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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

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Received 11th February 2003, Accepted 7th April 2003
First published as an Advance Article on the web 24th April 2003

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 complexes[1] (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 species[3] 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]

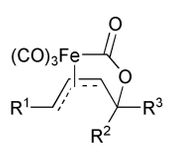


Fig. 1 π-Allyltricarbonyliron lactone complexes.

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 full[8] 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]

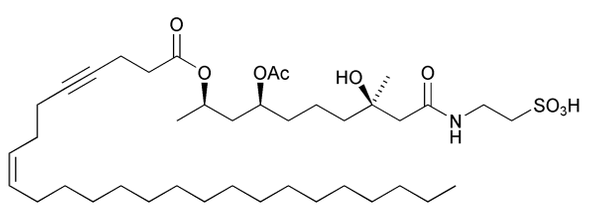


Fig. 2 Taurospongin A.

Results and discussion

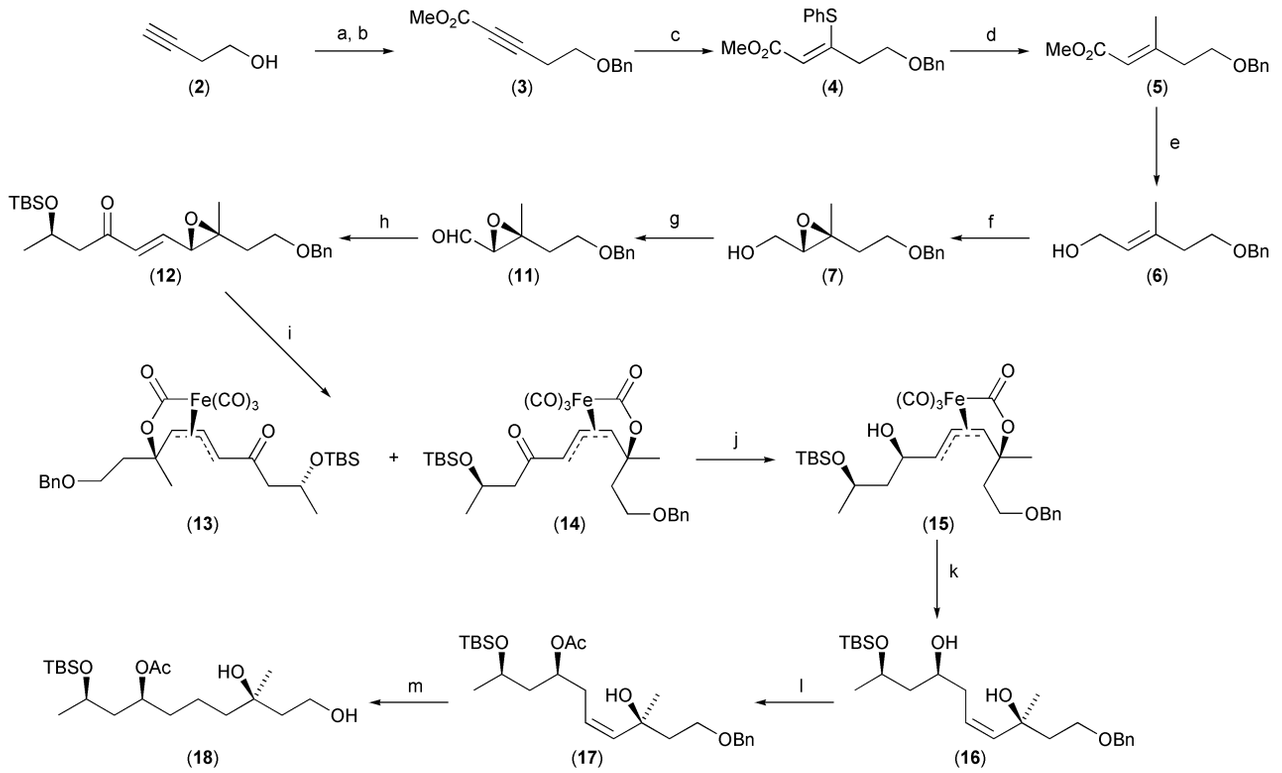
In our first approach, 3-butyn-1-ol (**2**) was converted to ester (**3**) in two steps by first protecting the primary hydroxyl group as a benzyl ether. The resulting benzyl ether was then subjected to lithium diisopropylamide (LDA) followed by methyl chloroformate to yield ester (**3**) in excellent 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.

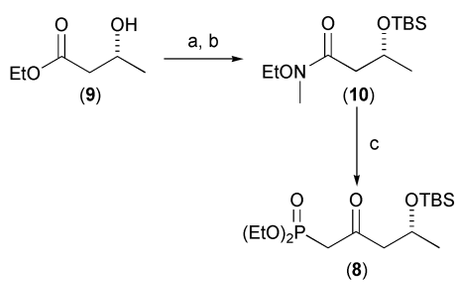
Before continuing with the synthesis we needed to prepare a further coupling partner, namely ketophosphonate (**8**). This was readily achieved by protection of the known β-hydroxyester (**9**)[10] with *tert*-butyldimethylsilyl chloride and conversion to the corresponding Weinreb amide (**10**) using 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]

DOI: 10.1039/b301676p



Scheme 1 *Reagents and conditions*: (a) BnBr, NaH, 0 °C, 98%; (b) LDA, THF, −78 °C then $ClCO_2Me$, −78 °C ⟶ rt, 89%; (c) PhSH, NaOMe, MeOH, rt, 88% of *Z* (*Z* : *E* = 10 : 1); (d) CuI, MeMgBr, THF, −78 °C, 98%; (e) DIBAL-H, PhMe, 0 °C, 91%; (f) $Ti(O\textit{i}\text{-}Pr)_4$, diisopropyl L-tartrate, *t*-BuOOH, 4 Å MS, CH_2Cl_2, −20 °C, 83%; (g) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 86%; (h) **8**, NaH, THF, 0 °C, 82%; (i) $Fe_2(CO)_9$, THF, rt, **13** 36%, **14** 29%; (j) $Al(\textit{i}\text{-}Bu)_3$ (1 M in PhMe), CH_2Cl_2, 0 °C, 72%; (k) $NaBH(OAc)_3$, THF, rt, 73%; (l) Ac_2O, DMAP, Et_3N, CH_2Cl_2, 0 °C, 96%; (m) H_2, $Pd(OH)_2$, 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 ⟶ 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 known[7] polyol fragment (**18**) (Scheme 1).

