Supporting Information

Enantioselective Synthesis of Iridal, the Parent Molecule of the Iridal Triterpenoid Class

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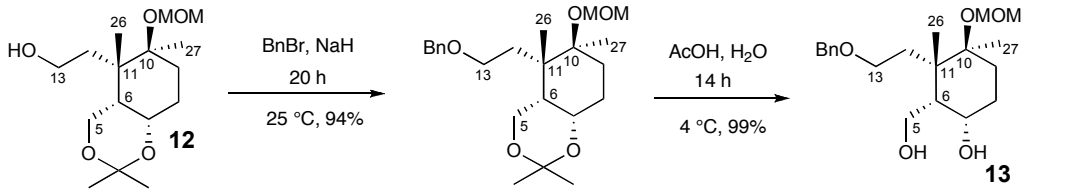
Experimental Section

General Experimental Section: "Usual work up" means washing of the organic layer with brine, drying over anhydrous $MgSO_4$, and evaporating *in vacuo* with a rotary evaporator at aspirator pressure. Melting points (uncorrected) were determined with the aid of a Büchi B-540 apparatus. IR spectra were recorded on a Perkin-Elmer Spectrum BX instrument with an FT-IR system. Absorptions are given in cm^{-1}. Optical Rotations were measured on a JASCO-810 polarimeter using a cell of 1 dm-path length. NMR spectra were run in $CDCl_3$ unless otherwise noted. Experimental evidence favoring the structures investigated came from a comprehensive range of ^1H and ^{13}C NMR data (500/125 and 300/75 MHz respectively, 1D and 2D experiments). ^1H chemical shifts are expressed in ppm downfield from TMS using the residual nondeuterated solvent as internal standard ($CDCl_3$ ^1H, 7.26 ppm). ^{13}C chemical shifts are reported relative to $CDCl_3$ triplet centered at 77.0 ppm. Mass spectra acquired in the positive ion mode under electron spray ionization (ES^+) using a mobile phase of methanol, will be abbreviated as ESIMS (MeOH). HR will be added for the high resolution mass measurements (HRESIMS).

Preparation of TBS-protected aldol 14



Chemical Formula: $C_{16}H_{30}O_5$
Exact Mass: 302,2093
Elemental Analysis: C, 63.55; H, 10.00;

Chemical Formula: $C_{23}H_{36}O_5$
Exact Mass: 392,2563
Elemental Analysis: C, 70.38; H, 9.24;

Chemical Formula: $C_{20}H_{32}O_5$
Exact Mass: 352,2250
Elemental Analysis: C, 68.15; H, 9.15;

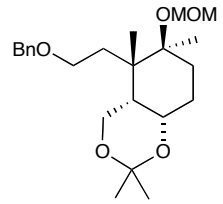
Benzyl protection

Sodium hydride (60% w/w in mineral oil; 6.0 g, 115.0 mmol) was washed twice with dry hexane under argon atmosphere and the remainder of the hexane removed *via* syringe and the flask vacuumed then filled with argon. *N*, *N*-dimethylformamide (80 mL) and the known[1] isopropylidene alcohol **12** (7.0 g, 23.1 mmol) were added. After stirring for 0.5 h the reaction mixture was cooled to 0 °C, BnBr (11.9 g, 69.3 mmol) and *N*, *N*-dimethylformamide (20 mL) were added and the mixture was stirred for 20 h. Water and ether were added, the two phases separated and the organic phase was worked up as usual. Chromatography of the residue (hexane-EtOAc, 3:1) gave the corresponding benzyl ether (8.5 g, 94%).

[1] ([1]) Corbu, A. , Gauron, G., Castro, J. M., Dakir, M., Arseniyadis, S. *Org. Lett*. **2007**, *9*, 4745–4748.

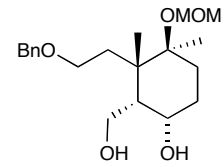
Acetonide deprotection

A mixture of acetic acid and water (120 mL, 3:1) was added to benzyl ether thus obtained (8.5 g, 21.7 mmol) at 0 °C. The reaction mixture was stirred at 4 °C for 14 h. The media was diluted with EtOAc, washed with a saturated solution of $NaHCO_3$ (until pH = 7) and brine. The organic layer was dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. A flash chromatography (heptane-EtOAc, 1:1) gave 7.6 g (99%) of diol **13**.



Chemical Formula: $C_{23}H_{36}O_5$
Exact Mass: 392,26

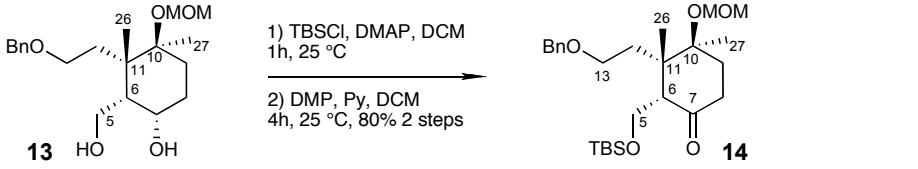
Colorless oil; $[\alpha]_D^{20}$ = 61 (*c* 1.6, $CHCl_3$); IR (film): ν = 3547, 1454, 1365, 1198, 1115, 1094, 1027, 962, 917, 735, 698 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.00 (s, 3H), 1.23 (s, 3H), 1.40 (s, 3H), 1.46 (s, 3H), 1.47-1.54 (m, 2H), 1.56 (bt, *J* = 3.6 Hz, 1H), 1.74 (ddd, *J* = 6.1, 9.1, 14.2 Hz, 1H), 1.84-1.94 (m, 2H), 2.76 (ddd, *J* = 5.5, 8.9, 14.3 Hz, 1H), 3.35 (s, 3H), 3.6 (dt, *J* = 6.0, 8.9 Hz, 1H), 3.80 (dt, *J* = 5.4, 9.0 Hz, 1H), 3.98 (bd, *J* = 12.8 Hz, 1H), 4.03 (dd, *J* = 4.1, 12.5 Hz, 1H), 4.15 (dt, *J* = 2.1, 3.3 Hz, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.53 (d, *J* = 11.9 Hz, 1H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 7.24-7.35 (m, 5H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 16.8, 19.0, 20.5, 26.5, 26.7, 29.7, 32.9, 38.4, 42.2, 55.3, 61.2, 67.2, 68.9, 72.8, 80.7, 90.4, 98.2, 127.2, 127.6 (2C), 128.2 (2C), 138.9; ESIMS (MeOH): 415.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{23}H_{36}O_5Na$ *m/z* 415.2460, found 415.2451; Analysis calcd. for $C_{23}H_{36}O_5$ (392.26): C 70.38, H 9.24; found C 70.59, H 9.26.



Chemical Formula: $C_{20}H_{32}O_5$
Exact Mass: 352,22

White crystals; Mp: 98.2-99.1 °C; $[\alpha]_D^{20}$ = 31 (*c* 1.0, $CHCl_3$); IR (film): ν = 3354, 1456, 1373, 1142, 1103, 1030, 938, 916 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.09 (s, 3H), 1.14 (s, 3H), 1.55 (ttd, *J* = 3.4, 6.6, 13.0 Hz, 1H), 1.59-1.64 (m, 1H), 1.68-1.78 (m, 2H), 1.84 (ddd, *J* = 3.9, 9.0, 14.3 Hz, 1H), 1.91 (td, *J* = 3.3, 6.8 Hz, 1H), 2.31 (bs, 1H), 3.32 (s, 3H), 3.56-3.62 (m, 2H), 3.77 (dd, *J* = 2.4, 11.0 Hz, 1H), 3.95 (dd, *J* = 6.8, 11.2 Hz, 1H), 4.21 (td, *J* = 3.8, 6.1 Hz,

1H), 4.47 and 4.50 (ABquartet, J = 11.7 Hz, 2H), 4.62 and 4.66 (ABquartet, J = 6.7 Hz, 2H), 7.27-7.33 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 19.0, 20.2, 28.3 (2C), 33.2, 43.0, 48.6, 55.2, 61.8, 68.1, 69.2, 73.2, 79.9, 90.3, 127.6, 127.7 (2C), 128.3 (2C), 137.8; ESIMS (MeOH): 375.2 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{20}H_{32}O_5Na$ *m/z* 375.2147, found 375.2153.

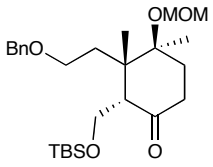


Chemical Formula: $C_{20}H_{32}O_5$
Exact Mass: 352.2250
Elemental Analysis: C, 68.15; H, 9.15; O, 22.70

Chemical Formula: $C_{26}H_{44}O_5Si$
Exact Mass: 464.2958
Elemental Analysis: C, 67.20; H, 9.54; O, 17.21; Si, 6.04

Selective primary hydroxyl group protection and Dess-Martin oxidation

A solution of diol **13** (5.7 g, 14.3 mmol, 1.0 equiv), DMAP (6.2 g, 45.8 mmol, 3.2 equiv), and *tert*-butyldimethylsilyl chloride (3.9 g, 22.9 mmol, 1.6 equiv), in CH_2Cl_2 (150 mL), was stirred at 0 °C to room temperature for 1 h. The reaction mixture was then diluted with CH_2Cl_2, washed with 1N HCl, then saturated aq. $NaHCO_3$ and worked up as usual to give the corresponding silyl ether that was filtered on silica and taken as such to the next step. To a solution of the silyl ether thus obtained (7.5 g, 14.3 mmol) in CH_2Cl_2 (200 mL) and pyridine (12 mL) were added 19.0 g (45.0 mmol) of Dess-Martin periodinane and stirring continued at room temperature for 4 h. The reaction mixture was then diluted with CH_2Cl_2, quenched with a saturated aqueous solution of sodium bicarbonate and washed with brine. Usual work up and chromatography (heptane-EtOAc, 3:1) afforded 5.3 g (80% over two steps) of the TBS-protected aldol **14**:

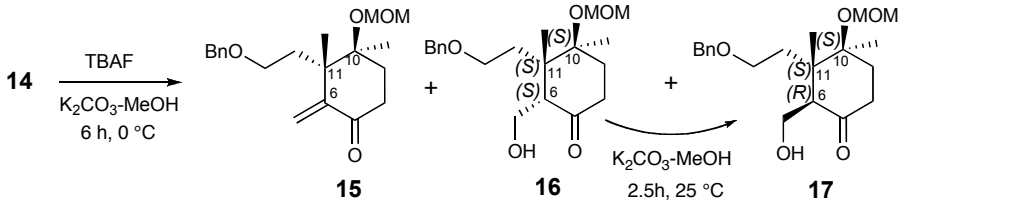


Chemical Formula: $C_{26}H_{44}O_5Si$
Exact Mass: 464,30

Colorless oil; $[\alpha]_D^{20}$ = 3 (*c* 0.8, $CHCl_3$); IR (film): ν = 1714, 1462, 1253, 1154, 1092, 1020, 919, 836, 777, 735, 698 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 1.17 (s, 3H), 1.24 (s, 3H), 1.52 (t, J = 7.9 Hz, 2H), 1.9 (ddd, J = 5.6, 13.1, 14.5 Hz, 1H), 2.07 (dd, J = 7.2, 15.1 Hz, 1H), 2.19 (dd, J = 5.5, 13.8 Hz, 1H), 2.60 (ddd, J = 7.3, 12.8, 13.9 Hz, 1H), 3.20 (m, 1H), 3.40-3.42 (m, 2H), 3.43 (s, 3H), 3.60 (dd, J = 3.9, 10.3 Hz,

1H), 4.13 (dd, J = 6.4, 10.3 Hz, 1H), 4.44 (bs, 2H), 4.79 and 4.84 (ABquartet, J = 7.6 Hz, 2H), 7.27-7.32 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.4, –5.3, 17.8, 18.2, 19.4, 25.9 (3C), 32.8, 33.5, 38.2, 48.5, 55.8, 57.9, 58.6, 67.5, 73.0, 79.8, 90.9, 127.5 (3C), 128.3 (2C), 138.2, 211.2; ESIMS (MeOH): 487.3 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{26}H_{44}O_5SiNa$ *m/z* 487.2856, found 487.2874; Analysis calcd. for $C_{26}H_{44}O_5Si$ (464.7): C 67.2, H 9.54; found C 66.91, H 9.77.

