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Synthetic studies towards the phomactins. Concise syntheses of the tricyclic furanochroman and the oxygenated bicyclo[9.3.1]pentadecane ring systems in phomactin A

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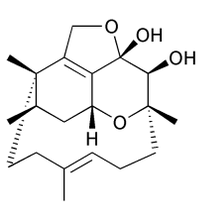
A concise synthesis of the tricyclic furanochroman unit **3** found in the PAF antagonist phomactin A (**1**) isolated from the marine fungus *Phoma* sp., is described. In complementary studies, a variety of synthetic routes towards the bicyclo[9.3.1]pentadecane ring system **4** in phomactin A were explored. These studies culminated in a synthesis of the substituted ring system **79** containing all the carbon atoms and all the necessary oxygen centres for elaboration to phomactin A itself.

Introduction

The phomactins are a novel class of oxygenated diterpenes isolated from the marine fungus *Phoma* sp.,[1] which show pronounced platelet activating factor (PAF) antagonistic activity. PAF is an ether phospholipid that mediates a range of cellular functions, including platelet aggregation, and has been implicated as a causative agent for asthma and other inflammatory diseases.[2] The structures of thirteen members of the phomactins have been determined and, although phomactin D (**2**) is the most biologically active[1d,3] phomactin A (**1**), with its unusual reduced furanochroman ring system **3** embedded in a macrocyclic bicyclo[9.3.1]pentadecane core **4**, is easily the most structurally complex and synthetically demanding of this family of PAF antagonists. Since its isolation in 1991, a plethora of strategies towards the synthesis of both the furanochroman **3**[4,5] and the bicyclopentadecane unit **4**,[6,7] in phomactin A have been reported.[8] However, it was not until recently that our research group,[9] and later Mohr and Halcomb,[10] succeeded in synthesising this intriguing target. In this paper we summarise our synthetic approaches towards the tricyclic furanochroman unit **3** and to the oxy-substituted bicyclo[9.3.1]pentadecatriene core **4** in phomactin A. In the accompanying paper[11] we describe how these model studies were brought together, culminating in the first total synthesis of phomactin A.



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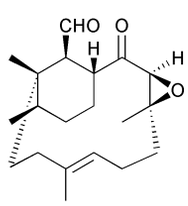

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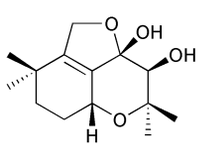

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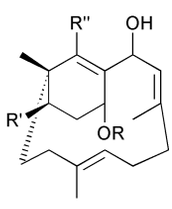

4

As a family the phomactins, with their bicyclo[9.3.1]pentadecane ring system, are related biogenetically to the more familiar taxane group of diterpenoid natural products, *e.g.* taxol **5**.[12] Thus, the unique 6,8,6-taxadiene ring system **6** in the taxanes can be represented as originating from geranylgeranyl pyrophosphate **8** *via* successive electrophilic transannulation reactions, *i.e.* **9** ⟶ **10**; **7** ⟶ **6** from the first-formed 14-membered ("cembranoid") carbocation intermediate **9** (Scheme 1).[13] However, a 1,2-H shift, followed by a 1,2-Me group shift from the intermediate carbocation **10**[14] would lead to **12** and then, by proton loss, to the phomactatriene **11**, a logical precursor of the naturally occurring oxygenated phomactins. Interestingly, until the isolation of the phomactins, only cleomeolide **13** found in the herb *Cleome viscose*, containing the bicyclo[9.3.1]pentadecane core **11**, had been isolated from nature.[15,16]

It seems likely that phomactin A (**1**) originates in the fungus *Phoma* sp. *via* sequential enzymatic oxidation and cyclisation of a hydrocarbon precursor similar to the phomactatriene **11**. Indeed, some of its congeners, particularly phomactin C (**14**), phomactin G (**15**) and the metabolite Sch 49028 (**16**), may represent key intermediates in the biosynthetic pathway. It was our contention that the successful synthesis of intermediates akin to **16** and **17**, in particular, would lead us ultimately to phomactin A itself. To achieve this objective we required: i, a reliable synthetic approach to the oxy-substituted bicyclo-[9.3.1]pentadecatriene core **17** (*cf.* **4**), and ii, confidence that once this objective had been realised we could elaborate the unusual furanochroman system, *viz.* **3**, from it. Accordingly we first examined synthetic routes to the model tricyclic reduced furanochroman **3**, and then studied a range of macrocyclisation strategies to the bicyclopentadecatriene units **4** and **17**. These studies will now be summarised.

Results and discussion

The tricyclic reduced furanochroman core 3

A concise route to the tricyclic reduced furanochroman unit **3** found in phomactin A was developed starting from the known 3-ethoxycyclohex-2-enone **18**[17] and proceeding *via* the 3-hydroxymethyl substituted cyclohexenone **22** and the dihydrofuran **23** as key intermediates.[4] Thus, bromination of **18**, followed by metallation of the resulting 2-bromo derivative **19** and quenching with 3-methylbut-2-enal first gave the substituted allyl alcohol **20a** (Scheme 2). A Peterson methylenation of

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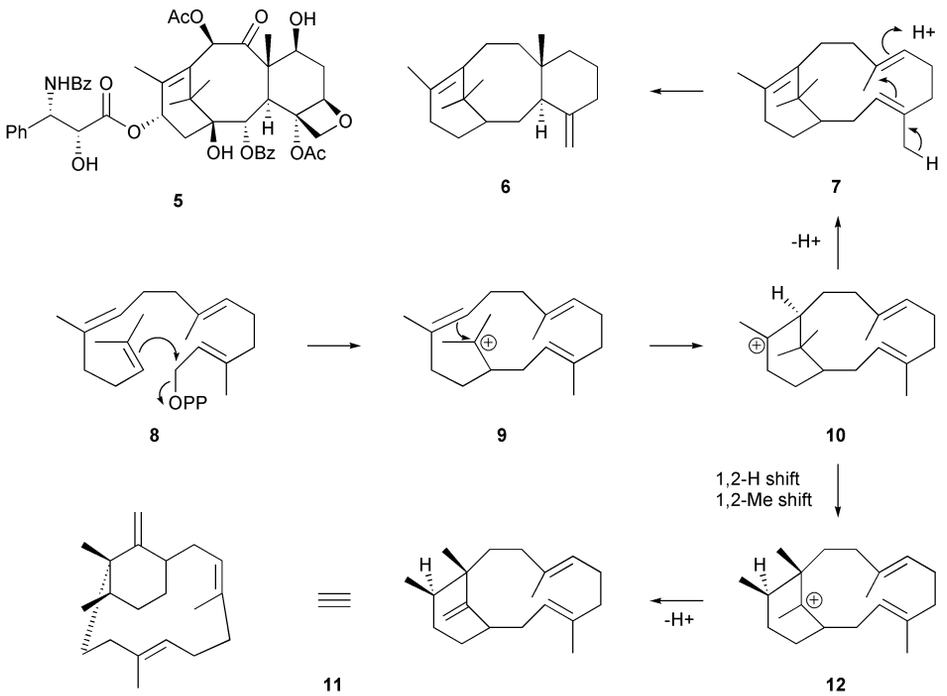
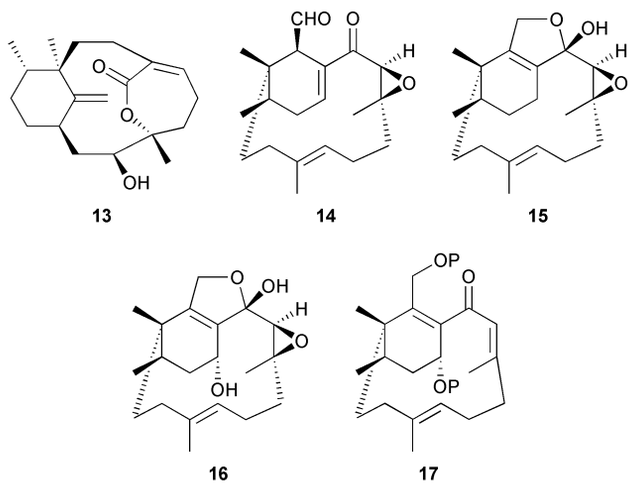
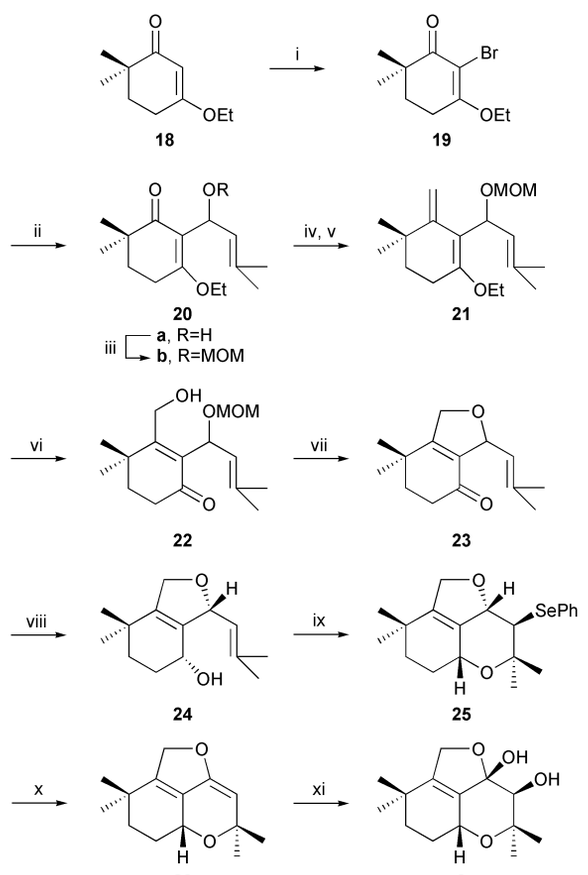


Scheme 1

the MOM ether **20b** derived from **20a**, next gave the conjugated diene ether **21** which, on epoxidation and work-up led to the rearranged cyclohexenone **22**. Deprotection of the MOM ether group in **22**, using camphorsulfonic acid, was accompanied by cyclisation leading to the dihydrofuran **23**. The same dihydrofuran **23** was obtained *via* addition of (tetrahydropyran-2-yl)methyl lithium to the vinylogous ester **20b**, followed by treatment of the resulting β-hydroxyether with *p*-toluenesulfonic acid in dichloromethane. Reduction of the carbonyl group in **23** with DIBALH, led to a 1 : 1 mixture of the α-OH epimer **24** and its corresponding 4β-epimer, which could be separated by chromatography and recycled to **24** by a Mitsunobu inversion sequence. Treatment of the α-alcohol **24** with phenylselenyl chloride resulted in a smooth cyclisation to the pyran **25** which was produced as a single diastereoisomer. Oxidation of the selenide **25**, with *m*-CPBA followed by thermal base-catalysed elimination of phenylselenic acid next led to the enol ether dihydrofuran **26**. Finally, oxidation of the enol ether **26** with dimethyldioxirane gave a 1 : 1 mixture of the required *syn*-vicinal diol **3** and its *anti*-diastereoisomer **27** which could be separated by chromatography. In addition to the vicinal diols **3** and **27**, we also isolated small amounts of the furan **28**, resulting from *in situ* rearrangement of the starting material **26**, and the furan methanol **30** produced by rearrangement of the intermediate oxonium ion **29**.[4,18]

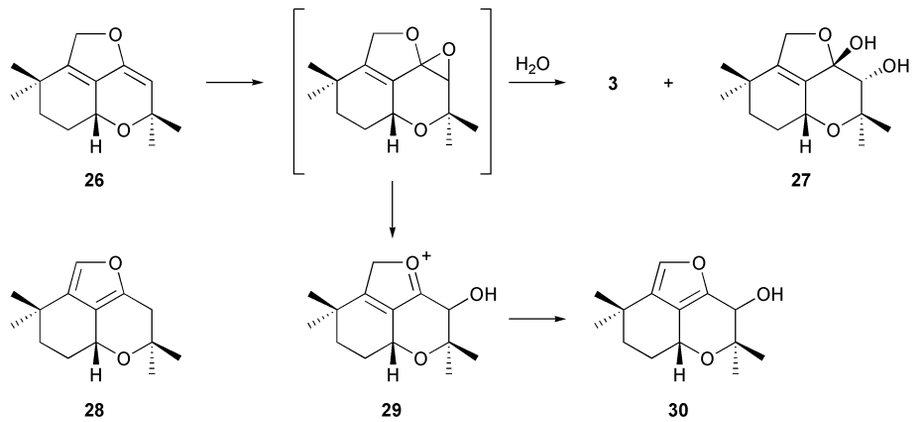




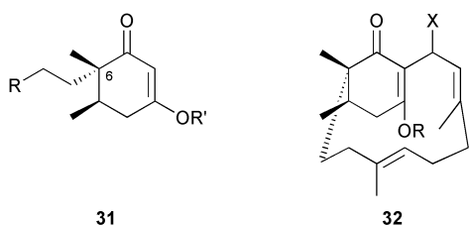
Scheme 2 *Reagents and conditions*: i, NBS, CCl_4, rt, 70%; ii, *t*-BuLi, THF, −78 °C; then 3-methylbutenal, −78 °C, 56%; iii, MOMCl, *i*-Pr_2EtN, CH_2Cl_2, 40 °C, 90%; iv, $TMSCH_2Li$, Et_2O, 0 °C; v, KH, THF, rt, 89% (2 steps); vi, *m*-CPBA, EtOH, rt, 31%; vii, CSA, CH_2Cl_2, rt, 91%; viii, *i*-Bu_2AlH, PhMe, −78 °C, 46%; ix, PhSeCl, K_2CO_3, CH_2Cl_2, −78 °C, 79%; x, *m*-CPBA, CH_2Cl_2, 0 °C; then THF, KOH, 65 °C; xi, DMDO, Me_2CO, H_2O, 22% (2 steps).

The bicyclo[9.3.1]pentadecane ring system 4

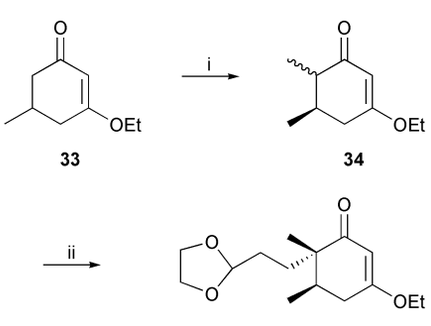
Central to any strategy for a synthesis of phomactin A, using principles employed in elaborating the model furanochroman **3**



from the vinylogous ester **18**, were: i) the requirement of a method to introduce the quaternary centre at C-6 in the intermediate **31** with the correct *syn*-stereochemistry of the vicinal methyl substituents, and ii) the need to develop a synthetic method for constructing the macrocyclic component in intermediates akin to **32**, *cf.* **4**.



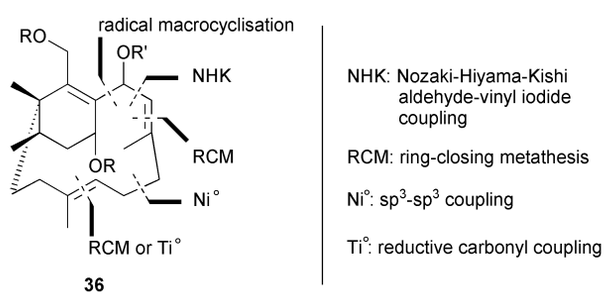
A solution of the first issue was relatively straightforward,[17a,19] since a facile synthesis of the intermediate **35** was smoothly accomplished by deprotonation and methylation of the vinylogous ester **33**, leading to **34**, followed by a further deprotonation of **34** and quenching the resulting enolate with 1,2-ethylenedioxa-3-iodopropane (Scheme 3).[20] In this manner a 3 : 1 mixture of C-6-epimers of **35** was obtained with the required α-side chain epimer **35** in preponderance. The use of electrophiles other than 1,2-ethylenedioxa-3-iodopropane in this sequence gave similar outcomes and similar ratios of α:β-substituted epimers (see later discussion).



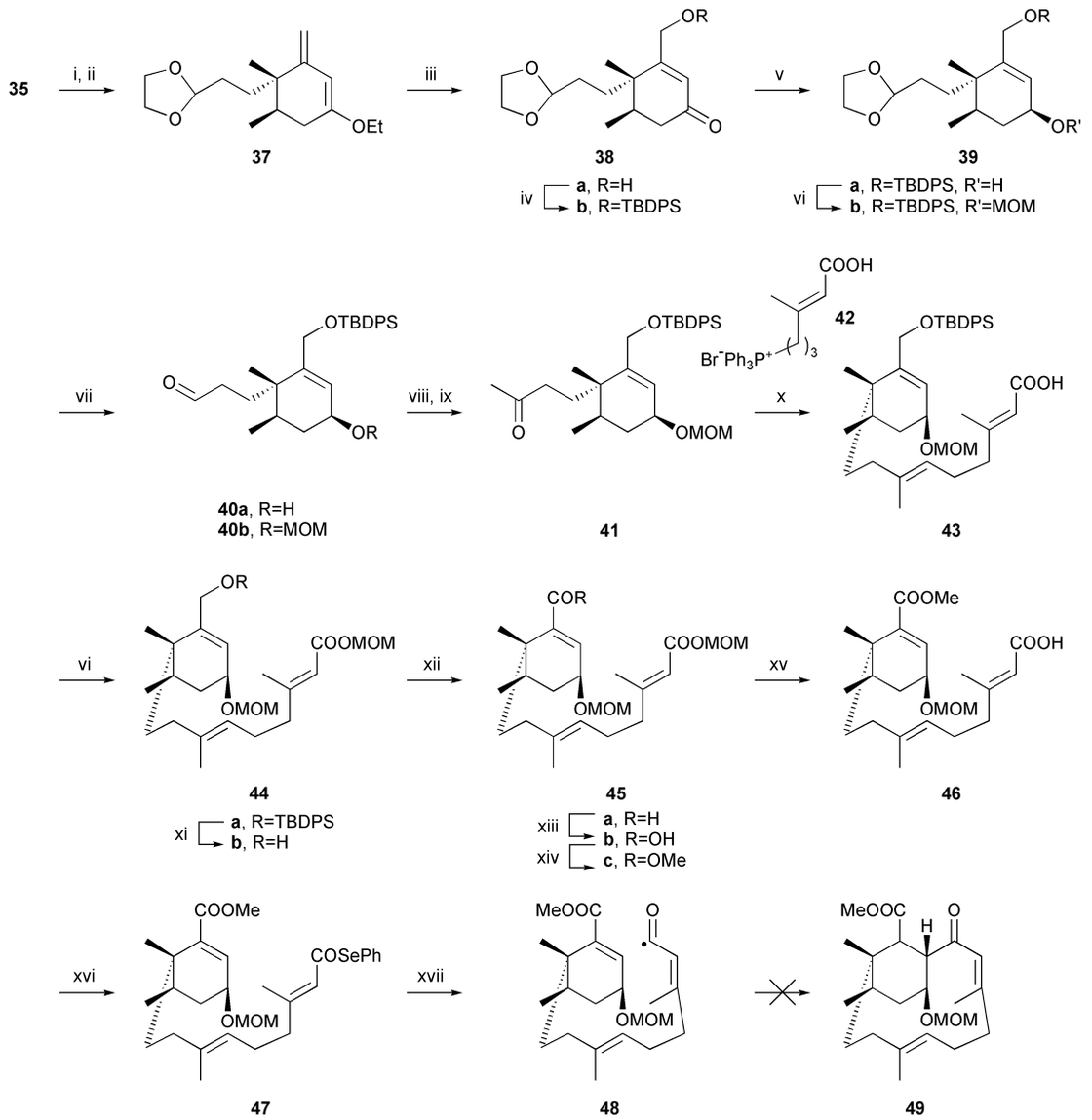
Scheme 3 *Reagents and conditions*: i, LDA, THF, −78 °C; then MeI, −78 °C to rt, 92%; ii, LDA, THF, −78 °C; then 1,1-ethylenedioxa-3-iodopropane, −78 °C to rt, 71%.

