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TETRAHEDRON

trans-C-Glycosides from 8-Oxabicyclo[3.2.1]oct-6-en-3-one – Synthesis of the C3-C13 Segment of the Phorboxazoles A and B

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Abstract: The enantiopure and fully resolved C3-C13 segment of the phorboxazoles A and B has been prepared in 14 steps in 24% overall yield starting from 8-oxabicyclo[3.2.1]oct-6-en-3-one. Key steps are the desymmetrization of the oxabicyclic ketone, the anomeric allylation and the asymmetric allylboration.

The phorboxazoles A and B, first described by Molinski in 1995,[1] are two new highly cytotoxic macrolides. They inhibit growth of tumor cells at subnanomolar concentrations *in vitro* (mean GI_{50} 1.58×10^{-9} M). Unlike antimitotic natural products such as Taxol®[2] or the epothilones[3] they rather arrest the cell cycle during S phase. The structural assignment has resulted from exhaustive NMR studies and comparison of synthetic samples with derivatized fragments of the phorboxazoles after degradation. Since the discovery only few synthetic approaches have been published[4] including a total synthesis of phorboxazole A.[5] The structural novelty and the biological activity has prompted us to start a program towards the total synthesis of these new marine natural products.

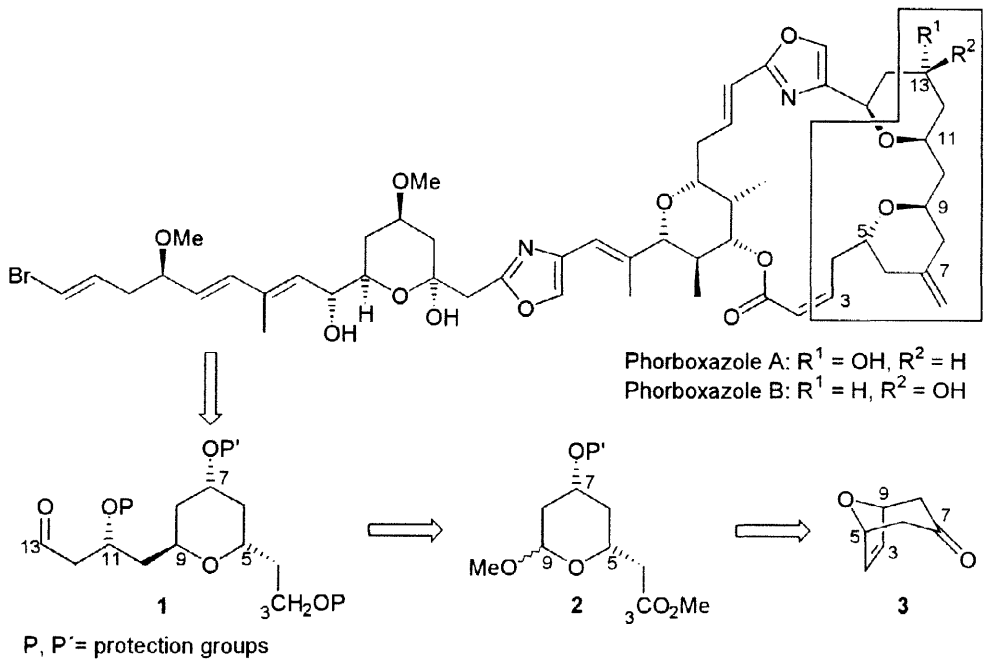

Figure 1 Retrosynthesis for the C3-C13 segment

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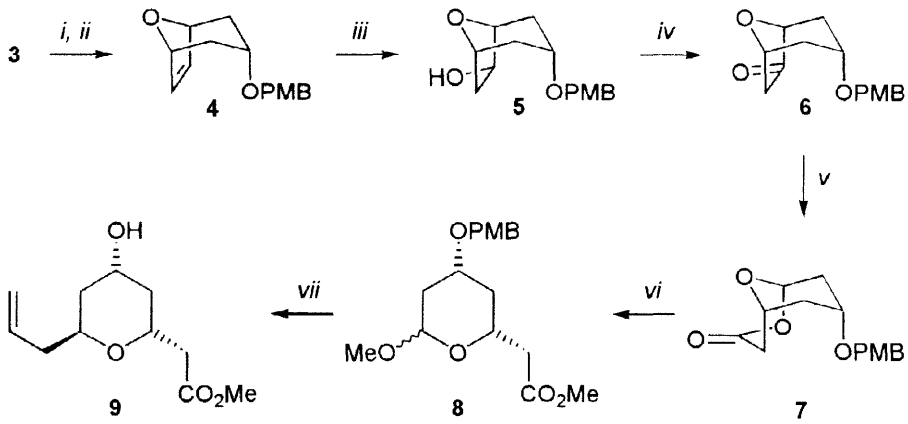
The 21-membered ring system contains three tetrahydropyran rings which can be regarded as 2,6-*trans* and 2,6-*cis* C-glycosides.[6] Our retrosynthetic analysis (Figure 1) involves disconnections between the C2/C3 and the C13/C14 bonds of the phorboxazoles. The C3-C13 segment **1** was to be prepared from methoxyacetal ester **2** which in turn can be generated from oxabicylo[3.2.1]oct-6-en-3-one **3**.[7]

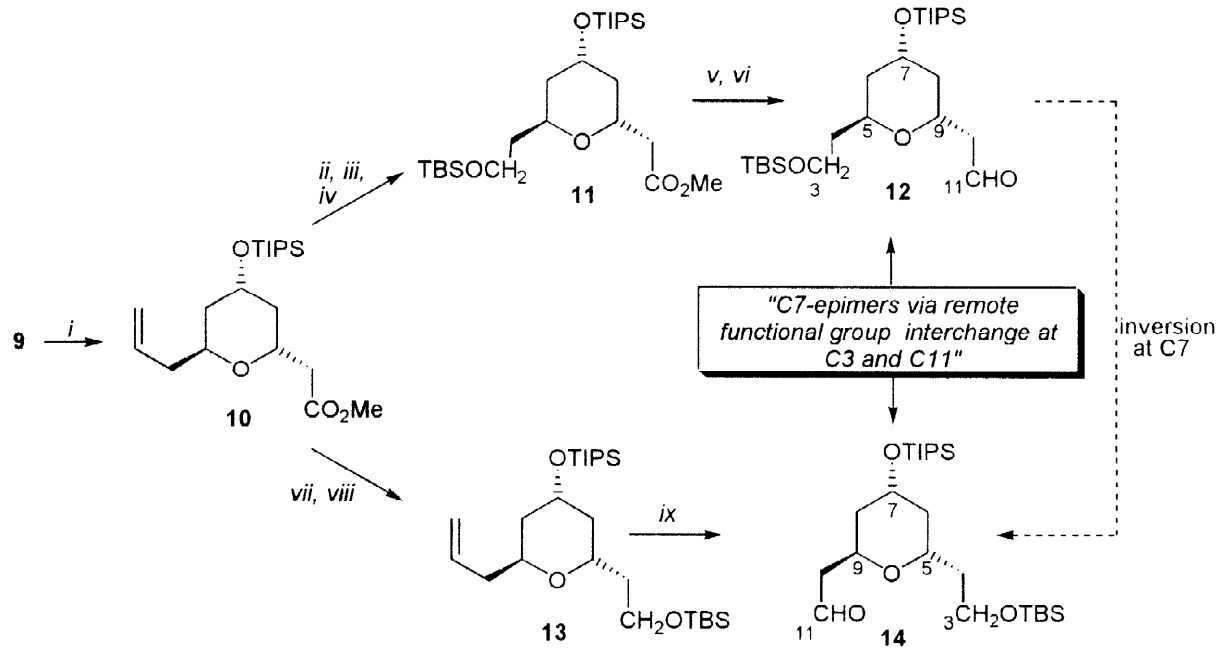
Starting from *meso* oxabicyclic ketone **3**, which can be prepared on a molar scale, stereoselective reduction with L-Selectride® and protection afforded PMB ether **4**. Desymmetrization of the olefinic double bond by asymmetric hydroboration led to alcohol **5** in high chemical yield. Oxidation of the alcohol **5** to the ketone **6** using PCC in dichloromethane and subsequent Baeyer-Villiger oxidation gave lactone **7**. Methoxyacetal ester **8** was generated by methanolysis in the presence of catalytic amounts of sulphuric acid with excellent overall yield over six steps starting from *meso* oxabicyclic ketone **3**. Treatment of methoxyacetal ester **8** with allyltrimethylsilane in the presence of trimethylsilyl triflate in acetonitrile gave diastereomerically pure 2,6-*trans* C-glycoside **9** in excellent yield.[8] The PMB protecting group is not stable to these conditions.



