The use of π-allyltricarbonyliron lactone complexes in the synthesis of the resorcylic macrolides α- and β-zearalenol

Svenja Burckhardt and Steven V. Ley *

Department of Chemistry, University of Cambridge, Lensfield Rd, Cambridge, UK CB2 1EW

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A highly stereoselective synthesis of the natural products α- and β-zearalenol **1** and **2** has been achieved using π-allyltricarbonyliron lactone complexes to control the 1,5-stereochemical relationship of the oxygen functionalities found in these resorcylic macrolides.

Introduction

The 14-membered resorcylic macrolides α- and β-zearalenol **1** and **2** are estrogenic mycotoxins produced by a species of the fungus *Fusarium*.[1] The zearalenols **1** and **2**, together with the reduced isomer α-zearalanol **3**, belong to a class of biologically important compounds whose progenitor is considered to be zearalenone **4** (Fig. 1). The hormonal activity of these

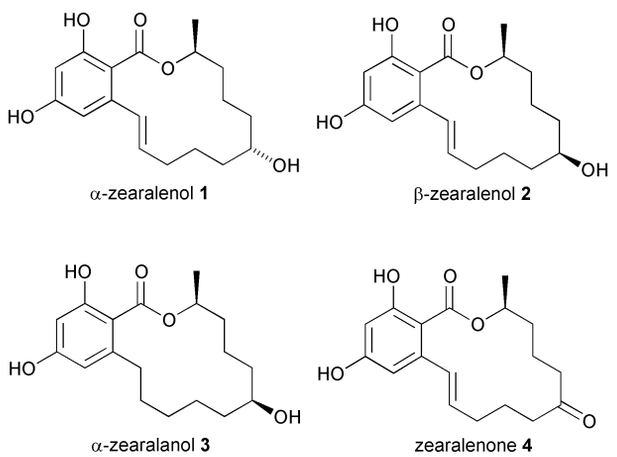

Fig. 1 The resorcylic acid lactones α-zearalenol **1**, β-zearalenol **2**, α-zearalanol **3** and zearalenone **4**.

compounds is linked to their close spatial similarity to 17β-estradiol,[2] with the α-isomer **1** being three to four times as active as the β-isomer **2**.[3] Furthermore this class of compounds has attracted attention due to their anabolic activity. For example, α-zearalanol **4** is employed as a cattle-growth stimulant[4] and also has undergone clinical trials as a potential treatment for menopausal and post-menopausal syndrome.[5] While several total syntheses of zearalenone **4** have been accomplished over the last 30 years,[6] to our knowledge no independent direct syntheses of **1** or **2** have been described. Here we report in full on the first enantioselective route to **1** and **2** employing π-allyltricarbonyliron lactone complexes as unusual precursor molecules to these natural products.[7]

We have shown previously that organoaluminium reagents, possessing an active β-hydrogen atom, such as tripropyl- or triisobutylaluminium, will reduce carbonyl groups appended to the allyl ligand of π-allyltricarbonyliron lactone complexes with excellent diastereoselectivity.[8] We have also shown that sodium triacetoxyborohydride efficiently decomplexes π-allyltricarbonyliron lactone complexes bearing a hydroxy group in the side-chain to generate stereodefined 1,5-diols.[9] Here we exploit these processes to show that π-allyltricarbonyliron lactone complexes can be used to control the required stereochemical arrangement found in **1** and **2**.

Results and discussion

The synthesis begins with the reduction of the ester **5**[10] to the corresponding alcohol, followed by Swern oxidation and Horner–Wadsworth–Emmons homologation using the phosphonate **6**, prepared according to the method of Grieco and Pogonowski,[11] providing the (*E*)-enone **7** in 83% yield over three steps (Scheme 1). Deprotection of the acetonide under acidic conditions and transformation of the liberated diol **8** to the cyclic sulfite **9** using thionyl chloride[12] afforded **9** as a mixture of diastereoisomers in 82% overall yield. Treatment of **9** with nonacarbonyldiiron in benzene under sonication conditions[13] provided the two diastereoisomeric π-allyltricarbonyliron lactone complexes, *endo*-**10a** and *exo*-**10b**, in 70% combined yield and in a ratio of *ca.* 1 : 1. Separation of the two isomers **10a** and **10b** was readily achieved by flash column chromatography. This 1 : 1 mixture was ideal since it should be possible to process these isomers individually to synthesise selectively the two natural products **1** and **2**. For example, for α-zearalenol **1**, reduction of the side-chain ketone in the *endo* complex **10a** was achieved in 94% yield using tripropylaluminium[8] to give **11a**, as the sole product as determined by 600 MHz ^{1}H NMR analysis. Analogously, the *exo* complex **10b** provided diastereomerically pure **11b** in 80% yield for the synthesis of β-zearalenol **2**. Treatment of **11a** and **11b** with sodium triacetoxyborohydride in tetrahydrofuran[9] resulted in a highly stereoselective decomplexation to afford, after TBDMS-protection and hydrogenation, the alcohols **12a** and **12b** in 61 and 66% yield over three steps, respectively (Scheme 1). Next, Swern oxidation of **12a** and **12b** provided the corresponding aldehydes **13a** and **13b** which in turn were transformed into the vinylstannanes **14a** and **14b** by applying the procedure developed by Hodgson *et al.*[14] utilising chromium(II) chloride and Bu_3SnCHI_2 in dimethylformamide (Scheme 2). With these stannanes in hand, we then examined their palladium catalysed coupling to the aromatic iodide **15**, previously synthesised by Hegedus *et al.*[6f] It soon became apparent that the nature of the ligand played a critical role in this Stille coupling reaction. The optimised conditions required the use of tetrakis(tri-2-furylphosphine)palladium,[15] which was prepared *in situ*, to provide independently the coupled products **16a** and **16b** in 82 and 85% yields, respectively. Treatment of **16a** or **16b** with HF·pyridine followed by hydrolysis of the methyl ester functionality using aqueous potassium hydroxide in ethane-1,2-diol at 120 °C

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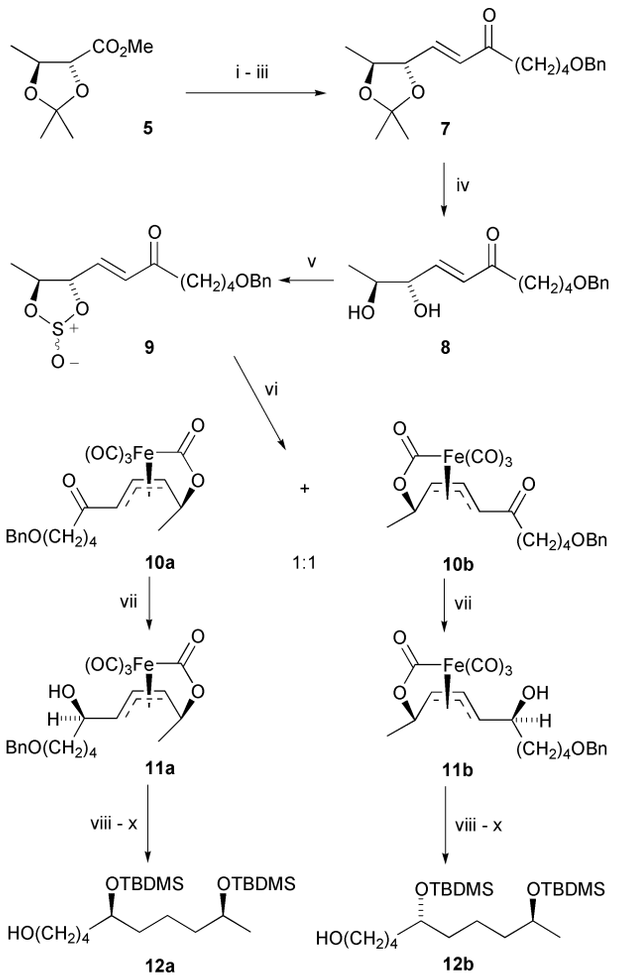


Scheme 1 *Reagents and conditions*: i. $LiAlH_4$, Et_2O, 0 °C, 2 h; ii. $(COCl)_2$, DMSO, Et_3N, DCM, −78 °C, 3 h; iii. $(EtO)_2P(O)CH_2CO(CH_2)_4OBn$ **6**, NaH, THF, −78 °C, 1 h, 83% (over 3 steps); iv. AcOH–H_2O (1 : 1), 40 °C, 24 h, 92%; v. $SOCl_2$, Et_3N, Et_2O, 0 °C, 30 min, 89%; vi. $Fe_2(CO)_9$, benzene, sonication, 30 °C, 3 h, 35% **10a**, 35% **10b**; vii. $AlPr^n_3$, DCM, 0 °C, 94% **11a**, 80% **11b**; viii. $NaBH(OAc)_3$, THF, 3 d; ix. TBDMSCl, imidazole, DMF, 0 °C, 30 min, then rt, 24 h; x. Pd/C (10%), H_2, EtOAc, 30 min, 61% **12a** (over three steps), 66% **12b** (over three steps).

provided the corresponding seco acids **18a** and **18b** in 83 and 85% yield over two steps.

Finally we investigated methods for the macrolactonisation of these seco acids to the 14-membered MEM-protected α- and β-zearalenone products **19a** and **19b**. Application of the Corey–Nicolaou procedure,[6b,16] involving the formation of pyridine-2-thiol esters and thermal cyclisation, did not provide any of the cyclised products, while the use of the Yamaguchi macrolactonisation[17] gave a low yielding and disappointing 1 : 1 mixture of the 10- and 14-membered lactones, arising from cyclisation of the acid functionality with the C-6′ or the C-10′ hydroxy group respectively. Pleasingly however, cyclisation of **18a** using Mukaiyama's protocol[18] afforded the desired MEM-protected α-zearalenol **19a** in 64% yield, while the corresponding MEM-protected β-zearalenol **19b** was obtained in 62% yield from **18b**. In both cases only very minor traces of the corresponding 10-membered lactones were observed by 600 MHz ^{1}H NMR analysis in the crude mixture. Final deprotection of the MEM-ethers in **19a** and **19b** proceeded in 93% yield using aqueous hydrochloric acid in tetrahydrofuran at 40 °C to provide α-zearalenol **1** and β-zearalenol **2**, respectively (Scheme 2). The products were identical in all respects to authentic samples.

