# Supporting Information I

# Total Synthesis (–)-Dactylolide and 13-Desmethylene-(–)-dactylolide and their Effects on Tubulin

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## 1. General Methods

All solvents used for reactions were purchased as anhydrous grade from Fluka (puriss.; dried over molecular sieves; $H_2O$ <0.005%) and used without further purification. Solvents for extractions, flash column chromatography (FC) and thin layer chromatography (TLC) were purchased as commercial grade and distilled prior to use. All non-aqueous reactions were performed under an argon atmosphere using flame-dried glassware and standard syringe/septa techniques. All other commercially available reagents were used without further purification, unless otherwise noted. In general, reactions were magnetically stirred and monitored by TLC performed on Merck TLC aluminum sheets (silica gel 60 $F_{254}$). Spots were visualized with UV light ($\lambda$ = 254 nm) or through staining with $Ce_2(SO_4)_3$/phosphomolybdic acid/$H_2SO_4$ (CPS) or $KMnO_4/K_2CO_3$. Chromatographic purification of products (FC) was performed using Fluka silica gel 60 for preparative column chromatography (particle size 40-63 μm).

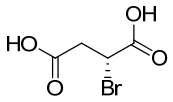
**Melting points** were obtained in open capillary tubes using a Büchi melting point apparatus B-540 and are uncorrected. **$^1$H-** and **$^{13}$C-NMR** spectra were recorded in $CDCl_3$ or MeOH-$d_4$ (unless otherwise noted) on Bruker AV-400 400 MHz and AV-500 500 MHz instruments at room temperature. Chemical shifts ($\delta$) are reported in ppm and are referenced to the solvent signal as an internal standard (chloroform $\delta$ 7.26 ppm for $^1$H, $\delta$ 77.16 ppm for $^{13}$C and MeOH-$d_4$ $\delta$ 3.31 ppm for $^1$H, $\delta$ 49.00 ppm for $^{13}$C). All $^{13}$C-NMR spectra were measured with complete proton decoupling. Data for NMR spectra are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, m = multiplet, br = broad signal, J = coupling constant in Hz.

**Infrared spectra (IR)** were recorded on a Jasco FT/IR-6200 instrument as thin film. Resonance frequencies are given as wavenumbers in $cm^{-1}$.

**Optical rotations** were measured on a Jasco P-1020 polarimeter operating at the sodium D line with a 10 mm or 100 mm path length cell and are reported as follows: $[a]_D^T$, concentration (g/100 ml), and solvent.

**Mass spectra** were recorded by the ETH Zürich MS service; HRMS (ESI) spectra were obtained on a Bruker Daltonics maxis (UHR-TOF) and HRMS (EI) on a Waters Micromass AutoSpec Ultima instrument.

## 2. Synthesis of alcohol 7



**(*R*)-2-Bromosuccinic acid (23)**.[1] To a solution of (*R*)-aspartic acid (5.00 g, 37.56 mmol, 1.00 equiv) in $H_2SO_4$ (13.3 ml of conc. $H_2SO_4$, 250 mmol, 6.60 equiv, in 100 ml of water) at –5 °C (NaCl/ice) was added KBr (20.11 g, 169 mmol, 4.5 equiv) followed by slow addition of a solution of $NaNO_2$ (4.6 g, 68.7 mmol, 1.80 equiv.) in $H_2O$ (9 ml) during 1 h (ATTENTION: Nitrous gases are formed and a an experimental set-up with a washing flask should be used!). After 3 h at 0 °C the brown mixture was extracted with EtOAc (4 x 60 ml). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure, to give **23** (6.67 g, 33.89 mmol, 90%) as a yellow solid. The compound was used without purification.

**TLC**: $R_f$ = 0.52 (EtOAc/Hex 1/1, 5% AcOH, UV, $KMnO_4$).

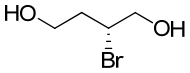
**Mp.**: 166-167 °C.

**$^1$H-NMR** (400 MHz, MeOH-$d_4$): δ 5.00 (br, s, 2 H), 4.59 (dd, J = 8.7, 6.3, 1 H), 3.22 (dd, J = 17.2, 8.7, 1 H), 2.98 (dd, J = 17.2, 6.3, 1 H).

**$^{13}$C-NMR** (100 MHz, MeOH-$d_4$): δ 173.2, 172.3, 40.7, 40.1.

**IR** (thin film): ν 3010, 2902, 2642, 2532, 1700, 1418, 1404, 1303, 1287, 1185, 935, 648.

$[\alpha]_D^{24}$: +60.83° (c 0.90, MeOH).



**(*R*)-2-Bromobutane-1,4-diol (24).**[1] To a solution of **23** (6.64 g, 33.7 mmol, 1.00 equiv) in dry THF (90 ml) was added a solution of $BH_3$ (1M in THF, 100 ml, 100 mmol, 3 equiv) slowly via a dropping funnel during 1 h at 0 °C. The yellow solution formed was stirred for 1 h at 0 °C and the cooling bath was removed; after 15 min a white precipitate was formed (exothermic process). Stirring was continued for additional 1.5 h, the mixture was cooled to 0 °C and $H_2O$ (5 ml) and of $K_2CO_3$ (10 g) were slowly added. The suspension was stirred for 10 min at rt, then filtered and the residue was washed with $Et_2O$ (3x 50 ml). Concentration of the solution under reduced pressure and purification of the residue by flash chromatography (EtOAc/MeOH 50/1) afforded **24** (5.47 g, 32.38 mmol, 96%) as a yellow oil.

[1] Frick, J. A.; Klassen, J. B.; Bathe, A.; Abramson, J. M.; Rapoport, H. *Synthesis*, **1992**, 621. (Preparation of (*S*)-2-bromosuccinic acid).

**Note:** The reaction also works well with neat BMS in around 93% yield. It is advisable to extemd the initial cooling period, if the reaction is performed on larger scale and at higher concentrations, due to substantial exothermicity!

**TLC**: $R_f$ = 0.53 (EtOAc/MeOH 50/1, $KMnO_4$).

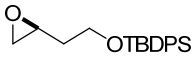
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 4.28 (dq, J = 8.1, 5.3, 1 H), 3.88-3.74 (m, 4 H), 3.45 (br, s, 1 H), 3.00 (br, s, 1H), 2.15 (ddt, J = 15.0, 8.1, 4.9, 1 H), 2.10-2.02 (m, 1 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 67.2, 60.1, 54.7, 37.9.

**IR** (thin film): ν 3307, 2935, 2886, 1452, 1419, 1378, 1052, 1023, 639.

**HRMS (ESI)**: calculated for $C_4H_9BrNaO_2$ [$(M+Na)^+$] 190.9678, found 190.9667

**$[\alpha]_D^{24}$ :** +33.30° (c 15.19, $CHCl_3$).




**(*S*)-*tert*-Butyl-(2-(oxiran-2-yl)ethoxy)diphenylsilane (11).**[2] To a suspension of NaH (60% in mineral oil, 2.74 g, 68.5 mmol, 3.00 equiv) in THF (30 ml) at –16 °C (NaCl/ice) was added a solution of **24 (**3.86 g, 22.83 mmol, 1.00 equiv) in THF (20 ml) over a 15 min period, during which the temperature rose to –10 °C. A solution of TBDPSCl (6.59 g, 23.97 mmol, 1.05 equiv) in THF (15 ml) was added at that temperature after 30 min and the cooling bath was removed. After additional 45 min, $H_2O$ (20 ml) was added carefully at 0 °C followed by saturated aqueous $NH_4Cl$ (20 ml). The phases were separated and the aqueous phase was extracted with EtOAc (3 x 30 ml). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/Hex 1/20), to give **11** (6.73 g, 20.61 mmol, 90%) as a colorless oil that converts to a white solid upon storage.

**TLC**: $R_f$ = 0.51 (EtOAc/Hex 1/10, UV, CPS).

**Mp:** 39.7-41.2 °C.

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.68-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 3.87-3.78 (m, 2 H), 3.12-3.07 (m, 1 H), 2.78 (dd, J = 5.1, 4.1, 1 H), 2.51 (dd, J = 5.1, 2.8, 1 H), 1.80-1.75 (m, 2 H), 1.06 (s, 9 H).

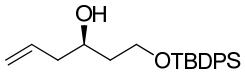
**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 135.7, 135.7, 133.8, 133.8, 129.8, 127.8, 61.0, 50.2, 47.4, 35.8, 26.9, 19.3.

**IR** (thin film): ν 3070, 2956, 2930, 2857, 1472, 1427, 1389, 1110, 823, 738, 701.

**HRMS (ESI)**: calculated for $C_{20}H_{26}NaO_2Si$ [$(M+Na)^+$] 349.1594, found 379.1592.

**$[\alpha]_D^{24}$** : –6.74° (c 1.87, $CHCl_3$).

[2] Analytical data: Hanessian, S.; Tehim, A.; Chen, P. *J. Org. Chem,* **1993**, *58*, 7768.




**(*R*)-1-(*tert*-Butyldiphenylsilyloxy)hex-5-en-3-ol (12).**[3] To a solution of vinylmagnesium bromide (1 M in THF, 40.5 ml, 40.5 mmol, 2.00 equiv) was added CuI (395 mg, 2.03 mmol, 0.10 equiv) at –60 °C. After 5 min a solution of **11** (6.62 g, 20.28 mmol, 1.00 equiv.) in THF (25 ml) was added, such that the interior temperature did not exceed –55 °C. The temperature was then allowed to rise slowly to –30 °C over a period of 1.5 h; then saturated aqueous $NH_4Cl$ (50 ml) was added slowly followed by $H_2O$ (20 ml). The cooling bath was removed, the mixture was stirred for 15 min, 25% aqueous $NH_4OH$ (10 ml) was added and stirring was continued for additional 10 min. The phases were separated, the blue aqueous phase was extracted with EtOAc (3 x 30ml), and the combined organic phases were dried over $MgSO_4$. Concentration of this solution under reduced pressure and purification of the residue by flash chromatography (EtOAc/Hex 1/10→1/5) afforded **12** (7.07 g, 19.94 mmol, 98%) as a pale-yellow, viscous oil.

**TLC**: $R_f$ = 0.40 (EtOAc/Hex 1/5, UV, CPS).

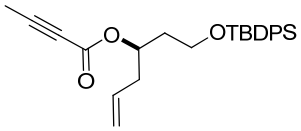
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.69-7.67 (m, 4 H), 7.46-7.38 (m, 6 H), 5.85 (ddt, J = 17.1, 10.2, 7.2, 1 H), 5.14-5.08 (m, 2 H), 4.00-3.93 (m, 1 H), 3.91-3.81 (m, 2 H), 3.15 (d, J = 2.6, 1 H), 2.33-2.21 (m, 2 H), 1.78-1.65 (m, 2 H), 1.06 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 135.7, 135.7, 135.1, 133.2, 133.1, 129.9, 127.9, 117.5, 71.0, 63.5, 42.1, 38.0, 27.0, 19.2.

**IR** (thin film): ν 3446, 3071, 2953, 2930, 2857, 1472, 1427, 1390, 1361, 1108, 1077, 997, 914, 822, 737, 700, 613, 503, 487.

**HRMS (ESI)**: calculated for $C_{22}H_{30}NaO_2Si$ [$(M+Na)^+$] 377.1907, found 377.1903.

$[\alpha]_D^{24}$: +4.31° (c 1.34, $CHCl_3$).




**(*R*)-1-(*tert*-Butyldiphenylsilyloxy)hex-5-en-3-yl but-2-ynoate (25).** To a solution of **12** (1.84 g, 5.2 mmol, 1.00 equiv) in dry DCM (15 ml) were added sequentially DMAP (65 mg, 0.52 mmol, 0.10 equiv), 2-butynoic acid (0.49 g, 5.70 mmol, 1.10 equiv), and a solution of DCC (1.30 g, 6.30 mmol, 1.20 equiv) in DCM (15 ml) at 0 °C. The suspension formed was allowed to warm to rt and stirring was continued for 16 h. $Et_2O$ (100 ml) was then added, the mixture was filtered, and the filter cake was washed with $Et_2O$ (50 ml). The filtrate was concentrated under reduced pressure to give a brown-red oil that was again treated

[3] a) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117. b) Clive, D. L. J. et al. *J. Am. Chem. Soc.* **1990**, *112*, 3018.

with $Et_2O$ (100 ml) followed by re-filtration of the mixture and washing of the precipitate with $Et_2O$ (50 ml). The combined filtrate and washing were concentrated under reduced pressure and the residue was purified by flash chromatography (EtOAc/Hex 1/30→1/20), to give **25** (1.87 g, 4.44 mmol, 85%) as a colorless oil.

**TLC**: $R_f$ = 0.44 (EtOAc/Hex 1/10, UV, CPS).

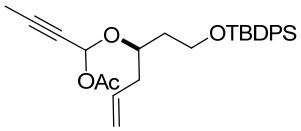
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.67-7.65 (m, 4 H), 7.46-7.37 (m, 6 H), 5.77 (ddt, J = 17.4, 9.7, 7.0, 1 H), 5.29-5.23 (m, 1 H), 5.13-5.07 (m, 2 H), 3.77-3.68 (m, 2 H), 2.46-2.34 (m, 2 H), 1.98 (s, 3 H), 1.89-1.83 (m, 2 H), 1.07 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 153.3, 135.7, 135.6, 133.8, 133.6, 133.2, 129.7, 127.8, 118.2, 85.3, 72.8, 72.6, 60.0, 38.6, 36.1, 26.9, 19.2, 3.9.

**IR** (thin film): ν 3071, 3050, 2957, 2359, 2342, 2243, 1706, 1472, 1428, 1389, 1249, 1110, 1063, 700.

**HRMS (ESI)**: calculated for $C_{23}H_{27}O_3Si$ [$(M\text{-}CH_3H_5)^+$] 379.1730, found 379.1724.

$[\alpha]_D^{24}$ : –18.04° (c 0.93, $CHCl_3$).




**1-((*R*)-1-(*tert*-butyldiphenylsilyloxy)hex-5-en-3-yloxy)but-2-ynyl acetate (10).** To a solution of **25** (1.77 g, 4.20 mmol, 1.00 equiv) in DCM (40 ml) at –78 °C was added slowly DIBALH (1M in toluene, 8.40 ml, 8.40 mmol, 2.00 equiv); after 30 min pyridine (1 ml, 12.60 mmol, 3.00 equiv), DMAP (1.54 g, 12.60 mmol, 3.00 equiv), and $Ac_2O$ (2.37 ml, 25.20 mmol, 6.00 equiv) were added seqentially –78 °C and the mixture was stirred at that temperature for 22 h. Saturated aqueous $NH_4Cl$ (20 ml) and saturated aqueous Rochelle salt (40 ml) were added at –78 °C and the mixture was allowed to warm to rt. Vigorous stirring was continued for 90 min in a beaker, resulting in the formation of two clear phases that were readily separable. The aqueous phase was extracted with DCM (3 x 40 ml) and the combined organic phases were washed with saturated aqueous $NaHCO_3$ (2 x 20ml) and brine (10 ml, once), and then dried over $MgSO_4$. Concentration of the solution under reduced pressure and purification of the residue by flash chromatography on a deactivated stationary silica phase (EtOAc/Hex 1/30→1/20, 2% $NEt_3$ (v/v)) afforded **10** (1.80 g, 3.87 mmol, 92%) as a 1.6/1 mixture of diastereomers as a colorless, viscous oil. Spectroscopic data are reported for the diastereomeric mixture.

