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Use of π -allyltricarbonyliron lactone complexes in the synthesis of taurospongin A: a potent inhibitor of DNA polymerase β and HIV reverse transcriptase

Christopher J. Hollowood, Shigeo Yamanoi and Steven V. Ley*

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, UK CB2 1EW. E-mail: svl1000@cam.ac.uk; Fax: +44 (0)1223 336442; Tel: +44 (0)1223 336398

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The total synthesis of taurospongin A by two new approaches has been achieved where π -allyltricarbonyliron lactone complexes have been used to control highly stereoselective additions of the nucleophiles to a carbonyl unit located in the side chain of these complexes.

Introduction

We have published extensively on the use of π -allyltricarbonyliron lactone complexes¹ (Fig. 1) as conceptually interesting precursors to a number of natural products.² Our work makes use of the many interesting aspects and structural features of these complexes to generate lactones or lactams of various types and stereodefined alcohols, diols and dienes. Crucial to the success of these syntheses are the methods of detachment of the ligating iron species³ and the predictable stereochemical control that comes from the tethering effect of the (CO)₃FeCO bridge.⁴ Furthermore, these complexes can be easily prepared from a range of different building blocks.^{1,5}



Fig. 1 π -Allyltricarbonyliron lactone complexes.

Taurospongin A (1), isolated from a purple sponge *Hippospongia sp.*⁶ displays potent inhibitory action of DNA polymerase β and HIV reverse transcriptase. It has an interesting molecular architecture consisting of a taurine unit and two fatty acid fragments, one unsaturated and one highly oxygenated and differentially substituted. Such complex natural products provide a challenging target for the synthetic chemist while providing a platform for the development of new tools for molecular assembly.

The first synthesis of (1), (Fig. 2) accomplished in 1998 by Jacobsen *et al.*, made use of three separate reagent controlled processes to set-up the three stereogenic centres.⁷ Here we report in full⁸ on two new approaches to Taurospongin A (1) incorporating the use of π -allyltricarbonyliron lactone complexes. The iron complexes were used to transfer chiral information, through tethering, to achieve a highly stereoselective addition of a nucleophile to a carbonyl unit appended to the side-chain of the molecule. This general process has already



been established by our group to install 1,5-, 1,7- and 1,5,7- hydroxylated stereogenic centres in alkyl chains.^{4h-j}

Results and discussion

In our first approach, 3-butyn-1-ol (2) was converted to ester (3) in two steps by first protecting the primary hydroxyl group as a benzyl ether. The resulting benzyl ether was then subjected to lithium diisopropylamide (LDA) followed by methyl chloroformate to yield ester (3) in excellent yield. Subsequent treatment of (3) with benzenethiol in the presence of sodium methoxide gave (4) in 88% yield in favour of the Z-isomer (Z : E = 10 : 1). Thioether (4) was then reacted with methyl magnesium bromide and CuI at -78 °C to give α,β -unsaturated ester (5) in 98% yield (Scheme 1).

Further elaboration of (5) required reduction of the ester group with DIBAL-H in toluene at 0 °C. The resulting alcohol (6) was immediately treated with diisopropyl L-tartrate under Sharpless epoxidation conditions.⁹ Both reactions proceeded in good overall yield (76%) with the asymmetric epoxidation giving greater than 94% ee.

Before continuing with the synthesis we needed to prepare a further coupling partner, namely ketophosphonate (8). This was readily achieved by protection of the known β -hydroxy-ester (9)¹⁰ with *tert*-butyldimethylsilyl chloride and conversion to the corresponding Weinreb amide (10) using standard conditions. Reaction of (10) with the corresponding anion of diethyl methylphosphonate gave ketophosphonate (8) in anticipation of a subsequent Horner–Wadsworth–Emmons coupling (Scheme 2).

Alcohol (7) was then oxidised under activated dimethylsulfoxide (Swern conditions) to give aldehyde (11), which was reacted rapidly with ketophosphonate (8) to give (12) in good overall yield (Scheme 1). Treatment of (12) with diironnonacarbonyl in degassed THF^{5f} for 3 h gave complexes (13) and (14) as an orange gum which, after flash chromatography gave pure compounds (13) and (14) in 36 and 29% yields respectively. Optimisation of this reaction, using a variety of conditions, in favour of the desired tricarbonyliron lactone complex (14) proved fruitless. However, complex (13) was not wasted and used to pilot further reactions albeit with the wrong relative stereochemistry. After some initial test reactions using complex (13), complex (14) could be confidently progressed via highly stereoselective reduction with triisobutylaluminium (1 M in PhMe) at 0 °C to give (15) in 72% isolated yield. As previously reported, the high degree of stereoselectivity observed in this reduction is a result of the direct influence of the π -allyltricarbonyliron lactone complex.^{4h-j}

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Scheme 1 Reagents and conditions: (a) BnBr, NaH, 0 °C, 98%; (b) LDA, THF, -78 °C then ClCO₂Me, -78 °C \rightarrow rt, 89%; (c) PhSH, NaOMe, MeOH, rt, 88% of Z (Z : E = 10 : 1); (d) Cul, MeMgBr, THF, -78 °C, 98%; (e) DIBAL-H, PhMe, 0 °C, 91%; (f) Ti(O*i*-Pr)₄, diisopropyl L-tartrate, *t*-BuOOH, 4 Å MS, CH₂Cl₂, -20 °C, 83%; (g) (COCl)₂, DMSO, Et₃N, CH₂Cl₂, -78 °C, 86%; (h) **8**, NaH, THF, 0 °C, 82%; (i) Fe₂(CO)₉, THF, rt, **13** 36%, **14** 29%; (j) Al(*i*-Bu)₃ (1 M in PhMe), CH₂Cl₂, 0 °C, 72%; (k) NaBH(OAc)₃, THF, rt, 73%; (l) Ac₂O, DMAP, Et₃N, CH₂Cl₂, 0 °C, 96%; (m) H₂, Pd(OH)₂, EtOAc, rt, 88%.



Scheme 2 Reagents and conditions: (a) TBDMSCl, imidazole, DMF, 0 °C, 100%; (b) *i*-PrMgCl, Me(MeO)NH·HCl, THF, -20 °C, 91%; (c) *n*-BuLi, (EtO)₂P(O)Me, THF, -78 °C \rightarrow rt, 72%.

Detachment of the iron tether in (15) with sodium triacetoxyborohydride 3g,4k in THF gave alkenyl 1,5-diol product (16) in 73% yield in which the Z-geometric isomer predominated. Diol (16) was then readily acetylated and simultaneously hydrogenated and debenzylated to give known⁷ polyol fragment (18) (Scheme 1).

Fragment (18) gave the same spectroscopic data and similar optical rotation data to an identical fragment previously synthesised by Jacobsen *en route* to taurospongin A (1).⁷ Although we had achieved a formal synthesis of taurospongin A (1), we were unhappy with the poor selectivity in the formation of the required *endo*-tricarbonyliron complex (14). Additionally, we wished to investigate a new route to the enyne fatty acid fragment and effect its coupling with a derivative of fragment (18).

Therefore, we devised an alternative route to the same polyol fragment (18) using a tricarbonyliron lactone complex but in this case installing the required carbinol centre by a stereo-selective addition of a methyl group to a carbonyl unit located in the side-chain of the complex. Our second approach to taurospongin A (1) began with a Sharpless asymmetric epoxidation of the known allylic alcohol (19)¹¹ followed by Swern oxidation to afford aldehyde (21) (Scheme 3).

In order to provide a coupling partner for (21), β -propiolactone was cleaved with sodium methoxide in methanol at 50 °C and the resulting hydroxy ester (22) immediately protected as its *tert*-butyldimethylsilyl derivative (23). Both reactions proceeded in quantitative yield. Subsequent reaction of (23) with the anion from diethyl methylphosphonate gave the Horner–Wadsworth–Emmons coupling partner (24) in 78% yield (Scheme 4).

Union of (21) with ketophosphonate derivative (24) following standard protocols proceeded smoothly to give (25) in 76% yield (Scheme 3). Epoxide (25) was then reacted with diironnonacarbonyl in THF^{5f} to produce the exo- and endotricarbonyliron lactone complexes (26) and (27). Pleasingly, after easy separation by silica gel flash chromatography the major desired endo complex (27) and the minor undesired exocomplex (26) were isolated in 48% and 14% yield respectively. Complex (27) was then reacted with trimethylaluminium to give tertiary alcohol complex (28) in 81% yield. The excellent stereocontrol observed in this addition reaction is due to the preferred s-cis conformation of the carbonyl group in the appended sidechain.^{4h} Reductive decomplexation of (28) as before using sodium triacetoxyborohydride, followed by hydrogenation with H₂ and Pd/C gave protected polyol fragment (29) (81% overall yield). Finally, acetylation using acetic anhydride and N,N-dimethylaminopyridine (DMAP) and triethylamine followed by selective removal of the primary tert-butyldimethylsilyl protecting group using tetra(n-butyl)ammonium fluoride (TBAF) in THF-AcOH at 0 °C gave the same polyol building block (18) as described above (Scheme 3). Fragment (18) gave identical spectroscopic and similar optical rotational data to (18) obtained by the route described in Scheme 1 and to that prepared previously by Jacobsen et al.⁷

We next turned our attention to the synthesis of the enyne fatty acid component (30). Octadec-1-yne (31) was deprotonated with *n*-butyllithium and coupled with 2-(3-bromopropoxy)tetrahydro-2*H*-pyran to give alcohol (32).



Scheme 3 Reagents and conditions: (a) Ti(Oi-Pr)₄, diisopropyl D-tartrate, *t*-BuOOH, 4 Å MS, CH₂Cl₂, -20 °C, 82%; (b) (COCl)₂, DMSO, Et₃N, CH₂Cl₂, -78 °C, 88%; (c) **24**, NaH, THF, 0 °C, 76%; (d) Fe₂(CO)₉, THF, rt, **26** 14%, **27** 48%; (e) AlMe₃, CH₂Cl₂, 0 °C, 81%; (f) NaBH(OAc)₃, THF, rt; (g) H₂, Pd/C, EtOAc, rt, 81% for two steps; (h) Ac₂O, DMAP, Et₃N, CH₂Cl₂, 0 °C, 98%; (i) TBAF, AcOH, THF, 0 °C \rightarrow rt, 87%.



Scheme 4 Reagents and conditions: (a) NaOMe, MeOH, 50 °C, 100%; (b) TBDMSCl, imidazole, DMF, 0 °C, 100%; (c) *n*-BuLi, $(EtO)_2$ -P(O)Me, THF, -78 °C \rightarrow rt, 78%.

Hydrogenation of (**32**) with the Lindlar catalyst (H₂, Pd/C, quinoline) proceeded smoothly to give Z-alkene (**33**). Subsequent oxidation using Dess–Martin periodinane followed by homologation of the resulting aldehyde (**34**) using the Ohira reagent (**36**)¹³ gave terminal acetylene (**35**) in 87% over the 3 steps. Further homologation of (**35**) was achieved by firstly deprotonating the acetylene group with *n*-butyllithium and alkylating with 2-(3-bromopropoxy)tetrahydro-2*H*-pyran to give intermediate THP-protected alcohol (**37**) in 82% yield. Subsequent deprotection and oxidation with Jones' reagent afforded the required acid (**30**) in 92% yield (Scheme 5).

The final steps in the synthesis of taurospongin A (1) were carried out using a modification of Jacobsen's previously published route.⁷ Diol (18) was selectively oxidised using TEMPO, KBr, NaHCO₃ and sodium hypochlorite. The resulting acid (38) was then easily converted to allyl ester (39) using allyl bromide in the presence of Hünig's base in 87% (over two steps). After removal of the *tert*-butyldimethylsilyl protecting group in (39) using HF–pyridine the resulting free alcohol was coupled with acid (30) under standard conditions to afford adduct (40) in 63% yield (over two steps) (Scheme 6).

Completion of the natural product merely required a few simple transformations. After ester deprotection with $Pd(PPh_3)_4$ and pyrrolidine, carboxylic acid (41) was activated by standard methods and coupled with taurine ($H_2NCH_2CH_2$ -SO₃H) to give taurospongin A (1). The NMR data for (1) was consistent with the previously synthesized material.⁷ For full characterisation, our synthetic sample was treated with diazomethane to give the corresponding methyl ester (42), which was identical in all respects to previously reported data of samples derived either from isolated or synthetic natural products.^{6,7}



Scheme 5 Reagents and conditions: (a) *n*-BuLi, 2-(3-bromopropoxy)tetrahydro-2*H*-pyran, HMPA, THF, 0 °C \rightarrow rt, then 6 M H₂SO₄, 0 °C, 73%; (b) H₂, Lindlar cat., quinoline, EtOAc, MeOH, rt, 100%; (c) Dess– Martin periodinane, CH₂Cl₂, rt, 95%; (d) **36**, K₂CO₃, MeOH, rt, 92%; (e) *n*-BuLi, 2-(3-bromopropoxy)tetrahydro-2*H*-pyran, HMPA, THF, -15 \rightarrow 0 °C, 82%; (f) Jones' reagent, acetone, 0 °C \rightarrow rt, 92%.

While there is a complete spectroscopic match with our material and the literature, data discrepancies do occur in the optical rotational data and so for completeness, we have summarized these data in Table 1.

Since all the rotations listed in Table 1 are small we can ascribe differences due to solvent effects or possible typographical errors in the published work. Correspondence with the authors has failed to resolve the optical rotation discrepancies.

Nevertheless, we have achieved new syntheses of the two fatty acid components that are used to construct taurospongin A (1).