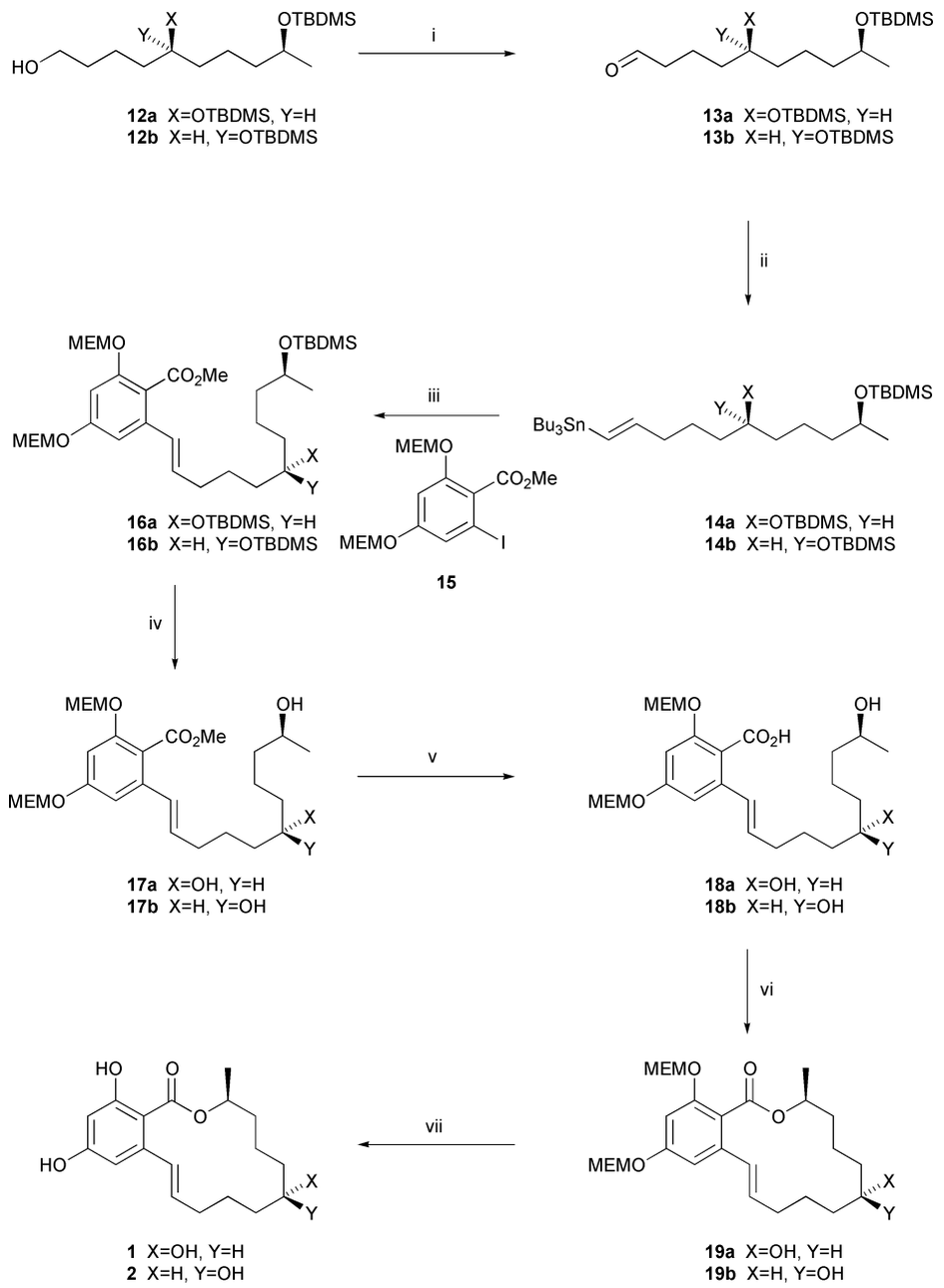
In summary, a synthetic route to the estrogenic mycotoxins α- and β-zearalenol has been achieved whereby π-allyltricarbonyliron lactone complexes serve as key precursor molecules to install the relative 1,5-carbon to oxygen stereocentres.

Experimental

^{1}H NMR spectra were recorded in $CDCl_3$ unless stated otherwise on Bruker DPX-200, Bruker DPX-400 or Bruker DRX-600 spectrometers and are reported as follows: chemical shift δ (ppm), (number of protons, multiplicity, coupling constant J/Hz, assignment). Residual protic solvent $CHCl_3$ (δ_H = 7.26 ppm) was used as the internal reference. ^{13}C NMR spectra were recorded in $CDCl_3$ unless stated otherwise at 50 MHz, 100 MHz or 150 MHz on Bruker DPX-200, Bruker DPX-400 or Bruker DRX-600 spectrometers, respectively, using the central resonance of $CDCl_3$ (δ_C = 77.0 ppm) as the internal reference. Infra-red spectra were recorded as thin films between sodium chloride plates, deposited from chloroform solution on Perkin-Elmer 983G or FTIR 1620 spectrometers. Mass spectra were obtained on a Kratos MS890MS spectrometer using electron ionisation or fast atom bombardment techniques, on a Kratos MS50 spectrometer using the fast ion bombardment technique or on a Bruker BIOAPEX 4.7 T FTICR or a Micromass Q-Tof spectrometer using the electrospray technique at the Department of Chemistry, University of Cambridge. Microanalyses were determined in the microanalytical laboratories at the University of Cambridge. Optical rotations were measured with an Optical Activity AA-1000 polarimeter and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Flash column chromatography was carried out using Merck Kieselgel (230–400 mesh) unless otherwise indicated. All reactions were carried out under an argon atmosphere in oven-dried glassware which was cooled under a continuous stream of argon immediately prior to use. Reactions involving the preparation of iron complexes were carried out using degassed benzene. The solvent was degassed by successively evacuating and purging the solvent three times with argon while simultaneously subjecting the solvent to sonication using an 80 W, 55 kHz cleaning bath. PE refers to petroleum ether, bp 40–60 °C, which was distilled prior to use. Et_2O and THF were distilled from sodium benzophenone ketyl and DCM; benzene and acetonitrile were distilled from calcium hydride. Other reagents and solvents were used as supplied. Aqueous solutions are saturated unless otherwise specified.

Diethyl (6-benzyloxy-2-oxo-1-hexyl)phosphonate (6)

A solution of diethyl (2-oxopropyl)phosphonate (68.0 g, 350 mmol) in THF (300 ml) was added dropwise to a stirred slurry of NaH [15.3 g of a 60% dispersion in mineral oil, prewashed with THF (2 × 30 ml), 382 mmol] in THF (375 ml) at 0 °C. The reaction mixture was allowed to warm to rt and stirred at this temperature for 1 h. After recooling to 0 °C, ^{n}BuLi (153 ml of a 2.5 M solution in hexane, 382 mmol) was added and the reaction mixture was stirred for another 30 min at 0 °C. A solution of 1-benzyloxy-3-bromopropane (72.8 g, 318 mmol) in THF (300 ml) was added dropwise, the reaction mixture was allowed to warm to rt and stirred for 1.5 h. The reaction mixture was carefully poured into ice-cold aqueous NH_4Cl solution (1000 ml) and the aqueous phase was extracted with Et_2O (3 × 500 ml). The combined organic extracts were washed with brine (200 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, neat Et_2O to 5% MeOH in Et_2O) afforded the phosphonate **6** (89 g, 82%) as a light yellow liquid; ν_{max}(film)/cm^{-1} 2981, 2940, 2860, 1713 (C=O), 1453, 1393, 1366, 1251 (P=O), 1100, 1023, 965; δ_H(400 MHz) 7.33–7.20 (5H, m, 5 × Ph-*H*), 4.45 (2H, s, PhCH_2), 4.15–4.03 (4H, m, 2 × OCH_2CH$_3$), 3.44 (2H, t, *J* 6.1, 2 × 6-H), 3.02 (2H, d, *J* 22.8, 2 × 1-H), 2.61 (2H, t, *J* 7.0, 2 × 3-H), 1.71–1.54 (4H, m, 2 × 4-H, 2 × 5-H), 1.29 (6H, t, *J* 7.0, 2 × OCH$_2$CH_3); δ_C(100 MHz) 201.8 (d, $^2J_{CP}$ 6.2, 2-C), 138.5 (quat. Ph-C), 128.3 (Ph-C), 127.6



Scheme 2 *Reagents and conditions*: i. $(COCl)_2$, DMSO, Et_3N, DCM, −78 °C, 3 h, 86% **13a**, 80% **11b**; ii. Bu_3SnCHI_2, $CrCl_2$, DMF, 0 °C, 67% **14a**, 69% **14b**; iii. methyl 4,6-bis[(2-methoxyethoxy)methyloxy]-2-iodobenzoate **15**, $Pd_2(dba)_3$, P(2-furyl)$_3$, toluene, 100 °C, 4 h, 82% **16a**, 85% **16b**; iv. HF·pyridine, pyridine, THF, 12 h, 95% **17a**, 93% **17b**; v. 10 M aqueous KOH, ethane-1,2-diol, 120 °C, 4 h, 87% **18a**, 91% **18b**; vi. syringe pump addition of a solution of the seco acid and Et_3N in MeCN over 10 h to 1-methyl-2-chloropyridinium iodide, MeCN, reflux, 64% **19a**, 62% **19b**; vii. 1.5 M aqueous HCl, THF, 40 °C, 93% **1**, 93% **2**.

(Ph-C), 127.5 (Ph-C), 72.9 (PhCH_2), 69.9 (6-C), 62.5 (d, $^2J_{CP}$ 6.4, 2 × OCH_2CH$_3$), 43.7 (d, $^3J_{CP}$ 0.8, 3-C), 42.3 (d, $^1J_{CP}$ 126.4, 1-C), 28.9 (4-C or 5-C), 20.2 (5-C or 4-C), 16.2 (d, $^3J_{CP}$ 6.2, 2 × OCH$_2$$CH_3$); *m/z* (EI) 342 ($M^+$, 1%), 284 (6), 251 ($M^+$ − Bn, 6), 207 (25), 194 (57), 179 (26), 91 (100) [Found (M^+) 342.1604. $C_{17}H_{27}O_5P$ requires M, 342.1596].

(1′*E*,4*R*,5*S*)-4-(7′-Benzyloxy-3′-oxohept-1′-en-1′-yl)-2,2,5-trimethyl-1,3-dioxolane (7)

$LiAlH_4$ (69.0 ml of a 1 M solution in Et_2O, 69 mmol) was added dropwise to a solution of the ester **5** (20.0 g, 115 mmol) in Et_2O (120 ml) at 0 °C and the reaction mixture was stirred at this temperature for 2 h. Water (2.6 ml) was added followed by 15% NaOH solution (2.6 ml) and water (7.8 ml) and the reaction mixture was stirred at rt for 12 h. The reaction mixture was filtered, washing the residue with Et_2O (2 × 50 ml). Concentration of the filtrate under reduced pressure afforded the crude alcohol which was used without further purification. A solution of DMSO (21.2 ml, 299 mmol) in DCM (280 ml) was added dropwise to a solution of $(COCl)_2$ (13.0 ml, 150 mmol) in DCM (280 ml) at −78 °C and the reaction mixture was stirred for 30 min. A solution of the crude alcohol in DCM (280 ml) was added dropwise and after 30 min Et_3N (56.0 ml, 403 mmol) was added dropwise at −78 °C. Stirring was continued at −78 °C for 1 h before the mixture was allowed to warm to rt. The reaction mixture was concentrated under reduced pressure, taken up in Et_2O (200 ml) and filtered through a plug of silica gel, washing the residue with Et_2O (500 ml). Concentration of the filtrate under reduced pressure afforded the corresponding crude aldehyde which was used without further purification. A solution of the phosphonate **6** (79.0 g, 230 mmol) in THF (140 ml) was added dropwise to a stirred slurry of NaH [9.2 g of a 60% dispersion in mineral oil, prewashed with THF (2 × 5 ml), 230 mmol] in THF (140 ml) at 0 °C. The reaction mixture was allowed to warm to rt and stirred at this temperature for 1 h.

