HETEROCYCLES, Vol. 62, 2003, pp. 619 - 633
Received, 28th August, 2003, Accepted, 31st October, 2003, Published online, 14th November, 2003

THE SYNTHESIS OF (-)-GLOEOSPORONE, A POTENT FUNGAL AUTOINHIBITOR OF SPORE GERMINATION USING A π-ALLYLTRICARBONYLIRON LACTONE COMPLEX AND A NEW REDUCTIVE DECOMPLEXATION PROCEDURE FOR THE INSTALLATION OF THE EMBEDDED 1,7-DIOL COMPONENT OF THE NATURAL PRODUCT

Ed Cleator, Jürgen Harter, and Steven V. Ley*

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, UK. CB2 1EW. e-mail svl1000@cam.ac.uk

Dedicated to Professor Leo A. Paquette on the occasion of his 70th Birthday and with thanks for his friendship and phenomenal contribution to organic chemistry over many years.

Abstract – The synthesis of (-)-gloeosporone has been achieved *via* a π-allyltricarbonyliron complex (**7**). The stereogenic centers observed in the natural product were constructed by a highly stereoselective Makaiyama aldol reaction to afford a new complex that upon reductive iron decomplexation gave a 1,7-diol motif found in the natural product.

INTRODUCTION

We have published extensively on the synthetic applications of π-allyltricarbonyliron complexes,[1] (Figure 1) these complexes have been shown to react in a highly dependable manner furnishing a wide range of functionality in a highly stereoselective fashion, and are therefore readily adapted to natural product syntheses.[2]

Crucial to the success of all these syntheses is the methods of detachment of the ligating iron species, coupled with the predictable stereochemical outcome of reactions being performed on these compexes.[3] Furthermore π-allyltricarbonyliron complexes are easily accessible from a large number of different starting materials.[1,4]

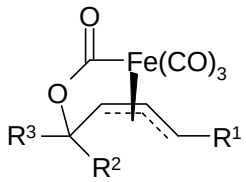
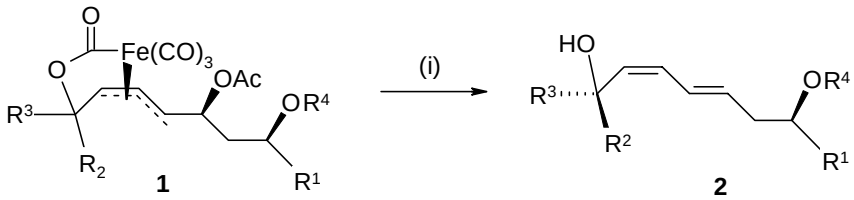


Figure 1

Recently we reported on a new reductive detachment of the ligating iron species.[5] This detachment occurs by treatment of a π-allyltricarbonyliron complexes such as **1** with lithium naphthalenide in THF, to give the corresponding 1,7-diol **(2)** (Scheme 1). Here we wish to report in full how this decomplexation technique can be readily applied as a key step in the synthesis of (-)-gloeosporone.



Scheme 1. (i) Li naphthalenide, THF, -78°C → rt, 17 h, 66-97%.

The isolation of the germination self inhibitor (-)-gloeosporone **(3)** from conidia of *Collectotrichum gloeosporioides*[6] generated much interest, both for its observed antifungal properties and the unique oxocane structure **(4)**, as originally reported[7] (Figure 2). Elegant synthesis studies of **(4)** by the Holmes groups[8] showed that the assigned oxocane structure to be incorrect, and enabled the correct macrocyclic structure **(3)** to be assigned. The total synthesis of **3** has also been achieved by a number of groups.[9]

Here we report a conceptually different approach to the synthesis of **3**, employing π-allyltricarbonyliron complex at a templating architecture to produce the 1,7-diol motif exhibited in the natural product.

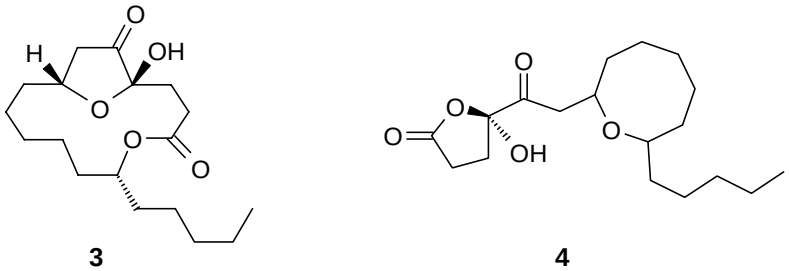
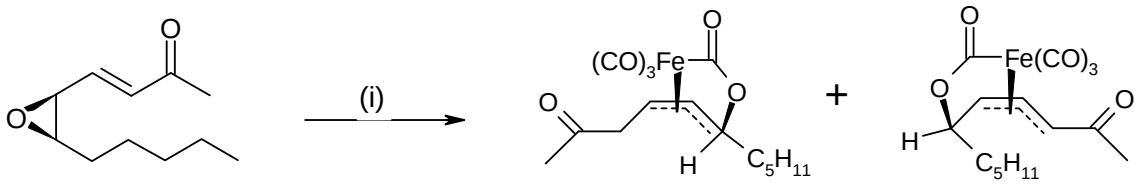


Figure 2.

RESULTS AND DISCUSSION

The synthesis of the key π-allyltricarbonyliron lactone complex **(7)** is readily accomplished upon treatment of **5** with diironnonacarbonyl in degassed THF (Scheme 2), providing a 4 : 1 mixture of

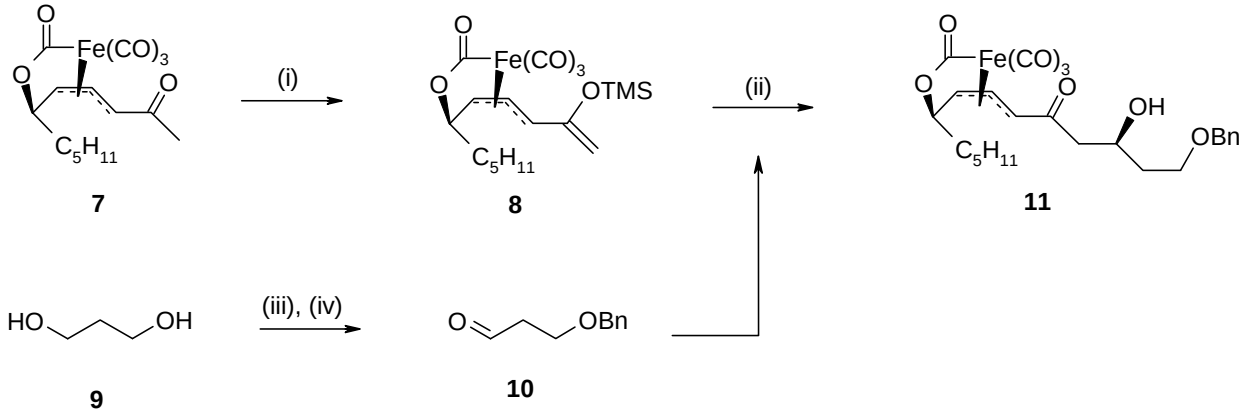
complexes **(7)** and **(6)** in a 64% yield.[10] The desired *endo* complex **(7)** (major) and the *exo* complex **(6)** (minor) were readily separated by SiO_2 column chromatography and are available in gramme quantities.



5 **6** **7**

Scheme 2. (i) $Fe_2(CO)_9$, THF, rt, 3 h, 64%, **7** : **6** in a 4 : 1 ratio.

Following our established method,[11] treatment of a dichloromethane solution of **7** with trimethylsilyl triflate in the presence of NEt_3 gave an intermediate trimethylsilyl enol ether **(8)** in an 84% yield. This silyl enol ether was used immediately in the highly diastereoselective Mukaiyama aldol coupling. The coupling partner for this reaction, 3-benzyloxypropionaldehyde **(10)**, was readily prepared following literature methods from 1,3-propanediol **(9)**.[12] (Scheme 3). The resulting alcohol **(11)** was formed as a single diastereomer, in 63% yield after work-up with HF-pyridine complex in THF.