The development of an acceptable macrocyclisation strategy to synthesise the macrocyclic core **32** in phomactin A was not so straightforward.[6–8] Indeed, we examined a range of C ⟶ C bond forming and coupling protocols and these are captured in a conceptual manner on the diagram of **36**.[21]

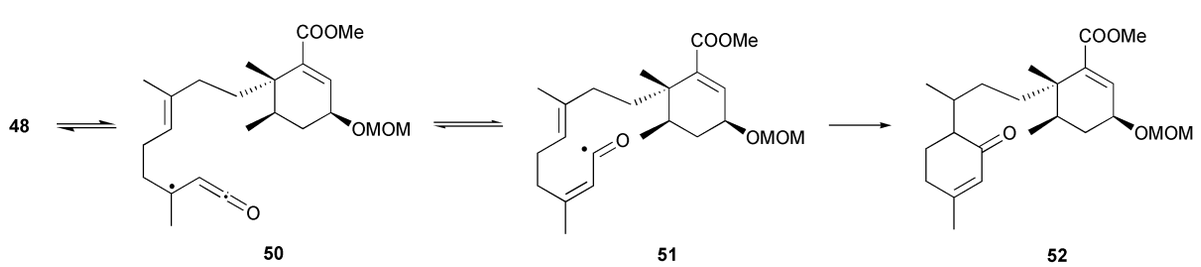
Thus, the very first macrocyclisation strategy we investigated was an unprecedented 12-*endo*-trig unsaturated acyl radical cyclisation from the selenyl ester precursor **47**, with the aim of elaborating the macrocyclic dienone **49**.[22,23] This led to a rather interesting outcome! The selenyl ester **47** was produced from the substituted vinylogous ester **35** as summarised in Scheme 4, following: i, Peterson olefination to **37**; ii, epoxidation of **37** to the 3-hydroxymethylcyclohex-2-enone **38a**; iii, functional group manipulation of **38a** to the MOM-ether **40b** *via* the *syn*-dimethyl alcohol **39a**, which was separated from the *anti*-diastereoisomer by chromatography; iv, conversion of the aldehyde **40b** into the corresponding methyl ketone **41**; v, a Wittig reaction between **41** and the phosphonium ylide derived from the salt **42**, leading to the *E*-alkene **43**; vi, MOM ester protection and oxidation of **43** to the acid ester **46** *via* **44** and **45**, and finally; vii, phenylselenylation of **46** to **47**.[18] Much to our chagrin however, when a benzene solution of the *E*-unsaturated selenyl ester **47** was treated with Bu_3SnH–AIBN, none of the product **49** from an anticipated 12-*endo*-trig macrocyclisation from the intermediate acyl radical **48** was produced. Instead, the cyclohex-2-enone product **52** was isolated resulting from a competing 6-*exo*-trig cyclisation from the corresponding *Z*-α,β-unsaturated acyl radical intermediate **51** into the adjacent C-6–C-7 alkene double bond. Subsequent detailed investigation of this unexpected outcome demonstrated that the facile *E*- to *Z*-isomerisation of the acyl radical species **48** took place *via* the corresponding α-alkyl ketene radical species **50**.[24,25]



The next approach we made towards a synthesis of the macrocyclic core in phomactin A, was based on an intramolecular reductive coupling of the keto-aldehyde **61** using low-valent transition metal reagents, *e.g.* Ti^0, SmI_2, in the expectation of producing **62**.[26] The keto-aldehyde **61** was prepared from the substituted vinylogous ester **35** following: i, bromination with *N*-bromosuccinimide, leading to the *syn*-dimethyl vinyl bromide **53**, which was separated from the *anti*-diastereoisomer by crystallisation; ii, lithiation of **53** and alkylation of the resulting vinyl lithium species with the unsaturated aldehyde **54**,[27] which led to the diastereoisomeric secondary alcohols **55a**; iii, protection of **55a** as its MOM ether and conversion of the latter to the hydroxymethyl substituted cyclohexenone **56** using chemistry established earlier in the synthesis of **38** from **35**; iv, acid-catalysed ring formation from **56**, producing a mixture of diastereoisomers of the dihydrofuran **57**; v, reduction of **57** to **58a** and, finally; vi, functional group manipulation of **58a** *via* **59** and **60**, including separation of the diastereoisomers of **58b**, to the keto-aldehyde **61** (Scheme 5).

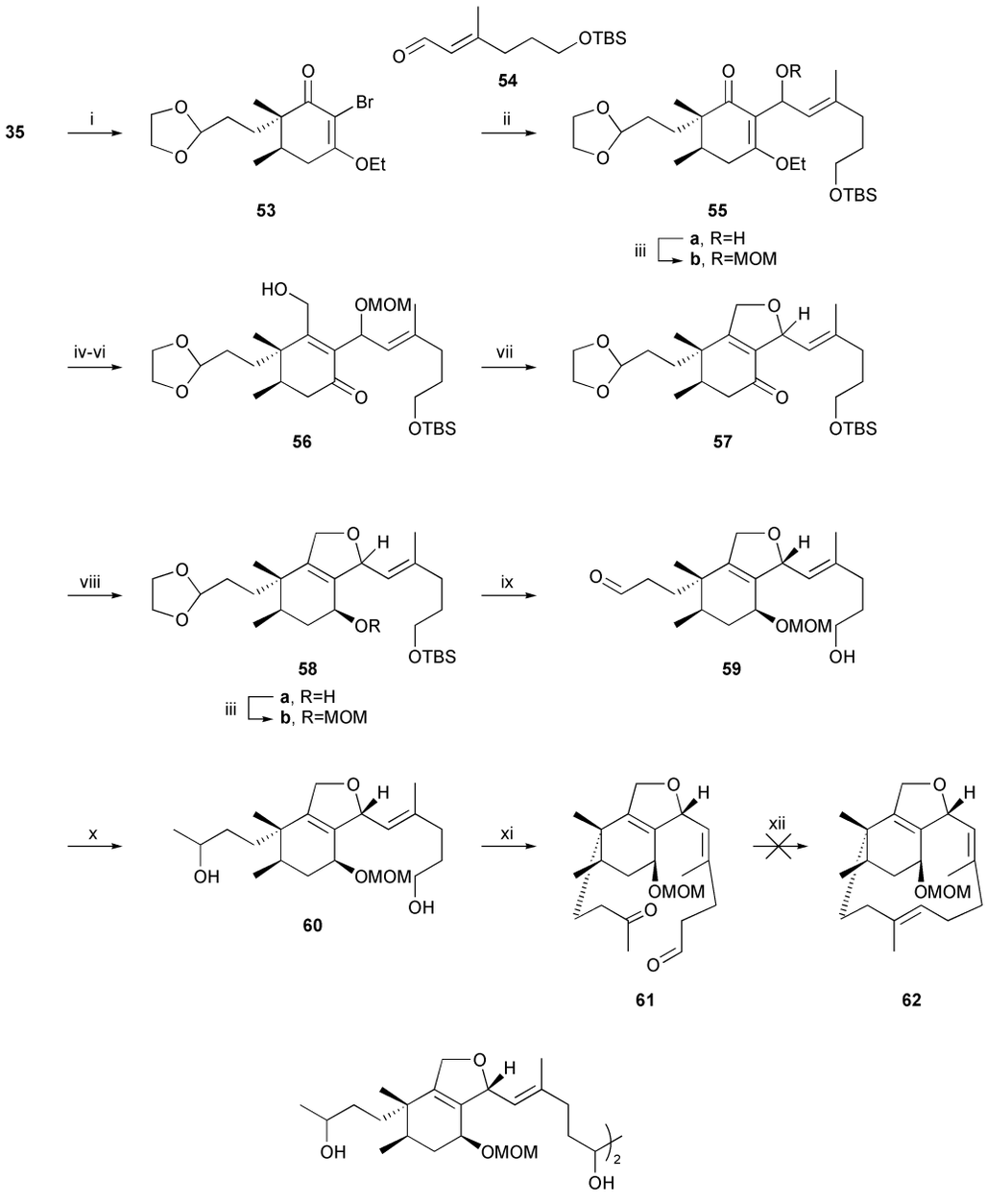


Scheme 4 *Reagents and conditions*: i, $TMSCH_2Li$, Et_2O, 0 °C; ii, KH, THF, rt; iii, *m*-CPBA, EtOH, rt, 31%; (3 steps); iv, TBDPSCl, DMAP, Et_3N, CH_2Cl_2, rt, 82%; v, $NaBH_4$, Et_2O, MeOH, 0 °C, 66%; vi, MOMCl, *i*-Pr_2EtN, CH_2Cl_2, rt, 96–98%; vii, CSA, THF, H_2O, reflux, 60% (**40a**) or 41% (**40b**); viii, MeMgI, Et_2O, 0 °C; ix, Dess–Martin periodinane, CH_2Cl_2, rt, 86% (2 steps from **40b**); x, **42**, KHMDS, THF, 0 °C, 71%; xi, TBAF, THF, rt, 69%; xii, Dess–Martin periodinane, CH_2Cl_2, rt, 85%; xiii $NaClO_2$, NaH_2PO_4, $H_2C{=}C(CH_3)_2$, *i*-BuOH, H_2O, rt, 96%; xiv, MeI, K_2CO_3, Me_2CO, rt, 81%; xv, *p*-TSA, THF, H_2O, reflux, 72%; xvi, *N*-phenylselenophthalimide, Bu_3P, CH_2Cl_2, −20 °C, 74%; xvii, AIBN, Bu_3SnH, PhH, 80 °C, 70% (**52**).



Unfortunately, all our attempts to effect reductive coupling of **61** to **62**, using low valent titanium (McMurry) and samarium diiodide protocols, instead led to either the corresponding diol **60** or to the tetrol **63** resulting from intermolecular pinacol coupling of the aldehyde group in **61**.[28,29]

It was at this time in our studies, *i.e.* 1994, that the now ubiquitous ring closure metathesis (RCM)[30] reaction was beginning to unleash its potential in macrocycle constructions, including interesting macrocyclic natural products.[31] We therefore examined the scope for RCM in the synthesis of the phomactin ring system **68** from their corresponding ω,ω-diene precursors, *i.e.* **67b** and **71** respectively. The syntheses of both **67** and **71** were achieved in a straightforward manner starting from the easily available vinyl bromide **53** already described (Schemes 6 and 7). Unfortunately, and perhaps not unexpected at the time of these studies, exposure of the polyene **67b** to Grubbs' first generation ruthenium pre-catalyst led only to the product resulting from dimerisation at the mono-substituted double bond in **67b**. Gratifying however, when the isomeric polyene **71b** (R′ = H) was treated with the same Grubbs′ pre-catalyst, the macrocyclic structure **72** was isolated in an unoptimised 27% yield, with exclusive *E*-geometry at the newly introduced alkene bond. Although the successful synthesis of the macrocycle **72**, using RCM, was a significant achievement, in its time, we were not persuaded that the RCM approach to the phomactins was the solution to our problem and, once



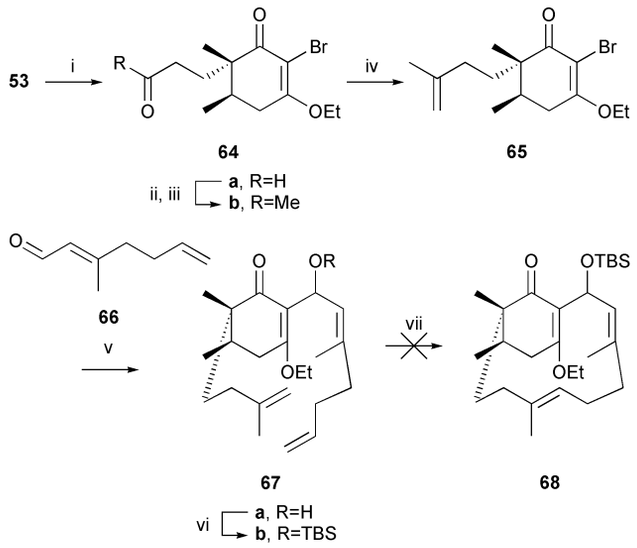
Scheme 5 *Reagents and conditions*: i, NBS, CCl_4, rt, 68%; ii, *t*-BuLi, THF, −90 °C; then **54**, −78 °C, 67%; iii, MOMCl, *i*-Pr_2EtN, CH_2Cl_2, 40 °C, 89–92%; iv, $TMSCH_2Li$, Et_2O, rt; v, KH, THF, rt; vi, *m*-CPBA, EtOH, 0 °C, 10% (3 steps); vii, CSA, CH_2Cl_2, 0 °C; viii, *i*-Bu_2AlH, PhMe, −78 °C, 45% (2 steps); ix, CSA, THF, H_2O, reflux, 68%; x, MeMgCl, THF, rt, 68%; xi, Dess–Martin periodinane, CH_2Cl_2, 0 °C to rt, 72%; xii, SmI_2, Sm, HMPA, *t*-BuOH, THF, −78 °C to rt.

again, we turned our attentions to alternative strategies to the phomactatriene **32**.

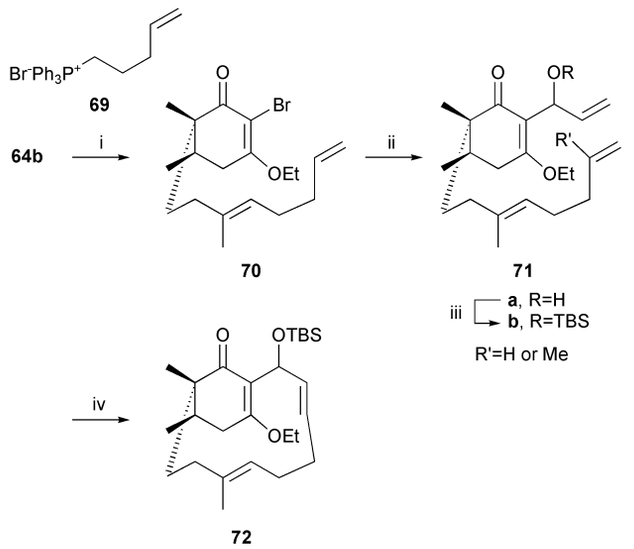
The next approach we examined in order to elaborate the macrocyclic core in phomactin A was based on an intramolecular Cr(II)-mediated coupling reaction from the aldehyde vinyl iodide intermediate **78**, the so-called Nozaki–Hiyama–Kishi (NHK) reaction.[32] Although we had ample precedent, from earlier work, to elaborate **78** swiftly it was also at this time in our studies that we decided to dispense with the ethyl vinylogous ester precursor **33**, and instead use the corresponding substituted dioxin **73a** containing an intact masked C-2 aldehyde function[21,33] as starting material.

Thus, 5-methylcyclohexan-1,3-dione was first converted into the corresponding dioxin **73a** by reaction with 1,3,5-trioxane in the presence of BF_3-etherate. Methylation of the kinetic enolate derived from **73a**, next produced a 1 : 1 mixture of diastereoisomers of the dimethyl dioxin **73b** which, on further deprotonation and quenching with the homoallylic iodide **85** led to the *bis*-alkylated product **74** as a 3 : 1 mixture of *syn*- and *anti*-dimethyl epimers (Scheme 8). The homoallylic iodide **85** was synthesised by way of Negishi's procedure[34] using a palladium-catalysed cross-coupling reaction between the homopropargylic iodide **81** and the *E*-vinyl iodide **80** leading to **82** followed by desilylation and a zirconium assisted carboalumination–iodination process as key steps (Scheme 9).[35]

Addition of *p*-methoxybenzyloxymethyl lithium[36] to the dioxin **74**, followed by work-up with dilute acid next led to the corresponding enone **75a**, *cf.* **35** ⟶ **38** and **55** ⟶ **56**. Protection of the alcohol group in **75a** as its PNB ester **75b**, followed by reduction of the ketone function then led to the β-orientated secondary alcohol **76**. The *syn*-dimethyl alcohol **76** was separated from the *anti*-epimer by chromatography. The resulting alcohol group in **76** was protected as its MOM ether, and then saponification led to the primary alcohol **77**. Oxidation of the primary alcohol group in **77** finally led to the key aldehyde vinyl iodide **78**. Using a similar series of transformations the intermediate **74** was also converted into the less substituted analogues, **88a** and **88b**, of **78** (Scheme 10).



Scheme 6 *Reagents and conditions*: i, $(CH_3CN)_2PdCl_2$, Me_2CO, rt, 52%; ii, MeMgCl, THF, 0 °C, 66%; iii, Dess–Martin periodinane, CH_2Cl_2, 0 °C, 99%; iv, *n*-BuLi, $MePPh_3Br$, Et_2O, −78 °C to rt, 44%; v, *t*-BuLi, **66**, THF, −78 °C, 76%; vi, TBDMSOTf, *i*-Pr_2EtN, CH_2Cl_2, 0 °C to rt, 82%; vii, $RuCl_2(=CHPh)(PCy_3)_2$, CH_2Cl_2, 40 °C.



Scheme 7 *Reagents and conditions*: i, *n*-BuLi, **69**, Et_2O, −78 °C to rt, 58%; ii, *t*-BuLi, acrolein, THF, −78 °C, 76%; iii, TBDMSOTf, *i*-Pr_2EtN, CH_2Cl_2, 0 °C to rt, 86%; iv, $RuCl_2(=CHPh)(PCy_3)_2$, CH_2Cl_2, 40 °C, 27%.

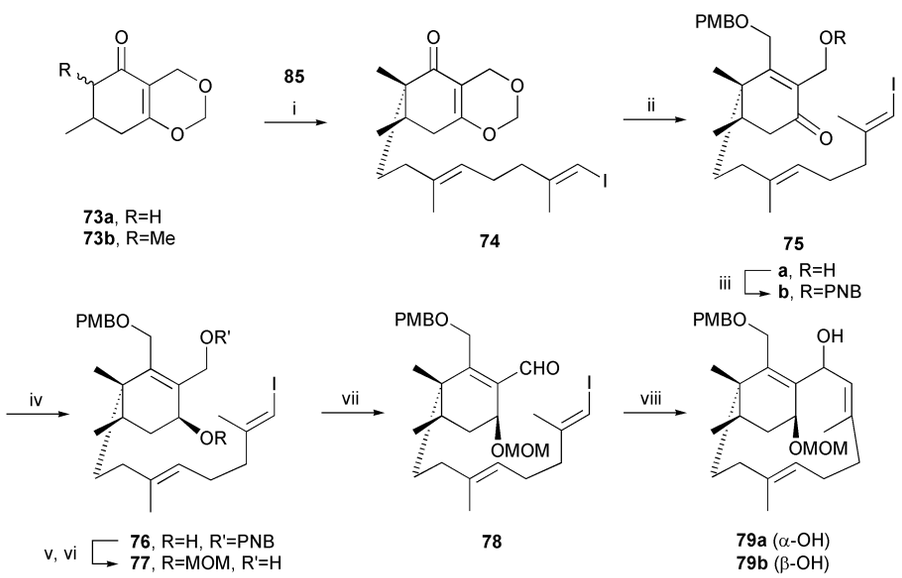
Treatment of a solution of the aldehyde vinyl iodide **78** in DMSO and THF with $CrCl_2$ and catalytic $NiCl_2$, under the NHK reaction conditions, resulted in smooth macrocyclisation and the formation of a 1 : 1 mixture of α- and β-OH epimers of **79** in a combined yield of 52%. Likewise, the analogue **88a** lacking substitution at C-3 underwent cyclisation under the same conditions producing a single crystalline macrocyclic alcohol **91** in 63% yield (see Scheme 10). An X-ray crystal analysis[37] showed that this alcohol had exclusively the α-stereochemistry shown in structure **91**. Finally, the iodoaldehyde **88b** led to a 3 : 1 mixture of diastereoisomers of the alcohol **92** following NHK macrocyclisation, in a combined yield of 62%. Application of molecular modelling,[38] in concert with NOE experiments suggested that the major diastereoisomeric alcohol had the α-configuration shown in **92**.

