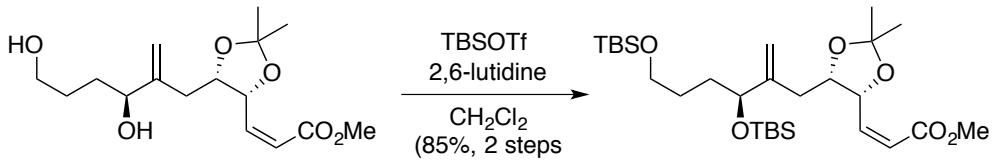
Data for (*E*)-enoate 45 (5.2 : 1, *E* : *Z* mixture): $[\alpha]_D^{25}$ -32.0 (c = 1.02, $CHCl_3$)

HRMS (NSI): *m/z* calcd for $C_{16}H_{26}O_6Na$ $[M+Na]^+$ 337.1622, found 337.1620.

IR (neat): 3381, 2988, 2934, 1719, 1660, 1437, 1372, 1262, 1215, 1163, 1119, 1049, 984, 903, 734, 699, 541 cm^{-1}.

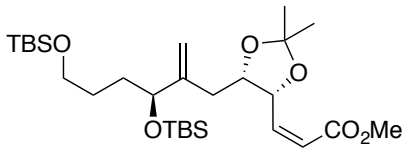
^{1}H NMR (600 MHz, $CDCl_3$, major isomer reported) δ 6.86 (dd, *J* = 15.6, 5.7 Hz, 1H), 6.12 (dd, *J* = 15.6, 1.5 Hz, 1H), 5.13 (s, 1H), 4.95 (s, 1H), 4.78 (ddd, *J* = 7.0, 5.8, 1.5 Hz, 1H), 4.56 – 4.38 (m, 1H), 4.18 – 4.01 (m, 2H), 3.76 (s, 3H), 3.70 – 3.59 (m, 2H), 2.31 (dd, *J* = 14.9, 9.1 Hz, 1H), 2.17 (m, 1H), 2.11 (m, 1H), 2.10 – 2.07 (m, 2H), 1.70 – 1.59 (m, 2H), 1.53 (s, 3H), 1.38 (s, 3H). $(C_6H_5)_3PO$ impurity (#H relative to **45**): δ 7.68 (ddt, *J* = 10.8, 6.9, 1.4 Hz, 0.5H), 7.56 (td, *J* = 7.3, 1.4 Hz, 0.25H), 7.47 (td, *J* = 7.7, 7.2, 2.9 Hz, 0.5H).

^{13}C NMR (151 MHz, $CDCl_3$, minor isomer denoted by *) δ 166.7, 166.3*, 148.3*, 148.1, 146.8*, 143.6, 132.3 (PPh_3O), 132.21 (PPh_3O), 132.20 (PPh_3O), 128.77 (PPh_3O), 128.69 (PPh_3O), 123.0, 121.7*, 114.2*, 113.6, 109.4, 109.2*, 79.0*, 78.2, 77.3*, 75.5, 75.4*, 63.03*, 62.99, 52.0, 51.9*, 33.3*, 33.1, 32.8, 32.5*, 29.6*, 29.5, 28.02*, 27.93, 25.5, 25.3*.



14 **15**

Bis-silyl ether 15: Diol **14** (256 mg, 0.82 mmol) was dissolved in CH_2Cl_2 (6 mL), and cooled to 0 °C with stirring. 2,6-lutidine (350 µL, 3.0 mmol) and TBSOTf (415 µL, 1.80 mmol) were added. The ice bath was removed, and the reaction mixture was stirred at ambient temperature for 2 h, whereupon it was quenched by addition of saturated aqueous NH_4Cl (2 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 mL x 3). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (2% EtOAc in hexanes to 3% EtOAc in hexanes) to afford *Z*-alkenoate bis-silyl ether **15** as a clear pale yellow oil (379 mg, 0.69 mmol, 85% yield).



15

Data for 15:

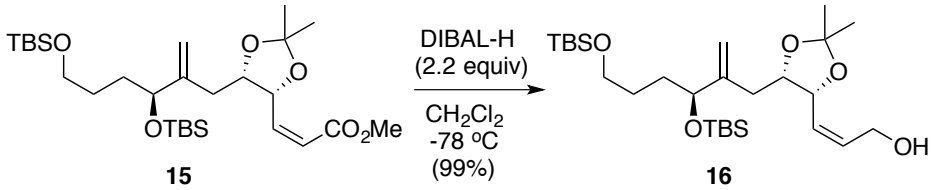
$[\alpha]_D^{25}$ -61.2 (c = 1.06, $CHCl_3$)

HRMS (NSI): *m/z* calcd for $C_{28}H_{54}O_6Si_2Na$ $[M+Na]^+$ 565.3351, found 565.3360.

IR (neat): 2967, 2953, 2929, 2857, 1723, 1649, 1472, 1463, 1407, 1380, 1253, 1219, 1196, 1181, 1093, 1053, 1004, 939, 901, 835, 775, 740, 665 cm^{-1}.

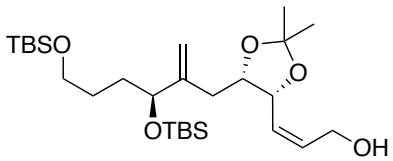
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.24 (dd, *J* = 11.7, 8.4 Hz, 1H), 5.94 (dd, *J* = 11.7, 1.4 Hz, 1H), 5.68 (ddd, *J* = 8.2, 6.4, 1.4 Hz, 1H), 5.05 (s, 1H), 4.95 (d, *J* = 1.7 Hz, 1H), 4.60 (ddd, *J* = 9.4, 6.4, 3.9 Hz, 1H), 4.08 (m, 1H), 3.72 (s, 3H), 3.59 (m, 2H), 2.18 – 2.05 (m, 2H), 1.51 (m, 8H), 1.39 (s, 3H), 0.89 (app. d, *J* = 2.5 Hz, 18H), 0.04 (app d, *J* = 2.3 Hz, 9H), 0.00 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 147.8, 146.6, 146.5, 121.6, 111.6, 108.9, 76.59, 76.55, 76.01, 75.93, 74.96, 74.92, 63.4, 33.0, 31.8, 28.9, 28.54, 28.51, 26.18, 26.05, 25.72, 25.69, 18.5, 18.4, -4.5, -4.80, -4.83, -5.05, -5.07.



15 **16**

Diene-alcohol 16: The ester **15** (193 mg, 0.35 mmol) was dissolved in CH_2Cl_2 (7 mL), and the solution was cooled to -78 °C. DIBAL-H (1.0 M in hexanes, 0.76 mL) was added dropwise to the solution at -78 °C. After 1.5 h, the reaction mixture was warmed to 0 °C and diluted with ether before addition of water (30 µL), 15% aqueous NaOH (30 µL), and more water (75 µL). After stirring for 15 min, the ice bath was removed and $MgSO_4$ was added. The slurry was stirred for 30 min at room temperature before filtration to remove the solids and concentration under reduced pressure. The primary alcohol **16** was obtained as a clear oil (182 mg, 0.35 mmol, 99% yield) and used without further purification.



16

Data for 16:

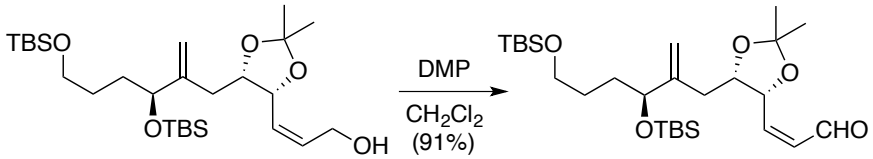
$[\alpha]_D^{25}$ -1.3 (c = 1.10, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{27}H_{55}O_5Si_2$ $[M+H]^+$: 515.3583, found 515.3588.

IR (thin film): 3412, 2985, 2953, 2929, 2885, 2856, 1648, 1507, 1472, 1462, 1380, 1370, 1521, 1217, 1162, 1091, 1042, 106, 939, 896, 833, 773, 665, 542 cm^{-1}.

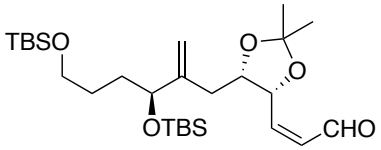
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (dddd, *J* = 11.3, 7.1, 6.0, 1.2 Hz, 1H), 5.58 (ddt, *J* = 11.0, 9.3, 1.5 Hz, 1H), 5.04 (q, *J* = 1.2 Hz, 1H), 4.93 (ddd, *J* = 9.2, 6.0, 1.2 Hz, 1H), 4.87 (q, *J* = 1.6 Hz, 1H), 4.45 (dt, *J* = 7.7, 5.9 Hz, 1H), 4.29 (ddd, *J* = 13.3, 7.0, 1.4 Hz, 1H), 4.15 (ddd, *J* = 13.3, 6.1, 1.6 Hz, 1H), 4.07 (t, *J* = 5.7 Hz, 1H), 3.59 (m, 2H), 2.34 (ddt, *J* = 16.4, 7.8, 1.4 Hz, 1H), 2.11 (ddt, *J* = 16.0, 5.4, 1.1 Hz, 1H), 1.82 (br s, -OH), 1.53 (m, 3H), 1.48 (s, 3H), 1.44 (m, 1H), 1.38 (s, 3H), 0.88 (s, 18H), 0.04 (s, 9H), 0.01 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.9, 133.0, 128.2, 111.3, 108.4, 77.5, 77.2, 77.0, 76.4, 76.3, 74.0, 73.9, 63.4, 58.7, 32.9, 31.4, 28.57, 28.54, 26.06, 26.05, 25.9, 18.6, 18.4, -4.5, -4.8, -5.1.



16 **17**

Diene-aldehyde 17: The primary alcohol **16** (182 mg, 0.35 mmol) was dissolved in CH_2Cl_2 (7 mL). DMP (225 mg, 0.52 mmol) and $NaHCO_3$ (88 mg, 1.04 mmol) were added. After 1.5 h, the reaction mixture was poured into a rapidly stirred solution of $Na_2S_2O_3$ (1 g) in saturated aqueous $NaHCO_3$ (10 mL). The suspension was stirred for 45 min until the layers turned clear. The layers were separated and the organic layer was washed with saturated aqueous $NaHCO_3$ (5 mL), water (8 mL x 2), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude oil was purified by silica gel flash column chromatography (8% EtOAc in hexanes) to furnish compound **17** as a yellow oil (162 mg, 0.32 mmol, 91% yield).



17

Data for 17:

$[\alpha]_D^{25}$ -29.6 (c = 1.0, $CHCl_3$)

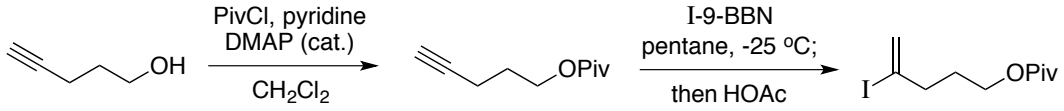
HRMS (NSI): *m/z* calcd. for $C_{27}H_{52}O_5Si_2Na$ $[M+Na]^+$: 535.3246, found 535.3241.

IR (neat): 2953, 2929, 2886, 2856, 1697, 1686, 1253, 1217, 1093, 1054, 1005, 836, 776 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.09 (d, *J* = 7.0 Hz, 1H), 6.47 (dd, *J* = 11.5, 8.8 Hz, 1H), 6.10 (ddd, *J* = 11.5, 7.0, 1.3 Hz, 1H), 5.41 (ddd, *J* = 8.9, 6.2, 1.3 Hz, 1H), 5.05 (s, 1H), 4.88 (d, *J* = 1.6 Hz, 1H), 4.63 (dt, *J* = 8.2, 5.9 Hz, 1H), 4.06 (t, *J* = 5.7 Hz, 1H), 3.58 (t, *J* = 5.8 Hz, 2H), 2.35 (ddt, *J* = 16.2, 8.2, 1.4 Hz, 1H), 2.15 – 2.03 (m, 1H), 1.52 (s, 5H), 1.51 – 1.45 (m, 1H), 1.45 – 1.37 (m, 3H), 0.89 (s, 6H), 0.88 (s, 9H), 0.04 (s, 8H), -0.00 (s, 2H).

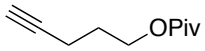
^{13}C NMR (126 MHz, $CDCl_3$) δ 190.8, 147.3, 146.1, 131.3, 112.0, 109.4, 77.2, 76.51, 76.47, 76.31, 76.24, 74.13, 74.10, 63.2, 32.9, 31.5, 28.9, 28.5, 26.17, 26.16, 26.05, 26.04, 25.73, 25.70, 18.5, 18.4, -4.5, -4.8, -5.1.

Vinylic iodide 18: This compound was prepared in two steps from pent-4-yn-1-ol (**46**).



4-pentyn-1-ol (**46**) **47** **18**

Preparation of 4-pentyn-1-ol, pivalate ester 47: 4-Pentyn-1-ol (**46**, 9.62 g, 114 mmol) was dissolved in CH_2Cl_2 (375 mL) at 0 °C. Pivaloyl chloride (PivCl, 16.54 g, 137 mmol) was added slowly prior to addition of pyridine (13.57 g, 172 mmol) and *N,N*-dimethylaminopyridine (DMAP, 200 mg). The reaction mixture was stirred overnight at room temperature before further addition of PivCl (6.36 g, 52.8 mmol), pyridine (5.40 g, 68.2 mmol), and DMAP (100 mg). After 5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (100 mL) and extracted with diethyl ether (5 x 75 mL). The combined organic layers were washed with brine (40 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (hexanes to 5% ethyl acetate in hexanes) to afford the pivalate ester **47** as a clear oil (19.18 g, 114 mmol, in 99% yield). ^{1}H NMR data for **47** matched the literature values.[6]



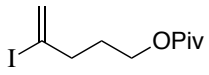
47

Data for 47:

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (t, *J* = 6.2 Hz, 2H), 2.30 (td, *J* = 7.1, 2.7 Hz, 2H), 1.98 (t, *J* = 2.7, 1H), 1.94 – 1.76 (p, *J* = 6.8 Hz, 2H), 1.21 (s, 9H).