After recooling to −78 °C a solution of the crude aldehyde in THF (140 ml) was added and the reaction mixture was stirred for 1 h. The reaction mixture was quenched by addition of NH_4Cl solution (20 ml), allowed to warm to rt and poured into aqueous NH_4Cl solution (400 ml). The aqueous phase was extracted with Et_2O (3 × 300 ml). The organic extracts were washed with brine (150 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 10 to 50% Et_2O in PE) afforded the enone **7** (31.8 g, 83% over three steps) as a light yellow liquid; $[\alpha]_D^{31}$ +6.6 (*c* 1.00 in $CHCl_3$) (Found: C, 72.4; H, 8.6. $C_{20}H_{28}O_4$ requires C, 72.3; H, 8.5%); ν_{max}(film)/cm^{-1} 2984, 2933, 2866, 1698, 1678 (C=O), 1638 (C=C), 1454, 1379, 1240, 1173, 1105, 1036, 979, 858, 736, 698; δ_H(600 MHz) 7.34–7.22 (5H, m, 5 × Ph-*H*), 6.67 (1H, dd, *J* 15.9, 5.8, 1′-H), 6.35 (1H, dd, *J* 15.9, 1.0, 2-H), 4.46 (2H, s, PhCH_2), 4.04 (1H, ddd, *J* 8.2, 5.8, 1.0, 4-H), 3.83–3.77 (1H, m, 5-H), 3.46 (2H, t, *J* 6.2, 2 × 7′-H), 2.57 (2H, t, *J* 7.3, 2 × 4′-H), 1.74–1.67 (2H, m, 2 × 5′-H), 1.66–1.58 (2H, m, 2 × 6′-H), 1.43 (3H, s, 2-CH_3), 1.40 (3H, s, 2-CH_3), 1.28 (3H, d, *J* 6.1, 5-CH_3); δ_C(150 MHz) 199.6 (3′-C), 140.9 (1′-C), 138.5 (quat. Ph-C), 130.5 (2′-C), 128.3 (Ph-C), 127.6 (Ph-C), 127.5 (Ph-C), 109.2 (2-C), 81.9 (4-C), 76.5 (5-C), 72.8 (PhCH_2), 69.9 (7′-C), 40.4 (4′-C), 29.1 (6′-C), 27.3 (2-CH_3), 26.7 (2-CH_3), 20.7 (5′-C), 16.7 (5-CH_3); *m*/*z* (EI) 332 (M^+, 1%), 214 (41), 185 (46), 172 (53), 169 (45), 127 (54), 111 (66), 97 (100), 91 (43) [Found (M^+) 332.1997. $C_{20}H_{28}O_4$ requires M, 332.1988].

(6*E*,8*S*,9*S*)-1-Benzyloxy-8,9-dihydroxydec-6-en-5-one (8)

AcOH (75 ml) and water (75 ml) were added to the acetonide **7** (15.0 g, 45 mmol) and the reaction mixture was stirred at 40 °C for 20 h. The reaction mixture was carefully poured into an aqueous $NaHCO_3$ solution (300 ml) and solid $NaHCO_3$ was added until effervescence stopped. The mixture was extracted with EtOAc (4 × 300 ml), the combined organic extracts were washed with brine (100 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (75% EtOAc in PE to neat EtOAc) afforded the diol **8** (12.1 g, 92%) as a colourless oil; $[\alpha]_D^{30}$ −10.6 (*c* 1.00 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3420 (OH), 2936, 2867, 1654 (C=O), 1638 (C=C), 1558, 1540, 1507, 1496, 1456, 1365, 1319, 1154, 1076, 986; δ_H(400 MHz) 7.37–7.24 (5H, m, 5 × Ph-*H*), 6.75 (1H, dd, *J* 15.9, 5.1, 7-H), 6.38 (1H, dd, *J* 15.9, 1.4, 6-H), 4.48 (2H, s, PhCH_2), 4.06–3.98 (1H, m, 8-H), 3.73–3.64 (1H, m, 9-H), 3.48 (2H, t, *J* 6.3, 2 × 1-H), 2.99 (1H, br s, O*H*), 2.66 (1H, br s, O*H*), 2.58 (2H, t, *J* 7.3, 2 × 4-H), 1.76–1.58 (4H, m, 2 × 2-H, 2 × 3-H), 1.21 (3H, d, *J* 6.3, 3 × 10-H); δ_C(100 MHz) 200.3 (5-C), 144.2 (7-C), 138.4 (quat. Ph-C), 130.1 (6-C), 128.4 (Ph-C), 127.7 (Ph-C), 127.6 (Ph-C), 75.7 (8-C), 72.9 (Ph*C*H$_2$), 70.3 (9-C), 70.0 (1-C), 40.6 (4-C), 29.1 (2-C or 3-C), 20.8 (3-C or 2-C), 19.2 (10-C); *m*/*z* (EI) 293 (MH^+, 11%), 185 (8), 168 (59), 91 (100) [Found (MH^+) 293.1753. $C_{17}H_{25}O_4$ requires MH, 293.1753].

(1′*E*,2*RS*,4*S*,5*S*)-4-(7′-Benzyloxy-3′-oxohept-1′-en-1′-yl)-5-methyl-1,3-dioxa-2-thiolane 2-oxide (9)

Freshly distilled $SOCl_2$ (2.11 ml, 26.9 mmol) was added dropwise to a solution of the diol **8** (5.23 g, 17.9 mmol) and Et_3N (7.47 ml, 53.7 mmol) in Et_2O (100 ml) at 0 °C. After 90 min the reaction mixture was poured into aqueous $NaHCO_3$ solution (100 ml), the phases were separated and the aqueous phase was extracted with Et_2O (3 × 100 ml). The combined organic extracts were washed with brine (40 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 50% Et_2O in PE) afforded the cyclic sulfite **9** (5.37 g, 89%) as a yellow oil; (1 : 1 mixture of diastereoisomers at sulfur); ν_{max}(film)/cm^{-1} 2933, 2847, 1677 (C=O), 1640 (C=C), 1451, 1358, 1209, 1100, 1046, 956, 867; δ_H(200 MHz) 7.40–7.22 (5H, m, 5 × Ph-*H*), {[6.75 (dd, *J* 15.8, 6.3), 6.64 (dd, *J* 15.8, 5.9)] 1H, 1′-H}, {[6.45 (dd, *J* 15.8, 1.0), 6.43 (dd, *J* 15.8, 1.0)] 1H, 2′-H}, {[5.05 (ddd, *J* 8.8, 5.9, 1.0), 4.55–4.44 (m)] 1H, 4-H}, {[4.79 (dq, *J* 9.1, 6.1), 4.27 (dq, *J* 8.8, 6.3)] 1H, 5-H}, 4.49 (2H, s, PhCH_2), 3.55–3.43 (2H, m, 2 × 7′-H), 2.69–2.54 (2H, m, 2 × 4′-H), 1.85–1.55 (4H, m, 2 × 5′-H, 2 × 6′-H), {[1.59 (d, *J* 6.3), 1.51 (d, *J* 6.1)] 3H, 5-*C*H$_3$}; δ_C(50 MHz) [198.8, 198.6 (3′-C)], 138.4 (quat. Ph-C), [136.8, 134.8, 132.9, 132.6 (1′-C, 2′-C)], 128.3 (Ph-C), 127.6 (Ph-C), 127.5 (Ph-C), [87.0, 83.7, 82.6, 79.0 (4-C, 5-C)], 72.9 (Ph*C*H$_2$), 69.8 (7′-C), [41.1, 40.7 (4′-C)], [29.0, 20.6, 20.5 (5′-C, 6′-C)], [18.0, 15.7 (5-*C*H$_3$)]; *m*/*z* (FAB) 361 (MNa^+, 10%), 339 (MH^+, 68), 231 (M^+ − Bn, 38) [Found (MH^+) 339.1265. $C_{17}H_{23}O_5S$ requires MH, 339.1266].

[(4*E*,2*S*,3*R*)-2-(Carbonyloxy-κ*C*)-10-benzyloxy-6-oxo-(3,4,5-η)-dec-4-en-3-yl]tricarbonyliron (10a) and [(4*E*,2*S*,3*S*)-2-(carbonyloxy-κ*C*)-10-benzyloxy-6-oxo-(3,4,5-η)-dec-4-en-3-yl]-tricarbonyliron (10b)