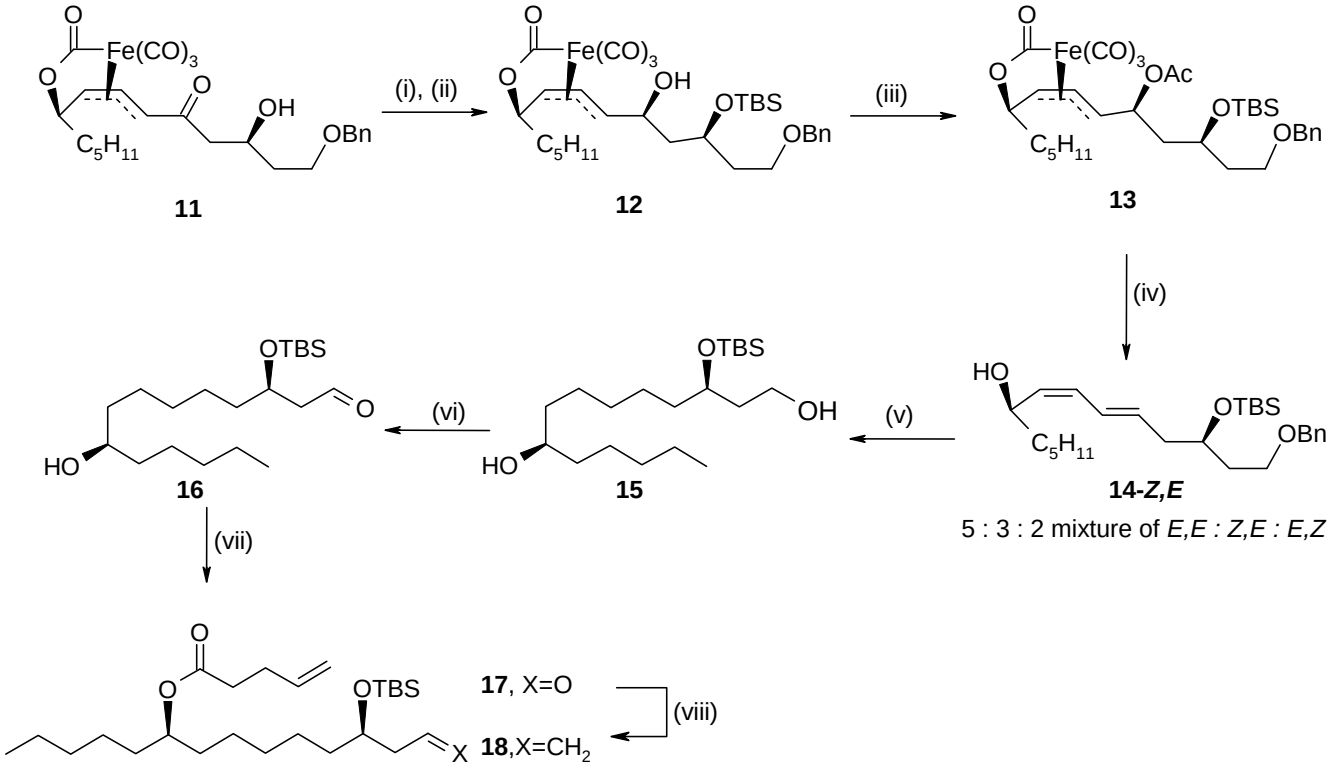
7 **8** **11**

9 **10**

Scheme 3. (i) TMSOTf, Et_3N, CH_2Cl_2, 0°C, 1 h, 84%; (ii) $OHC(CH_2)_2OBn$ (**10**), $BF_3.OEt_2$, CH_2Cl_2, -78°C then Et_3N, HF-pyr, THF, 63%; (iii) BnBr, THF, TBAI, NaH, rt, 16 h, 73%; (iv) DMSO, $(COCl)_2$, CH_2Cl_2, NEt_3, -78°C → rt, 1.5 h, 69%.

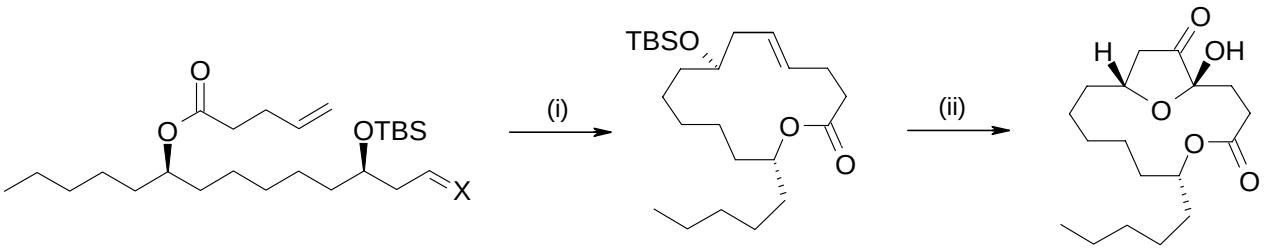
The Mukaiyama aldol coupling of complexes such as **8** to generate 1,7-diols has a predictable stereochemical outcome which has been thoroughly investigated by our group.[13] This outcome has been shown to be a consequence of the bulky tricarbonyl lactone moiety shielding the top face of enol ether **(8)**. Notably the iron tether also ensures that **8** has an s-*trans* conformation, this coupled with the *endo* orientated pentyl group ensures only one reactive conformation is achievable, thus generating desired 1,7-diol relationship. Reprotection of the hydroxyl group in **11** with *t*-butyldimethylsilyl triflate, followed by stereoselective reduction with *i*-Bu_3Al in a toluene / dichloromethane mixture[14] gave the

mono-protected diol **(12)** in an 83% yield over two steps. The acetate intermediate for the key reductive removal of the ligating iron moiety **(13)** was prepared in a 98% yield upon treatment of **12** with acetic anhydride in dichloromethane. Subjecting complex **(13)** to the new reductive decomplexation conditions, namely lithium naphthalenide in THF at -78°C, afforded a mixture of alkenes **(14)** in an excellent 98% yield after warming the reaction mixture to room temperature[5] (Scheme 4). Reduction of the intermediate diene mixture with simultaneous benzyl deprotection gave mono-protected triol **(15)** (83%). The primary alcohol was then selectively oxidized to aldehyde **(16)** using Oshima conditions.[15] It was noted that in order for this reaction to proceed smoothly two equivalents of K_2CO_3 needed to be added to the reaction mixture, however aldehyde **(16)** could be prepared in a respectable 78% yield. The sensitivity of this aldehyde became apparent during subsequent acylation with 4-pentenoyl chloride which occurred in a 65% yield. This reaction was found to be capricious and often led to incomplete conversion which necessitated recycling of unreacted **16** under the described conditions. Attempting the reaction under a variety of other conditions led loss of the OTBS moiety and formation of the corresponding α,β-unsaturated ester. Nevertheless **17** could be readily methylenated with methyl phosphonium chloride upon treatment with *t*-BuOK in THF,[16] to provide the known precursor **(18)** to (-)-gloeosporone.



Scheme 4. *Reagents and conditions*: (i) TBSOTf, Et_3N, CH_2Cl_2, 0°C, 18 h, 100%; (ii) *i*-Bu_3Al (1M solution in toluene), CH_2Cl_2, 0°C, 30 min, 83%; (iii) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 0°C → rt, 2h, 98%.(iv) Li naphthalenide, THF, -78°C → rt, 17 h, 98%; (v) Pd/C, H_2, EtOAc, 12 h, 83%; (vi) $RuCl_2(PPh_3)_3$, benzene, K_2CO_3 (2 eq.) rt, 20 h, 78%; (vii) 4-pentenoyl chloride, DMAP (6 eq.), CH_2Cl_2, 0°C → rt, 3 h, 65%; (viii) $(Ph)_3PCH_3Cl$, *t*-BuOK, THF, 0°C → rt, 85%.