Preparation of 4-iodopent-4-en-1-yl pivalate 18: I-9-BBN (1.0 M in hexanes, 50 mL, 50.0 mmol) was diluted with pentane (80 mL) and cooled to -25 °C, at which point a solution of alkyne **47** (3.36 g, 20.0 mmol) in pentane (35 mL) was added slowly. The reaction mixture turned light yellow and clear. The reaction mixture was stirred at -25 °C for 5 h, followed by addition of acetic acid (12 mL), which resulted in vigorous bubbling and produced a white, cloudy precipitate. The suspension was then warmed to 0 °C, where it was stirred for 1 h, followed by addition of 3M NaOH (280 mL) and 30% aqueous H_2O_2 (48 mL), resulting in vigorous bubbling upon addition. The suspension was then warmed to room temperature and stirred for 45 min. The layers turned clear and colorless. The aqueous layer was separated and extracted with CH_2Cl_2 (4 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel

flash column chromatography (hexanes to 2.5% ethyl acetate in hexanes) to afford vinylic iodide **18** as a light-yellow oil (5.17 g, 17.5 mmol, 88% yield).



18

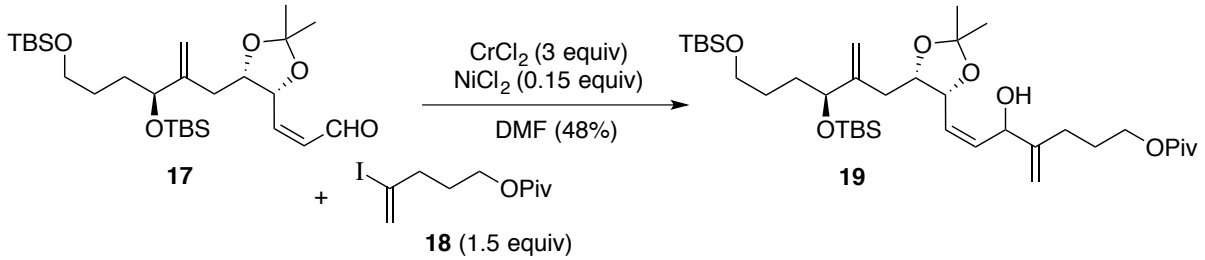
Data for 18:

HRMS (NSI): *m/z* calcd. for $C_{10}H_{18}O_2I$ $[M+H]^+$ 297.0346, found 297.0347.

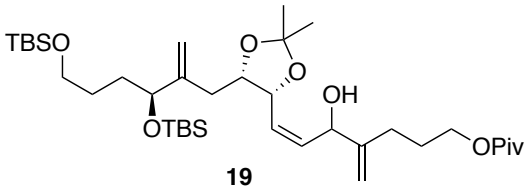
IR (thin film): 2969, 2958, 1726, 1619, 1479, 1282, 1151, 892 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (s, 1H), 5.74 (s, 1H), 4.08 (t, *J* = 6.3 Hz, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 1.91 – 1.83 (m, 2H), 1.21 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.7, 126.5, 110.8, 62.7, 42.0, 39.0, 28.3, 27.4.



Bis-allylic alcohol 19: $CrCl_2$ (70 mg, 0.47 mmol) and $NiCl_2$ (0.3 mg, 0.02 mmol) were weighed out in a glove box, and the flask was flushed with argon for 10 min. The flask was cooled to 0 °C and dry DMF (2 mL) was added. The ice bath was removed after 10 min and the solvated salts were warmed to room temperature. A solution of vinyl iodide **18** (71 mg, 0.23 mmol) in DMF (0.7 mL) was added in one portion, and the reaction mixture was stirred for 10 min before aldehyde **17** (66 mg, 0.16 mmol) in DMF (0.33 mL + 0.2 mL rinsate) was added over 30 min by syringe pump. The reaction mixture was stirred at room temperature for 2 h before being diluted with aqueous NH_4Cl (5 mL) and EtOAc (5 mL). After stirring for 1 h the layers were separated. The aqueous layer was extracted with EtOAc (10 mL × 6). The combined organic layers were washed with water (10 mL x 3), 10% aqueous LiCl, and brine before being dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (6% EtOAc in hexanes to 14% EtOAc in hexanes) to afford compound **19** as a clear pale yellow oil (52 mg, 0.077 mmol, 48% yield, 1:1 mixture of diastereomers).



19

Data for 19:

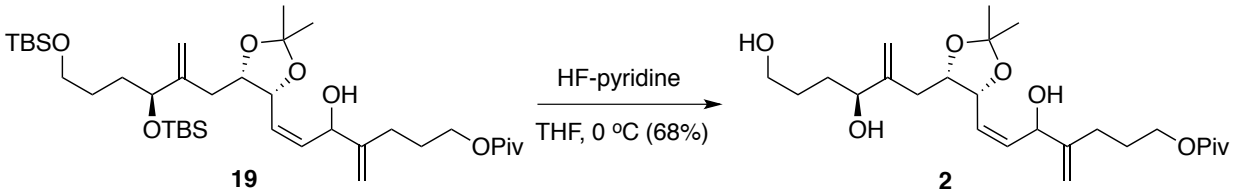
$[\alpha]_D^{25}$ +2.0 (c = 1.00, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{37}H_{70}O_7Si_2Na$ $[M+Na]^+$ 705.4552, found 705.4575.

IR (neat): 3412, 2954, 2928, 2856, 1729, 1253, 1159, 1095, 1054, 1006, 835, 775 cm^{-1}.

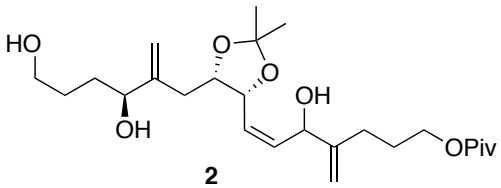
^{1}H NMR (600 MHz, C_6D_6) δ 5.87 – 5.71 (m, 2H), 5.17 (m, 1H), 5.12 (t, *J* = 1.1 Hz, 0.5H), 5.09 (t, *J* = 1.2 Hz, 0.5H), 5.03 (d, *J* = 1.6 Hz, 0.5H), 5.02 (d, *J* = 1.6 Hz, 0.5H), 5.00 (m, 1H), 4.80 (d, *J* = 1.5 Hz, 1H), 4.52 (dt, *J* = 9.8, 6.6 Hz, 1H), 4.45 (m, 1H), 4.42 (m, 1H), 4.20 (t, *J* = 5.9 Hz, 1H), 4.04 (m, 2H), 3.60 (m, 2H), 2.53 (ddd, *J* = 20.5, 16.2, 8.4 Hz, 1H), 2.23 (td, *J* = 15.7, 5.0 Hz, 1H), 2.13 (m, 1H), 2.01 (m, 1H), 1.77 – 1.59 (m, 6H), 1.53 (s, 1.5H), 1.52 (s, 1.5H), 1.34 (s, 1.5H), 1.33 (s, 1.5H), 1.20 (s, 9H), 1.02 (s, 9H), 0.99 (m, 9H), 0.13 (s, 6H), 0.08 (s, 6H).

^{13}C NMR (151 MHz, C_6D_6) δ 177.8, 150.0, 149.9, 148.3, 135.13, 135.08, 128.4, 128.1, 111.89, 111.86, 110.82, 110.6, 108.24, 108.17, 79.1, 79.0, 76.7, 75.3, 75.2, 63.95, 63.93, 63.42, 63.39, 38.8, 33.38, 33.35, 32.52, 32.50, 30.2, 29.3, 28.6, 28.3, 28.2, 27.51, 27.49, 27.43, 26.23, 26.18, 25.8, -4.3, -4.8, -5.1.



19 **2**

Triene-triol 2: Bis-silyl ether **19** (52 mg, 0.077 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. HF·pyridine (1 mL) was added dropwise. The reaction mixture was warmed to room temperature gradually and stirred for 4 h, at which point the reaction mixture was cooled to 0 °C before addition of saturated sodium bicarbonate (10 mL in 1 mL portions). The mixture was stirred for 45 min before dilution with EtOAc (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (10 mL x 5). The combined organic layers were washed with saturated aqueous bicarbonate (10 mL) and brine (10 mL) before being dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by silica gel flash column chromatography (50 % EtOAc in hexanes to EtOAc) to afford triene-triol **2** as a clear pale yellow oil (23 mg, 0.052 mmol, 68% yield, 1:1 mixture of diastereomers).



2

Data for 2:

$[\alpha]_D^{25}$ -5.5 (c = 1.10, $CHCl_3$)

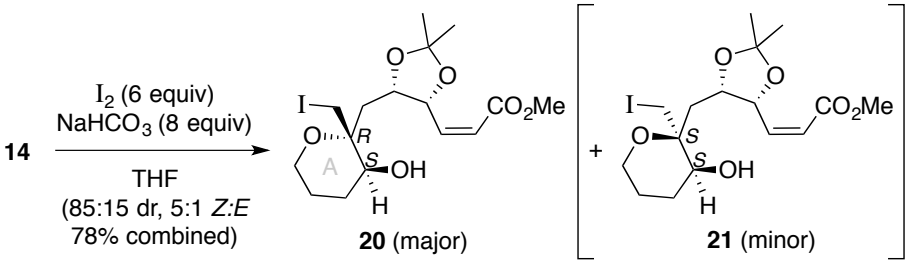
HRMS (NSI): *m/z* calcd. for $C_{25}H_{42}O_7Na$ $[M+Na]^+$: 477.2823, found 477.2826.

IR (neat): 3385, 2931, 2871, 1725, 1648, 1552, 1480, 1457, 1369, 1285, 1250, 1216, 1159, 1044, 976, 901, 795, 773 cm^{-1}.

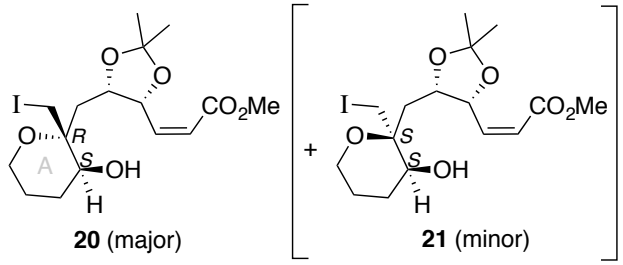
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.82 – 5.72 (m, 2H), 5.16 (s, 0.5H), 5.15 (s, 1H), 5.13 (s, 0.5H), 4.95 (d, *J* = 1.3 Hz, 1H), 4.94 (s, 0.5H), 4.93 (s, 0.5H), 4.68 – 4.62 (m, 2H), 4.37 (dddd, *J* = 17.5, 10.0, 6.2, 4.5 Hz, 1H), 4.11 (m, 1H), 4.08 (td, *J* = 6.8, 1.7 Hz, 2H), 3.68 (m, 2H), 2.34 (ddd, *J* = 20.2, 15.0, 9.2 Hz, 1H), 2.18 – 2.08 (m, 3H), 1.89 – 1.78 (m, 2H), 1.76 – 1.60 (m, 4H), 1.52 (s, 1.5H), 1.51 (s, 1.5H), 1.38 (s, 3H), 1.20 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.9, 149.2, 149.1, 148.4, 148.3, 135.4, 135.2, 127.5, 127.3, 113.2, 112.8, 111.2, 111.0, 108.68, 108.63, 78.75, 78.67, 78.40, 78.27, 75.4, 75.2, 75.0, 64.11, 64.09, 62.9, 39.0, 33.30, 33.26, 32.76, 32.74, 29.9, 29.4, 28.20, 28.16, 28.11, 27.4, 27.13, 27.11, 25.5.

3) Sequential oxacyclizations to form the AB rings from diene-diol 14 (Scheme 2):



Iodomethyl tetrahydropyranols 20 and 21: Diol **14** (338 mg, contaminated with ca. 10% Ph_3PO) was dissolved in THF (10 mL) and cooled to 0 °C. $NaHCO_3$ (735 mg, 8.70 mmol) was added, followed by I_2 (1.47 g, 5.80 mmol). The reaction mixture warmed to room temperature and was stirred for 2 h. The reaction mixture was quenched with addition of aqueous $Na_2S_2O_3$ and diluted with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 5mL). The combined organic extracts were combined and washed with brine before being dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting crude oil was purified by silica gel flash column chromatography (35% ether in pentane) to afford cyclized compound favoring diastereomer **20** (335 mg, 0.76 mmol, 78% yield over 2 steps, 85:15 dr, 5:1 *Z:E*).



Data for 20 (from 85:15 mixture of 20:21)

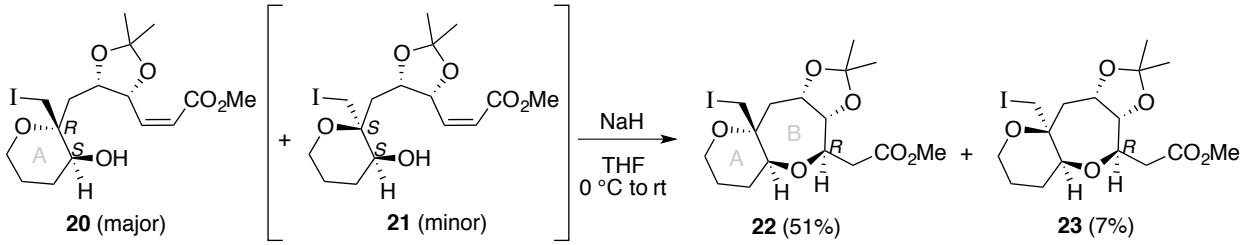
$[\alpha]_D^{25}$ -110.0 (c = 1.00, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{16}H_{26}O_6I$ $[M+H]^+$ 441.0769, found 441.0771.