The C6 epimerization

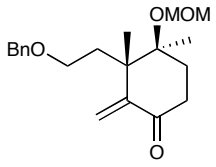


Chemical Formula: $C_{20}H_{28}O_4$
Exact Mass: 332.1988
Elemental Analysis: C, 72.26; H, 8.49; O, 19.25

Chemical Formula: $C_{20}H_{30}O_5$
Exact Mass: 350.2093
Elemental Analysis: C, 68.54; H, 8.63; O, 22.83

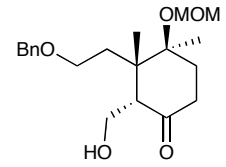
To a magnetically stirred solution (15 mL of THF) of TBS-protected aldol **14** (3.0 g, 6.5 mmol) was added tetrabutylammonium fluoride (TBAF, 7.7 mmol, 7.7 mL, 1M in THF). The reaction was stirred at 0 °C for 2 h before an additional 0.6 equiv of tetrabutylammonium fluoride (3.9 mmol, 3.9 mL) were added. After another 2 h, an extra 0.6 equiv of TBAF (3.9 mmol, 3.9 mL) were added, and the reaction was stopped following a 2 h stirring (TLC monitoring) by dilution with EtOAc, washed with brine and worked up as usual. Silica gel column chromatography (heptane-EtOAc, 4:1 to 1:2) afforded the enone **15** (252 mg, 12%), the C6(*S*) aldol **16** (1.17 g, 52%) along with the desired C6(*R*) aldol **17** (570 mg, 25%).

To a solution of C6(*S*) aldol **16** (300 mg, 0.86 mmol) in MeOH (4 mL) was added K_2CO_3 (35 mg, 0.26 mmol) and the reaction mixture was stirred for 1 h at 25 °C, then diluted with brine and the methanol was evaporated in *vacuo*. The aqueous layer was extracted five times with ethyl acetate. The organic layer was dried over $MgSO_4$ and evaporated, yielding 280 mg of crude product that was subjected to flash-chromatography (heptane-EtOAc, 3:1 to 1:2) yielding the enone **15** (48 mg, 16%), the C6(*S*) aldol **16** (130 mg, 43%) and the desired C6(*R*) aldol **17** (90 mg, 30%).



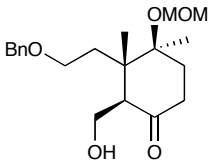
Chemical Formula: $C_{20}H_{28}O_4$
Exact Mass: 332,20

Enone 15: Yellow oil; $[\alpha]_D^{20}$ = – 3 (*c* 1.0, $CHCl_3$); IR (film): ν = 1692, 1453, 1380, 1148, 1100, 1029, 915, 737, 697 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.18 (s, 3H), 1.30 (s, 3H), 1.60-1.69 (m, 1H), 1.79 (ddd, *J* = 6.2, 9.3, 13.3 Hz, 1H), 2.04-2.09 (m, 2H), 2.41 (ddd, *J* = 3.8, 6.2, 17.5 Hz, 1H), 2.59 (ddd, *J* = 8.4, 10.4, 18.2 Hz, 1H), 3.33 (s, 3H), 3.36-3.48 (m, 2H), 4.38 and 4.45 (ABquartet, *J* = 12.0 Hz, 2H), 4.69 and 4.75 (ABquartet, *J* = 7.0 Hz, 2H), 5.14 (s, 1H), 5.85 (s, 1H), 7.27-7.36 (m, 5H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 17.2, 19.7, 29.5, 34.9, 35.6, 47.5, 55.7, 66.8, 73.2, 79.5, 90.8, 118.9, 127.6, 127.7 (2C), 128.4 (2C), 138.1, 151.2, 202.9; ESIMS (MeOH): 355.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{20}H_{28}O_4Na$ *m/z* 355.1885, found 355.1878.



Chemical Formula: $C_{20}H_{30}O_5$
Exact Mass: 350,21

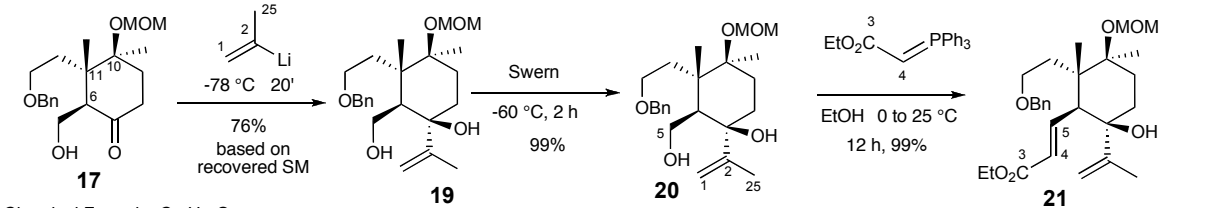
Aldol 16: Colorless oil; $[\alpha]_D^{20}$ = 30 (*c* 1.0, $CHCl_3$); IR (film): ν = 3445, 1698, 1455, 1152, 1094, 1028, 917, 736, 668 cm^{-1}; ^{1}H-NMR (C_6D_6, 500 MHz): δ = 1.03 (s, 3H), 1.06 (s, 3H), 1.47-1.62 (m, 3H), 1.65 (ddd, *J* = 1.3, 7.4, 15.2 Hz, 1H), 2.15 (ddd, *J* = 2.0, 5.4, 14.7 Hz, 1H), 2.42 (ddd, *J* = 7.4, 13.3, 14.6 Hz, 1H), 2.90 (bs, 1H), 3.20 (s, 3H), 3.29-3.38 (m, 3H), 3.81 (t, *J* = 8.0 Hz, 1H), 4.26 (bt, *J* = 9.9 Hz, 1H), 4.34 (s, 2H), 4.50 (d, *J* = 7.5 Hz, 1H), 4.53 (d, *J* = 7.5 Hz, 1H), 7.20-7.39 (m, 5H); ^{13}C-NMR (C_6D_6, 125 MHz): δ = 17.3, 19.2, 31.8, 33.9, 38.0, 47.7, 55.6, 57.6, 59.2, 67.7, 73.0, 79.5, 90.9, 127.7 (2C), 128.3, 128.5 (2C), 139.0, 213.7; ESIMS (MeOH): 373.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{20}H_{30}O_5Na$ *m/z* 373.1991, found 373.2008; Analysis calcd. for $C_{20}H_{30}O_5$ (350.4): C 68.54, H 8.63; found C 68.26, H 8.52.



Chemical Formula: $C_{20}H_{30}O_5$
Exact Mass: 350,21

Aldol 17: Colorless oil; $[\alpha]_D^{20}$ = 1 (*c* 1.0, $CHCl_3$); IR (film): ν = 3433, 1702, 1453, 1150, 1098, 1027, 917, 738, 698 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.99 (s, 3H), 1.41 (s, 3H), 1.70 (ddd, *J* = 5.3, 9.1, 14.0 Hz, 1H), 1.87 (ddd, *J* = 6.2, 9.4, 14.0 Hz, 1H), 2.00-2.06 (m, 2H), 2.31 (td, *J* = 7.7, 15.4 Hz, 1H), 2.44-2.54 (m, 2H), 3.35 (s, 3H), 3.51-3.67 (m, 2H), 3.72 (dd, *J* = 3.6, 11.5 Hz, 1H) 4.01 (dd, *J* = 8.2, 11.5 Hz, 1H), 4.48 (s, 2H), 4.69 and 4.77 (ABquartet, *J* = 7.7 Hz, 2H), 7.28-7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 16.5, 18.9, 32.3, 36.9, 37.1, 46.3, 55.9, 59.2, 60.4, 67.2, 73.1, 79.1, 90.7, 127.6, 127.7 (2C), 128.4 (2C), 138.2, 213.6; ESIMS (MeOH): 373.2 ([*M* + Na]$^+$, 100); HRESIMS: calcd. for $C_{20}H_{30}O_5Na$ *m/z* 373.1991, found 373.1987; Analysis calcd. for $C_{20}H_{30}O_5$ (350.4): C 68.54, H 8.63; found C 68.26, H 8.52.

Elaboration of the south part: the two carbon homologation and formylolefination



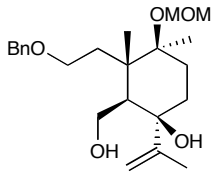
Chemical Formula: $C_{20}H_{30}O_5$
Exact Mass: 350,2093
Elemental Analysis:
C, 68.54; H, 8.63;

Chemical Formula: $C_{23}H_{36}O_5$
Exact Mass: 392.2563
Elemental Analysis:
C, 70.38; H, 9.24; O, 20.38

Chemical Formula: $C_{23}H_{34}O_5$
Exact Mass: 390.2406
Elemental Analysis:
C, 70.74; H, 8.78; O, 20.49

Chemical Formula: $C_{27}H_{40}O_6$
Exact Mass: 460.2825
Elemental Analysis:
C, 70.41; H, 8.75; O, 20.84

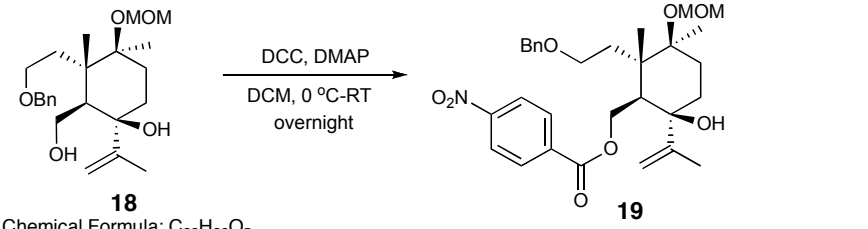
To a flame dried flask purged with Ar was added 2-bromopropene (1.8 mL, 16.30 mmol) dissolved in THF (20 mL). The flask was cooled to –78 °C and *t*-BuLi (19.1 mL, 32.60 mmol, 1.7M in pentane) was added slowly. The mixture was allowed to stir for 20 min. Aldol **17** (570 mg, 1.63 mmol) in THF (10 mL) (dried over 4Å molecular sieves) was slowly added to the (2-propenyl)lithium by syringe. The reaction was quenched with a saturated solution of NH_4Cl at –78 °C after 20 min. The mixture was allowed to warm to room temperature. The aqueous layer was extracted with Et_2O. The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash chromatography (heptane-EtOAc, 1:2) gave 160 mg of the diol **19** (25%), 340 mg of the starting aldol **17 (**60%) and 43 mg of enone **15** (7%).