The synthesis of (-)-gloeosporone **(3)** was completed from **18** *via* a modified method. Thus treatment of a boiling dichloromethane solution of compound **(18)** with 3 mol% of tricyclohexylphosphine[1,3-bis-(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidine][benzylidine]ruthenium(IV)dichloride (Grubbs' second generation RCM catalyst),[17] formed cyclic lactone **(19)** as a mixture of mixture of alkene isomers(1 : 1 mixture of geometric isomers by ^{13}C NMR spectrometry) in an excellent 99% yield (Scheme 5). This compound was known to undergo oxidation of the alkene mixture with $KMnO_4$ in acetic anhydride,[18] and following desilylation / cyclization by treatment with HF in acetonitrile produces **(1)** in a 56% yield.[9b,9g]



18 **19-*E*** **3**

1 : 1 mixture of *E : Z*

Scheme 5. *Reagents and conditions*: (i) $RuCl_2(=CHPh)[1,3\text{-}ImH_2]P(Cy)_3$, CH_2Cl_2, 40°C, 5 h, 99%; (ii) $KMnO_4$, Ac_2O, then HF, MeCN, 4 h, 56%

In summary, this work further demonstrates the power of π-allyltricarbonyliron lactone complexes for natural product synthesis. In particularly the use of the new lithium naphthalenide decomplexation protocol has been shown to be an especially attractive route to enantiopure 1,7-diol units found in the natural product (-)-gloeosporone but also could find applications in other systems.

EXPERIMENTAL

^1H NMR spectra were recorded in $CDCl_3$ or C_6D_6 on Bruker DRX-600 or DRX-400 spectrometer and are reported as follows: chemical shift, δ (ppm) [number of protons, multiplicity, coupling constant *J* (Hz), and assignment]. Residual protic solvent $CHCl_3$ (δ_H = 7.26 ppm) or C_6H_6 (δ_H = 7.20 ppm) was used as the internal reference. ^{13}C NMR spectra were recorded in $CDCl_3$ or C_6D_6 at 150 MHz or 100 MHz on Bruker DRX-600 or DRX-400 or spectrometer, using the central resonance of $CDCl_3$ (δ_C = 77.0 ppm) or C_6D_6 (δ_C = 128.0 ppm) as the internal reference. In distortionless enhancement by polarisation transfer experiments (DEPT135) signals with an odd number of protons attached are designated (–) and those with an even number (+). For those cases where an inseperable mixture of compounds was produced, the data reported was obtained on the mixture. IR spectra were recorded on Perkin-Elmer 983G, FTIR 1620 or Perkin Elmer ATR Spectrum 1 spectrophorometer. MS spectra were obtained on Kratos MS890MS, Bruker BIOAPEX 4.7 T FTICR or Micromass Q-TOF spectrometers at the Department of Chemistry, University of

Cambridge. The following ionisation techniques were used: electron ionisation (EI), chemical ionisation (CI), fast atom bombardment (FAB) and electrospray (ES). Optical rotation measurements are reported in 10^{-1} deg cm^2 g^{-1}; concentrations (*c*) are in g 100 dm^{-3}. Flash column chromatography was carried out using Merck Kieselgel (230–400 mesh) unless otherwise indicated. Analytical thin layer chromatography was performed using precoated glass-backed plates (Merck Kieselgel 60 F254) and visualised by ultraviolet, acidic ammonium molybdate(IV) or acidic potassium permanganate solutions. Aqueous solutions were saturated unless otherwise specified. Petrol refers to petroleum ether boiling point 40–60 °C. In cases where mixtures of solvents were utilised, the ratios given refer to the volumes used. 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 unless otherwise stated. Et_2O and THF were distilled from sodium benzophenone ketyl. CH_2Cl_2 and PhMe were distilled from calcium hydride.

Preparation of lithium naphthalenide solution

A suspension of naphthalene (6.5 g, 50.7 mmol) and lithium (1.15 g, 50.0 mmol, ~30 wt.% dispersion in mineral oil) in THF (50 mL) was sonicated for 30 min to yield a dark green solution (~1 mol dm^{-3}).

(3*E*,5*R*,6*R*)-5,6-Epoxy-2-oxoundec-3-ene (**5**)

Diethyl (2-oxopropyl)phosphonate (1.2 eq., 13.9 mmol, 2.7 g, 2.67 mL, d=1.010) was added dropwise to a stirred solution of NaH (MW 24.0, 0.51 g of a 60% dispersion in mineral oil) in THF (110 mL) over 5 minutes before cooling to 0°C. A solution of (2*S*,3*R*)-2,3-epoxyoctanal (1.65 g, 11.6 mmol) in THF (10 mL) was then added dropwise over 10 min. After 30 min the reaction mixture was poured into brine (50 mL) and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 100 mL) and the combined organic extracts were washed with brine (50 mL), and then dried ($MgSO_4$). Concentration *in vacuo* followed by flash column chromatography of the residue (eluent Et_2O : PE 1:19 to 1:9, gradient) afforded epoxy enone **(5)** (1.60 g, 876%) as a colourless oil; ν_{max} (film)/cm^{-1}: 2956, 2929, 2858, 1698, 1679 (C=O), 1628 (C=C), 1466, 1432, 1360, 1299, 1257, 1180, 1146, 976, 883, 827, 726; δ_H (400 MHz, $CDCl_3$): 0.88 (3H, t, J 7.2, 11-H x 3), 1.21-1.62 (8H, m, 7-H x 2, 8-H x 2, 9-H x 2, 10-H x 2), 2.24 (3H, s, 1-H x 3), 2.89 (1H, td, *J* 5.3, 2.0, 6-H), 3.20 (1H, dd, *J* 6.7, 2.1, 5-H), 6.32 (1H, d, *J* 16.8, 3-H), 6.46 (1H, dd, *J* 16.8, 6.7, 4-H); δ_C (100 MHz, $CDCl_3$): 197.3 (C=O), 143.5 (CH), 132.4 (CH), 61.5 (CH), 6.4 (CH), 31.7 (CH_2), 31.4 (CH_2), 27.2 (CH_3), 25.4 (CH_2), 22.5 (CH_2), 13.9 (CH_3); m/z (+EI): Found: $[M]^+$ 182.1308. $C_{11}H_{18}O_2$ requires 182.1307. $[\alpha]_D^{25}$ +23.8° (c 1.00 in $CHCl_3$) [optical rotation reported in lit.[19] $[\alpha]_D^{27}$ +27.1° (c 1.0 in $CHCl_3$)]; Data were consistent with those reported in the literature.[19]

[(3*E*,5*S*,6*R*)-6-(Carbonyloxy-κC)-2-oxo-(3,4,5-η)-undec-3-en-5-yl]tricarbonyliron (6) and

[(3*E*,5*R*,6*R*)-6-(carbonyloxy-κC)-2-oxo-(3,4,5-η)-undec-3-en-5-yl]tricarbonyliron (**7**)