**TLC**: $R_f$ = 0.40 (EtOAc/Hex 1/10, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.72-7.66 (m, 4 H), 7.45-7.36 (m, 6 H), 6.45 (q, J = 1.8, 0.37 H), 6.44 (q, J = 1.8, 0.63 H), 5.87-5.75 (m, 1 H), 5.12-5.02 (m, 2 H), 4.17-4.06 (m, 1 H), 3.85-3.71 (m, 2 H), 2.41-2.30

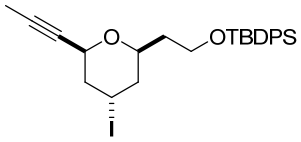
(m, 2 H), 2.05 (s, 1.12 H), 1.99 (s, 1.88 H), 1.86 (d, J = 1.8, 1.15 H), 1.84 (d, J = 1.8, 1.85 H), 1.83-1.71 (m, 2 H), 1.07 (s, 3.38 H), 1.06 (s, 5.62 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 169.9, 169.7, 135.7, 135.7, 135.6, 135.6, 134.5, 134.1, 134.0, 133.9, 133.9, 129.7, 129.7, 129.7, 127.8, 127.8, 118.0, 117.2, 87.2, 86.2, 83.1, 82.9, 76.4, 74.9, 74.4, 74.1, 60.6, 60.3, 39.7, 39.2, 37.4, 37.4, 27.0, 26.9, 21.2, 21.2, 19.3, 19.3, 3.7, 3.7.

**IR** (thin film): ν 3072, 2956, 2857, 2259, 1740, 1472, 1370, 1228, 1082, 903, 822, 701.

**HRMS (ESI)**: calculated for $C_{28}H_{36}NaO_4Si$ [$(M+Na)^+$], 487.2281, found 487.2265.

$[\alpha]_D^{24}$: –19.24° (c 0.99, $CHCl_3$).




***tert*-Butyl-(2-((2*S*,4*S*,6*S*)-4-iodo-6-(prop-1-ynyl)tetrahydro-2H-pyran-2-yl)ethoxy)diphenylsilane (13).** To a solution of **10** (1.79 g, 3.85 mmol, 1.00 equiv) in DCM (55 ml) at –19 °C (NaCl/ice) was added 2,6-dimethylpyridine (0.09 ml, 0.77 mmol, 0.20 equiv) followed by slow addition of TMSI (1.37 ml, 9.62 mmol, 2.50 equiv). The cooling bath was removed after 10 min and the yellow solution was allowed to warm to rt. After a total of 45 min saturated aqu $NaHCO_3$ (20 ml) was carefully added, the phases were separated, and the aqueous phase was extracted with DCM (3 x 10 ml). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/30→1/20) afforded **13** (1.78 g, 3.34 mmol, 85%) as a pale-yellow, viscous oil. Material obtained in this way is generally contaminated by 2-3 % of aldehyde **26** (see below). Spectroscopic data for **13** were acquired with a pure sample.

**TLC**: $R_f$ = 0.45 (EtOAc/Hex 1/10, UV, CPS).

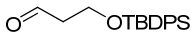
**$^1$H-NMR** (400 MHz, $CDCl_3$) δ 7.71-7.67 (m, 4 H), 7.44-7.36 (m, 6 H), 4.83 (quin, J = 3.1, 1 H), 4.57 (br. dquin, J = 10.8, 2.1, 1 H), 4.21-4.15 (m, 1 H), 3.86 (ddd, J = 10.5, 8.2, 4.9, 1 H), 3.73 (dt, J = 10.3, 5.4, 1 H), 2.16 (dq, J = 14.8, 2.3, 1 H), 1.99 (ddd, J = 14.7, 2.4, 2.1, 1 H), 1.93-1.82 (m, 2 H), 1.87 (d, J = 2.1, 3 H), 1.69 (ddt, J = 13.7, 8.3, 5.3, 1 H), 1.57-1.50 (m, 1 H), 1.07 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 135.7, 135.7, 134.1, 133.9, 129.7, 127.8, 127.8, 81.5, 77.9, 71.1, 65.1, 60.1, 41.8, 40.3, 38.3, 29.3, 27.0, 19.4, 3.8.

**IR** (thin film): ν 3070, 2953, 2856, 2360, 2341, 1472, 1427, 1389, 1232, 1107, 1095, 1049, 822, 737, 702.

**HRMS (EI)**: calculated for $C_{22}H_{24}IO_2Si$ [$(M-C_4H_9)^+$], 475.0590, found 475.0585.

$[\alpha]_D^{24}$: –3.30° (c 1.00, $CHCl_3$).




**3-(*tert*-Butyldiphenylsilyloxy-)propanal (26)**

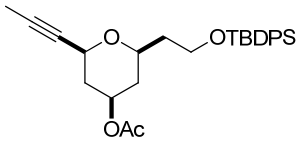
**TLC**: $R_f$ = 0.71 (EtOAc/Hex 1/10, UV, $KMnO_4$).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.82 (t, J = 2.2, 1 H), 7.67-7.64 (m, 4 H), 7.46-7.37 (m, 6 H), 4.03 (t, J = 6.1, 2 H), 2.61 (dt, J = 6.1, 2.2, 2 H), 1.04 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 202.0, 135.7, 133.4, 130.0, 127.9, 58.5, 46.5, 26.9, 19.3.

**IR** (thin film): ν 2957, 2888, 1727, 1427, 1105, 822, 700.

**HRMS (EI)**: calculated for $C_{15}H_{15}O_2Si$ [$(M-C_4H_9)^+$], 255.0836, found 255.0836.




**(2*S*,4*R*,6*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-(prop-1-ynyl)tetrahydro-2H-pyran-4-yl acetate (27).** To a solution of **13** (1.57 g, 2.95 mmol, 1.00 equiv) in toluene (130 ml) was added a solution of 18-c-6 (3.12 g, 11.80 mmol, 4.00 equiv) in toluene (20 ml) followed by CsOAc (5.67 g, 29.53 mmol, 10.00 equiv) at rt and the mixture was heated to 60 °C for 4 d. After cooling to rt $H_2O$ (50 ml) and EtOAc (50 ml) were added, the phases were separated, and the aqueous phase was extracted with EtOAc (3 x 30 ml). The combined organic extract were washed once with brine (30 ml), dried over $MgSO_4$ and the solution was concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/25→1/10) afforded **27** (987 mg, 2.12 mmol, 72%) as a colorless, viscous oil.

**TLC**: $R_f$ = 0.29 (EtOAc/Hex 1/10, UV, CPS or $KMnO_4$).

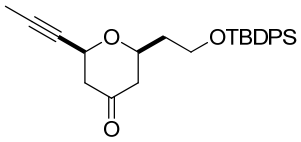
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.67-7.64 (m, 4 H), 7.44-7.36 (m, 6 H), 4.86 (tt, J = 11.3, 4.8, 1 H), 4.09 (br. dquin, J = 11.6, 2.1, 1 H), 3.87 (ddd, J = 10.3, 8.3, 4.9, 1 H), 3.72 (dt, J = 10.3, 5.4, 1 H), 3.67-3.61 (m, 1 H), 2.18 (dddd, J =12.6, 4.9, 2.4, 2.1, 1 H), 2.04 (s, 3 H), 1.94 (dddd, J = 12.3, 4.8, 2.4, 1.8, 1 H), 1.89-1.82 (m, 1 H), 1.86 (d, J = 2.1, 3 H), 1.72 (ddt, J = 14.1, 8.4, 5.4, 1 H), 1.64 (dd, J = 23.9, 11.5, 1 H), 1.31 (dd, J = 23.6, 11.5, 1 H), 1.05 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 170.5, 135.7, 135.7, 134.9, 134.1, 133.9, 129.7, 129.7, 127.8, 81.2, 77.7, 72.6, 69.7, 66.2, 60.0, 38.8, 38.4, 37.1, 27.0, 21.3, 19.3, 3.8.

**IR** (thin film): ν 3071, 2956, 2856, 2360, 2342, 1740, 1472, 1428, 1389, 1237, 1109, 1063, 1031, 907, 822.

**HRMS (ESI)**: calculated for $C_{22}H_{24}IO_2Si$ [$(M+Na)^+$], 487.2281, found 487.2275.

$[\alpha]_D^{24}$: –10.84° (c 2.39, $CHCl_3$).




**(2*S*,6*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-6-(prop-1-ynyl)dihydro-2H-pyran-4(3H)-one (28).** To a stirred solution of **27** (0.96 g, 2.07 mmol, 1.00 equiv) in MeOH (40 ml) were added $K_2CO_3$ (2.86 g, 20.70 mmol, 10.00 equiv) and $H_2O$ (2 ml) and stirring was continued for 6 h. Brine (20 ml) and EtOAc (20 ml) were then added and the phases were separated. The aqueous phase was extracted with EtOAc (3 x 10 ml) and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure.

The crude product was dissolved in DCM (20 ml) and DMP (1.32 g, 3.10 mmol, 1.50 equiv) was added in two equal portions (with the second portion added after 30 min) and the mixture was stirred for 3 h. A mixture of saturated aqu $Na_2S_2O_3$ (10 ml) and saturated aqueous $NaHCO_3$ (10ml) was then added and stirring was continued for 10 min. The phases were separated, the aqueous phase was extracted with DCM (3 x 20 ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/10→1/5) gave **28** (733.8 mg, 1.75 mmol, 85% for two steps) as a colorless oil.

**Note:** Swern oxidation using 1.5 equiv of oxalylchloride, 3 equiv of DMSO and 5 equiv of $NEt_3$ gave comparable overall yields and could be more suitable for large scale preparations.

**TLC**: $R_f$ = 0.33 (EtOAc/Hex 1/5, UV, CPS or $KMnO_4$).

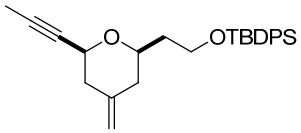
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.67-7.63 (m, 4 H), 7.45-7.36 (m, 6 H), 4.29 (ddq, J = 10.3, 4.1, 2.1, 1 H), 3.93-3.83 (m, 2 H), 3.75 (dt, J = 10.4, 5.3, 1 H), 2.61 (dd, J =15.0, 10.5, 1 H), 2.56 (ddd, J = 15.0, 4.0, 1.6, 1 H), 2.39 (ddd, J = 14.6, 2.6, 1.6, 1 H), 2.29 (dd, J = 14.6, 11.6, 1 H), 1.97-1.88 (m, 1 H), 1.89 (d, J = 2.1, 3 H), 1.82-1.73 (m, 1 H), 1.04 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 205.6, 135.7, 135.7, 133.8, 133.8, 129.8, 129.8, 127.9, 83.0, 77.0, 73.8, 67.3, 59.7, 48.3, 47.8, 39.1, 27.0, 19.3, 3.9.

**IR** (thin film): ν 2955, 2927, 2856, 1722, 1473, 1427, 1337, 1227, 1109, 1086, 702.

**HRMS (ESI)**: calculated for $C_{26}H_{32}NaO_3Si$ [$(M+Na)^+$], 443.2013, found 443.1999.

$[\alpha]_D^{24}$ : –26.81° (c 0.97, $CHCl_3$).




***tert*-Butyl-(2-((2*R*,6*S*)-4-methylene-6-(prop-1-ynyl-)tetrahydro-2H-pyran-2-yl)ethoxy-) diphenylsilane (14).** To a solution of $MePh_3PBr$ (1.20 g, 3.38 mmol, 2.00 equiv) in THF (20 ml) was added *n*-BuLi (1.6M in hexane, 2.00 ml, 3.20 mmol, 1.90 equiv) at –78 °C. After 15 min stirring at –78 °C the temperature was allowd to rise to 0 °C; stirring was continued for 30 min, a solution of **28** (0.71 g, 1.69 mmol, 1.00 equiv) in THF (10 ml) was added, and the mixture was then heated to 50 °C for 90 min After cooling to rt $H_2O$ (10 ml) and EtOAc (10 ml) were added, the phases were separated, and the aqueous phase was extracted with EtOAc (3 x 10 ml). The combined organic extracts were dried over $MgSO_4$ and the solution was concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/100 →1/50) gave **14** (0.66 g, 1.58 mmol, 94%) as a colorless oil.

**TLC**: $R_f$ = 0.62 (EtOAc/Hex 1/10, UV, CPS).

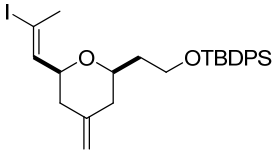
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.68-7.65 (m, 4 H), 7.44-7.35 (m, 6 H), 4.76-4.74 (m, 2 H), 4.00 (ddq, J = 11.0, 2.4, 2.1, 1 H), 3.87 (ddd, J = 10.2, 8.1, 5.0, 1 H), 3.74 (dt, J =10.2, 5.5, 1 H), 3.56-3.50 (m, 1 H), 2.43-2.39 (m, 1 H), 2.36-2.29 (m, 1 H), 2.24-2.20 (m, 1 H), 2.00-1.93 (m, 1 H), 1.92-1.85 (m, 1 H), 1.88 (d, J = 2.1, 3 H), 1.78-1.70 (m, 1 H), 1.04 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 143.5, 135.7, 135.7, 134.1, 134.0, 129.7, 129.7, 127.8, 109.6, 81.2, 78.5, 75.6, 69.0, 60.3, 42.0, 40.5, 39.1, 27.0, 19.3, 3.9.

**IR** (thin film): ν 3071, 2944, 2931, 2857, 2360, 2342, 1651, 1472, 1427, 1389, 1345, 1110, 1089, 1060, 998, 894, 823, 702.

**HRMS (ESI)**: calculated for $C_{27}H_{35}O_2Si$ [$(M+H)^+$], 419.2401, found 419.2404.

$[\alpha]_D^{24}$: –3.42° (c 0.55, $CHCl_3$).