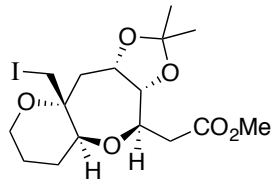
IR (neat): 3470, 2983, 2939, 2870, 1723, 1660, 1437, 1306, 1255, 1216, 1164, 1080, 985, 861, 832 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$, major diastereomer) δ 6.19 (dd, *J* = 11.7, 8.4 Hz, 1H), 5.99 (dd, *J* = 11.7, 1.4 Hz, 1H), 5.69 (ddd, *J* = 8.3, 6.7, 1.4 Hz, 1H), 4.66 (ddd, *J* = 10.5, 6.7, 1.2 Hz, 1H), 3.99 (dd, *J* = 9.3, 4.6 1H), 3.87 (d, *J* = 11.5 Hz, 1H), 3.74 (s, 3H), 3.65 (m, 1H), 3.39 (d, *J* = 11.5 Hz, 1H), 3.34 (m, 1H), 2.86 (d, *J* = 4.9 Hz, -OH), 2.00 (m 1H), 1.87 (m, 2H), 1.68 (m, 3H), 1.52 (s, 3H), 1.41 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.0, 165.8, 146.4, 145.7, 121.9, 121.8, 109.3, 109.0, 75.9, 75.4, 75.13, 75.09, 73.8, 68.6, 68.4, 61.2, 60.8, 53.9, 51.7, 39.3, 31.0, 29.3, 28.3, 28.0, 27.3, 26.6, 25.6, 25.3, 12.6.



Bicyclic polyethers 22 and 23: Tetrahydropyranol enoate **20** (550 mg, 1.25 mmol, 85:15 dr, 5:1 *Z:E*) was dissolved in THF (20 mL). The solution was cooled to 0 °C before addition of NaH (60% in mineral oil, 50 mg, 1.25 mmol). The reaction warmed to room temperature gradually and stirred for 1 h. The reaction was diluted with diethyl ether and quenched by addition of methanol (1 mL) and then concentrated under reduced pressure. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 x 7 mL). The combined organic extracts were combined and washed with brine before being dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude powder was purified by silica gel flash column chromatography (15% to 20% diethyl ether in pentane) to afford the cyclized compound **22** (280 mg, 0.64 mmol, 51% yield). At this stage, the *cis*-fused isomer **23** was isolated as a white powder (36 mg, 0.082 mmol, 7% yield, from the minor diastereomer **21** arising from the iodocyclization step).



22

Data for 22:

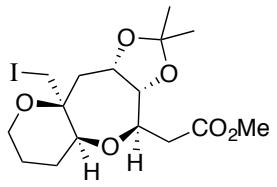
$[\alpha]_D^{25}$ +5.2 (c = 0.78, CH_3OH), -0.7 (c = 1.10, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{16}H_{26}O_6IH$ $[M+H]^+$ 441.0769, found 441.0765.

IR (neat): 2983, 2947, 2875, 1736, 1437, 1381, 1302, 1266, 1212, 1166, 1121, 1105, 1043, 998, 883, 800, 737 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.50 (ddd, *J* = 10.8, 6.9, 6.0 Hz, 1H), 3.98 (dd, *J* = 10.0, 6.9 Hz, 1H), 3.90 (td, *J* = 9.9, 2.8 Hz, 1H), 3.77 (dd, *J* = 12.1, 2.0 Hz, 1H), 3.71 (s, 3H), 3.63 (ddt, *J* = 12.3, 4.6, 2.3 Hz, 1H), 3.52 (dd, *J* = 12.1, 4.2 Hz, 1H), 3.34 (td, *J* = 12.2, 5.3 Hz, 1H), 3.06 (d, *J* = 12.1 Hz, 1H), 2.78 (dd, *J* = 16.1, 2.8 Hz, 1H), 2.52 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.42 (dd, *J* = 16.1, 9.9 Hz, 1H), 1.85 (ddd, *J* = 14.0, 10.8, 2.0 Hz, 1H), 1.79 – 1.64 (m, 3H), 1.51 (m, 1H), 1.42 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 109.0, 85.2, 79.2, 78.5, 74.0, 72.9, 60.0, 51.9, 42.1, 39.1, 27.3, 26.1, 25.5, 24.4, 8.1.



23

Data for 23:

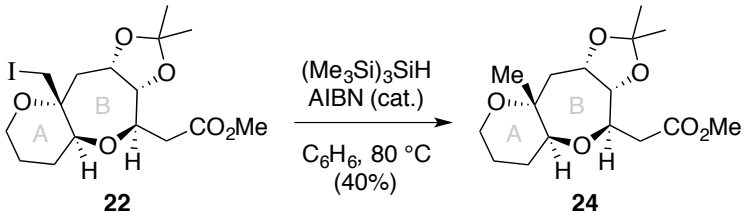
$[\alpha]_D^{25}$ -7.0 (c = 0.772, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{16}H_{26}O_6IH$ $[M+H]^+$ 441.0769, found 441.0773.

IR (neat): 2931, 2858, 1734, 1437, 1369, 1264, 1207, 1154, 1088, 1044, 1016, 995, 914, 870, 841, 800, 744, 648, 624, 589 cm^{-1}.

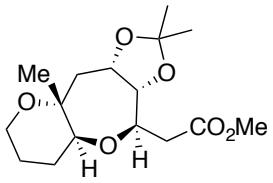
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 (ddd, *J* = 11.4, 7.0, 3.3 Hz, 1H), 4.09 (dd, *J* = 9.7, 7.0 Hz, 1H), 3.96 (td, *J* = 10.0, 2.5 Hz, 1H), 3.77 – 3.65 (m, 2H), 3.71 (s, 3H), 3.57 (d, *J* = 11.1 Hz, 1H), 3.53 (app dd, *J* = 12.2, 2.9 Hz, 1H), 3.19 (d, *J* = 11.1 Hz, 1H), 2.73 (dd, *J* = 16.4, 2.4 Hz, 1H), 2.52 (dd, *J* = 16.4, 10.3 Hz, 1H), 2.22 (dd, *J* = 14.3, 3.3 Hz, 1H), 1.92 (dd, *J* = 14.3, 11.4 Hz, 1H), 1.85 – 1.75 (m, 4H), 1.42 (s, 3H), 1.31 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.2, 109.4, 78.7, 77.7, 76.4, 74.0, 73.2, 61.8, 51.9, 41.4, 39.9, 27.8, 26.8, 25.0, 19.6, 13.3.



22 **24**

Bicyclic polyether 24: Alkyl iodide **22** (21 mg, 0.048 mmol) was dissolved in benzene (1 mL). A single crystal of AIBN was added along with $(Me_3Si)_3SiH$ (18 µL, 0.057 mmol). The reaction mixture was heated to reflux, where it was stirred for 45 min before cooling and solvent removal under reduced pressure. The resulting oil was purified by silica gel flash column chromatography (20% EtOAc in hexanes to 25% EtOAc in hexanes) to afford product **24** (6.0 mg, 0.019 mmol, 40% yield). NOESY of this compound revealed correlations that allowed for assignment of the stereochemistry at the new stereocenters.



24

Data for 24:

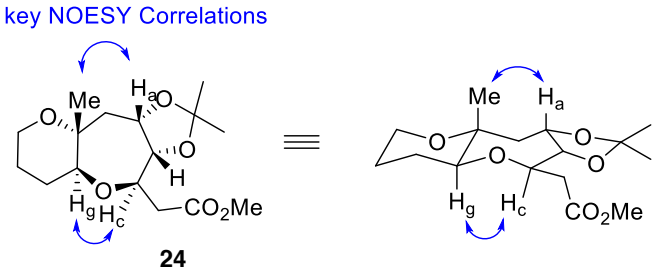
$[\alpha]_D^{25}$ +11.5 (c = 0.609 $CHCl_3$)

IR (thin film): 2983, 2875, 1737, 1383, 1221, 850 cm^{-1}.

HRMS (NSI): *m/z* calcd. for $C_{16}H_{27}O_6$ $[M+H]^+$ 315.1802, found 315.1805.

^{1}H NMR (400 MHz, Acetone-d_6) δ 4.54 (ddd, *J* = 10.8, 7.1, 6.1 Hz, 1H), 3.95 (dd, *J* = 10.0, 7.1 Hz, 1H), 3.82 (td, *J* = 10.0, 2.9 Hz, 1H), 3.64 (s, 3H), 3.59 – 3.50 (m, 1H), 3.46 (ddt, *J* = 12.0, 4.7, 1.7 Hz, 1H), 3.17 (dd, *J* = 11.4, 3.9 Hz, 1H), 2.67 (dd, *J* = 15.8, 2.9 Hz, 1H), 2.31 (dd, *J* = 15.8, 10.1 Hz, 1H), 2.15 – 2.10 (m, 1H), 1.85 (dd, *J* = 13.4, 10.9 Hz, 1H), 1.60 (m, 3H), 1.53 – 1.36 (m, 1H), 1.35 (s, 3H), 1.19 (s, 3H), 1.12 (s, 3H).

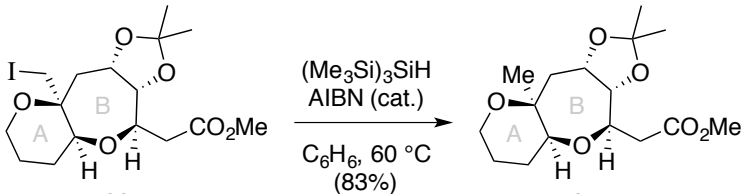
^{13}C NMR (151 MHz, Acetone-d_6) δ 171.8, 109.0, 82.6, 80.1, 78.8, 74.7, 60.2, 51.8, 45.3, 40.2, 30.8, 27.7, 26.9, 24.5, 23.1, 21.2.



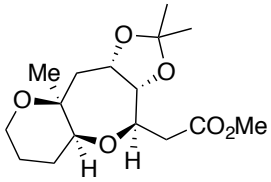
24

H_a = 4.54 ddd, *J* = 10.8, 7.1, 6.1 Hz
H_c = 3.82 td, *J* = 10.0, 2.9 Hz
H_g = 3.17 dd, *J* = 11.4, 3.9

Figure 2. Key NOE correlations for compound **24**



Bicyclic polyether 25 (from minor diastereomer 23): To confirm the stereochemistry across the AB ring fusion, the *cis*-fused diastereomer **25** was prepared. The minor diastereomer iodide **23** (10 mg, 0.023 mmol) was dissolved in benzene (0.4 mL). $(Me_3Si)_3SiH$ (18 µL, 0.057 mmol) and a single crystal of AIBN were added and the reaction was heated to 60 °C, where it was stirred for 10 min before cooling and removal of solvent under reduced pressure. The resulting oil was purified by silica gel flash column chromatography (15% EtOAc in hexanes to 20% EtOAc in hexanes) to afford product **25** (6.0 mg, 0.019 mmol, 83% yield, 5.7:1 mixture of *cis* : *trans* fused diastereomers. NOESY of this compound revealed correlations that allowed for assignment of the stereochemistry at the *cis*-AB ring fusion.



25

Data for 25:

$[\alpha]_D^{25}$ +26.0 (c = 0.40, $CHCl_3$)

IR (thin film): 2985, 2360, 1740, 1436, 1263, 1115, 1046 cm^{-1}.

HRMS (NSI): *m/z* calcd. for $C_{16}H_{26}O_6Na$ $[M+Na]^+$ 337.1608, found 337.1617.

^{1}H NMR (600 MHz, Acetone-d_6) δ 4.62 (ddd, *J* = 11.7, 6.9, 3.2 Hz, 1H), 4.07 (dd, *J* = 9.6, 6.9 Hz, 1H), 3.92 (td, *J* = 10.0, 2.6 Hz, 1H), 3.70 (td, *J* = 13.0, 2.5 Hz, 1H), 3.65 (s, *J* = 0.9 Hz, 3H), 3.59 (dd, *J* = 11.6, 5.1 Hz, 1H), 3.38 (t, *J* = 3.2 Hz, 1H), 2.63 (dd, *J* = 15.8, 2.7 Hz, 1H), 2.42 (dd, *J* = 16.1, 10.4 Hz, 1H), 2.04 – 2.00 (m, 1H), 1.96 – 1.85 (m, 1H), 1.80 – 1.70 (m, 2H), 1.60 (dd, *J* = 13.0, 3.8 Hz, 1H), 1.35 (s, 3H), 1.28 (d, *J* = 4.1 Hz, 1H), 1.26 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H).

^{13}C NMR (151 MHz, Acetone-d_6) δ 172.2, 109.7, 82.5, 79.9, 77.2, 74.8, 74.3, 61.7, 51.7, 44.5, 40.7, 28.3, 27.3, 25.4, 23.0, 21.2.

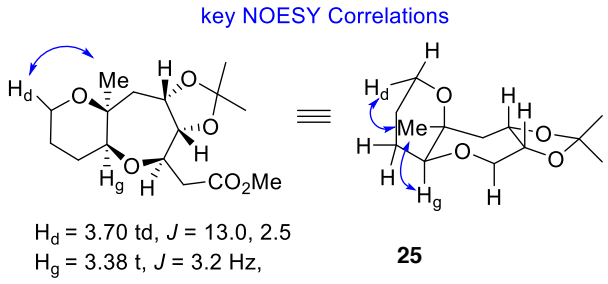
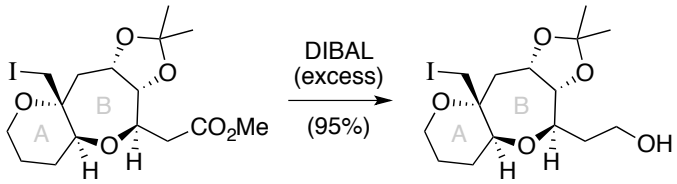
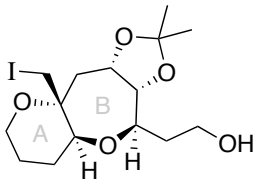


Figure 3. Key NOE correlations for compound **25**



22 **26**

Bicyclic alcohol 26: The ester **22** (122 mg, 0.277 mmol) was dissolved in CH_2Cl_2 (5.5 mL), and DIBAL-H (1.0 M in hexanes, 0.61 mL) was added dropwise. After 2 h, more DIBAL-H (0.3 mL) was added, and after 7 h, additional DIBAL-H (0.3 mL) was added, totaling about 4 equivalents. The reaction mixture was cooled to 0 °C, diluted with ether, and quenched by addition of Rochelle's salt (12 mL) and stirred for 4 h at room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 8 mL). The combined organic layers were washed with water (10 mL x 2), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude powder **26** (113 mg, 0.277 mmol, >95% yield) was recrystallized from heptane and benzene *via* vapor diffusion to afford colorless needle-like crystals.