Chemical Formula: $C_{23}H_{36}O_5$
Exact Mass: 392,26

Carbinol 18: Colorless oil; $[\alpha]_D^{20}$ = –42 (*c* 1.0, $CHCl_3$); IR (film): ν = 3390, 1452, 1375, 1143, 1090, 1033, 902, 736, 698 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.27 (s, 3H), 1.34-1.37 (m, 1H), 1.38 (s, 3H), 1.52 (t, *J* = 2.8 Hz, 1H), 1.61 (ddd, *J* = 3.2, 4.4, 12.9 Hz, 1H), 1.73-1.76 (m, 1H), 1.77 (s, 3H), 1.78-1.83 (m, 1H), 1.84-1.86 (ddd, *J* = 4.9, 9.7, 13.8 Hz, 1H), 2.19 (ddd, *J* = 4.0, 12.9, 13.9 Hz, 1H), 2.45 (bs, 1H), 3.32 (s, 3H), 3.36 (bs, 1H), 3.67 (ddd, *J* = 5.0, 9.6, 10.6 Hz, 1H), 3.76 (dt, *J* = 5.9, 9.9 Hz, 1H), 3.82 (dd, *J* = 3.2, 11.4 Hz, 1H), 4.02 (bd, *J* = 11.9 Hz, 1H), 4.49 and 4.52 (ABquartet, *J* = 11.4 Hz, 2H), 4.68 and 4.71 (ABquartet, *J* = 7.3 Hz, 2H), 4.93 (s, 1H), 5.23 (s, 1H), 7.27-7.34 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 17.1, 19.6, 19.7, 29.2, 34.2, 38.1, 43.7, 47.6, 55.4, 61.2, 68.2, 72.9, 78.4, 80.0, 90.2, 111.0, 127.5, 127.6 (2C), 128.3(2C), 138.6, 151.5; ESIMS (MeOH): 415.2 ([*M* + Na]$^+$, 100); HRESIMS: calcd. for $C_{23}H_{36}O_5Na$ *m/z* 415.2460, found 415.2442; Analysis calcd. for $C_{23}H_{36}O_5$ (392.4): C 70.38, H 9.24; found C 69.96, H 9.12.

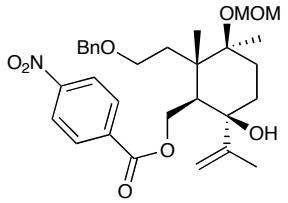
Preparation of the X-ray sample 19



18
Chemical Formula: $C_{23}H_{36}O_5$
Exact Mass: 392.2563
Elemental Analysis:
C, 70.38; H, 9.24; O, 20.38

19
Chemical Formula: $C_{30}H_{39}NO_8$
Exact Mass: 541.2676
Elemental Analysis: C, 66.52; H, 7.26; N, 2.59; O, 23.63

To a stirred solution of carbinol **18** (29 mg, 0.074 mmol) in dry CH_2Cl_2 was added *p*-nitro benzoic acid (32 mg, 0.192 mmol) and the mixture was cooled to 0 °C and DCC (39 mg, 0.192 mmol) was added. The reaction mixture was then left to stir at 25 °C overnight. The reaction mixture was diluted with CH_2Cl_2 and filtered on a celite pad. The filtrate was washed with 5% AcOH solution, worked up as usual and the crude purified by chromatography (heptane-EtOAc, 3:1) yielding the *p*-nitro benzoate **19** (40 mg, 99%). The white solid was crystallized from hexane-chloroform (10:1) at 25 °C.



Chemical Formula: $C_{30}H_{39}NO_8$
Exact Mass: 541,27

***p*-nitrobenzoyl ester 19:** White crystals; Mp: 104-106 °C; $[\alpha]_D^{20}$ = –10 (*c* 0.8, $CHCl_3$); IR (film): ν = 1722, 1527, 1351, 1280, 1109, 1034 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.33 (s, 3H), 1.40 (s, 3H), 1.38-1.42 (m, 1H), 1.71 (dt, *J* = 3.5, 13.2 Hz, 1H), 1.81 (s, 3H), 1.90-1.95 (m, 2H), 1.99 (dd, *J* = 3.8, 14.7 Hz, 1H), 2.05 (t, *J* = 4.8 Hz, 1H), 2.2 (ddd, *J* = 4.1, 12.9, 14.4 Hz, 1H), 3.37 (s, 3H), 3.65 (dt, *J* = 5.0, 9.9 Hz, 1H), 3.82 (dt, *J* = 6.5, 9.7 Hz, 1H), 4.45 (dd, *J* = 3.5, 12.1 Hz, 1H), 4.48 and 4.51 (ABquartet, *J* = 12.4 Hz, 2H), 4.70 and 4.72 (ABquartet, *J* = 4.2 Hz, 2H), 4.79 (d, *J* = 7.3 Hz, 1H), 4.84 (s, 1H), 5.11 (s, 1H), 7.28-7.33 (m, 5H), 8.14 (d, *J* = 8.9 Hz, 2H), 8.26 (d, *J* = 8.9 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 16.0, 19.8, 19.9, 29.0, 34.6, 38.5, 43.6, 46.6, 55.5, 64.6, 67.8, 72.8, 79.8, 90.3, 111.0, 123.5 (2C), 127.5 (2C), 128.3 (2C), 130.5 (2C), 135.7, 138.6, 150.4, 150.5, 164.5; ESIMS (MeOH): 564.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{30}H_{39}NO_8Na$ *m/z* 564.2573, found 564.2561.

***X-Ray Structure Analysis of* 19**

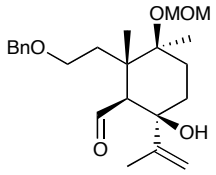
The following crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 680572.

Stick-type crystal with dimensions of 0.40 x 0.25 x 0.15 mm was used for data collection on a Nonius Kappa-CCD diffractometer, λ(Mo K_α) = 0.7107 Å, at 293(2)K. Empirical formula C_{30} H_{39} N O_8, M = 541.62. Orthorhombic system, space group P 2_1 2_1 2_1, Z = 4, a = 7.302 (2), b = 11.179 (3), c = 35.809 (6) Å, V = 2923.1 (12) $Å^3$, ρ_{calc}= 1.231 g cm^{-3}, F(000) = 1160, μ = 0.089 mm^{-1}. A total of 7781 intensity data was integrated using HKL2000 package up to θ = 18.9°, reduced to 1915 unique reflections (Friedel pairs averaged). The structure was solved by direct methods using SHELXS-97 and refined by full-matrix least-squares on F^2 (SHELXL-97), using $w=1/[2\sigma(F_o^2) + (0.0548P)^2 + 0.05929P]$, where $P=(F_o^2 + 2 F_c^2)/3$. All non-hydrogen atoms were refined anisotropically and all hydrogen atoms were positioned geometrically and treated as riding on their parent atoms with $U_{iso}(H)=1.2 U_{eq}$(parent atom) (or 1.5 for methyl group and hydroxyl group). Final R_1 =0.041, wR_2=0.094 for 357 parameters versus 1503 reflections with $I>2\sigma(I)$ and 0.41 < θ < 19.9° (corresponding R values based on

all (1912) reflections are 0.059 and 0.106, respectively). Goodness of fit = 1.027. Largest difference peak and hole are 0.218 and -0.159.

Swern Oxidation

To a solution of DMSO (1.1 ml, 15.0 mmol) in CH_2Cl_2 at –78 ^oC under argon was added $(COCl)_2$ (3.7 mL, 7.4 mmol, 2 M solution in CH_2Cl_2) and the reaction mixture was stirred for half an hour before adding the solution of **18** (980 mg, 2.5 mmol) in CH_2Cl_2. The reaction mixture was stirred at –78 ^oC for one hour and was quenched by the addition of Et_3N (3.3 mL, 25.0 mmol) at the same temperature. After allowing the reaction mixture to attain the room temperature, it was diluted by adding CH_2Cl_2, washed with 1N HCl followed by saturated aqueous solution of $NaHCO_3$ and worked up as usual. The crude was purified by chromatography (heptane-EtOAc, 3:1) affording 965 mg of the expected aldehyde **20** (99%).

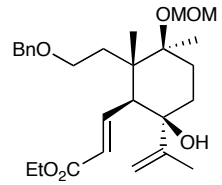


Chemical Formula: $C_{23}H_{34}O_5$
Exact Mass: 390,24

Aldehyde 20: Colorless oil; $[\alpha]_D^{20}$ = –32 (*c* 1.0, $CHCl_3$); IR (film): ν = 1712, 1453, 1377, 1110, 1034, 915 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.33 (s, 3H), 1.34 (s, 3H), 1.52-1.54 (m, 1H), 1.61-1.68 (m, 2H), 1.71-1.72 (m, 1H), 1.73 (s, 3H), 2.04-2.10 (m, 1H), 2.20 (dt, *J* = 4.0, 13.4 Hz, 1H), 2.80 (d, *J* = 2.8 Hz, 1H), 3.32 (s, 3H), 3.52 (ddd, *J* = 4.8, 9.3, 10.4 Hz, 1H), 3.71 (dt, *J* = 5.8, 9.7 Hz, 1H), 4.45 and 4.49 (ABquartet, *J* = 12.1 Hz, 2H), 4.69 and 4.72 (ABquartet, *J* = 7.6 Hz, 2H), 4.86 (s, 1H), 5.01 (s, 1H), 7.28-7.35 (m, 5H), 9.96 (d, *J* = 2.9 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 16.9, 19.5, 19.7, 29.3, 34.2, 38.4, 44.4, 55.5, 58.9, 67.3, 73.0, 76.0, 79.3, 90.4, 111.4, 127.6, 127.7 (2C), 128.4 (2C), 138.4, 150.3, 207.3; ESIMS (MeOH): 413.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{23}H_{34}O_5Na$ *m/z* 413.2304, found 413.2296.

The two-carbon homologation

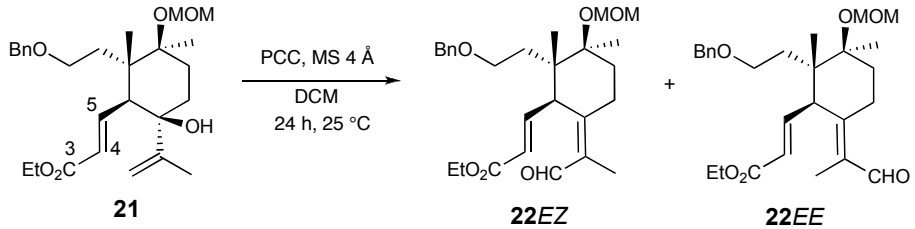
To a stirred solution of the aldehyde **20** (600 mg, 1.5 mmol) in ethanol (35 mL) was added at 0 ^oC (carbethoxymethylene)triphenylphosphorane (1.33 g, 3.8 mmol) and the reaction was stirred for 14 h at 25 ^oC. The suspension was evaporated to dryness and the residue directly passed to chromatography (heptane-EtOAc, 3:1) yielding 700 mg of the conjugated ester **21** (99%):



Chemical Formula: $C_{27}H_{40}O_6$
Exact Mass: 460,28

Colorless oil; $[\alpha]_D^{20} = -75$ (*c* 1.4, $CHCl_3$); IR (film): ν = 1714, 1644, 1452, 1371, 1263, 1033 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.28 (t, *J* = 7.4 Hz, 3H), 1.30 (s, 3H), 1.31 (s, 3H), 1.40-1.43 (m, 1H), 1.54 (ddd, *J* = 4.3, 11.1, 13.7 Hz, 1H), 1.64-1.70 (m, 2H), 1.68 (s, 3H), 1.88 (dt, *J* = 4.6, 14.4 Hz, 1H), 2.17-2.23 (m, 2H), 3.30 (s, 3H), 3.53 (ddd, *J* = 4.3, 9.6, 11.3 Hz, 1H), 3.72 (ddd, *J* = 5.9, 9.6, 11.0 Hz, 1H), 4.11-4.21 (m, 2H), 4.44 and 4.49 (ABquartet, *J* = 12.4 Hz, 2H), 4.65 and 4.72 (ABquartet, *J* = 7.3 Hz, 2H), 4.80 (s, 1H), 4.93 (s, 1H), 5.71 (d, *J* = 15.8 Hz, 1H), 6.97 (dd, *J* = 10.6, 15.7 Hz, 1H), 7.27-7.34 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 14.2, 15.8, 19.5, 29.2, 29.7, 34.4, 39.3, 43.4, 52.4, 55.5, 60.2, 67.7, 72.9, 79.5, 90.2, 111.0, 124.8, 127.4, 127.6, 127.7 (2C), 128.3 (2C), 138.7, 145.5, 149.9, 165.9; ESIMS (MeOH): 483.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{27}H_{40}O_6Na$ *m/z* 483.2723, found 483.2724; Analysis calcd. for $C_{27}H_{40}O_6$ (460.3): C 70.40, H 8.75; found C 69.64, H 8.82.