***tert*-Butyl-(2-((2*R*,6*S*)-6-((*E*)-2-iodoprop-1-enyl)-4-methylenetetrahydro-2H-pyran-2-yl)ethoxy) diphenylsilane (9).** To a suspension of CuCN (668 mg, 7.42 mmol, 5.00 equiv) in THF (16 ml) at –78 °C was added a solution of *n*-BuLi (1.6M in hexane, 9.30 ml, 14.82 mmol, 10.00 equiv). After 5 min the flask was immersed in a cooling bath at –40 °C, resulting in the formation of a pale-yellow, almost clear solution. The mixture was cooled back to –78 °C after 10 min, which made it become slightly heterogenous. Neat $Bu_3SnH$ (4.00 ml, 14.82 mmol, 10.00 equiv.) was then added dropwise, immediately leading to a turbid yellow solution with liberation of gas. After 20 min at –78 °C the mixture was stirred

for 5 min at –40 °C, giving an almost clear golden-yellow solution. After 10 min at –40 °C the solution was cooled back to –78 °C followed by addition of MeOH (6.60 ml, 163.00 mmol, 110.00 equiv) under vigorous stirring. After 10 min at –78 °C the flask was immersed in a cooling bath at –40 °C; the reaction mixture now was a clear red solution. After 10 min at –40 °C this solution was cooled back to – 78 °C and a solution of **14** (0.62 g, 1.48 mmol, 1.00 equiv) in THF (10 ml) was added. The mixture was stirred for 15 h, during which period the temperature was allowed to rise to –15 °C. Saturated aqu $NH_4Cl$ (30 ml) and 25% aqueous $NH_4OH$ (6 ml) were then added together with EtOAc (20 ml). Stirring was continued for 30 min, the two almost clear phases were separated, and the aqueous phase was extracted with EtOAc (3 x 10 ml). The combined organic extracts were dried over $MgSO_4$, the solution was concentrated under reduced pressure. Purification of the residue by flash chromatography on deactivated silica (Hex→EtOAc/Hex 1/100→1/50, 1% (v/v) $NEt_3$) gave the vinylstannane (1.02 g, 1.43 mmol, 97%) as a pale-yellow oil that was used immediately.

A solution of the above vinylstannane in THF (11 ml) was cooled to –17 °C (NaCl/ice) followed by addition of NIS (0.49 g, 2.10 mmol, 1.50 equiv) in THF (2 ml), to give an almost clear yellow solution. After 20 min a mixture of saturated aqu $Na_2S_2O_3$ (5 ml) and saturated aqu $NaHCO_3$ (5 ml) was added followed by EtOAc (5 ml). Stirring was continued for 2 min until two clear, colorless phases were formed. The phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 ml). The combined organic extracts were dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash chromatography (Hex/EtOAc 1/100) to afford the desired product **9** (0.79 g, 1.44 mmol, quant.) as a pale yellow oil.

**TLC**: $R_f$ = 0.64 (EtOAc/Hex 1/20, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.70-7.67 (m, 4 H), 7.47-7.38 (m, 6 H), 6.24 (dq, J = 7.7, 1.5, 1 H), 4.81-4.77 (m, 2 H), 3.99 (ddd, J =10.8, 7.7, 2.6, 1 H), 3.87 (ddd, J = 10.1, 8.1, 5.4, 1 H), 3.76 (dt, J = 10.1, 5.6, 1 H), 3.64-3.57 (m, 1 H), 2.44 (d, J = 1.5, 3 H), 2.27-2.20 (m, 2 H), 2.13-2.06 (m, 1 H), 2.00-1.94 (m, 1 H), 1.87-1.73 (m, 2 H), 1.08 (s, 9 H).

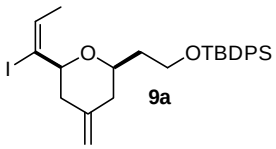
**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 141.6, 135.6, 135.6, 134.0, 133.9, 129.7, 127.7, 109.3, 98.5, 76.3, 75.3, 60.2, 40.6, 40.4, 39.0, 28.8, 26.9, 19.3.

**IR** (thin film): ν 3070, 2931, 2890, 2856, 1651, 1472, 1427, 1360, 1105, 1087, 998, 858, 700.

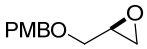
**HRMS (ESI)**: calculated for $C_{27}H_{36}IO_2Si$ [$(M+H)^+$], 547.1524, found 547.1503.

$[\alpha]_D^{24}$: +4.90° (c 1.81, $CHCl_3$).

The $^{1}$H-NMR spectrum indicated the presence of ca. 3 % of the undesired regioisomer **9a** (δ 6.45-6.39, m):




**9a**




**(*S*)-2-((4-methoxybenzyloxy)methyl)oxirane (8).**[4] To a suspension of NaH (60% in mineral oil, 0.73 g, 18.07 mmol, 1.20 equiv) in dry THF (15 ml) at 0 °C was added a solution of (*R*)-glycidol (1.16 g, 15.06 mmol, 1.00 equiv) in THF (2 ml). After stirring for 30 min at 0 °C 4-methoxybenzyl chloride (2.83 g, 18.07 mmol, 1.20 equiv) was added slowly followed by a spatula tip of TBAI and the mixture was allowed to warm to rt. After 20 h $H_2O$ (20 ml) was added carefully followed by EtOAc (10 ml); the phases were separated and the aqueous phase was extracted with $Et_2O$ (3 x 20 ml). The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was purified by flash chromatography (EtOAc/Hex 1/10→1/5>1/3) to give **8** (2.24 g, 11.5 mmol, 76%) as a colorless oil.

**TLC**: $R_f$ = 0.31 (EtOAc/Hex 1/3, UV, CPS).

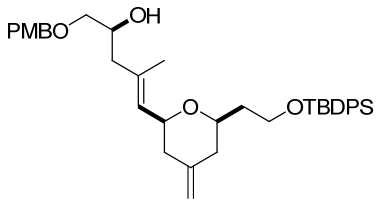
**$^{1}$H-NMR** (400 MHz, $CDCl_3$): δ 7.29-7.26 (m, 2 H), 6.90-6.86 (m, 2 H), 4.54 (d, J = 11.6, 1 H), 4.49 (d, J = 11.6, 1 H), 3.81 (s, 3 H), 3.73 (dd, J = 11.4, 3.1, 1 H), 3.42 (dd, J = 11.4, 5.8, 1 H), 3.19-3.15 (m, 1 H), 2.79 (dd, J = 5.0, 4.2, 1 H), 2.60 (dd, J = 5.1, 2.7, 1 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.5, 130.1, 129.6, 114.0, 73.1, 70.7, 55.4, 51.0, 44.5.

**IR** (thin film): ν 2999, 2934, 2836, 1731, 1612, 1512, 1464, 1384, 1301, 1244, 1174, 1086, 1031, 818.

**HRMS (EI)**: calculated for $C_{11}H_{14}O_3$ [$(M)^+$], 194.0937, found 197.0938.

$[\alpha]_D^{24}$: –5.98° (c 0.98, $CHCl_3$).




**(*S*,*E*)-5-((2*S*,6*R*)-6-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-methylenetetrahydro-2H-pyran-2-yl)-1-(4-methoxybenzyloxy)-4-methylpent-4-en-2-ol (7).** Vinyl iodide **9** (385 mg, 0.70 mmol, 1.00 equiv, azeotropically dried once with 2 ml of acetonitrile or toluene right before use) was dissolved in dry toluene (7 ml) and the solution was cooled to –78 °C. *t*-BuLi (1.6 M in pentane, 0.88 ml, 1.41 mmol, 2.00

[4] Ahmed, A.; Hoegenauer, K. E.; Enev, V. S.; Hanbauer, M.; Kaehlig, H.; Öhler, E.; Mulzer, J. *J. Org. Chem.* **2003**, *68*, 3026.

equiv) was then added and the near colorless solution was stirred for 30 min; it was then cooled to around –85 - –90 °C with liquid nitrogen and a solution of **8** (342 mg, 1.76 mmol, 2.50 equiv, azeotropically dried once with 2 ml of acetonitrile or toluene right before use) in dry toluene (2 ml) was added followed by $BF_3$•$OEt_2$ (0.22 ml, 1.76 mmol, 2.50 equiv; addition ca. 1 min after the addition of **8**) giving a pale yellow solution. Stirring was continued at –78 °C for 1 h; then the cooling bath was removed and saturated aqueous $NaHCO_3$ (10 ml) and 10 ml of EtOAc were added. After the mixture had reached rt, the phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 ml). The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure, and the residue purified by flash chromatography (EtOAc/Hex 1/5→1/4) to give 264.2 mg (0.43 mmol, 61%) of **7** as a colorless oil.

**Note:** Chromatographic separation was difficult and two FC runs were needed in order to remove the iodohydrine derived from competing epoxide opening by iodide.

**TLC**: $R_f$ = 0.17 (EtOAc/Hex 1/5, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.68-7.65 (m, 4 H), 7.44-7.34 (m, 6 H), 7.28-7.24 (m, 2 H), 6.90-6.87 (m, 2 H), 5.29 (dq, J = 7.7, 1.2, 1 H), 4.75-4.73 (m, 2 H), 4.49 (s, 2 H), 3.99 (ddd, J =10.9, 7.7, 2.7, 1 H), 3.98-3.91 (m, 1 H), 3.84 (ddd, J = 10.1, 8.0, 5.5, 1 H), 3.80 (s, 3 H), 3.74 (dt, J = 10.1, 5.7, 1 H), 3.60-3.54 (m, 1 H), 3.46 (dd, J = 9.5, 3.5, 1 H), 3.33 (dd, J = 9.5, 7.1, 1 H), 2.31 (d, J = 3.5, 1 H), 2.25-2.22 (m, 1 H), 2.20 (d, J = 6.8, 2 H), 2.16-2.12 (m, 1 H), 2.04-2.00 (m, 1 H), 1.97-1.90 (m, 1 H), 1.89-1.80 (m, 1 H), 1.77-1.71 (m, 1 H), 1.69 (d, J = 1.2, 3 H), 1.05 (s, 9 H).

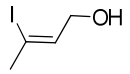
**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.4, 144.7, 135.7, 135.7, 135.4, 134.1, 134.0, 130.2, 129.7, 129.5, 129.0, 127.7, 127.7, 114.0, 108.7, 75.5, 75.3, 73.7, 73.2, 68.6, 60.4, 55.4, 43.7, 41.0, 40.7, 39.2, 27.0, 19.4, 17.3.

**IR** (thin film): ν 3070, 2932, 2857, 1612, 1513, 1471, 1427, 1247, 1106, 1087, 1058, 1036, 998, 821, 702.

**HRMS (ESI)**: calculated for $C_{38}H_{50}NaO_5Si$ [$(M+Na)^+$], 637.3320, found 637.3322.

$[\alpha]_D^{24}$ = +5.97° (c 0.88, $CHCl_3$).

## 3. Synthesis of unsaturated acid 6



**(*Z*)-3-Iodobut-2-en-1-ol (29).**[5] A solution of Red-Al (3.4 M in toluene, 64 ml, 218 mmol, 1.50 equiv) in a two-necked dry flask charged with a magnetic stirring bar, a reflux condenser, an addition funnel and an argon in/outlet was diluted with $Et_2O$ (150 ml) and then cooled to 0 °C. A solution of 2-butyn-1-ol (10.17 g, 145.10 mmol, 1.00 equiv) in $Et_2O$ (150 ml) was added dropwise via the addition funnel. After stirring at 0 °C for 30 min the reaction mixture was allowed to warm to rt (CAUTION: exothermicity after ca. 1.5 h !). After 15 h a white suspension had formed that was cooled to 0 °C; EtOAc (100 ml) was then slowly added via the addition funnel. A solution of iodine (55.3 g, 218 mmol, 1.50 equiv) in THF (150 ml) was then slowly added at −78 °C. After completion of the addition, the addition funnel was rinsed with THF (75 ml). After warming to rt the mixture was carefully added to a stirred mixture of saturated aqu $Na_2S_2O_3$ (200 ml) and saturated aqueous Rochelle salt (200 ml) followed by addition of EtOAc (100 ml). After stirring at rt for 30 min two clear phases were obtained that were separated. The aqueous phase was extracted with EtOAc (3 x 100 ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/6→1/3→1/1) gave **29** (25.25 g, 127.6 mmol, 88%) of a yellow oil.

**Note**: The product is not stable upon prolonged storage at rt.

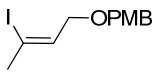
**TLC**: $R_f$ = 0.36 (EtOAc/Hex 1/3, UV, $KMnO_4$ or CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 5.75 (tq, J = 5.9, 1.5, 1 H), 4.14 (dq, J = 6.0, 1.3, 2 H), 2.52 (q, J = 1.3, 3 H), 2.20 (br s, 1 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 134.3, 102.5, 67.4, 33.7.

**IR** (thin film): 3313, 2950, 2911, 2871, 1720, 1649, 1426, 1375, 1256, 1222, 1073, 1005.

**HRMS (EI)**: calculated for $C_4H_6IO$ [$M^+$] 197.9458, found 197.9537.



**(*Z*)-1-((3-Iodobut-2-enyloxy)methyl)-4-methoxybenzene (15)**[6]

Preparation of PMB-trichloroacetimidate: A solution of 4-methoxybenzyl alcohol (13.82 g, 100.00 mmol, 1.00 equiv) in $Et_2O$ (15 ml) was added to a stirred suspension of NaH (60% in mineral oil, 0.40 g, 10.00

[5] Corey, E. J.; Katzenellenbogen, J. A.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 4245.

[6] PMB-imidate preparation: Mickel, S. J.; Sedelmeier, G. H.; Niederer, D.; Daeffler, R.; Osmani, A.; Schreiner, K.; Seeger-Weibel, M.; Bérod, B.; Schaer, K.; Gamboni R.; *Organic Process Research & Development* **2004**, *8,* 92. PMB-protection: Chau, A.; Paquin, J.-F.; Lautens, M. *J. Org. Chem.* **2006**, *71*, 1924.

mmol, 0.10 equiv) in $Et_2O$ (70 ml) at 0 °C. After the effervescence had ceased, stirring was continued for a total of 30 min. Neat $Cl_3CCN$ (10.53 ml, 105 mmol, 1.05 equiv) was then added dropwise, resulting in the formation of a pale yellow solution (with the interior temperature was kept between 0-8 °C) and the pale orange suspension was stirred at 0 °C for a total of 45 min. The mixture was then allowed to warm to rt and was concentrated under reduced pressure. The tan residue was treated with pentane (100 ml) and MeOH (0.40 ml, 10.00 mmol, 0.10 equiv), the mixture was stirred for 2 min at rt, and the solid material was removed by filtration and with pentane (washed once 100 ml). The combined filtrate and washing was conentrated under reduced pressure and the yellow residue was purified by flash chromatography (EtOAc/Hex 1/10→1/5, 1% $NEt_3$ to deactivate the stationary phase) giving PMB-trichloroacetimidate (24.63 g, 87.16 mmol, 87%) as a yellow oil that could be stored in the freezer over months and without loss of reactivity.

To a solution of **29** (1.02 g, 5.15 mmol, 1.00 equiv) in cyclohexane (20 ml) and DCM (10 ml) was added neat PMB-trichloroacetimidate dropwise at 0 °C followed by PPTS (0.12 g, 0.48 mmol, 0.10 equiv) (a clear solution was obtained after ca. 5 min). The cooling bath was removed and a white precipitate began to form. After 16 h saturated aqueous $NaHCO_3$ (10 ml) and $H_2O$ (10 ml) were added to the pale yellow mixture. The phases were separated, the aqueous layer was extracted with DCM (2 x 10ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/20) provided **15** (1.47 g, 4.64 mmol, 90 %) as a pale yellow oil.

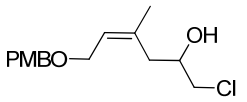
**TLC**: $R_f$ = 0.75 (EtOAc/Hex 1/5, UV, $KMnO_4$ or CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.29-7.27 (m, 2 H), 6.90-6.86 (m, 2 H), 5.75 (tq, J = 5.7, 1.5, 1 H), 4.45 (s, 2 H), 4.04 (dq, J = 5.7, 1.4, 2 H), 3.80 (s, 3 H), 2.54 (q, J = 1.4, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.4, 132.6, 130.3, 129.6, 114.0, 102.4, 74.5, 72.3, 55.4, 33.9.