A solution of the cyclic sulfite **9** (5.37 g, 15.9 mmol) in degassed PhH (300 ml) was added to $Fe_2(CO)_9$ (17.32 g, 47.6 mmol) and the reaction mixture was submitted to sonication at rt for 5 h. The mixture was filtered through a plug of Celite, washing the residue with Et_2O (1500 ml). After concentration of the filtrate under reduced pressure the residue was purified by flash column chromatography (silica gel, 1 to 70% Et_2O in PE) affording a 1 : 1 mixture of the *endo* complex **10a** and the *exo* complex **10b** (5.20 g, 74%). Separation of the diastereoisomeric complexes was achieved using a Biotage FLASH 40i system (FLASH 40M cartridge, 65% Et_2O in PE) giving, in order of elution, the *endo* complex **10a** (2.46 g, 35%) as a bright yellow oil; $[\alpha]_D^{27}$ +369.0 (*c* 1.00 in DCM); ν_{max}(film)/cm^{-1} 2934, 2860, 2088 (CO), 2023 (CO), 1675 (C=O), 1496, 1454, 1373, 1359, 1301, 1180, 1087, 1047, 996, 945, 831, 737, 697; δ_H(600 MHz) 7.38–7.24 (5H, m, 5 × Ph-*H*), 5.53 (1H, dd, *J* 11.2, 8.6, 4-H), 5.04 (1H, dd, *J* 8.6, 4.6, 3-H), 4.56–4.47 (3H, m [incl. 4.50, 2H, s, PhCH_2] 2-H, PhCH_2), 3.87 (1H, d, *J* 11.2, 5-H), 3.50 (2H, t, *J* 6.3, 2 × 10-H), 2.82–2.69 (2H, m, 2 × 7-H), 1.90–1.65 (4H, m, 2 × 8-H, 2 × 9-H), 1.37 (3H, d, *J* 6.4, 3 × 1-H); δ_C(150 MHz) 207.9 (CO), 205.0 (CO), 203.9 (CO), 202.6 (CO), 199.7 (CO), 138.5 (quat. Ph-C), 128.4 (Ph-C), 127.6 (2 × Ph-C), 92.0 (CH), 85.4 (CH), 73.0 (CH), 72.9 (Ph*C*H$_2$), 69.8 (10-C), 65.8 (CH), 43.0 (7-C), 29.1 (8-C or 9-C), 21.8 (1-C), 20.6 (9-C or 8-C); *m*/*z* (FIB) 443 (MH^+, 75%), 386 (M^+ − 2CO, 35), 358 (M^+ − 3CO, 32), 331 (MH^+ − 4CO, 100), 239 (M^+ − 4CO − Bn, 13), 223 (45) [Found (MH^+) 443.0785. $C_{21}H_{23}FeO_7$ requires MH, 443.0793]; and the *exo* complex **10b** (2.46 g, 35%) as a bright yellow oil; $[\alpha]_D^{27}$ −339.5 (*c* 1.00 in DCM); ν_{max}(film)/cm^{-1} 3033, 2933, 2861, 2082 (CO), 2017 (CO), 1665 (C=O), 1496, 1453, 1305, 1120, 1104, 1049, 995, 946, 739, 695, 652, 603; δ_H(600 MHz) 7.37–7.24 (5H, m, 5 × Ph-*H*), 5.68 (1H, dd, *J* 11.0, 8.4, 4-H), 4.80 (1H, d, *J* 8.4, 3-H), 4.50 (2H, s, PhCH_2), 4.27 (1H, q, *J* 6.5, 2-H), 3.72 (1H, d, *J* 11.0, 5-H), 3.50 (2H, t, *J* 6.4, 2 × 10-H), 2.79–2.66 (2H, m, 2 × 7-H), 1.85–1.63 (4H, m, 2 × 8-H, 2 × 9-H), 1.42 (3H, d, *J* 6.5, 3 × 1-H); δ_C(150 MHz) 208.1 (CO), 204.9 (CO), 203.9 (CO), 202.5 (CO), 200.0 (CO), 138.5 (quat. Ph-C), 128.3 (Ph-C), 127.6 (Ph-C), 127.5 (Ph-C), 93.6 (CH), 84.4 (CH), 72.9 (Ph*C*H$_2$), 70.7 (CH), 69.8 (10-C), 65.1 (CH), 42.9 (CH_2), 29.1 (8-C or 9-C), 24.0 (1-C), 20.6 (9-C or 8-C); *m*/*z* (FIB) 443 (MH^+, 28%), 386 (M^+ − 2CO, 13), 359 (MH^+ − 3CO, 7), 331 (MH^+ − 4CO, 100), 239 (M^+ − 4CO − Bn, 10), 223 (44) [Found (MH^+) 443.0811. $C_{21}H_{23}FeO_7$ requires MH, 443.0793].

General procedure for the preparation of alcohol complexes 11a and 11b

For a 1.45 mmol scale reaction: Al^{n}Pr$_3$ (1.0 M solution in PhMe, 3.0 equiv.) was added dropwise to a solution of the ketone complex (1.0 equiv.) in DCM (20 ml) at 0 °C. After 1 h 1 M aqueous HCl solution (10 ml) was added and the mixture

was partioned between water (30 ml) and Et_2O (30 ml). The aqueous phase was extracted with Et_2O (3 × 30 ml), the combined organic extracts were washed with brine (30 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 50 to 75% Et_2O in PE) afforded the alcohol complex.

[(4*E*,2*S*,3*R*,6*R*)-2-(Carbonyloxy-κ*C*)-10-benzyloxy-6-hydroxy-(3,4,5-η)-dec-4-en-3-yl]tricarbonyliron (11a)

Prepared according to the general procedure using *endo* complex **10a** (628 mg, 1.42 mmol). The alcohol complex **11a** (595 mg, 94%) was obtained as a yellow oil; $[a]_D^{30}$ +115.0 (*c* 1.00 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3417 (OH), 2933, 2862, 2079 (CO), 2023 (CO), 2002 (CO), 1665 (C=O), 1638, 1450, 1360, 1082, 1039, 995, 946, 831, 739, 695, 657; δ_H(600 MHz) 7.38–7.24 (5H, m, 5 × Ph-*H*), 4.75 (1H, dd, *J* 12.2, 8.3, 4-H), 4.60 (1H, dd, *J* 8.3, 4.7, 3-H), 4.50 (2H, s, PhCH_2), 4.46–4.40 (1H, m, 2-H), 4.14–4.08 (1H, m, 6-H), 4.03 (1H, dd, *J* 12.2, 3.6, 5-H), 3.52 (2H, t, *J* 6.1, 2 × 10-H), 2.54–2.45 (1H, m, O*H*), 1.84–1.50 (6H, m, 2 × 7-H, 2 × 8-H, 2 × 9-H), 1.34 (3H, d, *J* 6.4, 3 × 1-H); δ_C(150 MHz) 209.5 (CO), 206.6 (2 × CO), 203.4 (CO), 138.3 (quat. Ph-C), 128.4 (Ph-C), 127.7 (Ph-C), 127.6 (Ph-C), 88.5 (CH), 88.0 (CH), 76.8 (CH), 73.3 (CH), 73.0 (Ph*C*H$_2$), 71.7 (CH), 70.1 (10-C), 39.4 (7-C), 29.2 (8-C or 9-C), 22.8 (9-C or 8-C), 21.8 (1-C); *m*/*z* (FIB) 445 (MH^+, 12%), 387 (11), 371 ($MH^+ - 2CO - H_2O$, 7), 333 ($MH^+ - 4CO$, 13), 315 ($MH^+ - 4CO - H_2O$, 100) [Found (MH^+) 445.0976. $C_{21}H_{25}FeO_7$ requires MH, 445.0950].

[(4*E*,2*S*,3*S*,6*S*)-2-(Carbonyloxy-κ*C*)-10-benzyloxy-6-hydroxy-(3,4,5-η)-dec-4-en-3-yl]tricarbonyliron (11b)

Prepared according to the general procedure using *exo* complex **10b** (655 mg, 1.48 mmol). The alcohol complex **11b** (524 mg, 80%) was obtained as a yellow oil; $[a]_D^{30}$ +77.0 (*c* 1.00 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3418 (OH), 2936, 2862, 2076 (CO), 2025 (CO), 2003 (CO), 1660 (C=O), 1634, 1450, 1377, 1333, 1307, 1090, 1046, 1007, 950, 736, 698; δ_H(600 MHz) 7.37–7.25 (5H, m, 5 × Ph-*H*), 4.90 (1H, dd, *J* 12.1, 8.0, 4-H), 4.49 (2H, s, PhCH_2), 4.37 (1H, d, *J* 8.0, 3-H), 4.21 (1H, q, *J* 6.4, 2-H), 4.11–4.02 (1H, m, 6-H), 3.89 (1H, dd, *J* 12.1, 3.8, 5-H), 3.51 (2H, t, *J* 6.2, 2 × 10-H), 2.77–2.69 (1H, m, O*H*), 1.78–1.48 (6H, m, 2 × 7-H, 2 × 8-H, 2 × 9-H), 1.35 (3H, d, *J* 6.4, 3 × 1-H); δ_C(150 MHz) 209.8 (CO), 206.5 (CO), 206.1 (CO), 203.6 (CO), 138.3 (quat. Ph-C), 128.4 (Ph-C), 127.7 (Ph-C), 127.6 (Ph-C), 89.5 (4-C), 87.6 (5-C), 76.2 (3-C), 73.0 (Ph*C*H$_2$), 71.5 (6-C), 71.2 (2-C), 70.1 (10-C), 39.2 (7-C), 29.2 (8-C or 9-C), 23.8 (1-C), 22.8 (9-C or 8-C); *m*/*z* (FIB) 445 (MH^+, 6%), 371 ($MH^+ - 2CO - H_2O$, 10), 315 ($MH^+ - 4CO - H_2O$, 91), 133 (100) [Found (MH^+) 445.0936. $C_{21}H_{25}FeO_7$ requires MH, 445.0950].

General procedure for the preparation of alcohols 12a and 12b

For a 1.2 mmol scale reaction: $NaBH(OAc)_3$ (5.0 equiv.) was added to a solution of the iron complex (1.0 equiv.) in THF (10 ml) at rt. After three days, acetone (10 ml) was added and the mixture was stirred for 1 h. The suspension was filtered through a plug of Celite, washing the residue with acetone (50 ml) and the filtrate was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 65% EtOAc in PE) afforded the diol (mixture of at least three double bond isomers).

TBDMSCl (4.0 equiv.) was added to a solution of the diol (1.0 equiv.) and imidazole (5.0 equiv.) in DMF (2 ml) at 0 °C. The mixture was stirred at 0 °C for 30 min and then at rt for 24 h. Water (15 ml) was added and the mixture was extracted with Et_2O (3 × 15 ml). The combined organic extracts were washed with brine (10 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 5% Et_2O in PE) afforded the bis-silyl ether (mixture of at least three double bond isomers).

Palladium on activated carbon (0.1 equiv., 10% Pd) was added to a solution of the benzyl ether (1.0 equiv.) in EtOAc (5 ml) and stirred under a hydrogen atmosphere for 12 h. The reaction mixture was filtered through Celite, washing the residue with EtOAc (30 ml) and the filtrate was concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 30% Et_2O in PE) afforded the alcohol.

(5*R*,9*S*)-5,9-Bis(*tert*-butyldimethylsilyloxy)decan-1-ol (12a). Prepared according to the general procedure using *endo* complex **11a** (0.52 g, 1.2 mmol). The alcohol **12a** (268 mg, 61% over three steps) was obtained as a colourless oil; $[a]_D^{31}$ +11.6 (*c* 1.00 in $CHCl_3$) (Found: C, 63.3; H, 11.8. $C_{22}H_{50}O_3Si_2$ requires C, 63.1; H, 12.0%); ν_{max}(film)/cm^{-1} 3358 (OH), 2953, 2930, 2857, 1472, 1462, 1406, 1375, 1360, 1254, 1129, 1110, 1052, 1005, 938, 835, 773; δ_H(200 MHz) 3.87–3.54 (4H, m [incl. 3.61, 2H, t, *J* 6.4, 2 × 1-H] 2 × 1-H, 5-H, 9-H), 1.71 (1H, br s, O*H*), 1.64–1.18 (12H, m, 2 × 2-H, 2 × 3-H, 2 × 4-H, 2 × 6-H, 2 × 7-H, 2 × 8-H), 1.10 (3H, d, *J* 6.1, 3 × 10-H), 0.87 (18H, s, 2 × SiC(CH_3)$_3$), 0.03 (6H, 2, Si(CH_3)$_2$), 0.02 (6H, 2, Si(CH_3)$_2$); δ_C(50 MHz) 72.1 (CH), 68.6 (CH), 62.8 (1-C), 39.9 (CH_2), 37.1 (CH_2), 36.7 (CH_2), 32.9 (CH_2), 25.8 (2 × SiC(*C*H$_3$)$_3$), 23.7 (10-C), 21.4 (CH_2), 21.3 (CH_2), 18.0 (2 × Si*C*(CH$_3$)$_3$), −4.5 (2 × Si*C*H$_3$), −4.8 (2 × Si*C*H$_3$); *m*/*z* (FIB) 419 (MH^+, 7%), 345 (10), 287 (19), 229 (33), 185 (31), 159 (61), 155 (100), 137 (65), 115 (64) [Found (MH^+) 419.3410. $C_{22}H_{51}O_3Si_2$ requires MH, 419.3377].