Scheme 6 Reagents and conditions: (a) cat. TEMPO, Aliquat[®] 336, KBr, aq. NaOCl, aq. NaHCO₃, CH₂Cl₂, 0 °C; (b) allyl bromide, i-Pr₂NEt, CH₂Cl₂, rt, 87% for two steps; (c) HF·py, THF, rt; (d) **30**, DIC, i-Pr₂NEt, DMAP, CH₂Cl₂, rt, 63% for two steps; (e) Pd(PPh₃)₄, pyrrolidine, CH₂Cl₂, rt; (f) *N*-hydroxysuccinimide, DCC, 1,4-dioxane, rt; (g) taurine, Et₃N, 1,4-dioxane, H₂O, rt, 100% for three steps; (h) CH₂N₂, Et₂O, rt, 75%.

Table 1 Specific rotation values			
Compound	Natural product ⁶	Jacobsen ⁷	This work
18		-2.54	-4.3
39		+1.16	-1.17
40		-1.77	-1.68
1	+2.4	Not measured	-3.5
42	-1.4	-3.0	-1.4

In addition, exploitation of our π -allyltricarbonyliron complex methodology generated the required stereochemistry of the natural product.

Experimental

¹H NMR spectra were recorded in CDCl₃ or C₆D₆ on Bruker DRX-600 or DRX-400 spectrometers and are reported as follows: chemical shift, δ (ppm) [number of protons, multiplicity, coupling constant J (Hz), and assignment]. Residual protic solvent CHCl₃ ($\delta_{\rm H} = 7.26$ ppm) or C₆H₆ ($\delta_{\rm H} = 7.20$ ppm) was used as the internal reference. ¹³C NMR spectra were recorded in CDCl₃ or C₆D₆ at 150 MHz or 100 MHz on Bruker DRX-600 or DRX-400 spectrometers, using the central resonance of CDCl₃ ($\delta_{\rm C}$ = 77.0 ppm) or C₆D₆ ($\delta_{\rm C}$ = 128.0 ppm) as the internal reference. Infra-red spectra were recorded on Perkin-Elmer 983G, FTIR 1620 or Perkin Elmer ATR Spectrum 1 spectrometers. Mass spectra were obtained on Kratos MS890MS, Bruker BIOAPEX 4.7 T FTICR or Micromass Q-TOF spectrometers. The following ionisation techniques were used: electron ionisation (EI), chemical ionisation (CI), fast atom bombardment (FAB) and electrospray (ES). Optical rotations were measured with an Perkin Elmer Model 343 Polarimeter, and are reported in 10⁻¹ deg cm² g⁻¹; concentration (c) is in g/100 ml. Flash column chromatography was carried out using Merck Kieselgel (230-400 mesh) unless otherwise indicated. Analytical thin layer chromatography (TLC) 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 bp 40-60 °C. In cases where mixtures of solvents were used, 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. Reactions involving preparation of the iron complexes were carried out using degassed THF. Et_2O and THF were distilled from sodium benzophenone ketyl, and CH_2Cl_2 from calcium hydride. Other reagents and solvents were used as supplied or purified using standard procedures as required.

Methyl 1-benzyloxybut-3-ynecarboxylate (3)

3-Butyn-1-ol (2) (14.0 g, 0.20 mol, 1.0 eq.) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 8.4 g, 0.21 mol, 1.05 eq.), which was pre-washed with pentane, in DMF (250 ml) at 0 °C. The resulting solution was stirred for 15 min before dropwise addition of BnBr (34.2 g, 0.20 mol) at 0 °C. The solution was then allowed to warm to room temperature overnight. The reaction mixture was poured onto H₂O (600 ml) and extracted with Et₂O (3 × 200 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Filtration through a pad of silica and concentration *in vacuo* afforded the corresponding benzyl ether as an oil (31.4 g, 98%), which was used without further purification. Data were consistent with those reported in the literature.¹⁴

n-BuLi (1.6 M, 100 ml, 1.06 eq.) was added via cannula to a solution of HNi-Pr₂ (21.7 g, 0.17 mol, 1.13 eq.) in THF (400 ml) at -78 °C. After complete addition the solution was warmed to 0 °C and cooled back to -78 °C. The above benzyl ether (24. 4 g 0.15 mol, 1.0 eq.) was then added dropwise. After stirring for 15 min MeCO₂Cl (43.2 g, 0.46 mol, 3.0 eq.) was added over 3 min and the solution was allowed to warm to room temperature. The mixture was poured onto 1 M aq. HCl (400 ml) and extracted with Et₂O (3×200 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (Et₂O-petrol = 1 : 10 \rightarrow 1 : 3) afforded alkynoate ester 3 as an oil (29.6 g, 89%); v_{max} (film)/cm⁻¹ 2239 (C=C), 1710 (C=O), 1435 (Ph); δ_H(400 MHz; CDCl₃) 7.37–7.26 (5 H, m, C₆H₅CH₂O), 4.56 (2 H, s, C₆H₅CH₂O), 3.76 (3 H, s, CO₂CH₃), 3.64 (2 H, t, J 6.8, 5-H × 2), 2.64 (2 H, t, J 6.8, 4-H × 2); δ_c(100 MHz; CDCl₃) 154.0 (1-C), 137.7 (Ph ipso), 128.5 (Ph meta × 2), 127.8 (Ph para), 127.7 (Ph ortho × 2), 86.4 (3-C), 73.6 (2-C), 73.1 (PhCH₂), 67.0 (5-C), 52.6 (CO₂CH₃), 20.2 (4-C); m/z (ES) 241 (100%, MNa⁺); [Found (MNa⁺) 241.0842. C₁₃H₁₄NaO₃ requires MNa, 241.0841].

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Methyl (2Z)-5-benzyloxy-3-(phenylthio)pent-2-enoate (4)

NaOMe (0.32 g, 6 mmol, 5 mol%) was added to a solution of alkynoate ester 3 (26.2 g, 0.12 mol, 1.0 eq.) and PhSH (13.9 g, 0.13 mol, 1.1 eq.) in MeOH (300 ml). After stirring overnight the mixture was filtered through a pad of silica and concentrated in vacuo. Purification of the crude product by flash column chromatography (Et₂O-petrol = $1 : 10 \rightarrow 1 : 3$) afforded alkenoate ester 4 as a pale yellow oil (34.7 g, 88%); v_{max} (film)/ cm⁻¹ 1701 (C=O), 1580 (C=C), 1434 (Ph); δ_H(400 MHz; CDCl₃) 7.50 (2 H, dd, J 6.8 and 1.4, PhS ortho × 2), 7.43-7.22 (8 H, m, $C_6H_5CH_2O$, PhS para and PhS meta \times 2), 5.94 (1 H, s, 2-H), 4.35 (2 H, s, C₆H₅CH₂O), 3.76 (3 H, s, CO₂CH₃), 3.43 (2 H, t, J 6.8, 5-H \times 2), 2.43 (2 H, t, J 6.8, 4-H \times 2); $\delta_{\rm C}(100$ MHz; CDCl₃) 166.4 (1-C), 157.9 (3-C), [137.9, 135.8, 130.6, 129.4, 129.2, 128.4, 127.7, 127.6 (PhCH₂ × 6 and PhS × 6)], 112.8 (2-C), 72.9 (PhCH₂), 68.4 (5-C), 51.2 (CO₂CH₃), 36.6 (4-C); m/z (ES) 351 (100%, MNa⁺) [Found (MNa⁺) 351.1028. C₁₉H₂₀NaO₃S requires MNa, 351.1031].

Methyl (2E)-5-benzyloxy-3-methylpent-2-enoate (5)

MeMgBr (3.0 M in Et₂O, 40 ml, 0.12 mol, 1.2 eq.) was added dropwise to a suspension of CuI (24.8 g, 0.13 mol, 1.3 eq.) in THF (400 ml) at -78 °C. After complete addition the solution was warmed to 0 °C and cooled back to -78 °C before dropwise addition of alkenoate ester 4 (32.8 g, 0.10 mol, 1.0 eq.). The reaction mixture was stirred at 0 °C for 1 h, then poured onto sat. NH₄Cl solution and filtered through a pad of Celite. The filtrate was extracted with $Et_2O(2 \times 150 \text{ ml})$ and the combined organic fractions washed with brine and dried (MgSO₄). Filtration through a pad of silica and concentration in vacuo afforded tri-substituted alkene 5 as a pale yellow oil (23.0 g, 98%), which was used without further purification; $v_{max}(film)/$ cm^{-1} 1715 (C=O), 1652 (C=C), 1435 (Ph); δ_{H} (400 MHz; CDCl₃) 7.37-7.26 (5 H, m, C₆H₅CH₂O), 5.74 (1 H, m, 2-H), 4.52 (2 H, s, C₆H₅CH₂O), 3.69 (3 H, s, CO₂CH₃), 3.61 (2 H, t, J 6.5, 5-H × 2), 2.46 (2 H, t, J 6.5, 4-H × 2), 2.19 (3 H, d, J 0.9, 3-CCH₃); $\delta_{\rm C}(100 \text{ MHz}; \text{CDCl}_3)$ 167.0 (1-C), 156.9 (3-C), 138.1 (Ph *ipso*), 128.4 (Ph meta × 2), 127.6 (Ph para), 127.6 (Ph ortho × 2), 116.6 (2-C), 73.0 (PhCH₂), 67.8 (5-C), 50.8 (CO₂CH₃), 40.8 (4-C), 18.9 (3-CCH₃); m/z (ES) 257 (100%, MNa⁺) [Found (MNa⁺) 257.1150. C14H18NaO3 requires MNa, 257.1154].

(2E)-5-Benzyloxy-3-methylpent-2-en-1-ol (6)

DIBAL-H (1 M in PhMe, 200 ml, 0.20 mol, 2.2 eq.) was added via cannula to a solution of ester **5** (21.1 g, 90 mmol, 1.0 eq.) in PhMe (200 ml) at 0 °C. The reaction mixture was stirred for 15 min before pouring slowly onto 1 M aq. HCl (500 ml). The resulting reaction mixture was stirred vigorously for a few minutes before the phases were separated and the aqueous layer was extracted with Et_2O (200 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O -petrol = 1 : 2 \rightarrow 3 : 1) afforded alcohol **6** as an oil (16.9 g, 91%). Data were consistent with those reported in the literature.¹⁵

(2S,3S)-5-Benzyloxy-2,3-epoxy-3-methylpentan-1-ol (7)

t-BuOOH (~5–6 M in decanes, 46 ml, 0.23 mol, 2.5 eq.) stored over 4 Å MS was added *via* cannula to a solution of diisopropyl L-tartrate (2.60 g, 11 mmol, 0.12 eq.) and Ti(O*i*-Pr)₄ (2.62 g, 9.2 mmol, 0.10 eq.) in CH₂Cl₂ (30 ml) over 4 Å MS at -20 °C. After 30 min this solution was added *via* cannula to a solution of allylic alcohol **6** (19.0 g, 92 mmol, 1.0 eq.) in CH₂Cl₂ (40 ml) over 4 Å MS at -20 °C. The resulting reaction mixture was stirred at -20 °C for 18 h. The mixture was then poured slowly onto a slurry of Celite in 1.5 M aq. FeSO₄ (500 ml) and filtered through a pad of Celite washing with CH₂Cl₂ (150 ml). The filtrate was separated and the aqueous layer was extracted with ether (200 ml). The CH₂Cl₂ and ether fractions were washed with brine, then combined and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (Et₂O-petrol = $1: 2 \rightarrow 10: 1$) afforded epoxide 7 as an oil (17.0 g, 83%, 94% ee); $[a]_{D}^{30}$ +1.3 (c 2.12, CH₂Cl₂); v_{max} (film)/ cm⁻¹ 3418 (OH), 1454 (Ph); $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.39–7.28 (5 H, m, C₆H₅CH₂O), 4.54 (1 H, d, J 12.0, C₆H₅CH₄H_BO), 4.50 (1 H, d, J 12.0, C₆H₅CH₄H_BO), 3.84 (1 H, m, 1-H₄), 3.70 (1 H, m, 1-H_B), 3.60 (2 H, m, 5-H \times 2), 3.06 (1 H, dd, J 6.5 and 4.5, 2-H), 1.99 (1 H, dt, J 14.3 and 5.9, 4-H_A), 1.91 (1 H, br s, OH), 1.82 (1 H, dt, J 14.3 and 6.7, 4-H_B), 1.34 (3 H, s, 3-CCH₃); $\delta_{\rm C}(100 \text{ MHz}; \text{CDCl}_3) 138.6 \text{ (Ph ipso)}, 128.8 \text{ (Ph meta <math>\times 2$), 128.1 (Ph ortho × 2), 128.0 (Ph para), 73.5 (PhCH₂), 66.8 (5-C), 63.2 (2-C), 61.7 (1-C), 60.1 (3-C), 38.7 (4-C), 17.6 (3-CCH₃); m/z (ES) 245 (100%, MNa⁺) [Found (MNa⁺) 245.1168. C₁₃H₁₈NaO₃ requires MNa, 245.1154].