**IR** (thin film): ν 2998, 2951, 2933, 2911, 2852, 1649, 1611, 1585, 1510, 1462, 1440, 1427, 1353, 1245, 1173, 1092, 1057, 1034, 817.

**HRMS (EI)**: calculated for $C_{12}H_{15}IO_2$ [$M^+$] 318.0117, found 318.0112.




**(*Z*)-1-Chloro-6-(4-methoxybenzyloxy)-4-methylhex-4-en-2-ol (16).** To a solution of **15** (952.20 mg, 2.99 mmol, 1.00 equiv) in toluene (15 ml) was added *n*-BuLi (1.6M in hexane, 2.05 ml, 3.29 mmol, 1.10 equiv) dropwise at –85 °C. After 30 min freshly distilled epichlorohydrin (0.70 ml, 8.98 mmol, 3.00 equiv) was added followed by $BF_3$•$OEt_2$ (0.50 ml, 3.89 mmol, 1.30 equiv.). After additional 15 min

saturated aqueous $NaHCO_3$ (15 ml), $H_2O$ (10 ml), and EtOAc (20 ml) were added and the mixture was allowed to warm to rt. The phases were separated and the aqueous phase was extracted with EtOAc (3 x 10 ml); the combined organic extracts were washed once with brine (10 ml), dried over $MgSO_4$, and then concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/5->1/3) afforded **16** (544.2 mg, 1.91 mmol, 64%) as a colorless oil.

**Note**: Isolated yields varied between 60 and 70%.

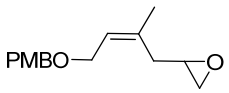
**TLC**: $R_f$ = 0.28 (EtOAc/Hex 1/3, UV, $KMnO_4$ or CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.30-7.28 (m, 2 H), 6.92-6.88 (m, 2 H), 5.69 (t, J = 7.0, 1 H), 4.48 (s, 2 H), 3.99 (dd, J = 11.2, 7.1, 1 H), 3.95-3.89 (m, 1 H), 3.87 (dd, *J* = 11.0, 7.3, 1 H), 3.82 (s, 3 H), 3.55 (d, J = 5.2, 2 H), 3.39 (d, J = 4.9, 1 H), 2.47 (dd, J = 13.5, 9.2, 1 H), 2.26 (dd, J = 13.5, 4.1, 1 H), 1.83 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.5, 139.0, 129.9 (3xC), 124.4, 114.0 (2xC), 72.5, 68.8, 65.2, 55.4, 49.9, 37.4, 23.8.

**IR** (thin film): ν 3404, 2954, 2935, 2911, 2858, 2837, 1612, 1513, 1464, 1442, 1380, 1361, 1301, 1246, 1173, 1063, 1032, 819.

**HRMS (ESI)**: calculated for $C_{15}H_{21}ClNaO_3$ $[(M+Na)^+]$ 307.1077, found 307.1071.




**(*Z*)-2-(4-(4-Methoxybenzyloxy)-2-methylbut-2-enyl-)oxirane (30).** To a solution of **16** (2.67 g, 9.38 mmol, 1.00 equiv) in EtOH (100 ml) was added crushed KOH (0.59 g, 10.50 mmol, 1.10 equiv) at 0 °C and the mixture was stirred for 20 h at 0 °C. It was then concentrated under reduced pressure and the residue was partitioned between $H_2O$ (10 ml) and EtOAc (20 ml). The phases were separated and the aqueous phase was extracted with EtOAc (3x10 ml); the combined organic extracts were washed once with brine (10 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/5→1/3) afforded **30** (2.08 g, 8.39 mmol, 89%) as a colorless oil.

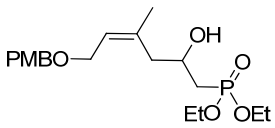
**TLC**: $R_f$ = 0.44 (EtOAc/Hex 1/3, UV, $KMnO_4$ or CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.28-7.24 (m, 2 H), 6.89-6.85 (m, 2 H), 5.55 (t, J = 6.8, 1 H), 4.43 (s, 2 H), 4.02-3.94 (m, 2 H), 3.80 (s, 3 H), 2.96-2.91 (m, 1 H), 2.73 (dd, J = 4.9, 4.0, 1 H), 2.46 (dd, J = 5.0, 2.6, 1 H), 2.34 (dd, J = 14.2, 5.9, 1 H), 2.25 (dd, J = 14.2, 5.3, 1 H), 1.83 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.3, 136.3, 130.6, 129.5, 124.3, 113.9, 72.0, 66.0, 55.4, 51.2, 46.9, 35.2, 24.5.

**IR** (thin film): ν 3039, 2934, 2853, 1612, 1511, 1454, 1442, 1301, 1245, 1173, 1072, 1034, 819.

**HRMS (ESI)**: calculated for $C_{15}H_{20}NaO_3$ $[(M+Na)^+]$ 271.1305, found 271.1305.




**(*Z*)-Diethyl 2-hydroxy-6-(4-methoxybenzyloxy)-4-methylhex-4-enylphosphonate (17).**[7] To a solution of diethylphosphite (3.48 g, 25.17 mmol, 3.00 equiv) in THF (55 ml) was added *n*-BuLi (1.6M in hexane, 15.70 ml, 25.17 mmol, 3.00 equiv) at –78 °C (interior temperature reached around –60 °C during addition). After 30 min a solution of **30** (2.08 g, 8.39 mmol, 1.00 equiv) in THF (15 ml) was added slowly followed by $BF_3$•$OEt_2$ (3.2 ml, 25.17 mmol, 3.00 equiv.). After 6 h at –78 °C saturated aqueous $NaHCO_3$ (50 ml) was added and the mixture was allowed to reach rt. The phases were separated, the aqueous phase was extracted with $Et_2O$ (3 x 40 ml), and the combined organic extracts were washed once with brine (10 ml) and dried over $MgSO_4$. Concentration of the solution under reduced pressure and purification of the residue by flash chromatography (EtOAc→EtOAc/acetone 5/1) gave **17** (2.58 g, 6.68 mmol, 80%) as a pale yellow oil.

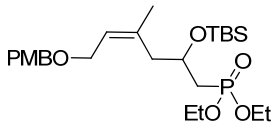
**TLC**: $R_f$ = 0.27 (EtOAc, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.27-7.24 (m, 2 H), 6.89-6.85 (m, 2 H), 5.61 (t, J = 7.0 Hz, 1 H), 4.43 (s, 2 H), 4.15-4.06 (m, 5 H), 3.99-3.90 (m, 2 H), 3.80 (s, 3 H), 3.55 (br s, 1 H), 2.41 (ddd, J = 13.5, 8.2, 1.5, 1 H), 2.24 (dd, J = 13.5, 5.2, 1 H), 1.99-1.83 (m, 2 H), 1.79 (d, J = 1.1, 3 H), 1.32 (td, J = 7.1, 1.7, 6 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.4, 138.0, 130.4, 129.7, 124.8, 113.9, 72.3, 65.8, 64.8 (J = 4.2 Hz), 62.0 (J = 6.1 Hz), 61.9 (J = 6.7 Hz), 55.4, 41.0 (J = 15.2 Hz), 33.8 ( J = 138.8 Hz), 24.0, 16.5 (J = 6.0 Hz).

**IR** (thin film): ν 3386, 2931, 1612, 1513, 1443, 1365, 1245, 1023, 958, 818.

**HRMS (ESI)**: calculated for $C_{19}H_{31}NaO_6P$ [$(M+Na)^+$] 409.1750, found 409.1758.




**(*Z*)-diethyl2-(tert-butyldimethylsilyloxy)-6-(4-methoxybenzyloxy)-4-methylhex-4-enylphosphonate (31).** To a solution of **17** (2.56 g, 6.62 mmol, 1.00 equiv.) in DMF (15 ml) were added sequentially ImH (2.70 g, 40 mmol, 6.00 equiv), DMAP (0.80 g, 6.62 mmol, 1.00 equiv) and TBSCl (3.00 g, 20 mmol, 3.00 equiv) at rt. The mixture formed was stirred for 1.5 d; $H_2O$ (20 ml) and $Et_2O$ (20 ml) were then added, the phases were separated, and the organic phase was extracted with $H_2O$ (2 x 10 ml). The combined aqueous extracts were then re-extracted with $Et_2O$ (2 x 10 ml) and the combined organic phases were dried over

[7]For NMR data on β-hydroxyphosphonates Zymanczyk-Duda, E.; Lejczak, B.; Kafarski, P. *Tetrahedron*, **1995**, *51*, 11809.

$MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 2/1→5/1) afforded **31** (2.78 g, 5.55 mmol, 84%) as a colorless oil.

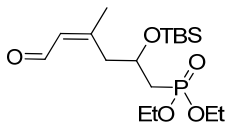
**TLC**: $R_f$ = 0.70 (EtOAc, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.27-7.24 (m, 2 H), 6.87-6.84 (m, 2 H), 5.50 (t, J = 6.7 Hz, 1 H), 4.41 (s, 2 H), 4.16-4.03 (m, 6 H), 3.96 (dd, J = 11.7, 6.5, 1 H), 3.79 (s, 3 H), 2.43 (dd, J = 13.5, 4.8, 1 H), 2.27 (ddd, J = 13.5, 7.8, 1.8, 1 H), 2.03-1.87 (m, 2 H) 1.77 (d, J = 1.1, 3 H), 1.31 (td, J = 7.0, 1.2, 6 H), 0.86 (s, 9 H), 0.07 (s, 3 H), 0.02 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.3, 137.0, 130.8, 129.5, 124.9, 113.9, 72.1, 67.0, 66.5, 61.5 (J = 6.6), 55.4, 41.4 (J = 6.4), 34.9 ( J = 136.1), 26.0, 24.4, 18.0, 16.6 (J = 6.1 Hz), 16.6 (J = 6.1 Hz), -4.5, -4.6.

**IR** (thin film): ν 2954, 2929, 2856, 1613, 1513, 1471, 1389, 1246, 1025, 958, 936, 808, 776.

**HRMS (EI)**: calculated for $C_{21}H_{36}O_6PSi$ [$(M-C_4H_9)^+$] 443.2013, found 443.2014.




**(*Z*)-Diethyl 2-(tert-butyldimethylsilyloxy)-4-methyl-6-oxohex-4-enylphosphonate (18).** To a solution of **31** (2.60 g, 5.19 mmol, 1.00 equiv) in DCM (40 ml) was added $H_2O$ (2 ml) followed by DDQ (1.77 g, 7.80 mmol, 1.50 equiv; added in 3 equal portions in 10 min intervals) at 0 °C under vigorous stirring. After 90 min the orange-tan coloured mixture was diluted with saturated aqu $NaHCO_3$ (10 ml), DCM (50ml) and $H_2O$ (10 ml). The clear phases were separated, the aqueous phase was extracted with DCM (3 x 20 ml), and the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The crude pale red oil, which contained the deprotected primary alcohol as well as the corresponding aldehyde, was directly used in the subsequent oxidation step.

To a stirred solution of oxalylchloride (0.50 ml, 5.71 mmol, 1.10 equiv) in DCM (10 ml) was slowly added a solution of DMSO (0.81 ml, 11.40 mmol, 2.20 equiv) in DCM (1 ml) at –78 °C. After 10 min, a solution of the crude alcohol/aldehyde in DCM (20 ml) was added and stirring was continued for another 30 min. $NEt_3$ (3.60 ml, 26.00 mmol, 5.00 equiv) was then added and after 15 additional min at –78 °C the mixture was allowed to warm to rt. After 1.5 h the yellow solution was diluted with $H_2O$ (10 ml) and the phases were separated. The aqueous phase was extracted with DCM (3 x 10 ml) and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 3/1→5/1→6/1) gave **18** (1.72 g, 4.54 mmol, 88% over two steps) as a pale red oil.

**Note**: The aldehyde decomposes upon prolonged storage at rt.

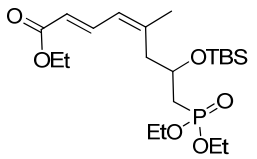
**TLC**: $R_f$ = 0.42 (EtOAc/Hex 5/1, UV, $KMnO_4$ or CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.93 (d, J = 8.2, 1 H), 5.93 (d, J = 8.2, 1 H), 4.21-4.13 (m, 1 H), 4.14-4.04 (m, 4 H), 2.90-2.88 (m, 2 H), 2.08-2.00 (m, 2 H), 1.99 (d, J = 1.3, 3 H), 1.32 (td, J = 7.1, 2.0, 6 H), 0.82 (s, 9 H), 0.05 (s, 3 H), -0.04 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 191.8, 160.3, 130.9, 67.2 (d, *J* = 2.2), 61.9 (d, *J* = 6.8), 61.8 (d, *J* = 6.8), 41.1 (d, *J* = 2.2), 35.7 (d, *J* = 134.9), 25.9, 25.8, 17.9, 16.6 (d, *J* = 6.2), -4.6, -4.7.

**IR** (thin film): ν 2954, 2857, 1674, 1472, 1463, 1392, 1251, 1151, 1048, 1021, 959, 936, 835, 826, 775.

**HRMS (EI)**: calculated for $C_{13}H_{26}O_5PSi$ [$(M-C_4H_9)^+$], 321.1282, found 321.1282.




**(2*E*,4*Z*)-Ethyl 7-(tert-butyldimethylsilyloxy)-8-(diethoxyphosphoryl)-5-methylocta-2,4-dienoate (32).** To a solution of triethyl phosphonoacetate (1.17 ml, 5.90 mmol, 1.30 equiv) in THF (10 ml) was added *n*-BuLi (1.6M in hexane, 3.55 ml, 5.67 mmol, 1.25 equiv) at 0 °C. After stirring for 30 at min 0 °C a solution of **18** (1.72 g, 4.54 mmol, 1.00 equiv) in THF (10 ml) was added, resulting in the formation of pale yellow-orange solution, which was stirred at 0 °C for 1.5 h. Saturated aqu $NH_4Cl$ (20 ml), $H_2O$ (5 ml) and EtOAc (5 ml) were then added, the phases were separated and the aqueous phase was extracted with EtOAc (2 x 20 ml). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc/Hex 2/1) to afford **32** (1.96 g, 4.38 mmol, 97%) as a pale purple oil.

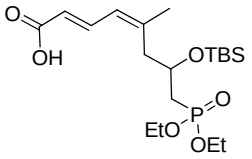
**TLC**: $R_f$ = 0.54 (EtOAc/Hex 5/1, UV, $KMnO_4$ or CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.56 (dd, J = 15.2, 11.6, 1 H), 6.06 (d, J = 11.5, 1 H), 5.76 (d, J = 15.2, 1 H), 4.18 (dq, J = 7.1, 1.4, 2 H), 4.16-4.07 (m, 5 H), 2.62 (dd, J = 13.4, 4.2, 1 H), 2.55 (dd, J = 13.4, 8.1, 1 H), 2.03 (d, J = 6.2, 1 H), 1.98 (d, J = 6.2, 1 H), 1.89 (s, 3 H), 1.33 (td, J = 7.1, 2.8, 6 H), 1.28 (t, J = 7.1, 3 H), 0.83 (s, 9 H), 0.05 (s, 3 H), -0.02 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 167.5, 146.1, 141.0, 126.8, 119.8, 67.0, 61.7 (d, J = 6.5), 60.2, 41.7 (d, J = 5.1), 35.3 (d, J = 135.3), 25.9, 25.3, 17.9, 16.6 (d, J = 6.1), 14.5, -4.6, -4.7.