(5*S*,9*S*)-5,9-Bis(*tert*-butyldimethylsilyloxy)decan-1-ol (12b). Prepared according to the general procedure using *exo* complex **11b** (0.53 g, 1.2 mmol). The alcohol **12b** (293 mg, 66% over three steps) was obtained as a colourless oil; $[a]_D^{31}$ +7.7 (*c* 1.00 in $CHCl_3$) (Found: C, 63.3; H, 12.0. $C_{22}H_{50}O_3Si_2$ requires C, 63.1; H, 12.0%); ν_{max}(film)/cm^{-1} 3344 (OH), 2954, 2930, 2857, 1472, 1462, 1375, 1361, 1255, 1130, 1049, 1005, 939, 835, 773; δ_H(600 MHz) 3.82–3.73 (1H, m, 5-H or 9-H), 3.68–3.62 (3H, m [incl. 3.64, 2H, t, *J* 6.5, 2 × 1-H] 2 × 1-H, 9-H or 5-H), 1.68–1.20 (13H, m, 2 × 2-H, 2 × 3-H, 2 × 4-H, 2 × 6-H, 2 × 7-H, 2 × 8-H, O*H*), 1.11 (3H, d, *J* 6.1, 3 × 10-H), 0.99 (9H, s, SiC(CH_3)$_3$), 0.88 (9H, s, SiC(CH_3)$_3$), 0.07–0.03 (12H, m, 2 × Si(CH_3)$_2$); δ_C(150 MHz) 72.2 (CH), 68.6 (CH), 63.0 (1-C), 40.1 (CH_2), 37.2 (CH_2), 36.7 (CH_2), 33.0 (CH_2), 25.9 (2 × SiC(*C*H$_3$)$_3$), 23.8 (10-C), 21.6 (CH_2), 21.3 (CH_2), 18.11 (Si*C*(CH$_3$)$_3$), 18.10 (Si*C*(CH$_3$)$_3$), −4.4 (2 × Si*C*H$_3$), −4.7 (Si*C*H$_3$); *m*/*z* (FIB) 419 (MH^+, 8%), 345 (12), 287 (20), 285 (20), 229 (31), 185 (40), 159 (46), 155 (100), 137 (71), 133 (68), 115 (65) [Found (MH^+) 419.3363. $C_{22}H_{51}O_3Si_2$ requires MH, 419.3377].

General procedure for the preparation of aldehydes 13a and 13b

For a 0.70 mmol scale reaction: a solution of DMSO (2.6 equiv.) in DCM (1.5 ml) was added dropwise to a solution of $(COCl)_2$ (1.3 equiv.) in DCM (2.0 ml) at −78°C and the reaction mixture was stirred for 30 min. A solution of the alcohol (1.0 equiv.) in DCM (1.5 ml) was added dropwise and after 30 min Et_3N (3.5 equiv.) was added dropwise at −78 °C. Stirring was continued at −78 °C for 1 h before the mixture was allowed to warm to rt. The reaction mixture was poured into water (10 ml) and extracted with Et_2O (3 × 10 ml). The combined organic extracts were washed with brine (5 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 10% Et_2O in PE) afforded the aldehyde.

(5*S*,9*S*)-5,9-Bis(*tert*-butyldimethylsilyloxy)decanal (13a). Prepared according to the general procedure using alcohol **12a** (253 mg, 0.61 mmol). The aldehyde **13a** (218 mg, 86%) was obtained as a colourless liquid; $[a]_D^{31}$ +10.6 (*c* 1.00 in $CHCl_3$)

(Found: C, 63.7; H, 11.5. $C_{22}H_{48}O_3Si_2$ requires C, 63.4; H, 11.6%); ν_{max}(film)/cm^{-1} 2953, 2929, 2894, 2857, 2710 (O=C–H), 1729 (C=O), 1472, 1462, 1375, 1360, 1255, 1129, 1073, 1048, 1005, 835, 774; δ_H(200 MHz) 9.74 (1H, t, *J* 1.8, 1-H), 3.85–3.55 (2H, m, 5-H, 9-H), 2.40 (2H, dt, *J* 7.1, 1.8, 2 × 2-H), 1.85–1.15 (10H, m, 2 × 3-H, 2 × 4-H, 2 × 6-H, 2 × 7-H, 2 × 8-H), 1.09 (3H, d, *J* 6.1, 3 × 10-H), 0.87 (18H, s, 2 × SiC(CH_3)$_3$), 0.02 (12H, s, 2 × Si(CH_3)$_2$); δ_C(50 MHz) 202.5 (1-C), 71.7 (5-C or 9-C), 68.5 (9-C or 5-C), 43.9 (CH_2), 39.9 (CH_2), 37.0 (CH_2), 36.2 (CH_2), 25.8 (2 × SiC(*C*H$_3$)$_3$), 23.7 (10-C), 21.3 (CH_2), 18.0 (2 × Si*C*(CH$_3$)$_3$), 17.8 (CH_2), −4.5 (2 × Si*C*H$_3$), −4.6 (Si*C*H$_3$), −4.8 (Si*C*H$_3$); *m*/*z* (FIB) 415 (M^+ − H, 5%), 401 (13), 399 (M^+ − OH, 2), 359 (M^+ − ^{t}Bu, 68), 285 (12), 227 (71), 185 (100) [Found (M^+ − H) 415.3083. $C_{22}H_{47}O_3Si_2$ requires M − H, 415.3064].

(5*R*,9*S*)-5,9-Bis(*tert*-butyldimethylsilyloxy)decanal (13b). Prepared according to the general procedure using alcohol **12b** (340 mg, 0.81 mmol). The aldehyde **13b** (269 mg, 80%) was obtained as a colourless liquid; $[\alpha]_D^{31}$ +5.8 (*c* 1.00 in $CHCl_3$) (Found: C, 63.5; H, 11.6. $C_{22}H_{48}O_3Si_2$ requires C, 63.4; H, 11.6%); ν_{max}(film)/cm^{-1} 2954, 2930, 2900, 2857, 2710 (O=C–H), 1730 (C=O), 1472, 1462, 1375, 1360, 1255, 1129, 1047, 1005, 835, 773; δ_H(200 MHz) 9.75 (1H, t, *J* 1.8, 1-H), 3.87–3.55 (2H, m, 5-H, 9-H), 2.41 (2H, dt, *J* 7.1, 1.8, 2 × 2-H), 1.85–1.20 (10H, m, 2 × 3-H, 2 × 4-H, 2 × 6-H, 2 × 7-H, 2 × 8-H), 1.10 (3H, d, *J* 6.1, 3 × 10-H), 0.88 (18H, s, 2 × SiC(CH_3)$_3$), 0.03 (12H, s, 2 × Si(CH_3)$_2$); δ_C(150 MHz) 202.4 (1-C), 71.8 (5-C or 9-C), 68.5 (9-C or 5-C), 44.0 (CH_2), 40.0 (CH_2), 37.1 (CH_2), 36.2 (CH_2), 25.8 (2 × SiC(*C*H$_3$)$_3$), 23.7 (10-C), 21.5 (CH_2), 18.1 (Si*C*(CH$_3$)$_3$), 18.0 (Si*C*(CH$_3$)$_3$), 17.8 (CH_2), −4.5 (2 × Si*C*H$_3$), −4.6 (Si*C*H$_3$), −4.8 (Si*C*H$_3$); *m*/*z* (FIB) 415 (M^+ − H, 4%), 359 (M^+ − ^{t}Bu, 62), 227 (68), 185 (100), 149 (75) [Found (M^+ − H) 415.3075. $C_{22}H_{47}O_3Si_2$ requires M − H, 415.3064].

General procedure for the preparation of stannanes 14a and 14b

For a 0.50 mmol scale reaction: a solution of tributyldiiodomethylstannane[14] (2.0 equiv.) and the aldehyde (1.0 equiv.) in DMF (10 ml) was added to a solution of $CrCl_2$ (10.0 equiv.) in DMF (30 ml) and the reaction mixture was stirred for 5 h. The reaction mixture was carefully poured into ice–water (100 ml) and extracted with Et_2O (3 × 50 ml). The combined organic extracts were washed with water (30 ml) and brine (30 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel 100 C_{18}-reversed phase, 30% DCM in MeOH) afforded the stannane (*ca.* 19 : 1 mixture of *E*–*Z* isomers).

(1*E*,6*R*,10*S*)-6,10-Bis(*tert*-butyldimethylsilyloxy)-1-tributylstannylundec-1-ene (14a). Prepared according to the general procedure using aldehyde **13a** (216 mg, 0.52 mmol). The stannane **14a** (248 mg, 67%) was obtained as a colourless liquid; ν_{max}(film)/cm^{-1} 2956, 2928, 2956, 1598 (C=C), 1462, 1376, 1254, 1048, 835, 773; NMR data quoted only for *E*-isomer: δ_H(400 MHz) 6.15–5.55 (2H, m, 1-H, 2-H), 3.84–3.73 (1H, m, 10-H), 3.70–3.58 (1H, m, 6-H), 2.18–2.06 (2H, m, 2 × 3-H), 1.65–1.20 (22H, m, 2 × 4-H, 2 × 5-H, 2 × 7-H, 2 × 8-H, 2 × 9-H, 3 × Sn(CH_2)$_2$CH_2CH$_3$), 1.12 (3H, d, *J* 6.1, 3 × 11-H), 0.96–0.83 (33H, m, 2 × SiC(CH_3)$_3$, 3 × Sn(CH$_2$)$_2$CH_2CH_3), 0.5 (6H, s, Si(CH_3)$_2$), 0.04 (6H, s, Si(CH_3)$_2$); δ_C(100 MHz) 149.5 (1-C or 2-C), 127.2 (2-C or 1-C), 72.2 (6-C or 10-C), 68.6 (10-C or 6-C), 40.0 (CH_2), 37.9 (CH_2), 37.2 (CH_2), 36.6 (CH_2), 29.1 (3 × CH_2), 27.2 (3 × CH_2), 25.9 (2 × SiC(*C*H$_3$)$_3$), 24.6 (CH_2), 23.7 (11-C), 21.5 (CH_2), 18.1 (2 × Si*C*(CH$_3$)$_3$), 13.7 (Sn[(CH$_2$)$_3$*C*H$_3$]$_3$), 9.4 (3 × CH_2), −4.4 (2 × Si*C*H$_3$), −4.7 (2 × Si*C*H$_3$).