The aforementioned studies, based on a chromium(II) mediated cyclisation, provided a satisfactory synthesis of the phomactin A ring system containing all the carbon atoms and all the necessary oxygen centres in readiness for elaboration to the target natural product itself. The development of these studies, which culminated in the first synthesis of phomactin A (**1**) is described in the accompanying paper.

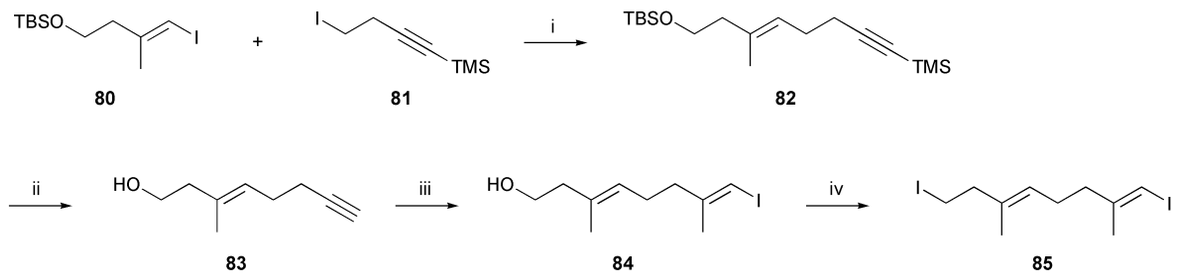
Experimental

General details

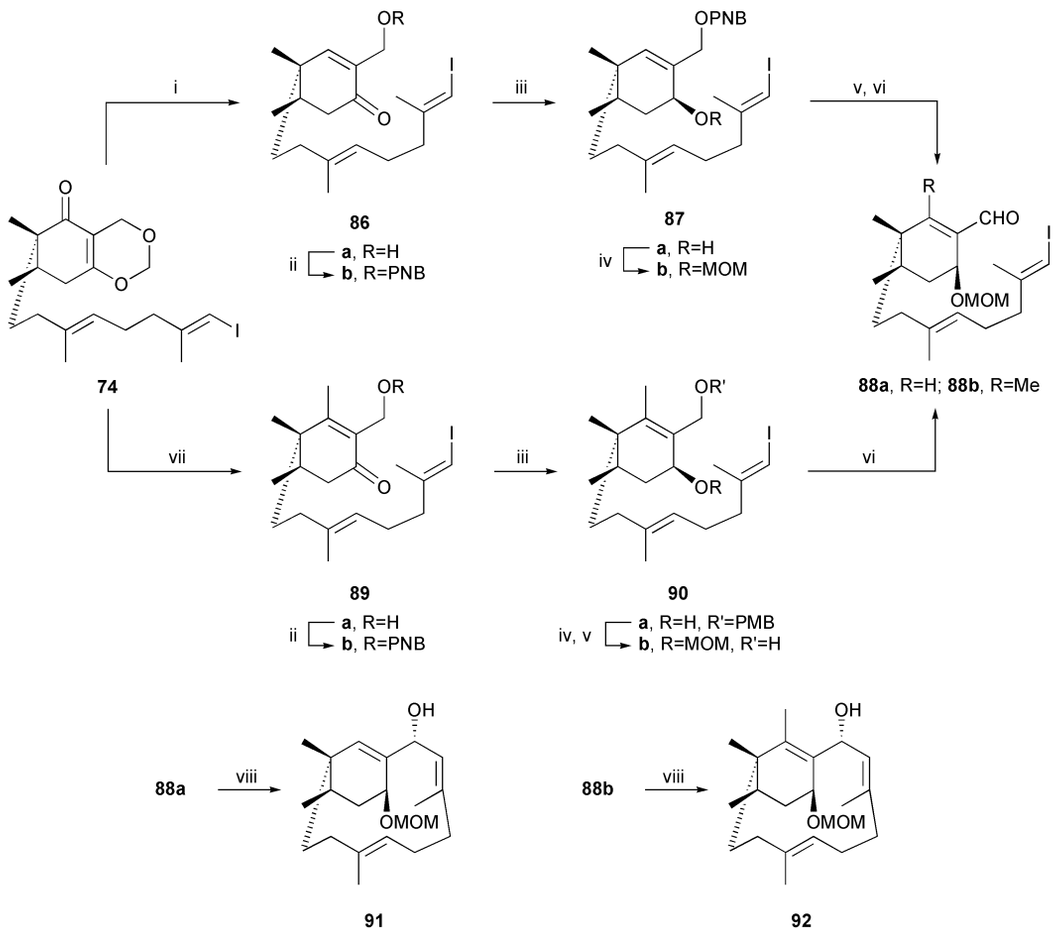
Melting points were determined on either a Stuart Scientific SMP3 melting point apparatus or a Köfler, or Reichert, hot-stage apparatus and are uncorrected. Ultraviolet spectra were obtained using a Phillips PU 8700 spectrophotometer as solutions in spectroscopic grade ethanol. Infrared spectra were recorded on a Perkin-Elmer 1600 Series FT-IR spectrometer as liquid films or as dilute solutions in spectroscopic grade chloroform or deuterochloroform. Proton NMR spectra were recorded on either a Bruker WM250 (250 MHz), a Joel JNM-EX270 (270 MHz), a Bruker DPX360 (360 MHz), a Bruker AM400 (400 MHz), or a Bruker DRX500 (500 MHz) spectrometer as dilute solutions in deuterochloroform, benzene-d_6, or d_4-methanol. Chemical shifts are referenced to residual proton-



Scheme 8 *Reagents and conditions*: i, LDA, DMPU, THF, −78 °C; then **85**, −78 °C to rt, 76%; ii, *n*-BuLi, $PMBOCH_2SnBu_3$, Et_2O, toluene, −78 °C to −25 °C; then 2N HCl, THF, rt, 69%; iii, *p*-NO_2-C_6H_4COCl, Et_3N, DMAP, CH_2Cl_2, −25 °C to 0 °C, 99%; iv, $CeCl_3 \cdot 7H_2O$, $NaBH_4$, MeOH, CH_2Cl_2, −78 °C to −40 °C, 77%; v, MOMCl, *i*-Pr_2EtN, Bu_4NI, CH_2Cl_2, 0 °C to rt; vi, KOH, MeOH, 73% (2 steps); vii, Dess–Martin periodinane, C_5H_5N, CH_2Cl_2, 0 °C, 99%; viii, $CrCl_2$ (6 eq.), $NiCl_2$ (0.25 eq.), DMSO, THF, rt, 52%.



Scheme 9 *Reagents and conditions*: i, *t*-BuLi, **81**, Et_2O, −78 °C; then $ZnCl_2$, −78 °C to 0 °C; then **80**, $Pd(PPh_3)_4$, 0 °C to rt, 94%; ii, TBAF, THF, 0 °C to rt, 91%; iii, Me_3Al, Cp_2ZrCl_2, CH_2Cl_2, −5 °C to rt; then I_2, THF, −25 °C to 0 °C, 91%; iv, PPh_3, imidazole, I_2, CH_2Cl_2, 0 °C to rt, 99%.



Scheme 10 *Reagents and conditions*: i, *i*-Bu_2AlH, $PhCH_3$, −70 °C; then 2N HCl, THF, rt, 96%; ii, *p*-NO_2-C_6H_4COCl, Et_3N, DMAP, CH_2Cl_2, −25 °C to 0 °C, 95% (**86b**) or 91% (**89b**); iii, $CeCl_3{\cdot}7H_2O$, $NaBH_4$, MeOH, CH_2Cl_2, −30 °C, 79% (**87a**) or 70% (**90a**); iv, MOMCl, *i*-Pr_2EtN, Bu_4NI, CH_2Cl_2, 0 °C to rt, 87% (**87b**); v, K_2CO_3, CH_2Cl_2, MeOH, rt, 99% (from **87b**) or 75% (**90b**, 2 steps); vi, Dess–Martin periodinane, C_5H_5N, CH_2Cl_2, 0 °C to rt, 99%; vii, MeLi, $PhCH_3$, −78 °C to −20 °C; then 2N HCl, THF, rt, 90%; viii, $CrCl_2$ (6 eq.), $NiCl_2$ (0.25 eq.), DMSO, rt, 63% (**91**) or 62% (**92**).

ated solvent (δ_H = 7.27 for $CDCl_3$ and C_6D_6, and 3.34 for CD_3OD) and are quoted in parts per million (ppm). The multiplicity of a signal is designated by one of the following abbreviations: s = singlet; d = doublet; t = triplet; q = quartet; br. = broad; m = multiplet; app. = apparent; and obs. = obscured. All coupling constants, *J*, are reported in Hertz and quoted to the nearest 0.1 Hz. Carbon-13 NMR spectra were recorded on either a Jeol JNM-EX270 (67.8 MHz), a Bruker DPX360 (90 MHz), a Bruker AM400 (100 MHz), or a Bruker DRX500 (125 MHz) spectrometer as dilute solutions in deuterochloroform or d_4-methanol on a broad band decoupled mode. Chemical shifts are referenced to residual protonated solvent (δ_C = 77.0 for $CDCl_3$ and 49.0 for CD_3OD) and are quoted in parts per million (ppm). The multiplicity of a signal was obtained using a DEPT sequence, and are designated by one of the following abbreviations: q = primary methyl; t = secondary methylene; d = tertiary methine; s = C(4°) = quarternary. Where required, assignments for ^1H and ^{13}C NMR spectra were confirmed by two-dimensional homonuclear (^1H–^1H) and/or heteronuclear (^1H–^{13}C) correlation spectroscopy recorded on a Bruker DPX360 spectrometer. Matrix dimensions for two dimensional spectra were either 1024 points × 128 columns (homonuclear ^1H–^1H) or 1024 points × 256 columns (heteronuclear ^1H–^{13}C). Mass spectra were recorded on a MM-70E, a Micromass LCT, an AEI MS-902, a VG Micromass 7070E, a VG Autospec or a MM-701CF spectrometer using electron ionisation (EI) at 70eV, chemical ionisation (CI), electrospray (ES) or fast atom bombardment (FAB) ionisation techniques. Microanalytical data were obtained on either an Exeter Analytical CE-440 or a Perkin-Elmer 240B elemental analyser.

All reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F_{254} precoated aluminium plates, which were visualised with ultraviolet light and then developed with either iodine on silica, acidic alcoholic vanillin solution, basic potassium permanganate, acidic anisaldehyde solution or ethanolic phosphomolybdic acid. Flash chromato-

graphy was performed on Merck silica gel 60, Davisil silica gel 60, or neutral alumina (Brockman grade 1) as the stationary phase and the solvents employed were either of analytical grade or were distilled before use.

Unless stated otherwise, all commercially available reagents were used as received. When necessary, commonly used organic solvents were dried prior to use. Tetrahydrofuran (THF), diethyl ether, benzene, and toluene were distilled from sodium benzophenone ketyl or dried by passing through towers of activated alumina. Dichloromethane was distilled from calcium hydride or obtained in high-grade form from Fisher Scientific. Methanol was distilled from magnesium methoxide and triethylamine from calcium hydride. Anhydrous dimethyl sulfoxide (DMSO) was either obtained from Fluka or distilled from, and stored over, activated 4 Å molecular sieves under an atmosphere of argon. Solvents were removed on a Büchi rotary evaporator using water aspirator pressure. Petroleum ether refers to light petroleum ether boiling in the range 40–60 °C. Where necessary, reactions requiring anhydrous conditions were performed under an atmosphere of nitrogen in flame dried or oven dried apparatus.

All of the compounds prepared in this paper are racemic.

6,6-Dimethyl-3-ethoxycyclohex-2-en-1-one 18

A solution of *n*-butyllithium (1.6 M in hexane, 93.0 mL, 150 mmol) was added dropwise over 15 minutes to a solution of diisopropylamine (21.0 mL, 150 mmol) in THF (225 mL) at 0 °C and the mixture was then stirred at 0 °C for 1 hour. The temperature was lowered to −78 °C and a solution of 3-ethoxy-6-methylcyclohex-2-en-1-one[17] (19.1 g, 120 mmol) in THF (25 mL) was added dropwise over 0.5 hour whilst maintaining the internal temperature below −65 °C; the solution was then stirred at −78 °C for 2 hours. Methyl iodide (15.5 mL, 250 mmol) was added dropwise over 5 minutes and the solution was then allowed to warm to room temperature overnight. Water (150 mL) was added and the mixture was then extracted with ether (200 mL, 2 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. Distillation gave the dimethylated vinylogous ester (19.8 g, 95%) as a colourless oil; bp. 82–84 °C (0.6 mmHg); (Found: C, 70.9; H, 9.7. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%); λ_{max} (EtOH)/nm (ε) 243 (12,400), 254 (14,400); ν_{max} (film)/cm^{-1} 1652, 1611, 1378 and 1191; δ_H (250 MHz, $CDCl_3$) 5.22 (1H, s, :C*H*), 3.86 (2H, q, *J* 7.0, OCH_2), 2.40 (2H, t, *J* 6.4, :CCH_2), 1.78 (2H, t, *J* 6.4, :CCH$_2$CH_2), 1.33 (3H, t, *J* 7.0, OCH$_2$CH_3), 1.09 (6H, s, C(CH_3)$_2$); δ_C (67.8 MHz, $CDCl_3$) 203.6 (s), 175.1 (s), 100.3 (d), 63.5 (t), 39.5 (s), 34.5 (t), 25.7 (t), 24.0 (q), 13.6 (q); *m*/*z* (EI) 168.1128 (M^+, $C_{10}H_{16}O_2$ requires 168.1150).

2-Bromo-6,6-dimethyl-3-ethoxycyclohex-2-en-1-one 19

N-Bromosuccinimide (10.6 g, 60 mmol) was added portionwise over 5 minutes to a stirred solution of the dimethylated vinylogous ester **18** (10.0 g, 60 mmol) in carbon tetrachloride (100 mL) at 0 °C. The resulting suspension was allowed to warm to room temperature over 1 hour and then stirred in the dark for 5 hours. The mixture was filtered and the residue was then washed with carbon tetrachloride (50 mL). The filtrate was concentrated *in vacuo* to leave the crude product as a yellow oil. Crystallisation from diethyl ether gave the *bromide* (10.1 g, 70%) as a colourless solid, mp. 70–72 °C; (Found: C, 48.4; H, 6.0; Br, 32.6. $C_{10}H_{15}BrO_2$ requires C, 48.6; H, 6.1; Br, 32.3%); λ_{max} (EtOH)/nm (ε) 273 (15,000); ν_{max} ($CHCl_3$)/cm^{-1} 1660, 1588 and 1360; δ_H (250 MHz, $CDCl_3$) 4.21 (2H, q, *J* 7.0, OCH_2), 2.70 (2H, t, *J* 6.2, :CCH_2), 1.87 (2H, t, *J* 6.2, :CCH$_2$CH_2), 1.44 (3H, t, *J* 7.0, OCH$_2$CH_3), 1.16 (6H, s, C(CH_3)$_2$); δ_C (67.8 MHz, $CDCl_3$) 195.9 (s), 170.7 (s), 101.8 (s), 64.8 (t), 41.3 (s), 33.9 (t), 24.6 (q), 15.0 (q), 24.4 (t); *m*/*z* (EI) 246.0256 (M^+, $C_{10}H_{15}BrO_2$ requires 246.0255).

6,6-Dimethyl-3-ethoxy-2-(1-hydroxy-3-methylbut-2-enyl)-cyclohex-2-en-1-one 20a

A solution of *tert*-butyllithium (1.7 M in pentane, 12.0 mL, 20 mmol) was added dropwise over 15 minutes to a stirred solution of the bromide **19** (2.54 g, 10 mmol) in THF (175 mL) at −78 °C and the bright orange solution was then stirred at −78 °C for 1 hour. 3-Methylbutenal (2.0 mL, 21 mmol) was added in one portion and the mixture was then stirred at −78 °C for 1 hour. Water (10 mL) was added and the mixture was then allowed to warm to room temperature. The mixture was poured into water (150 mL) and then extracted with ether (150 mL, 2 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 0.5% triethylamine and 50% diethyl ether in petroleum ether as eluent to give the *allylic alcohol* (1.45 g, 56%) as a colourless gum; λ_{max} (EtOH)/nm (ε) 209 (8,600), 213 (9,400), 267 (12,900); ν_{max} ($CHCl_3$)/cm^{-1} 3470, 1608, 1356, 1240 and 1036; δ_H (250 MHz, $CDCl_3$) 5.51–5.40 (2H, m, C(OH)*H* and :C*H*), 4.53 (1H, d, *J* 9.3, O*H*), 4.13–4.01 (2H, m, OCH_2), 2.56 (2H, m, :CCH_2), 1.81 (2H, m, :CCH$_2$CH_2), 1.71 (3H, s, :CCH_2), 1.67 (3H, s, :CCH_2), 1.35 (3H, t, *J* 7.0, OCH$_2$CH_2), 1.09 (3H, s, CCH_2), 1.07 (3H, s, CCH_2); δ_C (67.8 MHz, $CDCl_3$) 205.3 (s), 170.0 (s), 132.8 (s), 126.6 (d), 117.8 (s), 64.3 (d), 63.6 (t), 39.5 (s), 34.0 (t), 25.7 (q), 24.3 (q), 24.0 (q), 22.3 (t), 17.8 (q), 14.9 (q); *m*/*z* (EI) 251.1637 (M^+ − H, $C_{15}H_{23}O_3$ requires 251.1647).

6,6-Dimethyl-3-ethoxy-2-(1-methoxymethoxy-3-methylbut-2-en-1-yl)-cyclohex-2-en-1-one 20b

Chloromethylmethyl ether (0.80 mL, 10.5 mmol) was added dropwise over *ca*. 1 minute to a stirred solution of the allylic alcohol **20a** (0.90 g, 3.6 mmol) and diisopropylethylamine (3.7 mL, 21.2 mmol) in dichloromethane (30 mL) at room temperature. The mixture was heated under reflux for 12 hours, then allowed to cool to room temperature, and poured into a saturated aqueous solution of sodium hydrogencarbonate (30 mL). The organic layer was separated and the aqueous layer was then extracted with dichloromethane (15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give (0.95 g, 90%) as a colourless solid, mp. 55–58 °C (ether–petrol); (Found: C, 69.1; H, 9.8. $C_{17}H_{28}O_4$ requires C, 68.9; H, 9.5%); λ_{max} (EtOH)/nm (ε) 202 (7,900), 265 (14,400); ν_{max} ($CHCl_3$)/cm^{-1} 1644, 1609, 1375 and 1362; δ_H (250 MHz, $CDCl_3$) 5.76 (1H, m, :C*H*), 5.68 (1H, d, *J* 8.9, OC*H*), 4.61 (1H, d, *J* 6.6, OC*H*(H)O), 4.53 (1H, d, *J* 6.6, OC(H)*H*O), 4.12–4.06 (2H, m, OCH_2), 3.31 (3H, s, OCH_3), 2.58 (2H, m, :CCH_2), 1.80 (2H, t, *J* 6.3, :CCH$_2$CH_2), 1.69 (3H, d, *J* 1.1, :CCH_3), 1.65 (3H, d, *J* 1.2, :CCH_3), 1.37 (3H, t, *J* 7.0, OCH$_2$CH_3), 1.09 (3H, s, CCH_3), 1.08 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 201.5 (s), 171.2 (s), 134.3 (s), 124.5 (d), 117.0 (s), 93.6 (t), 66.1 (d), 63.5 (t), 55.0 (q), 39.6 (s), 34.1 (t), 25.8 (q), 24.5 (q), 24.4 (q), 22.7 (t), 18.0 (q), 15.1 (q); *m*/*z* (EI) 251.1653 (M^+ − C_2H_5O, $C_{17}H_{28}O_4$ requires 251.1647).