**IR** (thin film): ν 2980, 2955, 2929, 2905, 2857, 1711, 1636, 1472, 1390, 1367, 1252, 1146, 1046, 1021, 934, 836, 808, 775.

**HRMS (ESI)**: calculated for $C_{21}H_{42}O_6PSi$ [$(M+H)^+$] 449.2483, found 449.2471.




**(2*E*,4*Z*)-7-(*tert*-Butyldimethylsilyloxy)-8-(diethoxyphosphoryl)-5-methylocta-2,4-dienoic acid (6).** To a solution of **32** (1.41 g, 3.13 mmol, 1.00 equiv) in EtOH (24 ml) was added 1.0 M aqueous NaOH (9.40 ml, 9.40 mmol, 3.00 equiv) at 0 °C. The cooling bath was removed after 5 min and the yellow solution at was stirred at rt for 25 h. The reaction was then quenched by the addition of 2.0 M aqueous HCl (4.70 ml, 9.40 mmol, 3.00 equiv). Subsequently, EtOAc (20 ml) and brine (20 ml) were added, the phases were separated, and the aqueous phase was extracted with EtOAc (4 x 20 ml). The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was dried in high vacuum to give crude **6** (1.27 g, 3.03 mmol, 97%) which was used in the next step without further purification.

**TLC**: $R_f$ = 0.46 (EtOAc, UV, $KMnO_4$).

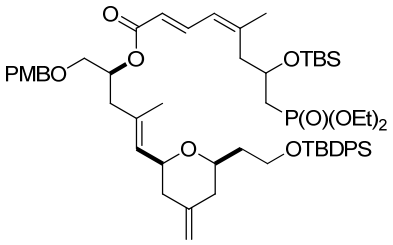
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 10.1 (br s, 1 H), 7.61 (dd, J = 15.0, 11.9, 1 H), 6.06 (d, J = 11.7, 1 H), 5.74 (d, J = 15.0, 1 H), 4.17-4.05 (m, 5 H), 2.65 (d, J = 13.0, 1 H), 2.49 (dd, J = 13.0, 8.2, 1 H), 2.03-2.00 (m, 1 H), 1.98-1.96 (m, 1 H), 1.88 (s, 3 H), 1.29 (td, J = 7.2, 2.8, 6 H), 0.81 (s, 9 H), 0.02 (s, 3 H), -.0.04 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 172.0, 146.9, 142.2, 126.6, 119.9, 67.2, 62.0 (d, J = 6.3), 41.6 (d, J = 3.4), 35.0 (d, J = 136.3), 25.8, 25.5, 17.9, 16.5 (d, J = 6.2), -4.7, -4.8.

**IR** (thin film): ν 2954, 2929, 2857, 1703, 1636, 1391, 1251, 1200, 1149, 1046, 1019, 935, 808, 774.

**HRMS (ESI)**: calculated for $C_{19}H_{37}O_6NaPSi$ [$(M+Na)^+$], 443.1989, found 443.1989.

## 3. Synthesis of (–)-Dactylolide ((–)-2)




**(2*E*,4*Z*)-((*S*,*E*)-5-((2*S*,6*R*)-6-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-methylenetetrahydro-2H-pyran-2-yl)-1-(4-methoxybenzyloxy)-4-methylpent-4-en-2-yl)7-(tert-butyldimethylsilyloxy)-8-(diethoxy phosphoryl)-5-methylocta-2,4-dienoate (33).** To a solution of **6** (218 mg, 0.52 mmol, 1.20 equiv, co-evaporated once with 2 ml of acetonitrile immediately before use) in toluene (3 ml) was added $NEt_3$ (0.16 ml, 1.12 mmol, 2.60 equiv) followed by 2,4,6-trichlorobenzoyl chloride (0.1 ml, 0.65 mmol, 1.5 equiv)

giving a pale yellow mixture. After 1.5 h at rt, a solution of **7** (266 mg, 0.43 mmol, 1.00 equiv, co-evaporated once with 2 ml of acetonitrile) and DMAP (53 mg, 0.43 mmol, 1.00 equiv, mixture sonicated to produce a clear solution) in toluene (1 ml; plus additional 1.5 ml form rinsing) was added, immediately leading to a yellow suspension. After stirring at rt for 18 h saturated aqu $NaHCO_3$ (5 ml), $H_2O$ (5 ml), and EtOAc (5 ml) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 ml). The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was purified by flash chromatography (EtOAc/Hex 1/3→1/2→1/1) to give **33** (375.9 mg, 0.37 mmol, 85%) as a pale yellow, viscous oil.

**TLC**: $R_f$ = 0.54 (EtOAc/Hex 1/1, UV, CPS).

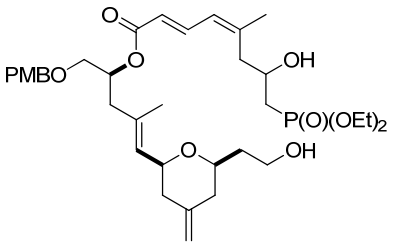
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.67-7.64 (m, 4 H), 7.59 (dd, J = 15.3, 11.9, 1 H), 7.43-7.32 (m, 6 H), 7.25-7.22 (m, 2 H), 6.87-6.84 (m, 2 H), 6.07 (d, J = 11.8, 1 H), 5.80 (d, J = 15.2, 1 H), 5.26 (d, J = 7.8, 1 H), 5.21-5.14 (m, 1 H), 4.73-4.71 (m, 2 H), 4.50 (d, J = 11.8, 1 H), 4.42 (dd, J = 11.8, 2.6, 1 H), 4.19-4.07 (m, 5 H), 3.96 (ddd, J = 10.9, 7.8, 2.6, 1 H), 3.85-3.80 (m, 1 H), 3.78 (s, br, 3 H), 3.72 (dt, 10.2, 5.5, 1 H), 3.60-3.51 (m, 1 H), 3.51-3.46 (m, 2 H), 2.64-2.54 (m, 2 H), 2.42 (dd, J = 13.7, 7.8, 1 H), 2.31 (ddd, J = 13.7, 5.7, 2.2, 1 H), 2.22 (d, J = 13.1, 1 H), 2.05 (d, J = 13.1, 1 H), 2.03-2.02 (m, 1 H), 1.99-1.97 (m, 1 H), 1.97-1.91 (m, 2 H), 1.89 (s, 3 H), 1.87-1.79 (m, 1 H), 1.76-1.71 (m, 1 H), 1.70 (s, 3 H), 1.32 (dt, J = 7.1, 3.0, 6 H), 1.03 (s, 9 H), 0.83 (s, 9 H), 0.06 (s, 3 H), -0.02 (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$; due to the diastereomeric nature of the product, the number of signals in the $^{13}$C-spectrum exceeds the number of carbon atoms): δ 166.8, 159.1, 146.3, 144.7, 141.4 (2), 135.6, 135.6, 134.6 (2), 134.1, 133.9, 130.3, 129.6, 129.4 (2C), 129.3 (2C), 127.7 (2C), 126.8, 119.7, 113.9, 108.6, 75.5, 75.2, 72.9 (2C), 71.4, 71.3, 70.1 (2C), 66.9, 61.6 (d, J = 6.5) (2C), 60.4 (2C), 55.3, 41.7, 40.9, 40.8, 40.7, 39.2, 35.2 (d, J = 135), 26.9, 25.9, 25.1, 21.1, 19.3, 17.9, 17.3 (2C), 16.5 (d, J = 6.3), -4.6, -4.7.

**IR** (thin film): ν 2952, 2930, 2893, 2857, 1710, 1636, 1612, 1514, 1248, 1146, 1111, 1089, 1049, 1024, 823, 703.

**HRMS (ESI)**: calculated for $C_{57}H_{85}NaO_{10}PSi_2$ [$(M+Na)^+$], 1039.5311, found 1039.5309.

$[\alpha]_D^{24}$: +9.46° (c 1.03, $CHCl_3$).




***(2E,4Z)-((S,E)*-5-((2*S*,6*R*)-6-(2-Hydroxyethyl)-4-methylenetetrahydro-2H-pyran-2-yl)-1-(4-methoxy benzyloxy)-4-methylpent-4-en-2-yl)-8-(diethoxyphosphoryl)-7-hydroxy-5-methyl-octa-2,4-dienoate (34).** To a stirred solution of **33** (27.3 mg, 0.027 mmol, 1.00 equiv) in THF (1 ml) in a plastic tube was added 70% HF•py (0.27 ml) at 0 °C (ice/$H_2O$). The cooling bath was removed after 5 min and stirring was continued at rt for 14 h. The solution was then carefully added to a vigorously stirred mixture of saturated aqu $NaHCO_3$ (20 ml) and EtOAc (10 ml) until two clear phases had formed (ca. 15 min). The phases were separated, the aqueous phase was extracted with EtOAc (3 x 10 ml), the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (10 ml) followed by drying over $MgSO_4$. Concentration under reduced pressure and purification using flash chromatography (EtOAc→EtOAc/acetone 1/1) afforded **34** (15.1 mg, 0.023 mmol, 85%) as a pale yellow, viscous oil.

**Note:** The use of less concentrated aqu $NaHCO_3$ is not recommended for workup, since not all HF may be neutralized, which would in turn lead decomposition of the product during concentration under reduced pressure. In any case the pH of the aqueous phase should be determined after workup and should not be acidic!

**TLC**: $R_f$ = 0.71 (EtOAc/Acetone 1/1, UV, CPS).

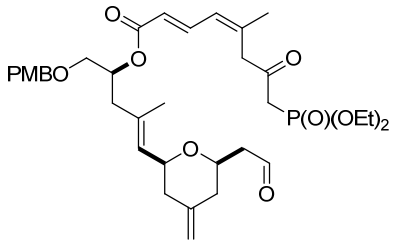
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.53 (ddd, J = 15.0, 11.6, 6.1, 1 H), 7.23-7.20 (m, 2 H), 6.86-6.83 (m, 2 H), 6.12 (d, J = 11.6, 1 H), 5.81 (d, J = 15.1, 1 H), 5.23-5.16 (m, 2 H), 4.71-4.69 (m, 2 H), 4.48 (dd, J = 11.8, 1.5, 1 H), 4.41 (dd, J = 11.8, 2.7, 1 H), 4.42-4.11 (m, 1 H), 4.17-4.05 (m, 4 H), 3.98-3.91 (m, 1 H), 3.77 (s, 3 H), 3.74-3.69 (m, 2 H), 3.60-3.56 (m, 1 H), 3.54-3.46 (m, 3 H), 2.89-2.76 (br s, 1 H), 2.60 (ddd, J = 15.2, 14.5, 8.1, 1 H), 2.47-2.40 (m, 1 H), 2.37-2.24 (m, 2 H), 2.17-2.12 (m 1 H), 2.09-2.04 (m, 1 H), 2.03-1.98 (m, 1 H), 1.98-1.95 (m, 1 H), 1.95-1.93 (m, 1 H), 1.92 (s, 3 H), 1.91-1.88 (m, 1 H), 1.81-1.70 (m, 2 H), 1.69, 1.68 (2 x s, 3 H), 1.31 (t, J = 7.1, 6 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$; due to the diastereomeric nature of the product, the number of signals in the $^{13}$C-spectrum exceeds the number of carbon atoms): δ 167.0, 159.3, 145.7, 145.6, 144.0 (2C), 140.6, 140.5, 134.9, 134.8, 130.2, 129.4, 129.0, 126.8 (2C), 120.1, 120.0, 113.9, 109.0 (2C), 78.3 (2C), 75.7, 72.9 (2C), 71.0, 70.8, 70.5, 70.4, 65.4 (d, J = 5.1), 65.3 (d, J = 5.1), 62.1 (d, J = 6.5), 62.0 (d, J = 6.5), 61.1, 55.3, 41.3 (d, J = 6.2), 41.2 (d, J = 6.2), 41.2, 41.0, 40.6, 40.6, 38.3, 38.2, 33.6 (d, J = 138), 33.5 (d, J = 138), 25.1, 24.8, 17.2, 17.1, 16.5 (d, J = 6.0) (2C).

**IR** (thin film): ν 3388, 2935, 2909, 2864, 1707, 1633, 1612, 1513, 1442, 1367, 1247, 1222, 1148, 1023, 975, 890, 802.

**HRMS (ESI)**: calculated for $C_{35}H_{54}O_{10}P$ [$(M+H)^+$], 665.3449, found 665.3442.

$[\alpha]_D^{24}$: –8.11° (c 0.99, $CHCl_3$).




**(2*E*,4*Z*)-((*S*,*E*)-1-(4-Methoxybenzyloxy)-4-methyl-5-((2*S*,6*R*)-4-methylene-6-(2-oxoethyl)tetrahydro-2H-pyran-2-yl)pent-4-en-2-yl)-8-(diethoxyphosphoryl)-5-methyl-7-oxoocta-2,4-dienoate (19).** To a solution of **34** (15 mg, 0.023 mmol, 1.00 equiv) in DCM (1 ml) was added DMP (67 mg, 0.16 mmol, 7.00 equiv; added in three equal portions in 30 min intervals) at rt. After 3 h stirring at rt, a mixture of DCM (5 ml), saturated aqu $NaHCO_3$ (5 ml), and saturated aqueous $Na_2S_2O_3$ (5 ml) and stirring was continued for 10 min, when two almost clear phases had formed. The phases were separated, the aqueous phase was extracted with DCM (3 x 10 ml), and the combined organic extracts were dried over $MgSO_4$. Concentration of the solution under reduced pressure and purrification of the residue by flash chromatography (EtOAc, 1% AcOH to deactivate the stationary phase) gave **19** (11.1 mg, 0.017 mmol, 74%) as a colorless oil.