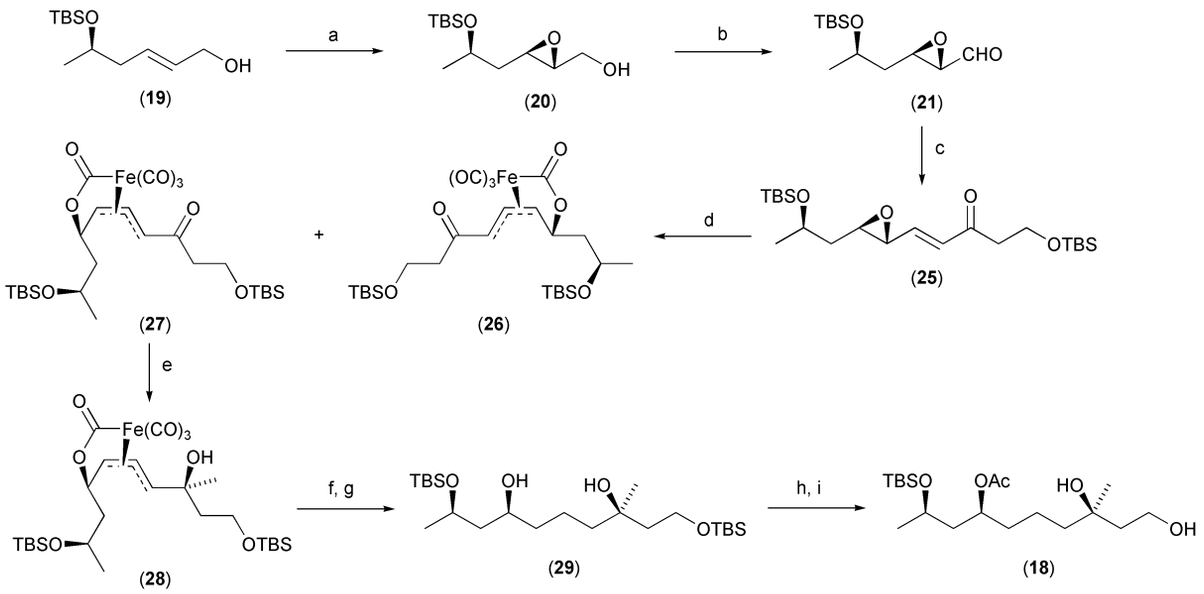
Fragment (**18**) gave the same spectroscopic data and similar optical rotation data to an identical fragment previously synthesised by Jacobsen *en route* to taurospongin A (**1**).[7] Although we had achieved a formal synthesis of taurospongin A (**1**), we were unhappy with the poor selectivity in 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 stereoselective 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).

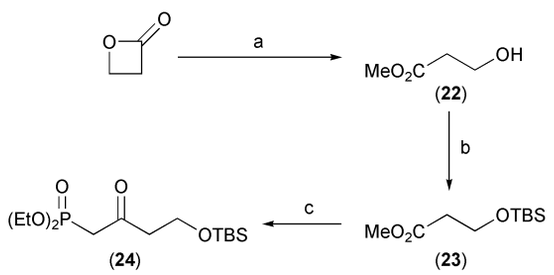
In order to provide a coupling partner for (**21**), β-propiolactone was cleaved with sodium methoxide in methanol at 50 °C and the resulting hydroxy ester (**22**) immediately protected as its *tert*-butyldimethylsilyl derivative (**23**). Both reactions proceeded in quantitative yield. Subsequent reaction 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 *endo*-tricarbonyliron lactone complexes (**26**) and (**27**). Pleasingly, after easy separation by silica gel flash chromatography the major desired *endo* complex (**27**) and the minor undesired *exo*-complex (**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 side-chain.[4h] Reductive decomplexation of (**28**) as before using sodium triacetoxyborohydride, followed by hydrogenation with H_2 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(O*i*-Pr)$_4$, diisopropyl D-tartrate, *t*-BuOOH, 4 Å MS, CH_2Cl_2, −20 °C, 82%; (b) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 88%; (c) **24**, NaH, THF, 0 °C, 76%; (d) $Fe_2(CO)_9$, THF, rt, **26** 14%, **27** 48%; (e) $AlMe_3$, CH_2Cl_2, 0 °C, 81%; (f) $NaBH(OAc)_3$, THF, rt; (g) H_2, Pd/C, EtOAc, rt, 81% for two steps; (h) Ac_2O, DMAP, Et_3N, CH_2Cl_2, 0 °C, 98%; (i) TBAF, AcOH, THF, 0 °C ⟶ rt, 87%.

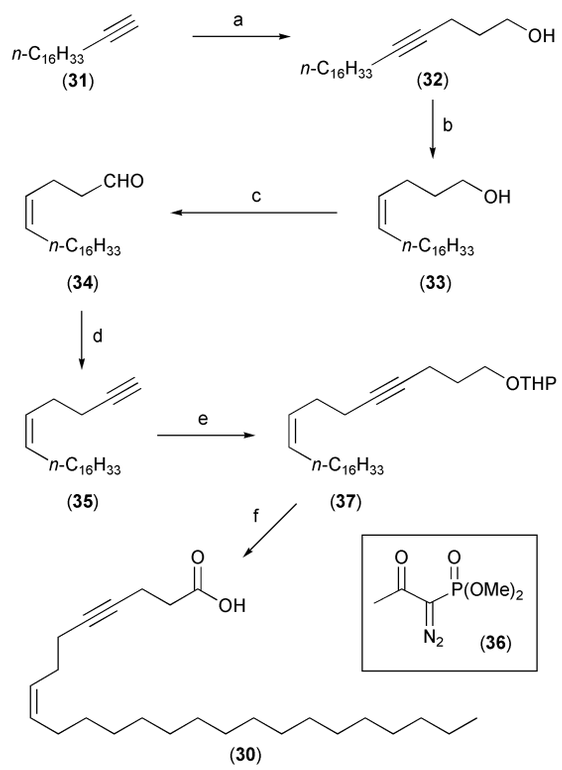


Scheme 4 *Reagents and conditions*: (a) NaOMe, MeOH, 50 °C, 100%; (b) TBDMSCl, imidazole, DMF, 0 °C, 100%; (c) *n*-BuLi, $(EtO)_2$-P(O)Me, THF, −78 °C ⟶ rt, 78%.

Hydrogenation of (**32**) with the Lindlar catalyst (H_2, 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, $NaHCO_3$ 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 ($H_2NCH_2CH_2$-SO_3H) 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]