(3*R*)-3-(*tert*-Butyldimethylsilyloxy)-*N*-ethoxy-*N*-methylbutyramide (10)

A solution of TBSDMCl (29.9 g, 0.20 mol, 1.05 eq.) in DMF (75 ml) was added *via* cannula to a solution of ethyl (*R*)-(–)-3-hydroxybutyrate (9) (99% ee, 25 g, 0.19 mol, 1.0 eq.) and imid-azole (14.8 g, 0.22 mol, 1.2 eq.) in DMF (250 ml) at 0 °C. The solution was then stirred overnight at room temperature. The reaction mixture was poured onto 1 M aq. HCl (600 ml) and extracted with Et₂O (3 × 200 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Filtration through a pad of silica and concentration *in vacuo* afforded the silyl ether as an oil, which was used without further purification (46.6 g, 100%); $[a]_D^{27} - 32.0$ (*c* 0.70, CH₂Cl₂). Data were consistent with those reported in the literature.¹¹

i-PrMgCl (2.0 M in THF, 110 ml, 0.22 mol, 3.0 eq.) was added *via* cannula to a suspension of *N*, *O*-dimethylhydroxyl-amine hydrochloride and the above silyl ether (18.0 g, 73 mmol, 1.0 eq.) in THF (200 ml) at -20 °C. 20 min after the final addition the mixture was poured onto 1 M aq. HCl and extracted with Et₂O (2 × 200 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et₂O-petrol = 1 : 1 \rightarrow 2 : 1) afforded Weinreb amide **10** as an oil (17.4 g, 91%). $[a]_{2D}^{2D} - 23.4$ (*c* 3.99, CH₂Cl₂). Data were consistent with those reported in the literature.¹⁰

Diethyl [(4*R*)-4-(*tert*-butyldimethylsilyloxy)-2-oxopentyl]phosphonate (8)

n-BuLi (1.6 M in hexanes, 14 ml, 22.5 mmol, 1.2 eq.) was added via cannula to a solution of (EtO)₂P(O)Me (3.67 g, 24 mmol, 1.3 eq.) in THF (400 ml) at -78 °C. After stirring for 1 h Weinreb amide 10 (4.85 g, 18.6 mmol, 1.0 eq.) was added dropwise. The solution was warmed to room temperature and stirred for a further 2 h before pouring onto 1 M aq. HCl (500 ml). After separation of the phases the aqueous phase was extracted with EtOAc (3 \times 100 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography $(Et_2O \rightarrow Et_2O - EtOAc [1:1])$ afforded β -keto-phosphonate 8 as an oil (4.71 g, 72%); $[a]_{\rm D}^{26}$ -24.9 (c 1.06, CH₂Cl₂); $v_{\rm max}$ (film)/cm⁻¹ 1714 (C=O), 1253 (P=O), 1124 (P–O); $\delta_{\rm H}$ (600 MHz; CDCl₃) 4.27 (1 H, m, 4-H), 4.05 (4 H, m, OCH₂CH₃ × 2), 3.10 (1 H, q, J 13.4, 1-H_A), 3.06 (1 H, q, J 13.4, 1-H_B), 2.78 (1 H, dd, J 15.7 and 7.0, 3-H_A), 2.63 (1 H, dd, J 15.7 and 5.2, 3-H_B), 1.31 (6 H, t, J 7.1, OCH₂CH₃ × 2), 1.15 (3 H, d, J 6.1, 5-H × 3), 0.83 (9 H, s, $SiC(CH_3)_3$, 0.04 (3 H, s, $Si(CH_3) \times 1$), 0.01 (3 H, s, $Si(CH_3) \times 1$) 1); $\delta_{\rm C}(150 \text{ MHz}; \text{CDCl}_3) 201.4 \text{ (d, } J = 39, 2\text{-C}), 65.9 \text{ (4-C)}, 62.9 \text{ (d)}$ (d, J = 38, OCH₂CH₃ × 2), 53.7 (3-C), 44.1 (d, J = 757, 1-C), 26.2 (SiC(CH₃)₃), 24.3 (5-C), 18.3 (SiC(CH₃)₃), 16.7 (d, J = 37, $OCH_2CH_3 \times 2$), -4.2 (Si(CH₃) × 1), -4.7 (Si(CH₃) × 1); δ_P (600 MHz; CDCl₃) 20.5; m/z (ES) 375 (100%, MNa⁺) [Found (MNa⁺) 375.1741. C₁₅H₃₃NaO₅PSi requires *M*Na, 375.1733].

(2R,3S)-5-Benzyloxy-2,3-epoxy-3-methylpentanal (11)

A solution of (COCl)₂ (1.93 g, 15.2 mmol, 1.25 eq.) in CH₂Cl₂ (10 ml) was added to a solution of DMSO (2.37 g, 30.4 mmol, 2.5 eq.) in CH_2Cl_2 (50 ml) at -78 °C. After 10 min alcohol 7 (2.70 g, 12.1 mmol, 1.0 eq.) was added and followed, after 15 min, by Et₃N (4.92 g, 48.6 mmol, 4.0 eq.). The reaction mixture was poured onto 1 M aq. HCl and the layers separated, the aqueous layer was extracted with Et₂O (200 ml) and the combined organic fractions washed with brine and dried (MgSO₄). Filtration through a pad of silica and concentration in vacuo afforded aldehyde 11 as an oil, which was used without further purification (2.29 g, 86%); v_{max}(film)/cm⁻¹ 1720 (C=O), 1454 (Ph); $\delta_{\rm H}$ (400 MHz; CDCl₃) 9.41 (1 H, d, J 4.7, 1-H), 7.30–7.20 (5 H, m, C₆H₅CH₂O), 4.45 (1 H, d, J 12.0, C₆H₅CH_AH_BO), 4.41 (1 H, d, J 12.0, $C_6H_5CH_AH_BO$), 3.50 (2 H, t, J 6.1, 5-H × 2), 3.24 (1 H, d, J 4.7, 2-H), 1.95 (1 H, dt, J 14.6 and 6.1, 4-H_A), 1.78 (1 H, dt, J 14.6 and 6.1, 4-H_B), 1.38 (3 H, s, 3-CCH₃); $\delta_{\rm C}(100 \text{ MHz}; \text{CDCl}_3)$ 199.2 (1-C), 138.0 (Ph *ipso*), 128.4 (Ph meta × 2), 127.7 (Ph para), 127.6 (Ph ortho × 2), 73.1 (PhCH₂), 65.8 (5-C), 63.5 (2-C), 62.7 (3-C), 38.3 (4-C), 17.6 (3-CCH₂).

(5*E*,2*R*,7*S*,8*S*)-10-Benzyloxy-2-(*tert*-butyldimethylsilyloxy)-7,8-epoxy-8-methyldec-5-en-4-one (12)

Phosphonate 8 (4.22 g, 12.0 mmol, 1.2 eq.) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 0.44 g, 11.0 mmol, 1.1 eq.) in THF (30 ml) at 0 °C followed, after 20 min, by aldehyde 11 (2.20 g, 10.0 mmol, 1.0 eq.) in THF (10 ml). After 10 min the reaction was poured onto sat. aq. NH₄Cl solution and extracted with Et₂O (2 \times 100 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (Et₂O-petrol = $1 : 3 \rightarrow 1 : 1$) afforded alkenone 12 as a pale yellow oil (3.43 g, 82%); $[a]_{D}^{30}$ -8.0 (c 1.25, CH₂Cl₂); v_{max} (film)/cm⁻¹ 1670 (C=O), 1627 (C=C), 1455 (Ph); $\delta_{\rm H}$ (400 MHz; CDCl₃) 7.32–7.22 (5 H, m, C₆H₅CH₂O), 6.61 (1 H, dd, J 15.9 and 6.4, 6-H), 6.31 (1 H, d, J 15.9, 5-H), 4.45 (2 H, s, C₆H₅CH₂O), 4.28 (1 H, m, 2-H), 3.53 (2 H, t, J 6.2, 10-H × 2), 3.36 (1 H, d, J 6.4, 7-H), 2.74 (1 H, dd, J 14.9 and 7.1, 3-H_A), 2.47 (1 H, dd, J 14.9 and 5.3, 3-H_B), 1.97 (1 H, dt, J 14.4 and 6.2, 9-H_A), 1.81 (1 H, dt, J 14.4 and 6.2, 9-H_B), 1.24 (3 H, s, 8-CCH₃), 1.14 (3 H, d, J 6.1, 1-H × 3), 0.79 $(9 \text{ H}, \text{ s}, \text{SiC}(\text{CH}_3)_3), 0.00 (3 \text{ H}, \text{ s}, \text{Si}(\text{CH}_3) \times 1), -0.04 (3 \text{ H}, \text{ s}, \text{Si}(\text{CH}_3) \times 1)$ Si(CH₃) × 1); $\delta_{\rm C}$ (100 MHz; CDCl₃) 198.5 (4-C), 141.3 (6-C), 138.5 (Ph ipso), 134.1 (5-C), 128.8 (Ph meta × 2), 128.1 (Ph para), 128.0 (Ph ortho \times 2), 73.5 (PhCH₂), 66.7 (10-C), 66.2 (2-C), 63.1 (8-C), 62.0 (7-C), 50.7 (3-C), 38.7 (9-C), 26.2 (SiC(CH₃)₃), 24.6 (1-C), 18.4 (SiC(CH₃)₃), 17.5 (8-CCH₃), -4.2 (Si(CH₃) × 1), -4.5 (Si(CH3) × 1); m/z (ES) 441 (100%, MNa⁺) [Found (MNa⁺) 441.2433. C₂₄H₃₈NaO₄Si requires MNa, 441.2437].

[(5*E*,3*S*,4*S*,9*R*)-1-Benzyloxy-9-(*tert*-butydimethylsilyloxy)-3-(carbonyloxy-κC)-3-methyl-7-oxo-(4,5,6-η)-dec-5-en-4-yl]tricarbonyliron (13) and [(5*E*,3*S*,4*R*,9*R*)-1-benzyloxy-9-(*tert*-butyldimethylsilyloxy)-3-(carbonyloxy-κC)-3-methyl-7-oxo-(4,5,6-η)-dec-5-en-4-yl]tricarbonyliron (14)

Degassed THF (30 ml) was added to diironnonacarbonyl (5.0 g, 13.7 mmol, 2.6 eq.) *via* cannula and the mixture was stirred vigorously in the absence of light for 20 min at room temperature. Alkenyl epoxide **12** (2.20 g, 5.3 mmol, 1.0 eq.) was then added and the reaction mixture was stirred vigorously. After 3 h the green mixture was filtered through a pad of Celite and washed with Et₂O (60 ml). PhMe (5 ml) was added to the filtrate and the solution was concentrated *in vacuo*. Purification of the residue by flash column chromatography (petrol until all Fe₃(CO)₁₂ had been removed, then Et₂O–petrol = 1 : 3 \rightarrow 1 : 1) afforded, in order of elution, *endo* iron lactone complex **14** as

an orange gum (0.90 g, 29%); $[a]_{D}^{33}$ +191.1 (c 0.45, CH₂Cl₂); v_{max} (film)/cm⁻¹ [2086, 2014 (FeCO)], 1669 (C=O), 1455 (Ph); $\delta_{\rm H}(600 \text{ MHz}; C_6D_6)$ 7.36–7.18 (5 H, m, $C_6H_5CH_2O$), 5.27 (1 H, m, 5-H), 4.41-4.30 (3 H, m, C₆H₅CH₂O and 9-H), 4.07 (1 H, d, J 8.5, 4-H), 3.88 (1 H, d, J 11.3, 6-H), 3.44 (2 H, m, 1-H × 2), 2.66 (1 H, dd, J 16.9 and 7.5, 8-H_A), 2.26 (1 H, dd, J 16.9 and 3.2, 8-H_B), 1.86 (2 H, m, 2-H \times 2), 1.29 (3 H, s, 3-CCH₃), 1.11 (3 H, d, J 5.9, 10-H × 3), 1.07 (9 H, s, SiC(CH₃)₃), 0.23 (3 H, s, Si(CH₃) × 1), 0.19 (3 H, s, Si(CH₃) × 1); $\delta_{\rm C}(150 \text{ MHz}; C_6 D_6)$ [209.6, 205.4, 200.8, 200.3, 197.6 $(Fe(CO) \times 4 \text{ and } 7-C)$], 138.5 (Ph *ipso*), 128.4 (Ph *meta* \times 2), [128.1-127.6 (Ph ortho × 2 and Ph para)], 91.2 (5-C), 90.0 (4-C), 78.9 (3-C), 73.1 (PhCH₂), 66.9 (1-C), 66.0 (6-C), 64.2 (9-C), 52.4 (8-C), 42.8 (2-C), 28.7 (3-CCH₃), 25.8 (SiC(CH₃)₃), 23.7 (10-C), 18.0 (SiC(CH₃)₃), -4.8 (Si(CH₃) × 2); m/z (ES) 609 (70%, MNa⁺) and 529 (100) [Found (MNa⁺) 609.1580. C₂₈H₃₈FeNaO₈Si requires MNa, 609.1583]; exo iron lactone complex **13** as an orange gum (1.10 g, 36%); $[a]_{\rm D}^{33}$ -221.2 (c 0.32, CH₂Cl₂); $v_{\rm max}$ (film)/cm⁻¹ [2087, 2014 (FeCO)], 1669 (C=O), 1455 (Ph); $\overline{\delta}_{H}(600 \text{ MHz}; C_6D_6)$ 7.33–7.18 (5 H, m, C₆H₅CH₂O), 5.24 (1 H, m, 5-H), 4.62 (1 H, d, J 8.6, 4-H), 4.46 (1 H, m, 9-H), 4.33 (1 H, d, J 12.0, C₆H₅CH₄H_BO), 4.29 (1 H, d, J 12.0, C₆H₅CH_AH_BO), 3.94 (1 H, d, J 11.2, 6-H), 3.49 (1 H, m, 1-H_A), 3.42 (1 H, m, 1-H_B), 2.71 (1 H, dd, J 15.7 and 7.9, 8-H_A), 2.42 (1 H, dd, J 15.7 and 4.4, 8-H_B), 2.03 (1 H, quintet, J 7.0, 2-H_A), 1.94 (1 H, m, 2-H_B), 1.25 (3 H, s, 3-CCH₃), 1.10 (3 H, d, J 5.9, 10-H × 3), 1.05 (9 H, s, $SiC(CH_3)_3$, 0.18 (3 H, s, $Si(CH_3) \times 1$), 0.15 (3 H, s, $Si(CH_3)$ × 1); $\delta_{\rm C}(150$ MHz; C₆D₆) [209.5, 205.8, 202.2, 200.0, 197.4 (Fe(CO) × 4 and 7-C)], 138.6 (Ph ipso), 128.4 (Ph meta × 2), [128.1–127.6 (Ph ortho × 2 and Ph para)], 91.2 (4-C), 91.0 (5-C), 79.0 (3-C), 72.9 (PhCH₂), 67.1 (6-C), 65.8 (9-C), 65.6 (1-C), 52.2 (8-C), 43.6 (2-C), 26.9 (3-CCH₃), 25.8 (SiC(CH₃)₃), 23.8 (10-C), 17.9 (SiC(CH₃)₃), -4.7 (Si(CH₃) × 1), -5.0 $(Si(CH_3) \times 1); m/z$ (ES) 609 (85%, MNa⁺) and 443 (100) [Found (MNa⁺) 609.1582. C₂₈H₃₈FeNaO₈Si requires MNa, 609.1583].