4,4-Dimethyl-1-ethoxy-2-(1-methoxymethoxy-3-methylbut-2-en-1-yl)-3-methylenecyclohex-1-ene 21

A solution of trimethylsilylmethyl lithium (1.0 M in pentane, 5.0 mL, 5.0 mmol) was added dropwise over 5 minutes to a stirred solution of the MOM ether **20b** (1.35 g, 4.6 mmol) in diethyl ether (40 mL) at 0 °C and the mixture was stirred at 0 °C for 1 hour and then poured into water (40 mL). The separated aqueous layer was extracted with ether (20 mL) and the combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a pale yellow oil. The crude *β-hydroxysilane* intermediate was dissolved in THF (40 mL),

and potassium hydride (35% wt/wt oil dispersion, *ca.* 1 mL) was then added dropwise over 1 minute. The red suspension was stirred at room temperature for 2 hours and then water (40 mL) was carefully added and the mixture was extracted with ether (40 mL, 2 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$ and then concentrated *in vacuo* to leave the *diene ether* (1.2 g, 89%) as a yellow oil; ν_{max} (film)/cm^{-1} 1628, 1370, 1360, 1093 and 1036; δ_H (250 MHz, $CDCl_3$) 5.93 (1H, d, *J* 8.7, OC*H*), 5.64 (1H, br. d, *J* 8.7, :C*H*), 5.37 (1H, s, :C*H*(H)), 4.92 (1H, s, :C(H)*H*), 4.62 (1H, d, *J* 6.7, OC*H*(H)O), 4.54 (1H, d, *J* 6.7, OC(H)*H*O), 3.94–3.77 (2H, m, OCH_2), 3.39 (3H, s, OCH_3), 2.43–2.22 (2H, m, :CCH_2), 1.76 (3H, d, *J* 1.2, :CCH_3), 1.73 (3H, d, *J* 1.1, :CCH_3), 1.59–1.51 (2H, m, :CH$_2$CH_2), 1.29 (3H, t, *J* 7.0Hz, OCH$_2$CH_3), 1.10 (3H, s, CCH_3), 1.02 (3H, s, CCH_3); δ_C (90 MHz, $CDCl_3$) 153.7 (s), 148.5 (s), 135.6 (s), 124.2 (d), 116.4 (s), 106.2 (t), 93.0 (t), 67.8 (d), 63.2 (t), 55.2 (q), 35.7 (t), 34.2 (s), 27.9 (q), 26.9 (q), 25.9 (q), 23.0 (t), 18.1 (q), 15.3 (q); *m*/*z* (EI) 294.2197 (M$^+$, $C_{18}H_{30}O_3$ requires 294.2195), which was used without further purification.

4,4-Dimethyl-3-hydroxymethyl-2-(1-methoxymethoxy-3-methyl-but-2-en-1-yl)-cyclohex-2-en-1-one 22

m-Chloroperoxybenzoic acid (56–86%, 0.79 g) was added portionwise over 1 minute to a stirred solution of the crude diene ether **21** (1.3 g, 4.6 mmol) in ethanol (40 mL) at room temperature and the mixture was then stirred at room temperature for 1 hour. A 5% aqueous solution of sodium thiosulfate (10 mL) was added in one portion and the mixture was then stirred at room temperature for 10 minutes. The majority of the solvent was removed *in vacuo* to leave an oily residue which was partitioned between a saturated aqueous solution of sodium hydrogencarbonate (40 mL) and ether (40 mL). The organic layer was separated and the aqueous phase was then extracted with ether (2 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *cyclohexenone* (0.38 g, 31%) as a colourless oil; (Found: C, 68.0; H, 9.5. $C_{16}H_{26}O_4$ requires C, 68.0; H, 9.3%); λ_{max} (EtOH)/nm (ε) 243 (4,700); ν_{max} (film)/cm^{-1} 3504 and 1668; δ_H (250 MHz, $CDCl_3$) 5.78 (1H, d, *J* 9.1, OC*H*), 5.30 (1H, br. d, *J* 9.1, :C*H*), 4.69 (1H, d, *J* 6.5, OC*H*(H)O), 4.56 (1H, d, *J* 6.5, OC(H)*H*O), 4.51 (1H, dd, *J* 12.1 and 4.9, C*H*(H)OH), 4.13 (1H, dd, *J* 12.1 and 9.4, C(H)*H*OH), 3.46 (1H, dd, *J* 9.4 and 4.9, O*H*), 3.33 (3H, s, OCH_3), 2.49–2.45 (2H, m, C(O)CH_2), 1.96–1.79 (2H, m, C(O)CH$_2$CH_2), 1.76 (3H, d, *J* 1.3, :CCH_3), 1.72 (3H, d, *J* 1.2, :CCH_3), 1.29 (3H, s, CCH_3), 1.20 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 198.1 (s), 163.9 (s), 138.5 (s), 136.3 (s), 122.4 (d), 93.7 (t), 68.8 (d), 58.8 (t), 55.5 (q), 37.0 (t), 36.0 (s), 34.5 (t), 27.1 (q), 26.0 (q), 25.8 (q), 18.2 (q); *m*/*z* (EI) 237.1495 (M$^+$ − MOM, $C_{14}H_{21}O_3$ requires 237.1491).

7,7-Dimethyl-3-(2-methylpropenyl)-3,5,6,7-tetrahydro-1*H*-isobenzofuran-4-one 23

(i) *From the cyclohexenone* **22**; Camphorsulfonic acid (10 mg, 0.04 mmol) was added in one portion to a stirred solution of the cyclohexenone **22** (0.15 g, 0.53 mmol) in dichloromethane (10 mL) at 0 °C and the mixture was stirred at 0 °C for 10 minutes and then at room temperature for 10 minutes. The solvent was removed *in vacuo* to leave a yellow oil which was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *dihydrofuran* (0.11 g, 91%) as a colourless oil; (Found: C, 75.9; H, 9.4. $C_{14}H_{20}O_2$ requires C, 76.3; H, 9.1%) λ_{max} (EtOH)/nm (ε) 209 (3,600), 248 (6,200); ν_{max} (film)/cm^{-1} 1669; δ_H (250 MHz, $CDCl_3$) 5.63 (1H, ddd, *J* 8.9, 4.9 and 3.0, OC*H*), 5.09–5.05 (1H, m, :C*H*), 4.82 (1H, dd, *J* 15.7 and 4.9, C*H*(H)O), 4.68 (1H, dd, *J* 15.7 and 3.0, C(H)*H*O), 2.47–2.41 (2H, m, C(O)CH_2), 1.94–1.88 (2H, m, C(O)CH$_2$CH_2), 1.80 (3H, d, *J* 1.3, :CCH_3), 1.72 (3H, d, *J* 1.3, :CCH_3), 1.21 (3H, s, CCH_3), 1.19 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 194.2 (s), 166.7 (s), 137.4 (s), 133.7 (s), 123.2 (d), 81.3 (d), 72.8 (t), 38.3 (t), 35.3 (t), 32.4 (s), 26.5 (q), 26.0 (q), 25.9 (q), 18.2 (q); *m*/*z* (EI) 220.1465 (M$^+$, $C_{14}H_{20}O_2$ requires 220.1463);

(ii) *From the vinylogous ester* **20b**; A solution of *n*-butyllithium (1.6 M in hexane, 0.55 mL, 0.88 mmol) was added dropwise over 5 minutes to a stirred solution of tributyl(tetrahydropyran-2-yloxymethyl)stannane[39] (0.37 g, 0.91 mmol) in THF (5 mL) at −78 °C. The yellow organolithium solution was stirred at −78 °C for 10 minutes and was then added dropwise over 5 minutes to a solution of the MOM ether **20b** (0.22 g, 0.73 mmol) in THF (5 mL) at −78 °C. The mixture was stirred at −78 °C for 1 hour, then water (10 mL) was added and the mixture was allowed to warm to room temperature. The mixture was extracted with ether (3 × 15 mL), and the combined organic extracts were then washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless oil. *p*-Toluenesulfonic acid monohydrate (14 mg, 0.07 mmol) was added in one portion to an ice-cooled solution of the crude *β-hydroxyether* in dichloromethane (10 mL) and the solution was stirred at 0 °C for 15 minutes and then at room temperature for 30 minutes. The mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate (10 mL) and the separated aqueous layer was then extracted with dichloromethane (10 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 0.5% triethylamine and 50% diethyl ether in petroleum ether as eluent to give the dihydrofuran (0.12 g, 73%) as a colourless oil, which showed identical spectroscopic data to those summarised under (i).

(3*R*,4*R*)-7,7-Dimethyl-3-(2-methylpropenyl)-1,3,4,5,6,7-hexahydroisobenzofuran-4-ol 24

A solution of diisobutylaluminium hydride (1.5 M in toluene, 1.2 mL, 1.8 mmol) was added dropwise over 5 minutes to a stirred solution of the dihydrofuran **23** (0.31 g, 1.4 mmol) in toluene (12 mL) at −78 °C and the yellow mixture was then stirred at −78 °C for 3 hours. Ethyl acetate (1.2 mL) was added dropwise over 1 minute and the solution was then allowed to warm to room temperature. Methanol (6.0 mL) was next added, in one portion, and the mixture was then stirred at room temperature for 10 minutes. Magnesium sulfate (*ca.* 2 g) was added portionwise and the mixture was stirred at room temperature for 1 hour. The mixture was filtered through Celite and the residue was then washed repeatedly with ethyl acetate (5 × 5 mL). The solvent was removed *in vacuo* to leave a mixture of diastereoisomeric alcohols as a colourless oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give: (i) the 4α-epimer (0.14 g, 46%) (eluted first) as a colourless oil, ν_{max} (film)/cm^{-1} 3440, 1058 and 1011; δ_H (400 MHz, $CDCl_3$) 5.48–5.43 (1H, m, OC*H*), 5.30 (1H, obs. dsep, *J* 9.5 and 1.1, :C*H*), 4.68 (1H, dd, *J* 12.3 and 5.2, C*H*(H)O), 4.54 (1H, ddd, *J* 12.3, 3.3 and 2.1, C(H)*H*O), 4.17 (1H, br. s, C*H*OH), 1.8–1.6 (3H, m), 1.79 (3H, d, *J* 1.1, :CCH_3), 1.77 (3H, d, *J* 1.1, :CCH_3), 1.42 (1H, ddd, *J* 12.8, 5.0 and 3.4), 1.08 (3H, s, CCH_3), 1.01 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 144.0 (s), 136.8 (s), 132.5 (s), 125.6 (d), 83.6 (d), 72.8 (t), 62.5 (d), 33.8 (t), 31.4 (s), 28.4 (t), 28.0 (q), 25.9 (q), 18.1 (q); *m*/*z* (EI) 222.1615 (M$^+$, $C_{14}H_{22}O_2$ requires 222.1620), and (ii) the corresponding 4β-epimer (0.13 g, 42%) (eluted second) as a colourless oil; ν_{max} (film)/cm^{-1} 3415, 1063 and 1010; δ_H (400 MHz, $CDCl_3$) 5.59–5.56 (1H, m, OC*H*), 5.08 (1H, obs. dsep, *J* 9.6 and 1.1, :C*H*), 4.60 (1H, ddd, *J* 12.2, 5.2 and 2.4, OC*H*(H)), 4.55 (1H, ddd, *J* 12.2, 3.3 and 1.3, OC(H)*H*), 4.07 (1H, br. s, C*H*OH), 1.92–1.86 (1H, m), 1.81–1.69 (1H, m), 1.76 (3H, d, *J* 1.1, :CCH_3),

1.75 (3H, d, *J* 1.1, :CCH_3), 1.65–1.59 (1H, m), 1.45 (1H, ddd, *J* 13.4, 7.8 and 3.2), 1.06 (3H, s, CCH_3), 1.01 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 143.2 (s), 136.9 (s), 133.7 (s), 124.3 (d), 82.6 (d), 73.1 (t), 62.9 (d), 34.8 (t), 31.1 (s), 29.6 (t), 27.6 (q), 26.7 (q), 25.9 (q), 18.1 (q); *m*/*z* (EI) 222.1617 (M^+, $C_{14}H_{22}O_2$ requires 222.1620).

Diethyl azodicarboxylate (0.12 mL, 0.73 mmol) was added dropwise over 1 minute to a stirred solution of triphenylphosphine (0.19 g, 0.72 mmol) in THF (5 mL) at 0 °C; the mixture was then stirred at 0 °C for 10 minutes. A solution of the 4β-alcohol (0.107 g, 0.48 mmol) (from above) and benzoic acid (0.094 g, 0.77 mmol) in THF (2 mL) was added dropwise over 5 minutes and the mixture was then stirred at 0 °C for 2 hours. A saturated aqueous solution of sodium hydrogencarbonate (7 mL) was added and the mixture was then extracted with ether (3 × 10 mL). The combined organic fractions were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 0.5% triethylamine and 25% diethyl ether in petroleum ether as eluent to give the corresponding *benzoate* (0.11 g, 70%) as a colourless oil; (Found: C, 77.5; H, 8.2. $C_{21}H_{26}O_3$ requires C, 77.3; H, 8.0%); λ_{max} (EtOH)/nm (ε) 207 (12,600), 228 (12,100), 273 (870); ν_{max} (film)/cm^{-1} 1715, 1270, 1108, 711 and 687; δ_H (250 MHz, $CDCl_3$) 8.02–7.98 (2H, m, Ar*H*), 7.57–7.50 (1H, m, Ar*H*), 7.45–7.39 (2H, m, Ar*H*), 5.65 (1H, br. s, C*H*OCOPh), 5.48–5.41 (1H, m, OC*H*), 5.10–5.06 (1H, m, :C*H*), 4.73 (1H, ddd, *J* 12.5, 5.1 and 1.1, OC*H*(H)), 4.58 (1H, ddd, *J* 12.5, 5.8 and 5.8, OC(H)*H*), 2.03–1.93 (2H, m), 1.80–1.69 (1H, m), 1.59–1.50 (1H, m), 1.59 (3H, d, *J* 1.2, :CCH_3), 1.21 (3H, d, *J* 1.1, :CCH_3), 1.16 (3H, s, CCH_3), 1.07 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 165.8 (s), 146.6 (s), 135.8 (s), 132.6 (d), 129.5 (d), 128.8 (s), 83.4 (d), 72.6 (t), 65.2 (d), 34.8 (t), 31.1 (s), 27.9 (q), 26.5 (t), 26.2 (q), 25.4 (q), 17.6 (q); *m*/*z* (EI) 326.1873 (M^+, $C_{21}H_{26}O_3$ requires 326.1882).

A solution of diisobutylaluminium hydride (1.5 M in toluene, 0.5 mL, 0.75 mmol) was added dropwise over 1 minute to a stirred solution of the 4β-benzoate (0.103 g, 0.32 mmol) in toluene (5 mL) at −78 °C and the mixture was then stirred at −78 °C for 2.5 hours. Ethyl acetate (0.5 mL) was added dropwise over 1 minute and the mixture was allowed to warm to room temperature. Methanol (2 mL) was added and the mixture was then stirred for 10 minutes. Magnesium sulfate (*ca*. 1 g) was added portionwise and the mixture was then stirred at room temperature for 1 hour. The mixture was filtered through Celite and the residue was washed with ethyl acetate (2 × 5 mL). The solvent was removed *in vacuo* to leave a colourless oil which was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the 4α-alcohol (0.047 g, 67%) whose spectroscopic data matched exactly those described earlier.

(3a*S*,8a*R*)-2,2,6,6-Tetramethyl-3-phenylselanyl-2,3,3a,5,6,7,8,8a-octahydrofuro[2,3,4-*de*]chromene 25

A solution of phenylselenyl chloride (0.114 g, 0.60 mmol) in dichloromethane (1 mL) was added dropwise over 1 minute to a stirred solution of the allylic alcohol **24** (0.12 g, 0.54 mmol) and potassium carbonate (0.37 g, 2.7 mmol) in dichloromethane (5 mL) at −78 °C and the mixture was then stirred at −78 °C for 15 minutes. The solution was allowed to warm to room temperature and then diluted with dichloromethane (15 mL). The mixture was washed with brine (10 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 5% diethyl ether in petroleum ether as eluent to give the *selenide* (0.16 g, 79%) as a colourless oil; (Found: C, 63.8; H, 7.1. $C_{20}H_{26}O_2Se$ requires C, 63.7; H, 6.9%); ν_{max} (film)/cm^{-1} 1378, 1363, 1063, 1018 and 740; δ_H (250 MHz, $CDCl_3$) 7.70–7.65 (2H, m, Ar*H*), 7.27–7.21 (3H, m, Ar*H*), 4.87–4.79 (1H, m, OC*H*), 4.68 (1H, ddd, *J* 12.1, 4.4 and 2.8, OC(H)*H*), 4.62 (1H, ddd, *J* 12.1, 5.1 and 1.4, OC*H*(H)), 4.27–4.24 (1H, m, C*H*O), 2.86 (1H, d, *J* 10.5, C(SePh)*H*), 2.03–1.96 (1H, m), 1.58–1.44 (2H, m), 1.36 (3H, s), 1.30 (3H, s), 1.10 (3H, s), 1.02 (3H, s); δ_C (67.8 MHz, $CDCl_3$) 141.0 (s), 134.4 (d), 130.9 (s), 130.5 (s), 128.8 (d), 127.2 (d), 84.0 (d), 72.6 (t), 69.7 (s), 65.7 (d), 59.9 (d), 36.8 (d), 31.7 (s), 29.5 (q), 28.5 (q), 27.1 (t), 25.4 (q), 19.5 (q); *m*/*z* (EI) 378.1107 (M^+, $C_{20}H_{26}O_2Se$ requires 378.1098).

(*R*)-2,2,6,6-Tetramethyl-2,5,6,7,8,8a-hexahydrofuro[2,3,4-*de*]-chromene 26

m-Chloroperoxybenzoic acid (56–86%, 0.046 g) was added portionwise over 30 minutes to a stirred solution of the selenide **25** (0.080 g, 0.21 mmol) in dichloromethane (8 mL) at 0 °C. The solvent was removed *in vacuo* to leave the crude *selenoxide* as a yellow oil. The selenoxide was dissolved in THF (8 mL), potassium hydroxide (0.12 g, 2.1 mmol) was then added in one portion, and the mixture was heated under reflux for 20 minutes. The suspension was filtered and the residue was washed with ether (10 mL). The filtrate was concentrated *in vacuo* to leave the crude *enol ether* (0.060 g) as a yellow gum, which was used without purification. The residue was purified by flash column chromatography on alumina using 10% diethyl ether in petroleum ether as eluent to give a small amount of the corresponding isomeric *furan* **28** as a colourless solid; ν_{max} ($CHCl_3$)/cm^{-1} 1666; δ_H (400 MHz, $CDCl_3$) 7.12 (1H, t, *J* 0.9, Fu*H*), 4.46–4.41 (1H, m, C*H*O), 2.62–2.50 (2H, m, FuCH_2), 2.01–1.95 (1H, m), 1.68–1.44 (3H, m), 1.42 (3H, s, CH_3), 1.40 (3H, s, CH_3), 1.30 (3H, s, CH_3), 1.18 (3H, s, CH_3); δ_C (67.8 MHz, $CDCl_3$) 145.4 (s), 136.0 (d), 130.1 (s), 118.8 (s), 73.3 (s), 66.5 (d), 38.4 (t), 36.1 (q), 31.6 (q), 31.3 (q), 30.7 (s), 30.4 (q), 27.6 (t), 24.7 (q); *m*/*z* (EI) 220.1427 (M^+, $C_{14}H_{20}O_2$ requires 220.1463).