The Dauben-Michno-Babler rearrangement of the allylic alcohol 21



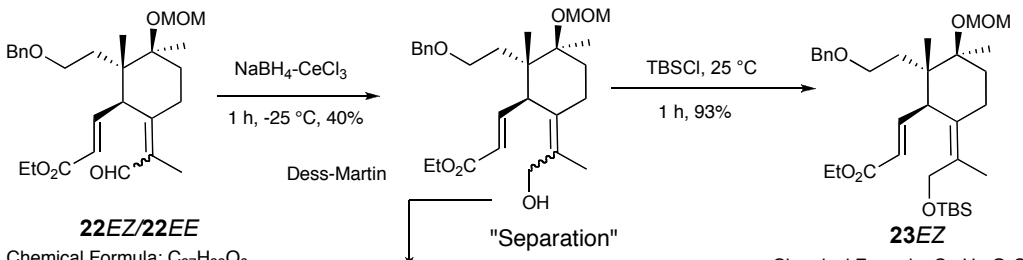
21

Chemical Formula: $C_{27}H_{40}O_6$
Exact Mass: 460,28
Elemental Analysis: C, 70.41; H, 8.75; O, 20.84

22EZ ***22EE***

Chemical Formula: $C_{27}H_{38}O_6$
Exact Mass: 458,27
Elemental Analysis: C, 70.71; H, 8.35; O, 20.93

To a stirring solution of **21** (500 mg, 1.08 mmol), in dry CH_2Cl_2 (10 mL), were added 400 mg of MS 4 Å and PCC (704 mg, 3.26 mmol). The reaction mixture was stirred at room temperature for 24 h, Et_2O was added and the supernatant was decanted. The operation was repeated five times and the combined organic phases were washed with NaOH (5%), HCl 1N, $NaHCO_3$ solution and worked up as usual to give 420 mg of an inseparable (6.4:1) mixture of ***22EZ***–***22EE*** and **21**. The crude was passed directly to the next step, a Luche reduction, allowing for chromatographic separation of the geometrical isomers. ***22EZ*** was prepared by re-oxidation only for characterization purposes.



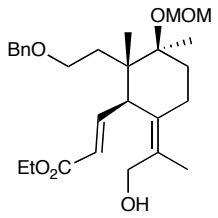
22*EZ*/22*EE*
Chemical Formula: $C_{27}H_{38}O_6$
Exact Mass: 458,27
Elemental Analysis: C, 70.71; H, 8.35; O, 20.93

22*EZ*

23*EZ*
Chemical Formula: $C_{33}H_{54}O_6Si$
Exact Mass: 574,37
Elemental Analysis: C, 68.95; H, 9.47; O, 16.70; Si, 4.89

Luche reduction

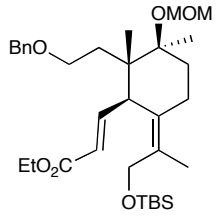
$CeCl_3.7H_2O$ (440 mg, 1.2 mmol) was added to a solution of **22*EZ*–22*EE*** (420 mg) in CH_2Cl_2 (6 mL) and EtOH (6 ml) at 0 °C. After 5 min, $NaBH_4$ (152 mg, 4.0 mmol) was added, the mixture was stirred for 15 min at –25 °C and then quenched by careful addition of brine followed by dilution with Et_2O. After being allowed to warm to room temperature, the organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic fractions were worked up as usual to afford after chromatography (heptane-EtOAc, 3:1 to 1:1) the allylic tertiary alcohol **21** (66 mg, 13% over two steps), the primary allylic alcohol *EZ* (200 mg, 40% over 2 steps) along with its geometrical isomer *EE* (34 mg, 7% over 2 steps).



Chemical Formula: $C_{27}H_{40}O_6$
Exact Mass: 460,28

Colorless oil; $[\alpha]_D^{20}$ = 103 (*c* 1.0, $CHCl_3$); IR (film): ν = 1713, 1637, 1368, 1273, 1153, 1104, 1028, 918, 699 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.02 (s, 3H), 1.09 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.37 (td, *J* = 5.2, 14.5 Hz, 1H), 1.49 (ddd, *J* = 5.1, 13.9, 14.6 Hz, 1H), 1.70 (ddd, *J* = 2.3, 4.4, 14.5 Hz, 1H), 1.82 (s, 3H), 1.89 (ddd, *J* = 6.2, 8.3, 14.4 Hz, 1H), 2.15 (dt, *J* = 2.5, 14.6 Hz, 1H), 2.36 (bd, *J* = 14.3 Hz, 1H), 3.36 (s, 3H), 3.54-3.56 (m, 2H), 3.59 (d, *J* = 12.2 Hz, 1H), 3.65 (d, *J* = 5.9 Hz, 1H), 4.14 (d, *J* = 12.2 Hz, 1H), 4.13-4.18 (m, 2H), 4.47 and 4.50 (ABquartet, *J* = 11.6 Hz, 2H), 4.63 and 4.68 (ABquartet, *J* = 7.5 Hz, 2H), 5.48 (dd, *J* = 1.7, 15.6 Hz, 1H), 7.31-7.38 (m, 5H), 7.42 (dd, *J* = 6.7, 15.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 14.3, 17.1, 17.4, 19.9, 21.8, 31.3, 34.0, 45.2, 48.7, 56.0, 59.9, 62.7, 67.6, 73.6,

79.8, 90.2, 117.6, 128.1, 128.4 (2C), 128.5 (2C), 131.4, 132.7, 137.2, 152.2, 167.4; ESIMS (MeOH): 483.2 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{27}H_{40}O_6Na$ *m/z* 483.2723, found 483.2708.

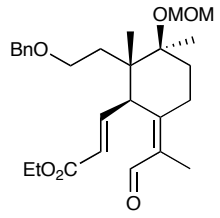


Chemical Formula: $C_{33}H_{54}O_6Si$
Exact Mass: 574,37

Silylether **23***EZ* was obtained after chromatography (heptane-EtOAc, 8:1) in 93% yield (470 mg, 0.82 mmol) under standard conditions (TBSCl-DMAP, CH_2Cl_2) as a colorless oil; $[\alpha]_D^{20}$ = 90 (*c* 1.0, $CHCl_3$); IR (film): ν = 1716, 1252, 1153, 1030, 836, 776 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.00 (s, 3H), 0.02 (s, 3H), 0.86 (s, 9H), 1.07 (s, 3H), 1.10 (s, 3H), 1.22-1.25 (m, 2H), 1.45-1.52 (m, 1H), 1.56 (dd, *J* = 4.8, 14.1 Hz, 1H), 1.67-1.71 (m, 1H), 1.72 (s, 3H), 1.79 (ddd, *J* = 7.1, 10.1, 153.7 Hz, 1H), 2.13 (tt, *J* = 3.4, 13.6 Hz, 1H), 2.35 (dd, *J* = 4.5, 14.2 Hz, 1H), 3.21 (d, *J* = 6.6 Hz, 1H), 3.35 (s, 3H), 3.45 (s, 2H), 3.47-3.50 (m, 2H), 4.00 (bs, 2H), 4.13 (dq, *J* = 1.9, 7.3 Hz, 1H), 4.45 (s, 2H), 4.62 and 4.67 (ABquartet, *J* = 7.5 Hz, 2H), 5.50 (d, *J* = 15.3 Hz, 1H), 7.27-7.31 (m, 5H), 7.39 (dd, *J* = 6.4, 15.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.4, 14.3, 15.3 15.7, 18.2, 18.3, 19.9, 21.9, 25.9, 31.3, 35.2, 44.7, 48.3, 56.0, 59.8, 62.7, 67.3, 73.2, 79.9, 90.2, 118.0, 127.6 (3C), 128.4 (2C), 130.5, 130.6, 138.3, 151.9, 167.4; ESIMS (MeOH): 597.3 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{33}H_{54}O_6SiNa$ *m/z* 597.3587, found 597.3610; Analysis calcd. for $C_{33}H_{54}O_6Si$ (574.9): C 68.95, H 9.47; found C 68.87, H 9.52.

Geometrically pure 22*EZ*

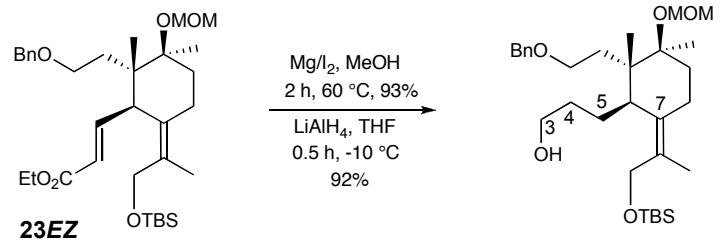
Following Luche reduction, the chromatographically separated *EZ* allylic alcohol (10 mg, 0.116 mmol) was re-oxidized with Dess-Martin periodinane (150 mg, 0.348 mmol) in CH_2Cl_2 (2 mL) and pyridine (0.1 mL) proceeding as above, to afford after silica gel column chromatography (heptane-EtOAc, 2:1) 8 mg (80%) of pure **22*EZ***.



Chemical Formula: $C_{27}H_{38}O_6$
Exact Mass: 458,27

22*EZ*: Colorless oil; $[\alpha]_D^{20}$ = 100 (*c* 1.0, $CHCl_3$); IR (film): ν = 1714, 1665, 1425, 1380, 1263, 1191, 1105, 1026 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.12 (s, 3H), 1.15 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.49 (ddd, *J* = 5.3, 6.2, 14.0 Hz, 1H), 1.65-1.71 (m, 1H), 1.72-1.78 (m, 1H), 1.82 (s, 3H), 1.87 (ddd, *J* = 2.6, 5.1, 14.6 Hz, 1H), 2.49 (dt, *J* = 5.3, 14.2 Hz, 1H), 2.57 (bd, *J* = 14.5 Hz, 1H), 3.39 (s, 3H), 3.49 (dd, *J* = 6.2, 7.4 Hz, 2H), 4.14 and 4.18 (ABquartet, *J* = 7.1 Hz, 2H), 4.30 (d, *J* = 6.6 Hz, 1H), 4.43 (s, 2H), 4.69 and 4.73 (ABquartet, *J* = 7.5 Hz, 2H), 5.50 (d, *J* = 15.7 Hz, 1H), 7.27-7.37 (m, 5H), 7.47 (dd, *J* = 6.6, 15.7 Hz, 1H), 9.92 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 11.0, 14.3, 18.0, 19.6, 24.3, 31.6, 35.0, 45.9, 47.0, 56.3, 60.1, 66.6, 73.4, 79.7, 90.4, 119.1, 127.8, 127.9 (2C), 128.5 (2C), 133.7, 137.8, 150.7, 157.3, 166.8, 190.4; ESIMS (MeOH): 481.2 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{27}H_{38}O_6Na$ *m/z* 481.2566, found 481.2562.

Selective reduction of the conjugated ester 23*EZ* and further reduction of the saturated ester thus obtained



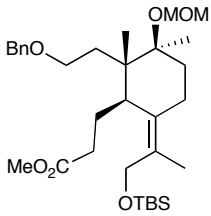
23*EZ*

Chemical Formula: $C_{33}H_{54}O_6Si$
Exact Mass: 574,37
Elemental Analysis: C, 68.95; H, 9.47; O, 16.70; Si, 4.89

Chemical Formula: $C_{31}H_{54}O_5Si$
Exact Mass: 534,3741
Elemental Analysis: C, 69.62; H, 10.18; O, 14.96; Si, 5.25

In a 2-neck flask containing magnesium turnings (930 mg, 38.70 mmol, 60.0 equiv) (activated, pre-dried in the oven for 6 h) was added dry, freshly distilled methanol (16 mL). To the mixture was then added iodine (49 mg, 0.19 mmol, 0.3 equiv) and the brown colored mixture was stirred at room temperature for 30 minutes as the color disappears and the solution becomes white. To the heterogeneous mixture was added the solution of **23*EZ*** (370 mg, 0.64 mmol, 1.0 equiv) in MeOH. The reaction mixture was then heated to 60 ^{o}C for two hours. The methanol was removed from the reaction mixture and the residue was neutralized with 1N HCl and the product was then extracted with ether. The organic layer was washed

with a saturated aqueous solution of $NaHCO_3$, worked up as usual and the crude was purified by column chromatography (heptane-EtOAc, 8:1) affording the corresponding saturated ester in 93% yield (335 mg) as a colorless oil.