[(5*E*,3*S*,4*R*,7*R*,9*R*)-1-Benzyloxy-9-(*tert*-butyldimethylsilyloxy)-3-(carbonyloxy-κC)-7-hydroxy-3-methyl-(4,5,6-η)-dec-5-en-4-yl]tricarbonyliron (15)

Al(i-Bu)₃ (1 M in PhMe, 2.3 ml, 2.3 mmol, 2.0 eq.) was added dropwise to a solution of ketone 14 (660 mg, 1.1 mmol, 1.0 eq.) in CH₂Cl₂ (6 ml) at 0 °C. After 30 min the solution was poured onto pre-cooled (0 °C) 1 M aq. HCl (30 ml) and stirred vigorously for 20 min. CH₂Cl₂ (20 ml) was added and the layers separated. The aqueous phase was extracted with Et₂O (30 ml) and the combined organic fractions washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (Et₂O–petrol = $1 : 2 \rightarrow 1 : 1$) afforded alcohol 15 as a gum (480 mg, 72%); $[a]_{D}^{27}$ +97.7 (c 1.13, CH₂Cl₂); v_{max}(film)/cm⁻¹ 3423 (OH), [2078, 1999 (FeCO)], 1450 (Ph); $\delta_{\rm H}(600 \text{ MHz}; C_6D_6)$ 7.37–7.21 (5 H, m, $C_6H_5CH_2O$), 4.70 (1 H, dd, J 12.0 and 8.4, 5-H), 4.39 (1 H, d, J 12.5, C₆H₅CH_AH_BO), 4.37 (1 H, d, J 12.5, C₆H₅CH_AH_BO), 4.25 (1 H, d, J 9.1, 7-H), 4.08 (1 H, d, J 12.0, 6-H), 3.86 (1 H, d, J 8.4, 4-H), 3.82 (1 H, s, OH), 3.80 (1 H, m, 9-H), 3.53 (2 H, m, 1-H × 2), 2.03 (1 H, m, 2-H_A), 1.99 (1 H, m, 2-H_B), 1.76 (1 H, dd, J 14.2 and 9.8, 8-H_A), 1.53 (1 H, d, J 14.2, 8-H_B), 1.35 (3 H, s, 3-CCH₃), 1.02 (3 H, d, J 6.0, 10-H × 3), 0.96 (9 H, s, SiC(CH₃)₃), 0.11 (3 H, s, Si(CH₃) × 1), 0.06 (3 H, s, Si(CH₃) × 1); $\delta_{\rm C}(150 \text{ MHz}; \text{ C}_6\text{D}_6)$ [211.4, 207.8, 203.8, 200.7 (Fe(CO) × 4)], 138.8 (Ph ipso), 128.3 (Ph meta × 2), [128.1–127.6 (Ph ortho × 2 and Ph para)], 87.5 (5-C), 86.4 (4-C), 82.0 (7-C), 78.9 (3-C), 72.9 (PhCH₂), 70.3 (6-C), 67.3 (1-C), 65.9 (9-C), 47.9 (8-C), 42.9 (2-C), 28.7 (3-CCH₃), 25.6 (SiC(CH₃)₃), 24.0 (10-C), 17.7 $(SiC(CH_3)_3)$, -4.0 $(Si(CH_3) \times 1)$, -5.1 $(Si(CH_3) \times 1)$; m/z (ES) 611 (70%, MNa⁺) and 476 (100) [Found (MNa⁺) 611.1751. C₂₈H₄₀FeNaO₈Si requires MNa, 611.1740].

(4Z,3S,7S,9R)-1-Benzyloxy-9-(*tert*-butyldimethylsilyloxy)-3-methyldec-4-ene-3,7-diol (16)

NaBH(OAc)_a (1.58 g, 7.5 mmol, 10 eq.) was added to a solution of iron complex 15 (440 mg, 0.75 mmol, 1.0 eq.) in THF (10 ml). After 40 h the red mixture was filtered through a pad of Celite and the residue washed with Et₂O (60 ml). Concentration of the filtrate in vacuo followed by flash column chromatography (Et₂O-petrol = $1 : 2 \rightarrow 1 : 1$) afforded a mixture of regioisomeric alkene diols as an oil with diol 16 as the major component (230 mg, 73%); v_{max}(film)/cm⁻¹ 3408 (OH), 1668 (C=C), 1455 (Ph); $\delta_{\rm H}(600~{\rm MHz};~{\rm CDCl_3})$ 7.36–7.28 (5 H, m, C₆H₅CH₂O), 5.52 (1 H, d, J 12.1, 4-H), 5.44 (1 H, dt, J 12.1 and 8.1, 5-H), 4.50 (2 H, m, J 11.9, C₆H₅CH₂O), 4.07 (1 H, m, 9-H), 3.79 (1 H, m, 7-H), 3.68 (2 H, m, 1-H × 2), 2.60 (1 H, dt, J 14.0 and 8.1, 6-H_A), 2.34 (1 H, ddd, J 14.0, 8.1 and 3.6, 6-H_B), 1.92 (1 H, m, 2-H_A), 1.88 (1 H, m, 2-H_B), 1.62 (1 H, dt, J 14.2 and 9.2, 8-H_A), 1.52 (1 H, ddd, J 14.2, 3.7 and 2.9, 8-H_B), 1.31 (3 H, s, 3-CCH₃), 1.17 (3 H, d, J 6.0, 10-H × 3), 0.89 (9 H, s, SiC(CH₃)₃), 0.10 (3 H, s, Si(CH₃) × 1), 0.09 (3 H, s, Si(CH₃) × 1); δ_{c} (150 MHz; CDCl₃) 138.4 (4-C), 138.0 (Ph *ipso*), 128.4 (Ph meta × 2), 127.6 (Ph ortho × 2), 127.6 (Ph para), 125.3 (5-C), 73.9 (3-C), 73.2 (PhCH₂), 70.2 (7-C), 69.5 (9-C), 67.8 (1-C), 45.9 (8-C), 41.7 (2-C), 35.2 (6-C), 29.9 (3-CCH₃), 25.8 (SiC(CH₃)₃), 24.4 (10-C), 17.9 (SiC(CH₃)₃), -3.9 (Si(CH₃) × 1), -4.8 (Si(CH₃) × 1); m/z (ES) 445 (100%, MNa⁺) [Found (MNa⁺) 445.2758. C₂₄H₄₂NaO₄Fe requires MNa, 445.2750].

(4Z,3S,7S,9R)-7-Acetoxy-1-benzyloxy-9-(*tert*-butyldimethyl-silyloxy)-3-methyldec-4-en-3-ol (17)

Ac₂O (32 mg, 0.31 mmol, 1.1 eq.) was added to a solution of diol 16 (120 mg, 0.28 mmol, 1.0 eq.), Et₃N (29 mg, 0.37 mmol, 1.3 eq.) and DMAP (4 mg, 0.03 mmol, 0.1 eq.) in CH₂Cl₂ (2.5 ml) at 0 °C. The reaction was allowed to warm to room temperature, stirred for 2 h, filtered through a pad of silica and the residue washed with Et₂O (50 ml). Concentration of the filtrate in vacuo afforded a mixture of alkene diols as an oil, with the major component diol 17. The diols were used without further purification (127 mg, 96%); $v_{max}(film)/cm^{-1}$ 3515 (OH), 1735 (C=O), 1667 (C=C), 1455 (Ph); $\delta_{\rm H}$ (600 MHz; CDCl₃) 7.35-7.27 (5 H, m, C₆H₅CH₂O), 5.44 (1 H, d, J 12.0, 4-H), 5.33 (1 H, m, 5-H), 5.00 (1 H, m, 7-H), 4.52 (1 H, d, J 12.0, C₆H₅CH_AH_BO), 4.49 (1 H, d, J 12.0, C₆H₅CH_AH_BO), 3.83 (1 H, m, 9-H), 3.73 (1 H, m, 1-H_A), 3.67 (1 H, m, 1-H_B), 3.54 (1 H, s, OH), 2.81 (1 H, m, 6-H_A), 2.68 (1 H, m, 6-H_B), 2.02 (3 H, s, COCH₃), 1.92 (1 H, m, 2-H_A), 1.82 (2 H, m, 2-H_B and 8-H_A), 1.61 (1 H, m, 8-H_B), 1.31 (3 H, s, 3-CCH₃), 1.14 (3 H, d, J 6.0, 10-H × 3), 0.88 (9 H, s, SiC(CH₃)₃), 0.04 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}(150 \text{ MHz}; \text{CDCl}_3)$ 170.5 (COCH₃), 137.8 (Ph *ipso*), 137.7 (4-C), 128.4 (Ph meta × 2), 127.7 (Ph ortho × 2), 127.7 (Ph para), 125.4 (5-C), 74.3 (3-C), 73.4 (PhCH₂), 71.7 (7-C), 67.9 (1-C), 65.6 (9-C), 44.0 (8-C), 41.5 (2-C), 32.7 (6-C), 29.5 (3-CCH₃), 25.8 (SiC(CH₃)₃), 23.4 (10-C), 21.2 (COCH₃), 18.1 $(SiC(CH_3)_3), -4.5 (Si(CH_3) \times 1), -4.8 (Si(CH_3) \times 1); m/z (ES)$ 487 (100%, MNa⁺) [Found (MNa⁺) 487.2850. C₂₆H₄₄NaO₅Si requires MNa, 487.2856].

(3*R*,7*S*,9*R*)-7-Acetoxy-9-(*tert*-butyldimethylsilyloxy)-3-methyl-decane-1,3-diol (18)

[From alkene diol 17 (Scheme 1)]. Pd(OH)₂ (20 wt. % Pd (dry basis) on carbon, 62 mg) was suspended in a solution of alkene diol **17** (62 mg, 0.13 mmol, 1 eq.) and Et₃N (26 mg, 0.26 mmol, 2.0 eq.) in EtOAc (2 ml). The mixture was purged 5 times with H₂ and stirred under an atmosphere of H₂. After 24 h the mixture was filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (EtOAc–petrol = $1 : 1 \rightarrow 3 : 1$) to afford diol **18** as an oil (44 mg, 88%); $[a]_{D}^{25} - 4.3$ (c 1.43, CHCl₃); v_{max} (film)/cm⁻¹ 3359 (OH), 1736 (C=O); δ_{H} (600

MHz; CDCl₃) 4.98 (1 H, m, 7-H), 3.91 (1 H, m, 1-H_A), 3.83 (2 H, m, 1-H_B and 9-H), 2.51 (1 H, s, OH), 2.29 (1 H, s, OH), 2.03 (3 H, s, COCH₃), 1.78 (2 H, m, 2-H_A and 8-H_A), 1.67–1.45 (7 H, m, 2-H_B, 4-H × 2, 6-H × 2 and 8-H_B), 1.37 (1 H, m, 5-H_A), 1.31 (1 H, m, 5-H_B), 1.23 (3 H, s, 3-CCH₃), 1.15 (3 H, d, *J* 6.1, 10-C × 3), 0.88 (9 H, s, SiC(CH₃)₃), 0.05 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}$ (150 MHz; CDCl₃) 170.7 (COCH₃), 73.6 (3-C), 71.5 (7-C), 65.6 (9-C), 59.8 (1-C), [44.3, 42.4, 41.5, 35.0 (2-C, 4-C, 6-C and 8-C)], 26.8 (3-CCH₃), 25.8 (SiC(CH₃)₃), 23.4 (10-C), 21.2 (COCH₃), 19.6 (5-C), 18.1 (SiC(CH₃)₃), -4.4 (Si(CH₃) × 1), -4.8 (Si(CH₃) × 1); *m*/*z* (ES) 399 (100%, MNa⁺) [Found (MNa⁺) 399.2555. C₁₉H₄₀NaO₅Si requires *M*Na, 399.2543]. Data were consistent with those reported in the literature.⁷