Degassed THF (150 mL) was added to $Fe_2(CO)_9$ (MW 363.79, 2.2 eq., 19.4 mmol, 7.04 g) under an argon atmosphere, the resultant solution was stirred in the absence of light for 30 min Epoxy enone **(5)** (1.60 g, 8.8 mmol) dissolved in THF (20 mL) was then added dropwise and stirring was continued for a further 3 h. The reaction mixture was then filtered through a pad of celite washing with Et_2O (3 x 100 mL). The organics were combined and toluene (5 mL) was added, and the solvents were removed *in vacuo*. The residue was the purificatied by flash column chromatography (eluent PE : Et_2O 1:1) *endo* complex **(7)** (1.58 g, 51%) as an orange-brown solid; ν_{max} (film)/cm^{-1}: 3057, 2957, 2932, 2861, 2086 (CO), 2016 (CO), 1681 (C=O), 1499, 1467, 1362, 1310, 1267, 1234, 1174, 1114, 1019, 738, 703, 655, 613; δ_H (400 MHz, $CDCl_3$): 0.88 (3H, t, *J* 6.5, 11-H x 3), 1.20-1.64 (8H, m, 7-H x 2, 8-H x 2, 9-H x 2, 10-H x 2), 2.43 (3H, s, 1-H x 3), 3.85 (1H, d, *J* 10.9, 3-H), 4.34 (1H, td, *J* 6.4, 4.8, 6-H), 5.03 (1H, dd, *J* 8.8, 4.8, 5-H), 5.55 (1H, dd, *J* 10.9, 8.8, 4-H); δ_C (100 MHz, $CDCl_3$): 207.8 (CO), 204.9 (CO), 202.4 (CO), 201.6 (CO), 199.7 (CO), 92.0 (CH), 84.6 (CH), 77.3 (CH), 65.8 (CH), 36.7 (CH_2), 31.5 (CH_2), 30.2 (CH_3 ,1-C), 26.5 (CH_2), 22.5 (CH_2), 13.9 (CH_3 ,11-C); *m/z* (CI): Found: $[MH]^+$ 351.0556. $C_{15}H_{19}O_6Fe$ requires 351.0531; $[\alpha]_D^{25}$ -419.3° (*c* 1.00 in $CHCl_3$) [optical rotation reported in lit.[19] $[\alpha]_D^{26}$ -482.6° (*c* 1.00 in $CHCl_3$)]; Data were consistent with those reported in the literature;[21] and then *exo* complex **(6)** (0.39 g, 13%) as an orange-brown solid; ν_{max} (film)/cm^{-1}: 2957, 2930, 2861, 2089 (CO), 2021 (CO), 1666 (C=O), 1496, 1467, 1420, 1361, 1315, 1227, 1175, 1114, 1069, 1046, 1004, 913, 734, 648; δ_H (400 MHz, $CDCl_3$): 0.89 (3H, t, *J* 7.2, 11-H x 3), 1.21-1.69 (8H, m, 7-H x 2, 8-H x 2, 9-H x 2, 10-H x 2), 2.30 (3H, s, 1-H x 3), 3.74 (1H, d, *J* 11.2, 3-H), 4.05 (1H, t, *J* 5.9, 6-H), 4.86 (1H, d, *J* 8.3, 5-H), 5.73 (1H, dd, *J* 11.2, 8.3, 4-H); δ_C (100 MHz, $CDCl_3$): 208.0 (CO), 204.9 (CO), 202.2 (CO), 201.3 (CO), 199.7 (CO), 93.6 (CH), 83.5 (CH), 74.4 (CH), 64.8 (CH), 38.0 (CH_2), 31.3 (CH_2), 30.1 (CH_3 , 1-C), 25.1 (CH_2), 22.5 (CH_2), 13.9 (CH_3 , 11-C); *m/z* (CI): Found: $[MH]^+$ 351.0567. $C_{15}H_{19}O_6Fe$ requires, 351.0531; $[\alpha]_D^{25}$ +411.8° (*c* 1.00 in $CHCl_3$) [optical rotation reported in lit.[19] $[\alpha]_D^{26}$ +410.4° (*c* 1.00 in $CHCl_3$)]; Data was consistent with those reported in the literature.[19]

[(3*E*,5*S*,6*R*)-6-(Carbonyloxy-κC)-2-trimethylsilanyloxy-(3,4,5-η)-undec-1,3-dien-5-yl]-tricarbonyliron (**8**)

Triethylamine (MW=101.19, d=0.726, 1.2 eq., 5.4 mmol, 0.55 g, 0.75 mL) and trimethylsilyl trifluoromethanesulfonate (MW=222.26, d=1.228, 1.1 eq., 4.95 mmol, 1.10 g, 0.89 mL) were added sequentially to a cooled (0°C) solution of the *endo* ketone complex **(7)** (MW=350.14, 1.58 g, 4.5 mmol) in CH_2Cl_2 (20 mL) and the reaction mixture was stirred at 0°C for 1 h. The reaction mixture was then poured onto H_2O (100 mL) , the layers separated and the aqueous fraction extracted with Et_2O (50 mL). The organic fractions were washed with brine (100 mL) and dried ($MgSO_4$). Concentration of the filtrate *in*

vacuo followed by rapid flash column chromatography (Florisil, eluent PE : Et_2O 5:1 to 1:1, gradient) afforded the silyl enol ether complex **(8)** (1.62 g, MW=422.33, 84%) as a pale yellow solid; ν_{max} (film)/cm^{-1}: 2922, 2853, 2077 (CO), 2011 (CO), 2002 (CO), 1685 (C=O), 1654 (C=C), 1605, 1462; δ_H (400 MHz, $CDCl_3$): 0.25 (9H, s, Si(CH_3)$_3$), 0.89 (3H, t, *J* 6.0, 11-H), 1.19-1.68 (8H, m, 7-H x 2, 8-H x 2, 9-H x 2, 10-H x 2), 4.27 (1H, app. q, *J* 6.4, 6-H), 4.33-4.43 (2H, m, 1-H x 1, 3-H), 4.57-4.68 (2H, m, 1-H x 1, 5-H), 5.00 (1H, dd, *J* 11.9, 8.5, 4-H); δ_C (100 MHz, $CDCl_3$): 209.2 (CO), 206.2 (CO), 205.5 (CO), 204.3 (CO), 153.8 (quat. C), 94.3 (CH_2), 85.6 (CH), 79.4 (CH), 77.4 (CH), 76.2 (CH), 36.8 (CH_2), 31.6 (CH_2), 26.7 (CH_2), 22.5 (CH_2), 14.0 (CH_3), -0.3 (Si(CH_3)$_3$); *m/z* (CI): Found: $[MH]^+$ 423.0944. $C_{18}H_{27}O_6FeSi$ requires, 423.0926; $[\alpha]_D^{25}$ -287.9° (*c* 1.00 in $CHCl_3$); Data were consistent with those for the racemic complex reported in the literature.[3d,19]

3-Benzyloxy-1-propionaldehyde (**10**)

Propane-1,3-diol **(9)** (MW=76.1, d=1.053, 25 mmol, 1.9 g) in THF (70 mL) was treated with NaH (MW=24.0, 1.0 eq., 25 mmol, 0.6 g, 60% dispersion in oil). The reaction mixture was stirred for 30 min, and then *n*-Bu_4NI (MW=369.38, 2.5 mol%, 0.625 mmol, 0.23 g) was introduced. Benzyl bromide (MW=171.04, d=1.438, 1.0 eq., 25 mmol, 4.27 g, 2.97 mL) then added dropwise and the reaction mixture stirred for 1 h at rt and then refluxed for a further 2 h at 110°C. After cooling the reaction mixture was poured onto saturated aqueous NH_4Cl solution (200 mL) and H_2O (100 mL), the phases separated, the aqueous phase extracted with Et_2O (2 x 50 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification of the resultant oil, flash column chromatography (eluent PE : Et_2O 10:1 to 1:10, gradient) afforded monobenzylated product (2.8 g, 73%) as an oil; δ_H (400 MHz, $CDCl_3$): 1.85 (2H, q, *J* 6.1), 2.30-2.40 (1H, br s, OH), 3.67 (2H, t, *J* 6.1), 3.80 (2H, t, *J* 6.1), 4.53 (2H, s), 7.30 (5H, m); δ_C (100 MHz, $CDCl_3$): 138.1, 128.4, 127.7, 127.6, 73.2, 69.2, 61.7, 32.2; Data were consistent with those reported in the literature.[22]

Compound **(10)** was then prepared from mono-benzylated propane-1,3-diol **(10)** (2.8 g, 18.3 mmol), by standard Swern oxidation conditions,[12] using DMSO (MW=78.13, d=1.101, 2.5 eq., 45.9 mmol, 3.6 g, 3.26 mL), oxalyl chloride (MW=126.93, d=1.455, 1.2 eq., 21.9 mmol, 2.78 g, 1.91 mL) and NEt_3 (MW=101.19, d=0.726, 5.0 eq., 91.5 mmol, 9.25 g, 12.7 mL). The reaction was quenched by addition of saturate aqueous NH_4Cl solution (20 mL), the aqueous phase was extracted with DCM (2 x 50 mL). The combined organic phases were washed with saturated $NaHCO_3$ (2 x 10 mL), brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by distillation (T=120°C, water pump pressure p=20 mmHg) yielded pure, colorless aldehyde **(10)** (2.1 g, 69%); δ_H (400 MHz, $CDCl_3$): 2.60-2.70 (2H, m), 3.80-3.90 (2H, t, *J* 6.1), 4.51 (2H, s),