**TLC**: $R_f$ = 0.53 (EtOAc, UV, CPS).

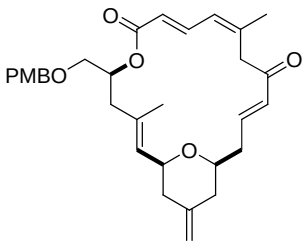
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.75 (t, J = 2.2, 1 H), 7.38 (dd, J = 15.1, 11.7, 1 H), 7.24-7.20 (m, 2 H), 6.87-6.83 (m, 2 H), 6.19 (d, J = 11.7, 1 H), 5.85 (d, J = 15.1, 1 H), 5.21-5.17 (m, 2 H), 4.77-4.74 (m, 2 H), 4.48 (d, J = 11.8, 1 H), 4.40 (d, J = 11.8, 1 H), 4.19-4.12 (m, 4 H), 3.98 (ddd, J = 11.6, 7.7, 2.7, 1 H), 3.84-3.79 (m, 1 H), 3.78 (s, 3 H), 3.61 (s, 2 H), 3.48 (d, J = 4.7, 2 H), 3.12 (s, 1 H), 3.07 (s, 1 H), 2.62 (ddd, J = 16.4, 7.6, 2.5, 1 H), 2.48 (ddd, J = 16.4, 4.9, 1.9, 1 H), 2.36 (dd, J = 13.6, 6.8, 1 H), 2.28 (dd, J = 13.6, 6.8, 1 H), 2.25-2.21 (m, 1 H), 2.10-2.05 (m, 1 H), 2.00-1.97 (m, 1 H), 1.94-1.91 (m, 1 H), 1.88 (s, 3 H), 1.68 (d, J = 1.2, 3 H), 1.33 (t, J = 7.1, 6 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 201.1, 198.2 (d, J = 6.5), 166.8, 159.4, 143.3, 141.0, 139.8, 135.1, 130.2, 129.4, 128.7, 127.5, 121.2, 113.9, 109.6, 75.7, 73.4, 72.9, 71.2, 70.3, 62.9 (d, J = 6.5), 55.4, 49.7, 47.7, 42.3 (d, J = 128), 41.0, 40.4, 40.3, 25.0, 17.2, 16.4 (d, J = 6.2).

**IR** (thin film): ν 2980, 2936, 2906, 2865, 1713, 1638, 1612, 1513, 1364, 1247, 1150, 1019, 971, 893.

**HRMS (ESI)**: calculated for $C_{35}H_{50}O_{10}P$ [$(M+H)^+$], 661.3136, found 661.3154.

$[\alpha]_D^{24}$: +6.22° (c 1.53, $CHCl_3$).




**(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-5-((4-Methoxybenzyloxy)methyl)-3,11-dimethyl-19-methylene-6,21-dioxa bicyclo [15.3.1]henicosa-2,8,10,14-tetraene-7,13-dione (20).** To a stirred solution of **19** (7.2 mg, 0.011 mmol, 1.00 equiv, co-evaporated before use with 1 ml of toluene) in THF (2 ml) at –78 °C was added a solution of NaHMDS (1M in THF, 0.013 ml, 0.013 mmol, 1.20 equiv, diluted with 1 ml of THF). The solution turned orange immediately. Stirring was continued while the cooling bath was slowly allowed to warm to rt. After 3.5 d, $H_2O$ (5 ml) and EtOAc (5 ml) were added and the phases were separated. The aqueous phase was extracted with EtOAc (3 x 5 ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/4) afforded **20** (2.54 mg, 0.005 mmol, 46%) as a colorless oil.

**Note:** Varying yields between 20% and 80% were observed independent of the scale of the reaction.

**Alternative procedure using $Ba(OH)_2$•0.8$H_2O$:**[8]

To a stirred solution of **19** (62.2 mg, 0.094 mmol, 1.00 equiv, co-evaporated with 3 ml of toluene immediately before use) in THF (31 ml) was added $H_2O$ (0.8 ml) followed by freshly activated $Ba(OH)_2$•0.8$H_2O$ at 0 °C. The cooling bath was removed after 30 min and stirring was continued at rt for additional 30 min more; 30 ml of $Et_2O$ were then added and the solution was washed first with saturated aqueous $NaHCO_3$ (2 x 10 ml) and then with brine (1 x 10 ml). The clear organic phase was dried over $MgSO_4$ and concentrated. The resulting yellow oil was purified by flash chromatography (EtOAc/Hex 1/3) to afford **20** (38.6 mg, 0.076 mmol, 81%) as a colorless oil.

**TLC**: $R_f$ = 0.40 (EtOAc/Hex 1/3, UV, $KMnO_4$, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.62 (dd, J = 15.1, 11.6, 1 H), 7.27-7.24 (m, 2 H), 6.90-6.86 (m, 2 H), 6.83 (ddd, J = 16.2, 9.8, 4.4, 1 H), 6.10 (d, J = 11.6, 1 H), 5.94 (d, J = 15.1, 1 H), 5.92 (d, J = 16.4, 1 H), 5.40-5.34 (m, 1 H), 5.17 (dd, J = 8.1, 0.9, 1 H), 4.74-4.70 (m, 2 H), 4.52 (d, J = 11.8, 1 H), 4.48 (d, J = 11.8, 1 H), 4.17 (d, J = 13.6, 1 H), 3.96 (ddd, J = 11.3, 8.1, 2.5, 1 H), 3.81 (s, 3 H), 3.58 (dd, J = 10.4, 6.0, 1 H), 3.51 (dd, J = 10.4, 4.9, 1 H), 3.30-3.24 (m, 1 H), 3.00 (d, J = 13.5, 1 H), 2.37 (dddd, J = 15.0, 10.1,

[8] (a) Paterson, I.; Yeung, K.-S.; Watson, C.; Ward, R. A; Wallace, P. A. *Tetrahedron* **1998**, *54*, 11935. (b) Barrios, J.; Marinas, J. M.; Sinisterra, J. V., *Bull. Soc. Chim. Belg.* **1986**, *95*, 107.

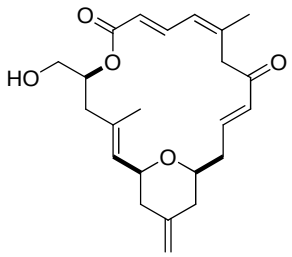
4.4, 2.0, 1 H), 2.26-2.20 (m, 1 H), 2.20 (d, J = 6.7, 2 H), 2.16-2.11 (m, 1 H), 2.11-2.05 (m, 1 H), 1.97-1.89 (m, 2 H), 1.79 (s, 3 H), 1.70 (d, J = 1.1, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 198.3, 166.9, 159.4, 146.5, 143.9, 142.9, 139.4, 132.6, 131.6, 130.2, 129.5, 129.5, 125.6, 121.3, 114.0, 109.1, 76.7, 76.1, 73.1, 71.6, 69.6, 55.4, 45.2, 42.8, 41.1, 40.9, 40.4, 23.6, 16.8.

**IR** (thin film): ν 3016, 2923, 2852, 1713, 1668, 1635, 1614, 1513, 1463, 1360, 1281, 1249, 1215, 1176, 1152, 1086, 1035, 978.

**HRMS (ESI)**: calculated for $C_{31}H_{38}NaO_6$ [$(M+Na)^+$], 529.2561, found 529.2571.

$[\alpha]_D^{24}$ : –158.79° (c 0.25, $CHCl_3$).




**(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-5-(Hydroxymethyl)-3,11-dimethyl-19-methylene-6,21-dioxabicyclo [15.3.1]henicosa-2,8,10,14-tetraene-7,13-dione (3).**[9] To a solution of **20** (4 mg, 0.008 mmol, 1.00 equiv) in DCM (0.5 ml) was added $H_2O$ (0.1 ml) followed by DDQ (5.4 mg, 0.024 mmol, 3.50 equiv) at rt. The mixture was vigorously stirred for 3 h; then saturated aqu $NaHCO_3$ (5 ml) and DCM (5 ml) were added and the phases were separated. The aqueous phase was extracted with DCM (3 x 5ml) and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the reisdue by flash chromatography (EtOAc/Hex 1/3->1/2) delivered **3** (2.49 mg, 0.0064 mmol, 82%) as a colorless solid.

**TLC**: $R_f$ = 0.30 (EtOAc/Hex 1/1, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.64 (dd, J = 15.1, 11.6, 1 H), 6.84 (ddd, J = 16.2, 9.6, 4.6, 1 H), 6.11 (d, J =11.7, 1 H), 5.94 (d, J = 15.1, 1 H), 5.93 (d, J = 16.5, 1 H), 5.28 (dddd. J = 10.8, 5.9, 4.1, 2.1, 1 H), 5.19 (d, J = 8.0, 1 H), 4.73 (d, J = 1.6, 1 H), 4.73 (d, J = 1.6, 1 H), 4.14 (d, J = 13.7, 1 H), 3.97 (ddd, J = 11.2, 8.2, 2.7, 1 H), 3.77- 3.70 (m, 2 H), 3.29 (ddt, J = 11.8, 9.5, 2.1, 1 H), 3.04 (d, J = 13.7, 1 H), 2.38 (dddd, J = 15.1, 10.1, 4.6, 2.0, 1 H), 2.30-2.08 (m, 5 H), 1.98-1.91 (m, 2 H), 1.81 (s, 3 H), 1.73 (d, J = 1.2, 3H).

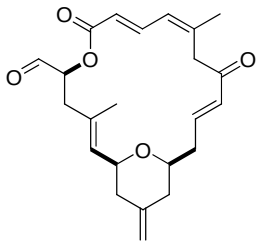
**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 198.1, 167.1, 146.5, 143.9, 143.3, 139.8, 132.6, 131.6, 129.6, 125.6, 121.0, 109.2, 76.7, 76.1, 71.9, 65.4, 45.2, 42.1, 41.1, 40.8, 40.3, 23.7, 16.8.

**IR** (thin film): ν 3389, 2925, 2853, 1715, 1669, 1634, 1553, 1449, 1436, 1357, 1280, 1259, 1148, 1086, 1049, 1019, 976, 799.

[9] Uenishi J.; Iwamoto, T.; Tanaka, J. *Org. Lett.* **2009**, *11*, 3262.

**HRMS (ESI)**: calculated for $C_{23}H_{30}NaO_5$ [$(M+Na)^+$], 409.1985, found 409.1983.

$[\alpha]_D^{24}$ : –136.26° (c = 0.11, $CHCl_3$).



**(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*S*)-3,11-Dimethyl-19-methylene-7,13-dioxo-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraene-5-carbaldehyde ((–)-2).**[10] To a stirred solution of **3** (2.33 mg, 0.006 mmol, 1.00 equiv) in DCM (0.5 ml) was added DMP (15 mg, 0.036 mmol, 6.00 equiv; added in 3 equal portions in 20 min intervals) at rt and stirring was continued for 60 min then a mixture of saturated aqueous $NaHCO_3$ (5 ml) and saturated aqueous $Na_2S_2O_3$ (5 ml) was added and stirring was continued for 10 min until two clear phases were formed. The phases were separated then the aqueous phase was extracted with DCM (3 x 10 ml), the combined organic phases were dried over $MgSO_4$, concentrated under reduced pressure then purified using flash chromatography (EtOAc/Hex 1/3) affording (–)-**2** (1.8 mg, 0.0048 mmol, 78%) of a colorless solid.

**TLC**: $R_f$ = 0.57 (EtOAc/Hex 1/1, UV, CPS or $KMnO_4$).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.67 (s, 1 H), 7.63 (dd, J = 15.1, 11.6, 1 H), 6.85 (ddd, J = 16.2, 8.6, 6.0, 1 H), 6.16 (d, J = 11.7, 1 H), 6.03-5.94 (m, 2 H), 5.32 (dd, J = 11.3, 2.5, 1 H), 5.24 (d, J = 8.0, 1 H), 4.75 (d, J = 1.6, 1 H), 4.75 (d, J = 1.6, 1 H), 3.97 (ddd, J = 11.5, 8.1, 2.7, 1 H), 3.94 (d, J = 14.3, 1 H), 3.33 (ddt, J = 11.1, 8.7, 2.7, 1 H), 3.24 (d, J = 14.5, 1 H), 2.55 (d, J = 14.3, 1 H), 2.36-2.28 (m, 3 H), 2.19-2.15 (m, 1 H), 2.14-2.09 (m, 1 H), 1.99-1.93 (m, 2 H), 1.87 (s, 3 H), 1.72 (d, J = 0.9, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 199.2, 197.6, 166.4, 146.1, 144.2, 143.6, 140.6, 131.6, 131.1, 130.7, 125.7, 119.9, 109.5, 76.6, 75.9, 75.5, 45.0, 40.9, 40.6, 39.9, 39.8, 24.3, 16.2.

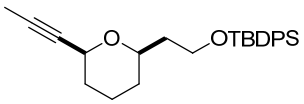
**IR** (thin film): ν 2936, 2858, 1733, 1716, 1706, 1670, 1635, 1438, 1355, 1278, 1256, 1144, 1086, 1050, 978, 890.

**HRMS (ESI)**: calculated for $C_{23}H_{28}NaO_5$ [$(M+Na)^+$], 407.1829, found 407.1820.

$[\alpha]_D^{20}$ : –258.33° (c 0.11, MeOH).

[10] See ref. 9 in this Supplementary information

## 4. Synthesis of 13-Desmethylene-(–)-Dactylolide (4)




***tert*-Butyldiphenyl(2-((2*R*,6*S*)-6-(prop-1-ynyl)tetrahydro-2H-pyran-2-yl)ethoxy-)silane (35).** To a solution of **13** (316.20 mg, 0.59 mmol, 1.00 equiv) in toluene (5 ml) was added $Bu_3SnH$ (0.18 ml, 0.07 mmol, 1.10 equiv) and a catalytic amount of AIBN. The solution was heated to 60 °C for 30 min; then the heating bath was removed and a solution of saturated aqueous KF[11] (10 ml) was added followed by EtOAc (5 ml). The mixture was stirred for 30 min at rt, the phases were separated, and the aqueous phase was extracted with EtOAc (2 x 5 ml). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/50) afforded **35** (211.2 mg, 0.52 mmol, 88 %) as a colorless oil that converted to a colorless solid at rt.

**TLC**: $R_f$ = 0.69 (EtOAc/Hex 1/10, UV, CPS).

**Mp:** 68-69 °C.

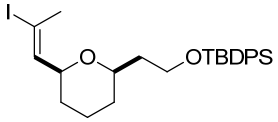
**$^1$H-NMR** (400 MHz, $CDCl_3$): 7.68-7.65 (m, 4 H), 7.44-7.35 (m, 6 H), 4.05 (ddq, J = 11.0, 2.4, 2.1, 1 H), 3.86 (ddd, J = 10.2, 8.0, 5.1, 1 H), 3.71 (dt, J =10.2, 5.6, 1 H), 3.59-3.53 (m, 1 H), 1.87-1.75 (m, 3 H), 1.86 (d, J = 2.1, 3 H), 1.72-1.63 (m, 1 H), 1.61-1.47 (m, 3 H), 1.28-1.19 (m, 1 H), 1.04 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 135.7, 135.6, 134.1, 134.0, 129.6, 129.6, 127.7, 80.4, 79.2, 75.0, 68.4, 60.3, 39.2, 33.0, 31.0, 27.0, 23.6, 19.3, 3.8.

**IR** (thin film): ν 3071, 2930, 2856, 2367, 2342, 1474, 1428, 1312, 1197, 1078, 822.

**HRMS (EI)**: calculated for $C_{22}H_{25}O_2Si$ [$(M-C_4H_9)^+$], 349.1618, found 349.1619.

$[\alpha]_D^{24}$ : –44.35° (c 1.09, $CHCl_3$).