[From alkene diol 29 (Scheme 3)]. Ac₂O (40 mg, 0.39 mmol, 1.1 eq.) was added to a solution of diol 29 (160 mg, 0.36 mmol, 1.0 eq.), Et₃N (43 mg, 0.43 mmol, 1.2 eq.) and DMAP (4 mg, 0.04 mmol, 0.1 eq.) in CH₂Cl₂ (3 ml) at 0 °C. The reaction was allowed to warm to room temperature, stirred for 2 h, filtered through a pad of silica and the residue washed with Et₂O (50 ml). Concentration of the filtrate in vacuo afforded (3R,7S,9R)-7-acetoxy-1,9-di(tert-butyldimethylsilyloxy)-3-methyldecan-3ol as an oil, which was used without further purification (171 mg, 98%); $[a]_{\rm D}^{25}$ -0.3 (c 1.23, CH₂Cl₂); $v_{\rm max}$ (film)/cm⁻¹ 3502 (OH), 1738 (C=O); $\delta_{\rm H}$ (600 MHz; CDCl₃) 4.96 (1 H, m, 7-H), 3.88 (2 H, m, 1-H × 2), 3.82 (1 H, m, 9-H), 3.77 (1 H, s, OH), 2.02 (3 H, s, COCH₃), 1.80 (1 H, ddd, J 13.9, 8.1 and 5.4, 8-H_A), 1.73 (1 H, ddd, J 14.5, 7.7 and 4.7, 2-H_A), 1.63-1.53 (4 H, m, 2-H_B, 6-H \times 2 and 8-H_B), 1.48–1.43 (3 H, m, 4-H \times 2 and 5-H_A), 1.30 (1 H, m, 5-H_B), 1.17 (3 H, s, 3-CCH₃), 1.15 (3 H, d, J 6.1, 10-H × 3), 0.90 (9 H, s, SiC(CH₃)₃ × 1), 0.88 (9 H, s, SiC(CH₃)₃ \times 1), 0.08 (6 H, s, Si(CH₃) \times 2), 0.08 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}$ (150 MHz, CDCl₃) 170.6 (COCH₃), 72.5 (3-C), 71.8 (7-C), 65.7 (9-C), 60.7 (1-C), 44.3 (8-C), [42.3, 41.3, 35.1 (2-C, 4-C and 6-C)], 26.2 (3-CCH₃), 25.8 (SiC(CH₃)₃ × 1), 25.8 $(SiC(CH_3)_3 \times 1), 23.5 (10-C), 21.2 (COCH_3), 19.6 (5-C), 18.1$ $(SiC(CH_3)_3 \times 1)$, 18.0 $(SiC(CH_3)_3 \times 1)$, -4.5 $(Si(CH_3) \times 1)$, -4.8 (Si(CH₃) × 1), -5.6 (Si(CH₃) × 1), -5.7 (Si(CH₃) × 1); m/z (ES) 513 (100%, MNa⁺) [Found (MNa⁺) 513.3416. C₂₅H₅₄NaO₅Si₂ requires MNa, 513.3408].

TBAF (1.0 M in THF, 0.20 ml, 0.51 mmol, 5.1 eq.) was added dropwise to a solution of the above alcohol (21.4 mg, 0.044 mmol, 1 eq.) and AcOH (12.8 mg, 0.21 mmol, 5 eq.) in THF (1 ml) at 0 °C. The reaction was allowed to warm to room temperature. After stirring for 4 h the reaction mixture was poured onto 1 M aq. HCl (10 ml) and the layers separated. The aqueous layer was extracted with Et₂O (3 × 5 ml) and the combined organic fractions washed with sat. aq. NaHCO₃ and brine and dried (MgSO₄). Concentration *in vacuo* followed by flash column chromatography (EtOAc–petrol = 1 : 1 \rightarrow 3 : 1) afforded diol **18** as an oil (14.3 mg, 87%); Data were consistent with those reported (*vide supra*).

(2*R*,3*R*,5*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,3-epoxyhexan-1-ol (20)

t-BuOOH (~5–6 M in decanes, 30 ml, 0.15 mol, 2.5 eq.), which was stored over 4 Å MS, was added *via* cannula to a solution of diisopropyl D-tartrate (1.71 g, 7.3 mmol, 0.12 eq.) and Ti(Oi-Pr)₄ (1.72 g, 6.1 mmol, 0.10 eq.) in CH₂Cl₂(20 ml) containing 4 Å MS at -20 °C. After 30 min this solution was added *via* cannula to a solution of allyl alcohol **19** (14.0 g, 60.7 mmol, 1.0 eq.) in CH₂Cl₂ (30 ml) over 4 Å MS at -20 °C and the reaction stirred at this temperature for 18 h. The mixture was poured slowly onto a slurry of Celite in 1.5 M aq. FeSO₄ (500 ml), then filtered through a pad of Celite and the residue was washed with CH₂Cl₂ (150 ml). The filtrate was separated and the aqueous layer was extracted with ether (200 ml). The CH₂Cl₂ and ether fractions were separately washed with brine,

then combined and dried (MgSO₄). Concentration in vacuo followed by flash column chromatography (Et₂O-petrol = 1:2 -10 : 1) afforded epoxide 20 as an oil (12.3 g, 82%, 93% de assessed by 400 MHz ¹H NMR of the crude product); $[a]_{D}^{25} + 9.8$ (c 1.23, CH_2Cl_2); v_{max} (film)/cm⁻¹ 3401 (OH); δ_H (400 MHz; CDCl₃) 3.97 (1 H, sextet, J 6.0, 5-H), 3.87 (1 H, dd, J 12.5 and 2.5, 1-H_A), 3.57 (1 H, dd, J 12.5 and 4.4, 1-H_B), 3.02 (1 H, td, J 6.0 and 2.3, 3-H), 2.86 (1 H, m, 2-H), 1.74 (1 H, dt, J 13.9 and 6.0, 4-H_A), 1.57 (2 H, m, 4-H_B and OH), 1.16 (3 H, d, J 6.0, $6-H \times 3$, 0.83 (9 H, s, SiC(CH₃)₃), 0.01 (3 H, s, Si(CH₃) × 1), 0.00 (3 H, s, Si(CH₃) × 1); $\delta_{\rm C}$ (100 MHz; CDCl₃) 66.4 (5-C), 61.67 (1-C), 58.1 (2-C), 53.2 (3-C), 41.5 (4-C), 25.8 (SiC(CH₃)₃), 23.6 (6-C), 18.0 (SiC(CH₃)₃), -4.5 (Si(CH₃) × 1), (Si(CH3) × 1); *m/z* (ES) 269 (100%, MNa⁺) [Found (MNa⁺) 269.1541. C₁₂H₂₆NaO₃Si₂ requires MNa, 269.1549].

(2S,3R,5R)-5-(tert-Butyldimethylsilyloxy)-2,3-epoxyhexanal (21)

A solution of (COCl)₂ (7.8 g, 61 mmol, 1.2 eq.) in CH₂Cl₂ (10 ml) was added to a solution of DMSO (9.6 g, 0.12 mol, 2.4 eq.) in CH₂Cl₂ (200 ml) at -78 °C. After 10 min alcohol 20 (12.1 g, 49 mmol, 1.0 eq.) was added and followed, after 15 min, by Et₃N (20 g, 0.20 mol, 4.0 eq.). The reaction mixture was poured onto 1 M aq. HCl and the layers separated, the aqueous layer was extracted with Et₂O (200 ml) and the combined organic fractions washed with brine and dried (MgSO₄). Filtration through a pad of silica and concentration in vacuo afforded aldehyde 21 as an oil, which was used without further purification (10.6 g, 88%); v_{max} (film)/cm⁻¹ 1731 (C=O); δ_{H} (400 MHz; CDCl₃) 8.95 (1 H, d, J 6.3, 1-H), 3.99 (1 H, sextet, J 6.0, 5-H), 3.31 (1 H, td, J 5.7 and 1.9, 3-H), 3.06 (1 H, dd, J 6.3 and 1.9, 2-H), 1.69 (2 H, m, 4-H × 2), 1.17 (3 H, d, J 6.0, 6-H × 3), $0.82 (9 \text{ H}, \text{ s}, \text{SiC}(\text{CH}_3)_3), 0.00 (3 \text{ H}, \text{ s}, \text{Si}(\text{CH}_3) \times 1), -0.03 (3 \text{ H}, \text{ s})$ s, Si(CH₃) × 1); $\delta_{\rm C}$ (100 MHz; CDCl₃) 198.3 (1-C), 66.3 (5-C), 58.6 (2-C), 54.2 (3-C), 40.9 (4-C), 25.8 (SiC(CH₃)₃), 23.6 (6-C), 18.0 (SiC(CH₃)₃), -4.5 (Si(CH₃) × 1), -4.9 (Si(CH₃) × 1).

Methyl 3-hydroxypropionoate (22)

 β -Propiolactone (12.0 g, 0.17 mol, 1.0 eq.) was added to a solution of NaOMe (0.90 g, 17 mmol, 10 eq.) in MeOH (50 ml). The solution was stirred at 50 °C for 1 h, cooled back to room temperature, filtered through a pad of silica and the residue washed with Et₂O (200 ml). Concentration of the filtrate in *vacuo* afforded ester **22** as an oil (17.3 g, 100%); $v_{max}(film)/cm^{-1}$ 3387 (OH), 1718 (C=O); $\delta_{\rm H}$ (400 MHz; CDCl₃) 3.88 (2 H, t, J 5.6, 3-H × 2), 3.72 (3 H, s, OCH₃), 2.59 (2 H, t, J 5.6, 2-H × 2), 2.36 (1 H, s, OH); δ_C(100 MHz; CDCl₃) 173.3 (1-C), 58.2 (3-C), 51.7 (OCH₃), 36.6 (2-C); *m/z* (ES) 127 (100%, MNa⁺) [Found (MNa⁺) 127.0375. C₄H₉NaO₃ requires *M*Na, 127.0371].

Methyl 3-(tert-butyldimethylsilyloxy)propionoate (23)

A solution of TBSC1 (30.4 g, 0.20 mol, 1.05 eq.) in DMF (75 ml) was added via cannula to a solution of alcohol 22 (20.0 g, 0.19 mol, 1.0 eq.) and imidazole (15.0 g, 0.22 mol, 1.15 eq.) in DMF (250 ml) at 0 °C and the solution allowed to warm to room temperature overnight. The reaction mixture was poured onto 1 M aq. HCl (600 ml) and extracted with Et₂O $(3 \times 200 \text{ ml})$. The combined organic fractions were washed with brine and dried (MgSO₄). Filtration through a pad of silica and concentration in vacuo afforded silyl ether 23 as an oil, which was used without further purification (42 g, 100%); $v_{max}(film)/$ cm⁻¹ 1727 (C=O); δ_H(400 MHz; CDCl₃) 3.84 (2 H, t, J 6.4, 3-H × 2), 3.63 (3 H, s, OCH₃), 2.48 (2 H, t, J 6.4, 2-H × 2), 0.82 (9 H, s, SiC(CH₃)₃), 0.00 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}$ (100 MHz; CDCl₃) 172.2 (1-C), 59.1 (3-C), 51.5 (OCH₃), 37.9 (2-C), 25.8 $(SiC(CH_3)_3)$, 18.2 $(SiC(CH_3)_3)$, -5.5 $(Si(CH_3) \times 2)$; m/z (ES) 241 (100%, MNa⁺) [Found (MNa⁺) 241.1241. C₁₀H₂₂NaO₃Si₂ requires MNa, 241.1236].

Diethyl [4-(tert-butyldimethylsilyloxy)-2-oxobutyl]phosphonate (24)

n-BuLi (1.6 M in hexanes, 100 ml, 0.16 mol, 1.0 eq.) was added via cannula to a solution of (EtO)₂P(O)Me (24.3 g, 0.16 mol, 1.0 eq.) in THF (400 ml) at -78 °C. After stirring for 1 h ester 23 (41 g, 0.19 mol, 1.2 eq.) was added dropwise. The solution was warmed to room temperature and stirred for a further 2 h before pouring onto 1 M aq. HCl (500 ml). After separation the aqueous phase was extracted with EtOAc (3×100 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration in vacuo followed by flash column chromatography (Et₂O \rightarrow Et₂O-EtOAc = 1 : 1) afforded β-ketophosphonate **24** as an oil (42 g, 78%); v_{max} (film)/cm⁻¹ 1715 (C=O), 1252 (P=O), 1014 (P–O); $\delta_{\rm H}$ (600 MHz; CDCl₃) 4.15 (4 H, m, OCH₂CH₃ × 2), 3.90 (2 H, t, J 6.2, 4-H × 2), 3.13 (2 H, d, J 22.6, 1-H × 2), 2.81 (2 H, t, J 6.2, 3-H), 1.34 (6 H, t, J 7.1, OCH₂CH₃ × 2), 0.87 (9 H, s, SiC(CH₃)₃), 0.05 (6 H, s, Si(CH₃) × 2); δ_{c} (100 MHz; CDCl₃) 201.5 (d, J 25, 2-C), 62.9 (d, J 26, OCH₂CH₃), 59.0 (4-C), 47.2 (3-C), 43.5 (d, J 506, 1-C), 26.2 (SiC(CH₃)₃), 18.6 (SiC(CH₃)₃), 16.6 (d, J 25, OCH₂CH₃), -5.1 (Si(CH₃) × 2); $\delta_{\rm P}$ (600 MHz; CDCl₃) 20.5; *m*/*z* (EI) 338 (15%, M⁺), 75 (100) [Found (M⁺) 338.1686. C₁₄H₃₁O₅PSi requires M, 338.1678].