(*R*)-2,2,6,6-Tetramethyl-2,3,6,7,8,8a-hexahydrofuro[2,3,4-*de*]-chromen-3-ol 30

m-Chloroperoxybenzoic acid (56–86%, 16 mg) was added portionwise to a solution of the enol ether **26** (0.029 g, 0.10 mmol) in dichloromethane (3 mL) at 0 °C; the mixture was then stirred at 0 °C for 30 minutes. The mixture was extracted with a saturated aqueous solution of sodium hydrogencarbonate (5 mL) and then the organic layer was washed with brine (5 mL). The organic layer was separated, dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow film. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *alcohol* (3 mg, 15%) as a colourless oil; δ_H (250 MHz, $CDCl_3$) 7.20 (1H, s, Fu*H*), 4.43 (1H, dd, *J* 10.6 and 4.2, OC*H*), 4.19 (1H, d, *J* 9.0, C(OH)*H*), 2.06–1.97 (1H, m), 1.69–1.43 (3H, m), 1.40 (6H, s), 1.31 (3H, s), 1.18 (3H, s); δ_C (100 MHz, $CDCl_3$) 146.8, 138.3, 130.2, 122.5, 69.4, 66.8, 38.7, 31.7, 31.6, 30.9, 27.8, 25.5, 22.4; *m*/*z* (EI) 219.1401 (M^+ − OH, $C_{14}H_{19}O_2$ requires 219.1385).

(3*S*,3a*S*,8a*R*)-2,2,6,6-Tetramethyl-2,3,6,7,8,8a-hexahydro-5*H*-furo[2,3,4-*de*]chromene-3,3a-diol 3

A solution of dimethyldioxirane (0.1 M in acetone, 3.0 mL, 0.3 mmol) was added dropwise over 30 minutes to a stirred solution of the crude enol ether **26** (0.060 g, 0.21 mmol) in acetone (4 mL) and water (4 mL) at 0 °C. The solvent was removed *in vacuo* to leave a yellow film which was partitioned between a saturated aqueous solution of sodium hydrogencarbonate (5 mL) and ethyl acetate (5 mL). The organic layer was separated and the aqueous layer was then extracted with ethyl acetate (2 × 5 mL). The combined organic extracts were washed with brine (5 mL), dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 25–50% diethyl ether in petroleum ether as eluent to give: (i) the *syn* vicinal diol (6 mg, 11%) (eluted first) as a colourless solid, δ_H (500 MHz, $CDCl_3$) 4.80 (1H, dd, *J* 12.9 and 2.8, 5*H*), 4.41

(1H, dd, *J* 12.9 and 1.3, 5*H*), 4.33 (1H, m, 8a*H*), 3.80 (1H, s, 3aO*H*), 3.56 (1H, d, *J* 6.0, 3*H*), 2.81 (1H, d, *J* 6.0, 3O*H*), 2.04–2.07 (1H, m, 8*H*), 1.51–1.57 (3H, m, 7*H* and 8*H*), 1.31 (3*H*, s), 1.30 (3*H*, s), 1.11 (3*H*, s), 1.08 (3*H*, s); δ_C (125.8 MHz, $CDCl_3$) 146.1 (s), 130.1 (s), 105.9 (s), 79.4 (d), 75.5 (s), 71.6 (t), 64.1 (d), 36.7 (t), 31.9 (s), 28.8 (q), 28.4 (q), 26.7 (t), 26.0 (q), 17.7 (q); *m*/*z* (FAB) 237.1472 ($M^+ - OH$, $C_{14}H_{21}O_3$ requires 237.1491), (ii) *(3R,3aS,8aR)-2,2,6,6-tetramethyl-2,3,6,7,8,8a-hexahydro-5H-furo[2,3,4-de]chromene-3,3a-diol* **27**, the *anti* vicinal diol (6 mg, 11%) (eluted second) as a colourless solid; δ_H (500 MHz, $CDCl_3$) 4.82 (1H, dd, *J* 13.1 and 2.9, 5*H*), 4.48 (1H, dd, *J* 13.1 and 1.4, 5*H*), 4.34 (1H, m, 8a*H*), 3.43 (1H, d, *J* 2.0, 3*H*), 2.57 (1H, s, 3aO*H*), 2.31 (1H, d, *J* 2.3, 3O*H*), 2.04–2.09 (1H, m, 8*H*), 1.57–1.66 (3H, m, 7*H* and 8*H*), 1.45 (3H, s), 1.33 (3H, s), 1.14 (3H, s), 1.08 (3H, s); δ_C (125.8 MHz, $CDCl_3$) 147.1 (s), 128.5 (s), 107.5 (s), 76.2 (d), 75.1 (s), 72.1 (t), 64.3 (d), 36.8 (t), 32.2 (s), 28.6 (q), 27.3 (q), 26.9 (t), 26.1 (q), 22.9 (q); *m*/*z* (EI) 236.1443 ($M^+ - H_2O$, $C_{14}H_{20}O_3$ requires 236.1412).

3-Ethoxy-5-methylcyclohex-2-en-1-one 33

The vinylogous ester **33** was prepared according to a modification of the method of Gannon and House.[17b,40] A solution of 5-methylcyclohexane-1,3-dione (25.0 g, 0.20 mmol) and *p*-toluenesulfonic acid monohydrate (1.0 g, 5.3 mmol) in benzene (450 mL) and ethanol (125 mL) was heated under reflux (Dean–Stark trap) for 8 hours with removal of the azeotropic mixture at a rate of 10 mL $hour^{-1}$. The solvent was removed *in vacuo* to leave a yellow oil which was partitioned between ether (300 mL) and a solution of sodium hydrogencarbonate (150 mL). The ethereal layer was separated and the aqueous layer was then extracted with ether (150 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a pale yellow oil. Distillation gave the vinylogous ester (27.9 g, 91%) as a colourless oil; bp. 82–84 °C (1.0 mmHg); (Found: C, 69.7; H, 9.5. $C_9H_{14}O_2$ requires C, 70.1; H, 9.2%); λ_{max} (EtOH)/nm (ε) 249 (14,400); ν_{max} (film)/cm^{-1} 1658, 1599, 1211 and 1030; δ_H (250 MHz, $CDCl_3$) 5.33 (1H, s, :C*H*), 3.84–3.76 (2H, m, OCH_2CH$_3$), 2.45–2.38 (2H, m), 2.26–1.98 (3H, m), 1.37 (3H, t, *J* 7.0, OCH$_2$CH_3), 1.08 (3H, d, *J* 6.1, CHCH_3); δ_C (67.8 MHz, $CDCl_3$) 199.6 (s), 177.1 (s), 102.1 (d), 64.0 (t), 44.9 (t), 37.1 (t), 28.7 (d), 20.7 (q), 13.9 (q); *m*/*z* (EI) 154.0994 (M^+, $C_9H_{14}O_2$ requires 154.0994).

5,6-Dimethyl-3-ethoxycyclohex-2-en-1-one 34

The vinylogous ester **33** was alkylated according to the method of Stork and Danheiser.[41] A solution of *n*-butyllithium (2.5 M in hexane, 78 mL, 200 mmol) was added dropwise over 20 minutes to a stirred solution of diisopropylamine (27 mL, 200 mmol) in THF (200 mL) at 0 °C and the mixture was then stirred at 0 °C for 1 hour. The mixture was cooled to −78 °C and then a solution of the vinylogous ester **33** (25 g, 160 mmol) in THF (50 mL) was added dropwise over 0.5 hour whilst maintaining the internal temperature below −65 °C. The resulting yellow solution was stirred at −78 °C for 2 hours and then methyl iodide (16 mL, 260 mmol) was added dropwise over 5 minutes. The solution was allowed to warm to room temperature overnight, then water (150 mL) and ether (200 mL) were added and the organic layer was separated. The aqueous phase was extracted with ether (200 mL) and the combined organic extracts were then washed with brine (100 mL), dried over $MgSO_4$ and concentrated *in vacuo* to leave a yellow oil. Distillation gave the methylated vinylogous ester (25.1 g, 92%) as an inseparable 1 : 1 mixture of diastereoisomers, as a colourless oil; data for the mixture of diastereoisomers, bp. 90–92 °C (1.0 mmHg); (Found: C, 71.4; H, 10.0. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%); λ_{max} (EtOH)/nm (ε) 248 (14,600); ν_{max} (film)/cm^{-1} 1658, 1614, 1379, 1216, 1191 and 1031; δ_H (270 MHz, $CDCl_3$) 5.39 (0.5H, d, *J* 1.3, :C*H*), 5.34 (0.5H, s, :C*H*), 3.92–3.86 (2H, m, OCH_2CH$_3$), 2.55–2.22 (3H, m), 2.08–1.87 (1H, m), 1.43 (1.5H, t, *J* 7.0, OCH$_2$CH_3), 1.42 (1.5H, t, *J* 7.0, OCH$_2$-CH_3), 1.22 (1.5H, d, *J* 6.6, CHCH_3), 1.15 (1.5H, d, *J* 6.3, CHCH'_3), 1.12 (1.5H, d, *J* 7.2, CHCH_3), 1.04 (1.5H, d, *J* 6.6, CHCH'_3); δ_C (67.8 MHz, $CDCl_3$) 202.9 (s), 201.5 (s), 175.6 (s), 175.4 (s), 101.5 (d), 100.9 (d), 64.0 (t), 63.9 (t), 47.0 (d), 44.8 (d), 36.7 (t), 34.7 (t), 34.5 (d), 31.8 (d), 19.7 (q), 15.6 (q), 14.0 (q), 12.7 (q), 10.9 (q); *m*/*z* (EI) 168.1165 (M^+, $C_{10}H_{16}O_2$ requires 168.1150).

6-(2-[1,3]Dioxolan-2-ylethyl)-5,6-dimethyl-3-ethoxycyclohex-2-enone 35

A solution of *n*-butyllithium (2.5 M in hexane, 29 mL, 72 mmol) was added dropwise over 20 minutes to a stirred solution of diisopropylamine (10 mL, 72 mmol) in THF (100 mL) at 0 °C and the mixture was stirred at 0 °C for 1 hour. The solution was cooled to −78 °C and a solution of a 1 : 1 mixture of diastereoisomers of the vinylogous ester **34** (10.0 g, 60 mmol) in THF (25 mL) was then added dropwise over 0.5 hour whilst maintaining the internal temperature below −65 °C. The yellow mixture was stirred at −78 °C for 2 hours and then a solution of 1,1-ethylenedioxa-3-iodopropane[20] (20 g, 88 mmol) in THF (10 mL) was added dropwise over 10 minutes at −78 °C. The mixture was allowed to warm to room temperature overnight and then stirred for 24 hours. Water (150 mL) and ether (150 mL) were added and the separated aqueous phase was then extracted with ether (150 mL). The combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 17–50% diethyl ether in petroleum ether as eluent to give the alkylated vinylogous ester (11.3 g, 71%) as an inseparable 3 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a viscous yellow oil; data for the *syn* isomer, λ_{max} (EtOH)/nm (ε) 248 (15,800); (Found: C, 67.1; H, 9.3. $C_{15}H_{24}O_4$ requires C, 67.1; H, 9.0%); ν_{max} (film)/cm^{-1} 1651, 1613, 1380, 1221, 1199 and 1030; δ_H (250 MHz, $CDCl_3$) 5.25 (1H, s, :C*H*), 4.82 (1H, dd, *J* 5.0 and 3.9, OC*H*O), 3.97–3.79 (6H, m, OCH_2CH_2O + OCH_2CH$_3$), 2.42–1.94 (4H, m), 1.55–1.41 (3H, m), 1.35 (3H, t, *J* 7.0, OCH$_2$CH_3), 0.97 (3H, d, *J* 7.0, CHCH_3), 0.96 (3H, s, CCH_3); δ_C (67.8 MHz, $CDCl_3$) 203.4 (s), 174.3 (s), 104.4 (d), 101.1 (d), 64.5 (t), 63.7 (t), 46.7 (s), 34.0 (t), 32.5 (d), 29.0 (t), 28.3 (t), 18.2 (q), 14.7 (q), 13.9 (q); *m*/*z* (EI) 268.1676 (M^+, $C_{15}H_{24}O_4$ requires 268.1675).

4-(2-[1,3]Dioxolan-2-ylethyl)-4,5-dimethyl-3-hydroxymethylcyclohex-2-enone 38a

Trimethylsilylmethyllithium (1.0 M in pentane, 21.0 mL, 21 mmol) was added dropwise over 30 minutes to a stirred, ice cooled, solution of a 3 : 1 mixture of diastereoisomers of the vinylogous ester **35** (5.0 g, 18.7 mmol) in diethyl ether (75 mL), and the resulting yellow solution was stirred at 4 °C for 1 hour. Water (50 mL) was added, the two layers were separated, and the aqueous layer was then extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine (50 mL) and then dried over $MgSO_4$. The solvent was removed *in vacuo* and replaced with THF (70 mL). Potassium hydride (2.5 g, 35 wt% dispersion in oil) was added dropwise, to the stirred THF solution at room temperature and, after stirring for 1 hour, water (50 mL) and ether (100 mL) were added and the two layers were separated. The aqueous phase was extracted with ether (3 × 50 mL) and the combined organic extracts were washed with brine (50 mL) and then dried over $MgSO_4$. The solvent was removed *in vacuo* to leave the olefination product **37** as an inseparable 3 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as an unstable oil. *m*-Chloroperoxybenzoic acid (6.4 g, 50–60%) was added to a solution of a 3 : 1 mixture of diastereoisomers of **37** in ethanol (40 mL) and the mixture was stirred at room temperature for 2 hours. Sodium thiosulfate (8 g) followed by potassium carbonate (10 g) in water (20 mL)

were added, and the mixture was then stirred for 1 hour. Most of the solvent was removed *in vacuo* and the residue was then partitioned between water (20 mL) and ethyl acetate (100 mL). The separated aqueous layer was extracted with ethyl acetate (5 × 50 mL) and the combined organic extracts were washed with brine (100 mL) and then dried over $MgSO_4$. The solvent was removed *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using diethyl ether as eluent to give the *enone* (1.45 g, 31%) as an inseparable 3 : 1 mixture of *syn*- and *anti*-dimethyl diastereoisomers; data for the *syn* isomer, (Found: C, 66.3; H, 8.9. $C_{14}H_{22}O_4$ requires C, 66.1; H, 8.7%); ν_{max} ($CHCl_3$)/cm^{-1} 3398, 2878, 1662, 1459, 1351, 1302, 1139, 980, 946, 908 and 862; δ_H (250 MHz, $CDCl_3$) 6.23 (1H, s, C:C*H*C(O)), 4.80 (1H, dd, *J* 4.4 and 3.5, $CH_2OCHOCH_2$), 4.36 (1H, dd, *J* 17.7 and 1.7, CH:CC*H*HO), 4.27 (1H, dd, *J* 17.7 and 1.7, CH:CCH*H*O), 3.96–3.76 (4H, m, OCH_2CH_2O), 3.18 (1H, br. s, O*H*), 2.32–2.01 (3H, m), 1.71–1.52 (3H, m), 1.38–1.23 (1H, m), 1.03 (3H, s, Me), 0.91 (3H, d, *J* 6.4, Me); δ_C (67.8 MHz, $CDCl_3$) 199.6 (s), 171.1 (s), 123.8 (d), 103.4 (d), 64.8 (t), 64.8 (t), 60.7 (t), 41.7 (t), 40.5 (s), 34.0 (d), 29.0 (t), 28.4 (t), 19.8 (q), 14.6 (q); *m*/*z* (EI) 254.1518 (M^+, $C_{14}H_{22}O_4$ requires 254.1518).

3-(*tert*-Butyldiphenylsilanyloxymethyl)-4-(2-[1,3]dioxolan-2-ylethyl)-4,5-dimethylcyclohex-2-enone 38b

tert-Butyldiphenylchlorosilane (11.26 mL, 43 mmol) was added, over 5 minutes, to a stirred solution of a 3 : 1 mixture of diastereoisomers of the alcohol **38a** (10.0 g, 39 mmol), DMAP (480 mg, 3.9 mmol), and triethylamine (12.07 mL, 86 mmol) in dichloromethane (10 mL), and the mixture was stirred at room temperature for 18 hour. Water (50 mL) was added and the separated aqueous layer was then extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 25% diethyl ether in petroleum ether as eluent to give the TBDPS ether (15.8 g, 82%) as the corresponding mixture of *syn*- and *anti*-dimethyl diastereoisomers; data for *syn* isomer, (Found: C, 73.1; H, 8.4. $C_{30}H_{40}O_4Si$ requires C, 73.1; H, 8.2%); λ_{max} 222 (10040) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2932, 2858, 1660, 1462, 1362, 1303, 1114, 998, 946, 908 and 861; δ_H (400 MHz, $CDCl_3$) 7.69–7.66 (4H, m, Ar), 7.45 (6H, m, Ar), 6.53 (1H, s, C:C*H*C(O)), 4.66 (1H, dd, *J* 4.9 and 3.8, $CH_2OCHOCH_2$), 4.47 (1H, dd, *J* 17.8 and 1.8, CH:CC*H*HO), 4.32 (1H, dd, *J* 17.8 and *J* 1.7, CH:CCH*H*O), 3.91–3.64 (4H, m, OCH_2CH_2O), 2.42–2.06 (3H, m), 1.66–1.39 (3H, m), 1.27–1.14 (1H, m), 1.09 (9H, s, *t*-Bu), 0.92 (3H, s, Me), 0.91 (3H, d, *J* 6.7, Me); δ_C (67.8 MHz, $CDCl_3$) 198.9 (s), 169.2 (s), 135.3 (d), 132.8 (s), 129.7 (d), 127.6 (d), 124.2 (d), 103.6 (d), 64.7 (t), 64.5 (t), 62.0 (t), 41.9 (t), 40.3 (s), 34.1 (d), 28.9 (t), 28.5 (t), 26.6 (q), 19.8 (q), 19.1 (s), 14.6 (q); *m*/*z* (FAB) 493 (M^+ + H, $C_{30}H_{41}O_4Si$ requires 493).

(1*S*,4*S*,5*R*)-3-(*tert*-Butyldiphenylsilanyloxymethyl)-4-(2-[1,3]-dioxolan-2-ylethyl)-4,5-dimethylcyclohex-2-enol 39a

Sodium borohydride (260 mg, 6.9 mmol) was added in one portion to a stirred solution of a 3 : 1 mixture of diastereoisomers of the cyclohexenone **38b** (3.0 g, 6.1 mmol) in dry ether (50 mL) and the resulting suspension was then cooled to 0 °C. Methanol (10 mL) was added dropwise over 10 minutes and the mixture was stirred at 0 °C for 1 hour. Ether (20 mL) and water (30 mL) were added and the separated aqueous phase was then extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (30 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 25% diethyl ether in petroleum ether as eluent to give the β-epimeric *alcohol* **39a** (1.98 g, 66%) as a colourless oil; (Found: C, 72.7; H, 8.8. $C_{30}H_{42}O_4Si$ requires C, 72.8; H, 8.6%); λ_{max} 220 (7380) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2931, 2857, 1960, 1894, 1827, 1661, 1589, 1462, 1428, 1374, 1362, 1112, 998, 984, 945, 907, 863, 835 and 611; δ_H (250 MHz, $CDCl_3$) 7.72–7.68 (4H, m, Ar), 7.46–7.35 (6H, m, Ar), 6.02 (1H, br. s, C:C*H*), 4.63 (1H, dd, *J* 4.7 and 4.4, $CH_2OCHOCH_2$), 4.28 (1H, m, C:CHC*H*O), 4.20 (2H, br. s, HC:CCH_2O), 3.87–3.70 (4H, m, OCH_2CH_2O), 1.87–1.61 (2H, m), 1.58–1.12 (5H, m), 1.09 (9H, s, *t*-Bu), 0.86 (3H, s, Me), 0.85 (3H, d, *J* 7.5, Me); δ_C (67.8 MHz, $CDCl_3$) 143.8 (s), 135.5 (d), 133.6 (s), 129.6 (d), 127.6 (d), 126.9 (d), 104.4 (d), 67.9 (d), 64.7 (t), 62.6 (t), 39.5 (s), 36.9 (t), 32.2 (d), 29.0 (t), 28.5 (t), 26.8 (q), 21.4 (q), 19.2 (s), 15.1 (q); *m*/*z* (FAB) 495 (M^+ + H, $C_{30}H_{43}O_4Si$ requires 495).