Reagents: (*i*) ref. 7, (*ii*) NaH, PMBCl, tetrabutylammonium iodide, THF, reflux, 6 h (85%), (*iii*) (+)-Ipc_2BH, THF, −10°C, 1 week (85%, 96% *ee*), (*iv*) PCC, DCM, rt, 5 h (92%), (*v*) *m*-CPBA, DCM, rt, overnight (96%), (*vi*) MeOH, conc. H_2SO_4 (catal.), rt, overnight (91%), (*vii*) allyltrimethylsilane, TMSOTf, acetonitrile, −20°C → rt, 1 h (85%, > 99% *de*).

Scheme 1

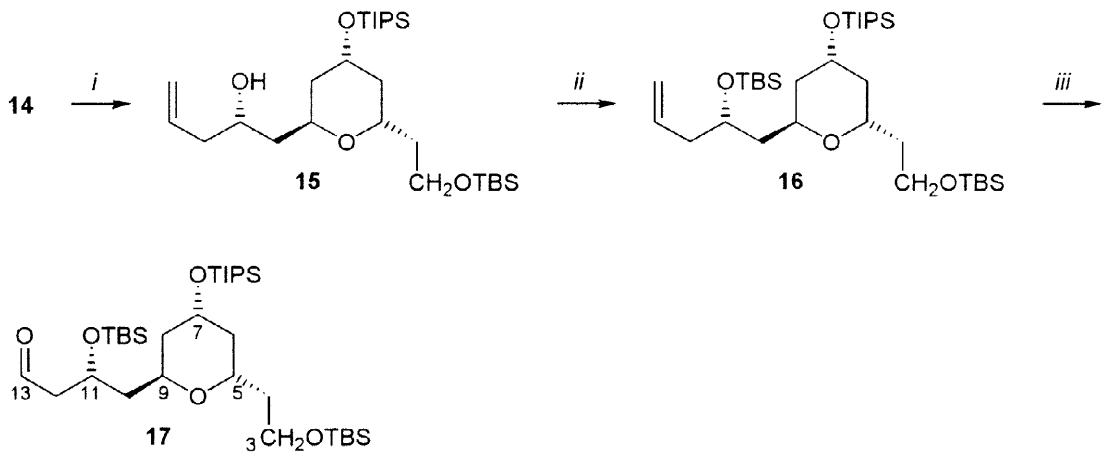
Hydroxy-ester **9** was *O*-silylated leading to the versatile 2,6-*trans* C-glycoside **10**. All three arms of this molecule are differentiated and functionalized chemoselectively (Scheme 2). Ozonolysis of ester **10**, reductive work up with triphenylphosphine,[9] reduction of the aldehyde by sodium borohydride and subsequent protection of the alcohol group led to ester **11**. On the other hand ester **10** was first reduced and then *O*-protected to provide TBS-ether **13**. Reduction of ester **11** and oxidation of the resulting primary alcohol using Dess-Martin periodinane[10] gave aldehyde **12**. Ozonolysis of bis-*O*-silylated ether **13** and subsequent reductive work up with triphenylphosphine afforded aldehyde **14**. The two aldehydes **12** and **14** are *C7-epimers via remote functional group interchange* of the chemodifferentiated side arms at C5 and C9.[11] Put another way, carbon C7 is not touched in our sequence (Scheme 2).



Reagents: (*i*) TIPSCl, imidazole, DMF, rt, 16 h (97%), (*ii*) O_3, DCM, −78°C then PPh_3 (99%), (*iii*) $NaBH_4$, MeOH, 0°C, 15 min (98%), (*iv*) TBSCl, imidazole, DMF, rt, 2 h (95%), (*v*) DIBAH, -20°C, THF, 1 h (92%), (*vi*) Dess-Martin periodinane, DCM, rt, 1 h (91%), (*vii*) DIBAH, -20°C, THF, 2 h, (*viii*) TBSCl, imidazole, DMF, rt, 16 h (88% over 2 steps), (*ix*) O_3, DCM, −78°C then PPh_3 (100%).

Scheme 2

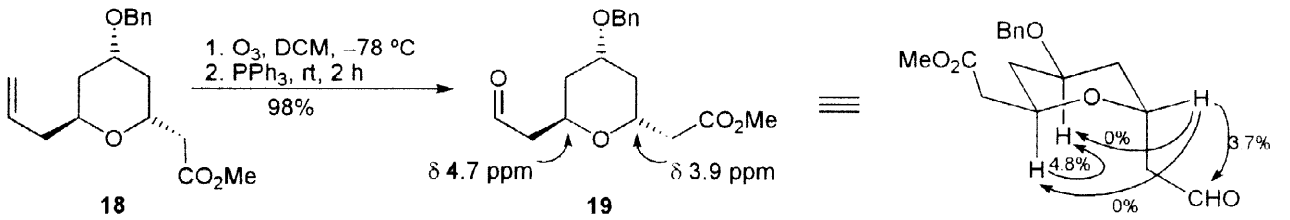
The C3-C13 segment synthesis was completed as shown in Scheme 3. Treatment of aldehyde **14** with (-)-*B*-allyl-β-diisopinocampheyl-borane[12] followed by oxidative work up ($NaOH/H_2O_2$) gave homoallylic alcohol **15** diastereoselectively and in good chemical yield. The alcohol was *O*-silylated with TBS-triflate in dichloromethane in the presence of 2,6-lutidine.[13] Ozonolysis of the allylic double bond led to aldehyde **17** and concluded the synthesis of the fully resolved C3-C13 segment of the phorboxazoles A and B.



Reagents: (*i*) (-)-*B*-allyl-β-diisopinocampheyl-borane, toluene, −78°C, 5 h then H_2O_2, NaOH, 1 h, rt (72%, 92% *de*), (*ii*) TBSOTf, 2,6-lutidine, DCM, 0°C, 30 min (93%), (*iii*) O_3, DCM, −78°C then PPh_3 (98%).