(4E,6R,7R,9R)-1,9-Di(tert-butyldimethylsilyloxy)-6,7-epoxydec-4-en-3-one (25)

Phosphonate 24 (3.00 g, 8.8 mmol, 1.2 eq.) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 0.32 g, 8.1 mmol, 1.1 eq.) in THF (200 ml) at 0 °C, followed, after 20 min, by aldehyde 21 (1.8 g, 7.4 mmol, 1.0 eq.). After 10 min the reaction was poured onto sat. aq. NH₄Cl and extracted with Et₂O (2 \times 100 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography $(Et_2O-petrol = 1 : 5 \rightarrow 1 : 2)$ afforded enone **25** as a pale yellow oil (2.40 g, 76%); $[a]_{D}^{25}$ +5.1 (c 0.93, CH₂Cl₂); v_{max} (film)/cm⁻¹ 1675 (C=O), 1631 (C=C); δ_H(600 MHz; CDCl₃) 6.53 (1 H, dd, J 16.0 and 7.0, 5-H), 6.41 (1 H, d, J 16.0, 4-H), 4.04 (1 H, sextet, J 6.0, 9-H), 3.92 (2 H, t, J 6.4, 1-H × 2), 3.21 (1 H, dd, J 7.0 and 1.8, 6-H), 3.02 (1 H, td, J 6.0 and 1.8, 7-H), 2.76 (2 H, m, 2-H × 2), 1.80 (1 H, dt, J 14.0 and 6.0, 8-H_A), 1.68 (1 H, dt, J 14.0 and 6.0, 8-H_B), 1.22 (3 H, d, J 6.0, 10-H \times 3), 0.88 (9 H, s, SiC(CH₃)₃), 0.87 (9 H, s, SiC(CH₃)₃), 0.10 (6 H, s, Si(CH₃) × 2), 0.04 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}$ (150 MHz; CDCl₃) 198.2 (3-C), 143.1 (5-C), 132.0 (4-C), 66.3 (9-C), 58.9 (1-C), 58.8 (7-C), 56.2 (6-C), 43.3 (2-C), 41.7 (8-C), 25.8 (SiC(CH₃)₃ × 1), 25.6 (SiC(CH₃)₃ × 1), 18.0 (10-C), 18.0 (SiC(CH₃)₃ × 1), 17.9 $(SiC(CH_3)_3 \times 1), -3.6 (Si(CH_3) \times 2), -5.5 (Si(CH3) \times 2); m/z$ (EI) 371 (12%, $M^+ - C_4H_9$), 75 (100) [Found ($M^+ - C_4H_9$) 371.2079. $C_{18}H_{35}O_4Si_2$ requires $M - C_4H_9$, 371.2074].

[(6E,2R,4R,5R)-4-(Carbonyloxy-кС)-2,10-di(tert-butyldimethylsilyloxy)-8-oxo-(5,6,7-n)-dec-6-en-5-yl]tricarbonyliron (26) and [(6E,2R,4R,5S)-4-(carbonyloxy-KC)-2,10-di(tertbutyldimethylsilyloxy)-8-oxo-(5,6,7-n)-dec-6-en-5-yl]tricarbonyliron (27)

Degassed THF (40 ml) was added to diironnonacarbonyl (5.0 g, 13.7 mmol, 2.2 eq.) via cannula and the mixture was stirred vigorously in the absence of light for 20 min at room temperature. Alkenyl epoxide 25 (2.70 g, 6.3 mmol, 1.0 eq.) was then added and the reaction mixture stirred vigorously. After 3 h the green mixture was filtered through a pad of Celite and washed with Et₂O (60 ml). PhMe (5 ml) was added to the filtrate and the solution was concentrated in vacuo. Purification of the residue by flash column chromatography (petrol until all Fe₃(CO)₁₂ had been removed, then Et_2O -petrol = 1 : 3 \rightarrow 1 : 1) afforded, in order of elution, endo iron lactone complex 27 as a yellow solid (1.80 g, 48%); $[a]_{D}^{25}$ -188.2 (c 0.44, CH₂Cl₂); $v_{max}(film)/cm^{-1}$

[2090, 2022 (FeCO)], 1674 (C=O); δ_H(600 MHz; C₆D₆) 5.29 (1 H, dd, J 11.2 and 8.6, 6-H), 4.25 (1 H, quintet, J 4.4, 4-H), 4.20 (1 H, dd, J 8.6 and 4.4, 5-H), 3.97 (1 H, d, J 11.2, 7-H), 3.95 (1 H, m, 2-H), 3.91 (1 H, m, 10-H_A), 3.79 (1 H, m, 10-H_B), 2.60 (1 H, ddd, J 16.6, 7.3 and 4.8, 9-H_A), 2.42 (1 H, ddd, J 16.6, 6.3 and 4.6, 9-H_B), 1.85 (1 H, ddd, J 13.7, 8.4 and 5.5, 3-H_A), 1.55 (1 H, ddd, J 13.7, 6.7 and 4.8, 3-H_B), 1.12 (3 H, d, J 6.1, $1-H \times 3$, 1.06 (18 H, s, SiC(CH₃)₃ × 2), 0.17 (3 H, s, Si(CH₃) × 1), 0.16 (3 H, s, Si(CH₃) × 1), 0.15 (3 H, s, Si(CH₃) × 1), 0.13 $(3 \text{ H}, \text{ s}, \text{Si}(\text{CH}_3) \times 1); \delta_{C}(150 \text{ MHz}; \text{C}_6\text{D}_6)$ [208.6, 205.5, 201.3, 200.2, 198.7 (Fe(CO) × 4 and 8-C)], 91.4 (6-C), 84.8 (5-C), 73.4 (4-C), 66.4 (7-C), 66.1 (2-C), 58.1 (10-C), 46.5 (3-C), 45.5 (9-C), 25.9 (SiC(CH₃)₃ × 1), 25.8 (SiC(CH₃)₃ × 1), 22.9 (1-C), 18.3 $(SiC(CH_3)_3 \times 1)$, 17.9 $(SiC(CH_3)_3 \times 1)$, -4.5 $(Si(CH_3) \times 1)$, -4.9 (Si(CH₃) × 1), -5.6 (Si(CH₃) × 2); m/z (ES) 619 (80%, MNa⁺), 453 (100) [Found (MNa⁺) 619.1816. C₂₆H₄₄FeNaO₈Si₂ requires MNa, 619.1822] and exo iron lactone 26 as a yellow solid (0.53 g, 14%); [a]²⁵_D +85.7 (c 0.37, CH₂Cl₂); v_{max}(film)/cm⁻ [2088, 2019 (FeCO)], 1670 (C=O); $\delta_{\rm H}$ (600 MHz; C₆D₆) 5.41 (1 H, dd, J 11.0 and 8.3, 6-H), 4.03-3.94 (3 H, m, 2-H, 4-H and 5-H), 3.87 (1 H, m, 10-H_A), 3.79 (1 H, m, 10-H_B), 3.76 (1 H, d, J 11.0, 7-H), 2.57 (1 H, ddd, J 16.5, 7.1 and 4.5, 9-H_A), 2.49 (1 H, ddd, J 16.5, 6.3 and 4.4, 9-H_B), 1.91 (1 H, ddd, J 13.7, 8.9 and 5.3, 3-H_A), 1.54 (1 H, ddd, J 13.7, 7.4 and 1.1, 3-H_B), 1.18 (3 H, d, J 6.1, 1-H × 3), 1.06 (9 H, s, SiC(CH₃)₃ × 1), 1.05 (9 H, s, SiC(CH₃)₃ \times 1), 0.17 (3 H, s, Si(CH₃) \times 1), 0.16 (3 H, s, Si(CH₃) × 1), 0.15 (3 H, s, Si(CH₃) × 1), 0.14 (3 H, s, Si(CH₃) × 1); δ_c(150 MHz; C₆D₆) 209.1, 201.4, 201.4, 200.6, 198.5, 92.8, 83.7, 70.9, 65.5, 65.0, 59.0, 47.9, 45.4, 25.9, 25.8, 22.8, 18.2, 17.9, -4.7, -5.0, -5.6, -5.7; m/z (ES) 619 (80%, MNa⁺), 525 (100) [Found (MNa⁺) 619.1819. C₂₆H₄₄FeNaO₈Si₂ requires MNa, 619.1822].

[(6*E*,2*R*,4*R*,5*S*,8*S*)-4-(Carbonyloxy-κC)-2,10-di(*tert*-butyldimethylsilyloxy)-8-hydroxy-8-methyl-(5,6,7-η)-dec-6-en-5-yl]tricarbonyliron (28)

AlMe₃ (2 M in PhMe, 1.4 ml, 2.8 mmol, 2.0 eq.) was added dropwise to a solution of ketone 27 (820 mg, 1.4 mmol, 1.0 eq.) in CH₂Cl₂ (10 ml) at 0 °C. After 30 min the solution was poured onto pre-cooled (0 °C) 1 M aq. HCl (30 ml) and stirred vigorously for 20 min. CH₂Cl₂ (20 ml) was added and the layers separated. The aqueous layer was extracted with Et₂O (30 ml) and the combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (Et₂O-petrol = $1: 3 \rightarrow 1: 1$) afforded alcohol **28** as a solid (682 mg, 81%); $[a]_{D}^{25} - 103.6$ (c 0.75, CH₂Cl₂); v_{max}(film)/cm⁻¹ 3449 (OH), [2082, 2003 (FeCO)], 1672 (C=O); $\delta_{\rm H}$ (600 MHz; C₆D₆) 4.81 (1 H, dd, J 12.3 and 8.4, 6-H), 4.26 (3 H, m, 4-H, 7-H and OH), 3.74 (1 H, td, J 11.1 and 1.5, 10-H_A), 3.60 (1 H, m, 10-H_B), 2.21 (1 H, ddd, J 14.3, 11.7 and 4.6, 9-H_A), 1.96 (1 H, ddd, J 13.6, 7.5 and 4.7, 3-H_A), 1.68 (1 H, ddd, J 13.6, 8.8 and 5.0, 3-H_B), 1.46 (3 H, s, 8-CCH₃), 1.43 (1 H, d, J 14.3, 9-H_B), 1.16 (3 H, d, J 6.1, 1-H × 3), 1.07 (9 H, s, SiC(CH₃)₃ × 1), 0.94 (9 H, s, SiC(CH₃)₃ × 1), 0.18 (3 H, s, Si(CH₃) × 1), 0.15 (3 H, s, Si(CH₃) × 1), 0.04 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}(150 \text{ MHz}; \text{ C}_6\text{D}_6)$ [210.6, 208.2, 203.8, 201.8 (Fe(CO) × 4)], 95.4 (7-C), 86.1 (6-C), 75.9 (5-C), 73.8 (4-C), 72.5 (8-C), 66.7 (2-C), 60.1 (10-C), 47.0 (3-C), 43.3 (9-C), 29.6 (8-CCH₃), 25.8 (SiC(CH₃)₃ × 1), 25.5 (SiC(CH₃)₃ × 1), 22.8 (1-C), 18.0 $(SiC(CH_3)_3 \times 1)$, 17.8 $(SiC(CH_3)_3 \times 1)$, -4.5 $(Si(CH_3) \times 1)$, -4.8 (Si(CH₃) × 1), -6.0 (Si(CH₃) × 1), -6.0 (Si(CH₃) × 1); m/z(ES) 635 (25%, MNa⁺), 551 (100) [Found (MNa⁺) 635.2120. C₂₇H₄₈FeNaO₈Si₂ requires MNa, 635.2135].

(3*R*,7*S*,9*R*)-1,9-Di(*tert*-butyldimethylsilyloxy)-3-methyldecane-3,7-diol (29)

NaBH(OAc)₃ (0.97 g, 4.6 mmol, 10 eq.) was added to a solution of iron complex **28** (280 mg, 0.46 mmol, 1 eq.) in THF (10 ml). After stirring for 40 h the red mixture was filtered through a pad

of Celite and the residue washed with Et₂O (60 ml). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et₂O-petrol = $1 : 1 \rightarrow 2 : 1$) afforded a mixture of alkene diols.

Pd/C (280 mg, 10 wt. % Pd on activated carbon,) was suspended in a solution of the above mixture of alkene diols in EtOAc (2.5 ml). The mixture was purged 5 times with H_2 and stirred under an atmosphere of H₂. After 3 h the mixture was filtered through a pad of Celite and the residue washed with EtOAc (50 ml). Concentrated of the filtrate in vacuo afforded alkane diol 29 as an oil which required no further purification (166 mg, 81%); $[a]_{\rm D}^{25}$ -14.9 (c 0.61, CH₂Cl₂); $v_{\rm max}$ (film)/cm⁻ 3435 (OH); $\delta_{\rm H}(600$ MHz; CDCl₃) 4.07 (1 H, m, 9-H), 3.89 (2 H, m, 1-H × 2), 3.77 (1 H, m, 7-H), 3.45 (1 H, s, OH), 1.75 (1 H, ddd, J 14.3, 7.4 and 4.8, 2-H_A), 1.65-1.60 (2 H, m, 2-H_B and 8- H_{A}), 1.58–1.46 (5 H, m, 4-H × 2, 6-H × 2 and 8- H_{B}), 1.19 (3 H, s, 3-CCH₃), 1.18 (3 H, d, J 6.1, 10-H × 3), 0.90 (18 H, s, SiC(CH₃)₃ × 2), 0.12 (3 H, s, Si(CH₃) × 1), 0.10 (3 H, s, Si(CH₃) × 1), 0.08 (6 H, s, Si(CH₃) × 2); $\delta_{\rm C}$ (150 MHz, CDCl₃) 72.7 (3-C), 71.3 (7-C), 70.2 (9-C), 60.7 (1-C), 45.7 (8-C), [42.2, 41.1, 38.1 (2-C, 4-C and 6-C)], 26.4 (3-CCH₃), 25.8 (SiC(CH₃)₃ × 2), 24.6 (10-C), 19.8 (5-C), 18.1 (SiC(CH₃)₃ × 1), 17.9 (SiC(CH₃)₃ × 1), -3.9 (Si(CH₃) × 1), -4.8 (Si(CH₃) × 1), -5.6 (Si(CH₃) × 1), -5.7 (Si(CH₃) × 1); m/z (ES) 471 (100%, MNa⁺) [Found (MNa⁺) 471.3325. C₂₃H₅₂NaO₄Si₂ requires *M*Na, 471.3302].