7.20-7.40 (5H, m), 9.77 (1H, t, *J* 1.8); δ_C (100 MHz, $CDCl_3$): 201.0, 137.9, 128.4, 127.7, 127.6, 127.6, 73.2, 63.8, 43.8. Data were consistent with those reported in the literature.[12]

[(8*E*,6*R*,7*S*,12*S*)-14-Benzyloxy-6-(carbonyloxy-κC)-12-hydroxy-10-oxo-(7,8,9-η)-tetradec-8-en-7-yl]-tricarbonyliron (**11**)

TMS enol ether **(8)** (560 mg, 1.33 mmol) was dissolved in 2 : 1 Et_2O : CH_2Cl_2 (13 mL) and cooled to -78°C. In a separate vessel 3-benzyloxy-1-propionaldehyde **(10)** (3.0 eq., 4.0 mmol, 650 mg) in Et_2O (5 mL) was treated with freshly distilled BF_3•OEt_2 (MW=141.93, d=1.120, 1.1 eq., 1.46 mmol, 207 mg, 185 μL). After 30 sec this solution was added dropwise to the cooled solution of **8** over 2 min. The reaction mixture the stirred for 3 h, then NEt_3 (1 mL) was added and the solution was allowed to come to rt. The resulting solution was filtered through a pad of celite washing with 1 : 1 Et_2O : CH_2Cl_2 (100 mL), and the solvent removed to give a crude mixture of silylated and non-silylated products. The mixture was dissolved in THF (5 mL) and HF.Pyridine complex (2.25 M in THF, 5 mL) was added. After stirring for 30 min the reaction mixture was discharged into saturated $NaHCO_3$, the organics were separated and dried ($MgSO_4$). After solvent removal the residue was Purified by flash column chromatography (eluent PE:Et_2O 2:1 to 1:2, gradient) affording the β-hydroxy ketone **(11)** (425 mg, 63%) as a yellow gum; ν_{max} (film)/cm^{-1}: 3492, 2931, 2861, 2248, 2087, 2005, 1735, 1668, 1497, 1454, 1364, 1309, 1242, 1205, 1017, 910, 821, 730, 698, 650; δ_H (600 MHz, $CDCl_3$): 0.86 (3H, t, *J* 6.8, 1-H x 3), 1.24-1.60 (8H, m, 2-H x 2, 3-H x 2, 4-H x 2, 5-H x 2), 1.83 (2H, m, 13-H x 2), 2.85 (2H, d, *J* 4.9, 11-H x 2), 3.27 (1H, d, *J* 3.3, OH), 3.70 (2H, m, 14-H x 2), 3.87 (1H, d, *J* 10.9, 9-H), 4.34 (1H, td, *J* 6.4, 4.4, 6-H), 4.38 (1H, m, 12-H), 4.52 (2H, s, $CH_2C_6H_5$), 5.02 (1H, dd, *J* 8.8, 4.4, 7-H), 5.56 (1H, dd, *J* 10.9, 8.2, 8-H), 7.22-7.40 (5H, m, $CH_2C_6H_5$); δ_C (150 MHz, $CDCl_3$): 207.8 (CO), 204.5 (CO), 203.6 (CO), 202.3 (CO), 199.6 (CO), 137.9 (Ph *ipso*), 128.4 (Ph *meta* x 2), 127.6 (Ph *para*), 127.6 (Ph *ortho* x 2), 92.0 (8-C), 84.6 (7-C), 76.8 (6-C), 73.2 ($CH_2C_6H_5$), 67.9 (14-C), 66.6 (12-C), 65.8 (9-C), 49.9 (11-C), 36.6 (5-C), 36.1 (13-C), 31.4 (4-C), 26.4 (3-C), 22.4 (2-C), 13.8 (1-C); *m/z* (ES): Found: $[MNa]^+$ 537.1188. $C_{25}H_{30}O_8FeNa$ requires, 537.1188; $[\alpha]_D^{25}$ -297.6° (*c* 1.00 in $CHCl_3$).[20]

[(8*E*,6*R*,7*S*,12*S*)-14-Benzyloxy-12-(*tert*-butyldimethylsilanyloxy)-6-(carbonyloxy-κC)-10-oxo-(7,8,9-η)-tetradec-8-en-7-yl]tricarbonyliron

TBSOTf (MW=264.34, d=1.151, 1.1 eq., 0.91 mmol, 0.241 g, 0.209 mL) was added dropwise to a solution of the β-hydroxy ketone **(11)** (425 mg, 0.83 mmol) and NEt_3 (MW=101.19, d=0.726, 1.25 eq., 1.04 mmol, 104 mg, 0.144 mL) in CH_2Cl_2 (5 mL) at 0°C. After 6 h the reaction mixture was purified by flash column chromatography (eluent PE : Et_2O 5:1 to 1:1) to afford the mono TBS protected iron lactone complex (522

mg, 100%) as a yellow oil; ν_{max} (neat)/cm^{-1}: 2929, 2857, 2087, 2010, 1671 (C=O), 1497, 1462, 1361, 1322, 1252, 1017, 910, 835, 776, 731, 697; δ_H (600 MHz, $CDCl_3$): 0.05 (3H, s, Si(CH_3)), 0.07 (3H, s, Si(CH_3)), 0.85 (9H, s, SiC(CH_3)$_3$), 0.89 (3H, t, *J* 7.1, 1-H x 3), 1.26-1.62 (8H, m, 2-H x 2, 3-H x 2, 4-H x 2, 5-H x 2), 1.86 (2H, app. q, *J* 6.5, 13-H x 2), 2.82 (1H, dd, *J* 15.9, 6.0, 11-H), 2.98 (1H, dd, *J* 15.9, 4.9, 11-H'), 3.56 (2H, m, 14-H x 2), 3.86 (1H, d, *J* 10.9, 9-H), 4.32 (1H, td, *J* 7.1, 4.9, 6-H), 4.42 (1H, m, 12-H), 4.49 (2H, m, C*H*$_2$C$_6$H$_5$), 5.01 (1H, dd, *J* 8.8, 4.9, 7-H), 5.52 (1H, dd, *J* 10.9, 8.8, 8-H), 7.20-7.38 (5H, m, CH$_2$C$_6$*H*$_5$); δ_C (150 MHz, $CDCl_3$): 207.9 (CO), 204.8 (CO), 202.2 (CO), 202.0 (CO), 199.8 (CO), 138.3 (Ph *ipso*), 128.3 (Ph *meta* x 2), 127.6 (Ph *para*), 127.5 (Ph *ortho* x 2), 91.8 (8-C), 84.4 (7-C), 76.7 (6-C), 72.9 (*C*H$_2$C$_6$H$_5$), 66.3 (14-C), 66.2 (9-C); 65.9 (12-C), 50.6 (11-C), 37.1 (13-C), 36.7 (5-C), 31.4 (4-C), 26.5 (3-C), 25.8 (SiC(*C*H$_3$)$_3$), 22.4 (2-C), 17.9 (Si*C*(CH$_3$)$_3$), 13.9 (1-C), -4.5 (Si(CH_3)), -4.8 (Si(CH_3)); *m/z* (ES): Found: [MNa]$^+$ 651.2054. $C_{31}H_{44}O_8FeNaSi$ requires, 651.2053; $[\alpha]_D^{25}$ -247.2° (*c* 1.00 in $CHCl_3$).