26

Data for 26:

Melting point: dec. at 181-184 °C then melts at 187-188 °C

$[\alpha]_D^{25}$ -8.1 (c = 1.02 $CHCl_3$)

IR (neat): 3490, 2936, 2873, 1382, 1266, 1169, 1049, 882 cm^{-1}.

HRMS (NSI): *m/z* calcd. for $C_{15}H_{26}IO_5$ $[M+H]^+$ 413.0819, found 413.0820.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.48 (ddd, *J* = 10.9, 7.1, 5.8 Hz, 1H), 4.03 (dd, *J* = 9.7, 7.1 Hz, 1H), 3.84 – 3.72 (m, 3H), 3.67 – 3.55 (m, 2H), 3.53 – 3.45 (m, 1H), 3.41 – 3.31 (m, 1H), 3.08 (d, *J* = 12.1 Hz, 1H), 2.53 – 2.47 (m, 1H), 2.09 – 1.96 (m, 1H), 1.87 – 1.77 (m, 2H), 1.77 – 1.64 (m, 2H), 1.63 – 1.52 (m, 1H), 1.42 (s, 3H), 1.36 (s, 3H), 0.91 – 0.87 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 108.0, 85.3, 81.3, 79.7, 73.9, 73.0, 60.6, 59.9, 42.2, 36.1, 27.4, 26.4, 25.5, 24.4, 7.8.

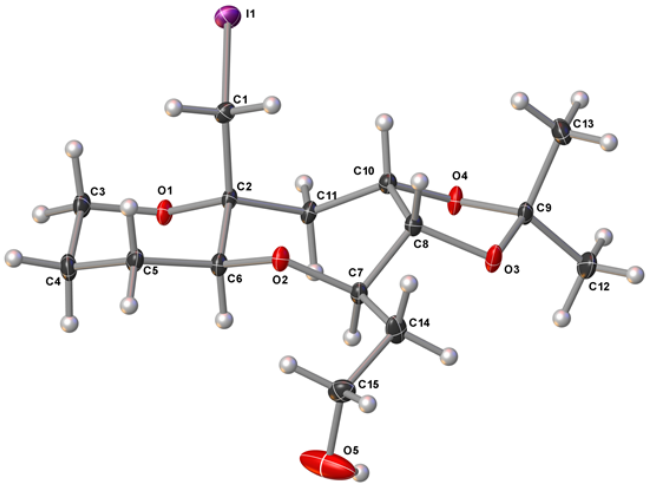
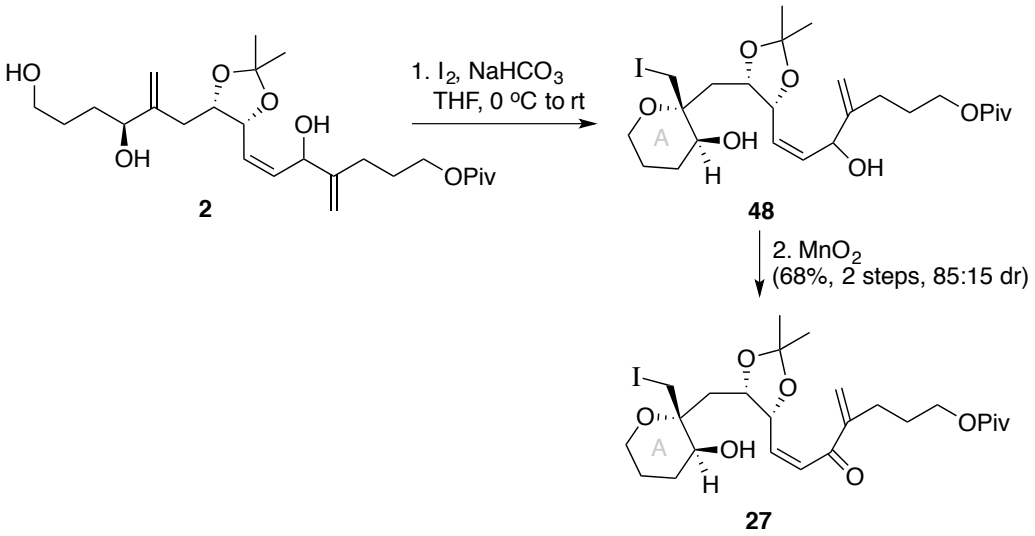
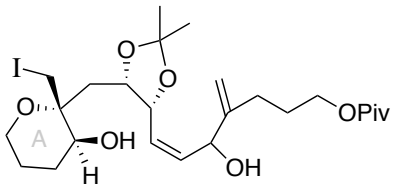


Figure 4. X-ray crystal structure of AB bicyclic compound **26**

4) Sequential oxacyclizations to form the AB rings from triene-triol 2 (Scheme 3):



<u>Tetrahydropyranol dienone 27:</u> Triene-triol **2** (23 mg, 0.052 mmol) was dissolved in THF (1 mL). The solution was cooled to 0 °C, then sodium bicarbonate (60 mg, 0.71 mmol) was added followed by iodine (120 mg, 0.47 mmol). The reaction mixture gradually warmed to ambient temperature. After 6 h, the reaction mixture was quenched by addition of saturated aqueous $Na_2S_2O_3$ (2 mL). The reaction mixture was diluted with EtOAc (2 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (4 x 2 mL) and the combined organic extracts were washed with brine before being dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by silica gel flash column chromatography (15% EtOAc in hexanes) to afford iodomethyl tetrahydropyranol **48** as a clear light-yellow film (20 mg, 0.034 mmol, 66% yield, 1:1.2 mixture of diastereomers of the bis-allylic alcohol. COSY, HMBC, and HMQC confirmed the structure. Additionally, dienone **27** was obtained (7.0 mg, 0.013 mmol, 25% yield).



48

Data for 48:

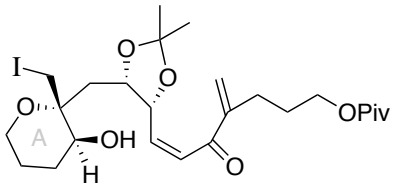
$[\alpha]_D^{25}$: -5.9 (c = 1.02, $CHCl_3$)

HRMS (NSI): m/z calcd. for $C_{25}H_{41}O_7INa$ $[M+Na]^+$ 603.1789, found 603.1800.

IR (neat): 3457, 2956, 2925, 2853, 2152, 1726, 1558, 1457, 1371, 1286, 1215, 1162, 1084, 1036, 975, 943, 905, 802 cm^{-1}.

^{1}H NMR (600 MHz, C_6D_6 * denotes minor diastereomer) δ 5.75 (ddd, *J* = 15.4, 7.7, 1.4 Hz, 0.45H)*, 5.67 (dd, *J* = 15.6, 7.9 Hz, 0.55H), 5.57 (app. t, *J* = 6.2 Hz, 0.55H), 5.55 (app. t, *J* = 6.2 Hz, 0.45H)*, δ 5.16 (s, 0.45H)*, 5.11 (d, *J* = 3.5 Hz, 0.55H), 4.84 (s, 0.55H), 4.82 (d, *J* = 1.6 Hz, 0.45H)*, 4.52 (m, 1H), 4.38 (dd, *J* = 17.5, 6.8 Hz, 1H), 4.32 (m, 1H), 4.08 (m, 4H), 3.67 (d, *J* = 11.5 Hz, 1H), 3.41 (d, *J* = 11.6 Hz, 1H), 3.37 (m, 1H), 3.05 (br t, *J* = 11.9 Hz, 1H), 2.15 (m, 2H), 2.03 (m, 1H), 1.73 (m, 2H), 1.69 – 1.59 (m, 3H), δ 1.36 (s, 1.65H), 1.35 (s, 1.55H)*, 1.34 (m, 2H), 1.21 (s, 4H)*, 1.20 (s, 5H).

^{13}C NMR (151 MHz, C_6D_6) δ 177.9, 149.6, 135.7, 135.5, 111.0, 110.7, 108.5, 79.7, 75.6, 75.3, 75.2, 74.1, 68.9, 64.1, 60.8, 40.33, 40.29, 38.9, 32.37(2), 30.2, 28.4, 28.3, 28.1, 27.6, 27.5, 25.8, 25.6, 14.4, 13.3.



27

Data for 27:

$[\alpha]_D^{25}$ +3.4 (c = 0.62, $CHCl_3$)

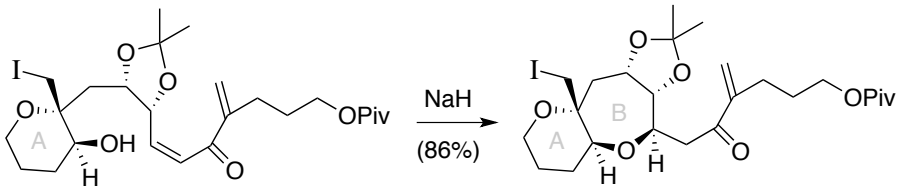
HRMS (APCI): m/z calcd. for $C_{25}H_{40}O_7I$ $[M+H]^+$ 579.1813, found 579.1814.

IR (neat): 2933, 2873, 234, 2481, 2365, 2230, 2183, 2046, 1725, 1674, 1561, 1510, 1479, 1370, 1285, 1215, 1162, 1081, 1046, 881 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$ 5:1 dr major diastereomer reported) δ 6.79 (dd, *J* = 11.7, 1.4 Hz, 1H), 6.16 (dd, *J* = 11.7, 8.1 Hz, 1H), 6.06 (s, 1H), 5.84 (s, 1H), 5.36 (t, *J* = 7.2 Hz, 1H), 4.73 (dd, *J* = 10.4, 6.8 Hz, 1H), 4.25 (m, 1H), 4.06 (m, 2H), 3.87 (d, *J* = 11.5 Hz, 1H), 3.65 (m, 1H), 3.40 (d, *J* = 11.5 Hz, 1H), 3.36 (m, 1H), 2.44 – 2.34 (m, 2H), 1.88 – 1.76 (m, 4H), 1.72 – 1.64 (m, 2H), 1.59 – 1.55 (m, 2H), 1.53 (s, 3H), 1.41 – 1.38 (s, 3H), 1.21 (s, 9H).

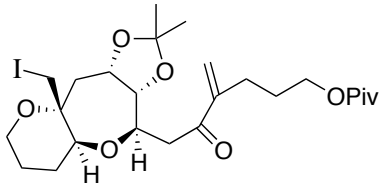
^{13}C NMR not obtained due to compound instability.

Preparation of tetrahydropyranol dienone 27 (from oxidation of 48): Bis-allylic alcohol **48** (11 mg, 0.019 mmol) was dissolved in CH_2Cl_2 (2.5 mL), and activated MnO_2 (80 mg, 0.95 mmol) was added. The reaction was stirred at ambient temperature for 16 h before it was filtered through a pad of Celite. ^{1}H NMR of the crude mixture revealed that the reaction proceeded to roughly 66% conversion to dienone **27**. The crude mixture was used in conjugate addition reactions, at which point the unreacted alcohol **48** was separated.



27 **28**

Bicyclic enone 28 (from cyclization of 27): The dienone **27** (44 mg, 0.076 mmol, obtained from **2** via several batches of iodocyclization and oxidation) was dissolved in THF (5 mL). The solution was cooled to 0 °C, and then sodium hydride (3.3 mg, 0.083 mmol) was added. The reaction mixture was stirred at 0 °C for 2 h, before being quenched with methanol. The solvent was removed under reduced pressure, and the resulting film was purified by silica gel column chromatography (40% diethyl ether in pentane) to afford bicyclic enone **28** as a light-yellow oil (37 mg, 0.65 mmol, 86% yield). This compound was produced as a single diastereomer at the newly formed chiral center, although as an 85:15 mixture of diastereomers across the AB ring fusion.



28

Data for 28:

$[\alpha]_D^{25}$ +8.4 (c = 1.06, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{25}H_{39}O_7INa$ $[M+Na]^+$ 601.1633, found 601.1631.

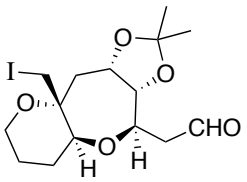
IR (neat): 2954, 2873, 2196, 1726, 1688, 1480, 1453, 1368, 1346, 1284, 1212, 1158, 1121, 1105, 1080, 1038, 973, 939, 884 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.04 (s, 1H), 5.79 (d, *J* = 1.3 Hz, 1H), 4.50 (dt, *J* = 10.4, 5.9 Hz, 1H), 4.04 (t, *J* = 6.5 Hz, 2H), 4.02 (app. dq, *J* = 3.3, 2.1, 1.4 Hz, 2H), 3.75 (dd, *J* = 12.0, 1.9 Hz, 1H), 3.61 (dd, *J* = 12.6, 5.2 Hz, 1H), 3.57 (dd, *J* = 12.1, 4.1 Hz, 1H), 3.33 (td, *J* = 12.3, 2.7 Hz, 1H), 3.05 (d, *J* = 12.0 Hz, 1H), 2.94 (m, 2H), 2.50 (dd, *J* = 14.0, 5.9 Hz, 1H), 2.35 (td, *J* = 7.4, 4.6 Hz, 2H), 1.87 (ddd, *J* = 13.4, 10.9, 1.9 Hz, 1H), 1.75 (p, *J* = 7.0 Hz, 2H), 1.72 – 1.62 (m, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.20 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.2, 178.7, 148.1, 125.4, 108.8, 85.0, 79.0, 77.8, 73.9, 73.0, 63.7, 60.0, 42.0, 41.8, 38.9, 27.56, 27.52, 27.39, 27.30, 25.9, 25.5, 24.3, 8.3.