Heneicos-4-yn-1-ol (32)

n-BuLi (1.6 M in hexanes, 1.40 ml, 2.24 mmol, 1.2 eq.) was added dropwise to a solution of 1-octadecyne (31) (470 mg, 1.87 mmol, 1.0 eq.) in THF (10.0 ml) at -15 °C. After stirring at -15 °C for 20 min, HMPA (6.5 ml) in THF (10.0 ml) was added and the solution stirred for a further 30 min at 0 °C before dropwise addition of 2-(3-bromopropoxy)tetrahydro-2H-pyran (501 mg, 2.25 mmol, 1.2 eq.) in THF (10.0 ml). The mixture was stirred for 3 h at 0 °C and for 15 h at room temperature, to which, after cooled back to 0 °C, 6 M aq. H₂SO₄ (5 ml) was added. After 2 h of stirring at 0 °C, the reaction mixture was poured onto H₂O (20 ml) and extracted with Et₂O (3 \times 15 ml). The combined organic fractions were washed successively with sat. aq. NaHCO₃ and brine, and dried (Na₂SO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (EtOAc-petrol = 1:4) afforded alcohol 32 as a white powder (425 mg, 73%); mp 51–52 °C; v_{max} (film)/cm⁻¹ 3552 (OH), 2955, 2917, 2848, 1459, 1065, 1053, 725; $\delta_{\rm H}$ (400 MHz; CDCl₃) 3.74 (2 H, t, J 6.1, 1-H × 2), 2.27 (2 H, m, 3-H × 2), 2.12 (2 H, m, 6-H × 2), 1.73 (2 H, quintet, J 6.5, 2-H × 2), 1.46 (2 H, m, 7-H × 2), 1.38–1.24 (27 H, m, 8-H–20-H and OH), 0.87 (3 H, t, J 6.8, 21-H \times 3); $\delta_{\rm C}$ (100 MHz; CDCl₃) 81.1 (5-C), 79.2 (4-C), 62.0 (1-C), 31.9 (19-C), 31.6 (2-C), 29.7-28.9 (7-C-18-C), 22.7 (20-C), 18.7 (6-C), 15.4 (3-C), 14.1 (21-C); m/z (ES) 331 (67%, MNa⁺) [Found (MNa⁺) 331.2977. C₂₁H₄₀NaO requires MNa, 331.2977].

Heneicos-4-en-1-ol (33)

Lindlar catalyst (5 wt.% Pd, 18.8 mg, 1.25 mol%) was added to a solution of alkyne **32** (219 mg, 0.709 mmol, 1.0 eq.) and quinoline (27.4 mg, 0.212 mmol, 30 mol%) in MeOH–EtOAc (1 : 2, 6.9 ml), which was purged 3 times with Ar. The resulting mixture was purged 3 times with H₂ and stirred at room temperature under an atmosphere of H₂. After the reaction was completed (monitored by TLC, 1 h), the mixture was filtered through a pad of Celite and concentrated *in vacuo*. The crude product was purified by flash column chromatography (EtOAc– petrol = 15 : 85) to afford alkene **33** as a waxy solid (221 mg, 100%); mp 34–35 °C; v_{max} (film)/cm⁻¹ 3334 (OH), 2916, 2849, 1468, 1059, 720; δ_{H} (400 MHz; CDCl₃) 5.42–5.35 (2 H, m, 4-H and 5-H), 3.65 (2 H, t, *J* 6.6, 1-H × 2), 2.12 (2 H, q, *J* 6.9, 3-H × 2), 2.03 (2 H, q, *J* 6.6, 6-H × 2), 1.64 (2 H, m, 2-H × 2), 1.43– 1.25 (29 H, m, 7-H–20-H and OH), 0.88 (3 H, t, *J* 6.7, 21-H ×

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3); $\delta_{\rm C}(100 \text{ MHz}; \text{CDCl}_3)$ 130.8 (5-C), 128.8 (4-C), 62.7 (1-C), 32.7 (2-C), 31.9 (19-C), 29.7–29.3 (7-C–18-C), 27.2 (6-C), 23.6 (3-C), 22.7 (20-C), 14.1 (21-C); *m/z* (ES) 333 (81%, MNa⁺) [Found (MNa⁺) 333.3135. C₂₁H₄₂NaO requires *M*Na, 333.3134].

Heneicos-4-enal (34)

Dess-Martin periodinane (176 mg, 0.415 mmol, 1.1 eq.) was added in one portion to a solution of alcohol 33 (116 mg, 0.373 mmol, 1.0 eq.) and pyridine (2.6 ml) in CH₂Cl₂ (7.5 ml) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. The mixture was poured onto a mixture of sat. aq. NaHCO₃ (5 ml) and sat. aq. Na₂S₂O₃ (5 ml) and extracted with CH_2Cl_2 (4 × 10 ml). The combined organic fractions were washed with brine and dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography $(Et_2O-petrol = 5:95)$ afforded aldehyde 34 as a colourless oil (109 mg, 95%); v_{max}(film)/cm⁻¹ 2922, 2852, 1729 (C=O), 1466, 721; δ_H(400 MHz; CDCl₃) 9.77 (1 H, s, 1-H), 5.43 (1 H, m, 5-H), 5.33 (1 H, m, 4-H), 2.48 (2 H, t, J 7.2, 2-H × 2), 2.37 (2 H, q, J 7.2, 3-H × 2), 2.04 (2 H, q, J 6.9, 6-H × 2), 1.36–1.25 (28 H, m, 7-H–20-H), 0.88 (3 H, t, J 6.8, 21-H \times 3); $\delta_{\rm C}$ (100 MHz; CDCl₃) 202.2 (1-C), 131.8 (5-C), 127.0 (4-C), 43.8 (2-C), 31.9 (19-C), 29.7-29.3 (7-C-18-C), 27.2 (6-C), 22.7 (20-C), 20.1 (3-C), 14.1 (21-C); m/z (ES) 331 (100%, MNa⁺) [Found (MNa⁺) 331.2975. C21H40NaO requires MNa, 331.2977].

Docos-5-en-1-yne (35)

Dimethyl 2-oxo-1-diazopropylphosphonate 36 (60.8 mg, 0.317 mmol, 1.2 eq.) was added to a solution of aldehyde 34 (81.5 mg, 0.264 mmol, 1.0 eq.) and K₂CO₃ (72.8 mg, 0.528 mmol, 2.0 eq.) in MeOH (5.0 ml). After stirring for 24 h at room temperature, the reaction mixture was diluted with petrol (10 ml) and poured into H₂O (10 ml). The aqueous phase was separated and extracted with petrol (3 \times 5 ml). The combined organic fractions were washed with brine and dried with MgSO4. Concentration of the filtrate in vacuo followed by column chromatography (petrol) afforded enyne 35 as a colourless oil (74.3 mg, 92%); $v_{max}(film)/cm^{-1}$ 3314 (=C–H), 2921, 2852, 1466, 721; $\delta_{\rm H}$ (400 MHz; CDCl₃) 5.49–5.37 (2 H, m, 5-H and 6-H), 2.28 (2 H, m, 4-H × 2), 2.22 (2 H, m, 3-H × 2), 2.04 (2 H, q, J 6.8, 7-H × 2), 1.94 (1 H, t, J 2.4, 1-H), 1.39–1.26 (28 H, m, 8-H–21-H), 0.88 (3 H, t, J 6.7, 22-H \times 3); $\delta_{\rm C}(100$ MHz; CDCl₃) 131.7 (6-C), 127.4 (5-C), 84.2 (2-C), 68.2 (1-C), 31.9 (20-C), 29.7-29.3 (8-C-19-C), 27.3 (7-C), 26.4 (4-C), 22.7 (21-C), 18.9 (3-C), 14.1 (22-C); m/z (EI) 304 (24%, M⁺), 131 (48) and 69 (100) [Found (M⁺) 304.3135. C₂₂H₄₀ requires M, 304.3130].

1-(Tetrahydro-2H-pyran-2'-yloxy)pentacos-8-en-4-yne (37)

n-BuLi (1.6 M in hexanes, 0.79 ml, 1.26 mmol, 1.2 eq.) was added dropwise to a solution of enyne 35 (322 mg, 1.06 mmol, 1.0 eq.) in THF (3 ml) at -15 °C. After stirring for 10 min, HMPA (2.0 ml) was added and the solution stirred for 20 min at -15 °C before dropwise addition of 2-(3-bromopropoxy)tetrahydro-2H-pyran (283 mg, 1.26 mmol, 1.2 eq.) in THF (2.0 ml). The mixture was allowed to warm to room temperature over 1 h and stirred for a further 1 h. After cooling to 0 °C, the reaction was quenched by addition of H₂O (10 ml) and extracted with Et_2O (3 × 10 ml). The combined organic fractions were washed with H₂O, and then dried (MgSO₄). Concentration of the filtrate in vacuo followed by flash column chromatography (EtOAc-petrol = 5:95) afforded THP ether 37 as a colourless oil (389 mg, 82%); v_{max}(film)/cm⁻¹ 2921, 2852, 1466, 1137, 1120, 1034, 721; $\delta_{\rm H}$ (400 MHz; CDCl₃) 5.46–5.36 (2 H, m, 8-H and 9-H), 4.60 (1 H, t, J 3.4, 2'-H), 3.90-3.78 (2 H, m, 1-H_A and 6'-H_A), 3.53–3.45 (2 H, m, 1-H_B and 6'-H_B), 2.26 $(2 \text{ H}, \text{ m}, 3\text{-H} \times 2), 2.23\text{--}2.14 (4 \text{ H}, \text{ m}, 6\text{-H} \times 2 \text{ and } 7\text{-H} \times 2),$

2.03 (2 H, q, *J* 6.7, 10-H × 2), [1.86–1.68 (4 H, m), 1.62–1.49 (4 H, m) (2-H × 2, 3'-H × 2, 4'-H × 2 and 5'-H × 2)], 1.36–1.25 (28 H, m, 11-H–24-H), 0.88 (3 H, t, *J* 6.9, 25-H × 3); $\delta_{\rm C}$ (100 MHz; CDCl₃) 131.2 (9-C), 128.0 (8-C), 98.7 (2'-C), 80.1 (5-C), 79.6 (4-C), 66.1 (1-C), 62.1 (6'-C), 31.9 (23-C), 30.7 (3'-C), 29.7–29.3 (11-C–22-C and 2-C), 27.3 (10-C), 27.0 (7-C), 25.5 (5'-C), 22.7 (24-C), 19.5 (4'-C), 19.2 (6-C), 15.7 (3-C), 14.1 (25-C); *m*/*z* (ES) 469 (45%, MNa⁺) [Found (MNa⁺) 469.4024. C₂₁H₄₀NaO requires *M*Na, 469.4022].

Pentacos-8-en-4-ynoic acid (30)

Jones Reagent (~2 M Cr(vI), 0.9 ml, 1.8 mmol, 5 eq.) was added dropwise to a solution of THP ether **37** (164 mg, 0.367 mmol, 1.0 eq.) in acetone (5.0 ml) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. i-PrOH (3 ml) was then added to the mixture before pouring into H₂O. After extraction with Et₂O (3 × 15 ml) the combined organic fractions were washed twice with H₂O and then dried (Na₂SO₄). Concentration of the filtrate *in vacuo* followed by flash column chromatography (EtOAc–petrol = 1 : 2) afforded carboxylic acid **30** as a white powder (128 mg, 92%); mp 75– 77 °C (lit.,⁷ 73–75 °C); v_{max} (film)/cm⁻¹ 2953, 2914, 2849, 1693 (C=O), 1471, 910, 718; *m*/z (ES) 399 (100%, MNa⁺) [Found (MNa⁺) 399.3237. C₂₅H₄₄NaO₂ requires *M*Na, 399.3239]; ¹H and ¹³C NMR data were consistent with those reported in the literature.⁷

Allyl (3*R*,7*S*,9*R*)-7-acetoxy-9-(*tert*-butyldimethylsilyloxy)-3-hydroxy-3-methyldecanoate (39)

TEMPO (0.4 mg, 2 µmol, 1 mol%), Aliquat[®] 336 (0.014 M in CH₂Cl₂, 0.75 ml, 11 µmol, 6 mol%), potassium bromide (0.28 M in H₂O, 0.10 ml, 28 µmol), sodium hypochlorite (~1.7 M in H₂O, 0.6 ml, 1.0 mmol, 6 eq.) and sat. aq. NaHCO₃ (0.3 ml) were added sequentially to a solution of diol **18** (66.2 mg, 0.18 mmol, 1 eq.) in CH₂Cl₂ (4.0 ml) at 0 °C. After stirring at 0 °C for 30 min, the reaction mixture was poured onto a mixture of CHCl₃ (5 ml) and 1 M aq. HCl (5 ml) and the layers separated. The aqueous layer was extracted with CHCl₃ (3 × 5 ml) and the combined organic fractions washed with brine (2 × 5 ml) and dried (Na₂SO₄). Concentration of the filtrate *in vacuo* afforded (3*R*,7*S*,9*R*)-7-acetoxy-9-(*tert*-butyldimethylsilyloxy)-3-hydroxy-3-methyldecanoic acid **38**, which was used immediately without further purification.