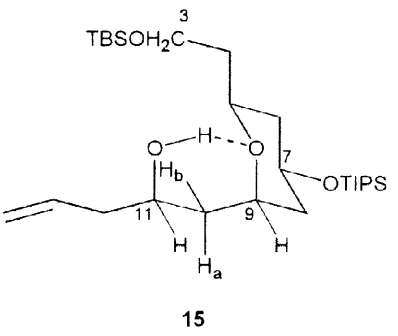
Scheme 3

Spectroscopic investigation of ester **19** *and homoallylic alcohol* **15**. Under conditions similar to those described above ester **19** was prepared from *O*-benzylated 2,6-*trans* C-glycoside **18**. The relative stereochemistry of ester **19** was confirmed by a NOE experiment.

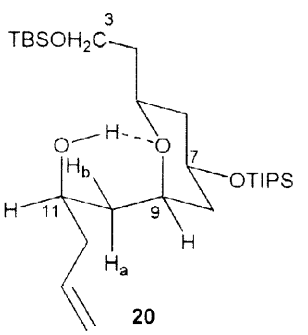


Scheme 4

The relative configuration of homoallylic alcohol **15** was confirmed by coupling constants[14] and spectroscopic comparison with the diastereomeric alcohol **20**, prepared by reaction of aldehyde **13** with (+)-*B*-allyl-β-diisopinocampheyl-borane (Figure 2). Thanks to intramolecular hydrogen bonding the signals of the H_aH_b protons at C10 are well resolved. The coupling constants show that the two alcohols **15** and **20** represent an epimeric pair.



$^2J_{10a,10b}$ = 14.4 Hz, $^3J_{9,10a}$ = 3.1 Hz, $^3J_{10a,11}$ = 3.1 Hz
$^2J_{10a,10b}$ = 14.4 Hz, $^3J_{9,10b}$ = 10.7 Hz, $^3J_{10b,11}$ = 9.2 Hz



$^2J_{10a,10b}$ = 14.4 Hz, $^3J_{9,10a}$ = 9.8 Hz, $^3J_{10a,11}$ = 2.9 Hz
$^2J_{10a,10b}$ = 14.4 Hz, $^3J_{9,10b}$ = 8.9 Hz, $^3J_{10b,11}$ = 3.4 Hz

Figure 2

In conclusion we have developed a straightforward synthesis towards the C3-C13 segment of the phorboxazoles. The 2,6-*trans* C-glycoside **10** is a versatile and attractive chiral building block in natural product synthesis.

Experimental

Infrared spectra were recorded on a Perkin-Elmer 1710 infrared spectrometer. – ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer in deuterated chloroform unless otherwise stated, with tetramethylsilane as internal standard. – Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer at rt unless otherwise stated. – Preparative column chromatography was performed on J. T. Baker silica gel (particle size 30 - 60 μm). – Analytical TLC was carried out on aluminium-backed 0.2-mm silica gel 60 F_{254} plates (E. Merck). – THF was distilled over sodium and benzophenone before use. CH_2Cl_2 (DCM) was distilled over CaH_2 before use. DMF was dried over BaO and distilled over CaH_2 before use. Methyl *t*-butyl ether (MTBE), ethyl acetate (EA) and light petroleum (PE, bp 40-60°C) were distilled before use.

endo-*3-(4-Methoxybenzyl)-oxy-8-oxa-bicyclo[3.2.1]oct-6-ene* **(4)**. To a solution of alcohol **3** (12.6 g, 100 mmol) in THF (130 ml) was added sodium hydride (8 g, 200 mmol, 60% suspension in mineral oil) portionwise under argon atmosphere. The suspension was refluxed for 2 h. Then 4-methoxybenzyl chloride (23.4 g, 20 ml, 150 mmol) and *n*-Bu_4NI (700 mg) were added. The mixture was refluxed for 6 h, stirred overnight at rt and terminated by careful addition of aq. NH_4Cl solution. Water (100 ml) was added and the aqueous layer was extracted with MTBE (5 × 100 ml). The combined organic layer was washed with brine, dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography (SiO_2; PE→MTB/PE, 1:1) and subsequently recrystallized (MTB/THF) to afford PMB ether **4** (20.92 g, 85%), colourless crystals, mp 87°C, $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2952, 2860, 2836, 2352, 1612, 1584, 1512, 1464, 1420, 1396, 1344, 1300, 1280, 1248, 1172, 1112, 1068, 1036, 960, 912, 888, 848, 824, 712. ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.21 (m, 2 H), 6.91-6.86 (m, 2 H), 6,34 (s, 2 H), 4.66 (d, ^2J 4.1 Hz, 2 H), 4.36 (s, 2 H), 3.76 (s, 3 H), 3.69-3.66 (dd, ^3J 5.9 Hz, ^3J 0.9 Hz, 1 H), 2.12-2.05 (ddd, ^2J 15.1 Hz, ^3J 5.9 Hz, ^3J 4.2 Hz, 2 H), 1.76 (dd, ^2J 15.1 Hz, ^3J 0.9 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (Ar-C), 133.8 (Ar-C), 131.1 (Ar-C), 128.7 (HC=CH), 113.7 (Ar-C), 77.6 (OCH), 70.9 (OCH), 69.9 (OCH_2), 55.3 (OCH_3), 32.2 (CH_2); MS (rt): $M^+ + 1$ = 247 (1.2), M^+ = 246 (6.7), 137 (2.6), 135 (3.2), 121 (100), 109 (3.1), 91 (3.4), 84 (33.9), 69 (13.1); HRMS calcd for $C_{15}H_{18}O_3$ (M^+) 246.1256, found 246.1250.

(1R,3R,5S,6R)-3-(4-Methoxybenzyl)-oxy-8-oxa-bicyclo[3.2.1]octan-6-ol **(5)**. To a solution of (–)-α-pinene (11.4 ml, 70.4 mmol) in THF (8.7 ml) was added BH_3·DMS (2.7 ml, 28 mmol) under argon. Stirring was stopped after 5 min yielding crystals of (+)-$(Ipc)_2BH$ overnight. The remaining solution was removed *via* syringe, the solid was powdered, washed with diethyl ether at –78°C and dried *in vacuo*. At –78°C alkene **4** (4.26 g, 17.3 mmol) in THF (5 ml) was added. The highly viscous mixture was stored for 1 week in a freezer (–10°C) and shaken occasionally. To the resulting homogeneous oil was added MeOH (2.5 ml), NaOH (12 ml, 2 M aq. solution) and 35% H_2O_2 (7 ml) at 0°C. The mixture was stirred for 30 min at rt, poured into water (20 ml) and extracted with DCM (5 × 20 ml). The combined organic layer was dried ($MgSO_4$) and evaporated. The crude product was chromatographed (SiO_2; EA) to give alcohol **5** (3.88 g, 85%, 96% *ee*), colourless crystals, mp 118°C, $[\alpha]_D^{20}$ = +3.1 (c = 1, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3592, 3000, 2952, 2864, 2836, 1612, 1584, 1512, 1464, 1440, 1420, 1396, 1364, 1336, 1300, 1248, 1172, 1084, 1060, 1032, 936, 864, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.21 (m, 2 H), 6.91-6.87 (m, 2 H), 4.66 (m, 1 H), 4.46 (m, 1 H), 4.34 (s, 2 H), 4.08 (m, 1 H), 3.77 (s, 3 H), 3.62 (m, 1 H), 2.80 (dd, ^3J 13 Hz, ^3J 7 Hz, 1 H), 2.04 (br. s, 1 H), 1.93-1.88 (m, 3 H), 1.75-1.69 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (Ar-C), 130.7 (Ar-C), 128.7 (Ar-C), 113.8 (Ar-C), 82.5 (OCH), 75.8 (OCH), 74.6 (OCH), 70.8 (OCH), 70.2 (OCH_2), 55.3 (OCH_3), 41.8 (CH_2), 34.6, 33.0 (CH_2); MS (rt): $M^+ + 1$ = 265 (1.2), M^+ = 264 (6.7), 167 (1), 149 (2.3), 137 (6.6), 136 (3.3), 135 (4.6), 123 (2.9), 122 (33.3), 121 (100), 109 (2.5), 107 (3.0), 91 (3.4), 84 (2.0), 82 (7.2), 77 (7.3), 69 (5.0); HRMS calcd for $C_{15}H_{20}O_4$ (M^+) 264.1362, found 264.1349.