5) Alternative synthesis of bicyclic enone 28 from bicyclic ester 22 (Scheme 4):

Bicyclic aldehyde 29: The ester **22** (445 mg, 1.01 mmol) was dissolved in CH_2Cl_2 (25 mL), and DIBAL-H (1.0 M in hexanes, 1.10 mL) was added dropwise. After stirring at room temperature for 2 h, the reaction mixture was cooled to 0 °C, diluted with ether, quenched by addition of Rochelle's salt (10 mL), and stirred for 4 h at room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 8 mL). The combined organic layers were washed with water (10 mL x 2), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude powder **29** (443 mg, 1.00 mmol) was used without further purification.



29

Data for 29:

$[\alpha]_D^{25}$ -6.4 (*c* = 1.00, $CHCl_3$)

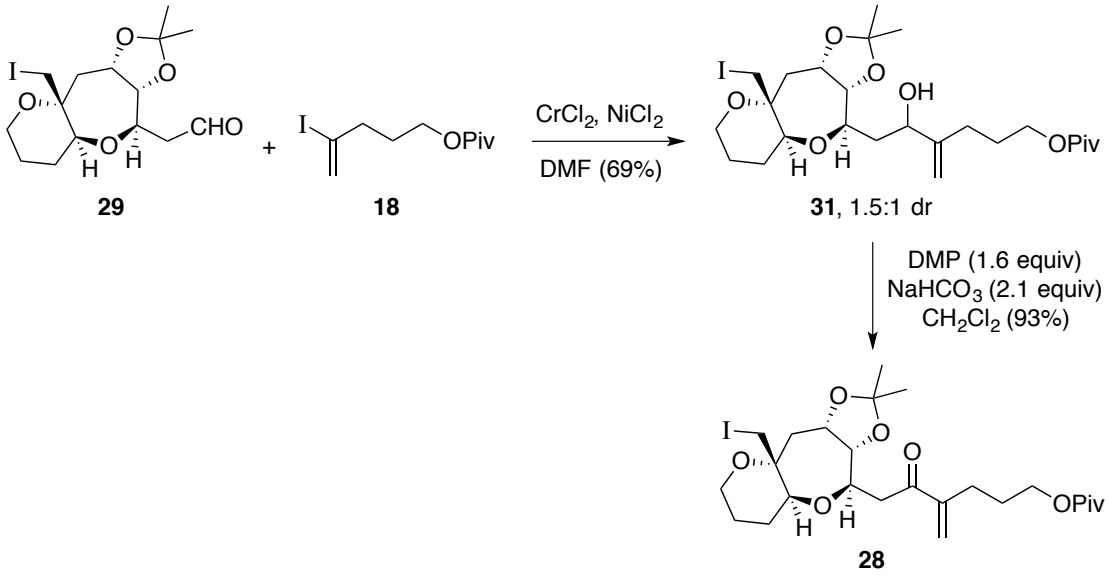
HRMS (NSI): *m/z* calcd for $C_{15}H_{24}IO_5$ $[M+H]^+$ 411.0663, found 411.0662.

IR (neat): 2939, 2870, 1971, 1725, 1454, 1382, 1212, 1078, 1050, 975, 881 cm^{-1}.

^{1}H NMR (399 MHz, $CDCl_3$) δ 9.79 (dd, *J* = 2.0, 1.1 Hz, 1H), 4.52 (dt, *J* = 10.8, 6.2 Hz, 1H), 4.09 – 3.86 (m, 2H), 3.77 (dd, *J* = 12.1, 2.0 Hz, 1H), 3.68 – 3.61 (m, 1H), 3.61 – 3.51 (m, 1H), 3.43 – 3.27 (m, 1H), 3.05 (d, *J* = 12.1 Hz, 1H), 2.91 – 2.71 (m, 1H), 2.61 (ddd, *J* = 17.3, 9.0, 2.0 Hz, 1H), 2.54 (dd, *J* = 14.0, 6.1 Hz, 1H), 1.85 (ddd, *J* = 14.1, 10.8, 2.0 Hz, 1H), 1.80 – 1.73 (m, 1H), 1.73 – 1.65 (m, 1H), 1.51 (m, 4.9 Hz, 1H), 1.41 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) 200.3, 108.9, 85.1, 79.1, 76.5, 73.9, 72.7, 59.9, 47.9, 42.0, 27.3, 26.0, 25.5, 24.3, 8.0.

Bicyclic enone 28 (from 18 + 29):



Preparation of allylic alcohol 31 (mixture of diastereomers): $CrCl_2$ (80 mg, 0.64 mmol) and $NiCl_2$ (0.5 mg, 0.03 mmol) were weighed out in a glove box and the flask was flushed with argon for 10 min. The flask was cooled to 0 °C, and dry DMF (2 mL) was added. The ice bath was removed after 10 min and the solvated salts were warmed to room temperature. A solution of vinylic iodide **18** (97 mg, 0.32 mmol) in DMF (0.6 mL) was added in one portion. The reaction mixture was stirred for 15 min and then a solution of aldehyde **29** (66 mg, 0.16 mmol) in DMF (0.33 mL) was added dropwise. The resulting suspension was stirred at room temperature for 4 h. The reaction mixture was diluted with water (15 mL) and extracted with EtOAc (10 mL × 6). The combined organic phase was washed with water (20 mL x 2) and brine before being dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (20% EtOAc in hexanes to 30% EtOAc in hexanes) to afford compound **31** as a clear pale-yellow oil (64 mg, 0.11 mmol, 69% yield, 1.5:1 mixture of diastereomers).

Data for 31 (mixture of diastereomers):

$[\alpha]_D^{25}$ -2.1 (c = 1.03, $CHCl_3$)

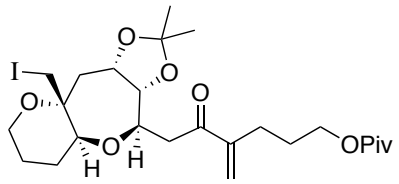
HRMS (NSI): *m/z* calcd. for $C_{25}H_{42}IO_7$ $[M+H]^+$ 581.1970, found 581.1962.

IR (neat): 3485, 2954, 2937, 2872, 1725, 1646, 1480, 1456, 1289, 1212, 1162, 1120, 1106, 1045, 997, 886, 800, 772 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.16 (d, *J* = 1.3 Hz, 0.4H), 5.10 (t, *J* = 1.2 Hz, 0.6H), 4.92 (t, *J* = 1.3 Hz, 0.4H), 4.88 (q, *J* = 1.5 Hz, 4.6H), 4.47 (dtd, *J* = 11.0, 7.1, 5.9 Hz, 1H), 4.31 (td, *J* = 11.1, 9.6, 5.5 Hz, 1H), 4.08 (dd, *J* = 6.4 Hz, 2H), 3.99 (ddd, *J* = 9.7, 7.1, 5.8 Hz, 1H), 3.76 (dt, *J* = 12.2, 2.3 Hz, 1H), 3.68 (dd, *J* = 9.8, 2.4 Hz, 0.4H), 3.63 (m, 1H), 3.57 (td, *J* = 9.8, 2.6 Hz, 0.6H), 3.48 (ddd, *J* = 14.9, 11.8, 4.4 Hz, 1H), 3.42 – 3.32 (m, 1H), 3.06 (dd, *J* = 12.1, 6.0 Hz, 1H), 2.49

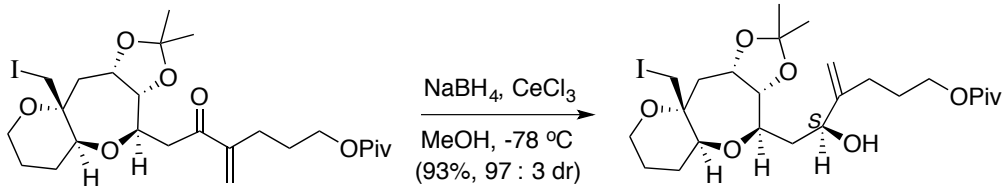
(dt, J = 14.0, 5.4 Hz, 1H), 2.16 (qd, J = 15.6, 14.4, 7.9 Hz, 1H), 2.06 (m, 1H), 1.96 (m, 1H), 1.88 – 1.77 (m, 4H), 1.74 – 1.67 (m, 2H), 1.67 – 1.55 (m, 1H), 1.41 (s, 3H), 1.34 (s, 3H), 1.20 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 178.7, 150.9, 150.1, 110.6, 109.7, 108.70, 108.67, 85.3, 85.0, 82.2, 79.8, 79.5, 79.3, 74.7, 73.9, 73.8, 72.9, 72.8, 71.8, 64.1, 64.0, 59.9, 54.0, 42.14, 42.07, 39.4, 38.9, 38.5, 31.9, 29.9, 29.5, 28.6, 27.5, 27.3, 27.2, 26.3, 25.52, 25.46, 24.4, 24.3, 7.9, 7.6.

Preparation of bicyclic enone 28 (from oxidation of 31): The allylic alcohol **31** (from coupling vinylic iodide **18** and aldehyde **29**; 60 mg, 0.10 mmol) was dissolved in CH_2Cl_2 (3 mL), and DMP (44 mg, 0.10 mmol) and $NaHCO_3$ (17 mg, 0.21 mmol) were added. After 2.5 h, additional DMP (27 mg, 0.06 mmol) was added. After 1 h, the reaction mixture was poured into a solution of aqueous $Na_2S_2O_3$ (5 g) and saturated aqueous $NaHCO_3$ (5 mL). The suspension was stirred for 30 min until the layers turned clear upon standing. The layers were separated and the aqueous layer was extracted with and CH_2Cl_2 (5 mL x 3). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (5 mL), water (5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford enone **28** (54 mg, 0.093 mmol, 93% yield).



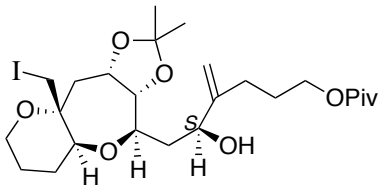
28

(Characterization data provided on page S-27)



28 **30**

<u>Bicyclic allylic alcohol 30</u> (enriched in (*S*)-diastereomer): The enone **28** (119 mg, 0.204 mmol) was dissolved in methanol (2 mL), and the solution was cooled to -78 °C. $CeCl_3 \cdot 7\ H_2O$ (96 mg, 0.26 mmol) and $NaBH_4$ (9.8 mg, 0.26 mmol) were added. After stirring at -78 °C for 1.5 h, the reaction mixture was quenched at low temperature by addition of acetone (0.5 mL), and allowed to warm to room temperature. The reaction mixture was concentrated under reduced pressure before being diluted saturated aqueous NH_4Cl (2 mL) and EtOAc (2 mL). The layers were separated and the aqueous later was extracted with EtOAc (3 mL x 3). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (20% EtOAc in hexanes to 25% EtOAc in hexanes) to afford compound **30** as a clear pale-yellow oil (110 mg, 0.189 mmol, 93% yield, 97:3 dr favoring the (*S*)-alcohol, based on Mosher ester analysis).



30

Data for 30:

$[\alpha]_D^{25}$ -7.3 (c = 1.02, $CHCl_3$)

HRMS (NSI): *m/z* calcd. for $C_{25}H_{42}IO_7$ $[M+H]^+$ 581.1970, found 581.1978.

IR (neat): 3504, 2954, 2935, 2872, 2360, 2342, 1726, 1457, 1381, 1285, 1080 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.10 (t, *J* = 1.2 Hz, 1H), 4.88 (q, *J* = 1.5 Hz, 1H), 4.46 (ddd, *J* = 11.0, 7.1, 5.9 Hz, 1H), 4.32 (dd, *J* = 8.4, 4.0 Hz, 1H), 4.09 (t, *J* = 6.5 Hz, 2H), 3.98 (dd, *J* = 9.7, 7.1 Hz, 1H), 3.76 (dd, *J* = 12.1, 1.9 Hz, 1H), 3.63 (dt, *J* = 12.7, 2.8 Hz, 1H), 3.57 (td, *J* = 9.9, 2.6 Hz, 1H), 3.50 (dd, *J* = 11.9, 4.5 Hz, 1H), 3.36 (ddd, *J* = 12.4, 8.3, 5.9 Hz, 1H), 3.09 (s, 1H), 3.05 (d, *J* = 12.1 Hz, 1H), 2.50 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.23 – 2.18 (m, 1H), 2.09 – 2.02 (m, 2H), 1.88 – 1.78 (m, 4H), 1.71 (app. qd, *J* = 6.4, 2.5 Hz, 2H), 1.68 – 1.56 (m, 2H), 1.41 (s, 3H), 1.34 (s, 3H), 1.20 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.7, 150.1, 110.6, 108.7, 85.3, 82.2, 79.8, 74.7, 73.8, 72.8, 64.1, 59.8, 42.1, 39.4, 38.9, 27.4, 27.3, 26.3, 25.5, 24.3, 7.6.