Further elution yielded a 1 : 2 mixture of C-5 α- and β-methyl epimers of the α-alcohol (951 mg, 32%) as an oil; ν_{max} (film)/cm^{-1} 3425, 3070, 3048, 2959, 2930, 2857, 1661, 1589, 1472, 1427, 1390, 1361, 1261, 1217, 1141, 1112, 1086, 1029, 942, 900, 822, 757 and 703; δ_H (250 MHz, $CDCl_3$) 7.72–7.66 (4H, m, Ar), 7.46–7.35 (6H, m, Ar), 6.18 and 6.08 (1H, d, *J* 4.8 and br. s respectively, C:C*H*), 4.68–4.61 (1H, m, $CH_2OCHOCH_2$), 4.27–4.12 (3H, m, C:CHC*H*O and HC:CCH_2O), 4.00–3.69 (4H, m, OCH_2CH_2O), 2.04–1.77 (1H, m), 1.68–1.17 (6H, m), 1.07 (9H, s, *t*-Bu), 0.98 and 0.84 (3H, d, *J* 6.8 and d, *J* 7.1 respectively, Me), 0.91 and 0.78 (3H, singlets, Me); δ_C (67.8 MHz, $CDCl_3$) 146.4 (s), 143.1 (s), 135.4 (d), 133.5 (s), 133.4 (s), 129.4 (d), 127.5 (d), 128.8 (d), 128.0 (d), 104.6 (d), 104.3 (d), 67.0 (d), 63.6 (d), 64.6 (t), 64.5 (t), 62.7 (t), 62.6 (t), 39.3 (s), 38.6 (s), 37.6 (t), 35.5 (t), 37.5 (d), 28.0 (d), 30.6 (t), 29.1 (t), 29.0 (t), 28.4 (t), 26.7 (q), 26.3 (q), 20.0 (q), 19.1 (s), 15.9 (q), 14.7 (q); *m*/*z* (CI, *methane*) 477.2824 (M^+−OH, $C_{30}H_{41}O_3Si$ requires 477.2825).

Tetrabutylammonium fluoride hydrate (90 mg, 0.34 mmol) was added in one portion, to a stirred solution of the silylether **39a** (90 mg, 0.18 mmol) in THF (5 mL), and the mixture was stirred at room temperature for 12 hours. Most of the solvent was removed *in vacuo* and the residue was partitioned between ether (10 mL) and water (10 mL). The separated aqueous layer was extracted with ether (3 × 10 mL) and the combined organic extracts were then washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using ethyl acetate as eluent to give the corresponding *diol* **39**, R = R′ = H, (46 mg, 99%) as a colourless oil, which crystallised from diethyl ether–petroleum ether as colourless crystals, mp. 110–112 °C; (Found: C, 65.6; H, 9.6. $C_{14}H_{24}O_4$ requires C, 65.6; H, 9.4%); ν_{max} ($CHCl_3$)/cm^{-1} 3366, 2857, 1461, 1358, 1139, 985, 905 and 861; δ_H (250 MHz, $CDCl_3$) 5.84 (1H, br. s, C:C*H*), 4.82 (1H, dd, *J* 4.7 and 3.9, $CH_2OCHOCH_2$), 4.27 (1H, m, C:CHC*H*O), 4.09 (2H, app. s, HC:CCH_2O), 4.02–3.81 (4H, m, OCH_2CH_2O), 2.47 (1H, br. s, O*H*), 2.16 (1H, br. s, O*H*), 1.84–1.29 (7H, m), 0.95 (3H, s, Me), 0.88 (3H, d, *J* 6.8, Me); δ_C (67.8 MHz, $CDCl_3$) 145.4 (s), 129.2 (d), 104.4 (d), 67.7 (d), 64.9 (t), 62.0 (t), 39.9 (s), 36.7 (t), 32.0 (d), 28.9 (t), 28.5 (t), 21.4 (q), 15.2 (q); *m*/*z* (FAB) 239 (M^+ − OH, $C_{14}H_{23}O_3$ requires 239). The relative stereochemistry assigned to this diol was determined by a single crystal X-ray structure determination.[37]

3-[(1*S*,4*S*,6*R*)-2-(*tert*-Butyldiphenylsilanyloxymethyl)-1,6-dimethyl-4-hydroxycyclohex-2-enyl]propionaldehyde 40a

Camphorsulfonic acid (60 mg, 0.26 mmol) was added in one portion to a stirred solution of the dioxolan **39a** (150 mg, 0.30 mmol) in THF (5 mL). Water (2.5 mL) was added and the mixture was heated at reflux for 4 hours, then cooled to room temperature. The mixture was diluted with water (5 mL) and ether (10 mL) and the separated aqueous layer was extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 33% diethyl

ether in petroleum ether as eluent to give the *aldehyde* (82 mg, 60%) as a colourless oil, which crystallised upon standing, mp. 40–42 °C; (Found: C, 74.3; H, 8.7. $C_{28}H_{38}O_3Si$ requires C, 74.6; H, 8.5%); ν_{max} ($CHCl_3$)/cm^{-1} 2932, 2858, 1721, 1661, 1462, 1362, 1112, 998, 908 and 862; δ_H (250 MHz, $CDCl_3$) 9.50 (1H, br. s, CH_2CHO), 7.71–7.68 (4H, m, Ar), 7.48–7.36 (6H, m, Ar), 6.06 (1H, br. s, C:C*H*), 4.29 (1H, m, C:CHCHO), 4.21 (1H, dt, *J* 14.4 and 1.6, HC:CCHHO), 3.97 (1H, dt, *J* 14.4 and 2.0, CH:CCHHO), 2.20 (1H, m, CH_2CHHCHO), 1.93–1.14 (6H, m), 1.10 (9H, s, *t*-Bu), 0.90 (3H, s, Me), 0.84 (3H, d, *J* 6.8, Me); δ_C (67.8 MHz, $CDCl_3$) 201.6 (d), 142.8 (s), 135.5 (d), 133.2 (s), 133.1 (s), 129.7 (d), 128.3 (d), 127.6 (d), 67.5 (d), 62.5 (t), 39.4 (s), 39.0 (t), 36.7 (t), 32.4 (d), 26.8 (q), 26.7 (t), 21.1 (q), 19.1 (s), 15.1 (q).

tert-Butyl-[(3*S*,5*R*,6*S*)-6-(2-[1,3]dioxolan-2-ylethyl)-5,6-dimethyl-3-methoxymethoxycyclohex-1-enylmethoxy]diphenylsilane 39b

Chloromethyl methyl ether (410 mL, 5.4 mmol) was added in one portion to a stirred solution of the alcohol **39a** (2.4 g, 4.9 mmol) and diisopropylethylamine (950 mL, 5.5 mmol) in dichloromethane (25 mL), and the mixture was stirred at room temperature for 18 hours. Water (10 mL) was added and the mixture was stirred for a further 1 hour, then diluted with water (20 mL) and dichloromethane (25 mL). The separated aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic extracts were then washed with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 25% diethyl ether in petroleum ether as eluent to give the *MOM ether* (2.55 g, 98%) as a colourless oil; λ_{max} 221 (8010) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2931, 2856, 2775, 1960, 1826, 1662, 1589, 1462, 1362, 1112, 998, 979, 949, 904, 863 and 836; δ_H (400 MHz, $CDCl_3$) 7.72–7.64 (4H, m, Ar), 7.44–7.33 (6H, m, Ar), 6.12 (1H, br. s, C:C*H*), 4.76 (2H, s, MeOCH_2O), 4.63 (1H, dd, *J* 4.6 and 4.5, $CH_2OCHOCH_2$), 4.24 (1H, m, C:CHCHO), 4.19 (2H, br. s, HC:CCH_2O), 3.93–3.70 (4H, m, OCH_2CH_2O), 3.41 (3H, s, MeO), 1.86–1.79 (1H, m), 1.77–1.72, (1H, m), 1.65–1.15 (5H, m), 1.09 (9H, s, *t*-Bu), 0.88 (3H, s, Me,), 0.86 (3H, d, *J* 6.9, Me); δ_C (67.8 MHz, $CDCl_3$) 143.9 (s), 135.3 (d), 133.4 (s), 133.3 (s), 129.4 (d), 129.3 (d), 127.8 (d), 127.4 (d), 124.5 (d), 104.2 (d), 94.9 (t), 73.2 (d), 64.5 (t), 64.4 (t), 62.4 (t), 55.0 (q), 39.3 (s), 33.8 (t), 32.2 (d), 28.8 (t), 28.4 (t), 26.6 (q), 21.1 (q), 19.0 (s), 15.0 (q); *m*/*z* (CI, *isobutane*) 539.3158 (M^+ + H, $C_{32}H_{47}O_5Si$ requires 539.3193).

3-[(1*S*,4*S*,6*R*)-2-(*tert*-Butyldiphenylsilanyloxymethyl)-1,6-dimethyl-4-methoxymethoxycyclohex-2-enyl]propionaldehyde 40b

An identical procedure to that described for the synthesis of the aldehyde **40a** was employed using the acetal **39b** (2.50 g, 4.6 mmol), camphorsulfonic acid (1.00 g, 4.3 mmol), THF (30 mL) and water (15 mL). The residue was purified by flash column chromatography on silica using 25% diethyl ether in petroleum ether as eluent to give the *aldehyde* (941 mg, 41%) as a colourless oil; λ_{max} 219 (7950) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2946, 2853, 2824, 2727, 1961, 1894, 1825, 1720, 1662, 1589, 1487, 1462, 1361, 1114, 998, 980, 951, 902, 863, 837, 647 and 609; δ_H (400 MHz, $CDCl_3$) 9.47 (1H, br. s, CH_2CHO), 7.72–7.67 (4H, m, Ar), 7.45–7.35 (6H, m, Ar), 6.13 (1H, br. s, C:C*H*), 4.75 (2H, s, MeOCH_2O), 4.25–4.20 (1H, m, C:CHCHO), 4.18 (1H, dt, *J* 14 and 2.0, HC:CCHHO), 3.96 (1H, dt, *J* 14 and 2.0, CH:CCHHO), 3.41 (3H, s, MeO), 2.22–2.14 (1H, m, CH_2CHHCHO), 1.90–1.79 (2H, m), 1.64–1.46, (4H, m), 1.08 (9H, s, *t*-Bu), 0.90 (3H, s, Me), 0.84 (3H, d, *J* 6.5, Me); δ_C (100 MHz, $CDCl_3$) 201.5 (d), 143.2 (s), 135.5 (d), 133.2 (s), 133.1 (s), 129.9 (d), 129.5 (d), 127.8 (d), 126.1 (d), 95.0 (t), 72.9 (d), 63.3 (t), 55.2 (q), 39.4 (s), 39.1 (t), 33.8 (t), 32.4 (d), 26.8 (q), 26.7 (t), 21.1 (q), 19.2 (s), 15.2 (q); *m*/*z* (CI, *methane*) 493.2746 (M^+ − H, $C_{30}H_{41}O_4Si$ requires 493.2774).

4-[(1*S*,4*S*,6*R*)-2-(*tert*-Butyldiphenylsilanyloxymethyl)-1,6-dimethyl-4-methoxymethoxycyclohex-2-enyl]butan-2-one 41

Methylmagnesium iodide (3.0 M in diethyl ether, 1.1 mL) was added dropwise, over 10 minutes, to a stirred solution of the aldehyde **40b** (1.40 g, 2.8 mmol) in ether (40 mL) at 0 °C. The pale yellow solution was stirred for 1 hour at 0 °C and then allowed to warm to room temperature. A saturated aqueous solution of ammonium chloride solution (5 mL) was added carefully, and the mixture was then diluted with ether (20 mL) and water (30 mL). The separated aqueous layer was extracted with ether (3 × 50 mL) and the combined organic extracts were then washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give *4-[(1S,4S,6R)-2-(tert-butyldiphenylsilanyloxymethyl)-1,6-dimethyl-4-methoxymethoxycyclohex-2-enyl]-butan-2-ol* (1.32 g, 91%) as an inseparable 1 : 1 mixture of diastereoisomers; data for the mixture of diastereoisomers, ν_{max} ($CHCl_3$)/cm^{-1} 2932, 2858, 1602, 1462, 1362, 1143, 1112, 998, 951, 909 and 862; δ_H (250 MHz, $CDCl_3$) 7.74–7.69 (4H, m, Ar), 7.47–7.37 (6H, m, Ar), 6.15 (1H, br. s, C:C*H*), 4.78 (2H, s, MeOCH_2O), 4.32–4.00 (3H, m, C:CHCHO, and HC:CCH_2O), 3.43 (3H, s, MeO), 3.51–3.42 (1H, m, MeCH(OH)CH_2), 1.87–1.71 (2H, m), 1.61–1.17, (5H, m), 1.09 (9H, s, *t*-Bu), 1.01 (3H, d, *J* 6.1, Me), 0.97 (3H, d, *J* 6.2, Me), 0.88 (3H, s, Me), 0.86 (3H, d, *J*6.9, Me), 0.84 (3H, d, *J* 6.8, Me); δ_C (67.8 MHz, $CDCl_3$) 144.2(s), 144.1 (s), 135.5 (d), 135.5 (d), 133.6 (s), 133.4 (s), 133.3 (s), 133.3 (s), 129.6 (d), 127.6 (d), 124.3 (d), 124.1 (d), 95.0 (t), 94.9 (t), 73.3 (d), 68.1 (d), 62.4 (t), 55.1 (q), 39.5 (s), 33.9 (t), 33.7 (t), 33.2 (t), 32.1 (d), 31.1 (t), 26.7 (q), 23.1 (q), 23.0 (q), 22.5 (q), 21.4 (q), 21.4 (q), 19.1 (s), 15.1 (q), 15.0 (q); *m*/*z* (CI, *methane*) 449.2832 (M^+ − OMOM, $C_{29}H_{41}O_2Si$ requires 449.2876).

Dess–Martin periodinane (1.30 g, 3.1 mmol) was added portionwise over 5 minutes, to a stirred solution of a 1 : 1 mixture of diastereoisomers of the alcohol (1.0 g, 2.0 mmol) in dichloromethane (20 mL) and the mixture was stirred at room temperature for 2 hours. A 10% aqueous solution of sodium thiosulfate (10 mL) was added and the mixture was stirred for 30 minutes, then diluted with dichloromethane (30 mL) and a 10% aqueous solution of potassium carbonate (20 mL). The separated aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic extracts were washed with brine (50 mL) and then dried over $MgSO_4$. The solvent was evaporated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 25% diethyl ether in petroleum ether as eluent to give the *ketone* (946 mg, 95%) as a colourless oil; (Found: C, 73.0; H, 8.8. $C_{31}H_{44}O_4Si$ requires C, 73.2; H, 8.7%); λ_{max} 217 (8120) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2931, 2857, 1712, 1589, 1467, 1428, 1361, 1147, 1112, 998, 951, 910, 862 and 836; δ_H (250 MHz, $CDCl_3$) 7.70–7.67 (4H, m, Ar), 7.44–7.37 (6H, m, Ar), 6.14 (1H, br. s, C:C*H*), 4.77 (2H, s, MeOCH_2O), 4.23 (1H, m, C:CHCHO), 4.18 (1H, d, *J* 14.5, HC:CCHHO), 3.96 (1H, d, *J* 14.5, CH:CCHHO), 3.42 (3H, s, MeO), 2.22 (1H, ddd, *J* 17.7, 10.9 and 5.3, MeC(O)CHHCH$_2$), 1.95 (3H, s, MeC(O)CH_2), 1.86–1.79 (1H, m, MeC(O)CHHCH$_2$), 1.67–1.37, (5H, m), 1.08 (9H, s, *t*-Bu), 0.88 (3H, s, Me), 0.84 (3H, d, *J* 6.4, Me); δ_C (67.8 MHz, $CDCl_3$) 208.2 (s), 143.6 (s), 135.5 (d), 133.3 (s),133.2 (s), 129.7 (d), 127.6 (d), 125.5 (d), 95.0 (t), 73.1 (d), 62.5 (t), 55.2 (q), 39.4 (s), 38.5 (t), 33.9 (t), 32.5 (d), 29.8 (q), 28.4 (t), 26.8 (q), 21.2 (q), 19.2 (s), 15.2 (q); *m*/*z* (FAB) 507.2914 (M^+−H, $C_{31}H_{43}O_4Si$ requires 507.2931).

4-Methylhex-4-enoic acid(triphenylphosphonium) bromide 42

Sodium borohydride (1.6 g, 42 mmol) was added to a stirred solution of the methyl 3-methyl-6-oxohex-2-enoate[42] (5.9 g, 38 mmol) in dry ether (100 mL) and the resulting suspension was cooled to 0 °C. Methanol (7 mL) was added in one portion

and the mixture was stirred at 0 °C for 1 hour. Ether (50 mL) and water (50 mL) were added, and the separated aqueous layer was extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine (30 mL) and dried over $MgSO_4$, and then concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the corresponding saturated alcohol (5.6 g, 93%) as a 4 : 1 *E* : *Z* mixture of double bond stereoisomers; data for *E*-isomer, ν_{max} (film)/cm^{-1} 3410, 2949, 2876, 1718, 1648, 1437, 1380, 1362, 1227, 1152, 1063, 1023, 918 and 734; δ_H (250 MHz, $CDCl_3$) 5.66–5.65 (1H, br. s, MeC:C*H*CO_2), 3.63 (3H, s, *Me*O), 3.59 (2H, t, *J* 6.4, CH_2CH_2OH), 2.21–2.17 (2H, m), 2.12 (3H, d, *J* 1.3, *Me*C:$CHCO_2$), 1.74–1.65 (2H, m); δ_C (67.8 MHz, $CDCl_3$) 167.1 (s), 159.9 (s), 115.1 (d), 61.5 (d), 50.7 (q), 36.9 (t), 30.0 (t), 18.6 (q); *m*/*z* (EI) 158.0905 (M^+, $C_8H_{14}O_3$ requires 158.0943).

A solution of triphenylphosphine (11.4 g, 43 mmol) in dichloromethane (25 mL) was added dropwise over 1 hour to a stirred solution of the alcohol (5.6 g, 35 mmol) and tetrabromomethane (21.7 g, 65 mmol) in dichloromethane (75 mL). The resulting pale yellow solution was stirred for 4 hours, after which time the solvent was removed *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 10% diethyl ether in petroleum ether as eluent to give: (i) the *Z*-methyl 6-bromo-3-methylhex-2-enoate (850 mg, 11%), as a colourless oil; ν_{max} (film)/cm^{-1} 2949, 2854, 1716, 1651, 1435, 1378, 1367, 1284, 1223, 1190, 1156, 1070, 1047, 1008, 960, 920, 855, 764, 739 and 642; δ_H (400 MHz, $CDCl_3$) 5.70 (1H, s, MeC:C*H*CO_2), 3.67 (3H, s, *Me*O), 3.43 (2H, t, *J*6.9, CH_2CH_2Br), 2.74 (2H, m, $CH_2CH_2CH_2Br$), 2.03 (2H, m, $CH_2CH_2CH_2Br$), 1.90 (3H, br. s, *Me*C:$CHCO_2$); δ_C (67.8 MHz, $CDCl_3$) 166.1 (s), 158.3 (s), 116.4 (d), 50.5 (q), 32.9 (t), 31.9 (t), 31.1 (t), 24.8 (q); *m*/*z* (EI) 220.0106 (M^+, $C_8H_{13}O_2Br$ requires 220.0099); and (ii) the corresponding *E*-isomer (3.4 g, 44%); (Found: C, 43.6; H, 6.2%. $C_8H_{13}O_2Br$ requires C, 43.5; H, 5.9%); ν_{max} (film)/cm^{-1} 2948, 1718, 1650, 1435, 1385, 1362, 1221 and 1152; δ_H (400 MHz, $CDCl_3$) 5.70–5.68 (1H, br. s, MeC:C*H*CO_2), 3.67 (3H, s, *Me*O), 3.38 (2H, t, *J* 6.55, CH_2CH_2Br), 2.31–2.27 (2H, m), 2.15 (3H, d, *J* 1.3, *Me*C:$CHCO_2$), 2.06–1.98 (2H, m); δ_C (67.8 MHz, $CDCl_3$) 165.9 (s), 157.3 (s), 115.6 (d), 50.1 (q), 38.3 (t), 32.1 (t), 29.7 (t), 17.9 (q); *m*/*z* (EI) 220.0094 (M^+, $C_8H_{13}O_2Br$ requires 220.0099).