***tert*-Butyl-(2-((2*R*,6*S*)-6-((*E*)-2-iodoprop-1-enyl)tetrahydro-2H-pyran-2-yl)ethoxy-)diphenylsilane (36).** To a suspension of CuCN (385 mg, 4.30 mmol, 10.00 equiv) in THF (8 ml) at –78 °C was added a solution of *n*-BuLi (1.6M in hexane, 5.40 ml, 8.60 mmol, 20.00 equiv). After 5 min the flask was immersed in a cooling bath at –40 °C and kept at this temperature for 10 min. The almost clear solution was then was re-cooled to –78 °C, producing a slightly heterogenous mixture, and $Bu_3SnH$ (2.30 ml, 8.60

[11] The use of KF-Workup: Askani, R.; Keller, U. *Liebigs Ann. Chem.* **1988**, 61.

mmol, 20.00 equiv) was added dropwise, resulting in the immediate formation of a yellow turbid solution with liberation of some gas. After 20 min at –78 °C the mixture was stirred for 15 min at –40 °C, giving an almost clear golden-yellow solution, and then re-cooled to –78 °C. MeOH (1.90 ml, 47.30 mmol, 110.00 equiv) was added under vigorous stirring, the mixture was stirred for 10 min at –78 °C, warmed to –40 °C for 10 min, and then re-cooled to –78 °C. A solution of **35** (175 mg, 0.43 mmol, 1.00 equiv) in THF (5 ml) was then added and the mixture was stirred for 1.5 d, with the temperature being allowed to gradually rise to –15 °C. Saturated aqu $NH_4Cl$ (10 ml) and 25% aqueous $NH_4OH$ (1 ml) were then added together with EtOAc (10 ml), the mixture was stirred for 30 min, and the two almost clear phases were formed that were separated. The aqueous phase was extracted with EtOAc (3 x 10 ml), the combined organic extracts were dried over $MgSO_4$, and the solution was concentrated under reduced pressure. Purification of the residue by flash chromatography on deactivated silica (Hex→EtOAc/Hex 1/100→1/50, 1%(v/v) $NEt_3$) gave the (*E*)-vinyl stannane (223 mg, 0.32 mmol, 74%) as a colorless oil. This material was immediately used in the next step.

A solution of the above (*E*)-vinyl stannane (223 mg, 0.32 mmol, 1.00 equiv) in THF (3 ml) was cooled to –17 °C (NaCl/ice) and a solution of NIS (108 mg, 0.48 mmol, 1.50 equiv) in THF (1 ml) was added with stirring. After 20 min a mixture of saturated aqu $Na_2S_2O_3$ (5 ml) and saturated aqu $NaHCO_3$ (5 ml) was added followed by EtOAc (5 ml). Stirring was continued for 5 min until two clear, colorless phases had formed; the pases were separated, the aqueous phase was extracted with EtOAc (3 x 5 ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (Hex/EtOAc 1/100) gave **36** (166 mg, 0.31 mmol, 98%) as a pale yellow oil.

**TLC**: $R_f$ = 0.72 (EtOAc/Hex 1/20, UV, CPS).

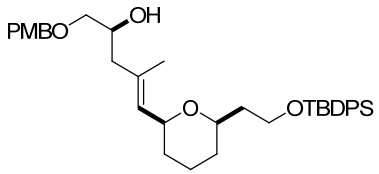
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.67-7.64 (m, 4 H), 7.44-7.35 (m, 6 H), 6.17 (dq, J = 7.7, 1.5, 1 H), 3.99 (ddd, J =11.2, 7.7, 2.1, 1 H), 3.83 (ddd, J = 10.1, 8.1, 5.5, 1 H), 3.70 (dt, J = 10.2, 5.6, 1 H), 3.62-3.56 (m, 1 H), 2.40 (d, J = 1.5, 3 H), 1.86-1.80 (m 1 H), 1.79-1.65 (m, 2 H), 1.58-1.51 (m, 3 H), 1.38-1.31 (m, 1 H), 1.24-1.18 (m, 1 H), 1.04 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 142.5, 135.7, 135.7, 134.1, 134.1, 129.7, 127.7, 98.5, 75.9, 74.6, 60.3, 39.3, 31.4, 31.3, 28.8, 27.0, 23.6, 19.4.

**IR** (thin film): ν 3070, 2931, 2856, 1472, 1428, 1260, 1197, 1105, 1076, 1036, 822, 799.

**HRMS (ESI)**: calculated for $C_{26}H_{35}INaO_2Si$ [$(M+Na)^+$], 557.1343, found 557.1305.

$[\alpha]_D^{24}$: –33.02° (c 0.44, $CHCl_3$).




**(*S*,*E*)-5-((2*S*,6*R*)-6-(2-(*tert*-Butyldiphenylsilyloxy-)ethyl-)tetrahydro-2H-pyran-2-yl)-1-(4-methoxybenzyloxy)-4-methylpent-4-en-2-ol (21).** To a solution of **36** (165.7 mg, 0.31 mmol, 1.00 equiv) in toluene (1 ml) was added *t*-BuLi (1.6M in pentane, 0.33 ml, 0.53 mmol, 1.70 equiv) at –78 °C. The near colorless solution was stirred for 30 min at –78 °C and then further cooled to around –85 °C. A solution of **8** (161 mg, 0.83 mmol, 2.70 equiv) in toluene (1.5 ml) was then added, followed, after 1 min, by $BF_3$•$OEt_2$ (0.10 ml, 0.77 mmol, 2.50 equiv), which produced a pale yellow solution. The mixture was stirred for 1 h at –78 °C; the cooling bath was then removed and saturated aqueous $NaHCO_3$ (10 ml) and EtOAc (10 ml) were added. After the mixture had reached rt, the phases were separated and the aqueous phase was extracted with EtOAc (3 x 5 ml). The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure, and the residue was purified by flash chromatography (EtOAc/Hex 1/7->1/5) to give **21** (58.3 mg, 0.097 mmol, 31%) as a colorless oil.

**Note:** Flash chromatography is difficult and needed to be performed twice (see comments for cpd. **7**), in order to remove the iodohydrine derived from competing epoxide opening by iodide. Best yields were obtained if the starting materials were purified by flash chromatography and azeotropically dried with toluene or acetonitrile immediately before use (see preparation for compound **7**).

**TLC**: $R_f$ = 0.28 (EtOAc/Hex 1/3, UV, CPS).

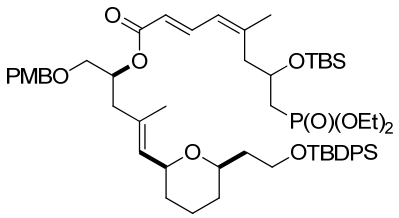
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.69-7.66 (m, 4 H), 7.44-7.34 (m, 6 H), 7.28-7.25 (m, 2 H), 6.90-6.87 (m, 2 H), 5.27 (dq, J = 7.7, 1.2, 1 H), 4.49 (s, 2 H), 4.03 (ddd, J =11.2, 7.6, 2.3, 1 H), 3.99-3.92 (m, 1 H), 3.84 (ddd, J = 10.3, 7.9, 5.5, 1 H), 3.80 (s, 3 H), 3.73 (dt, J = 10.2, 5.7, 1 H), 3.63-3.57 (m, 1 H), 3.46 (dd, J = 9.5, 3.5, 1 H), 3.33 (dd, J = 9.6, 7.1, 1 H), 2.41 (br s., 1 H), 2.20 (d, J = 6.9, 2 H), 1.86-1.76 (m, 2 H), 1.73-1.65 (m, 1 H), 1.68 (d, J = 1.2, 3 H), 1.60-1.48 (m, 3 H), 1.34-1.17 (m, 2 H), 1.06 (s, 9 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.4, 135.7, 135.6, 134.6, 134.2, 134.1, 130.2, 129.8, 129.6, 129.5, 127.7, 113.9, 74.9, 74.5, 73.7, 73.1, 68.6, 60.5, 55.4, 43.7, 39.5, 31.8, 31.4, 27.0, 23.8, 19.4, 17.3.

**IR** (thin film): ν 3442, 2931, 2856, 1612, 1513, 1429, 1388, 1302, 1247, 1110, 1037, 821, 702.

**HRMS (ESI)**: calculated for $C_{37}H_{50}NaO_5Si$ [$(M+Na)^+$], 625.3320, found 625.3320.

$[\alpha]_D^{24}$: –5.02° (c 0.43, $CHCl_3$).




**(2*E*,4*Z*)-((*S*,*E*)-5-((2*S*,6*R*)-6-(2-(tert-butyldiphenylsilyloxy)ethyl)tetrahydro-2H-pyran-2-yl)-1-(4-methoxybenzyloxy)-4-methylpent-4-en-2-yl) 7-(tert-butyldimethylsilyloxy)-8-(diethoxyphosphoryl)-5-methylocta-2,4-dienoate (37).** To a solution of **6** (82.8 mg, 0.20 mmol, 1.55 equiv) in toluene (1 ml) was added $NEt_3$ (0.06 ml, 0.39 mmol, 3.20 equiv) followed by 2,4,6-trichlorobenzoyl chloride (0.038 ml, 0.24 mmol, 1.90 equiv) at rt. The almost clear pale yellow solution was stirred for 1 h; then a solution of alcohol **21** (76.8 mg, 0.127 mmol, 1.00 equiv) and DMAP (23 mg, 0.19 mmol, 1.50 equiv) in toluene (1 ml (the mixture was sonicated to produce a clear solution); plus 2 x 0.5 ml from rinsing)) was added, resultin in the immediate formation of an off-white suspension. After 18 h saturated aqu $NaHCO_3$ (5 ml) and EtOAc (5 ml) were added and the phases were separated. The aqueous layer was extracted with EtOAc (3 x 5 ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash chromatography (EtOAc/Hex 1/3→1/1) afforded ester **37** (96.6 mg, 0.096 mmol, 74 %) as a colorless oil.

**TLC**: $R_f$ = 0.54 (EtOAc/hexane 1/1, UV, $KMnO_4$ or CPS).

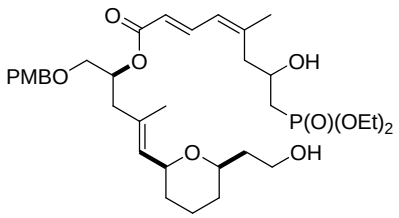
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.67-7.64 (m, 4 H), 7.59 (dd, J = 15.3, 11.9, 1 H), 7.43-7.32 (m, 6 H), 7.25-7.22 (m, 2 H), 6.87-6.84 (m, 2 H), 6.07 (d, J = 11.8, 1 H), 5.80 (d, J = 15.2, 1 H), 5.23 (d, J = 7.8, 1 H), 5.21-5.14 (m, 1 H), 4.48 (d, J = 11.7, 1 H), 4.41 (dd, J = 11.8, 2.6, 1 H), 4.20-4.06 (m, 5 H), 4.01-3.95 (m, 1 H), 3.84-3.78 (m, 1 H), 3.78 (s, 3 H), 3.71 (dt, 10.2, 5.6, 1 H), 3.60-3.53 (m, 1 H), 3.52-3.45 (m, 2 H), 2.64-2.59 (m, 1 H), 2.56 (dd, J = 13.4, 7.9. 1 H), 2.40 (dd, J = 13.6, 8.0, 1 H), 2.30 (ddd, J = 13.8, 5.9, 2.2, 1 H), 2.03 (d, J = 6.4, 1 H), 1.98 (d, J = 6.4, 1 H), 1.89 (s, 3 H), 1.85-1.74 (m, 3 H), 1.71-1.63 (m, 1 H), 1.69 (s, 3 H), 1.58-1.49 (m, 1 H), 1.44-1.40 (m, 1 H), 1.33 (dt, J = 7.1, 2.9, 6 H), 1.26-1.16 (m, 2 H), 1.04 (s, 9 H), 0.83 (s, 9 H), 0.06 (s, 3 H), -0.02, (s, 3 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$; due to the diastereomeric nature of the product, the number of signals in the $^{13}$C-spectrum exceeds the number of carbon atoms): δ 167.1, 159.3, 146.3, 141.5, 141.4, 135.7, 135.6, 134.2, 134.1, 133.9, 133.8, 130.3, 130.1 (2C), 129.6, 129.4 (2C), 127.7, 126.8, 119.8, 119.7, 113.9, 74.9, 74.5, 72.9 (2C), 71.5 (2C), 70.1 (2C), 66.8, 61.7 (d, J = 6.5) (2C), 60.5, 55.3, 41.8, 41.7, 41.0 (2C), 39.5, 35.2 (d, J = 135.0), 31.7, 31.4, 27.0, 25.9, 25.1, 23.8, 19.3, 17.9, 17.3 (2C), 16.5 (d, J = 6.3), -4.6, -4.7.

**IR** (thin film): ν 2930, 2856, 1710, 1636, 1612, 1513, 1472, 1363, 1302, 1248, 1146, 1026, 936, 823, 775, 703.

**HRMS (ESI)**: calculated for $C_{56}H_{85}NaO_{10}PSi_2$ [$(M+Na)^+$], 1027.5311, found 1027.5315.

$[\alpha]_D^{24}$: +1.30° (c 1.30, $CHCl_3$).




**(2*E*,4*Z*)-((*S*,*E*)-5-((2*S*,6*R*)-6-(2-Hydroxyethyl)tetrahydro-2H-pyran-2-yl)-1-(4-methoxybenzyloxy)-4-methylpent-4-en-2-yl) 8-(diethoxyphosphoryl)-7-hydroxy-5-methylocta-2,4-dienoate (38).** To a solution of **37** (96.90 mg, 0.096 mmol, 1.00 equiv) in THF (4 ml) in a polypropylene tube was added 70% HF•py (1 ml) at 0 °C (ice/$H_2O$). The cooling bath was removed after 5 min and stirring was continued at rt for 20 h. The solution was then carefully added to a vigorously stirred mixture of saturated aqu $NaHCO_3$ (50 ml) and EtOAc (10 ml); after ca. 15 min two clear phases had formed which were separated. The aqueous phase was extracted with EtOAc (4 x 10 ml), and the combined organic extracts were washed with saturated aqu $NaHCO_3$ (1x 5 ml) and dried over $MgSO_4$. Concentration under reduced pressure and purification of the residue by flash chromatography (EtOAc→EtOAc/Acetone 1/1) afforded **38** (50.6 mg, 0.078 mmol, 80%) as a colorless, viscous oil.

**Note:** The use of less concentrated aqu $NaHCO_3$ is not recommended for workup, since not all HF may be neutralized, which would in turn lead decomposition of the product during concentration under reduced pressure. In any case the pH of the aqueous phase should be determined after workup and should not be acidic!