(1R,3R,5S)-3-(4-Methoxybenzyl)-oxy-8-oxa-bicyclo[3.2.1]octan-6-one **(6)**. To a suspension of PCC (4.72 g, 22 mmol) on silica gel (6 g) in DCM (20 ml) was added alcohol **5** (3.8 g, 14.4 mmol) in DCM (20 ml) dropwise under argon. The mixture was stirred for 5 h at rt and chromatographed (SiO_2; EA/PE, 1:1) to afford ketone **6** (3.47 g, 92%), white crystals, mp 73°C, $[\alpha]_D^{20}$ = +27.9° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2960, 2928, 2872, 2836, 1756, 1612, 1512, 1464, 1440, 1420, 1400, 1348, 1324, 1304, 1248, 1176, 1148, 1072, 1032, 972, 884, 864, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.21 (m, 2 H), 6.89-6.87 (m, 2 H), 4.74 (m, 1 H), 4.50 (d, ^2J 11.2 Hz, 1 H), 4.23 (d, ^2J 11.2 Hz, 1 H), 3.99 (m, 1 H), 3.80 (m, 4 H), 2.80-2.75 (d, ^2J 16.5 Hz, 1 H), 2.61-2.55 (m, 1 H), 2.27-2.21 (m, 2 H), 2.03 (dt, ^2J 14.7 Hz, ^3J 4 Hz, 1 H), 1.89 (dd, ^2J 14.7 Hz, ^3J 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.2 (C=O), 159.1 (Ar-C), 130.1 (Ar-C), 129.0 (Ar-C), 113.8 (Ar-C), 75.2 (OCH), 73.7 (OCH), 70.5 (OCH), 69.8 (OCH_2), 55.3 (OCH_3), 42.5 (CH_2), 34.5, 33.1 (CH_2); MS (120°C): $M^+ + 1$ = 263 (2.3), M^+ = 262 (6.6), 191 (3.2), 143 (2.3), 141 (8.2), 137 (4.5), 135 (3.4), 123 (3.6), 122 (20.5), 121 (100), 109 (3.8), 97 (3.0), 91 (6.5), 85 (4.3), 77 (8.8), 69 (8.3); HRMS calcd for $C_{15}H_{18}O_4$ (M^+) 262.1205, found 262.1202.

(1R,5R,7R)-7-(4-Methoxybenzyl)-oxy-2,9-dioxa-bicyclo[3.3.1]nonan-3-one **(7)**. To a solution of ketone **6** (3.21 g, 12.2 mmol) in DCM (100 ml) was added $NaHCO_3$ (2.1 g, 25 mmol) followed by *m*-CPBA (5.2 g,

~70%, 21 mmol). The mixture was stirred overnight at rt, diluted with DCM (400 ml) and washed with sat. aq. $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (SiO_2; EA/PE, 1:1) to yield lactone **7** (3.26 g, 96%), colourless crystals, mp 101°C, $[\alpha]_D^{20}$ = +43.0° (c = 0.5, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2960, 2872, 2836, 1748, 1612, 1512, 1464, 1440, 1420, 1384, 1344, 1304, 1280, 1228, 1180, 1104, 1032, 972, 864, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27-7.24 (m, 2 H), 6.89-6.86 (m, 2 H), 5.72 (m, 1 H), 4.57 (d, ^2J 11.8 Hz, 1 H), 4.31 (d, ^2J 11.8 Hz, 1 H), 4.46-4.43 (m, 1 H), 3.91 (m, 1 H), 3.80 (m, 4 H), 2.97 (ddd, ^2J 17.7 Hz, ^3J 8.3 Hz, ^4J 0.9 Hz, 1 H), 2.64 (d, ^2J 17.7 Hz, 1 H), 2.40 (dq, ^2J 15.1 Hz, $^{3/4}J$ 2 Hz, 1 H), 2.20 (dt, ^2J 14.7 Hz, ^3J 4.7 Hz, 1 H), 2.00-1.95 (m, 1 H), 1.86 (dt, ^2J 15.1 Hz, ^3J 3.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (C=O), 159.2 (Ar-C), 132.1 (Ar-C), 129.5 (Ar-C), 113.8 (Ar-C), 96.8 (OCHO), 69.9 (OCH_2), 68.0 (OCH), 65.8 (OCH), 55.4 (OCH_3), 35.8 (CH_2), 33.6 (CH_2), 31.5 (CH_2); MS (130°C): M^+ = 278 (4.1), 189 (1.2), 176 (4.8), 163 (1.7), 150 (33.9), 137 (43.6), 135 (15.4), 124 (9.6), 122 (10.6), 121 (100), 109 (6.5), 96 (15.8), 91 (3.4), 83 (9.7), 82 (7.5), 77 (12.7); HRMS calcd for $C_{15}H_{18}O_5$ (M^+) 278.1154, found 278.1155.

[(2R,4R,6R)-6-Methoxy-4-(4-methoxybenzyl)-oxy-tetrahydropyran-2-yl]-acetic acid methyl ester (**α-8**). To a solution of lactone **7** (3.12 g, 11.2 mmol) in dry MeOH (20 ml) was added conc. H_2SO_4 (0.2 ml) and the mixture was stirred at rt overnight. The mixture was diluted with DCM (100 ml), washed with sat. aq. $NaHCO_3$ solution (20 ml), dried ($MgSO_4$) and evaporated. Column chromatography (SiO_2; EA/PE, 1:3) of the crude product afforded esters **α-8** and **β-8** (3.29 g, 91%, α:β > 10:1), colourless oil, $[\alpha]_D^{20}$ = −28.0° (c = 1.66, $CHCl_3$). Data for the α-anomer: $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2972, 2936, 2896, 2836, 1736, 1612, 1512, 1440, 1388, 1368, 1324, 1300, 1248, 1152, 1120, 1104, 1044, 972, 932, 876; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2 H), 6.89-6.87 (m, 2 H), 4.85 (d, ^3J 2.9 Hz, 1 H), 4.47 (s, 2 H), 4.21-4.15 (m, 1 H), 3.92-3.86 (m, 1 H), 3.80 (s, 3 H), 3.70 (s, 3 H), 3.33 (s, 3 H), 2.55 (d, ^3J 8.8 Hz, 1 H), 2.48 (d, ^3J 4.4 Hz, 1 H), 2.19-2.15 (m, 1 H), 2.11-2.07 (m, 1 H), 1.58-1.51 (m, 1 H), 1.32 (q, $^{2/3}J$ 11.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5 (C=O), 159.2 (Ar-C), 131.6 (Ar-C), 129.2 (Ar-C), 113.9 (Ar-C), 99.1 (OCHO), 70.3 (OCH), 69.7 (OCH_2), 64.6 (OCH), 55.3 (Ar-OCH_3), 54.6 (OCH_3), 51.7 (CO_2CH_3), 40.8 (CH_2), 37.6, 36.3 (CH_2); MS (90°C): M^+ − 324 (0.2), 292 (2.6), 274 (0.2), 248 (0.2), 186 (1.2), 176 (2.5), 163 (0.9), 150 (20.6), 137 (15.8), 122 (10.6), 121 (100), 109 (2.6), 97 (5.3), 85 (5.9), 78 (7.5); HRMS calcd for $C_{17}H_{24}O_6$ (M^+) 324.1573, found 324.1578.