i-Pr,NEt (0.46 ml, 2.7 mmol, 15 eq.) followed by allyl bromide (0.22 ml, 2.6 mmol, 14 eq.) were added to a solution of the above carboxylic acid 38 in CH₂Cl₂. The reaction mixture was stirred at room temperature for 46 h before a mixture of EtOAc (5 ml) and 1 M aq. HCl (5 ml) was added, and the layers separated. The aqueous layer was extracted with EtOAc (3 \times 5 ml) and the combined organic fractions washed successively with sat. aq. NaHCO₃ and brine and dried (Na₂SO₄). Concentration of the filtrate in vacuo afforded allyl ester 39 as an oil (65.9 mg, 87%); $[a]_{D}^{25}$ -1.17 (c 1.37, CHCl₃); $v_{max}(film)/cm^{-1}$ 3523, (OH), 2930, 2857, 1734 (C=O), 1463, 1373, 1243, 1181, 1136, 1019, 991, 835, 774; $\delta_{\rm H}(600~{\rm MHz};{\rm CDCl}_3)$ 5.92 (1 H, m, $CH=CH_2$), 5.33 (1 H, m, $CH=CH_2 \times 1$), 5.26 (1 H, m, $CH=CH_2$) × 1), 4.95 (1 H, m, 7-H), 4.61 (2 H, m, OCH₂CH=CH₂ × 2), 3.81 (1 H, m, 9-H), 3.41 (1 H, br s, OH), 2.52 (1 H, d, J 15.7, 2-H_A), 2.46 (1 H, d, J 15.7, 2-H_B), 2.02 (3 H, s, COCH₃), 1.79 (1 H, ddd, J 13.7, 8.1 and 5.5, 8-H_A), 1.59-1.52 (3 H, m, 8-H_B and 6-H × 2), 1.59 (2 H, m, 4-H × 2), 1.44–1.28 (2 H, m, 5-H × 2), 1.22 (3 H, s, 3-C(CH₃)), 1.14 (3 H, d, J 6.0, 10-H × 3), 0.88 (9 H, s, SiC(CH₃)), 0.04 (6 H, s, Si(CH₃) \times 2); δ_{c} (150 MHz; CDCl₃) 172.6 (1-C), 170.6 (COCH₃), 131.7 (CH=CH₂), 118.8 (CH= CH₂), 71.6 (9-C), 70.8 (3-C), 65.7 (OCH₂CH=CH₂), 65.3 (7-C), 44.9 (2-C), 44.3 (8-C), 41.7 (4-C), 34.9 (6-C), 26.6 (3-C(CH₃)), 25.8 (SiC(CH₃)₃), 23.5 (10-C), 21.2 (COCH₃), 19.5 (5-C), 18.1 $(SiC(CH_3)_3)$, -4.4 $(Si(CH_3) \times 1)$, -4.8 $(Si(CH_3) \times 1)$; m/z (ES) 453 (100%, MNa⁺) [Found (MNa⁺) 453.2639. C₂₂H₄₂NaO₆Si

requires MNa, 453.2649]. Data were consistent with those reported in the literature.⁷

Allyl (3*R*,7*S*,9*R*)-7-acetoxy-9-(pentacos-8-en-4-ynoyloxy)-3-hydroxy-3-methyldecanoate (40)

A solution, prepared by mixing commercial HF·pyridine (0.18 ml), pyridine (0.62 ml) and THF (1.80 ml) was added to TBS ether **39** (19.2 mg, 44.5 μ mol). The reaction mixture was stirred at room temperature for 6 h before a mixture of EtOAc (5 ml) and sat. aq. NH₄Cl (5 ml) was added and the layers separated. The aqueous layer was extracted with EtOAc (3 × 5 ml) and the combined organic fractions washed successively with 1 M aq. HCl, sat. aq. NaHCO₃ and brine and dried (Na₂SO₄). Concentration of the filtrate *in vacuo* afforded the desired alcohol, which was immediately used without further purification.

i-Pr₂NEt (23.0 mg, 0.178 mmol, 4 eq.) in CH₂Cl₂ (0.2 ml), diisopropyl carbodiimide (DIC) (22.5 mg, 0.178 mmol, 4 eq.) in CH₂Cl₂ (0.3 ml) and DMAP (2.7 mg, 22.1 µmol, 0.5 eq.) were sequentially added to a solution of the above alcohol and carboxylic acid 30 (24.4 mg, 64.7 µmol, 1.4 eq.) in CH₂Cl₂ (1.5 ml) at room temperature. The reaction mixture was stirred at room temperature for 46 h, before a mixture of EtOAc (5 ml) and sat. aq. NH₄Cl (5 ml) was added, and the layers separated. The aqueous layer was extracted with EtOAc (3 \times 5 ml) and the combined organic fractions washed successively with 1 M aq. HCl, sat. aq. NaHCO₃ and brine and dried (Na₂SO₄). Concentration in vacuo followed by column chromatography (EtOAcpetrol = 1 : 4) afforded ester 40 as an oil (18.8 mg, 63%); $[a]_{D}^{25}$ -1.68 (c 1.07, CHCl₃); v_{max}(film)/cm⁻¹ 3528, 2922, 2853, 1734, 1458, 1372, 1241, 1176; $\delta_{\rm H}$ (600 MHz; CDCl₃) 5.92 (1 H, m, CH=CH₂), 5.44-5.37 (2 H, m, 8'-H and 9'-H), 5.34 (1 H, m, CH=CHAH_B), 5.26 (1 H, m, CH=CH_AHB), 4.99–4.92 (2 H, m, 7-H and 9-H), 4.62 (2 H, d, J 5.9, OCH₂CH=CH₂ × 2), 3.41 (1 H, br s, OH), 2.52 (1 H, d, J 15.7, 2-H_A), 2.46 (1 H, d, J 15.7, 2-H_B), 2.45–2.40 (4 H, m, 2'-H and 3'-H), 2.20 (2 H, m, 7'-H × 2), 2.15 (2 H, m, 6'-H × 2), 2.04 (3 H, s, COCH₃), 2.02 (2 H, m, 10'-H × 2), 1.95 (1 H, m, 8-H_A), 1.67 (1 H, m, 8-H_B), 1.56 (2 H, m, 6-H × 2), 1.50 (2 H, m, 4-H × 2), 1.45–1.29 (2 H, m, 5-H × 2), 1.25 (28 H, br s, 11'-H-24'-H), 1.24 (3 H, d, J 7.3, 10-H), 1.22 (3 H, s, 3-C(CH₃)), 0.88 (3 H, t, J 7.0, 25'-H \times 3); δ_{C} (150 MHz; CDCl₃) 172.6 (1-C), 171.5 (1'-C), 170.6 (COCH₃), 131.8 (CH=CH₂), 131.2 (9'-C), 127.8 (8'-C), 118.8 (CH=CH₂), 80.7 (5'-C), 78.2 (4'-C), [70.85, 70.77 (3-C and 7-C)], 68.3 (9-C), 65.3 (OCH₂CH=CH₂), 44.9 (2-C), 41.6 (4-C), 40.2 (8-C), 34.6 (6-C), 34.3 (2'-C), 31.9 (23'-C), 29.7–29.3 (11'-C–22'-C), 27.3 (10'-C), 26.9 (7'-C), 26.6 (3-C(CH₃)), 22.7 (24'-C), 21.2 (COCH₃), 20.0 (10-C), 19.4 (5-C), 19.1 (6'-C), 14.8 (3'-C), 14.1 (25'-C); m/z (ES) 697 (61%, MNa⁺) [Found (MNa⁺) 697.5009 C₄₁H₇₀NaO₇ requires MNa, 697.5020]. Data were consistent with those reported in the literature.7

Taurospongin A (1)

Pyrrolidine (20 µl, 239 µmol, 8 eq.) followed by Pd(PPh₃)₄ (2.7 mg, 2.3 µmol, 14 mol%) were added to a solution of allyl ester **40** (21.3 mg, 31.6 µmol, 1 eq.) in CH₂Cl₂ (1.3 ml) at room temperature. The reaction mixture was stirred at room temperature for 40 min before a mixture of CHCl₃ (5 ml) and 1 M aq. HCl (5 ml) was added, and the layers separated. The aqueous layer was extracted with CHCl₃ (3 × 5 ml) and the combined organic fractions washed with brine and dried (Na₂SO₄). Concentration *in vacuo* gave carboxylic acid **41**, which was used immediately without further purification.

N-Hydroxysuccinimide (11.5 mg, 0.10 mmol, 3 eq.) followed by dicyclohexylcarbodiimide (DCC) (20.9 mg, 0.10 mmol, 3 eq.) was added to a solution of the above carboxylic acid **41** in 1,4-dioxane (1.0 ml) at room temperature. The reaction mixture was stirred at room temperature for 2 h, before addition of Et_2O (2 ml). The resulting white suspension was filtered and concentrated to afford the desired *N*-hydroxysuccinic ester, which was used immediately without further purification.

A solution, prepared by mixing taurine (16.4 mg, 0.13 mmol, 4 eq.), Et₃N (0.03 ml, 0.22 mmol, 8 eq.), 1,4-dioxane (0.6 ml) and H_2O (0.5 ml), was added to the above N-hydroxysuccinic ester. The reaction mixture was stirred at room temperature for 24 h. PhMe (2 ml) was added and the reaction mixture concentrated in vacuo to remove H₂O azeotropically (repeated twice). The resulting crude product was purified by column chromatography (Amberlite[®] IR-120 H⁺ form – silica gel column, MeOH- $CH_2Cl_2 = 1 : 4$, repeated three times) to afford taurospongin A (1) as a waxy solid (23.3 mg, 100%); $[a]_D^{25} - 3.5$ (c 0.37, CHCl₃); v_{max}(film)/cm⁻¹ 3315, 2922, 2853, 1734, 1639, 1372, 1240, 1175, 1060; δ_H(600 MHz; CDCl₃) 7.74 (1 H, br s), 5.44-5.35 (2 H, m), 4.95-4.91 (2 H, m), 4.70 (1 H, br s), 3.66 (2 H, br s), 3.13 (2 H, br s), 2.46–2.44 (4 H, m), 2.31 (2 H, br s), 2.22-2.14 (4 H, m), 2.05 (3 H, s), 2.04-1.99 (2 H, m), 1.95-1.91 (1 H, m), 1.68–1.67 (1 H, m), 1.60–1.42 (4 H, m), 1.33–1.23 (33 H, m), 1.18 (3 H, br s), 0.88 (3 H, t, J 7.0); $\delta_{\rm C}$ (150 MHz; CDCl₃) 173.2, 171.6, 171.0, 131.2, 127.8, 80.7, 78.2, 71.8, 71.1, 68.5, 50.0, 46.5, 42.2, 40.4, 35.2, 34.9, 34.3, 31.9-29.3, 27.3, 26.8, 26.1, 22.7, 21.2, 20.0, 19.6, 19.1, 14.8, 14.1; m/z (ES) 786 (100%, [MNa₂ - H]⁺), 764 (66, MNa⁺) [Found (MNa⁺) 764.4739. C₂₂H₄₂NaO₆Si requires *M*Na, 764.4747].

Taurospongin A methyl ester (42)

A solution of CH₂N₂ (~0.5 M in Et₂O, 2 ml) was added to taurospongin A (1) (16 mg, 21.6 µmol). The resulting solution was stirred at room temperature for 45 min. Concentration of the mixture in vacuo followed by column chromatography (acetone-petrol = 3:7) afforded methyl ester 42 (12.0 mg, 75%); $[a]_{D}^{25}$ -1.4 (c 0.49, CHCl₃); $v_{max}(film)/cm^{-1}$ 3379, 2922, 2853, 1733, 1650, 1539, 1458, 1354, 1242, 1162, 1022, 987, 790, 720; $\delta_{\rm H}(600 \text{ MHz}; \text{CDCl}_3) 5.80 (1 \text{ H}, \text{ br t}, J 5.5), 5.58-5.51 (2 \text{ H}, \text{m}),$ 5.22-5.15 (2 H, m), 4.33 (1 H, br s), 3.36-3.27 (2 H, m), 3.22 (3 H, s), 2.80–2.70 (2 H, m), 2.52–2.46 (2 H, m), 2.44–2.36 (2 H, m), 2.29 (2 H, q, J 6.5), 2.22–2.17 (2 H, m), 2.07 (2 H, q, J 6.7), 2.04 (1 H, d, J 14.7), 1.98 (1 H, quintet, J 7.1), 1.89 (1 H, d, J 14.7), 1.79 (3 H, s), 1.59–1.46 (7 H, m), 1.45–1.30 (28 H, m), 1.22 (3 H, d, J 6.2), 1.19 (3 H, s), 0.96 (3 H, t, J 6.8); δ_c(150 MHz; CDCl₃) 172.6, 171.3, 170.2, 131.3, 128.4, 80.9, 79.0, 71.1, 70.8, 68.3, 55.0, 48.5, 46.1, 42.0, 40.9, 35.1, 34.5, 34.0, 32.3, 30.2-29.7, 27.7, 27.3, 27.0, 23.1, 20.8, 20.2, 20.0, 19.6, 15.2, 14.3; m/z (ES) 778 (97%, MNa⁺), 734 (100) [Found (MNa⁺) 778.4908. C₂₂H₄₂NaO₆Si requires MNa, 778.4904]. Data were consistent with those reported in the literature.^{6,7}

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