Lithium hydroxide monohydrate (1.2 g, 29 mmol) was added in one portion to a stirred mixture of the above *E*-bromo ester (2.7 g, 12 mmol), THF (30 mL) and water (30 mL), and the resulting suspension was stirred at room temperature for 48 hours. Ether (30 mL) was added and the aqueous layer was then adjusted to pH 2.0 using hydrochloric acid (2 M, *ca*. 5 mL). The separated aqueous layer was extracted with ether (3 × 50 mL) and the combined organic extracts were then washed with brine (30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the corresponding *E*-unsaturated carboxylic acid (1.7 g, 67%) as a colourless crystalline solid, mp. 72–74 °C (pentane); (Found: C, 40.7; H, 5.4%. $C_7H_{11}O_2Br$ requires C, 40.6; H, 5.4%); ν_{max} ($CHCl_3$)/cm^{-1} 3180 (br), 2800 (br), 1694, 1645, 1456, 1349, 1299, 1153 and 1114; δ_H (400 MHz, $CDCl_3$) 5.74 (1H, br. s, MeC:C*H*CO_2), 3.40 (2H, t, *J* 6.6, CH_2CH_2Br), 2.36–2.32 (2H, m), 2.18 (3H, d, *J* 1.15, *Me*C:$CHCO_2$), 2.09–1.99 (2H, m); δ_C (100 MHz, $CDCl_3$) 172.3 (s), 161.1 (s), 116.2 (d), 39.3 (t), 32.6 (t), 30.2 (t), 19.1 (q); *m*/*z* (EI) 205.9927 (M^+, $C_7H_{11}O_2Br$ requires 205.9942).

Triphenylphosphine (4.0 g, 15 mmol) was added in one portion to a stirred solution of the aforementioned bromo-acid (1.7 g, 8 mmol) in benzene (40 mL), and the mixture was then heated at reflux for 6 days. Ether (10 mL) was added to the cooled solution and the solid *phosphonium salt* (3.2 g, 83%) was filtered off. Crystallisation from ether/light petrol gave an analytically pure sample of the *phosphonium salt* as colourless crystals, mp. 186–188 °C; (Found: C, 63.7; H, 5.7. $C_{25}H_{26}O_2BrP$ requires C, 64.0; H, 5.6%); λ_{max} 206 (21950) nm; ν_{max} ($CHCl_3$)/cm^{-1} 3260 (br), 2800 (br), 1716, 1649, 1589, 1439, 1368, 1113 and 997; δ_H (400 MHz, $CDCl_3$) 7.86–7.68 (15H, m, Ar), 5.99 (1H, br. s, MeC:C*H*CO_2), 3.77–3.70 (2H, m, CH_2CH_2P), 2.52–2.49 (2H, m), 1.97 (3H, d, *J*0.9, *Me*C:$CHCO_2$), 1.87–1.81 (2H, m); δ_C (67.8 MHz, $CDCl_3$) 168.7 (s), 157.1 (s), 134.8 (d), 133.1 (dd, *J* 11.0), 130.2 (dd, *J* 13.5), 118.1 (s), 116.8 (d), 39.9 (dt, *J* 17.1), 21.5 (td, *J* 51.2), 19.7 (t), 18.4 (q).

(2*E*,6*E*)-9-[(1*S*,4*S*,6*R*)-2-(*tert*-Butyldiphenylsilanyloxymethyl)-1,6-dimethyl-4-methoxymethoxycyclohex-2-enyl]-3,7-dimethyl-nona-2,6-dienoic acid 43

A solution of potassium *bis*(trimethylsilyl)amide (1.6 g, 8 mmol) in THF (2 mL), was added dropwise, over 10 minutes, to a stirred suspension of the phosphonium salt **42** (2.0 g, 4.3 mmol) in THF (20 mL) at 0 °C. The resulting orange solution was stirred at 0 °C for 15 min and then a solution of the ketone **41** (950 mg, 1.87 mmol) in THF (5 mL) was added dropwise over 5 minutes. The solution was stirred at 0 °C for 4 hours, and then allowed to warm to room temperature over 1 hour. The solution was acidified to pH ~2 with hydrochloric acid (2M, 4 mL) and then diluted with ether (25 mL) and water (20 mL). The separated aqueous layer was extracted with ether (3 × 25 mL) and the combined organic extracts were washed with brine (50 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *acid* (821 mg, 71%) as a colourless oil, which solidified upon standing overnight at 0 °C, mp. 79–81 °C; (Found: C, 73.4; H, 9.1. $C_{38}H_{54}O_5Si$ requires C, 73.7; H, 8.8%); ν_{max} ($CHCl_3$)/cm^{-1} 3175 (br), 2800 (br), 2929, 2856, 1713, 1645, 1589, 1462, 1361, 1303, 1112, 951, 901, 864 and 838; δ_H (400 MHz, $CDCl_3$) 7.72–7.69 (4H, m, Ar), 7.45–7.35 (6H, m, Ar), 6.15 (1H, br. s, C:C*H*CHO), 5.64 (1H, br. s, MeC:C*H*CO_2), 4.80–4.74 (1H, m, CH_2MeC:C*H*CH_2), 4.78 (2H, s, MeOCH_2O), 4.27 (1H, m, C:CHC*H*O), 4.19 (1H, br. d, *J* 14.5, HC:CC*H*HO), 4.08 (1H, br. d, *J* 14.5, HC:CCH*H*O), 3.42 (3H, s, *Me*O), 2.14 (3H, d, *J* 1.2, *Me*C:$CHCO_2$), 2.06–2.05 (4H, m), 1.86–1.77 (3H, m), 1.60–1.49 (2H, m), 1.44–1.36 (2H, m), 1.39 (3H, d, *J* 1.1, CH_2*Me*C:$CHCH_2$), 1.07 (9H, s, *t*-Bu), 0.86 (3H, s, Me), 0.85 (3H, obs. d, *J*8, Me); δ_C (67.8 MHz, $CDCl_3$) 171.9 (s), 162.8 (s), 144.4 (s), 136.6 (s), 135.6 (d), 135.5 (d), 133.6 (s), 133.5 (s), 129.6 (d), 127.7 (d), 124.2 (d), 122.4 (d), 114.8 (d), 95.1 (t), 73.5 (d), 62.7 (t), 55.2 (q), 41.1 (t), 39.8 (s), 34.3 (t), 34.1 (t), 32.2 (d), 26.8 (q), 26.0 (t), 21.5 (q), 19.3 (q), 19.1 (s), 15.9 (q), 15.2 (q); *m*/*z* (CI, *ammonia*) 636.4080 ($M^+ + NH_4$, $C_{38}H_{58}O_5NSi$ requires 636.4084).

(2*E*,6*E*)-9-[(1*S*,4*S*,6*R*)-2-(*tert*-Butyldiphenylsilanyloxymethyl)-1,6-dimethyl-4-methoxymethoxycyclohex-2-enyl]-3,7-dimethyl-nona-2,6-dienoic acid methoxymethyl ester 44a

Chloromethyl methyl ether (100 μL, 1.32 mmol) was added, in one portion, to a stirred solution of the acid **43** (620 mg, 1.00 mmol) and diisopropylethylamine (200 μL, 1.15 mmol) in dichloromethane (15 mL) and the mixture was stirred at room temperature for 18 hours. Water (10 mL) was added and the mixture was stirred for 1 hour, then diluted with water (10 mL) and dichloromethane (25 mL). The separated aqueous layer was extracted with dichloromethane (3 × 25 mL) and the combined organic extracts were washed with brine (30 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the MOM *ester* (640 mg, 96%) as a colourless oil; (Found: C, 72.5; H, 8.9. $C_{40}H_{58}O_6Si$ requires C, 72.5; H, 8.8%); λ_{max} 200 (8880) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2932, 2857, 1714, 1644, 1462, 1359, 1129, 1111, 969, 908, 864 and 838; δ_H (400 MHz, $CDCl_3$) 7.71–7.70 (4H, m, Ar), 7.44–7.36 (6H, m, Ar), 6.15 (1H,

br. s, C:C*H*CHO), 5.65 (1H, br. s, MeC:C*H*CO_2), 5.26 (2H, s, CO_2CH_2OMe), 4.79 (1H, m, CH_2MeC:C*H*CH_2), 4.78 (2H, s, MeOCH_2O), 4.27 (1H, m, C:CHC*H*O), 4.20 (1H, br. d, *J* 14.5, HC:CC*H*HO), 4.09 (1H, br. d, *J* 14.5, HC:CCH*H*O), 3.47 (3H, s, *Me*O), 3.42 (3H, s, *Me*O), 2.16 (3H, s, *Me*C:CHCO_2), 2.18–2.05 (4H, m), 1.84–1.79 (3H, m), 1.62–1.37 (4H, m), 1.40 (3H, s, CH_2*Me*C:CHCH_2), 1.08 (9H, s, *t*-Bu), 0.86 (3H, s, Me), 0.85 (3H, obs. d, *J* ~ 7, Me); δ_C (67.8 MHz, $CDCl_3$) 165.9 (s), 161.7 (s), 144.3 (s), 136.5 (s), 135.5 (d), 133.5/133.4 (s), 129.6 (d), 127.6 (d), 124.1 (d), 122.4 (d), 114.9 (d), 95.1 (t), 89.6 (t), 73.4 (d), 62.5 (t), 57.4 (q), 55.2 (q), 40.9 (t), 39.7 (s), 34.2 (t), 34.0 (t), 32.1 (d), 26.7 (q), 25.9 (t), 21.5 (q), 19.2 (s), 19.0 (q), 15.9 (q), 15.1 (q); *m*/*z* (CI, *methane*) 601.3646 (M^+ − OMOM, $C_{38}H_{53}O_4Si$ requires 601.3713).

(2*E*,6*E*)-9-((1*S*,4*S*,6*R*)-1,6-Dimethyl-2-hydroxymethyl-4-methoxymethoxycyclohex-2-enyl)-3,7-dimethylnona-2,6-dienoic acid methoxymethyl ester 44b

Tetrabutylammonium fluoride hydrate (320 mg, 1.22 mmol) was added in one portion to a stirred solution of the silylether **44a** (610 mg, 0.92 mmol) in THF (20 mL) at room temperature, and the mixture was stirred at room temperature for 12 hours. Most of the solvent was removed *in vacuo* and the residue was then partitioned between ether (20 mL) and water (10 mL). The separated aqueous layer was extracted with ether (3 × 10 mL) and the combined organic extracts were then washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the *alcohol* (270 mg, 69%) as a 15 : 1 mixture of the 2*E* and 2*Z* isomers; data for the 2*E*-isomer, λ_{max} 202 (7690) nm; ν_{max} ($CHCl_3$)/cm^{-1} 3527, 2992, 2945, 2845, 1714, 1644, 1462, 1402, 1357, 1325, 1129, 1102, 970, 910 and 836; δ_H (250 MHz, $CDCl_3$) 5.86 (1H, br. s, C:C*H*CHO), 5.69 (1H, br. s, MeC:C*H*CO_2), 5.27 (2H, s, CO_2CH_2OMe,), 5.06 (1H, m, CH_2MeC:C*H*CH_2), 4.75 (1H, d, *J* 6.9, MeOC*H*HO), 4.72 (1H, d, *J* 6.9, MeOCH*H*O), 4.23 (1H, m, C:CHC*H*O), 4.16 (1H, br. d, *J* 14.5, HC:CC*H*HO), 4.04 (1H, br. d, *J*14.5, HC:CCH*H*O), 3.48 (3H, s, *Me*O), 3.40 (3H, s, *Me*O), 2.18 (3H, s, *Me*C:CHCO_2), 2.30–2.13 (4H, m), 1.92–1.75 (3H, m), 1.59 (3H, s, CH_2*Me*C:CHCH_2), 1.67–1.31 (4H, m), 0.97 (3H, s, Me), 0.89 (3H, d, *J* 6.8, Me); δ_C (67.8 MHz, $CDCl_3$) 166.0 (s), 161.6 (s), 146.3 (s), 136.6 (s), 125.4 (d), 122.4 (d), 115.1 (d), 94.9 (t), 89.6 (t), 72.9 (d), 62.1 (t), 57.4 (q), 55.2 (q), 40.9 (t), 40.0 (s), 34.2 (t), 34.1 (t), 33.8 (t), 31.8 (d), 25.7 (t), 21.5 (q), 18.9 (q), 16.1 (q), 15.2 (q); *m*/*z* (CI, *methane*) 363.2518 (M^+ − OMOM, $C_{22}H_{35}O_4$ requires 363.2535).

(2*E*,6*E*)-9-((1*S*,4*S*,6*R*)-1,6-Dimethyl-2-formyl-4-methoxymethoxycyclohex-2-enyl)-3,7-dimethylnona-2,6-dienoic acid methoxymethyl ester 45a

Dess–Martin periodinane (300 mg, 0.71 mmol) was added portionwise over 5 minutes to a stirred solution of a 15 : 1 mixture of the 2*E* and 2*Z* isomers of the alcohol **44b** (260 mg, 0.61 mmol) in dichloromethane (10 mL), and the mixture was stirred at room temperature for 30 minutes. The mixture was diluted with dichloromethane (10 mL) and a 10% aqueous solution of potassium carbonate (5 mL) and the separated aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), then dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *aldehyde* (220 mg, 85%) as a 15 : 1 mixture of the 2*E* and 2*Z* isomers; data for the 2*E*-isomer, λ_{max} 215 (9290) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2944, 2844, 2778, 2725, 1714, 1691, 1644, 1449, 1402, 1374, 1359, 1324, 1130, 1099, 968, 912 and 863; δ_H (400 MHz, $CDCl_3$) 9.33 (1H, d, *J* 1.5, CH:CC*H*O), 6.59 (1H, br. s, C:C*H*CHO), 5.60 (1H, br. s, MeC:C*H*CO_2), 5.17 (2H, s, CO_2CH_2OMe), 4.93 (1H, m, CH_2MeC:C*H*CH_2), 4.70 (1H, d, *J*6.9, MeOC*H*HO), 4.66 (1H, d, *J* 6.9, MeOCH*H*O), 4.32–4.28 (1H, m, C:CHC*H*O), 3.38 (3H, s, *Me*O), 3.34 (3H, s, *Me*O), 2.09 (3H, s, *Me*C:CHCO_2), 2.24–1.92 (4H, m), 1.83–1.63 (3H, m), 1.46 (3H, s, CH_2*Me*C:CHCH_2), 1.55–1.20 (4H, m), 0.96 (3H, s, Me), 0.84 (3H, d, *J* 5.6, Me); δ_C (100 MHz, $CDCl_3$) 194.0 (d), 165.7 (s), 161.4 (s), 153.8 (d), 147.4 (s), 136.2 (s), 122.4 (d), 114.9 (d), 95.1 (t), 89.3 (t), 72.6 (d), 57.1 (q), 55.2 (q), 40.7 (t), 39.3 (s), 34.6 (t), 32.9 (t), 32.3 (t), 31.7 (d), 25.6 (t), 20.0 (q), 18.7 (q), 15.8 (q), 14.7 (q); *m*/*z* (FAB) 299 (M^+ + H− 2 × HOMOM, $C_{20}H_{27}O_2$ requires 299).

(3*S*,5*R*,6*S*)-5,6-Dimethyl-3-methoxymethoxy-6-((3*E*,7*E*)-8-methoxymethoxycarbonyl-3,7-dimethylocta-3,7-dienyl)cyclohex-1-enecarboxylic acid 45b

A solution of sodium chlorite (600 mg, 6.6 mmol) and sodium dihydrogen orthophosphate (600 mg, 5.0 mmol) in water (5 mL), was added in one portion to a stirred solution of a 15 : 1 mixture of the 2*E* and 2*Z* isomers of the aldehyde **45a** (215 mg, 0.51 mmol), 2-methyl-2-butene (2.5 mL) and *tert*-butanol (12.5 mL) and the resulting pale yellow mixture was stirred at room temperature for 4 hours. The mixture was concentrated *in vacuo* and the residue was then partitioned between water (10 mL) and ether (20 mL). The separated aqueous extract was extracted with ether (3 × 25 mL), and the combined organic extracts were then washed with brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the *acid* (215 mg, 96%) as a 15 : 1 mixture of the 7*E* and 7*Z* isomers; data for the 7*E*-isomer, λ_{max} 221 (9070) nm; ν_{max} ($CHCl_3$)/cm^{-1} 3200 (br), 2800 (br), 2944, 2847, 1711, 1644, 1457, 1359, 1324, 1130, 1089, 969, 911 and 864; δ_H (400 MHz, $CDCl_3$) 6.89 (1H, br. s, C:C*H*CHO), 5.61 (1H, br. s, MeC:C*H*CO_2), 5.18 (2H, s, CO_2CH_2OMe), 4.96 (1H, m, CH_2MeC:C*H*CH_2), 4.68 (1H, d, *J* 6.9, MeOC*H*HO), 4.65 (1H, d, *J* 6.9, MeOCH*H*O), 4.21 (1H, m, C:CHC*H*O), 3.39 (3H, s, *Me*O), 3.33 (3H, s, *Me*O), 2.09 (3H, s, *Me*C:CHCO_2), 2.14–1.95 (4H, m), 1.88–1.61 (3H, m), 1.48 (3H, s, CH_2*Me*C:CHCH_2), 1.59–1.36 (4H, m), 1.08 (3H, s, Me), 0.86 (3H, d, *J* 6.7, Me); δ_C (100 MHz, $CDCl_3$) 171.6 (s), 165.8 (s), 161.5 (s), 142.8 (d), 138.3 (s), 136.3 (s), 122.4 (d), 114.9 (d), 94.8 (t), 89.4 (t), 72.1 (d), 57.1 (q), 55.1 (q), 40.7 (t), 39.8 (s), 34.6 (t), 33.6 (t), 32.8 (t), 31.9 (d), 25.7 (t), 20.6 (q), 18.8 (q), 15.7 (q), 15.3 (q); *m*/*z* (CI, *methane*) 377.2309 (M^+ − OMOM, $C_{22}H_{33}O_5$ requires 377.2328).