[(2R,4S,6S)-6-Allyl-4-hydroxy-tetrahydropyran-2-yl]-acetic acid methyl ester (**9**). To a solution of ester **α/β-8** (3.24 g, 10 mmol) and allyltrimethylsilane (9 ml, 6.47 g, 56.8 mmol) in acetonitrile (15 ml) was added TMSOTf (1.82 ml, 2.22 g, 10 mmol) dropwise at −20°C. The mixture was warmed up slowly to rt, stirred for 1 h, diluted with MTBE (25 ml) and washed with sat. aq. $NaHCO_3$ solution. The aqueous layer was extracted with MTBE (5 × 20 ml) and the combined organic layer was dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography (SiO_2; MTB/PE, 1:1) to give ester **9** (1.85 g, 85%), colourless oil, $[\alpha]_D^{20}$ = −50.5° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3608, 3080, 3000, 2952, 2840, 1732, 1632, 1612, 1584, 1512, 1440, 1380, 1356, 1316, 1304, 1248, 1176, 1068, 1036, 920, 832, 540; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84-5.71 (m, 1 H), 5.09-5.02 (m, 2 H), 4.13-4.01 (m, 3 H), 3.67 (s, 3 H), 2.69-2.45 (m, 2 H), 2.49-2.41 (m, 1 H), 2.22-2.15 (m, 1 H), 2.12 (s, 1 H), 2.01-1.95 (m, 1 H), 1.84-1.78 (m, 1 H), 1.57 (ddd, ^2J 12.8 Hz, ^3J 9.6 Hz, ^3J 5.3 Hz, 1 H), 1.53 (dt, $^{2/3}J$ 12.8 Hz, ^3J 9.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8 (C=O), 134.8 (=CH), 116.9 (=CH_2), 71.3, 66.0, 65.3 (OCH), 51.6 (OCH_3), 40.7 (CH_2), 39.6, 37.1 (CH_2), 36.8 (CH_2); MS (rt): $M^+ - OCH_3$ = 183 (1.4), $M^+ - C_3H_5$ = 173 (6.1), 155 (76.5), 141 (10.6), 123 (25.6), 113 (6.8), 102 (9.8), 97 (18.8), 81 (100); HRMS calcd for $C_8H_{13}O_4$ ($M^+ - C_3H_5$) 173.0813, found 173.0802.

(2R,4S,6S)-(6-Allyl-4-triisopropylsilyloxy-tetrahydropyran-2-yl)-acetic acid methyl ester (**10**). A mixture of alcohol **9** (272 mg, 1.27 mmol), imidazole (218 mg, 3.25 mmol) and triisopropylsilyl chloride (293 mg, 1.5 mmol) in DMF (3 ml) was stirred for 16 h at rt. MTBE (5 ml) was added and the mixture was washed with sat. aq. $NaHCO_3$ solution. The aqueous layer was extracted with MTBE (3 × 10 ml) and the combined organic layer was dried ($MgSO_4$). The solvent was removed and the crude product was purified by column chromatography (SiO_2; MTBE/PE, 1:5) to afford ester **10** (446 mg, 97%), colourless oil, $[\alpha]_D^{20}$ = −29.8° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2944, 2892, 2864, 1732, 1464, 1436, 1384, 1324, 1284, 1164, 1124, 1064,

1036, 996, 916, 880, 808; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83-5.72 (m, 1 H), 5.10-5.03 (m, 2 H), 4.22-4.02 (m, 3 H), 3.67 (s, 3 H), 2.83-2.53 (m, 2 H), 2.45-2.37 (m, 1 H), 2.23-2.16 (m, 1 H), 1.96-1.91 (m, 1 H), 1.74-1.61 (m, 2 H), 1.49-1.41 (m, 1 H), 1.14-0.91 (m, 21 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0 (C=O), 134.9 (=CH), 116.7 (=CH_2), 69.8, 67.2, 64.8 (OCH), 51.6 (OCH_3), 40.3 (CH_2), 39.2, 38.0 (CH_2), 37.8 (CH_2), 17.7 ($SiCH(CH_3)_2$), 12.2 ($SiCH(CH_3)_2$); MS (90°C): M^+ = 370 (0), 339 (2.8), 327 (24.7), 309 (1.0), 286 (2.3), 259 (23.0), 229 (11.5), 205 (1.6), 185 (7.0), 155 (10.9), 145 (5.6), 131 (93.0), 103 (76.5), 89 (12.7), 75 (100); HRMS calcd for $C_{19}H_{35}O_3Si$ ($M^+ - OCH_3$) 339.2355, found 339.2361.

[(2R,4S,6S)-6-(2-tert.-Butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran-2-yl]-acetic acid methyl ester **(11)**. A solution of ester **10** (2.8 g, 7.6 mmol) in DCM (30 ml) was ozonized at –78°C until saturation with ozone occurred (light-blue colour). PPh_3 (5.9 g, 23 mmol) was added and the mixture was allowed to warm up to rt. After stirring for 2 h at rt the solvent was removed and the crude product purified by column chromatography (SiO_2; MTBE/PE, 1:5 → MTBE/PE, 1:1) to yield the aldehyde (2.8 g, 99%), colourless crystals. To a solution of the aldehyde (372 mg, 1 mmol) in MeOH (5 ml) was added sodium borohydride (40 mg, 1.06 mmol) portionwise at 0°C. The mixture was stirred for 15 min. Then sat. aq. solution of NH_4Cl (5 ml) was added and the mixture was allowed to warm up to rt. The aqueous layer was extracted with EA (3 × 20 ml), the combined organic layer was dried ($MgSO_4$) and evaporated. Column chromatography (SiO_2; MTBE/PE, 1:1) afforded the alcohol (367 mg, 98%) as colourless oil. A solution of the alcohol (187 mg, 0.5 mmol), imidazole (85 mg, 1.25 mmol) and *tert.*-butyldimethylsilyl chloride (95 mg, 0.6 mmol) in DMF (2 ml) was stirred overnight under argon atmosphere. MTBE (20 ml) was added and the mixture was washed with sat. aq. $NaHCO_3$ solution (10 ml). The aqueous layer was extracted with MTBE (3 × 10 ml) and the combined organic layer was dried ($MgSO_4$). After removal of the solvent the crude product was purified by column chromatography (SiO_2; MTBE/PE, 1:3) to give ester **11** (203 mg, 95%), colourless oil, $[\alpha]_D^{20}$ = –29.2° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)$/ cm^{-1} 3000, 2948, 2892, 2864, 1732, 1464, 1436, 1388, 1360, 1324, 1256, 1196, 1160, 1088, 1024, 956, 916, 880 836; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21-4.09 (m, 3 H), 3.68-3.65 (m, 2 H), 3.68 (s, 3 H), 2.74 (dd, ^2J 15.2 Hz, ^3J 8.6 Hz, 1 H), 2.51 (dd, ^2J 15.2 Hz, ^3J 4.8 Hz, 1 H), 1.97-1.89 (m, 2 H), 1.71-1.68 (m, 2 H), 1.59-1.51 (m, 1 H), 1.46-1.39 (m, 1 H), 1.07-1.03 (m, 21 H), 0.88 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1 (C=O), 67.4, 66.7, 65.0 (OCH), 59.8 (OCH_2), 51.5 (OCH_3), 40.5, 39.7, 39.0, 35.8 (CH_2), 25.7 ($SiC(CH_3)_3$), 18.3 ($SiCH(CH_3)_2$), 18.1 ($SiC(CH_3)_3$) 12.3 ($SiCH(CH_3)_2$), –5.4 ($Si(CH_3)_2$); MS (rt): M^+ = 488 (0), 473 (1.6), 457 (4.2), 445 (73.4), 431 (32.2), 359 (6.9), 285 (46.3), 259 (100), 229 (27.5), 197 (8.0), 171 (11.8), 157 (14.9), 131 (65.6), 115 (19.7), 89 (56), 73 (38.5); HRMS calcd for $C_{24}H_{49}O_5Si_2$ ($M^+ - CH_3$) 473.3117, found 473.3117.