(1*E*,6*S*,10*S*)-6,10-Bis(*tert*-butyldimethylsilyloxy)-1-tributylstannylundec-1-ene (14b). Prepared according to the general procedure using aldehyde **13b** (400 mg, 0.96 mmol). The stannane **14b** (467 mg, 69%) was obtained as a colourless liquid; ν_{max}(film)/cm^{-1} 2956, 2928, 2866, 1599 (C=C), 1463, 1376, 1360, 1264, 1048, 836, 773; NMR data quoted only for *E*-isomer: δ_H(400 MHz) 6.10–5.35 (2H, m, 1-H, 2-H), 3.85–3.72 (1H, m, 10-H), 3.70–3.57 (1H, m, 6-H), 2.19–2.06 (2H, m, 2 × 3-H), 1.60–1.24 (22H, m, 2 × 4-H, 2 × 5-H, 2 × 7-H, 2 × 8-H, 2 × 9-H, 3 × Sn(CH_2)$_2$CH_2CH$_3$), 1.11 (3H, d, *J* 6.0, 3 × 11-H), 0.94–0.84 (33H, m, 2 × SiC(CH_3)$_3$, 3 × Sn(CH$_2$)$_2$CH_2CH_3), 0.05 (6H, s, Si(CH_3)$_2$), 0.04 (6H, s, Si(CH_3)$_2$); δ_C(100 MHz) 149.5 (1-C or 2-C), 127.2 (2-C or 1-C), 72.2 (6-C or 10-C), 68.6 (10-C or 6-C), 40.1 (CH_2), 37.9 (CH_2), 37.3 (CH_2), 36.5 (CH_2), 29.1 (3 × CH_2), 27.2 (3 × CH_2), 25.9 (2 × SiC(*C*H$_3$)$_3$), 24.5 (CH_2), 23.8 (11-C), 21.6 (CH_2), 18.1 (2 × Si*C*(CH$_3$)$_3$), 13.7 (Sn[(CH$_2$)$_3$*C*H$_3$]$_3$), 9.4 (3 × CH_2), −4.4 (2 × Si*C*H$_3$), −4.7 (2 × Si*C*H$_3$).

General procedure for the Stille coupling of the stannanes 14a and 14b

For a 0.50 mmol scale reaction: $Pd_2(dba)_3$ (0.05 equiv.) and P(2-furyl)$_3$ (0.4 equiv.) were dissolved in PhMe (1 ml) and stirred at rt until the solution had turned from purple to yellow. This solution was added to a mixture of the stannane (1.0 equiv.) and the aryl iodide **15**[6f] (1.0 equiv.) and the reaction was heated to 80 °C for 4 h. The reaction mixture was poured into aqueous NH_4Cl solution (10 ml) and extracted with Et_2O (3 × 10 ml). The combined organic extracts were washed with brine (5 ml), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 70% Et_2O in PE) afforded the coupled product.

Methyl 4,6-bis[(2-methoxyethoxy)methyloxy]-2-[(1′*E*,6′*R*,10′*S*)-6′,10′-bis(*tert*-butyldimethylsilyloxy)undec-1′-en-1′-yl]-benzoate (16a). Prepared according to the general procedure using stannane **14a** (352 mg, 0.50 mmol). The coupled product **16a** (310 mg, 82%) was obtained as a colourless liquid; $[\alpha]_D^{30}$ +5.1 (*c* 1.00 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2956, 2925, 2855, 1733 (C=O), 1602 (C=C), 1456, 1254, 1107, 1024, 835, 772; δ_H(400 MHz) 6.84 (1H, d, *J* 2.0, Ar-*H*), 6.73 (1H, d, *J* 2.0, Ar-*H*), 6.30 (1H, d, *J* 15.7, 1′-H), 6.16 (1H, dt, *J* 15.7, 6.7, 2′-H), 5.25 (2H, s, OCH_2O), 5.23 (2H, s, OCH_2O), 3.87 (3H, s, CO_2CH_3), 3.84–3.74 (5H, m, 10′-H, 2 × OCH_2CH$_2$O), 3.68–3.60 (1H, m, 6′-H), 3.58–3.51 (4H, m, 2 × OCH$_2$CH_2O), 3.39 (3H, s, OCH_3), 3.36 (3H, s, OCH_3), 2.20–2.10 (2H, m, 2 × 3′-H), 1.55–1.20 (10H, m, 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H), 1.07 (3H, d, *J* 6.1, 3 × 11′-H), 0.88 (18H, s, 2 × SiC(CH_3)$_3$), 0.04 (12H, s, 2 × Si(CH_3)$_2$); δ_C(100 MHz) 168.3 (*C*O$_2$CH$_3$), 158.8, (quat. Ar-C), 155.3 (quat. Ar-C), 137.9 (quat. Ar-C), 134.7 (2′-C), 126.2 (1′-C), 117.4 (quat. Ar-C), 106.1 (Ar-C), 102.5 (Ar-C), 93.8 (O*C*H$_2$O), 93.3 (O*C*H$_2$O), 72.1 (6′-C), 71.5 (2 × O*C*H$_2$CH$_2$O), 68.6 (10′-C), 67.8 (OCH$_2$*C*H$_2$O), 67.7 (OCH$_2$*C*H$_2$O), 59.0 (2 × O*C*H$_3$), 52.1 (CO$_2$*C*H$_3$), 40.0 (CH_2), 37.3 (CH_2), 36.7 (CH_2), 33.4 (3′-C), 25.9 (2 × SiC(*C*H$_3$)$_3$), 24.9 (CH_2), 23.7 (11′-C), 21.5 (CH_2), 18.1 (2 × Si*C*(CH$_3$)$_3$), −4.4 (2 × Si*C*H$_3$), −4.7 (2 × Si*C*H$_3$); *m*/*z* (ES) 779 (MNa^+, 6%), 734 (4), 597 (100), 539 (16) [Found (MNa^+) 779.4534. $C_{39}H_{72}NaO_{10}Si_2$ requires MNa, 779.4562].

Methyl 4,6-bis[(2-methoxyethoxy)methyloxy]-2-[(1′*E*,6′*S*,10′*S*)-6′,10′-bis(*tert*-butyldimethylsilyloxy)undec-1′-en-1′-yl]-benzoate (16b). Prepared according to the general procedure using stannane **14b** (317 mg, 0.45 mmol). The coupled product **16b** (290 mg, 85%) was obtained as a colourless liquid; $[\alpha]_D^{30}$ +4.4 (*c* 1.00 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2951, 2928, 2856, 1732 (C=O), 1601 (C=C), 1578 (C=C), 1472, 1462, 1431, 1256, 1108, 1022, 835, 773; δ_H(600 MHz) 6.84 (1H, d, *J* 1.8, Ar-*H*), 6.73 (1H, d, *J* 1.8, Ar-*H*), 6.31 (1H, d, *J* 15.7, 1′-H), 6.17 (1H, dt, *J* 15.7, 6.8, 2′-H), 5.26 (2H, s, OCH_2O), 5.24 (2H, s, OCH_2O), 3.88 (3H, s, CO_2CH_3), 3.85–3.72 (5H, m, 10′-H, 2 × OCH_2-CH$_2$O), 3.70–3.62 (1H, m, 6′-H), 3.58–3.51 (4H, m, 2 × OCH$_2$-

CH_2O), 3.38 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 2.22–2.12 (2H, m, 2 × 3′-H), 1.55–1.23 (10H, m, 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H), 1.11 (3H, d, *J* 6.1, 3 × 11′-H), 0.88 (18H, s, 2 × $SiC(CH_3)_3$), 0.04 (12H, s, 2 × $Si(CH_3)_2$); δ_C(150 MHz) 168.3 (CO_2CH_3), 158.8 (quat. Ar-C), 155.2 (quat. Ar-C), 137.9 (quat. Ar-C), 134.7 (2′-C), 126.2 (1′-C), 117.4 (quat. Ar-C), 106.1 (Ar-C), 102.5 (Ar-C), 93.8 (OCH_2O), 93.3 (OCH_2O), 72.1 (6′-C), 71.5 (2 × OCH_2CH_2O), 68.6 (10′-C), 67.8 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (OCH_3), 58.9 (OCH_3), 52.1 (CO_2CH_3), 40.1 (CH_2), 37.3 (CH_2), 36.6 (CH_2), 33.4 (3′-C), 25.9 (2 × $SiC(CH_3)_3$), 24.8 (CH_2), 23.7 (11′-C), 21.6 (CH_2), 18.1 (2 × $SiC(CH_3)_3$), −4.4 (2 × $SiCH_3$), −4.7 (2 × $SiCH_3$); *m*/*z* (FAB) 779 (MNa^+, 100%), 756 (M^+, 17), 725 ($M^+ - CH_3O$), 12), 699 ($M^+ - {}^t$Bu, 59), 681 (93) [Found (MNa^+) 779.4616. $C_{39}H_{72}NaO_{10}Si_2$ requires MNa, 779.4562].

Preparation of stock solution of HF·py in pyridine and THF

HF·py (3.8 ml) was added carefully to a stirred solution of pyridine (14 ml) in THF (40 ml) in a polyvinylchloride bottle under argon. The resulting colourless solution was stored under argon at −20 °C and used as the stock solution in the following deprotections.

General procedure for the TBDMS-deprotection of bis-silyl ethers 16a and 16b

For a 0.10 mmol scale reaction: the bis-silyl ether (1.0 equiv.) was treated with HF·py stock solution (3 ml) at rt for 12 h. The reaction mixture was poured into aqueous $CuSO_4$ solution (10 ml) and extracted with EtOAc (3 × 10 ml). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 5% MeOH in Et_2O) afforded the diol.