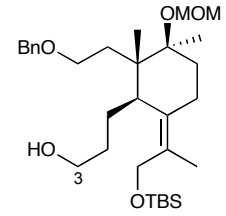


Chemical Formula: $C_{32}H_{54}O_6Si$
Exact Mass: 562,37

Saturated ester: $[\alpha]_D^{20}$ = 37 (*c* 1.0, $CHCl_3$); IR (film): ν = 1736, 1453, 1364, 1252, 1073, 1030, 836 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = –0.01 (s, 3H), 0.00 (s, 3H), 0.83 (s, 9H), 1.03 (s, 3H), 1.05 (s, 3H), 1.15 (t, *J* = 7.0 Hz, 1H), 1.38-1.43 (m, 1H), 1.46 (dd, *J* = 4.6, 14.4 Hz, 1H), 1.65 (s, 3H), 1.67-1.71 (m, 1H), 1.84-1.89 (m, 1H), 1.92-1.98 (m, 1H), 1.99-2.05 (m, 1H), 2.07-2.10 (m, 1H), 2.11-2.16 (m, 1H), 2.23 (ddd, *J* = 2.9, 4.2, 14.1 Hz, 1H), 2.33 (bd, *J* = 10.4 Hz, 1H), 3.34 (s, 3H), 3.37-3.47 (m, 2H), 3.56 (s, 3H), 3.87 and 4.02 (ABquartet, *J* = 10.3 Hz, 2H), 4.41 (s, 2H), 4.64 and 4.67 (ABquartet, *J* = 7.3 Hz, 2H), 7.23-2.29 (m, 5H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.3, –5.4, 15.9, 17.9, 18.4, 20.2, 21.4, 25.2, 25.9 (3C), 32.3, 33.5, 36.1, 44.1, 45.2, 51.2, 55.8, 62.7, 67.6, 73.1, 80.7, 90.2, 127.5, 127.6 (2C), 128.4 (2C), 128.9, 133.4, 138.5, 175.0; ESIMS (MeOH): 585.3 ([*M* + Na]$^+$, 100); HRESIMS: calcd. for $C_{32}H_{54}O_6SiNa$ *m/z* 585.3587, found 585.3590.

$LiAlH_4$ reduction

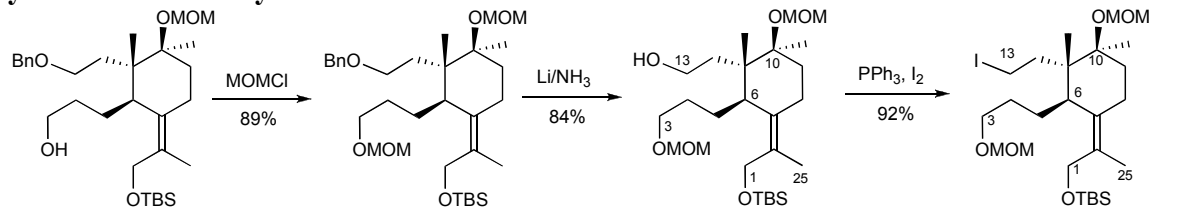
To a magnetically stirred suspension of $LiAlH_4$ (47 mg, 1.25 mmol, 2.0 equiv) in anhydrous THF (10 mL), cooled to –10 °C, was added dropwise a solution of the ester (350 mg, 0.62 mmol, 1.0 equiv) in anhydrous THF. After stirring at this temperature for 15 min (TLC monitoring) the mixture was diluted with wet Et_2O and treated with a small amount of saturated $NaHCO_3$ solution. The organic layer was filtered over a sintered glass funnel, and after silica gel chromatography (heptane-EtOAc, 2:1) the corresponding primary alcohol was obtained as a colorless oil (305 mg, 92%).



Chemical Formula: $C_{31}H_{54}O_5Si$
Exact Mass: 534,37

C3-free alcohol: $[\alpha]_D^{20}$ = 55 (*c* 1.5, $CHCl_3$); IR (film): ν = 1459, 1367, 1252, 1033, 836 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.05 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 1.06 (s, 3H), 1.10 (s, 3H), 1.21-1.28 (m, 2H), 1.39-1.48 (m, 2H), 1.52 (dd, *J* = 4.4, 14.5 Hz, 1H), 1.61-1.68 (m, 1H), 1.70-1.81 (m, 3H), 1.71 (s, 3H), 2.11 (dt, *J* = 4.0, 13.8 Hz, 1H), 2.29 (td, *J* = 3.2, 14.0 Hz, 1H), 2.37 (bd, *J* = 10.5 Hz, 1H), 3.38 (s, 3H), 3.44-3.53 (m, 2H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.98 and 4.13 (ABquartet, *J* = 11.1 Hz, 2H), 4.45 and 4.48 (ABquartet, *J* = 11.8 Hz, 2H), 4.68 and 4.72 (ABquartet, *J* = 7.7 Hz, 2H), 7.27-7.35 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.3, 15.7, 18.0, 18.4, 20.2, 21.4, 26.0 (3C), 26.1, 32.4, 32.7, 36.1, 44.1, 45.7, 55.6, 62.9, 63.6, 67.7, 73.1, 80.8, 90.2, 127.5, 127.6 (2C), 128.0 (2C), 128.3, 134.1, 138.5; ESIMS (MeOH): 557.3 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{31}H_{54}O_5Na$ *m/z* 557.3638, found 557.3613.

Synthesis of the alkyliodide 7



Chemical Formula: $C_{31}H_{54}O_5Si$
Exact Mass: 534,3741
Elemental Analysis:
C, 69.62; H, 10.18; O, 14.96;

Chemical Formula: $C_{33}H_{58}O_6Si$
Exact Mass: 578,4003
Elemental Analysis:
C, 68.47; H, 10.10;

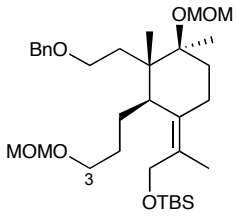
Chemical Formula: $C_{26}H_{52}O_6Si$
Exact Mass: 488,3533
Elemental Analysis:
C, 63.89; H, 10.72;

Chemical Formula: $C_{26}H_{51}IO_5Si$
Exact Mass: 598,2550
Elemental Analysis:
C, 52.16; H, 8.59;

MOM-protection

To an ice-cold solution of the alcohol thus obtained (310 mg, 0.73 mmol) in 4 mL of dry CH_2Cl_2, under argon, was added diisopropylethylamine (0.78 mL, 4.52 mmol) and chloromethyl methylether (0.33 mL, 4.37 mmol). The reaction mixture was allowed to warm and stirred at 25 °C for 16 h (while TLC-monitored), then quenched with water. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layers were washed with dilute HCl, a saturated aqueous solution of $NaHCO_3$, worked up as usual and purified by column

chromatography (heptane-EtOAc, 9:1) to give 303 mg (89%) of C3-OMOM protected derivative**.**

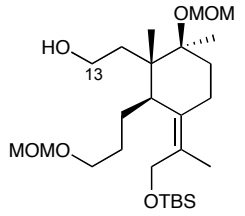


Chemical Formula: $C_{33}H_{58}O_6Si$
Exact Mass: 578,40

Colorless oil; $[\alpha]_D^{20}$ = 53 (*c* 1.0, $CHCl_3$); IR (film): ν = 2927, 1453, 1367, 1257, 1149, 1032, 918, 835 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.04 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.06 (s, 3H), 1.10 (s, 3H), 1.17-1.31 (m, 1H), 1.42-1.49 (m, 2H), 1.52 (dd, *J* = 4.1, 14.2 Hz, 1H), 1.63-1.69 (m, 1H), 1.71 (s, 3H), 1.71-1.81 (m, 2H), 2.12 (dt, *J* = 4.8, 13.8 Hz, 1H), 2.29 (bd, *J* = 14.2 Hz, 1H), 2.35 (bd, *J* = 11.2 Hz, 1H), 3.34 (s, 3H), 3.38 (s, 3H), 3.42-3.52 (m, 4H), 4.03 and 4.08 (ABquartet, *J* = 11.2 Hz, 2H), 4.45 and 4.48 (ABquartet, *J* = 11.7 Hz, 2H), 4.59 (s, 3H), 4.67 and 4.72 (ABquartet, *J* = 6.8 Hz, 2H), 7.27-7.35 (m, 5H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.3, 15.7, 18.0, 18.4, 20.2, 21.4, 26.0 (3C), 26.7, 29.5, 32.4, 36.2, 44.1, 45.8, 55.0, 55.7, 62.8, 67.7, 68.5, 73.1, 80.8, 90.2, 96.3, 127.5, 127.6 (2C), 128.1 (2C), 128.3, 133.9, 138.6; ESIMS (MeOH): 601.3 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{33}H_{58}O_6SiNa$ *m/z* 601.3900, found 601.3914; Analysis calcd. for $C_{33}H_{58}O_6Si$ (488.3): C 68.47, H 10.10; found C 68.20, H 10.16.

Debenzylation

To a stirred solution of the benzyl ether (278 mg, 0.48 mmol) in liquid ammonia (15 mL) and THF (10 mL) in the presence of *t*-BuOH (0.48mL) lithium metal (34 mg, 4.8 mmol, 10.0 equiv) was added portionwise at –78 °C. The mixture was stirred for 10 min (blue color). Ammonia was evaporated while technical Et_2O was added periodically along with solid NH_4Cl. Evaporation to dryness, dilution with ether and usual work up, afforded after chromatography (heptane-EtOAc, 3:1) the required debenzylated compound in 84% yield (197 mg) as a colorless oil.

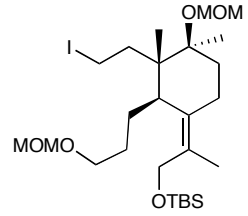


Chemical Formula: $C_{26}H_{52}O_6Si$
Exact Mass: 488,35

C13-free alcohol: $[\alpha]_D^{20}$ = 91 (*c* 1.0, $CHCl_3$); IR (film): ν = 1470, 1256, 1151, 1109, 1033, 918, 836 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.09 (s, 3H), 0.10 (s, 3H), 0.91 (s, 9H), 1.04 (s, 3H), 1.09 (s, 3H), 1.17-1.26 (m, 1H), 1.32-1.45 (m, 2H), 1.51 (dt, *J* = 4.4, 14.2 Hz, 1H), 1.62-1.75 (m, 3H), 1.73 (s, 3H), 1.78-1.86 (m, 2H), 2.12 (bt, *J* = 14.0 Hz, 1H), 2.29 (ddd, *J* = 2.9, 3.9, 13.6 Hz, 1H), 2.72 (bd, *J* = 11.1 Hz, 1H), 3.34 (s, 3H), 3.37 (s, 3H), 3.45 (t, *J* = 6.8 Hz, 2H), 3.61 (ddd, *J* = 5.8, 8.0, 10.7 Hz, 1H), 3.70 (ddd, *J* = 6.5, 8.4, 10.7 Hz, 1H), 3.82 (d, *J* = 10.9 Hz, 1H), 4.43 (d, *J* = 10.9 Hz, 1H), 4.59 (s, 2H), 4.67 and 4.71 (ABquartet, *J* = 7.4 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.3, –5.2, 16.2, 17.4, 18.5, 20.2, 21.3, 26.0 (3C), 26.3, 29.5, 32.3, 39.1, 44.3, 45.5, 55.0, 55.7, 59.9, 63.4, 68.5, 80.8, 90.1, 96.4, 127.4, 135.8; ESIMS (MeOH): 511.3 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{26}H_{52}O_6SiNa$ *m/z* 511.3431, found 511.3442.