2-[(2S,4R,6S)-6-(2-tert.-Butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran-2-yl]-ethanol **(12)**. To a solution of ester **11** (250 mg, 0.51 mmol) in toluene (5 ml) was added DIBAH (1.1 ml, 1.28 mmol, 1.2 M solution in toluene) dropwise at –20°C under N_2 and stirred for 1 h. MeOH (0.1 ml) was added carefully, followed by sat. aq. solution of potassium sodium tartrate (10 ml) and the mixture was stirred for 1 h. MTBE (20 ml) was added and the aqueous layer was extracted with MTBE (3 × 20 ml). The combined organic layer was dried ($MgSO_4$) and the solvent was removed. The crude product was purified by column chromatography (SiO_2; MTBE/PE, 1:3) to afford the alcohol (215 mg, 92%), colourless oil. To a solution of Dess-Martin periodinane (150 mg, 0.35 mmol) in DCM (1 ml) was added dropwise a solution of the alcohol (150 mg, 0.32 mmol) in DCM (1 ml). The mixture was stirred for 1 h and then poured into MTBE (20 ml). NaOH (10 ml, 2 N aq. solution) was added and the mixture was stirred for 10 min. The layers were separated and the aqueous layer was extracted with MTBE (3 × 20 ml). The combined organic layer was dried ($MgSO_4$), evaporated and purified by column chromatography (SiO_2; MTBE/PE, 1:3) to afford aldehyde **12** (135 mg, 91%), colourless oil, $[\alpha]_D^{20}$ = –33.0° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2948, 2892, 2864, 1724, 1464, 1384, 1360, 1256, 1172, 1120, 1088, 1032, 1012, 956, 916, 880, 836; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1 H), 4.28-4.12 (m, 3 H), 3.67 (dd, ^3J 7.4 Hz, ^3J 5.5 Hz, 2 H), 2.89 (m, 1 H), 2.60 (m, 1 H), 1.96-1.43 (m, 4 H), 1.65-1.55 (m, 1 H), 1.50-1.43 (m, 1 H), 1.26 (s, 1 H), 1.09-1.04 (m, 21 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0 (C=O), 66.9, 65.4, 64.9 (OCH), 59.7 (OCH_2), 48.9 (CH_2), 39.5, 39.0, 36.0 (CH_2), 25.9 ($SiC(CH_3)_3$), 18.3 ($SiCH(CH_3)_2$), 18.1 ($SiC(CH_3)_2$), 12.3 ($SiCH(CH_3)_2$), –5.4 ($Si(CH_3)_2$); MS (rt): M^+ 456 (0),

416 (36.8), 343 (23.4), 283 (12.8), 269 (8.3), 239 (9.6), 227 (100), 197 (12.6), 185 (26.2), 157 (20.5), 131 (39.3), 116 (22.4), 101 (28.3), 90 (56.3), 73 (49.9); HRMS calcd for $C_{21}H_{43}O_4Si_2$ ($M^+-C_3H_7$) 415.2700, found 415.2707.

(2S,4S,6S)-6-Allyl-2-(2-tert.-butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran **(13)**. To a solution of ester **10** (2 g, 5.4 mmol) in THF (40 ml) was added DIBAH (10.8 ml, 13 mmol, 1.2 M solution in toluene) at –20°C. The mixture was stirred for 2 h at –20°C. MeOH (1 ml) was added carefully, followed by sat. aq. potassium sodium tartrate solution (40 ml) and the mixture was strirred for 1 h. The aqueous layer was extracted with EA (3 × 30 ml) and the combined organic layer was dried ($MgSO_4$) and evaporated. Column chromatography (SiO_2; MTBE) afforded the alcohol (1.68 g, 91%). A mixture of the alcohol (1.5 g, 4.39 mmol), imidazole (746 mg, 11 mmol) and *tert.*-butyldimethylsilyl chloride (793 mg, 5.27 mmol) in DMF (15 ml) was stirred overnight at rt. MTBE (50 ml) was added and the mixture was washed with with sat. aq. $NaHCO_3$ solution (30 ml). The aqueous layer was extracted with MTBE (5 × 30 ml). The combined organic layer was dried ($MgSO_4$), evaporated and purified by column chromatography (SiO_2; MTB/PE, 1:5) to give alcohol **13** (2 g, 97%), colourless oil, $[\alpha]_D^{20}$ = –31.3° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2944, 2892, 2864, 1464, 1388, 1256, 1176, 1088, 1004, 964, 916, 880, 836; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84-5.74 (m, 1 H), 5.09-5.02 (m, 2 H), 4.13-3.98 (m, 2 H), 3.84-3.78 (m, 3 H), 2.44-2.37 (m, 1 H), 2.22-2.15 (m, 1 H), 1.98-1.87 (m, 2 H), 1.74 (ddd, ^2J 13.1 Hz, ^3J 4.2 Hz, ^3J 1.4 Hz, 1 H), 1.67-1.59 (m, 2 H), 1.36 (dt, $^{2/3}J$ 12.9 Hz, ^3J 8.7 Hz, 1 H), 1.05-1.03 (m, 21 H), 0.89-0.86 (s, 9 H), 0.05-0.03 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.2 (=CH), 116.6 ($=CH_2$), 70.3, 66.5, 65.0 (OCH), 59.9 (OCH_2), 40.5 (CH_2), 38.5, 38.2 (CH_2), 37.4 (CH_2), 25.9 ($SiC(CH_3)_3$), 18.3 ($SiC(CH_3)_3$), 18.1 ($SiCH(CH_3)_2$), 12.3 ($SiCH(CH_3)_2$), –5.3 ($Si(CH_3)_2$); MS (rt): M^+ = 456 (0.6), 442 (0.7), 414 (33.3), 400 (20.7), 372 (5.7), 346 (32.7), 241 (28.1), 227 (27.1), 197 (15.6), 185 (27.3), 157 (15.2), 131 (100), 115 (19.6), 101 (20.8), 89 (67.7), 73 (40.4); HRMS calcd for $C_{22}H_{45}O_3Si_2$ (M^+ – C_3H_7) 413.2907, found 413.2915.