Methyl 4,6-bis[(2-methoxyethoxy)methyloxy]-2-[(1′*E*,6′*R*,10′*S*)-6′,10′-dihydroxyundec-1′-en-1′-yl]benzoate (17a). Prepared according to the general procedure using bis-silyl ether **16a** (83 mg, 0.11 mmol). The diol **17a** (55 mg, 95%) was obtained as a colourless liquid; $[\alpha]_D^{29}$ +3.5 (*c* 1.30 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3416 (OH), 2928, 1729 (C=O), 1601 (C=C), 1577 (C=C), 1433, 1267, 1157, 1108, 1020, 849; δ_H(400 MHz) 6.84 (1H, d, *J* 2.0, Ar-*H*), 6.73 (1H, d, *J* 2.0, Ar-*H*), 6.32 (1H, d, *J* 15.7, 1′-H), 6.21–6.10 (1H, m, 2′-H), 5.26 (2H, s, OCH_2O), 5.23 (2H, s, OCH_2O), 3.88 (3H, s, CO_2CH_3), 3.85–3.76 (5H, m, 10′-H, 2 × OCH_2CH_2O), 3.67–3.58 (1H, m, 6′-H), 3.58–3.51 (4H, m, 2 × OCH_2CH_2O), 3.37 (3H, s, OCH_3), 3.36 (3H, s, OCH_3), 2.24–2.14 (2H, m, 2 × 3′-H), 1.70–1.30 (10H, m, 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H), 1.18 (3H, d, *J* 6.2, 3 × 11′-H); δ_C(100 MHz) 168.4 (CO_2CH_3), 158.8, (quat. Ar-C), 155.3 (quat. Ar-C), 137.8 (quat. Ar-C), 134.4 (2′-C), 126.6 (1′-C), 117.3 (quat. Ar-C), 106.0 (Ar-C), 102.5 (Ar-C), 93.8 (OCH_2O), 93.3 (OCH_2O), 71.6 (6′-C), 71.5 (2 × OCH_2CH_2O), 68.0 (10′-C), 67.8 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (2 × OCH_3), 52.2 (CO_2CH_3), 39.2 (CH_2), 37.3 (CH_2), 36.8 (CH_2), 32.9 (3′-C), 25.0 (CH_2), 23.5 (11′-C), 21.7 (CH_2); *m*/*z* (ES) 551 (MNa^+, 100%) [Found (MNa^+) 551.2793. $C_{27}H_{44}NaO_{10}$ requires MNa, 551.2832].

Methyl 4,6-bis[(2-methoxyethoxy)methyloxy]-2-[(1′*E*,6′*S*,10′*S*)-6′,10′-dihydroxyundec-1′-en-1′-yl]benzoate (17b). Prepared according to the general procedure using bis-silyl ether **16b** (68 mg, 0.09 mmol). The diol **17b** (44 mg, 93%) was obtained as a colourless liquid; $[\alpha]_D^{33}$ +5.4 (*c* 1.00 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3395 (OH), 2930, 1728 (C=O), 1600 (C=C), 1578 (C=C), 1433, 1268, 1157, 1109, 1020, 849; δ_H(400 MHz) 6.84 (1H, d, *J* 2.0, Ar-*H*), 6.73 (1H, d, *J* 2.0, Ar-*H*), 6.31 (1H, d, *J* 15.7, 1′-H), 6.16 (1H, dt, *J* 15.7, 6.8, 2′-H), 5.26 (2H, s, OCH_2O), 5.23 (2H, s, OCH_2O), 3.88 (3H, s, CO_2CH_3), 3.84–3.76 (5H, m, 10′-H, 2 × OCH_2CH_2O), 3.66–3.58 (1H, m, 6′-H), 3.57–3.51 (4H, m, 2 × OCH_2CH_2O), 3.37 (3H, s, OCH_3), 3.36 (3H, s, OCH_3), 2.25–2.14 (2H, m, 2 × 3′-H), 1.75–1.37 (10H, m, 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H), 1.18 (3H, d, *J* 6.2, 3 × 11′-H); δ_C(100 MHz) 168.5 (CO_2CH_3), 158.8, (quat. Ar-C), 155.2 (quat. Ar-C), 137.8 (quat. Ar-C), 134.4 (2′-C), 126.5 (1′-C), 117.2 (quat. Ar-C), 105.9 (Ar-C), 102.5 (Ar-C), 93.8 (OCH_2O), 93.2 (OCH_2O), 71.5 (6′-C, 2 × OCH_2CH_2O), 67.9 (10′-C), 67.8 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (2 × OCH_3), 52.3 (CO_2CH_3), 39.1 (CH_2), 37.2 (CH_2), 36.9 (CH_2), 33.0 (3′-C), 25.0 (CH_2), 23.6 (11′-C), 21.8 (CH_2); *m*/*z* (ES) 551 (MNa^+, 100%), 463 (4), 242 (8) [Found (MNa^+) 551.2818. $C_{27}H_{44}NaO_{10}$ requires MNa, 551.2832].

General procedure for the hydrolysis of methyl benzoates 17a and 17b

For a 0.08 mmol scale reaction: 10 M aqueous KOH solution (1 ml) was added to a solution of the methyl benzoate (1.0 equiv.) in ethane-1,2-diol (2 ml) and the reaction was heated to 120 °C for 3 h. The reaction mixture was poured into water (10 ml) and extracted with Et_2O (2 × 5 ml). The aqueous phase was acidified to pH 2 using 3 M aqueous HCl solution and extracted with $CHCl_3$ (3 × 10 ml). The combined $CHCl_3$ extracts were washed with brine (2 ml), dried over Na_2SO_4 and concentrated under reduced pressure to afford the seco acid, which was used without further purification.

4,6-Bis[(2-methoxyethoxy)methyloxy]-2-[(1′*E*,6′*R*,10′*S*)-6′,10′-dihydroxyundec-1′-en-1′-yl]benzoic acid (18a). Prepared according to the general procedure using methyl benzoate **17a** (48 mg, 0.09 mmol). The seco acid **18a** (40 mg, 87%) was obtained as a colourless liquid; ν_{max}(film)/cm^{-1} 3396 (OH), 2930, 1718 (C=O), 1601 (C=C), 1578 (C=C), 1456, 1284, 1172, 1158, 1109, 1020, 848; δ_H(400 MHz) 6.82 (1H, d, *J* 1.8, Ar-*H*), 6.73 (1H, d, *J* 1.8, Ar-*H*), 6.55 (1H, d, 15.7, 1′-H), 6.11 (1H, dt, *J* 15.7, 6.9, 2′-H), 5.25 (4H, s, 2 × OCH_2O), 4.31 (2H, br s, 2 × O*H*), 3.91–3.69 (5H, m, 10′-H, 2 × OCH_2CH_2O), 3.68–3.59 (1H, m, 6′-H), 3.58–3.48 (4H, m, 2 × OCH_2CH_2O), 3.37 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 2.26–2.11 (2H, m, 2 × 3′-H), 1.66–1.29 (10H, m, 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H), 1.18 (3H, d, *J* 6.1, 3 × 11′-H); δ_C(100 MHz) 169.3 (CO_2H), 158.9 (quat. Ar-C), 155.2 (quat. Ar-C), 138.7 (quat. Ar-C), 134.2 (2′-C), 127.6 (1′-C), 117.0 (quat. Ar-C), 106.8 (Ar-C), 102.4 (Ar-C), 93.8 (OCH_2O), 93.3 (OCH_2O), 71.6 (OCH_2CH_2O), 71.5 (OCH_2CH_2O), 71.3 (6′-C), 68.1 (10′-C), 68.1 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (OCH_3), 58.9 (OCH_3), 38.8 (CH_2), 37.1 (CH_2), 35.6 (CH_2), 32.2 (3′-C), 24.2 (CH_2), 23.3 (11′-C), 21.4 (CH_2); *m*/*z* (ES) 537 (MNa^+, 20%), 413 (59), 365 (100), 349 (79) [Found (MNa^+) 537.2709. $C_{26}H_{42}NaO_{10}$ requires MNa, 537.2676].

4,6-Bis[(2-methoxyethoxy)methyloxy]-2-[(1′*E*,6′*S*,10′*S*)-6′,10′-dihydroxyundec-1′-en-1′-yl]benzoic acid (18b). Prepared according to the general procedure using methyl benzoate **17b** (37 mg, 0.07 mmol). The seco acid **18b** (33 mg, 91%) was obtained as a colourless liquid; ν_{max}(film)/cm^{-1} 3376 (OH), 2932, 1720 (C=O), 1601 (C=C), 1579 (C=C), 1455, 1317, 1285, 1174, 1158, 1111, 1021, 849; δ_H(600 MHz) 6.82 (1H, d, *J* 1.9, Ar-*H*), 6.73 (1H, d, *J* 1.9, Ar-*H*), 6.58 (1H, d, 15.7, 1′-H), 6.12 (1H, dt, *J* 15.7, 6.9, 2′-H), 5.27 (2H, s, OCH_2O), 5.26 (2H, s, OCH_2O), 3.88–3.70 (5H, m, 10′-H, 2 × OCH_2CH_2O), 3.68–3.61 (1H, m, 6′-H), 3.58–3.51 (4H, m, 2 × OCH_2CH_2O), 3.37 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 2.26–2.18 (2H, m, 2 × 3′-H), 1.69–1.39 (10H, m, 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H), 1.18 (3H, d, *J* 6.2, 3 × 11′-H); δ_C(150 MHz) 169.1 (CO_2H), 158.9 (quat. Ar-C), 155.2 (quat. Ar-C), 139.0 (quat. Ar-C), 134.2 (2′-C), 127.7 (1′-C), 116.8 (quat. Ar-C), 106.9 (Ar-C), 102.3 (Ar-C), 93.7 (OCH_2O), 93.3 (OCH_2O), 71.6 (OCH_2CH_2O), 71.5 (OCH_2CH_2O), 71.3 (6′-C), 68.2 (10′-C), 68.2 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (OCH_3), 58.9 (OCH_3),

38.8 (CH_2), 37.0 (CH_2), 35.7 (CH_2), 32.2 (3′-C), 24.1 (CH_2), 23.5 (11′-C), 21.5 (CH_2); *m/z* (ES) 537 (MNa^+, 100%), 515 (MH^+, 17), 421 (8), 242 (9) [Found (MNa^+) 537.2700. $C_{26}H_{42}NaO_{10}$ requires MNa, 537.2676].

General procedure for the macrolactonisation of seco acids 18a and 18b using the Mukaiyama protocol

For a 0.10 mmol scale reaction: a solution of the seco acid (1.0 equiv.) and Et_3N (8.0 equiv.) in MeCN (10 ml) was added to a refluxing solution of 2-chloro-1-methylpyridinium iodide (4.0 equiv.) in MeCN (10 ml) over a 10 h period *via* syringe pump. After an additional 5 h at reflux, the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 3% MeOH in Et_2O) afforded the diprotected zearalenol.