[(8*E*,6*R*,7*S*,10*S*,12*S*)-14-Benzyloxy-12-(*tert*-butyldimethylsilanyloxy)-6-(carbonyloxy-κC)-10-hydroxy-(7,8,9-η)-tetradec-8-en-7-yl]tricarbonyliron (**12**)

i-Bu$_3$Al (1 M solution in toluene, d = 0.848, 2.0 eq., 1.34 mmol, 1.34 mL) was added dropwise to a solution of the TBS protected Mukaiyama aldol adduct (423 mg, 0.67 mmol) in CH_2Cl_2 (5 mL) at 0°C. after 2 h the reaction was quenched by addition of 1N HCl at 0°C, the organic was separated and the aqueous was back extracted with CH_2Cl_2 (2 x 10 mL). The combined organics were dried ($MgSO_4$), concentrated and the residue purified by flash column chromatography (eluent PE : Et_2O 5:1 to 3:1, gradient) afforded the secondary alcohol iron lactone complex **(12)** (353 mg, 83%) as a yellow oil; ν_{max} (neat)/cm^{-1}: 3419 (br, OH), 2929, 2857, 2077, 2000, 1667, 1636, 1462, 1360, 1252, 1004, 835, 775, 657; δ_H (400 MHz, $CDCl_3$): 0.05 (3H, s, Si(CH_3)), 0.08 (3H, s, Si(CH_3)), 0.85 (9H, s, SiC(C*H*$_3$)$_3$), 0.89 (3H, t, *J* 7.1, 1-H x 3), 1.30-1.64 (8H, m, 2-H x 2, 3-H x 2, 4-H x 2, 5-H x 2), 1.80 (2H, m, 11-H x 2), 1.86 (2H, m, 13-H x 2), 3.52 (2H, t, *J* 5.8, 14-H x 2), 3.70 (1H, s, OH), 3.94 (1H, d, *J* 9.5, 9-H), 4.16 (1H, m, 12-H), 4.25 (1H, td, *J* 6.9, 5.1, 6-H), 4.45 (1H, m, 10-H), 4.49 (2H, d, *J* 3.3, C*H*$_2$C$_6$H$_5$), 4.60 (1H, dd, *J* 8.4, 4.4, 7-H), 4.85 (1H, dd, *J* 12.1, 8.4, 8-H), 7.22-7.35 (5H, m, CH$_2$C$_6$*H*$_5$); δ_C (100 MHz, $CDCl_3$): 209.7 (CO), 207.1 (CO), 206.2 (CO), 203.3 (CO), 138.0 (Ph *ipso*), 128.4 (Ph *meta* x 2), 127.7 (Ph *para*), 127.6 (Ph *ortho* x 2), 88.2 (8-C), 87.0 (7-C), 77.3 (6-C), 75.9 (10-C), 73.1 (*C*H$_2$C$_6$H$_5$), 71.1 (14-C), 69.6 (9-C), 66.2 (12-C), 45.3 (11-C), 37.8 (13-C), 36.7 (5-C), 31.5 (4-C), 26.6 (3-C), 25.7 (SiC(*C*H$_3$)$_3$), 22.4 (2-C), 17.8 (Si*C*(CH$_3$)$_3$), 13.9 (1-C), -4.0 (Si(CH_3)), -4.7 (Si(CH_3)); *m/z* (CI) Found: [MH]$^+$ 631.2380. $C_{31}H_{47}O_8FeSi$ requires 631.2390; $[\alpha]_D^{25}$ -62.4° (*c* 1.00 in $CHCl_3$).

[(8*E*,6*R*,7*S*,10*S*,12*S*)-10-Acetoxy-14-benzyloxy-12-(*tert*-butyldimethylsilanyloxy)-6-(carbonyloxy-

κC)-(7,8,9-η)-tetradec-8-en-7-yl]tricarbonyliron (**13**)

Acetic anhydride (MW=102.09, d=1.082, 1.1 eq., 0.57 mmol, 58.3 mg, 53.8 μL) was added to a solution of the alcohol **(13)** (330 mg, 0.52 mmol), NEt_3 (MW=101.19, d=0.726, 1.3 eq., 0.68 mmol, 68.8 mg, 94.8 μL) and DMAP (MW=122.17, 0.1 eq., 0.052 mmol, 6.3 mg) in CH_2Cl_2 (5 mL) at 0°C. After 1 h the reaction mixture was filtered through a pad of celite washing with Et_2O (50 mL), solvent removal afforded acetate **(13)** (340 mg, 98%) as a colorless oil; ν_{max} (neat)/cm^{-1}: 2929, 2857, 2077, 2000, 1740 (C=O), 1667 (C=O), 1463, 1370, 1224, 1098, 1005, 835, 774, 734, 697, 655; δ_H (400 MHz, $CDCl_3$): 0.05 (3H, s, $Si(CH_3)$), 0.08 (3H, s, $Si(CH_3)$), 0.86 (9H, s, $SiC(CH_3)_3$), 0.89 (3H, t, *J* 7.1, 1-H x 3), 1.20-1.66 (8H, m, 2-H x 2, 3-H x 2, 4-H x 2, 5-H x 2), 1.80 (2H, app. q, *J* 5.8, 11-H x 2), 2.03 (3H, s, $COCH_3$), 2.10 (2H, m, 13-H x 2), 3.58 (2H, m, 14-H x 2), 3.90 (1H, dd, *J* 6.5, 5.1, 9-H), 3.96 (1H, m, 12-H), 4.20 (1H, td, *J* 6.9, 5.1, 6-H), 4.47 (1H, m, 10-H), 4.49 (2H, d, *J* 3.3, $CH_2C_6H_5$), 4.60 (1H, dd, *J* 8.4, 4.4, 7-H), 5.45 (1H, dd, *J* 12.1, 8.4, 8-H), 7.23-7.37 (5H, m, $CH_2C_6H_5$); δ_C (100 MHz, $CDCl_3$): 208.8, 206.4, 204.1, 202.9, 170.0, 138.4, 128.3, 127.7, 127.6, 127.5, 89.0, 81.7, 73.0, 71.7, 66.6, 66.3, 44.7, 36.5, 36.3, 31.5, 26.5, 25.8 ($SiC(CH_3)_3$), 22.4, 20.6, 17.9 ($SiC(CH_3)_3$), 13.9, -4.5 ($Si(CH_3)$), -4.6 ($Si(CH_3)$); *m/z* (ES): Found: $[MH]^+$ 673.2477. $C_{33}H_{49}O_9FeSi$ requires, 673.2495; $[\alpha]_D^{25}$ -139.7° (*c* 1.00 in $CHCl_3$).

(7*E*,9*E*,6*R*,12*R*)-14-Benzyloxy-12-(*tert*-butyldimethyl-silanyl-oxy)-6-hydroxy-tetradeca-7,9-diene (14-*E*,*E*),(7*E*,9*Z*,6*R*,12*R*)-14-benzyloxy-12-(*tert*-butyldimethylsilanyloxy)-6-hydroxytetradeca-7,9-diene(14-*E*,*Z*) and (7*Z*,9*E*,6*R*,12*R*)-14-benzyloxy-12-(*tert*-butyldimethylsilanyloxy)-6-hydroxytetradeca -7,9-diene (14-*Z*,*E*)

Acetate **(13)** (55 mg, 0.08 mmol, MW=672.66) in THF (1 mL) was cooled to -78°C and lithium naphthalenide (5 eq., 0.41 mmol, 0.41 mL, 1 M solution in THF, freshly prepared according to the above method) was added. The solution was stirred at this temperature overnight. The solution was warmed to room temperature and filtered thtough a pad of silica, washing with Et_2O, the solvent was then removed and the residue purified by flash column chromatography (eluent PE:Et_2O 5:1 to 1:1, gradient) to afford an inseparable mixture of dienes **(14-*E*,*E***, **14-*E*,*Z*** and **14-*Z*,*E*)** (0.5: 0.2:0.3) as an oil (36 mg, 98%); ν_{max} (neat)/cm^{-1}: 3358 (OH), 2927, 2855, 2079, 1973, 1455, 1361, 1252, 1092, 1043, 989, 835, 774, 734, 697; δ_H (400 MHz, $CDCl_3$): 0.05 (3H, s, $Si(CH_3)$), 0.08 (3H, s, $Si(CH_3)$), 0.84 (9H, s, $SiC(CH_3)_3$), 0.89 (3H, t, *J* 7.1, 1-H x 3), 1.21-1.63 (8H, m, 2-H x 2, 3-H x 2, 4-H x 2, 5-H x 2), 1.75 (2H, m, 11-H x 2), 2.26 (2H, m, 13-H x 2), 3.54 (1H, s, OH), 3.58 (1H, m, 12-H), 3.91 (0.5H, m, 6-H x 0.5), 4.12 (0.5H, m, 6-H x 0.5), 4.49 (2H, app. q, *J* 11.7, $CH_2C_6H_5$), 5.29 (0.3H, m, 7-H x 0.3), 5.49 (0.2H, m, 10-H x 0.2), 5.58 (0.5H, dd, *J* 15.0, 6.9, 7-H x 0.5), 5.69 (1H, m, 7-H x 0.2, 10-H x 0.8), 6.04 (1H, m, 8-H x 0.3, 9-H x 0.7), 6.17 (0.5H, dd, *J* 15.3