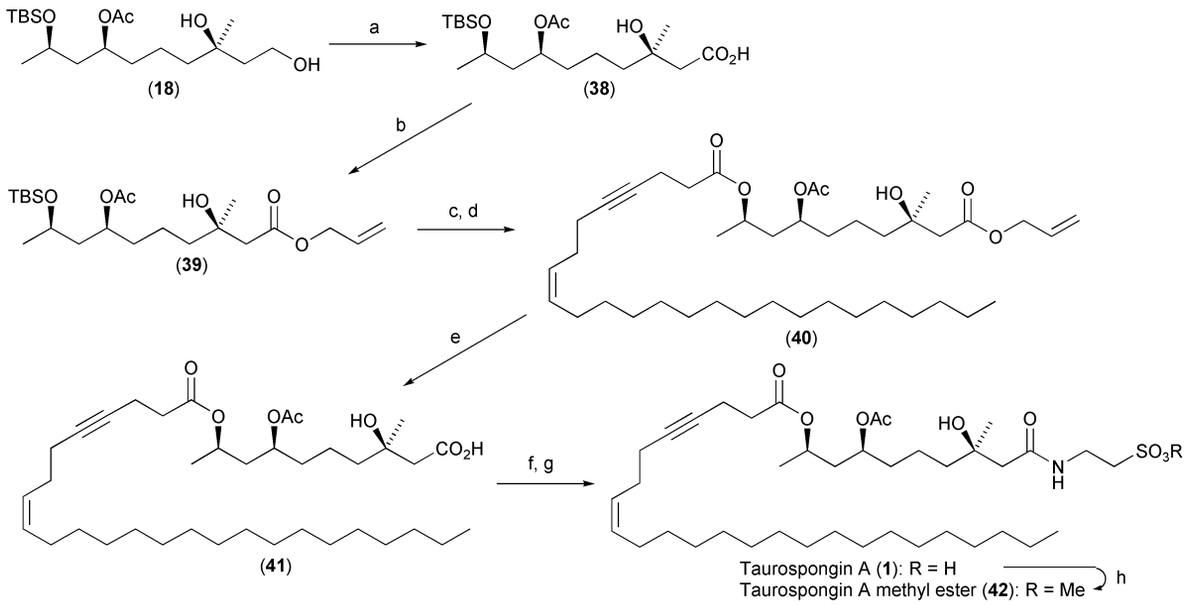


Scheme 5 *Reagents and conditions*: (a) *n*-BuLi, 2-(3-bromopropoxy)-tetrahydro-2*H*-pyran, HMPA, THF, 0 °C⟶rt, then 6 M H_2SO_4, 0 °C, 73%; (b) H_2, Lindlar cat., quinoline, EtOAc, MeOH, rt, 100%; (c) Dess–Martin periodinane, CH_2Cl_2, rt, 95%; (d) **36**, K_2CO_3, MeOH, rt, 92%; (e) *n*-BuLi, 2-(3-bromopropoxy)tetrahydro-2*H*-pyran, HMPA, THF, −15 ⟶ 0 °C, 82%; (f) Jones' reagent, acetone, 0 °C ⟶ 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. $NaHCO_3$, CH_2Cl_2, 0 °C; (b) allyl bromide, i-Pr_2NEt, CH_2Cl_2, rt, 87% for two steps; (c) HF·py, THF, rt; (d) **30**, DIC, i-Pr_2NEt, DMAP, CH_2Cl_2, rt, 63% for two steps; (e) $Pd(PPh_3)_4$, pyrrolidine, CH_2Cl_2, rt; (f) *N*-hydroxysuccinimide, DCC, 1,4-dioxane, rt; (g) taurine, Et_3N, 1,4-dioxane, H_2O, rt, 100% for three steps; (h) CH_2N_2, Et_2O, 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

^{1}H NMR spectra were recorded in $CDCl_3$ or C_6D_6 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 $CHCl_3$ (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 spectrometers, 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. 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 cm^2 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 H_2O (600 ml) and extracted with Et_2O (3 × 200 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). 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 HN*i*-Pr_2 (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 $MeCO_2Cl$ (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 Et_2O (3 × 200 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 10 ⟶ 1 : 3) afforded alkynoate ester **3** as an oil (29.6 g, 89%); ν_{max}(film)/cm^{-1} 2239 (C≡C), 1710 (C=O), 1435 (Ph); δ_H(400 MHz; $CDCl_3$) 7.37–7.26 (5 H, m, $C_6H_5CH_2O$), 4.56 (2 H, s, $C_6H_5CH_2O$), 3.76 (3 H, s, CO_2CH_3), 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; $CDCl_3$) 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 ($PhCH_2$), 67.0 (5-C), 52.6 (CO_2CH_3), 20.2 (4-C); *m*/*z* (ES) 241 (100%, MNa^+); [Found (MNa^+) 241.0842. $C_{13}H_{14}NaO_3$ requires *M*Na, 241.0841].

Methyl (2*Z*)-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 (Et_2O–petrol = 1 : 10 ⟶ 1 : 3) afforded alkenoate ester **4** as a pale yellow oil (34.7 g, 88%); ν_{max}(film)/cm^{-1} 1701 (C=O), 1580 (C=C), 1434 (Ph); δ_H(400 MHz; $CDCl_3$) 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* × 2), 5.94 (1 H, s, 2-H), 4.35 (2 H, s, $C_6H_5CH_2O$), 3.76 (3 H, s, CO_2CH_3), 3.43 (2 H, t, *J* 6.8, 5-H × 2), 2.43 (2 H, t, *J* 6.8, 4-H × 2); δ_C(100 MHz; $CDCl_3$) 166.4 (1-C), 157.9 (3-C), [137.9, 135.8, 130.6, 129.4, 129.2, 128.4, 127.7, 127.6 ($PhCH_2$ × 6 and PhS × 6)], 112.8 (2-C), 72.9 (PhCH_2), 68.4 (5-C), 51.2 (CO_2CH_3), 36.6 (4-C); *m*/*z* (ES) 351 (100%, MNa^+) [Found (MNa^+) 351.1028. $C_{19}H_{20}NaO_3S$ requires *M*Na, 351.1031].

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

MeMgBr (3.0 M in Et_2O, 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. NH_4Cl solution and filtered through a pad of Celite. The filtrate was extracted with Et_2O (2 × 150 ml) and the combined organic fractions washed with brine and dried ($MgSO_4$). 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; ν_{max}(film)/cm^{-1} 1715 (C=O), 1652 (C=C), 1435 (Ph); δ_H(400 MHz; $CDCl_3$) 7.37–7.26 (5 H, m, $C_6H_5CH_2O$), 5.74 (1 H, m, 2-H), 4.52 (2 H, s, $C_6H_5CH_2O$), 3.69 (3 H, s, CO_2CH_3), 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-CCH_3); δ_C(100 MHz; $CDCl_3$) 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 (PhCH_2), 67.8 (5-C), 50.8 (CO_2CH_3), 40.8 (4-C), 18.9 (3-CCH_3); *m*/*z* (ES) 257 (100%, MNa^+) [Found (MNa^+) 257.1150. $C_{14}H_{18}NaO_3$ requires *M*Na, 257.1154].

(2*E*)-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 ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 2 ⟶ 3 : 1) afforded alcohol **6** as an oil (16.9 g, 91%). Data were consistent with those reported in the literature.[15]

(2*S*,3*S*)-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 CH_2Cl_2 (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 CH_2Cl_2 (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. $FeSO_4$ (500 ml) and filtered through a pad of Celite washing with CH_2Cl_2 (150 ml). The filtrate was separated and the aqueous layer was extracted with ether (200 ml). The CH_2Cl_2 and ether fractions were washed with brine, then combined and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 2 ⟶ 10 : 1) afforded epoxide **7** as an oil (17.0 g, 83%, 94% ee); $[\alpha]_D^{30}$ +1.3 (*c* 2.12, CH_2Cl_2); ν_{max}(film)/cm^{-1} 3418 (OH), 1454 (Ph); δ_H(400 MHz; $CDCl_3$) 7.39–7.28 (5 H, m, $C_6H_5CH_2O$), 4.54 (1 H, d, *J* 12.0, $C_6H_5CH_AH_BO$), 4.50 (1 H, d, *J* 12.0, $C_6H_5CH_AH_BO$), 3.84 (1 H, m, 1-H_A), 3.70 (1 H, m, 1-H_B), 3.60 (2 H, m, 5-H × 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-CCH_3); δ_C(100 MHz; $CDCl_3$) 138.6 (Ph *ipso*), 128.8 (Ph *meta* × 2), 128.1 (Ph *ortho* × 2), 128.0 (Ph *para*), 73.5 (PhCH_2), 66.8 (5-C), 63.2 (2-C), 61.7 (1-C), 60.1 (3-C), 38.7 (4-C), 17.6 (3-CCH_3); *m*/*z* (ES) 245 (100%, MNa^+) [Found (MNa^+) 245.1168. $C_{13}H_{18}NaO_3$ requires *M*Na, 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 imidazole (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 Et_2O (3 × 200 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). 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%); $[\alpha]_D^{27}$ −32.0 (*c* 0.70, CH_2Cl_2). 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*-dimethylhydroxylamine 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 Et_2O (2 × 200 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 1 ⟶ 2 : 1) afforded Weinreb amide **10** as an oil (17.4 g, 91%). $[\alpha]_D^{29}$ −23.4 (*c* 3.99, CH_2Cl_2). 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 × 100 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O ⟶ Et_2O–EtOAc [1 : 1]) afforded β-keto-phosphonate **8** as an oil (4.71 g, 72%); $[\alpha]_D^{26}$ −24.9 (*c* 1.06, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1714 (C=O), 1253 (P=O), 1124 (P–O); δ_H(600 MHz; $CDCl_3$) 4.27 (1 H, m, 4-H), 4.05 (4 H, m, OCH_2CH_3 × 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, OCH_2CH_3 × 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, $Si(CH_3)$ × 1), 0.01 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; $CDCl_3$) 201.4 (d, *J* = 39, 2-C), 65.9 (4-C), 62.9 (d, *J* = 38, OCH_2CH_3 × 2), 53.7 (3-C), 44.1 (d, *J* = 757, 1-C), 26.2 ($SiC(CH_3)_3$), 24.3 (5-C), 18.3 ($SiC(CH_3)_3$), 16.7 (d, *J* = 37, OCH_2CH_3 × 2), −4.2 ($Si(CH_3)$ × 1), −4.7 ($Si(CH_3)$ × 1); δ_P(600 MHz; $CDCl_3$) 20.5; *m*/*z* (ES) 375 (100%, MNa^+) [Found (MNa^+) 375.1741. $C_{15}H_{33}NaO_5PSi$ requires *M*Na, 375.1733].