2,4-Bis[(2-methoxyethoxy)methyl]-α-zearalenol (19a). Prepared according to the general procedure using seco acid **18a** (50 mg, 0.10 mmol). The diprotected α-zearalenol **19a** (32 mg, 64%) was obtained as a colourless oil; $[\alpha]_D^{30}$ +43.4 (*c* 1.1 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3442 (OH), 2921, 1719 (C=O), 1600 (C=C), 1577 (C=C), 1453, 1261, 1155, 1104, 1022; δ_H(400 MHz) 6.82 (1H, d, *J* 2.0, Ar-*H*), 6.73 (1H, d, *J* 2.0, Ar-*H*), 6.46 (1H, d, *J* 16.1, 1′-H), 6.22 (1H, dt, *J* 16.1, 6.0, 2′-H), 5.30–5.19 (5H, m, 10′-H, 2 × OCH_2O), 3.83–3.77 (4H, m, 2 × OCH_2CH_2O), 3.77–3.69 (1H, m, 6′-H), 3.59–3.51 (4H, m, 2 × OCH_2CH_2O), 3.38 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 2.38–2.28 (1H, m, 3′-H), 2.24–2.12 (1H, m, 3′-H), 1.79–1.14 (13H, m [incl. 1.34, 3H, d, *J* 6.3, 3 × 11′-H] 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H, 3 × 11′-H); δ_C(100 MHz) 167.8 (Ar*C*O), 158.6 (quat. Ar-C), 154.8 (quat. Ar-C), 137.2 (quat. Ar-C), 133.8 (2′-C), 126.4 (1′-C), 118.4 (quat. Ar-C), 106.0 (Ar-C), 102.5 (Ar-C), 93.7 (OCH_2O), 93.4 (OCH_2O), 71.6 (OCH_2CH_2O), 71.5 (OCH_2CH_2O), 71.1 (6′-C or 10′-C), 70.6 (10′-C or 6′-C), 67.8 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (2 × OCH_3), 35.4 (CH_2), 34.5 (CH_2), 32.5 (CH_2), 30.4 (3′-C), 20.6 (CH_2), 20.4 (11′-C), 19.9 (CH_2); *m/z* (ES) 519 (MNa^+, 100%) [Found (MNa^+) 519.2545. $C_{26}H_{40}NaO_9$ requires MNa, 519.2570].

2,4-Bis[(2-methoxyethoxy)methyl]-β-zearalenol (19b). Prepared according to the general procedure using seco acid **18b** (50 mg, 0.10 mmol). The diprotected β-zearalenol **19b** (31 mg, 62%) was obtained as a colourless oil; $[\alpha]_D^{30}$ +40.0 (*c* 0.30 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3447 (OH), 2926, 1720 (C=O), 1600 (C=C), 1577 (C=C), 1447, 1264, 1157, 1104, 1024; δ_H(600 MHz) 6.87 (1H, d, *J* 1.7, Ar-*H*), 6.73 (1H, d, *J* 1.7, Ar-*H*), 6.38 (1H, d, *J* 15.8, 1′-H), 6.11–6.04 (1H, m, 2′-H), 5.41–5.33 (1H, m, 10′-H), 5.26 (2H, s, OCH_2O), 5.25 (1H, d, *J* 7.0, OC*H*HO), 5.22 (1H, d, *J* 7.0, OCH*H*O), 3.83–3.78 (4H, m, 2 × OCH_2CH_2O), 3.71–3.64 (1H, m, 6′-H), 3.53–3.48 (4H, m, 2 × OCH_2CH_2O), 3.39 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 2.34–2.27 (1H, m, 3′-H), 2.26–2.18 (1H, m, 3′-H), 1.83–1.19 (13H, m [incl. 1.30, 3H, d, *J* 6.4, 3 × 11′-H] 2 × 4′-H, 2 × 5′-H, 2 × 7′-H, 2 × 8′-H, 2 × 9′-H, 3 × 11′-H); δ_C(100 MHz) 167.6 (Ar*C*O), 158.6 (quat. Ar-C), 154.6 (quat. Ar-C), 136.9 (quat. Ar-C), 133.8 (2′-C), 127.6 (1′-C), 118.5 (quat. Ar-C), 105.6 (Ar-C), 102.5 (Ar-C), 93.6 (OCH_2O), 93.4 (OCH_2O), 71.6 (OCH_2CH_2O), 71.5 (OCH_2CH_2O), 70.8 (10′-C), 69.1 (6′-C), 67.8 (OCH_2CH_2O), 67.7 (OCH_2CH_2O), 59.0 (2 × OCH_3), 36.7 (CH_2), 34.9 (CH_2), 32.7 (CH_2), 30.3 (3′-C), 22.8 (CH_2), 19.5 (11′-C), 19.4 (CH_2); *m/z* (ES) 519 (MNa^+, 100%), 421 (13), 281 (37), 186 (18) [Found (MNa^+) 519.2605. $C_{26}H_{40}NaO_9$ requires MNa, 519.2570].

General procedure for the preparation of α- and β-zearalenol 1 and 2

For a 0.04 mmol scale reaction: THF (2 ml) and aqueous 1.5 M HCl solution (1 ml) were added to the diprotected zearalenol (1.0 equiv.) and the mixture was stirred at 40 °C for 48 h. Aqueous $NaHCO_3$ solution (2 ml) was added and the mixture was extracted with Et_2O (3 × 5 ml). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue using a Biotage FLASH 12i system (FLASH 12S cartridge, 1% MeOH in DCM) afforded the natural product zearalenol.

α-Zearalenol (1). Prepared according to the general procedure using diprotected α-zearalenol **19a** (20 mg, 0.04 mmol). α-Zearalenol **1** (12 mg, 93%) was obtained as a colourless oil. 600 MHz ^{1}H NMR analysis indicated a de of 94%; $[\alpha]_D^{32}$ −93.6 (*c* 0.55 in acetone) [optical rotation obtained on an authentic sample: $[\alpha]_D^{32}$ −97.3 (*c* 0.55 in acetone)]; ν_{max}(film)/cm^{-1} 3362 (OH), 2933, 2859, 1644 (C=O), 1608 (C=C), 1579 (C=C), 1454, 1391, 1354, 1314, 1258, 1204, 1162, 1110, 1026, 969, 910, 848, 812; δ_H(600 MHz, d_6-acetone) 12.17 (1H, s, 2-OH), 9.12 (1H, br s, 4-OH), 7.17 (1H, d, *J* 15.1, 1′-H), 6.45 (1H, d, *J* 2.4, Ar-*H*), 6.29 (1H, d, *J* 2.4, Ar-*H*), 5.76–5.69 (1H, m, 2′-H), 5.00–4.93 (1H, m, 10′-H), 3.80–3.72 (1H, m, 6′-H), 3.31 (1H, br s, 6′-OH), 2.34–2.27 (2H, m, 2 × 3′-H), 1.96–1.87 (2H, m, 4′-H, 9′-H), 1.72–1.41 (7H, m, 4′-H, 5′-H, 2 × 7′-H, 2 × 8′-H, 9′-H), 1.39 (3H, d, *J* 6.1, 3 × 11′-H), 1.12–1.08 (1H, m, 5′-H); δ_C(100 MHz, d_6-acetone) 171.8 (Ar*C*O), 165.9 (quat. Ar-C), 162.5 (quat. Ar-C), 144.3 (quat. Ar-C), 133.5 (2′-C), 132.7 (1′-C), 108.7 (Ar-C), 102.6 (quat. Ar-C), 101.9 (Ar-C), 73.8 (10′-C), 65.1 (6′-C), 36.8 (7′-C), 34.8 (9′-C), 31.8 (5′-C), 30.3 (3′-C), 22.6 (4′-C), 21.5 (8′-C), 20.3 (11′-C); *m/z* (ES) 343 (MNa^+, 88%), 325 (MNa − H_2O, 100), 307 (MNa − $2H_2O$, 5), 299 (MNa − CO_2, 28), 229 (19), 197 (4) [Found (MNa^+) 343.1503. $C_{18}H_{24}NaO_5$ requires MNa, 343.1516]. Data obtained on the synthetic α-zearalenol **1** were consistent (^{1}H NMR, ^{13}C NMR, TLC, $[\alpha]_D$) with those obtained for an authentic sample purchased from Sigma Aldrich.

β-Zearalenol (2). Prepared according to the general procedure using diprotected β-zearalenol **19b** (20 mg, 0.04 mmol). β-Zearalenol **2** (12 mg, 93%) was obtained as a white, amorphous solid. 600 MHz ^{1}H NMR analysis indicated a de of >95%; $[\alpha]_D^{32}$ −12.5 (*c* 1.00 in acetone) [optical rotation obtained on an authentic sample: $[\alpha]_D^{32}$ −12.9 (*c* 1.00 in acetone)]; ν_{max}(film)/cm^{-1} 3396 (OH), 2922, 2851, 1643 (C=O), 1608 (C=C), 1580 (C=C), 1452, 1378, 1353, 1311, 1258, 1197, 1162, 1109, 1024, 964, 904, 847; δ_H(600 MHz, d_6-acetone) 11.03 (1H, br s, 2-OH), 9.02 (1H, br s, 4-OH), 6.86 (1H, d, *J* 15.5, 1′-H), 6.53 (1H, d, *J* 2.2, Ar-*H*), 6.28 (1H, d, *J* 2.2, Ar-*H*), 5.97 (1H, ddd, *J* 15.5, 8.4, 6.1, 2′-H), 5.13–5.06 (1H, m, 10′-H), 3.81–3.71 (1H, m, 6′-H), 3.40 (1H, br s, 6′-OH), 2.36–2.28 (1H, m, 3′-H), 2.28–2.21 (1H, m, 3′-H), 1.96–1.86 (1H, m, 9′-H), 1.79–1.61 (5H, m, 2 × 4′-H, 5′-H, 7′-H, 9′-H), 1.59–1.52 (1H, m, 7′-H), 1.49–1.37 (2H, m, 2 × 8′-H), 1.34 (3H, d, *J* 6.3, 3 × 11′-H), 1.32–1.23 (1H, m, 5′-H); δ_C(100 MHz, d_6-acetone) 171.1 (Ar*C*O), 163.6 (quat. Ar-C), 161.8 (quat. Ar-C), 142.3 (quat. Ar-C), 132.2 (2′-C), 131.4 (1′-C), 107.4 (Ar-C), 105.2 (quat. Ar-C), 101.6 (Ar-C), 73.4 (10′-C), 67.6 (6′-C), 36.3 (7′-C), 34.2 (9′-C), 31.6 (5′-C), 31.0 (3′-C), 22.4 (4′-C), 19.1 (8′-C), 18.0 (11′-C); *m/z* (ES) 343 (MNa^+, 77%), 325 (MNa − H_2O, 100), 299 (MNa − CO_2, 29) [Found (MNa^+) 343.1510. $C_{18}H_{24}NaO_5$ requires MNa, 343.1516]. Data obtained for the synthetic β-zearalenol **2** were consistent (^{1}H NMR, ^{13}C NMR, TLC, $[\alpha]_D$) with those obtained for an authentic sample purchased from Sigma Aldrich.

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