The right-half segment, Iodide 7Z

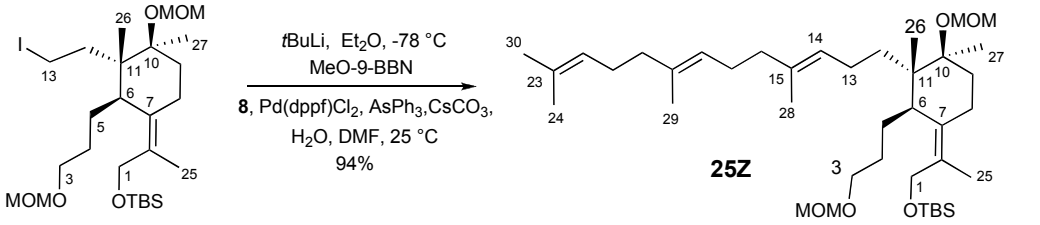
To a solution of alcohol (87 mg, 0.18 mmol), triphenylphosphine (186 mg, 0.71 mmol), and imidazole (46 mg, 0.71 mmol) in toluene (2 mL) at 25 °C was added iodine (135 mg, 0.53 mmol). After stirring for 1 h the solution was poured into a 1 M aqueous $Na_2S_2O_3$ solution (100 mL) and extracted with Et_2O (3 x 200 mL). The combined organic extracts were washed with brine (100 mL), dried, filtered, and concentrated. The material was then dissolved in CH_2Cl_2, silica gel was added to the solution, and the resulting slurry was concentrated to dryness. The product was passed through a short plug of silica (hexane-EtOAc, 95:5) to yield 97 mg (92%) of **7Z** as a colorless oil:



Chemical Formula: $C_{26}H_{51}IO_5Si$
Exact Mass: 598,26

$[\alpha]_D^{20}$ = 21 (*c* 1.2, $CHCl_3$); IR (film): ν = 1470, 1552, 1151, 1110, 1034, 836, 774 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.09 (s, 3H), 0.10 (s, 3H), 0.92 (s, 9H), 1.04 (s, 3H), 1.08 (s, 3H), 1.20 (qdd, *J* = 6.0, 12.3, 12.9 Hz, 1H), 1.41 (dtdd, *J* = 4.9, 6.5, 11.5, 13.2 Hz, 1H), 1.51 (dt, *J* = 4.4, 14.3 Hz, 1H), 1.59 (bs, 1H), 1.62-1.65 (m, 1H), 1.73 (s, 3H), 1.74-1.81 (m, 2H), 2.06 (dd, *J* = 5.2, 12.3 Hz, 1H), 2.11 (dd, *J* = 4.7, 12.9, 1H), 2.30 (ddd, *J* = 2.7, 4.0, 14.0 Hz, 1H), 2.40 (bd, *J* = 11.2 Hz, 1H), 3.12 (ddd, *J* = 4.1, 8.6, 12.8 Hz, 1H), 3.21 (ddd, *J* = 5.5, 8.6, 12.4 Hz, 1H), 3.34 (s, 3H), 3.37 (s, 3H), 3.41-3.49 (m, 2H), 3.98 and 4.21 (ABquartet, *J* = 11.2 Hz, 2H), 4.59 (s, 2H), 4.66 and 4.71 (ABquartet, *J* = 6.8 Hz, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.3, –5.2, 1.6, 15.8, 17.5, 18.5, 20.1, 21.2, 26.2 (3C), 26.5, 29.4, 32.4, 42.9, 44.3, 47.6, 55.0, 55.7, 62.8, 68.4, 80.2, 90.1, 96.4, 128.5, 133.4; ESIMS (MeOH): 621.2 ([*M* + Na]$^+$, 100); HRESIMS: calcd. for $C_{26}H_{51}O_5SiINa$ *m/z* 621.2448, found 621.2435.

Segment linking: Synthesis of iridal's core structure



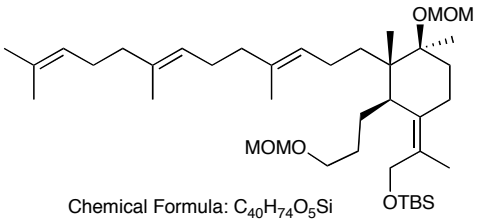
7*Z*
Chemical Formula: $C_{26}H_{51}IO_5Si$
Exact Mass: 598,2550
Elemental Analysis: C, 52.16; H, 8.59;

Chemical Formula: $C_{39}H_{72}O_5Si$
Exact Mass: 648,5149
Elemental Analysis: C, 72.17; H, 11.18;

The Marshall protocol[2] was used: To a stirring solution of alkyl iodide **7*Z*** (90 mg, 0.15 mmol, 1.0 equiv) in Et_2O (2 mL) was added β-MeO-9-BBN (0.6 mL, 1.0 M solution in hexane, 4.0 equiv) and the mixture was cooled to –78 °C. To this solution was rapidly added *tert*-butyllithium (0.31 mL, 1.7 M solution in pentane, 3.5 equiv). The mixture was stirred for 5 min, then THF (2.0 mL) was added and the reaction mixture was warmed to 25 °C for 1 h. In a separate flask, vinyl iodide **8** (38 mg, 0.12 mmol, 1.0 equiv), prepared in two steps from geranyl acetone using standard Negishi conditions, was dissolved in DMF (2 mL). To this solution was sequentially added $Pd(dppf)Cl_2$ (5 mg, 0.006 mmol, 0.050 equiv), $AsPh_3$ (5.5 mg, 0.018 mmol, 0.150 equiv), $CsCO_3$ (156 mg, 0.48 mmol, 4.0 equiv) and water (0.05 mL, 2.85 mmol, 24 equiv). The ethereal mixture of the alkylboronate was cannulated into the DMF solution and stirred overnight. The reaction mixture was then diluted with water and extracted

[2] Marshall, J.; Schaaf, G. M. *J. Org. Chem*. **2003**, *68*, 7428–7432.

with Et_2O. The organic extracts were washed with brine, worked up as usual and the residue was purified by column chromatography on silica gel (heptane-EtOAc, 5:1) to give 75 mg of the desired product **25*Z*** (94%).

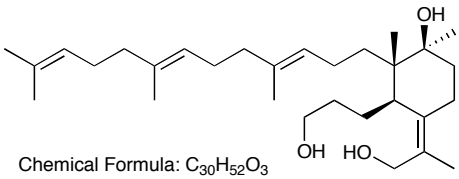


Chemical Formula: $C_{40}H_{74}O_5Si$
Exact Mass: 662,53

25*Z*: Colorless oil; $[\alpha]_D^{20}$ = 26 (*c* 1.5, $CHCl_3$); IR (film): ν = 1446, 1381, 1250, 1150, 1109, 1033, 919, 835 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.89 (s, 9H), 1.03 (s, 3H), 1.08 (s, 3H), 1.20-1.29 (m, 1H), 1.38 (ddd, *J* = 5.8, 11.9, 13.5 Hz, 1H), 1.43-1.49 (m, 1H), 1.53 (dd, *J* = 4.4, 14.5 Hz, 1H), 1.58 (s, 3H), 1.59 (s, 3H), 1.60 (s, 3H), 1.67 (bs, 5H), 1.71 (s, 3H), 1.72-1.84 (m, 3H), 1.87-1.91 (m, 1H), 1.93-1.98 (m, 4H), 2.03-2.08 (m, 4H), 2.13 (dd, *J* = 3.2, 13.8 Hz, 1H), 2.28 (d, *J* = 13.6 Hz, 1H), 2.47 (d, *J* = 10.9 Hz, 1H), 3.35 (s, 3H), 3.38 (s, 3H), 3.43-3.51 (m, 2H), 4.12 (s, 2H), 4.60 (s, 2H), 4.67 and 4.72 (ABquartet, *J* = 7.5 Hz, 2H), 5.04 (t, *J* = 6.9 Hz, 1H), 5.07-5.11 (m, 2H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.45, –5.4, 15.6, 16.0, 17.7, 18.1, 18.4, 20.2, 21.5, 22.6, 25.7, 26.0 (3C), 26.7, 26.8, 29.6, 32.4, 36.7, 39.7 (2C), 44.5, 44.6, 55.0, 55.6, 63.0, 68.6, 81.1, 90.1, 96.3, 124.3, 124.4, 125.3, 127.7, 128.6, 131.2, 133.7, 134.1, 134.4, 134.8; ESIMS (MeOH): 685.5 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{40}H_{74}O_5SiNa$ *m/z* 685.5216, found 685.5203.

Synthesis of the triol

To a solution of fully protected triol **25Z** (24 mg, 0.036 mmol) in THF (1 mL) was added HCl (0.5 mL 6M solution) and stirred at 25 °C for 36 h. The reaction was quenched with solid $NaHCO_3$ and extracted five times with Et_2O. The organic extracts were dried over Na_2SO_4, evaporated at reduced pressure and the residue purified by chromatography (heptane-EtOAc, 1:2) to give 10 mg (60%) of triol along with 8 mg of a less polar complex mixture of compounds.

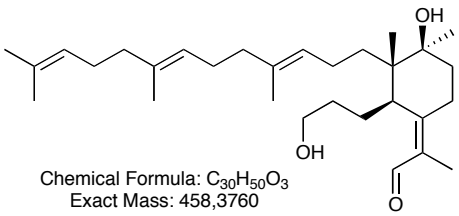


Chemical Formula: $C_{30}H_{52}O_3$
Exact Mass: 460,39

Colorless oil; $[\alpha]_D^{20}$ = 27 (*c* 0.75, $CHCl_3$); IR (film): ν = 3383, 2969, 1381, 1260, 1090, 1025 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.01 (s, 3H), 1.11 (s, 3H), 1.24-1.30 (m, 2H), 1.33-1.46 (m, 2H), 1.51 (ddd, *J* = 2.8, 3.7, 13.6 Hz, 1H), 1.57-1.62 (m, 1H), 1.59 (s, 3H), 1.60 (s, 6H), 1.68 (s, 3H), 1.69-1.75 (m, 1H), 1.81 (s, 3H), 1.85-1.92 (m, 3H), 1.95-1.98 (m, 4H), 2.03-2.08 (m, 4H), 2.26 (dt, *J* =3.8, 14.3 Hz, 1H), 2.34 (bd, *J* = 13.6 Hz, 1H), 2.57 (bd, *J* = 11.1 Hz, 1H), 3.60 (t, *J* = 6.7 Hz, 2H), 4.13 and 4.16 (ABquartet, *J* = 11.4 Hz, 2H), 5.0 (t, *J* = 6.6 Hz, 1H), 5.09 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 15.9, 16.0, 16.1, 17.7, 17.8, 21.3, 22.6, 25.7, 25.9, 26.5, 26.6, 26.8, 31.2, 32.6, 36.9, 39.7 (2C), 43.9, 44.3, 63.2, 63.4, 75.4, 124.1, 124.4, 124.7, 127.8, 131.2, 135.0, 135.3, 136.1; ESIMS (MeOH): 483.3 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{30}H_{52}O_3Na$ *m/z* 483.3814, found 483.3804.

Allylic oxidation

To a solution of triol (13 mg, 0.028 mmol) in CH_2Cl_2 (1 mL) was added 3,5-dimethylpyrazole (18 mg, 0.186 mmol), the mixture was cooled to 0 °C and PCC (36 mg, 0.168 mmol) was added. After 10 min the reaction mixture was diluted with Et_2O, washed with HCl 1N twice and then three times with brine and water. The organic phase was dried over Na_2SO_4 the solvent evaporated and the crude subjected to column chromatography (heptane-EtOAc, 1:1) to give Iridal **1** (11 mg, 88%) along with a small amount of the corresponding dialdehyde (1 mg, 7%).