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

A solution of $(COCl)_2$ (1.93 g, 15.2 mmol, 1.25 eq.) in CH_2Cl_2 (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 Et_3N (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 Et_2O (200 ml) and the combined organic fractions washed with brine and dried ($MgSO_4$). 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%); ν_{max}(film)/cm^{-1} 1720 (C=O), 1454 (Ph); δ_H(400 MHz; $CDCl_3$) 9.41 (1 H, d, *J* 4.7, 1-H), 7.30–7.20 (5 H, m, $C_6H_5CH_2O$), 4.45 (1 H, d, *J* 12.0, $C_6H_5CH_AH_BO$), 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-CCH_3); δ_C(100 MHz; $CDCl_3$) 199.2 (1-C), 138.0 (Ph *ipso*), 128.4 (Ph *meta* × 2), 127.7 (Ph *para*), 127.6 (Ph *ortho* × 2), 73.1 (Ph*C*H$_2$), 65.8 (5-C), 63.5 (2-C), 62.7 (3-C), 38.3 (4-C), 17.6 (3-C*C*H$_3$).

(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. NH_4Cl solution and extracted with Et_2O (2 × 100 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 3 ⟶ 1 : 1) afforded alkenone **12** as a pale yellow oil (3.43 g, 82%); $[\alpha]_D^{30}$ −8.0 (*c* 1.25, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1670 (C=O), 1627 (C=C), 1455 (Ph); δ_H(400 MHz; $CDCl_3$) 7.32–7.22 (5 H, m, $C_6H_5CH_2O$), 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, $C_6H_5CH_2O$), 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-CCH_3), 1.14 (3 H, d, *J* 6.1, 1-H × 3), 0.79 (9 H, s, $SiC(CH_3)_3$), 0.00 (3 H, s, $Si(CH_3)$ × 1), −0.04 (3 H, s, $Si(CH_3)$ × 1); δ_C(100 MHz; $CDCl_3$) 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* × 2), 73.5 (Ph*C*H$_2$), 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 ($SiC(CH_3)_3$), 24.6 (1-C), 18.4 ($SiC(CH_3)_3$), 17.5 (8-C*C*H$_3$), −4.2 ($Si(CH_3)$ × 1), −4.5 (Si(CH3) × 1); *m*/*z* (ES) 441 (100%, MNa^+) [Found (MNa^+) 441.2433. $C_{24}H_{38}NaO_4Si$ requires *M*Na, 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 Et_2O (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 $Fe_3(CO)_{12}$ had been removed, then Et_2O–petrol = 1 : 3 ⟶ 1 : 1) afforded, in order of elution, *endo* iron lactone complex **14** as an orange gum (0.90 g, 29%); $[\alpha]_D^{33}$ +191.1 (*c* 0.45, CH_2Cl_2); ν_{max}(film)/cm^{-1} [2086, 2014 (FeCO)], 1669 (C=O), 1455 (Ph); δ_H(600 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, $C_6H_5CH_2O$ 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 × 2), 1.29 (3 H, s, 3-CCH_3), 1.11 (3 H, d, *J* 5.9, 10-H × 3), 1.07 (9 H, s, $SiC(CH_3)_3$), 0.23 (3 H, s, $Si(CH_3)$ × 1), 0.19 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; C_6D_6) [209.6, 205.4, 200.8, 200.3, 197.6 (Fe(CO) × 4 and 7-C)], 138.5 (Ph *ipso*), 128.4 (Ph *meta* × 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 (Ph*C*H$_2$), 66.9 (1-C), 66.0 (6-C), 64.2 (9-C), 52.4 (8-C), 42.8 (2-C), 28.7 (3-C*C*H$_3$), 25.8 ($SiC(CH_3)_3$), 23.7 (10-C), 18.0 ($SiC(CH_3)_3$), −4.8 ($Si(CH_3)$ × 2); *m*/*z* (ES) 609 (70%, MNa^+) and 529 (100) [Found (MNa^+) 609.1580. $C_{28}H_{38}FeNaO_8Si$ requires *M*Na, 609.1583]; *exo* iron lactone complex **13** as an orange gum (1.10 g, 36%); $[\alpha]_D^{33}$ −221.2 (*c* 0.32, CH_2Cl_2); ν_{max}(film)/cm^{-1} [2087, 2014 (FeCO)], 1669 (C=O), 1455 (Ph); δ_H(600 MHz; C_6D_6) 7.33–7.18 (5 H, m, $C_6H_5CH_2O$), 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, $C_6H_5CH_AH_BO$), 4.29 (1 H, d, *J* 12.0, $C_6H_5CH_AH_BO$), 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-CCH_3), 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, $Si(CH_3)$ × 1), 0.15 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; C_6D_6) [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 (Ph*C*H$_2$), 67.1 (6-C), 65.8 (9-C), 65.6 (1-C), 52.2 (8-C), 43.6 (2-C), 26.9 (3-C*C*H$_3$), 25.8 ($SiC(CH_3)_3$), 23.8 (10-C), 17.9 ($SiC(CH_3)_3$), −4.7 ($Si(CH_3)$ × 1), −5.0 ($Si(CH_3)$ × 1); *m*/*z* (ES) 609 (85%, MNa^+) and 443 (100) [Found (MNa^+) 609.1582. $C_{28}H_{38}FeNaO_8Si$ requires *M*Na, 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 CH_2Cl_2 (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. CH_2Cl_2 (20 ml) was added and the layers separated. The aqueous phase was extracted with Et_2O (30 ml) and the combined organic fractions washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 2 ⟶ 1 : 1) afforded alcohol **15** as a gum (480 mg, 72%); $[\alpha]_D^{27}$ +97.7 (*c* 1.13, CH_2Cl_2); ν_{max}(film)/cm^{-1} 3423 (OH), [2078, 1999 (FeCO)], 1450 (Ph); δ_H(600 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, $C_6H_5CH_AH_BO$), 4.37 (1 H, d, *J* 12.5, $C_6H_5CH_AH_BO$), 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-CCH_3), 1.02 (3 H, d, *J* 6.0, 10-H × 3), 0.96 (9 H, s, $SiC(CH_3)_3$), 0.11 (3 H, s, $Si(CH_3)$ × 1), 0.06 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; C_6D_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 (Ph*C*H$_2$), 70.3 (6-C), 67.3 (1-C), 65.9 (9-C), 47.9 (8-C), 42.9 (2-C), 28.7 (3-C*C*H$_3$), 25.6 ($SiC(CH_3)_3$), 24.0 (10-C), 17.7 ($SiC(CH_3)_3$), −4.0 ($Si(CH_3)$ × 1), −5.1 ($Si(CH_3)$ × 1); *m*/*z* (ES) 611 (70%, MNa^+) and 476 (100) [Found (MNa^+) 611.1751. $C_{28}H_{40}FeNaO_8Si$ requires *M*Na, 611.1740].