Table 2. Selected resonances for MTPA-ester derivatives from compound **30**

alcohol **30** resonance	MTPA-ester resonance	δ *S*-ester (ppm)	δ *R*-ester (ppm)	$\Delta(\delta_S-\delta_R)$ (ppm)	$\Delta(\delta_S-\delta_R)$ (Hz)
5.10	a	5.21	5.14	0.07	42
4.88	b	5.11	5.05	0.06	36
2.06	j_2	2.13	2.08	0.05	30
4.32	c	5.69	5.67	n/a	n/a
3.76	e	3.77	3.77	0	0
2.50	i	2.50	2.50	0	0
3.63	f	3.62	3.63	-0.01	-6
3.36	g	3.35	3.36	-0.01	-6
3.05	h	3.04	3.07	-0.03	-18
3.98	d	3.95	4.00	-0.05	-30

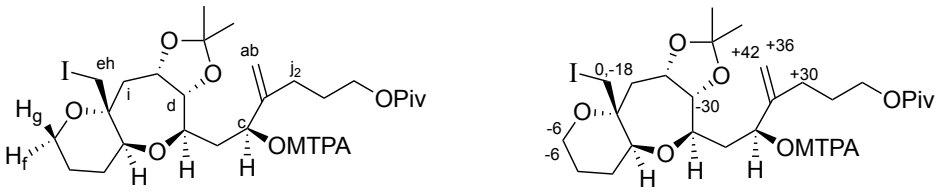
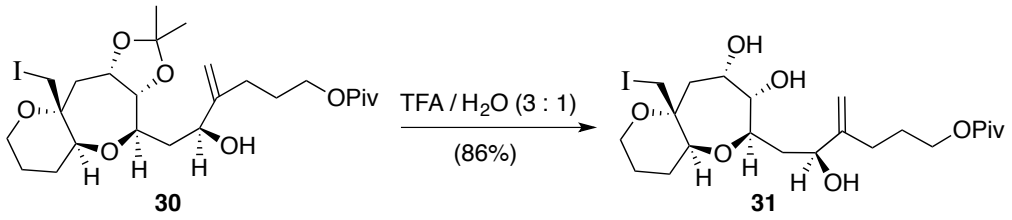
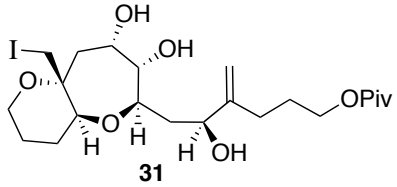


Figure 5. MTPA-ester data for compound **30**

6) Preparation of tricyclic polyether 33 from bicyclic allylic alcohol 30 (Scheme 5):



Bicyclic triol 31: Acetonide **30** (44 mg, 0.075 mmol) was added to a vial, and a mixture of trifluoroacetic acid and water (3:1, 1 mL) was added. The reaction mixture was stirred for 15 min, then cooled to 0 °C before slow addition of saturated aqueous sodium bicarbonate solution (4 mL) and dilution with EtOAc (2 mL). The biphasic mixture was stirred for 30 min before the layers were separated. The aqueous layer was extracted with EtOAc (5 mL x 5). The combined organic extracts were washed with brine, and dried over Na_2SO_4 before being filtered and concentrated under reduced pressure. The crude residue was purified by silica gel flash column chromatography (50% EtOAc in hexanes to 75% EtOAc in hexanes) to afford compound **31** as a clear pale-yellow film (35 mg, 0.065 mmol, 86% yield).



Data for 31:

$[\alpha]_D^{25}$ +20.1 (c = 1.01, $CHCl_3$)

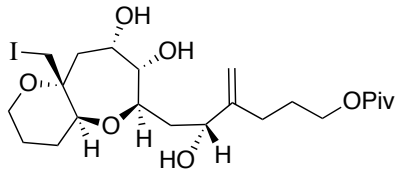
IR (neat): 3479 (br), 1722, 1479, 1283, 1158, 802 cm^{-1}.

HRMS (NSI): *m/z* calcd. for $C_{22}H_{37}IO_7Na$ $[M+Na]^+$ 563.1476, found 563.1475.

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.11 (s, 1H), 4.88 (q, *J* = 1.4 Hz, 1H), 4.29 (dd, *J* = 8.7, 3.5 Hz, 1H), 4.09 (td, *J* = 6.6, 2.5 Hz, 2H), 3.96 (ddd, *J* = 10.3, 3.7, 1.9 Hz, 1H), 3.89 (ddd, *J* = 9.8, 4.0, 2.6 Hz, 1H), 3.86 (m, 2H), 3.79 (dd, *J* = 11.9, 1.9 Hz, 1H), 3.62 (ddd, *J* = 10.8, 5.1, 3.0 Hz, 1H), 3.45 (d, *J* = 11.9 Hz, 1H), 3.34 (d, *J* = 11.8 Hz, 1H), 3.33 (m, 1H), 2.23 – 1.99 (m, 4H), 1.91 – 1.75 (m, 4H), 1.75 – 1.64 (m, 2H), 1.51 (m, 2H), 1.21 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 179.0, 149.7, 110.7, 83.7, 79.1, 77.9, 74.4, 73.4, 68.3, 64.1, 60.2, 42.2, 40.8, 39.0, 27.8, 27.2, 26.4, 25.2, 10.3.

The same procedure was conducted on the diastereomer mixture of allylic alcohol **30** (1.5 : 1 dr) obtained directly from the coupling of vinylic iodide **18** and aldehyde **29**. Careful silica gel flash column chromatography (50% EtOAc in hexanes to 75% EtOAc in hexanes) provided separation of diastereomers **31** and **37**.



37

Data for 37:

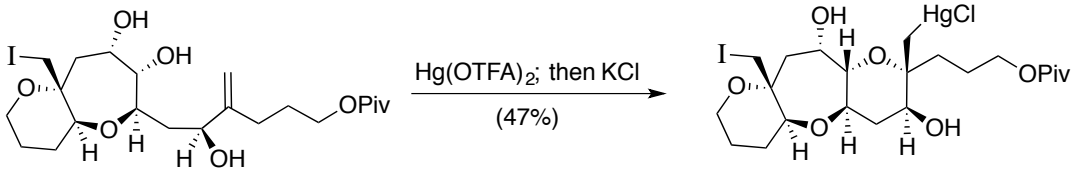
$[\alpha]_D^{25}$ -7.0 (c = 0.827, $CHCl_3$)

IR (neat): 3406 (br), 2955, 2922, 1480, 1275, 1161, 763 cm^{-1}.

HRMS (APCI): *m/z* calcd. for $C_{22}H_{38}O_7I$ $[M+H]^+$ 541.1657, found 541.1643.

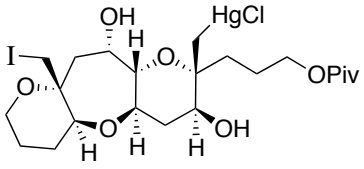
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.17 (t, *J* = 1.2 Hz, 1H), 4.96 (q, *J* = 1.3 Hz, 1H), 4.26 (dd, *J* = 6.9, 2.6 Hz, 1H), 4.13 (dt, *J* = 10.9, 6.7 Hz, 1H), 4.08 (dt, *J* = 10.8, 6.4 Hz, 1H), 3.96 (ddd, *J* = 10.6, 3.2, 2.2 Hz, 1H), 3.92 (dt, *J* = 9.8, 3.1 Hz, 1H), 3.85 (t, *J* = 2.4 Hz, 1H), 3.81 (ddd, *J* = 11.9, 6.9, 3.4 Hz, 2H), 3.62 (ddd, *J* = 13.8, 4.9, 1.9 Hz, 1H), 3.44 (d, *J* = 11.9 Hz, 1H), 3.34 (td, *J* = 11.8, 4.1 Hz, 1H), 2.18 – 2.09 (m, 3H), 2.09 – 1.99 (m, 1H), 1.91 – 1.78 (m, 4H), 1.67 (m, 3H), 1.57 – 1.42 (m, 1H), 1.21 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 179.0, 149.9, 110.2, 81.7, 79.1, 78.2, 73.4, 72.3, 68.6, 64.0, 60.2, 42.5, 39.3, 39.0, 27.4, 27.1, 26.5, 25.3, 10.2.



31 **32**

Tricyclic polyether organomercurial 32: Alkenyl triol **31** (32 mg, 0.059 mmol) was dissolved in THF (1.2 mL), and the solution was cooled to 0 °C. $Hg(O_2CCF_3)_2$ (48 mg, 0.088 mmol) was added. The ice bath was removed after 5 min, and the reaction mixture was stirred at ambient temperature for 2 h before addition of saturated aqueous KCl (60 μL), and stirring for an addition 1.5 h. The reaction mixture was diluted with water (1 mL) and EtOAc (2 mL). The layers were separated and the organic layer was extracted with EtOAc (2 mL x 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by silica gel flash column chromatography (35% EtOAc in hexanes to 45% EtOAc in hexanes) to afford organomercurial intermediate **32** (0.028 mmol, 22 mg, 47% yield). HRMS was complicated by the multiple isotopes of mercury. In addition, another slightly more polar product was isolated (21 mg, 0.027 mmol and 45% yield calcd. assuming mercury incorporation). This other product underwent decomposition upon attempted demercuration, when following the same protocol that was successful for converting compound **32** into compound **33** (see below).



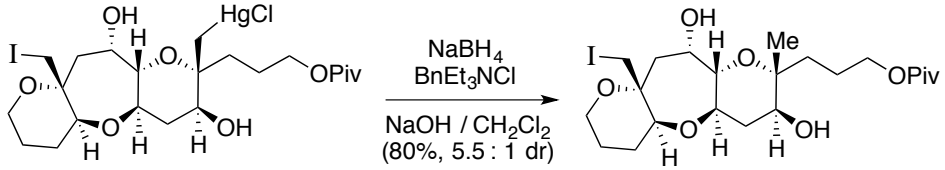
32

Data for 32:

IR (neat): 3426, 2957, 2854, 2360, 2342, 1725, 1554, 1480, 1285, 1160, 1082, 1014 cm^{-1}.

^{1}H NMR (600 MHz, C_6D_6) δ 4.13 (dd, *J* = 11.9, 5.0 Hz, 1H), 4.05 (dt, *J* = 10.7, 7.1 Hz, 1H), 3.93 (dt, *J* = 10.6, 6.8 Hz, 1H), 3.86 (t, *J* = 4.8 Hz, 1H), 3.73 (d, *J* = 11.5 Hz, 1H), 3.50 (ddd, *J* = 11.6, 9.4, 4.7 Hz, 1H), 3.43 (d, *J* = 11.6 Hz, 1H), 3.40 (dd, *J* = 12.7, 5.0 Hz, 1H), 3.10 (dd, *J* = 12.0, 4.5 Hz, 1H), 3.03 (dd, *J* = 9.5, 1.8 Hz, 1H), 2.95 (td, *J* = 12.5, 2.4 Hz, 1H), 2.39 (dd, *J* = 16.1, 4.9 Hz, 1H), 2.20 (dd, *J* = 16.2, 4.4 Hz, 1H), 1.75 (dt, *J* = 12.0, 4.6 Hz, 1H), 1.63 (d, *J* = 14.5 Hz, 1H), 1.49 (m, 2H), 1.42 – 1.24 (m, 3H), 1.21 (s, 9H), 1.11 – 1.06 (m, 1H), 1.01 – 0.89 (m, 1H), 0.82 (d, *J* = 12.0 Hz, 1H).

^{13}C NMR (151 MHz, C_6D_6) δ 178.3, 79.4, 77.1, 76.0, 75.3, 72.7, 70.1, 67.9, 64.3, 60.0, 46.0, 36.9, 35.0, 29.9, 27.1, 26.8, 26.1, 25.1, 22.3, 14.9.



32 **33**

Tricyclic polyether 33: Organomercurial **32** (12 mg, 0.016 mmol) was added to a 0.3 mL conical vial containing CH_2Cl_2 (40 µL). Benzyltriethylammonium chloride (14 mg, 0.061 mmol) and 10% aqueous sodium hydroxide (150 µL) were added, and the resulting biphasic mixture was rapidly stirred, followed by addition of $NaBH_4$ (0.012 mmol dissolved in 25 µL of 10% aqueous NaOH). The biphasic mixture was stirred for 10 min, at which time it was diluted with water (1 mL) and CH_2Cl_2 (1 mL). The layers were separated and the aqueous layer was washed with CH_2Cl_2 (3 x 1 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a crude oil. The crude compound was purified by silica gel flash column chromatography (30% - 40% EtOAc in hexanes) to afford **33** as a clear pale-yellow oil (7 mg, 80% yield, 5.5:1 dr). COSY, HMBC, and HMQC support the structural assignment and NOE supports the axial methyl assignment.

H_a δ 4.15, dd, *J* = 11.8, 5.0 Hz
H_d δ 3.90, dt, *J* = 6.0, 2.9 Hz
H_f δ 3.55, ddd, *J* = 11.9, 9.4, 4.8 Hz
H_i δ 3.12, dd, *J* = 11.9, 4.8 Hz
H_j δ 3.05, dd, *J* = 9.5, 1.9 Hz

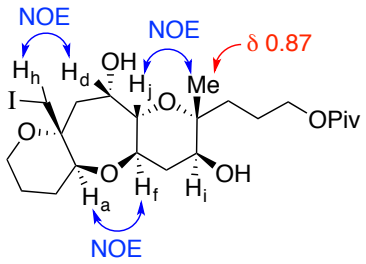


Figure 6. Key NOE correlations of compound **33**

Data for 33:

$[\alpha]_D^{25}$ -15.7 (c = 0.60, $CHCl_3$)

IR (neat): 3465 (br), 2956, 2925, 2854, 1721, 1462, 1261, 1158, 1015, 798 cm^{-1}.

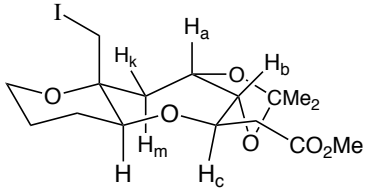
HRMS (NSI): *m/z* calcd. for $C_{22}H_{38}IO_7$ $[M+H]^+$ 541.1657, found 541.1663.

^{1}H NMR (600 MHz, C_6D_6) δ 4.18 – 4.11 (m, 2H), 3.98 (dt, *J* = 10.6, 6.8 Hz, 1H), 3.90 (dt, *J* = 4.6, 3.0 Hz, 1H), 3.68 (d, *J* = 11.5 Hz, 1H), 3.55 (ddd, *J* = 11.6, 9.4, 4.7 Hz, 1H), 3.40 (dd, *J* = 12.2, 5.0 Hz, 1H), 3.33 (d, *J* = 11.5 Hz, 1H), 3.12 (dd, *J* = 11.7, 4.7 Hz, 1H), 3.05 (dd, *J* = 9.4, 1.9 Hz, 1H), 2.93 (td, *J* = 12.4, 2.5 Hz, 1H), 2.36 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.26 (dd, *J* = 16.1, 4.6 Hz, 1H), 1.92 (dt, *J* = 11.8, 4.7 Hz, 1H), 1.61 (p, *J* = 7.2 Hz, 3H), 1.55 – 1.44 (m, 2H), 1.42 – 1.27 (m, 5H), 1.19 (s, 9H), 0.87 (s, 3H).