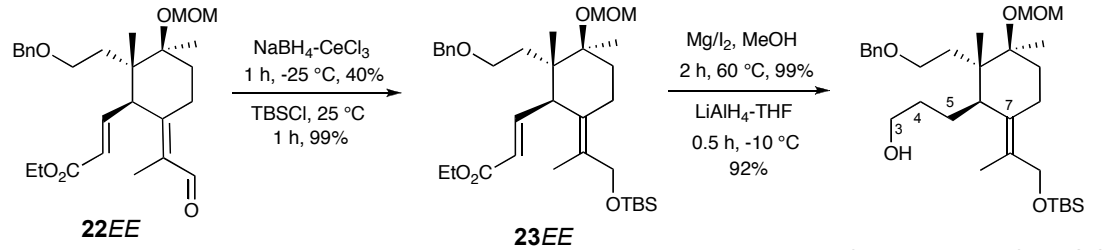


Chemical Formula: $C_{30}H_{50}O_3$
Exact Mass: 458,3760

1: Colorless oil; $[\alpha]_D^{20}$ = 33 (*c* 0.7, $CHCl_3$); IR (film): ν = 3411, 1650, 1609, 1445, 1375, 1093, 1053, 905 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.09 (s, 3H), 1.06-1.45 (m, 1H), 1.16 (s, 3H), 1.24-1.33 (m, 2H), 1.37-1.43 (m, 1H), 1.52 (s, 3H), 1.58 (s, 3H), 1.60 (s, 3H), 1.64-1.69 (m, 1H), 1.68 (s, 3H), 1.75-1.81 (m, 1H), 1.82-1.92 (m, 4H), 1.84 (s, 3H), 1.92-1.97 (m, 4H), 2.01-2.06 (m, 4H), 2.53 (bd, *J* = 13.9 Hz, 1H), 2.60 (dt, *J* = 5.3, 14.0 Hz, 1H), 3.32 (bd, *J* = 11.1 Hz, 1H), 3.61 (t, *J* = 6.4 Hz, 2H), 4.96 (t, *J* = 7.1 Hz, 1H), 5.08 (dt, *J* = 6.5, 7.8 Hz,

2H), 10.18 (s, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 10.9, 15.9, 16.0. 17.7, 17.9, 22.1, 23.8, 25.7, 26.3, 26.5, 26.6, 26.8, 32.7, 37.0, 37.2, 39.6, 39.7, 43.4, 44.7, 63.1, 75.1, 123.9, 124.1, 124.4, 131.2, 133.2, 135.0, 135.5, 162.7, 190.0; ESIMS (MeOH): 481.3 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{30}H_{50}O_3Na$ *m/z* 481.3658, found 481.3658.

Route to the geometrical isomer of Iridal



22*EE*

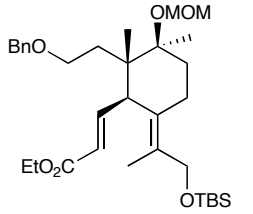
Chemical Formula: $C_{27}H_{38}O_6$
Exact Mass: 458,27
Elemental Analysis: C, 70.71; H, 8.35; O, 20.93

23*EE*

Chemical Formula: $C_{33}H_{54}O_6Si$
Exact Mass: 574,37
Elemental Analysis: C, 68.95; H, 9.47; O, 16.70; Si, 4.89

Chemical Formula: $C_{31}H_{54}O_5Si$
Exact Mass: 534,37
Elemental Analysis: C, 69.62; H, 10.18; O, 14.96; Si, 5.25

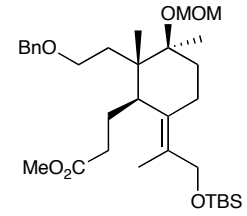
TBS protection



Chemical Formula: $C_{33}H_{54}O_6Si$
Exact Mass: 574,37

Proceedeing as above on a 220 mg (0.48 mmol) scale, the silyl ether was obtained after chromatography (heptane-EtOAc, 8:1) in 90% yield (250 mg, 0.43 mmol) as a yellow oil: $[\alpha]_D^{20}$ = 112 (*c* 1.0, $CHCl_3$); IR (film): ν = 1715, 1641, 1432, 1382, 1256, 1190, 1030, 837 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.05 (s, 6H), 0.90 (s, 9H), 1.06 (s, 3H), 1.13 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.50-1.56 (m, 2H), 1.58 (s, 3H), 1.70 (ddd, *J* = 2.2, 5.0, 14.3 Hz, 1H), 1.79 (ddd, *J* = 6.0, 9.0, 13.3 Hz, 1H), 2.14 (bt, *J* = 14.1 Hz, 1H), 2.42 (bd, *J* = 14.5 Hz, 1H), 3.16 (d, *J* = 6.8 Hz, 1H), 3.37 (s, 3H), 3.45-3.54 (m, 2H), 4.12 and 4.22 (ABquartet, *J* = 11.5 Hz, 2H), 4.15 (q, *J* = 6.8 Hz, 2H), 4.46 and 4.49 (ABquartet, *J* = 11.2 Hz, 2H), 4.66 and 4.69 (ABquartet, *J* = 6.6 Hz, 2H), 5.53 (d, *J* = 15.6 Hz, 1H), 7.27-2.34 (m, 5H), 7.36 (dd, *J* = 6.4, 15.7 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.2, 14.3, 15.4, 18.2, 18.3, 19.9, 21.3, 25.9, 31.6, 35.2, 44.8, 48.9, 56.0, 59.8, 63.2, 67.5, 73.2, 79.9, 90.2, 117.9, 127.6, 127.7, 128.4, 130.8, 130.9, 138.2, 151.1, 167.3; ESIMS (MeOH): 597.4 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{33}H_{54}O_6SiNa$ *m/z* 597.3587, found 597.3597.

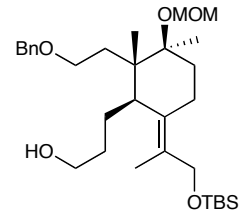
Selective reduction of the conjugated ester



Chemical Formula: $C_{32}H_{54}O_6Si$
Exact Mass: 562,37

Proceedeing as above on a 157 mg (0.27 mmol) scale, the saturated ester was obtained after chromatography (heptane-EtOAc, 5:1) in 95% yield (150 mg, 0.26 mmol) as a colorless oil: $[\alpha]_D^{20}$ = 54 (*c* 1.0, $CHCl_3$); IR (film): ν = 1737, 1456, 1363, 1253, 1164, 1075, 1031, 836, 776 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.05 (s, 6H), 0.89 (s, 9H), 1.08 (s, 3H), 1.11 (s, 3H), 1.43-1.52 (m, 2H), 1.59 (s, 3H), 1.71-1.75 (m, 2H), 1.90-1.97 (m, 1H), 2.00-2.05 (m, 1H), 2.07-2.12 (m, 1H), 2.12-2.21 (m, 2H), 2.32-2.39 (m, 2H), 3.39 (s, 3H), 3.46-3.54 (m, 2H), 3.62 (s, 3H), 4.16 (s, 2H), 4.45 and 4.49 (ABquartet, *J* = 12.1 Hz, 2H), 4.69 and 4.72 (ABquartet, *J* = 7.1 Hz, 2H), 7.28-7.34 (m, 5H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.2 (2C), 16.4, 17.8, 18.3, 20.1, 20.8, 25.5, 25.9 (3C), 32.8, 33.1, 35.9, 44.2, 45.3, 51.3, 55.7, 63.4, 68.0, 73.2, 80.8, 90.2, 127.5, 127.7 (2C), 128.3 (2C), 129.6, 133.5, 138.4, 174.8; ESIMS (MeOH): 585.3 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{32}H_{54}O_6SiNa$ *m/z* 585.3587, found 585.3584.

$LiAlH_4$ reduction

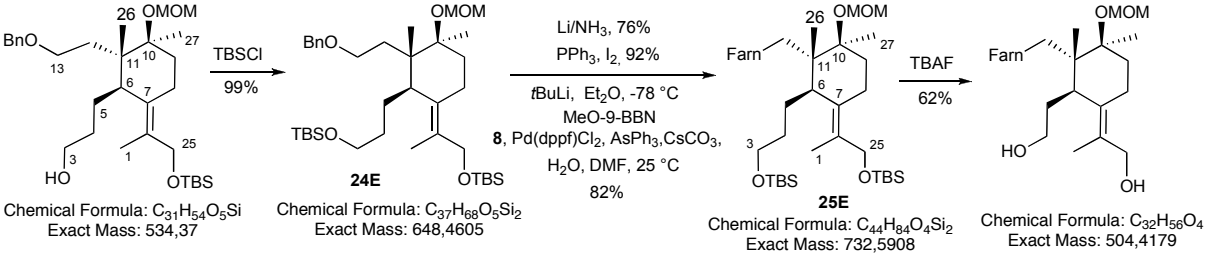


Chemical Formula: $C_{31}H_{54}O_5Si$
Exact Mass: 534,37

Proceedeing as above on a 140 mg scale (0.25 mmol), the primary alcohol was obtained after chromatography (heptane-EtOAc, 2:1) in 92% yield (126 mg, 0.23 mmol) as a colorless oil: $[\alpha]_D^{20}$ = 59 (*c* 0.85, $CHCl_3$); IR (film): ν = 1456, 1392, 1215, 1032, 836, 775 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.05 (s, 6H), 0.89 (s, 9H), 1.05 (s, 3H), 1.10 (s, 3H), 1.27 (ddt, *J* = 5.5, 11.8, 12.4 Hz, 1H), 1.42-1.51 (m, 3H), 1.63 (bs, 3H), 1.64-1.68 (m, 1H), 1.69-1.76 (m, 2H), 1.82 (dq, *J* = 4.1, 12.2 Hz, 1H), 2.10 (bt, *J* = 13.8 Hz, 1H), 2.33-2.37 (m, 2H), 3.38 (s, 3H), 3.51 (dd, *J* = 6.8, 8.2 Hz, 2H), 3.57 (t, *J* = 6.6 Hz, 2H), 4.15 and 4.18 (ABquartet, *J* = 11.3 Hz, 2H), 4.45 and 4.50 (ABquartet, *J* = 12.1 Hz, 2H), 4.68 and 4.71 (ABquartet,

J = 6.8 Hz, 2H), 7.27-7.35 (m, 5H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.2 (2C), 16.6, 18.0, 18.3, 20.2, 20.9, 25.9 (3C), 26.4, 32.4, 32.8, 36.0, 44.2, 45.9, 55.6, 63.5, 63.6, 68.0, 73.2, 80.8, 90.2, 127.5, 127.7 (2C), 128.3 (2C), 128.7, 134.3, 138.5; ESIMS (MeOH): 557.3 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{31}H_{54}O_5SiNa$ *m/z* 557.3638, found 557.3626.