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

$NaBH(OAc)_3$ (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 Et_2O (60 ml). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 2 ⟶ 1 : 1) afforded a mixture of regioisomeric alkene diols as an oil with diol **16** as the major component (230 mg, 73%); ν_{max}(film)/cm^{-1} 3408 (OH), 1668 (C=C), 1455 (Ph); δ_H(600 MHz; $CDCl_3$) 7.36–7.28 (5 H, m, $C_6H_5CH_2O$), 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, $C_6H_5CH_2O$), 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-CCH_3), 1.17 (3 H, d, *J* 6.0, 10-H × 3), 0.89 (9 H, s, $SiC(CH_3)_3$), 0.10 (3 H, s, $Si(CH_3)$ × 1), 0.09 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; $CDCl_3$) 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 ($PhCH_2$), 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-CCH_3), 25.8 ($SiC(CH_3)_3$), 24.4 (10-C), 17.9 ($SiC(CH_3)_3$), −3.9 ($Si(CH_3)$ × 1), −4.8 ($Si(CH_3)$ × 1); *m*/*z* (ES) 445 (100%, MNa^+) [Found (MNa^+) 445.2758. $C_{24}H_{42}NaO_4Fe$ requires *M*Na, 445.2750].

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

Ac_2O (32 mg, 0.31 mmol, 1.1 eq.) was added to a solution of diol **16** (120 mg, 0.28 mmol, 1.0 eq.), Et_3N (29 mg, 0.37 mmol, 1.3 eq.) and DMAP (4 mg, 0.03 mmol, 0.1 eq.) in CH_2Cl_2 (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 Et_2O (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%); ν_{max}(film)/cm^{-1} 3515 (OH), 1735 (C=O), 1667 (C=C), 1455 (Ph); δ_H(600 MHz; $CDCl_3$) 7.35–7.27 (5 H, m, $C_6H_5CH_2O$), 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, $C_6H_5CH_AH_BO$), 4.49 (1 H, d, *J* 12.0, $C_6H_5CH_AH_BO$), 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, $COCH_3$), 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-CCH_3), 1.14 (3 H, d, *J* 6.0, 10-H × 3), 0.88 (9 H, s, $SiC(CH_3)_3$), 0.04 (6 H, s, $Si(CH_3)$ × 2); δ_C(150 MHz; $CDCl_3$) 170.5 ($COCH_3$), 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 ($PhCH_2$), 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-CCH_3), 25.8 ($SiC(CH_3)_3$), 23.4 (10-C), 21.2 ($COCH_3$), 18.1 ($SiC(CH_3)_3$), −4.5 ($Si(CH_3)$ × 1), −4.8 ($Si(CH_3)$ × 1); *m*/*z* (ES) 487 (100%, MNa^+) [Found (MNa^+) 487.2850. $C_{26}H_{44}NaO_5Si$ requires *M*Na, 487.2856].

(3*R*,7*S*,9*R*)-7-Acetoxy-9-(*tert*-butyldimethylsilyloxy)-3-methyldecane-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 Et_3N (26 mg, 0.26 mmol, 2.0 eq.) in EtOAc (2 ml). The mixture was purged 5 times with H_2 and stirred under an atmosphere of H_2. After 24 h the mixture was filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (EtOAc–petrol = 1 : 1 ⟶ 3 : 1) to afford diol **18** as an oil (44 mg, 88%); $[a]_D^{25}$ −4.3 (*c* 1.43, $CHCl_3$); ν_{max}(film)/cm^{-1} 3359 (OH), 1736 (C=O); δ_H(600 MHz; $CDCl_3$) 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, $COCH_3$), 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-CCH_3), 1.15 (3 H, d, *J* 6.1, 10-C × 3), 0.88 (9 H, s, $SiC(CH_3)_3$), 0.05 (6 H, s, $Si(CH_3)$ × 2); δ_C(150 MHz; $CDCl_3$) 170.7 ($COCH_3$), 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-CCH_3), 25.8 ($SiC(CH_3)_3$), 23.4 (10-C), 21.2 ($COCH_3$), 19.6 (5-C), 18.1 ($SiC(CH_3)_3$), −4.4 ($Si(CH_3)$ × 1), −4.8 (Si(CH3) × 1); *m*/*z* (ES) 399 (100%, MNa^+) [Found (MNa^+) 399.2555. $C_{19}H_{40}NaO_5Si$ requires *M*Na, 399.2543]. Data were consistent with those reported in the literature.[7]

[From alkene diol 29 (Scheme 3)]. Ac_2O (40 mg, 0.39 mmol, 1.1 eq.) was added to a solution of diol **29** (160 mg, 0.36 mmol, 1.0 eq.), Et_3N (43 mg, 0.43 mmol, 1.2 eq.) and DMAP (4 mg, 0.04 mmol, 0.1 eq.) in CH_2Cl_2 (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 Et_2O (50 ml). Concentration of the filtrate *in vacuo* afforded (3*R*,7*S*,9*R*)-7-acetoxy-1,9-di(*tert*-butyldimethylsilyloxy)-3-methyldecan-3-ol as an oil, which was used without further purification (171 mg, 98%); $[a]_D^{25}$ −0.3 (*c* 1.23, CH_2Cl_2); ν_{max}(film)/cm^{-1} 3502 (OH), 1738 (C=O); δ_H(600 MHz; $CDCl_3$) 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, $COCH_3$), 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 × 2 and 8-H_B), 1.48–1.43 (3 H, m, 4-H × 2 and 5-H_A), 1.30 (1 H, m, 5-H_B), 1.17 (3 H, s, 3-CCH_3), 1.15 (3 H, d, *J* 6.1, 10-H × 3), 0.90 (9 H, s, $SiC(CH_3)_3$ × 1), 0.88 (9 H, s, $SiC(CH_3)_3$ × 1), 0.08 (6 H, s, $Si(CH_3)$ × 2), 0.08 (6 H, s, $Si(CH_3)$ × 2); δ_C(150 MHz, $CDCl_3$) 170.6 ($COCH_3$), 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-CCH_3), 25.8 ($SiC(CH_3)_3$ × 1), 25.8 ($SiC(CH_3)_3$ × 1), 23.5 (10-C), 21.2 ($COCH_3$), 19.6 (5-C), 18.1 ($SiC(CH_3)_3$ × 1), 18.0 ($SiC(CH_3)_3$ × 1), −4.5 ($Si(CH_3)$ × 1), −4.8 ($Si(CH_3)$ × 1), −5.6 ($Si(CH_3)$ × 1), −5.7 ($Si(CH_3)$ × 1); *m*/*z* (ES) 513 (100%, MNa^+) [Found (MNa^+) 513.3416. $C_{25}H_{54}NaO_5Si_2$ requires *M*Na, 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 Et_2O (3 × 5 ml) and the combined organic fractions washed with sat. aq. $NaHCO_3$ and brine and dried ($MgSO_4$). Concentration *in vacuo* followed by flash column chromatography (EtOAc–petrol = 1 : 1 ⟶ 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 $Ti(O\textit{i}\text{-}Pr)_4$ (1.72 g, 6.1 mmol, 0.10 eq.) in CH_2Cl_2(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 CH_2Cl_2 (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. $FeSO_4$ (500 ml), then filtered through a pad of Celite and the residue was washed with CH_2Cl_2 (150 ml). The filtrate was separated and the aqueous layer was extracted with ether (200 ml). The CH_2Cl_2 and ether fractions were separately washed with brine,