10.2, 8-H x 0.5), 6.32 (0.3H, dd, *J* 15.0 10.9, 9-H x 0.3), 6.44 (0.2H, dd, *J* 15.0 10.9, 8-H x 0.2), 7.24-7.38 (5H, m, $CH_2C_6H_5$); δ_C (100 MHz, $CDCl_3$): 138.5, 134.3, 131.9, 130.6, 128,3, 127.7, 127.4, 125.8, 72.9, 72.7, 69.2, 67.0, 41.2, 41.0, 37.4, 37.3, 36.9, 31.8, 25.8 (SiC(CH_3)$_3$), 25.1, 24.9, 22.6, 18.1 (SiC(CH_3)$_3$), 14.0, -4.3 (Si(CH_3)), -4.7 (Si(CH_3)); *m/z* (ES) Found: $[MH]^+$ 447.3267. $C_{27}H_{47}O_3Si$ requires, 447.3294.

(3*R*,9*R*)-3-(*tert*-Butyldimethylsilanyloxy)tetradecane-1,9-diol (**15**)

The diene mixture **(14-*E,E*)**, **(14-*E,Z*)** and **(14-*Z,E*)** (120 mg, 0.27 mmol, MW=446.74), Pd/C (1 eq., 10 wt %, 0.27 mmol, 283 mg) was stirred at rt under H_2 atmosphere in ethyl acetate (5 mL). After 12 h, the solution was filtered through a pad of celite, the solvent was removed and the residue was purified by flash column chromatography (eluent PE:Et_2O 2:1 to 1:1, gradient) affording diol **(15)** as an oil (81 mg, 83%); ν_{max} (neat)/cm^{-1}: 3394 (O MHz, $CDCl_3$): 0.07 (3H, s, Si(CH_3)), 0.09 (3H, s, Si(CH_3)), 0.89 (9H, s, SiC(CH_3)$_3$), 0.89 (3H, t, *J* 7.1, H), 2928, 2856, 2370, 2358, 2299, 1462, 1254, 1059, 835, 773, 734, 661; δ_H (400 14-H x 3), 1.25-1.52 (18H, m, 4-H x 2, 5-H x 2, 6-H x 2, 7-H x 2, 8-H x 2, 10-H x 2, 11-H x 2, 12-H x 2, 13-H x 2), 1.65 (1H, m, 2-H), 1.81 (1H, m, 2-H'), 2.40 (2H, s, 1-OH, 9-OH), 3.58 (1H, m, 9-H), 3.70 (1H, m, 1-H), 3.83 (1H, m, 1-H'), 3.91 (1H, m, 3-H); δ_C (100 MHz, $CDCl_3$): 71.9, 71.8, 60.3, 37.7, 37.4, 37.3, 36.7, 31.9, 29.8, 25.8 (SiC(CH$_3$)$_3$), 25.5, 25.3, 25.3, 25.2, 22.6, 17.9 (SiC(CH_3)$_3$), 14.0, -4.4 (Si(CH_3)), -4.7 (Si(CH_3)); *m/z* (+ES) Found: $[MNa]^+$ 383.2966. $C_{20}H_{44}O_3NaSi$ requires, 383.2957.

(3*R*,9*R*)-3-(*tert*-Butyldimethylsilanyloxy)-9-hydroxytetradecanal (16)

A solution of diol **(15)** (70 mg, 0.19 mmol, MW=360.65) in benzene (3 mL) was added *via* cannula to a stirred solution of tris(triphenylphosphine)ruthenium dichloride (1 eq., 0.19 mmol, 186 mg, MW=958.85) in benzene (5 mL) containing K_2CO_3 (52 mg, 0.38 mmol). The reaction mixture was stirred at rt for 12 h, then filtered through a pad of Florisil®. The residue was washed with Et_2O (3 x 50 mL). Concentration of the filtrate *in vacuo* followed by flash column chromatography (PE : Et_2O 1:1) afforded aldehyde **(16)** (53 mg, 78%) as an oil; ν_{max} (neat)/cm^{-1}: 3432 (OH), 2928, 2857, 1725 (C=O), 1463, 1434, 1361, 1255, 1094, 1005, 938, 806, 744, 693; δ_H (400 MHz, $CDCl_3$): 0.07 (3H, s, Si(CH_3)), 0.09 (3H, s, Si(CH_3)), 0.89 (9H, s, SiC(CH_3)$_3$), 0.89 (3H, t, *J* 7.1, 14-H x 3), 1.19-1.61 (18H, m, 4-H x 2, 5-H x 2, 6-H x 2, 7-H x 2, 8-H x 2, 10-H x 2, 11-H x 2, 12-H x 2, 13-H x 2), 2.05 (1H, s, 9-OH), 2.51 (2H, m, 2-H x 2), 3.58 (1H, m, 9-H), 4.17 (1H, quint., *J* 5.5, 3-H), 9.81 (1H, t, *J* 2.2, 1-H); δ_C (100 MHz, $CDCl_3$): 202.3 (C=O), 71.9, 68.2, 50.8, 37.7, 37.4, 37.3, 34.2, 31.8, 30.3, 29.6, 25.7 (SiC(CH$_3$)$_3$), 25.5, 25.3, 25.1, 22.6, 18.0 (SiC(CH_3)$_3$), 14.0, -4.5 (Si(CH_3)), -4.7 (Si(CH_3)); *m/z* (+ES) Found: $[MNa]^+$ 381.2803. $C_{20}H_{42}O_3NaSi$ requires, 381.2801; $[\alpha]_D^{25}$ -2.6° (*c* 0.75 in $CHCl_3$).

(3*R*,9*R*)-3-(*tert*-Butyldimethylsilanyloxy)tetradecanal-9-yl pent-4'-enoate (17)

4-Pentenoyl chloride (2 eq., 14.5 mg, 13.5 μL, MW=118.56, d=1.074) was added to aldehyde **(16)** (22 mg, 0.061 mmol, MW=358.63) and DMAP (3 eq., 0.18 mmol, 22.3 mg, MW=122.17) in CH_2Cl_2 (2 mL) at 0°C. The reaction mixture was stirred and allowed to warm to rt over 3 h, then filtered through a pad of Florisil®. The residue was washed with Et_2O (3 x 10 mL). Concentration of the filtrate *in vacuo* followed by flash column chromatography (PE : Et_2O 9:1 to 2:1) afforded ester **(17)** (5.3 mg, 30% conversion, 65% yield, based on recovered starting material) as an oil.[21] δ_H (400 MHz, $CDCl_3$): 0.07 (3H, s, $Si(CH_3)$), 0.09 (3H, s, $Si(CH_3)$), 0.89-0.94 (12H, s, $SiC(CH_3)_3$, 14-H x 3), 1.23-1.69 (18H, m, 4-H x 2, 5-H x 2, 6-H x 2, 7-H x 2, 8-H x 2, 10-H x 2, 11-H x 2, 12-H x 2, 13-H x 2), 2.30 (4H, m, 2'-H x 2, 3'-H x 2), 2.43 (2H, m, 2-H x 2), 4.08 (1H, app. t, *J* 5.5, 9-H), 4.79 (1H, quint., *J* 5.2, 3-H), 4.95 (2H, app. q, 5'-H x 2), 5.75 (1H, m, 4'-H), 9.78 (1H, t, *J* 2.2, 1-H).