Completion of the synthesis



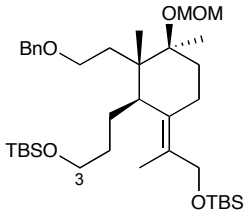
Chemical Formula: $C_{31}H_{54}O_5Si$
Exact Mass: 534,37

Chemical Formula: $C_{37}H_{68}O_5Si_2$
Exact Mass: 648,4605

Chemical Formula: $C_{44}H_{84}O_4Si_2$
Exact Mass: 732,5908

Chemical Formula: $C_{32}H_{56}O_4$
Exact Mass: 504,4179

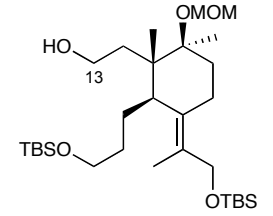
TBS protection at C-3



Chemical Formula: $C_{37}H_{68}O_5Si_2$
Exact Mass: 648,4605

Proceeding as above on a 151 mg scale (0.28 mmol), the silyl ether was obtained after chromatography (heptane-EtOAc, 12:1) in 99% yield (183 mg, 0.28 mmol) as a colorless oil: $[\alpha]_D^{20}$ = 47 (*c* 1.3, $CHCl_3$); IR (film): ν = 1468, 1383, 1249, 1102, 1037, 835, 772 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.03 (s, 6H), 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 0.89 (s, 9H), 1.04 (s, 3H), 1.10 (s, 3H), 1.20 (qt, J = 5.8, 12.7 Hz, 1H), 1.36-1.43 (m, 1H), 1.44-1.51 (m, 2H), 1.63 (bs, 3H), 1.64-1.68 (m, 1H), 1.68-1.83 (m, 3H), 2.10 (bt, J = 13.8 Hz, 1H), 2.33 (bd, J = 13.0 Hz, 2H), 3.37 (s, 3H), 3.50-3.56 (m, 4H), 4.16 (s, 2H), 4.46 and 4.50 (ABquartet, J = 12.0 Hz, 2H), 4.66 and 4.73 (ABquartet, J = 7.1 Hz, 2H), 7.27-7.35 (m, 5H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.2 (2C), –5.1 (2C), 16.6, 18.0, 18.3, 18.4, 20.2, 20.8, 25.9 (3C), 26.0 (3C), 26.8, 32.4, 32.9, 36.0, 44.2, 46.0, 55.6, 63.5, 63.9, 68.1, 73.2, 80.9, 90.1, 127.5, 127.7 (2C), 128.3 (2C), 128.5, 134.4, 138.5; ESIMS (MeOH): 671.4 ([M + Na]$^+$, 100); HRESIMS: calcd. for $C_{37}H_{68}O_5Si_2Na$ *m/z* 671.4503, found 671.4487.

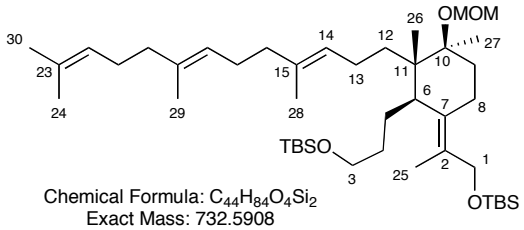
Debenzylation



Chemical Formula: $C_{30}H_{62}O_5Si_2$
Exact Mass: 558,4136

Proceedeing as above on a 111 mg scale (0.17 mmol), the C13-free alcohol (chromatography heptane-EtOAc 3:1) was obtained in 76% yield (72 mg, 0.13 mmol) as a white solid: Mp: 62-64 °C; $[\alpha]_D^{20}$ = 58 (*c* 0.7, $CHCl_3$); IR (film): ν = 1470, 1255, 1104, 1033, 835, 776 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.03 (s, 6H), 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 0.89 (s, 9H), 1.05 (s, 3H), 1.11 (s, 3H), 1.22 (qt, *J* = 6.0, 12.8 Hz, 1H), 1.38-1.46 (m, 2H), 1.48 (dd, *J* = 4.0, 14.0 Hz, 1H), 1.62-1.69 (m, 2H), 1.71 (s, 3H), 1.72-1.76 (m, 1H), 1.79 (dddd, *J* = 4.3, 11.2, 12.2, 13.1 Hz, 1H), 2.11 (dd, *J* = 13.5, 14.2 Hz, 1H), 2.32-2.36 (m, 2H), 3.38 (s, 3H), 3.55 (dt, *J* = 2.7, 6.4 Hz, 2H), 3.69 (td, *J* = 5.8, 9.3 Hz, 2H), 4.15 and 4.20 (ABquartet, *J* = 11.6 Hz, 2H), 4.67 and 4.73 (ABquartet, *J* = 7.1 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.3, –5.2 (2C), –5.1, 16.7, 18.0, 18.3, 18.4, 20.3, 20.8, 25.9 (3C), 26.0 (3C), 26.8, 32.4, 32.9, 39.5, 44.4, 46.1, 55.6, 60.4, 63.5, 63.8, 80.7, 90.1, 128.5, 134.7; ESIMS (MeOH): 581.4 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{30}H_{62}O_5Si_2Na$ *m/z* 581.4034, found 581.4036.

The corresponding iodide, to be used in the sp^3-sp^2 coupling was prepared and immediately taken to the next step without characterization.

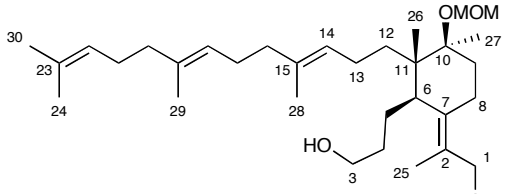


Chemical Formula: $C_{44}H_{84}O_4Si_2$
Exact Mass: 732.5908

The Marshall protocol for the Suzuki-Miyaura coupling employed for the Iridal synthesis was applied on a 44 mg scale (0.066 mmol), yielding the desired adduct **25*E*** (40 mg, 0.054 mmol, 82%) as a yellow oil; $[\alpha]_D^{20}$ = 15 (*c* 1.5, $CHCl_3$); IR (film): ν = 1472, 1381, 1148, 1100, 1035, 839, 770 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 0.03 (s, 6H), 0.04 (s, 6H), 0.89 (bs, 18H), 1.03 (s, 3H), 1.04-1.08 (m, 1H), 1.09 (s, 3H), 1.23-1.28 (m, 1H), 1.32-1.39 (m, 1H), 1.41-1.45 (m, 1H), 1.46-1.52 (m, 1H), 1.59 (bs, 6H), 1.60 (s, 3H), 1.68 (s, 3H), 1.69-1.71 (m, 1H), 1.72 (s, 3H), 1.78-1.81 (m, 1H), 1.89-1.98 (m, 7H), 2.04-2.13 (m, 5H), 2.33 (bd, , *J* = 13.3 Hz,

1H), 2.48 (bd, *J* = 12.1 Hz, 1H), 3.38 (s, 3H), 3.56 (t, *J* = 6.5 Hz, 2H), 4.12 and 4.23 (ABquartet, *J* = 12.0 Hz, 2H), 4.67 and 4.74 (ABquartet, *J* = 7.0 Hz, 2H), 5.02 (t, *J* = 6.9 Hz, 1H), 5.07-5.11 (m, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = –5.2 (2C), –5.1 (2C), 16.0, 16.1, 16.8, 17.7, 18.0, 18.3, 18.4, 20.2, 20.9, 23.2, 25.7, 25.9 (3C), 26.0 (3C), 26.7, 26.8, 26.9, 32.6, 32.9, 36.5, 39.7, 39.8, 44.8, 44.9, 55.6, 63.5, 64.0, 81.2, 90.1, 124.3, 124.4, 125.1, 128.2, 131.2, 134.6, 134.8, 134.9; ESIMS (MeOH): 755.6 ([*M* + Na]$^+$, 100); HRESIMS: calcd. for $C_{44}H_{84}O_4Si_2Na$ *m/z* 755.5806, found 755.5814.

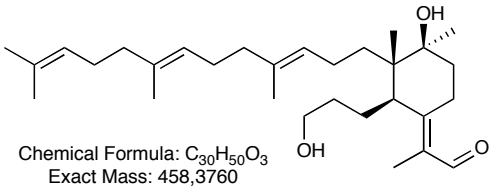
Fluoride deprotection: Preparation of C3, C1-free diol



Chemical Formula: $C_{32}H_{56}O_4$
Exact Mass: 504.4179

To a magnetically stirred solution of the fully protected alcohol **25*E*** (25 mg, 0.034 mmol) was added tetrabutylammonium fluoride (0.15 mL, 1M in THF). The reaction was stirred at 25 °C for 4 h. After dilution with EtOAc, usual work up and chromatography on SiO_2 (heptane-EtOAc 1:2) gave the expected compound (10 mg, 0.020 mmol, 58%) as a yellow oil; $[\alpha]_D^{20}$ = 42 (*c* 1.5, $CHCl_3$); IR (film): ν = 3339, 1447, 1379, 1150, 1104, 1031, 920 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 1.04 (s, 3H), 1.07-1.14 (m, 1H), 1.09 (s, 3H), 1.29-1.37 (m, 2H), 1.44-1.53 (m, 2H), 1.59 (s, 6H), 1.60 (s, 3H), 1.68 (s, 3H), 1.74 (dt, *J* = 3.0, 14.7 Hz, 1H), 1.81 (s, 3H), 1.83-1.89 (m, 1H), 1.91-1.94 (m, 2H), 1.95-1.98 (m, 5H), 2.03-2.08 (m, 4H), 2.19 (bt, *J* = 13.5 Hz, 1H), 2.40 (bd, *J* = 14.0 Hz, 1H), 2.52 (bd, *J* = 11.7 Hz, 1H), 3.39 (s, 3H), 3.6 (t, *J* = 6.7 Hz, 2H), 4.11 and 4.21 (ABquartet, *J* = 11.0 Hz, 2H), 4.70 and 4.72 (ABquartet, *J* = 6.9 Hz, 2H), 5.02 (dd, *J* = 6.4, 7.0 Hz, 1H), 5.09 (dd, *J* = 5.5, 8.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 16.0 (3C), 17.6, 17.9, 20.1, 21.1, 23.2, 25.7, 26.6, 26.6, 26.8, 32.5, 33.1, 36.6, 39.7 (2C), 44.8, 44.9, 55.7, 63.7, 63.8, 81.1, 90.2, 124.2, 124.4, 124.9, 128.1, 131.3, 134.8, 134.9, 137.7; ESIMS (MeOH): 527.4 ([*M* + Na]$^+$, 100); HRESIMS: calcd. for $C_{32}H_{56}O_4Na$ *m/z* 527.4076, found 527.4084.

Geometrical isomer of Iridal 26



Chemical Formula: $C_{30}H_{50}O_3$
Exact Mass: 458,3760

The C10-MOM protected diol thus obtained (3.5 mg, 0.07 mmol) was subjected to HCl-*t*BuOH treatment at room temperature for 20 h (TLC monitoring) affording the desired triol, which was directly subjected to allylic oxidation as above to give the spectroscopically pure **26** (3 mg, 0.006 mmol, 88% two steps) as a colorless oil; IR (film): ν = 3427, 1651, 1456, 1379, 1260, 1091, 1023, 903, 797 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 1.08 (s, 3H), 1.13-1.20 (m, 1H), 1.16 (s, 3H), 1.23-1.33 (m, 2H), 1.34-1.43 (m, 1H), 1.57 (s, 3H), 1.58 (s, 3H), 1.59 (s, 3H), 1.64-1.70 (m, 1H), 1.68 (s, 3H), 1.75-1.87 (m, 5H), 1.80 (s, 3H), 1.89-1.99 (m, 6H), 2.02-2.10 (m, 4H), 2.59 (bt, *J* = 13.2 Hz, 1H), 2.80 (bd, *J* = 11.2 Hz, 1H), 3.23 (bd, *J* = 13.6 Hz, 1H), 3.61 (t, *J* = 6.4 Hz, 2H), 4.97 (t, *J* = 6.8 Hz, 1H), 5.05-5.11 (m, 2H), 10.24 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 11.9, 16.0, 16.1, 17.7, 17.8, 20.0, 23.3, 25.7, 26.4, 26.6, 26.8, 27.2, 32.1, 37.2, 38.0, 39.7 (2C), 45.2, 47.3, 63.3, 75.2, 124.1, 124.2, 124.4, 131.2, 133.1, 135.0, 135.4, 163.5, 190.7; ESIMS (MeOH): 481.3 ($[M + Na]^+$, 100); HRESIMS: calcd. for $C_{30}H_{50}O_3Na$ *m/z* 481.3658, found 481.3644.