then combined and dried ($MgSO_4$). Concentration *in vacuo* followed by flash column chromatography (Et_2O–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); ν_{max}(film)/cm^{-1} 3401 (OH); δ_H(400 MHz; $CDCl_3$) 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 × 3), 0.83 (9 H, s, $SiC(CH_3)_3$), 0.01 (3 H, s, $Si(CH_3)$ × 1), 0.00 (3 H, s, $Si(CH_3)$ × 1); δ_C(100 MHz; $CDCl_3$) 66.4 (5-C), 61.67 (1-C), 58.1 (2-C), 53.2 (3-C), 41.5 (4-C), 25.8 ($SiC(CH_3)_3$), 23.6 (6-C), 18.0 ($SiC(CH_3)_3$), −4.5 ($Si(CH_3)$ × 1), −4.9 (Si(CH3) × 1); *m*/*z* (ES) 269 (100%, MNa^+) [Found (MNa^+) 269.1541. $C_{12}H_{26}NaO_3Si_2$ requires *M*Na, 269.1549].

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

A solution of $(COCl)_2$ (7.8 g, 61 mmol, 1.2 eq.) in CH_2Cl_2 (10 ml) was added to a solution of DMSO (9.6 g, 0.12 mol, 2.4 eq.) in CH_2Cl_2 (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 Et_3N (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 Et_2O (200 ml) and the combined organic fractions washed with brine and dried ($MgSO_4$). 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%); ν_{max}(film)/cm^{-1} 1731 (C=O); δ_H(400 MHz; $CDCl_3$) 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 H, s, $SiC(CH_3)_3$), 0.00 (3 H, s, $Si(CH_3)$ × 1), −0.03 (3 H, s, $Si(CH_3)$ × 1); δ_C(100 MHz; $CDCl_3$) 198.3 (1-C), 66.3 (5-C), 58.6 (2-C), 54.2 (3-C), 40.9 (4-C), 25.8 ($SiC(CH_3)_3$), 23.6 (6-C), 18.0 ($SiC(CH_3)_3$), −4.5 ($Si(CH_3)$ × 1), −4.9 ($Si(CH_3)$ × 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 Et_2O (200 ml). Concentration of the filtrate *in vacuo* afforded ester **22** as an oil (17.3 g, 100%); ν_{max}(film)/cm^{-1} 3387 (OH), 1718 (C=O); δ_H(400 MHz; $CDCl_3$) 3.88 (2 H, t, *J* 5.6, 3-H × 2), 3.72 (3 H, s, OCH_3), 2.59 (2 H, t, *J* 5.6, 2-H × 2), 2.36 (1 H, s, OH); δ_C(100 MHz; $CDCl_3$) 173.3 (1-C), 58.2 (3-C), 51.7 (OCH_3), 36.6 (2-C); *m*/*z* (ES) 127 (100%, MNa^+) [Found (MNa^+) 127.0375. $C_4H_9NaO_3$ requires *M*Na, 127.0371].

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

A solution of TBSCl (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 Et_2O (3 × 200 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). 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%); ν_{max}(film)/cm^{-1} 1727 (C=O); δ_H(400 MHz; $CDCl_3$) 3.84 (2 H, t, *J* 6.4, 3-H × 2), 3.63 (3 H, s, OCH_3), 2.48 (2 H, t, *J* 6.4, 2-H × 2), 0.82 (9 H, s, $SiC(CH_3)_3$), 0.00 (6 H, s, $Si(CH_3)$ × 2); δ_C(100 MHz; $CDCl_3$) 172.2 (1-C), 59.1 (3-C), 51.5 (OCH_3), 37.9 (2-C), 25.8 ($SiC(CH_3)_3$), 18.2 ($SiC(CH_3)_3$), −5.5 ($Si(CH_3)$ × 2); *m*/*z* (ES) 241 (100%, MNa^+) [Found (MNa^+) 241.1241. $C_{10}H_{22}NaO_3Si_2$ requires *M*Na, 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 ($MgSO_4$). Concentration *in vacuo* followed by flash column chromatography (Et_2O ⟶ Et_2O–EtOAc = 1 : 1) afforded β-ketophosphonate **24** as an oil (42 g, 78%); ν_{max}(film)/cm^{-1} 1715 (C=O), 1252 (P=O), 1014 (P–O); δ_H(600 MHz; $CDCl_3$) 4.15 (4 H, m, OCH_2CH_3 × 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, OCH_2CH_3 × 2), 0.87 (9 H, s, $SiC(CH_3)_3$), 0.05 (6 H, s, $Si(CH_3)$ × 2); δ_C(100 MHz; $CDCl_3$) 201.5 (d, *J* 25, 2-C), 62.9 (d, *J* 26, OCH_2CH_3), 59.0 (4-C), 47.2 (3-C), 43.5 (d, *J* 506, 1-C), 26.2 ($SiC(CH_3)_3$), 18.6 ($SiC(CH_3)_3$), 16.6 (d, *J* 25, OCH_2CH_3), −5.1 ($Si(CH_3)$ × 2); δ_P(600 MHz; $CDCl_3$) 20.5; *m*/*z* (EI) 338 (15%, M^+), 75 (100) [Found (M^+) 338.1686. $C_{14}H_{31}O_5PSi$ requires *M*, 338.1678].

(4*E*,6*R*,7*R*,9*R*)-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. NH_4Cl and extracted with Et_2O (2 × 100 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 5 ⟶ 1 : 2) afforded enone **25** as a pale yellow oil (2.40 g, 76%); $[a]_D^{25}$ +5.1 (*c* 0.93, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1675 (C=O), 1631 (C=C); δ_H(600 MHz; $CDCl_3$) 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 × 3), 0.88 (9 H, s, $SiC(CH_3)_3$), 0.87 (9 H, s, $SiC(CH_3)_3$), 0.10 (6 H, s, $Si(CH_3)$ × 2), 0.04 (6 H, s, $Si(CH_3)$ × 2); δ_C(150 MHz; $CDCl_3$) 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 ($SiC(CH_3)_3$ × 1), 25.6 ($SiC(CH_3)_3$ × 1), 18.0 (10-C), 18.0 ($SiC(CH_3)_3$ × 1), 17.9 ($SiC(CH_3)_3$ × 1), −3.6 ($Si(CH_3)$ × 2), −5.5 (Si(CH3) × 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].