(4*R*,10*R*)-4-(*tert*-Butyldimethylsilanyloxy)pentadec-1-en-10-yl pent-4'-enoate (**18**)

Methyltriphenylphosphonium chloride[22] (0.2 mmol, 63 mg, MW=312.78) was deprotonated by stirring with *t*-BuOK (0.16 mmol, 17.9 mg) in THF (2 mL) at rt for 30 min. The solution was cooled to O°C and aldehyde **(17)** (5.3 mg, 12 μmol, MW=440.74) in THF (1 mL) was added. The reaction mixture was stirred and allowed to warm to rt overnight, then filtered through a pad of Florisil®. The residue was washed with Et_2O (3 x 5 mL). Concentration of the filtrate *in vacuo* followed by flash column chromatography (PE:Et_2O 40:2 to 40:3) afforded diene **(18)** (4.5 mg, 85%) as an oil; ν_{max} (neat)/cm^{-1}: 2928, 2858, 1735 (C=O), 1255, 1093, 835, 822; δ_H (400 MHz, $CDCl_3$): 0.07 (3H, s, $Si(CH_3)$), 0.09 (3H, s, $Si(CH_3)$), 0.79-0.89 (12H, s, $SiC(CH_3)_3$, 15-H x 3), 1.21-1.50 (18H, m, 5-H x 2, 6-H x 2, 7-H x 2, 8-H x 2, 9-H x 2, 11-H x 2, 12-H x 2, 13-H x 2, 14-H x 2), 2.15 (2H, t, *J* 6.8, 3-H x 2), 2.29-2.35 (4H, m, 2'-H x 2, 3'-H x 2), 3.61 (1H, quint., *J* 5.5, 4-H), 4.80 (1H, quint., *J* 6.1, 10-H), 4.98-5.11 (4H, m, 1-H x 2, 5'-H x 2), 5.65-5.80 (2H, m, 2-H, 4'-H); δ_C (100 MHz, $CDCl_3$): 172.9 (C=O), 136.8 (C=C), 135.4 (C=C), 116.6 (C=C), 115.4 (C=C), 74.3, 71.9, 41.9, 36.7, 34.0, 33.8, 31.7, 29.7, 29.6, 29.0, 25.9 ($SiC(CH_3)_3$), 25.3, 25.2, 24.9, 22.5, 18.1 ($SiC(CH_3)_3$), 14.0, 13.9, 1.0, -4.4 ($Si(CH_3)$), -4.5 ($Si(CH_3)$); *m/z* (+ES) Found: $[MNa]^+$ 461.3431. $C_{26}H_{50}O_3NaSi$ requires, 461.3427; $[\alpha]_D^{25}$ +10.5° (*c* 0.1 in $CHCl_3$). Data were consistent with those reported in the literature.[9g]

ACKNOWLEDGEMENTS

We gratefully acknowledge the financial support from the ESPRC, the BP endowment and the Novartis Research Fellowship (to SVL).

REFERENCES AND NOTES

1. (a) S. V. Ley and G. Meek, *J. Chem. Soc., Chem. Commun.*, 1996, 317. (b) S. V. Ley and L. R. Cox, *J. Chem. Soc., Chem. Commun.*, 1996, 657. (c) S. V. Ley, L. R. Cox, G. Meek, K. H. Metten, C. Piqué, and J. M. Worrall, *J. Chem. Soc., Perkin Trans. I*, 1997, 3299. (d) S. V. Ley, S. Burckhardt, L. R. Cox, and G. Meek, *J. Chem. Soc., Perkin Trans. I*, 1997, 3327.
2. (a) S. V. Ley, C. J. Hollowood, and S. Yamanoi, *Chem. Commun.*, 2002, **15**, 1624; (b) S. V. Ley and G. Meek, *J. Chem. Soc., Perkin Trans. I*, 1997, **8**, 1125; (c) D. Diez-Martin, N. R. Kotecha, S. V. Ley, S. Mantegani, J. C. Manendez, H. M. Organ, A. D. White, and B. J. Banks, *Tetrahedron*, 1992, **48**, 7899; and references cited within.
3. (a) S. V. Ley, S. Burckhardt, L. R. Cox, and G. Meek, *J. Chem. Soc., Perkin Trans. I*, 1997, 3327. (b) S. V. Ley and L. R. Cox, *Chem. Commun.*, 1998, 227. (c) S. V. Ley, L. R. Cox, and J. M. Worrall, *J. Chem. Soc., Perkin Trans. I*, 1998, 3349. (d) S. V. Ley, L. R. Cox, B. Middleton, and J. M. Worrall, *Tetrahedron*, 1999, **55**, 3515.
4. (a) S. V. Ley, L. R. Cox, and G. Meek, *Chem. Rev.*, 1996, **96**, 423; (b) L. R. Cox and S. V. Ley, *Chem. Soc. Rev.*, 1998, **27**, 301.
5. (a) S. V. Ley and C. J. Hollowood, *Chem Commun.*, 2002, 2130.
6. A. R. Lax, G. E. Templeton, and W. L. Myers, *Phytopathology*, 1982, **74**, 503.
7. W. L. Meyer, A. R. Lax, G. E. Templeton, and M. J. Brannon, *Tetrahedron Lett.*, 1983, **24**, 5059.
8. R. W. Carling and A. B. Holmes, *Tetrahedron Lett.*, 1986, **27**, 6133.
9. (a) G. Adam, R. Zibuck, and D. J. Seebach, *J. Am. Chem. Soc.*, 1987, **109**, 6176; (b) S. L. Schreiber, S. E. Kelly, J. A. Porco, T. Sammakia, and E. M. Suh, *J. Am. Chem. Soc.*, 1988, **110**, 6210; (c) D. Seebach, G. Adam, R. Zibuck, W. Simon, M. Rouilly, W. L. Meyers, J. F. Hinton, T. A. Privett, G. E. Templeton, D. K. Heiny, U. Gisi, and H. Binder, *Liebig. Ann. Chem.*, 1989, 1233; (d) N. R. Curtis, A. B. Holmes, M. G. Looney, N. D. Pearson, and G. C. Slim, *Tetrahedron Lett.*, 1991, **32**, 537; (e) S. Takano, Y. Shimazaki, M. Takahashi, and K. J. Ogasawara,. *Chem. Commun.*, 1988, 1004; (f) M. Matsushita, M. Yoshida, Y. Yhang, M. Miyashita, H. Irie, T. Ueno, and T. Tsurushima, *Chem. Pharm. Bull.*, 1992, **40**, 524; (g) A. Fürstner and K. Langemann, *J. Am. Chem. Soc.*, 1997, **119**, 9130.
10. S. V. Ley and L. R. Cox, *J. Chem. Soc., Perkin Trans. I*, 1997, 3315.
11. S. V. Ley, L. R. Cox, B. Middleton, and J. M. Worrall, *Chem. Commun.*, 1998, 1339.
12. F. A. Davis, H. Qi, and G. Sundarababu, *Tetrahedron*, 2000, **56**, 5303.
13. S. V. Ley and E. A. Wright, *J. Chem. Soc., Perkin Trans. I*, 2000, **11**, 1677.
14. S. V. Ley and C. J. Hollowood, *Org. Biomol. Chem.*, 2003, **1**, 3197.
15. H. Tomioka, K. Takai, K. Oshima, and H. Nozaki, *Tetrahedron lett.*, 1983, **24**, 2185.

16. A. J. Pearson and M. K. O'Brien, *J. Org. Chem.*, 1989, **54**, 4663.
17. M. Scholl, T. M. Trnka, J. P. Morgan, and R. H. Grubbs, *Tetrahedron Lett*, 1999, **40**, 2247.
18. P. Jensen and K. B. Sharpless, *J. Org. Chem.*, 1974, **39**, 2314.
19. L. R. Cox, 'p-Allyltricarbonyliron Lactone Complexes in Asymmetric Synthesis', PhD thesis, Cambridge University, Cambridge, 1997.
20. The minor diastereoisomer was not isolated due to its low abundance. However, analysis of the 400 MHz ^{1}H NMR spectrum of the crude reaction mixture after silyl deprotection allowed an estimation of the d.e. of the aldol products, specifically by integration of the 9-H resonance; δ_H (400 MHz) 3.87 (0.98H, d), 3.83 (0.02H, d). Calculated d.e. = 96%.
21. Due to the instability of the aldehyde it was used immediately in the Wittig reaction.
22. Methyltriphenylphosphonium chloride was dried *prior* to use by dissolving it in little toluene and concentration *in vacuo* (2 x) and leaving it on a high vacuum pump overnight.