^{13}C NMR (151 MHz, C_6D_6) δ 178.5, 77.9, 76.9, 76.7, 76.3, 73.8, 71.1, 71.0, 65.2, 60.7, 46.6, 36.4, 35.9, 27.7, 27.4, 25.8, 23.2, 15.9.

Attempts to remove the iodine from compound **33** began with classical methods of radical deiodination, with tributyltin hydride and with *tris*-trimethyl silane, initiated by AIBN over a range of temperatures with varying equivalents of hydride source.[7,8] We then attempted Stephenson's photocatalytic methodology for reduction of unactivated alkyl iodides using *fac*-$Ir(ppy)_3$ and Hantzsch ester,[9] however this resulted in decomposition of starting material with trace iodomethylene protons still visible in the crude NMR. Attempted hydrogenolysis[10] of compound **33** with 10% Pd/C and triethylamine at 30 bar for 22 hours gave no reaction, which we have attributed to steric congestion of the tricyclic compound.

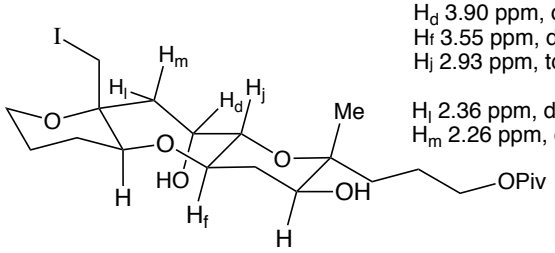
In particular, the B ring exhibits different chemical shifts and couplings for key resonances H_a, H_b, H_c, H_k and H_m in compound **22**, vs. the corresponding resonances H_d, H_f, H_j, H_l and H_m in tricyclic compound **33**. The conformational drawings for compounds **22** and **33** (Figure 7) are based on these coupling constants.



H_a 4.50 ppm, ddd, *J* = 10.8, 6.9, 6.0 Hz
H_b 3.98 ppm, dd, *J* = 10.0, 6.9 Hz
H_c 3.90 ppm, td, *J* = 9.9, 2.8 Hz

H_k 2.52 ppm, dd, *J* = 14.0, 6.0 Hz
H_m 1.85 ppm, ddd, *J* = 14.0, 10.8, 2.0 Hz

compound **22**



H_d 3.90 ppm, dt, *J* = 4.6, 3.0 Hz
H_f 3.55 ppm, ddd, *J* = 11.6, 9.4, 4.7 Hz
H_j 2.93 ppm, td, *J* = 12.4, 2.5 Hz

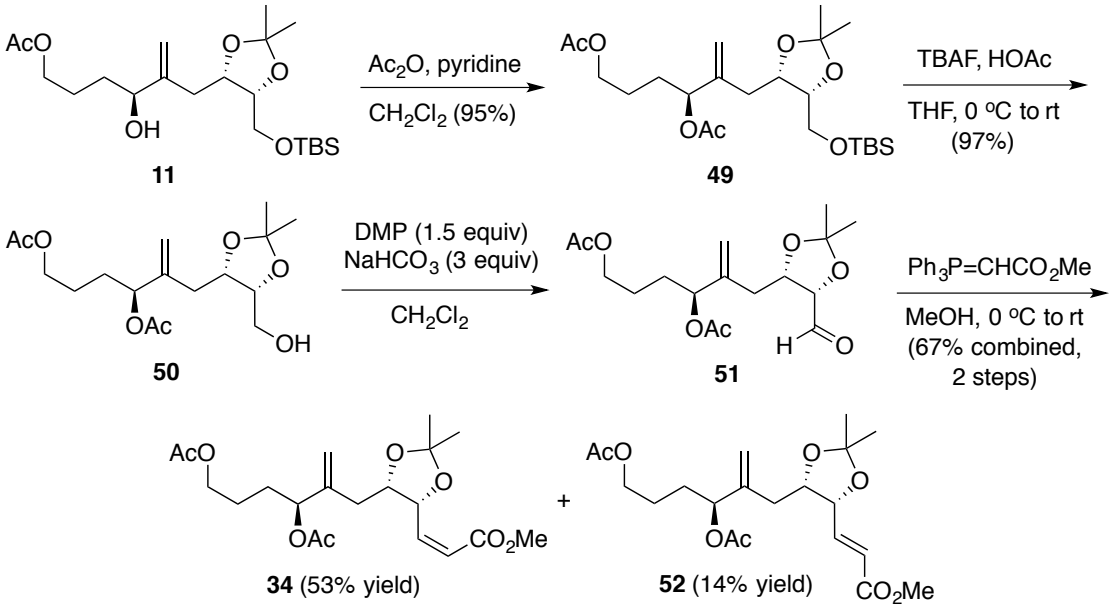
H_l 2.36 ppm, dd, J = 16.0, 4.8 Hz
H_m 2.26 ppm, dd, J = 16.1, 4.6 Hz

compound **33**

Figure 7. Key ^{1}H resonances and coupling constants for the seven-membered rings of compounds **22** and **33**

7) Preparation of bis-acetate dienoate 34 and its conversion to bicyclic 36 (footnote 25):

Dienoate ester, diacetate 34 was prepared in four steps from the allylic alcohol **11**:



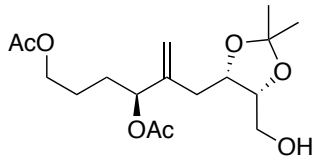
Preparation of bis-acetate ester 49: Alcohol **11** (from page S-23, 948 mg, 2.27 mmol) was dissolved in CH_2Cl_2 (25 mL), acetic anhydride (0.9 mL) and pyridine (0.9 mL) were added, and the reaction mixture was stirred overnight. The crude was concentrated under reduced pressure and purified by silica gel flash column chromatography (20% EtOAc in hexanes) to afford bis-acetate ester **49** as pale yellow, clear oil (929 mg, 2.27 mmol, 95% yield).

Data for 49:

HRMS (NSI): *m/z* calcd. for $C_2H_{42}O_7NaSi$ $[M+Na]^+$ 481.2592, found 481.2583.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.21 (t, *J* = 6.4 Hz, 1H), 5.16 (s, 1H), 5.11 (q, *J* = 1.4 Hz, 1H), 4.39 (ddd, *J* = 9.4, 5.9, 3.1 Hz, 1H), 4.13 (ddd, *J* = 7.8, 6.3, 4.8 Hz, 1H), 4.07 (td, *J* = 6.5, 1.7 Hz, 2H), 3.68 (dd, *J* = 10.4, 7.7 Hz, 1H), 3.63 (dd, *J* = 10.4, 4.7 Hz, 1H), 2.44 (dd, *J* = 16.3, 3.1 Hz, 1H), 2.32 (dd, *J* = 16.0, 9.8 Hz, 1H), 2.07 (s, 3H), 2.05 (s, 3H), 1.80 – 1.70 (m, 2H), 1.69 (s, 3H), 1.44 (s, 3H), 1.35 (s, 3H), 0.90 (s, 9H), 0.08 (s, 6H).

Preparation of primary alcohol 50: Silyl ether **49** (929 mg, 2.02 mmol) was dissolved in THF (20 mL) and cooled to 0 °C, followed by addition of acetic acid (90 µL, 1.5 mmol) and TBAF (1.0 M in THF, 3.0 mL, 3.0 mmol). The reaction mixture was gradually warmed to room temperature and stirred for 2 h before removal of solvent under reduced pressure. The resulting oil was purified by silica gel flash column chromatography (60% EtOAc in hexanes) to afford the product **50** as a pale-yellow oil (675 mg, 1.96 mmol, 97% yield).



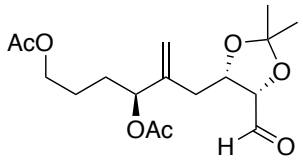
50

Data for 50:

HRMS (NSI): *m/z* calcd. for $C_{17}H_{28}O_7Na$ $[M+Na^+]$ 367.1727, found 367.1721.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.17 (t, *J* = 6.4 Hz, 1H), 5.16 (d, *J* = 1.0 Hz, 1H), 5.05 (t, *J* = 1.5 Hz, 1H), 4.46 (ddd, *J* = 8.0, 6.2, 5.3 Hz, 1H), 4.22 (td, *J* = 6.3, 4.6 Hz, 1H), 4.08 (td, *J* = 6.4, 4.4 Hz, 2H), 3.64 (m, 2H), 2.41 (ddt, *J* = 16.2, 8.1, 1.3 Hz, 1H), 2.28 (dd, *J* = 16.0, 5.4 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.90 (s, 1H), 1.77 – 1.67 (m, 3H), 1.67 – 1.60 (m, 1H), 1.49 (s, 3H), 1.39 (s, 3H).

Preparation of aldehyde 51: To a stirred solution of primary alcohol **50** (675 mg, 1.96 mmol) in CH_2Cl_2 (40 mL) was added DMP (1.27 g, 3.03 mmol) and $NaHCO_3$ (503 mg, 6.05 mmol). After 2 h, the reaction was poured into a rapidly stirred solution of $Na_2S_2O_3$ (25 g) in saturated aqueous $NaHCO_3$ (100 mL). The suspension was stirred for 30 min until the layers turned clear. The layers were separated and the organic layer was washed with saturated aqueous $NaHCO_3$ (25 mL), water (15 mL x 2), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude aldehyde **51** was used immediately without further purification.



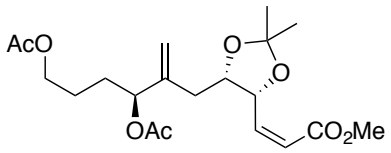
51

Data for 51:

HRMS (NSI): *m/z* calcd. for $C_{17}H_{26}O_7Na$ $[M+Na]^+$: 365.1570, found 365.1567.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.68 (d, *J* = 3.3, Hz, 1H), 5.18 (s, 1H), 5.16 (m, 1H), 5.09 (s, 1H), 4.62 – 4.55 (m, 1H), 4.34 (dd, *J* = 7.0, 3.2 Hz, 1H), 4.08 (dt, *J* = 5.8, 2.8 Hz, 2H), 2.38 – 2.20 (m, 2H), 2.07 (s, 3H), 2.06 (s, 3H), 1.81 – 1.63 (m, 4H), 1.61 (s, 3H), 1.44 (s, 3H).

Preparation of dienoate ester 34: The crude aldehyde **51** (688 mg) was dissolved in methanol (6.5 mL) and cooled to 0 °C, then the Wittig reagent (803 mg, 2.4 mmol) was added. The reaction mixture was stirred at 0 °C for 2 h, whereupon the solvent was removed under reduced pressure and the resulting viscous yellow oil was purified by silica gel flash column chromatography (15% EtOAc in hexanes). The alkene isomers were separated cleanly to afford **34**, *Z*-α,β unsaturated ester (398 mg, 1.07 mmol, 53% yield) and **52**, *E*-α,β unsaturated ester (107 mg, 0.29 mmol, 14% yield).

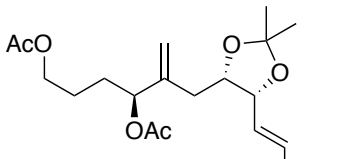


34

Data for 34, *Z*-α,β unsaturated ester:

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.24 (dd, *J* = 11.7, 8.1 Hz, 1H), 5.95 (dd, *J* = 11.7, 1.5 Hz, 1H), 5.64 (ddd, *J* = 8.1, 6.5, 1.5 Hz, 1H), 5.17 (dd, *J* = 7.1, 5.3 Hz, 1H), 5.12 (s, 1H), 5.07 (t, *J* = 1.3 Hz, 1H), 4.60 (ddd, *J* = 8.6, 6.6, 4.5 Hz, 1H), 4.05 (t, *J* = 6.3 Hz, 2H), 3.72 (s, 3H), 2.13 – 2.09 (m, 2H), 2.05 (s, 3H), 2.04 (s, 3H), 1.75 – 1.57 (m, 4H), 1.50 (s, 3H), 1.38 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 171.2, 170.4, 166.1, 146.7, 144.2, 121.7, 113.8, 109.0, 77.0, 76.1, 75.2, 64.2, 51.7, 33.4, 29.8, 28.4, 25.6, 24.8, 21.4, 21.1.



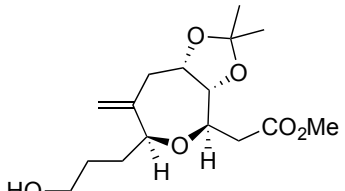
52

Data for 52, *E*-α,β unsaturated ester:

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.86 (dd, *J* = 15.6, 6.0 Hz, 1H), 6.11 (dd, *J* = 15.6, 1.4 Hz, 1H), 5.17 (s, 1H), 5.15 (s, 1H), 5.06 – 5.01 (m, 1H), 4.74 (td, *J* = 6.3, 1.5 Hz, 1H), 4.52 (ddd, *J* = 8.4,

6.4, 5.0 Hz, 1H), 4.07 (td, *J* = 6.1, 1.6 Hz, 2H), 3.76 (s, 3H), 2.31 – 2.24 (m, 1H), 2.11 (dd, *J* = 15.9, 5.1 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.74 – 1.59 (m, 4H), 1.53 (s, 3H), 1.40 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$): δ 143.7, 123.2, 113.8, 109.2, 77.3, 76.6, 76.2, 64.2, 51.9, 33.3, 29.8, 28.1, 25.6, 24.9, 21.4, 21.2.