[(6*E*,2*R*,4*R*,5*R*)-4-(Carbonyloxy-κC)-2,10-di(*tert*-butyldimethylsilyloxy)-8-oxo-(5,6,7-η)-dec-6-en-5-yl]tricarbonyliron (26) and [(6*E*,2*R*,4*R*,5*S*)-4-(carbonyloxy-κC)-2,10-di(*tert*-butyldimethylsilyloxy)-8-oxo-(5,6,7-η)-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 Et_2O (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 $Fe_3(CO)_{12}$ had been removed, then Et_2O–petrol = 1 : 3 ⟶ 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, CH_2Cl_2); ν_{max}(film)/cm^{-1}

[2090, 2022 (FeCO)], 1674 (C=O); δ_H(600 MHz; C_6D_6) 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 × 3), 1.06 (18 H, s, $SiC(CH_3)_3$ × 2), 0.17 (3 H, s, $Si(CH_3)$ × 1), 0.16 (3 H, s, $Si(CH_3)$ × 1), 0.15 (3 H, s, $Si(CH_3)$ × 1), 0.13 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; C_6D_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 ($SiC(CH_3)_3$ × 1), 25.8 ($SiC(CH_3)_3$ × 1), 22.9 (1-C), 18.3 ($SiC(CH_3)_3$ × 1), 17.9 ($SiC(CH_3)_3$ × 1), −4.5 ($Si(CH_3)$ × 1), −4.9 ($Si(CH_3)$ × 1), −5.6 ($Si(CH_3)$ × 2); *m*/*z* (ES) 619 (80%, MNa^+), 453 (100) [Found (MNa^+) 619.1816. $C_{26}H_{44}FeNaO_8Si_2$ requires *M*Na, 619.1822] and *exo* iron lactone **26** as a yellow solid (0.53 g, 14%); $[\alpha]_D^{25}$ +85.7 (*c* 0.37, CH_2Cl_2); ν_{max}(film)/cm^{-1} [2088, 2019 (FeCO)], 1670 (C=O); δ_H(600 MHz; C_6D_6) 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, $SiC(CH_3)_3$ × 1), 1.05 (9 H, s, $SiC(CH_3)_3$ × 1), 0.17 (3 H, s, $Si(CH_3)$ × 1), 0.16 (3 H, s, $Si(CH_3)$ × 1), 0.15 (3 H, s, $Si(CH_3)$ × 1), 0.14 (3 H, s, $Si(CH_3)$ × 1); δ_C(150 MHz; C_6D_6) 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. $C_{26}H_{44}FeNaO_8Si_2$ requires *M*Na, 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)

$AlMe_3$ (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 CH_2Cl_2 (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. CH_2Cl_2 (20 ml) was added and the layers separated. The aqueous layer was extracted with Et_2O (30 ml) and the combined organic fractions were washed with brine and dried ($MgSO_4$). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 3 ⟶ 1 : 1) afforded alcohol **28** as a solid (682 mg, 81%); $[\alpha]_D^{25}$ −103.6 (*c* 0.75, CH_2Cl_2); ν_{max}(film)/cm^{-1} 3449 (OH), [2082, 2003 (FeCO)], 1672 (C=O); δ_H(600 MHz; C_6D_6) 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-CCH_3), 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, $SiC(CH_3)_3$ × 1), 0.94 (9 H, s, $SiC(CH_3)_3$ × 1), 0.18 (3 H, s, $Si(CH_3)$ × 1), 0.15 (3 H, s, $Si(CH_3)$ × 1), 0.04 (6 H, s, $Si(CH_3)$ × 2); δ_C(150 MHz; C_6D_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-CCH_3), 25.8 ($SiC(CH_3)_3$ × 1), 25.5 ($SiC(CH_3)_3$ × 1), 22.8 (1-C), 18.0 ($SiC(CH_3)_3$ × 1), 17.8 ($SiC(CH_3)_3$ × 1), −4.5 ($Si(CH_3)$ × 1), −4.8 ($Si(CH_3)$ × 1), −6.0 ($Si(CH_3)$ × 1), −6.0 ($Si(CH_3)$ × 1); *m*/*z* (ES) 635 (25%, MNa^+), 551 (100) [Found (MNa^+) 635.2120. $C_{27}H_{48}FeNaO_8Si_2$ requires *M*Na, 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 Et_2O (60 ml). Concentration of the filtrate *in vacuo* followed by flash column chromatography (Et_2O–petrol = 1 : 1 ⟶ 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 H_2. 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%); $[\alpha]_D^{25}$ −14.9 (*c* 0.61, CH_2Cl_2); ν_{max}(film)/cm^{-1} 3435 (OH); δ_H(600 MHz; $CDCl_3$) 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-CCH_3), 1.18 (3 H, d, *J* 6.1, 10-H × 3), 0.90 (18 H, s, $SiC(CH_3)_3$ × 2), 0.12 (3 H, s, $Si(CH_3)$ × 1), 0.10 (3 H, s, $Si(CH_3)$ × 1), 0.08 (6 H, s, $Si(CH_3)$ × 2); δ_C(150 MHz, $CDCl_3$) 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-CCH_3), 25.8 ($SiC(CH_3)_3$ × 2), 24.6 (10-C), 19.8 (5-C), 18.1 ($SiC(CH_3)_3$ × 1), 17.9 ($SiC(CH_3)_3$ × 1), −3.9 ($Si(CH_3)$ × 1), −4.8 ($Si(CH_3)$ × 1), −5.6 ($Si(CH_3)$ × 1), −5.7 ($Si(CH_3)$ × 1); *m*/*z* (ES) 471 (100%, MNa^+) [Found (MNa^+) 471.3325. $C_{23}H_{52}NaO_4Si_2$ 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-2*H*-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. H_2SO_4 (5 ml) was added. After 2 h of stirring at 0 °C, the reaction mixture was poured onto H_2O (20 ml) and extracted with Et_2O (3 × 15 ml). The combined organic fractions were washed successively with sat. aq. $NaHCO_3$ and brine, and dried (Na_2SO_4). 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; ν_{max}(film)/cm^{-1} 3552 (OH), 2955, 2917, 2848, 1459, 1065, 1053, 725; δ_H(400 MHz; $CDCl_3$) 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 × 3); δ_C(100 MHz; $CDCl_3$) 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. $C_{21}H_{40}NaO$ requires *M*Na, 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 H_2 and stirred at room temperature under an atmosphere of H_2. 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; ν_{max}(film)/cm^{-1} 3334 (OH), 2916, 2849, 1468, 1059, 720; δ_H(400 MHz; $CDCl_3$) 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 ×

3); δ_C(100 MHz; $CDCl_3$) 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. $C_{21}H_{42}NaO$ 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 CH_2Cl_2 (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. $NaHCO_3$ (5 ml) and sat. aq. $Na_2S_2O_3$ (5 ml) and extracted with CH_2Cl_2 (4 × 10 ml). The combined organic fractions were washed with brine and dried ($MgSO_4$). 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%); ν_{max}(film)/cm^{-1} 2922, 2852, 1729 (C=O), 1466, 721; δ_H(400 MHz; $CDCl_3$) 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 × 3); δ_C(100 MHz; $CDCl_3$) 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. $C_{21}H_{40}NaO$ requires *M*Na, 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 K_2CO_3 (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 H_2O (10 ml). The aqueous phase was separated and extracted with petrol (3 × 5 ml). The combined organic fractions were washed with brine and dried with $MgSO_4$. Concentration of the filtrate *in vacuo* followed by column chromatography (petrol) afforded enyne **35** as a colourless oil (74.3 mg, 92%); ν_{max}(film)/cm^{-1} 3314 (≡C–H), 2921, 2852, 1466, 721; δ_H(400 MHz; $CDCl_3$) 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 × 3); δ_C(100 MHz; $CDCl_3$) 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. $C_{22}H_{40}$ requires *M*, 304.3130].