[(2R,4R,6S)-6-(2-tert.-Butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran-2-yl]-acetaldehyde **(14)**. A solution of bis-*O*-silylether **13** (456 mg, 1 mmol) in DCM (10 ml) was ozonized at –78°C until saturation with ozone occurred (light-blue colour). PPh_3 (524 mg, 2 mmol) was added and the mixture was allowed to reach rt. After stirring for 2 h at rt the solvent was removed and the crude product purified by column chromatography (SiO_2; MTBE/PE, 1:15 → MTB/PE, 1:3) to yield aldehyde **14** (458 mg, 100%), colourless oil, $[\alpha]_D^{20}$ = –32.4° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3000, 2948, 2892, 2864, 2728, 1724, 1464, 1388, 1360, 1296, 1256, 1204, 1176, 1100, 1036, 1012, 956, 920, 880, 836; ^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (dd, ^3J 2.3 Hz, ^3J 2 Hz, 1 H), 4.62-4.58 (m, 1 H), 4.14-4.09 (m, 1 H), 3.92-3.85 (m, 1 H), 3.65 (dd, ^3J 7.4 Hz, ^3J 5.5 Hz, 2 H), 2.77-2.72 (m, 1 H), 2.46-2.41 (m, 1 H), 2.08-2.01 (m, 1 H), 1.87 (dt, $^{2/3}J$ 12.8 Hz, ^3J 4.2 Hz, 1 H), 1.72-1.63 (m, 3 H), 1.47-1.41 (m, 1 H), 1.05 (m, 21 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0 (C=O), 67.3, 64.9, 64.8 (OCH), 59.7 (OCH_2), 47.2 (CH_2), 39.3, 38.9, 37.9 (CH_2), 25.9 ($SiC(CH_3)_3$), 18.09 ($SiCH(CH_3)_2$), 18.07 ($SiC(CH_3)_3$), 12.3 ($SiCH(CH_3)_2$), –5.4 ($Si(CH_3)_2$); MS (rt): M^+ = 458 (0.9), 443 (2.8), 415 (44.3), 401 (52.5), 371 (9.5), 357 (8.6), 329 (20.1), 284 (9.6), 255 (5.4), 241 (18.1), 229 (100), 197 (17.9), 185 (32.6), 157 (23.1), 131 (53.0), 115 (25.1), 101 (36.5), 89 (71.2), 73 (51.2), HRMS calcd for $C_{21}H_{43}O_4Si_2$ (M^+ – C_3H_7) 415.2700, found 415.2708.

(2S)-1-[(2S,4R,6S)-6-(2-tert.-Butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran-2-yl]-pent-4-en-2-ol **(15)**. To a solution of (–)-*B*-methoxy-β-diisopinocampheyl-borane (840 mg, 2.66 mmol) in toluene (10 ml) was added allylmagnesium bromide (2.6 ml, 2.6 mmol, 1 M in diethyl ether) at –78°C under argon. The mixture was stirred for 15 min at the same temperature and for 2 h at rt. Then 7 ml of the (–)-*B*-allyl-β-diisopinocampheyl-borane solution (1.47 mmol, 0.21 M solution) were added *via* syringe to aldehyde **14** (458 mg, 1 mmol) in toluene (5 ml) at –78°C. The mixture was stirred for 3 h at the same temperature and then allowed to warm up to rt. NaOH (3 ml, 2 M aq. solution) and 35% H_2O_2 (3 ml) were added, the mixture was stirred for 1 h and then neutralized with H_2SO_4 (2 M). The aqueous layer was extracted with MTBE (3 × 20 ml), the combined organic layer washed with brine and dried ($MgSO_4$). Column chromatography (SiO_2; MTB/PE, 1:5) afforded alcohol **15** (349 mg, 72%, 92% *de*), colourless oil, $[\alpha]_D^{20}$ = –28.1° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3464, 2944, 2892, 2864, 1464, 1432, 1388, 1360, 1328, 1308, 1256, 1180, 1100, 996, 960,

920, 880, 836; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88-5.79 (m, 1 H), 5.12-5.06 (m, 2 H), 4.23-4.17 (m, 1 H), 4.14-4.09 (m, 1 H), 4.01-3.95 (m, 1 H), 3.89-3.83 (m, 1 H), 3.71-3.67 (m, 2 H), 3.49 (br. s, 1 H), 2.26-2.20 (m, 2 H), 2.14-2.06 (m, 2 H), 1.72-1.63 (m, 2 H), 1.91 (dt, $^{2/3}J$ 13.5 Hz, ^3J 4.3 Hz, 1 H), 1.77 (ddd, ^2J 14.4 Hz, ^3J 10.7 Hz, ^3J 9.2 Hz, 1 H), 1.46 (dt, $^{2/3}J$ 13.5 Hz, ^3J 7.0 Hz, 1 H), 1.45 (ddd, ^2J 14.4 Hz, ^3J 3.1 Hz, ^3J 3.1 Hz, 1 H), 1.05 (m, 21 H), 0.87 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.0 (=CH), 117.2 (=CH_2), 71.2, 69.5, 67.6, 64.8 (OCH), 69.9 (OCH_2), 41.8, 39.9, 39.5, 38.8, 37.8 (CH_2), 25.9 ($SiC(CH_3)_3$), 18.3 ($SiCH(CH_3)_2$), 18.1 ($SiC(CH_3)_3$), 12.2 ($SiCH(CH_3)_2$), −5.3, −5.4 ($Si(CH_3)_2$); MS (110°C): M^+ = 500 (1.3), 458 (24.6), 443 (30.2), 371 (8.2), 345 (51.2), 269 (20.1), 242 (23.3), 201 (25.1), 171 (18.4), 145 (18.4), 131 (100), 115 (24.0), 89 (81.2), 73 (49.8); HRMS calcd for $C_{27}H_{56}O_4Si_2$ (M^+) 500.3717, found 500.3712.