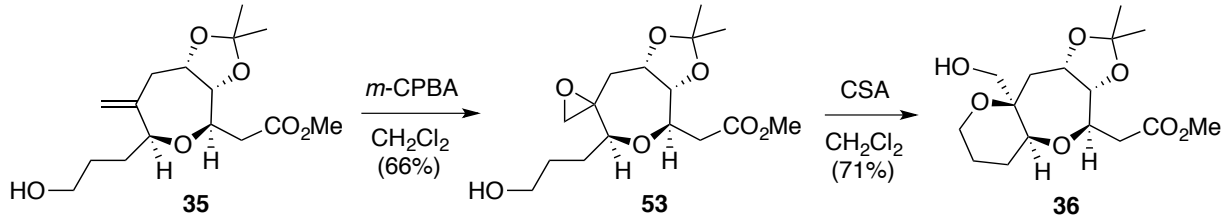
Unexpected formation of methylene-oxepane 35: Bis-acetate **34** (398 mg, 1.07 mmol) was dissolved in methanol (11 mL), and then K_2CO_3 (30 mg, 0.21 mmol) was added. The reaction mixture was stirred at room temperature for 4 h. The methanol was removed by rotary evaporation before immediate purification by silica gel flash column chromatography (40% EtOAc in hexanes to 60% EtOAc in hexanes) to afford methylene-oxepane **35** as a light-yellow oil (138 mg, 0.44 mmol, 41% yield, 9:1 dr).



35

Data for 35:
^{1}H NMR (600 MHz, C_6D_6) δ 5.06 (d, *J* = 0.9 Hz, 1H), 4.93 (t, *J* = 1.3 Hz, 1H), 4.31 (dd, *J* = 8.4, 5.4 Hz, 0.1 H), 4.26 (dd, *J* = 8.6, 5.3 Hz, 0.9 H), 4.04 (td, *J* = 10.2, 2.7 Hz, 1H), 3.99 (ddd, *J* = 5.6, 4.5, 3.2 Hz, 1H), 3.65 (dd, *J* = 10.0, 5.8 Hz, 0.1H), 3.52 (dd, *J* = 10.2, 5.5 Hz, 0.9H), 3.40 (dd *J* = 12.4, 6.1 Hz, 2H), 3.38 (s, 3H), 2.93 (dd, *J* = 15.9, 2.6 Hz, 0.1H), 2.89 (dd, *J* = 16.0, 2.7 Hz, 0.9H), 2.49 (dd, *J* = 16.0, 10.3 Hz, 1H), 2.41 (dd, *J* = 14.0, 4.4 Hz, 1H), 2.35 (ddd, *J* = 14.0, 3.2, 1.0 Hz, 1H), 1.69 – 1.61 (m, 1H), 1.58 – 1.45 (m, 2H), 1.43 – 1.37 (m, 1H), 1.36 (s, 3H), 1.24 (s, 3H).

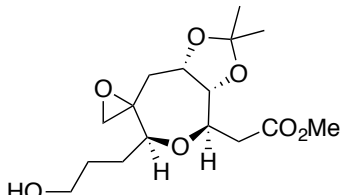
***Cis*-fused bicyclic polyether 36:** Epoxidation of **35** was diastereoselective, although the stereochemistry of the epoxide intermediate **53** could not be determined. Acid-catalyzed cyclization produced bicyclic **36**, which was unambiguously characterized by X-ray crystallography.



35 **53** **36**

Preparation of epoxide 53: Methylene-oxepane **35** (138 mg, 0.44 mmol) was dissolved in a rapidly stirred biphasic mixture of CH_2Cl_2 (9 mL) and aqueous pH 7 buffer (9 mL). *m*-CPBA (77% purity, 295 mg, 1.31 mmol) was added. The suspension was stirred overnight until alkene

had been consumed, at which time the reaction mixture was diluted with EtOAc (20 mL). The organic layer was separated and washed with aqueous $Na_2S_2O_2$ (10 mL), aqueous $NaHCO_3$ (15 mL), water (15 mL), and brine before being dried over $MgSO_4$, filtered, concentrated, and purified by silica gel flash column chromatography (50% EtOAc in hexanes) to afford the product with benzoic acid, which was re-subjected to column chromatography (40% EtOAc in hexanes) to afford the epoxide **53** as a light-yellow film (95 mg, 0.29 mmol, 66% yield).

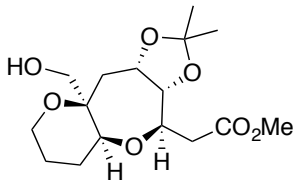


53

Data for 53:

^{1}H NMR (600 MHz, C_6D_6) δ 4.26 (td, *J* = 10.1, 2.4 Hz, 1H), 4.14 (ddd, *J* = 9.6, 6.8, 4.1 Hz, 1H), 3.82 (dd, *J* = 9.9, 6.8 Hz, 1H), 3.71 (dd, *J* = 10.7, 2.1 Hz, 1H), 3.39 (m, 2H), 3.37 (s, 3H), 2.84 (dd, *J* = 15.9, 2.5 Hz, 1H), 2.49 (dd, *J* = 15.9, 10.3 Hz, 1H), 2.38 (dd, *J* = 4.5, 1.4 Hz, 1H), 2.23 (ddd, *J* = 14.0, 9.6, 1.5 Hz, 1H), 2.08 (d, *J* = 4.5 Hz, 1H), 1.67 (dd, *J* = 14.1, 4.1 Hz, 1H), 1.65 – 1.60 (m, 1H), 1.44 (m, 1H), 1.40 (s, 3H), 1.36 (m, 2H), 1.19 (s, 3H).

Preparation of bicyclic polyether 36: Epoxide **53** (49.0 mg, 0.148 mmol) was dissolved in dry CH_2Cl_2 (3 mL), and camphorsulfonic acid (CSA, 17.2 mg, 0.074 mmol) was added. The reaction was stirred at room temperature for 14 h, and then concentrated under reduced pressure. Silica gel flash column chromatography (40% ether in pentane to 50% ether in pentane) afforded bicyclic polyether **36** as a white powder (35.0 mg, 0.106 mmol, 71% yield). The powder was recrystallized from heptane and benzene *via* vapor diffusion to afford colorless needle-like crystals.



36

Data for 36:

Melting point: 126-127 °C

$[\alpha]_D^{25}$ +5.4 (c = 0.65, $CHCl_3$)

IR (neat): 3435, 2924, 2854, 1739, 1439, 1370, 1263, 1209, 1106, 1044 cm^{-1}.

HRMS (NSI): *m/z* calcd. for $C_{16}H_{25}O_6INa$ $[M+Na]^+$ 463.0588, found 463.0585.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.68 (ddd, *J* = 11.6, 6.9, 3.1 Hz, 1H), 4.14 (dd, *J* = 9.6, 6.9 Hz, 1H), 4.02 (td, *J* = 10.2, 2.5 Hz, 1H), 3.96 (d, *J* = 11.3 Hz, 1H), 3.77 (dd, *J* = 11.6, 5.0 Hz, 1H),

3.70 (s, 3H), 3.62 (td, *J* = 12.9, 11.6, 2.5 Hz, 1H), 3.44 (t, *J* = 3.1 Hz, 1H), 3.24 (d, *J* = 11.3 Hz, 1H), 2.77 (dd, *J* = 16.3, 2.5 Hz, 1H), 2.55 (dd, *J* = 16.3, 10.4 Hz, 1H), 2.34 (dd, *J* = 14.6, 3.1 Hz, 1H), 1.92 – 1.82 (m, 2H), 1.82 – 1.71 (m, 3H), 1.68 (m, 1H), 1.45 (s, 3H), 1.35 (s, 3H).

^{1}H NMR (600 MHz, C_6D_6) δ 4.93 (ddd, *J* = 11.6, 6.9, 3.1 Hz, 1H), 4.15 (td, *J* = 10.0, 2.4 Hz, 1H), 4.07 (dd, *J* = 9.6, 6.9 Hz, 1H), 3.44 (d, *J* = 11.2 Hz, 1H), 3.39 (m, 2H), 3.33 (s, 3H), 3.11 (ddd, *J* = 13.1, 11.6, 2.5 Hz, 1H), 2.87 (d, *J* = 11.2 Hz, 1H), 2.79 (dd, *J* = 16.3, 2.4 Hz, 1H), 2.56 (dd, *J* = 16.3, 10.3 Hz, 1H), 2.47 (dd, *J* = 14.5, 3.1 Hz, 1H), 1.93 – 1.83 (m, 2H), 1.67 – 1.61 (m, 1H), 1.46 (s, 3H), 1.33 (tdd, *J* = 13.9, 4.6, 3.2 Hz, 2H), 1.21 (s, 3H), 0.94 – 0.90 (m, 1H), 0.77 (ddq, *J* = 13.2, 4.3, 2.3 Hz, 1H).

^{13}C NMR (151 MHz, C_6D_6) δ 171.9, 128.7, 109.7, 79.8, 79.1, 76.7, 76.4, 74.8, 62.8, 61.8, 51.4, 40.5, 38.4, 30.6, 28.4, 27.1, 25.5, 20.5.

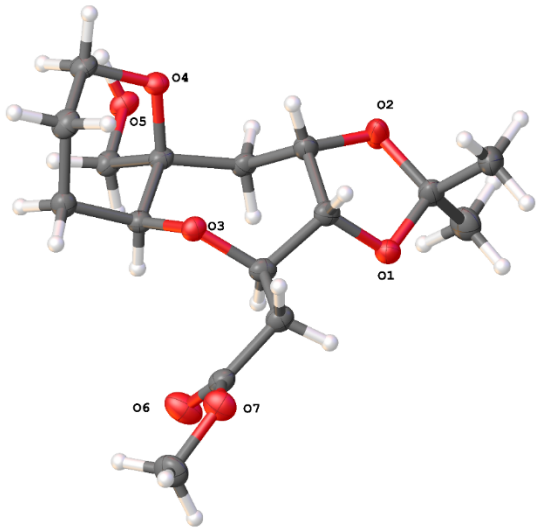
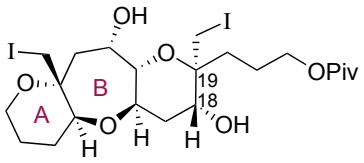


Figure 8. X-ray crystal structure of *cis*-fused bicyclic compound **36**

8) Iodocyclization of alkenyl triol 37 to tricyclic polyether 38 (footnote 28):

Preparation of tricyclic polyether 38: Alkenyl triol **37** (see page S-42, 9.0 mg, 0.017 mmol) was dissolved in THF (1.5 mL), and the solution was cooled to 0 °C. Sodium bicarbonate (14 mg, 0.16 mmol) was added followed by iodine (26 mg, 0.10 mmol). The reaction mixture gradually warmed to ambient temperature. After 10 h, the reaction mixture was quenched by addition of saturated aqueous $Na_2S_2O_3$ (2 mL). The reaction mixture was diluted with EtOAc (2 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (4 x 2 mL) and the combined organic extracts were washed with brine before being dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by silica gel flash column chromatography (50% EtOAc in hexanes) to afford tricyclic polyether diiodide **38** (7.0 mg, 0.012 mmol, 70 % yield).



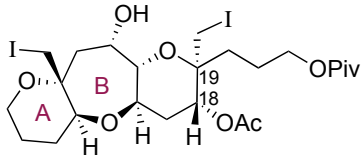
38

Data for 38:

HRMS (NSI): *m/z* calcd for $C_{22}H_{37}O_7I_2$ $[M+H]^+$ 667.0623, found 667.0635.

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.15 (dd, *J* = 12.0, 4.9 Hz, 1H), 4.11 (td, *J* = 5.4, 2.0 Hz, 2H), 4.04 (td, *J* = 12.2, 11.0, 4.7 Hz, 1H), 3.98 (t, *J* = 3.2 Hz, 1H), 3.87 (d, *J* = 11.5 Hz, 1H), 3.64 (dd, *J* = 12.7, 4.7 Hz, 1H), 3.41 (dd, *J* = 10.0, 1.7 Hz, 1H), 3.26 (dd, *J* = 9.1, 2.8 Hz, 1H), 3.25 (d, *J* = 11.4 Hz, 1H), 3.12 (d, *J* = 10.1 Hz, 1H), 2.26 – 2.21 (m, 1H), 2.21 – 2.15 (m, 2H), 2.09 – 2.02 (m, 1H), 1.95 – 1.75 (m, 4H), 1.68 (m, 2H), 1.58 (m, 2H), 1.25 (s, 9H).

Tricyclic polyether **38** was derivatized as the acetate ester **54**: Compound **38** was dissolved in CH_2Cl_2 (1 mL), and Ac_2O (0.1 mL) and pyridine (0.1 mL) were added. The reaction mixture was stirred overnight. The crude product was concentrated under reduced pressure and purified by silica gel flash column chromatography to afford the acetate ester **54** as a yellow oil.



54

Data for 54:

$[\alpha]_D^{25}$ -10.5 (c = 0.327, $CHCl_3$)

IR (neat): 3477, 2958, 2925, 2854, 1729, 1460, 1259, 1241, 1316, 1028, 797 cm^{-1}.

HRMS (APCI): *m/z* calcd. for $C_{24}H_{39}O_8I_2$ $[M+H]^+$ 709.0729, found 709.0703.

^{1}H NMR (600 MHz, C_6D_6) δ 5.00 (t, *J* = 3.1 Hz, 1H), 4.19 (dd, *J* = 11.8, 4.9 Hz, 1H), 4.06 (ddd, *J* = 11.9, 9.3, 4.6 Hz, 1H), 3.85 (m, 3H), 3.67 (d, *J* = 11.4 Hz, 1H), 3.35 (dd, *J* = 12.5, 4.7 Hz, 1H), 3.28 (d, *J* = 11.4 Hz, 1H), 3.15 (app. ddd, *J* = 18.3, 9.9, 1.8 Hz, 2H), 2.91 (td, *J* = 12.5, 2.7 Hz, 1H), 2.85 (d, *J* = 10.2 Hz, 1H), 2.38 (dt, *J* = 14.5, 4.0 Hz, 1H), 2.31 (dd, *J* = 16.2, 4.4 Hz, 1H), 1.66 (s, 3H), 1.41 – 1.29 (m, 8H), 1.27 (s, 9H).

^{13}C NMR (151 MHz, C_6D_6) δ 177.3, 168.9, 77.7, 77.3, 75.9, 75.8, 71.4, 70.7, 70.0, 63.2, 60.1, 45.9, 38.6, 29.9, 29.5, 27.3, 25.1, 22.8, 21.2, 20.2, 14.8, 6.9.

9) References

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