1-(Tetrahydro-2*H*-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-2*H*-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 H_2O (10 ml) and extracted with Et_2O (3 × 10 ml). The combined organic fractions were washed with H_2O, and then dried ($MgSO_4$). 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%); ν_{max}(film)/cm^{-1} 2921, 2852, 1466, 1137, 1120, 1034, 721; δ_H(400 MHz; $CDCl_3$) 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 H, m, 3-H × 2), 2.23–2.14 (4 H, m, 6-H × 2 and 7-H × 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); δ_C(100 MHz; $CDCl_3$) 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. $C_{21}H_{40}NaO$ 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 H_2O. After extraction with Et_2O (3 × 15 ml) the combined organic fractions were washed twice with H_2O and then dried (Na_2SO_4). 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); ν_{max}(film)/cm^{-1} 2953, 2914, 2849, 1693 (C=O), 1471, 910, 718; *m*/*z* (ES) 399 (100%, MNa^+) [Found (MNa^+) 399.3237. $C_{25}H_{44}NaO_2$ requires *M*Na, 399.3239]; ^1H and ^{13}C 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 CH_2Cl_2, 0.75 ml, 11 μmol, 6 mol%), potassium bromide (0.28 M in H_2O, 0.10 ml, 28 μmol), sodium hypochlorite (~1.7 M in H_2O, 0.6 ml, 1.0 mmol, 6 eq.) and sat. aq. $NaHCO_3$ (0.3 ml) were added sequentially to a solution of diol **18** (66.2 mg, 0.18 mmol, 1 eq.) in CH_2Cl_2 (4.0 ml) at 0 °C. After stirring at 0 °C for 30 min, the reaction mixture was poured onto a mixture of $CHCl_3$ (5 ml) and 1 M aq. HCl (5 ml) and the layers separated. The aqueous layer was extracted with $CHCl_3$ (3 × 5 ml) and the combined organic fractions washed with brine (2 × 5 ml) and dried (Na_2SO_4). 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_2NEt (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 CH_2Cl_2. 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 × 5 ml) and the combined organic fractions washed successively with sat. aq. $NaHCO_3$ and brine and dried (Na_2SO_4). Concentration of the filtrate *in vacuo* afforded allyl ester **39** as an oil (65.9 mg, 87%); $[\alpha]_D^{25}$ −1.17 (c 1.37, $CHCl_3$); ν_{max}(film)/cm^{-1} 3523, (OH), 2930, 2857, 1734 (C=O), 1463, 1373, 1243, 1181, 1136, 1019, 991, 835, 774; δ_H(600 MHz; $CDCl_3$) 5.92 (1 H, m, C*H*=CH_2), 5.33 (1 H, m, CH=CH_2 × 1), 5.26 (1 H, m, CH=CH_2 × 1), 4.95 (1 H, m, 7-H), 4.61 (2 H, m, OCH_2CH=CH_2 × 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, $COCH_3$), 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(CH_3)), 1.14 (3 H, d, *J* 6.0, 10-H × 3), 0.88 (9 H, s, SiC(CH_3)), 0.04 (6 H, s, Si(CH_3) × 2); δ_C(150 MHz; $CDCl_3$) 172.6 (1-C), 170.6 (*C*OCH_3), 131.7 (*C*H=CH_2), 118.8 (CH=*C*H_2), 71.6 (9-C), 70.8 (3-C), 65.7 (O*C*H_2CH=CH_2), 65.3 (7-C), 44.9 (2-C), 44.3 (8-C), 41.7 (4-C), 34.9 (6-C), 26.6 (3-C(*C*H_3)), 25.8 (SiC(*C*H_3)$_3$), 23.5 (10-C), 21.2 (CO*C*H_3), 19.5 (5-C), 18.1 (Si*C*(CH_3)$_3$), −4.4 (Si(CH_3) × 1), −4.8 (Si(CH_3) × 1); *m*/*z* (ES) 453 (100%, MNa^+) [Found (MNa^+) 453.2639. $C_{22}H_{42}NaO_6Si$

requires *M*Na, 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 μmol). The reaction mixture was stirred at room temperature for 6 h before a mixture of EtOAc (5 ml) and sat. aq. NH_4Cl (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. $NaHCO_3$ and brine and dried (Na_2SO_4). Concentration of the filtrate *in vacuo* afforded the desired alcohol, which was immediately used without further purification.

i-Pr_2NEt (23.0 mg, 0.178 mmol, 4 eq.) in CH_2Cl_2 (0.2 ml), diisopropyl carbodiimide (DIC) (22.5 mg, 0.178 mmol, 4 eq.) in CH_2Cl_2 (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 CH_2Cl_2 (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. NH_4Cl (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. $NaHCO_3$ and brine and dried (Na_2SO_4). Concentration *in vacuo* followed by column chromatography (EtOAc–petrol = 1 : 4) afforded ester **40** as an oil (18.8 mg, 63%); $[\alpha]_D^{25}$ −1.68 (*c* 1.07, $CHCl_3$); ν_{max}(film)/cm^{-1} 3528, 2922, 2853, 1734, 1458, 1372, 1241, 1176; δ_H(600 MHz; $CDCl_3$) 5.92 (1 H, m, C*H*=CH_2), 5.44–5.37 (2 H, m, 8′-H and 9′-H), 5.34 (1 H, m, CH=C*HA*H_B), 5.26 (1 H, m, CH=CH_A*HB*), 4.99–4.92 (2 H, m, 7-H and 9-H), 4.62 (2 H, d, *J* 5.9, OCH_2CH=CH_2 × 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, $COCH_3$), 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(CH_3)), 0.88 (3 H, t, *J* 7.0, 25′-H × 3); δ_C(150 MHz; $CDCl_3$) 172.6 (1-C), 171.5 (1′-C), 170.6 (*C*OCH_3), 131.8 (*C*H=CH_2), 131.2 (9′-C), 127.8 (8′-C), 118.8 (CH=*C*H_2), 80.7 (5′-C), 78.2 (4′-C), [70.85, 70.77 (3-C and 7-C)], 68.3 (9-C), 65.3 (O*C*H_2CH=CH_2), 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(*C*H_3)), 22.7 (24′-C), 21.2 (CO*C*H_3), 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 $C_{41}H_{70}NaO_7$ requires *M*Na, 697.5020]. Data were consistent with those reported in the literature.[7]

Taurospongin A (1)

Pyrrolidine (20 μl, 239 μmol, 8 eq.) followed by $Pd(PPh_3)_4$ (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 CH_2Cl_2 (1.3 ml) at room temperature. The reaction mixture was stirred at room temperature for 40 min before a mixture of $CHCl_3$ (5 ml) and 1 M aq. HCl (5 ml) was added, and the layers separated. The aqueous layer was extracted with $CHCl_3$ (3 × 5 ml) and the combined organic fractions washed with brine and dried (Na_2SO_4). 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.), Et_3N (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 H_2O 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%); $[\alpha]_D^{25}$ −3.5 (*c* 0.37, $CHCl_3$); ν_{max}(film)/cm^{-1} 3315, 2922, 2853, 1734, 1639, 1372, 1240, 1175, 1060; δ_H(600 MHz; $CDCl_3$) 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); δ_C(150 MHz; $CDCl_3$) 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%, $[MNa_2 - H]^+$), 764 (66, MNa^+) [Found (MNa^+) 764.4739. $C_{22}H_{42}NaO_6Si$ requires *M*Na, 764.4747].

Taurospongin A methyl ester (42)

A solution of CH_2N_2 (~0.5 M in Et_2O, 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%); $[\alpha]_D^{25}$ −1.4 (*c* 0.49, $CHCl_3$); ν_{max}(film)/cm^{-1} 3379, 2922, 2853, 1733, 1650, 1539, 1458, 1354, 1242, 1162, 1022, 987, 790, 720; δ_H(600 MHz; $CDCl_3$) 5.80 (1 H, br t, *J* 5.5), 5.58–5.51 (2 H, 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; $CDCl_3$) 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. $C_{22}H_{42}NaO_6Si$ requires *M*Na, 778.4904]. Data were consistent with those reported in the literature.[6,7]

Acknowledgements

We gratefully acknowledge the financial support from EPSRC, Bristol-Myers Squibb and the Isaac Newton Trust (to CJH), the BP endowment and the Novartis Research Fellowship (to SVL), Uehara Memorial Foundation for a Postdoctoral Fellowship (to SY).

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