**TLC**: $R_f$ = 0.33 (EtOAc/Acetone 1/1, UV, $KMnO_4$ or CPS).

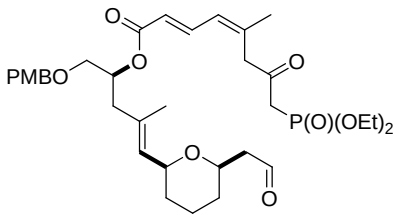
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.54 (ddd, J = 14.7, 11.6, 6.0, 1 H), 7.24-7.21 (m, 2 H), 6.87-6.84 (m, 2 H), 6.13 (d, J = 11.7, 1 H), 5.82 (d, J = 15.1, 1 H), 5.23-5.16 (m, 2 H), 4.48 (dd, J = 11.8, 2.0, 1 H), 4.42 (dd, J = 11.8, 2.5, 1 H), 4.23-4.15 (m, 1 H), 4.18-4.07 (m, 4 H), 4.03-3.97 (m, 1 H), 3.79 (s, 3 H), 3.73-3.64 (m, 3H), 3.62 (br s, 1H), 3.60-3.52 (m, 1H), 3.48 (d, J = 4.8, 2H), 2.98 (br s, 1H), 2.66-2.57 (m, 1H), 2.45 (ddd, J = 13.6, 9.1, 5.5, 1 H), 2.36-2.23 (m, 2 H), 1.96-1.89 (m, 2 H), 1.93 (s, 3 H), 1.81-1.75 (m, 1 H), 1.75-1.61 (m, 2 H), 1.67 (d, J = 1.0, 3 H), 1.52-1.40 (m, 3 H), 1.31, 1.30 (2 x t, J = 7.1, 6 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$; due to the diastereomeric nature of the product, the number of signals in the $^{13}$C-spectrum exceeds the number of carbon atoms): δ 167.0, 159.3, 145.6, 145.5, 140.5, 140.4, 134.0, 133.9, 130.2, 129.8, 129.7, 129.4, 126.8 (2C), 120.2, 120.1, 113.8, 78.2, 78.1, 75.0, 72.9, 71.1, 70.9, 70.5, 70.3, 65.4 (d, J = 5.0), 65.2 (d, J = 5.0), 62.1 (d, J = 6.6), 62.0 (d, J = 6.6), 61.4, 55.3, 41.3 (d, J = 5.9), 41.2 (d, J = 5.9), 41.1, 41.0, 38.3 (2C), 33.6 (d, J = 138.0), 33.5 (d, J = 138.0), 31.4 (2C), 31.3, 31.2, 25.0, 24.8, 23.4 (2C), 17.1 (2C), 16.5 (d, J = 6.2) (2C).

**IR** (thin film): ν 3398, 2929, 2857, 1707, 1633, 1612, 1513, 1367, 1301, 1247, 1148, 1025, 974, 818.

**HRMS (ESI)**: calculated for $C_{34}H_{53}NaO_{10}P$ [$(M+Na)^+$], 675.3269, found 675.3278.

$[\alpha]_D^{24}$: –10.42° (c 1.02, $CHCl_3$).




**(2*E*,4*Z*)-((*S*,*E*)-1-(4-methoxybenzyloxy)-4-methyl-5-((2*S*,6*R*)-6-(2-oxoethyl)tetrahydro-2H-pyran-2-yl)pent-4-en-2-yl) 8-(diethoxyphosphoryl)-5-methyl-7-oxoocta-2,4-dienoate (39)**. To a stirred solution of **38** (32.30 mg, 0.050 mmol, 1.00 equiv) in DCM (1 ml) was added DMP (126 mg, 0.297 mmol, 6.00 equiv, addition in two equal portions, second addition after 30 min) at rt. After 3 h DCM (5 ml) and a mixture of saturated aqueous $NaHCO_3$ (5 ml) and saturated aqueous $Na_2S_2O_3$ (5 ml) were added then stirring was continued for 10 min, when two clear phases had formed. The phases were separated, the aqueous phase was extracted with DCM (3 x 5 ml), and the combined organic extracts were dried over $MgSO_4$. Concentration of the solution under reduced pressure and purification of the residue by flash chromatography (EtOAc, 1% AcOH to deactivate the stationary phase) gave **39** (23.3 mg, 0.036 mmol, 72%) as a pale yellow oil.

**TLC**: $R_f$ = 0.33 (EtOAc, UV, CPS or $KMnO_4$).

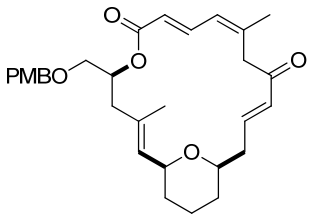
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.74 (t, J = 2.2, 1 H), 7.38 (dd, J = 15.1, 11.7, 1 H), 7.24-7.20 (m, 2 H), 6.87-6.83 (m, 2 H), 6.19 (d, J = 11.5, 1 H), 5.85 (d, J = 15.1, 1 H), 5.21-5.15 (m, 2 H), 4.47 (d, J = 11.8, 1 H), 4.40 (d, J = 11.8, 1 H), 4.19-4.12 (m, 4 H), 4.02 (ddd, J = 11.2, 7.7, 2.3, 1 H), 3.89-3.83 (m, 1 H), 3.79 (s, 3 H), 3.62 (br s, 2 H), 3.49-3.44 (m, 2 H), 3.13 (s, 1 H), 3.07 (s, 1 H), 2.57 (ddd, J = 16.3, 7.7, 2.5, 1 H), 2.43 (ddd, J = 16.3, 4.9, 2.0, 1 H), 2.34 (dd, J = 13.7, 6.9, 1 H), 2.26 (dd, J = 13.7, 7.0, 1 H), 1.88 (s, 3 H), 1.86-1.81 (m, 2 H), 1.67 (d, J = 1.2, 3 H), 1.62-1.56 (m, 1 H), 1.47-1.43 (m, 1 H), 1.33 (t, J = 7.1, 6 H), 1.28-1.20 (m, 2 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 201.8, 198.3 (d, J = 6.8), 166.8, 159.3, 140.9, 139.8, 134.3, 130.2, 129.5, 129.4, 127.6, 121.2, 113.9, 75.1, 72.9, 72.9, 71.3, 70.3, 62.9 (d, J = 6.5), 55.4, 50.1, 47.7, 42.2 (d, J = 127), 41.0, 31.2, 31.1, 25.0, 23.4, 17.2, 16.4 (d, J = 6.0).

**IR** (thin film): ν 2977, 2932, 2915, 2858, 1714, 1638, 1612, 1514, 1440, 1365, 1248, 1020, 971.

**HRMS (ESI)**: calculated for $C_{34}H_{50}O_{10}P$ $[(M+H)^+]$, 649.3136, found 649.3158.

$[\alpha]_D^{24}$ : –0.76° (c 1.15, $CHCl_3$).




**(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*R*)-5-((4-methoxybenzyloxy)methyl)-3,11-dimethyl-6,21-dioxabicyclo [15.3.1]henicosa-2,8,10,14-tetraene-7,13-dione (22)**. To a solution of **39** (22.9 mg, 0.035 mmol, 1.00 equiv, co-evaporated before use with 1 ml of dry toluene) in THF (18 ml) was added a solution of NaHMDS (1M in THF, 0.05 ml, 0.05 mmol, 1.40 equiv, diluted with 5 ml of THF) at –78 °C; an orange color was produced immediately. Stirring was continued while the cooling bath was slowly allowed to warm to rt. After 2 d saturated aqueous $NH_4Cl$ (5 ml), $H_2O$ (1 ml) and EtOAc (5 ml) were added and the phases were separated. The aqueous phase was extracted with EtOAc (3 x 5 ml) and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (EtOAc/Hex 1/4) afforded **22** (8.6 mg, 0.017 mmol, 49%) as a colorless oil.

**Note**: Varying yields between 49% and 90% were observed independent of the scale of the reaction.

**TLC**: $R_f$ = 0.35 (EtOAc/Hex 1/3, UV, CPS or $KMnO_4$).

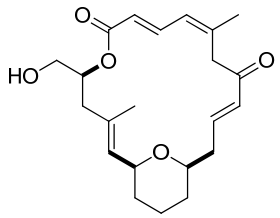
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.62 (dd, J = 15.1, 11.6, 1 H), 7.27-7.24 (m, 2 H), 6.89-6.87 (m, 2 H), 6.84 (ddd, J = 16.5, 9.8, 4.3, 1 H), 6.09 (d, J = 11.6, 1 H), 5.94 (d, J = 15.1, 1 H), 5.90 (d, J = 16.5, 1 H), 5.40-5.34 (m, 1 H), 5.13 (dd, J = 8.0, 0.9, 1 H), 4.52 (d, J = 11.8, 1 H), 4.48 (d, J = 11.8, 1 H), 4.18 (d, J = 13.5, 1 H), 3.99 (ddd, J = 11.3, 8.0, 2.3, 1 H), 3.81 (s, 3 H), 3.57 (dd, J = 10.4, 6.0, 1 H), 3.50 (dd, J = 10.4, 4.9, 1 H), 3.32-3.26 (m, 1 H), 2.99 (d, J = 13.6, 1 H), 2.32 (dddd, J = 15.0, 10.1, 4.4, 2.0, 1 H), 2.19-2.17 (m, 2 H), 2.17-2.12 (m, 1 H), 1.83-1.79 (m, 1 H), 1.78 (s, 3 H), 1.69 (d, J = 1.2, 3 H), 1.55-1.51 (m, 1 H), 1.51-1.42 (m, 2 H), 1.27-1.18 (m, 2 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 198.5, 166.9, 159.4, 147.2, 142.8, 139.3, 131.6, 131.3, 130.3, 130.3, 129.4, 125.6, 121.4, 114.0, 76.1, 75.4, 73.0, 71.7, 69.6, 55.4, 45.1, 42.8, 40.7, 32.0, 31.7, 23.6, 23.5, 16.7.

**IR** (thin film): ν 2978, 2932, 2915, 2858, 1714, 1638, 1612, 1514, 1365, 1248, 1151, 1020, 972.

**HRMS (ESI)**: calculated for $C_{30}H_{39}O_6$ [$(M+H)^+$], 495.2741, found 495.2741.

$[\alpha]_D^{24}$: –198.92° (c 0.36, $CHCl_3$).



**(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*R*)-5-(hydroxymethyl)-3,11-dimethyl-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraene-7,13-dione (5).** To a solution of **22** (8.6 mg, 0.017 mmol, 1.00 equiv) in DCM (0.5 ml) was added $H_2O$ (0.1 ml) followed by DDQ (12 mg, 0.052 mmol, 3.00 equiv) at rt. The mixture was vigorously stirred for 2 h; then saturated aqueous $NaHCO_3$ (5 ml) and DCM (5 ml) were added and the phases were separated. The aqueous phase was extracted with DCM (3 x 5ml) and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the reisdue by flash chromatography (EtOAc/Hex ½→1/1) delivered **5** (4.7 mg, 0.013 mmol, 72%) as an amorphous off-white solid.

**TLC**: $R_f$ = 0.41 (EtOAc/Hex 1/1, UV, CPS or $KMnO_4$).

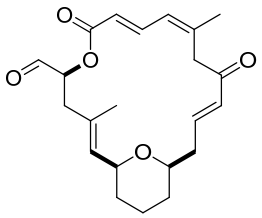
**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.64 (dd, J = 15.1, 11.5, 1 H), 6.85 (ddd, J = 16.2, 9.7, 4.6, 1 H), 6.09 (d, J = 11.9, 1 H), 5.94 (d, J = 15.1, 1 H), 5.94-5.89 (m, 1 H), 5.27 (dddd, J = 10.6, 5.9, 4.1, 2.2, 1 H), 5.15 (d, J = 8.0, 1 H), 4.15 (d, J = 13.7, 1 H), 4.00 (ddd, J = 11.2, 8.0, 2.3, 1 H), 3.77- 3.69 (m, 2 H), 3.34-3.28 (m, 1 H), 3.02 (d, J = 13.7, 1 H), 2.32 (dddd, J = 15.0, 10.2, 4.5, 2.0, 1 H), 2.23 (dd, J = 13.6, 10.8, 1 H), 2.19-2.12 (m, 2 H), 1.84-1.81 (m, 1 H), 1.79 (s, 3 H), 1.71 (d, J = 1.1, 3 H), 1.62-1.58 (m, 2 H), 1.56-1.50 (m, 1 H), 1.48-1.42 (m, 1 H), 1.25-1.17 (m, 2 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 198.3, 167.1, 147.2, 143.3, 139.7, 131.6, 131.3, 130.4, 125.5, 121.0, 76.2, 75.4, 71.9, 65.4, 45.1, 42.1, 40.6, 31.9, 31.7, 23.7, 23.6, 16.7.

**IR** (thin film): ν 3445, 2931, 2856, 1715, 1668, 1635, 1437, 1359, 1280, 1209, 1177, 1150, 1044, 979.

**HRMS (ESI)**: calculated for $C_{22}H_{30}NaO_5$ [$(M+Na)^+$], 397.1985, found 397.1981.

$[\alpha]_D^{24}$: –163.24° (c 0.18, $CHCl_3$).



**(1*S*,2*E*,5*S*,8*E*,10*Z*,14*E*,17*R*)-3,11-dimethyl-7,13-dioxo-6,21-dioxabicyclo[15.3.1]henicosa-2,8,10,14-tetraene-5-carbaldehyde (4).** To a stirred solution of **5** (4.7 mg, 0.013 mmol, 1.00 equiv) in DCM (0.5 ml) was added DMP (22 mg, 0.05 mmol, 4.00 equiv, addition in 2 equal portions, second portion added after 20 min) and stirring was continued for 60 min. A mixture of saturated aqueous $NaHCO_3$ (5 ml) and

saturated aqueous $Na_2S_2O_3$(5 ml) was then added together with DCM (5 ml) and stirring was continued for 10 min, when two practically clear phases had formed. The phases were separated, the aqueous phase was extracted with DCM (3 x 5 ml), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (EtOAc/Hex 1/5→1/3→1/1) afforded **4** (3.7 mg, 0.01 mmol, 77%) as a semi-solid.

**TLC**: $R_f$ = 0.53 (EtOAc/Hex 1/1, UV, CPS).

**$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.67 (s, 1 H), 7.63 (dd, J = 15.2, 11.7, 1 H), 6.85 (ddd, J = 16.2, 8.7, 6.0, 1 H), 6.14 (d, J = 11.7, 1 H), 5.98 (d, J = 16.2, 1 H), 5.96 (d, J = 15.2, 1 H), 5.31 (dd, J = 11.3, 2.5, 1 H), 5.20 (d, J = 8.0, 1 H), 4.00 (ddd, J = 11.5, 8.0, 2.4, 1 H), 3.95 (d, J = 14.4, 1 H), 3.35 (ddt, J = 11.8, 8.9, 2.5, 1 H), 3.23 (d, J = 14.4, 1 H), 2.52 (d, J = 14.1, 1 H), 2.33-2.22 (m, 3 H), 1.86 (s, 3 H), 1.83-1.77 (m, 1 H), 1.71 (d, J = 0.9, 3 H), 154-1.47 (m, 3 H), 1.28-1.21 (m, 2 H).

**$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 199.3, 197.7, 166.5, 146.8, 144.2, 140.5, 131.5, 131.4, 130.1, 125.7, 120.0, 76.1, 75.6, 75.3, 45.0, 40.1, 39.9, 31.8, 31.4, 24.2, 23.5, 16.1.

**IR** (thin film): ν 2929, 2855, 1715, 1669, 1635, 1437, 1354, 1279, 1257, 1208, 1146, 1078, 1045, 979.

**HRMS (ESI)**: calculated for $C_{22}H_{29}O_5$ [$(M+H)^+$], 373.2010, found 373.2021.

$[\alpha]_D^{24}$: –236.81° (c 0.23, $CHCl_3$).