[(2S,4R,6R)-2-(2-tert.-Butyldimethylsilyloxy-ethyl)-6-{(2S)-2-tert.-butyldimethylsilyloxy-pent-4-enyl}-4-tri-isopropylsilyloxy]-tetrahydropyran **(16)**. To a solution of alcohol **15** (400 mg, 0.8 mmol) and 2,6-lutidine (0.17 ml, 1.72 mmol) in DCM (1 ml) was added *tert.*-butyldimethylsilyl trifluoromethanesulfonate (0.224 ml, 0.96 mmol) dropwise at 0°C. The mixture was stirred for 30 min, then silica gel was added and the crude product was purified by column chromatography (SiO_2; MTB/PE, 1:20) to yield tris-*O*-silylether **16** (457 mg, 93%), colourless oil, $[\alpha]_D^{20}$ = −26.3° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 2952, 2928, 2892, 2856, 1472, 1388, 1360, 1256, 1072, 1004, 936, 916, 880, 836, 796; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87-5.77 (m, 1 H), 5.06-5.02 (m, 2 H), 4.17-4.02 (m, 4 H), 3.71-3.65 (m, 2 H), 2.38-2.19, 1.92-1.55 and 1.38-1.29 (3 m, 10 H), 1.05 (m, 21 H), 0.89 (s, 18 H), 0.06, 0.05 (2 s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.1 (=CH), 117.0 (=CH_2), 69.3, 67.6, 66.7, 65.2 (OCH), 60.0 (OCH_2), 40.8, 40.7, 39.4, 38.9, 38.7 (CH_2), 25.9, 25.7 ($SiC(CH_3)_3$), 18.2 ($SiCH(CH_3)_2$), 18.1 ($SiC(CH_3)_3$), 12.3 ($SiCH(CH_3)_2$), −4.4, −4.5, −5.3, −5.5 ($Si(CH_3)_2$); MS (60°C): M^+ = 574 (4.3), 558 (13.2), 440 (2.1), 400 (3.5), 372 (18.1), 346 (18.2), 332 (6.4), 241 (28.3), 213 (16.6), 185 (100), 171 (54.9), 145 (10.4), 131 (46.4), 115 (24.5), 89 (44.8), 73 (74.5); HRMS calcd for $C_{29}H_{61}O_4Si_3$ ($M^+ - C_4H_9$) 557.3878, found 557.3878.

(3R)-4-[(2R,4R,6S)-6-(2-tert.-Butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran-2-yl]-3-tert.-butyldimethylsilyloxy-butyraldehyde **(17)**. A solution of bis-silylether **16** (500 mg, 0.8 mmol) in DCM (5 ml) was ozonized at -78°C until saturation with ozone occurred (5 min, light-blue colour). PPh_3 (630 mg, 2.4 mmol) in DCM (3 ml) was added and the mixture was allowed to reach rt. After stirring for 2 h at rt the solvent was removed and the crude product purified by column chromatography (SiO_2; MTB/PE, 1:20 → MTB/PE, 1:15 → MTB/PE, 1:5) to give aldehyde **17** (500 mg, 98%), colourless oil, $[\alpha]_D^{20}$ = −24.1° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 2984, 2948, 2892, 2864, 1724, 1464, 1388, 1360, 1256, 1176, 1096, 1004, 964, 936, 916, 880, 836; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83-9.81 (m, 1 H), 4.38-4.32, 4.20-4.06 and 3.84-3.78 (3 m, 4 H), 3.73-3.68 (m, 2 H), 2.66 (ddd, ^2J 15.8 Hz, ^3J 4.7 Hz, ^3J 1.8 Hz, 1 H), 2.52 (ddd, ^2J 15.8 Hz, ^3J 7.0 Hz, ^3J 3.0 Hz, 1 H), 2.05-1.90, 1.72-1.63 and 1.57-1.50 (3 m, 7 H), 1.39 (dt, $^{2/3}J$ 13.0 Hz, ^3J 8.3 Hz, 1 H), 1.06 (m, 21 H), 0.90 and 0.87 (2 s, 18 H), 0.10, 0.06 and 0.04 (3 s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1 (C=O), 66.9, 66.5, 65.6, 65.1 (OCH), 59.9 (OCH_2), 50.6 (CH_2), 40.3, 40.1, 39.5, 38.4 (CH_2), 26.0, 25.7 ($SiC(CH_3)_3$), 18.2 ($SiCH(CH_3)_2$), 18.1 ($SiC(CH_3)_3$), 12.3 ($SiCH(CH_3)_2$), -4.34, −4.73, −5.30, −5.32 ($Si(CH_3)_2$); MS (130°C): M^+ = 616 (0), 574 (8.9), 559 (3.3), 441 (15.3), 427 (8.5), 371 (10.3), 345 (13.6), 331 (8.1), 255 (12.4), 241 (57.5), 187 (19.3), 171 (51.4), 131 (70.3), 115 (27.2), 89 (54.1), 75 (100); HRMS calcd for $C_{29}H_{61}O_5Si_3$ ($M - C_3H_7$) 573.3827, found 573.3835.

(2R)-1-[(2S,4R,6S)-6-(2-tert.-Butyldimethylsilyloxy-ethyl)-4-triisopropylsilyloxy-tetrahydropyran-2-yl]-pent-4-en-2-ol **(20)**. Aldehyde **12** (400 mg, 0.87 mmol) and (+)-*B*-allyl-β-diisopinocampheyl-borane (6 ml, 1.28 mmol, 0.21 M solution) were allowed to react as described for aldehyde **14** to give after chromatography (SiO_2; MTB/PE, 1:5) alcohol **20** (306 mg, 70%, 92% *de*), colourless oil, $[\alpha]_D^{20}$ = −25.3° (c = 1, $CHCl_3$). $\nu_{max}(CHCl_3)/cm^{-1}$ 3500, 3000, 2944, 2892, 2864, 1464, 1432, 1388, 1360, 1256, 1176, 1100, 996, 956, 920, 908, 880, 836, 796; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87-5.77 (m, 1 H), 5.15-5.09 (m, 2 H), 4.35-4.29 (m, 1 H), 4.16-4.10 (m, 2 H), 3.91-3.84 (m, 1 H), 3.74-3.66 (m, 2 H), 2.54 (br. s, 1 H), 2.28-2.24 (m, 2 H), 2.11-2.02 (m, 2 H), 1.74-1.63 (m, 2 H), 1.93-1.88 (m, 1 H), 1.85 (ddd, ^2J 14.4 Hz, ^3J 9.8 Hz, ^3J 2.9 Hz, 1 H), 1.44 (ddd, ^2J 14.4 Hz, ^3J 8.9 Hz, ^3J 3.4 Hz, 1 H), 1.45 (dt, $^{2/3}J$ 14.1 Hz, ^3J 8.9 Hz, 1 H), 1.06 (m, 21 H), 0.88 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.0 (=CH), 117.7 (=CH_2), 67.8, 67.0, 66.3, 65.1 (OCH), 59.9

(OCH_2), 42.0, 41.4, 39.4, 39.0, 38.0 (CH_2), 26.0 ($SiC(CH_3)_3$), 18.3 ($SiCH(CH_3)_2$), 18.1 ($SiC(CH_3)_2$), 12.3 ($SiCH(CH_3)_2$), −5.3 ($Si(CH_3)_2$); MS (60°C): M^+ = 500 (0), 457 (15.9), 443 (23.5), 372 (3.6), 345 (35.4), 331 (5.9), 271 (14.7), 241 (39.7), 227 (9.6), 201 (25.2), 171 (16.0), 145 (18.9), 131 (100), 115 (22.7), 97 (20.7), 89 (89.4), 81 (23.6), 73 (51.5); HRMS calcd for $C_{24}H_{49}O_4Si_2$ ($M^+ - C_3H_7$) 457.3169, found 457.3163.

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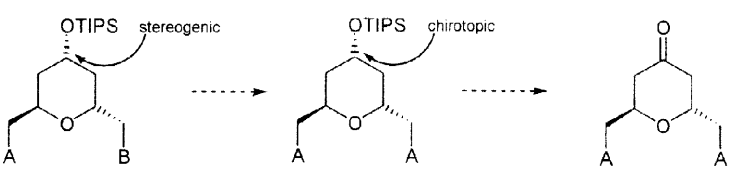

pro-pseudo-C_2-symmetric **pseudo-C_2-symmetric** **C_2-symmetric**
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