(3*S*,5*R*,6*S*)-5,6-Dimethyl-3-methoxymethoxy-6-((3*E*,7*E*)-8-methoxymethoxycarbonyl-3,7-dimethylocta-3,7-dienyl)cyclohex-1-enecarboxylic acid methyl ester 45c

Methyl iodide (200 μL, 3.21 mmol) was added in one portion, to a stirred suspension of a 15 : 1 mixture of the 7*E* and 7*Z* isomers of the acid **45b** (215 mg, 0.49 mmol) and potassium carbonate (200 mg, 1.45 mmol) in acetone (10 mL), and the resulting mixture was stirred at room temperature for 12 hours. Most of the solvent was removed *in vacuo* and the residue was then partitioned between ether (20 mL) and water (10 mL). The separated aqueous layer was extracted with ether (3 × 20 mL) and the combined organic extracts were then washed with brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 25% diethyl ether in petroleum ether as eluent to give the *ester* (180 mg, 81%) as a 15 : 1 mixture of the 7*E* and 7*Z* isomers; data for the 7*E*-isomer, (Found: C, 66.4; H, 9.0%. $C_{25}H_{40}O_7$ requires C, 66.4; H, 8.9%); λ_{max} 218 (10050) nm; ν_{max} ($CHCl_3$)/cm^{-1} 2948, 2846, 1713, 1644, 1459, 1358, 1324, 1130, 1107, 986, 912 and 864; δ_H (400 MHz, $CDCl_3$) 6.69 (1H, br. s, C:C*H*CHO), 5.63 (1H, br. s, MeC:C*H*CO_2), 5.20 (2H, s, CO_2CH_2OMe), 4.96 (1H, m, CH_2MeC:C*H*CH_2), 4.68 (1H, d, *J* 6.8, MeOC*H*HO), 4.65 (2H, d, *J* 6.8, MeOCH*H*O),

4.20 (1H, m, C:CHC*H*O), 3.66 (3H, s, *Me*O), 3.41 (3H, s, *Me*O), 3.34 (3H, s, *Me*O), 2.12 (3H, s, *Me*C:CHCO$_2$), 2.18–2.06 (4H, m), 1.99–1.74 (3H, m), 1.49 (3H, s, CH$_2$*Me*C:CHCH$_2$), 1.61–1.40 (4H, m), 1.10 (3H, s, Me), 0.87 (3H, d, *J* 6.7, Me); δ_C (100 MHz, CDCl$_3$) 167.4 (s), 165.8 (s), 161.5 (s), 140.3 (d), 139.3 (s), 136.4 (s), 122.4 (d), 114.9 (d), 94.9 (t), 89.4 (t), 72.1 (d), 57.2 (q), 55.2 (q), 51.3 (q), 40.8 (t), 40.0 (s), 34.6 (t), 33.8 (t), 33.0 (t), 31.9 (d), 25.8 (t), 20.9 (q), 18.8 (q), 15.8 (q), 15.4 (q); *m*/*z* (CI, *methane*) 391.2463 (M$^+$ − OMOM, $C_{23}H_{35}O_5$ requires 391.2485).

(3*S*,5*R*,6*S*)-6-((3*E*,7*E*)-8-Carboxy-3,7-dimethylocta-3,7-dienyl)-5,6-dimethyl-3-methoxymethoxycyclohex-1-enecarboxylic acid methyl ester 46

p-Toluenesulfonic acid monohydrate (15 mg, 0.08 mmol) was added in one portion to a stirred solution of a 15 : 1 mixture of the 7*E* and 7*Z* isomers of the ester **45c** (60 mg, 0.13 mmol) in THF (5 mL). Water (2.5 mL) was added and the mixture was heated at reflux for 12 hours, and then cooled to room temperature. The mixture was diluted with water (5 mL) and ether (10 mL) and the separated aqueous layer was extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), then dried over MgSO$_4$, and concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *acid* (39 mg, 72%) as a 15 : 1 mixture of the 7*E* and 7*Z* isomers; data for the 7*E*-isomer, λ_{max} 216 (6094) nm; ν_{max} (CHCl$_3$)/cm^{-1} 3200 (br), 2800 (br), 2949, 2855, 1713, 1643, 1459, 1663, 1300, 1146, 1110, 959, 910, 865 and 650; δ_H (270 MHz, CDCl$_3$) 6.74 (1H, br. s, C:C*H*CHO), 5.67 (1H, br. s, MeC:C*H*CO$_2$), 5.01 (1H, m, CH$_2$MeC:C*H*CH$_2$), 4.75 (1H, d, *J*6.9, MeOC*H*HO), 4.64 (1H, d, *J* 6.9, MeOC*H*HO), 4.26 (1H, ddd, *J* 10.2, 6 and 2, C:CHC*H*O), 3.71 (3H, s, *Me*O), 3.40 (3H, s, *Me*O), 2.16 (3H, d, *J* 1.3, *Me*C:CHCO$_2$), 2.22–2.11 (4H, m), 2.06–1.71 (4H, m), 1.54 (3H, d, *J* 1.3, CH$_2$*Me*C:CHCH$_2$), 1.61–1.46 (3H, m), 1.15 (3H, s, Me), 0.92 (3H, d, *J*6.6, Me); δ_C (67.8 MHz, CDCl$_3$) 171.8 (s), 167.6 (s), 162.8 (s), 140.4 (d), 139.5 (s), 136.6 (s), 122.4 (d), 115.1 (d), 95.0 (t), 72.3 (d), 55.3 (q), 51.5 (q), 41.1 (t), 40.2 (s), 34.7 (t), 33.9 (t), 33.1 (t), 32.0 (d), 25.9 (t), 21.0 (q), 19.1 (q), 15.9 (q), 15.5 (q); *m*/*z* (FAB) 409.2560 (M$^+$ + H, $C_{23}H_{37}O_6$ requires 409.2590).

(3*S*,5*R*,6*S*)-6-((3*E*,7*E*)-3,7-Dimethyl-8-phenylselanylcarbonylocta-3,7-dienyl)-5,6-dimethyl-3-methoxymethoxycyclohex-1-enecarboxylic acid methyl ester 47

N-Phenylselenophthalimide (23 mg, 0.08 mmol) was added in one portion to stirred solution of a 15 : 1 mixture of the 7*E* and 7*Z* isomers of the carboxylic acid **46** (20 mg, 0.05 mmol) and tributylphosphine (25 mL, 8.10 mmol) in dichloromethane (20 mL) at −20 °C and the mixture was stirred at −20 °C for 1.5 hours. Water (5 mL) and dichloromethane (5 mL) were added, and the mixture was then allowed to warm to room temperature. The separated organic layer was washed with water (2 × 5 mL), potassium carbonate (2 × 5 mL) (10% aqueous) and brine (5 mL), and then dried over MgSO$_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 11% diethyl ether in petroleum ether as eluent to give the *selenol ester* (20 mg, 74%) as a 15 : 1 mixture of the 7*E* and 7*Z* isomers; data for the 7*E*-isomer, λ_{max} 202 (1170) nm; ν_{max} (CHCl$_3$)/cm^{-1} 2948, 2848, 1711, 1614, 1457, 1361, 1266, 1147, 1108, 984, 909 and 832; δ_H (400 MHz, CDCl$_3$) 7.56–7.52 (2H, m, Ar), 7.41–7.37 (3H, m, Ar), 6.76 (1H, br. s, C:C*H*CHO), 6.09 (1H, br. s, MeC:C*H*COSe), 5.02 (1H, m, CH$_2$MeC:C*H*CH$_2$), 4.75 (1H, d, *J*6.9, MeOC*H*HO), 4.72 (1H, d, *J*6.9, MeOC*H*HO), 4.28 (1H, ddd, *J* 10.1, 6 and 2, C:CHC*H*O), 3.73 (3H, s, *Me*O), 3.41 (3H, s, *Me*O), 2.08 (3H, d, *J* 1.2, *Me*C:CHCOSe), 2.18–2.07 (4H, m), 1.89–1.81 (4H, m), 1.56 (3H, s, CH$_2$*Me*C:CHCH$_2$), 1.57–1.45 (3H, m), 1.18 (3H, s, Me), 0.95 (3H, d, *J* 6.8, Me,); δ_C (67.8 MHz, CDCl$_3$) 189.5 (s), 167.6 (s), 157.9 (s), 139.5 (s), 138.4 (d), 136.9 (s), 135.8 (d), 129.2 (d), 128.6 (d), 127.2 (s), 124.4 (d), 122.4 (d), 95.0 (t), 72.3 (d), 55.4 (q), 51.5 (q), 40.7 (t), 40.2 (s), 34.8 (t), 34.0 (t), 33.1 (t), 32.1 (d), 25.8 (t), 21.0 (q), 20.4 (q), 16.0 (q), 15.6 (q).

5,6-Dimethyl-3-methoxymethoxy-6-[3-(4-methyl-2-oxocyclohex-3-enyl)butyl]-cyclohex-1-enecarboxylic acid methyl ester 52

AIBN (2 mg, 0.1 eq) was added in one portion, under an atmosphere of argon, to a stirred solution of the selenol ester **47** (20 mg, 0.04 mmol) in dry, argon degassed benzene (11 mL), and the resulting solution was heated at reflux. Tributyltin hydride (10 μL, 0.04 mmol) was added in one portion and the solution was then heated at reflux for 1.5 hours. The mixture was cooled to room temperature, and then concentrated *in vacuo* to leave a residue. The residue was purified by flash column chromatography on silica using 33% diethyl ether in petroleum ether as eluent to give the *cyclohexenone* (10 mg, 70%) as a mixture of 4 diastereoisomers; data for the mixture of diastereoisomers, λ_{max} 228 (15200) nm; ν_{max} (CHCl$_3$)/cm^{-1} 2951, 1712, 1658, 1458, 1380, 1145, 1108, 960 and 912; δ_H (400 MHz, CDCl$_3$) 6.76/6.73/6.70 (1H, br. s, C:C*H*CHO), 5.85/5.83/5.80 (1H, br. s, MeC:C*H*CO), 4.75–4.69 (2H, m, MeOCH_2O), 4.29–4.21 (1H, m, C:CHC*H*O), 3.74/3.71 (3H, s, *Me*O), 3.40/3.39 (3H, s, *Me*O), 2.29–2.26 (2H, m), 1.95/1.93/1.92 (3H, s, *Me*C:CHCO), 2.20–1.66 (8H, m), 1.55–1.23 (3H, m), 1.16/1.15 (3H, s, Me), 0.91/0.76 (3H, d, *J* 6.8, Me), 0.86/0.73 (3H, d, *J* 6.7, Me); δ_C (100 MHz, CDCl$_3$) 200.9 (s), 167.8/167.7 (s), 161.1/160.9/160.4 (s), 140.7/140.2/140.0/139.9 (d), 127.1/126.9 (d), 95.0 (t), 72.3 (d), 55.4 (q), 51.5/51.4 (q), 51.1/50.9/50.2/48.9 (d), 40.2 (s), 33.1 (t), 32.1/32.0 (d), 31.4/31.1/31.0 (d), 30.9/30.7 (t), 30.3/29.7/29.5 (t), 28.8/28.3/27.7 (t), 24.1 (q), 23.9/23.3/22.4/22.2 (t), 21.1, 17.4/17.2/15.5 (q); *m*/*z* (FAB) 393.2655 (M$^+$ + H, $C_{23}H_{37}O_5$ requires 393.2641).

(5*R*,6*S*)-2-Bromo-6-(2-[1,3]dioxolan-2-ylethyl)-5,6-dimethyl-3-ethoxycyclohex-2-enone 53

N-Bromosuccinimide (7.7 g, 43.3 mmol) was added portionwise over 5 minutes to a stirred solution of a 3 : 1 mixture of diastereoisomers of the vinylogous ester **35** (11.6 g, 43.3 mmol) in carbon tetrachloride (110 mL) at room temperature and the resulting suspension was then stirred at room temperature in the dark for 4.5 hours. The suspension was filtered and the residue was then washed with carbon tetrachloride (20 mL). The filtrate was concentrated *in vacuo* to leave a yellow oil which was purified by flash column chromatography on silica using 66% diethyl ether in petroleum ether as eluent to give the *bromide* (10.2 g, 68%) as a 3 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a colourless oil. The mixture was stirred in diethyl ether (100 mL) for 1 hour, and filtration gave the *anti*-epimer (2.01 g) as a colourless solid, mp. 148–150 °C; (Found %: C, 51.8; H, 6.8. $C_{15}H_{23}BrO_4$ requires C, 51.9; H, 6.7%); δ_H (360 MHz, CDCl$_3$) 4.81–4.79 (1H, m, OC*H*O), 4.23–4.14 (2H, m, OCH_2CH$_3$), 3.96–3.89 (2H, m, OCH_2CH$_2$O), 3.87–3.81 (2H, m, OCH$_2$CH_2O), 2.67 (1H, dd, *J* 18.0 and 5.2, :CC*H*(H)), 2.14–2.08 (1H, m), 1.64–1.56 (3H, m), 1.50–1.47 (2H, m), 1.44 (3H, t, *J* 7.0, OCH$_2$CH_3), 1.18 (3H, s, CCH_3), 1.08 (3H, d, *J* 6.9, CHCH_3); δ_C (90 MHz, CDCl$_3$) 195.3 (s), 169.4 (s), 104.5 (d), 101.7 (s), 64.8 (t), 64.7 (t), 47.4 (s), 36.7 (d), 32.6 (t), 28.2 (t), 24.9 (t), 20.3 (q), 15.3 (q), 15.1 (q); *m*/*z* (EI) 346.0780 (M$^+$, $C_{15}H_{23}BrO_4$ requires 346.0780). The filtrate was concentrated *in vacuo* to leave a residue which crystallised from ether–petrol to give the *syn*-epimer (8.1 g) as a colourless solid, mp. 80–83 °C; (Found: C, 51.8; H, 6.9; Br, 23.5. $C_{15}H_{23}BrO_4$ requires C, 51.9; H, 6.7; Br, 23.0%); λ_{max} (EtOH)/nm (ε) 274 (14,500); ν_{max} (CHCl$_3$)/cm^{-1} 1660 and 1592; δ_H (500 MHz, CDCl$_3$) 4.80 (1H, dd, *J* 5.2 and 4.3, OC*H*O), 4.23–4.12 (2H, m, OCH_2CH$_3$), 3.93–3.88 (2H, m, OCH_2CH$_2$O), 3.84–3.79 (2H, m, OCH$_2$-

CH_2O), 2.72 (1H, dd, *J* 17.7 and 4.9, :CC*H*(H)), 2.40 (1H, dd, *J* 17.7 and 9.4, :CC(H)*H*), 2.23–2.18 (1H, m), 2.07–2.02 (1H, m), 1.56–1.39 (3H, m), 1.41 (3H, t, *J* 7.0, OCH_2CH_3), 1.01 (3H, d, *J* 6.9, $CHCH_3$), 0.97 (3H, s, CCH_3); δ_C (125 MHz, $CDCl_3$) 195.3 (s), 169.7 (s), 104.4 (d), 102.2 (s), 64.7 (t), 48.0 (s), 32.3 (t), 32.2 (d), 29.6 (t), 28.4 (t), 18.5 (q), 15.0 (q), 14.8 (q); *m*/*z* (EI) 346.0764 (M^+, $C_{15}H_{23}BrO_4$ requires 346.0780).

(*E*)-6-(*tert*-Butyldimethylsilanyloxy)-3-methylhex-2-enal 54

The enal was prepared according to the methods of Danheiser and Marshall and their respective co-workers.[27] *tert*-Butyldimethylsilyl chloride (6.7 g, 45 mmol) was added in one portion to a stirred solution of 1-acetoxy-6-hydroxy-3-methylhex-2(*E*)-ene (7.0 g, 41 mmol), triethylamine (6.2 mL, 45 mmol) and DMAP (0.27 g, 2.2 mmol) in dichloromethane (100 mL) at 0 °C and the resulting solution was allowed to warm to room temperature and then stirred overnight. The mixture was diluted with dichloromethane (200 mL), then washed with a saturated aqueous solution of sodium hydrogencarbonate (200 mL) and then with a saturated aqueous solution of ammonium chloride (200 mL). The separated organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to leave the corresponding silyl ether (11.6 g, 99%) as a pale yellow oil; ν_{max} (film)/cm^{-1} 1740, 1234, 1102 and 836; δ_H (250 MHz, $CDCl_3$) 5.35 (1H, m, :C*H*), 4.58 (2H, d, *J* 7.2, CH_2OAc), 3.59 (2H, t, *J* 6.4, $TBSOCH_2$), 2.11–2.03 (2H, m, CH_2C:), 2.05 (3H, s, $COCH_3$), 1.70 (3H, br, s, :CCH_3), 1.67–1.58 (2H, m, $TBSOCH_2CH_2$), 0.89 (9H, s, $C(CH_3)_3$), 0.04 (6H, s, $Si(CH_3)_2$); δ_C (67.8 MHz, $CDCl_3$) 171.0 (s), 141.9 (s), 118.2 (d), 62.4 (t), 61.2 (t), 35.6 (t), 30.6 (t), 25.8 (q), 20.9 (q), 16.3 (q), −5.4 (q); *m*/*z* (EI) 229.1257 (M^+ − *t*Bu, $C_{11}H_{21}O_3Si$ requires 229.1260), which was used without further purification.

Potassium carbonate (11.3 g, 82 mmol) was added in one portion to a solution of the silyl ether acetate (11.6 g, 41 mmol) in methanol (150 mL) at room temperature and the resulting suspension was then stirred at room temperature for 1 hour. The solvent was removed *in vacuo* to leave a residue which was partitioned between water (200 mL) and ether (200 mL). The separated aqueous phase was extracted with ether (200 mL) and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave the *(E)-6-(tert-butyldimethylsilanyloxy)-3-methylhex-2-en-1-ol* (9.8 g, 99%) as a pale yellow oil; ν_{max} (film)/cm^{-1} 3354, 1255, 1101, 836 and 775; δ_H (400 MHz, $CDCl_3$) 5.44–5.40 (1H, m, :C*H*), 4.15 (2H, d, *J* 6.9, CH_2OH), 3.60 (2H, t, *J* 6.4, $TBSOCH_2$), 2.07 (2H, t, *J* 7.8, :CCH_2), 1.68 (3H, s, :CCH_3), 1.68–1.61 (2H, m, $TBSOCH_2CH_2$), 0.90 (9H, s, $C(CH_3)_3$), 0.05 (6H, s, $Si(CH_3)_2$); δ_C (67.8 MHz, $CDCl_3$) 139.2 (s), 123.3 (d), 62.7 (t), 59.2 (t), 35.7 (t), 30.8 (t), 25.9 (q), 18.2 (s), 16.2 (q), −5.4 (q); *m*/*z* (EI) 169.1049 (M^+ − *t*Bu − H_2O, $C_9H_{17}OSi$ requires 169.1049), which was used without further purification.

Manganese dioxide (10.0 g, 110 mmol) was added in one portion to a stirred solution of the above alcohol (2.0 g, 8 mmol) in dichloromethane (20 mL) at room temperature and the mixture was then stirred at room temperature for 2 hours. The mixture was filtered through Celite and the residue was then washed exhaustively with dichloromethane (5 × 10 mL). The solvent was evaporated *in vacuo* to leave a residue which was purified by flash column chromatography on silica using 5% diethyl ether in petroleum ether as eluent to give the aldehyde (1.5 g, 74%) as a colourless oil; λ_{max} (EtOH)/nm (ε) 237 (13,300); ν_{max} (film)/cm^{-1} 1676, 1104, 836 and 776; δ_H (250 MHz, $CDCl_3$) 10.05 (1H, d, *J* 8.1, C*H*O), 5.95 (1H, br. d, *J* 8.1, :C*H*), 3.69 (2H, t, *J* 6.1, $TBSOCH_2$), 2.34 (2H, t, *J* 7.2, :CCH_2), 2.23 (3H, d, *J* 1.0, :CCH_3), 1.83–1.72 (2H, m, $TBSOCH_2CH_2$), 0.95 (9H, s, $C(CH_3)_3$), 0.10 (6H, s, $Si(CH_3)_2$); δ_C (67.8 MHz, $CDCl_3$) 191.2 (d), 163.9 (s), 127.2 (d), 62.1 (t), 37.0 (t), 30.2 (t), 25.8 (q), 18.2 (s), 17.5 (q), −5.4 (q); *m*/*z* (CI) 241.1636 (M^+ − H, $C_{13}H_{25}O_2Si$ requires 241.1624).

2-[(*E*)-6-(*tert*-Butyldimethylsilanyloxy)-1-hydroxy-3-methylhex-2-enyl]-6-(2-[1,3]dioxolan-2-ylethyl)-5,6-dimethyl-3-ethoxycyclohex-2-enone 55a

A solution of *tert*-butyllithium (1.7 M in pentane, 9.8 mL, 17 mmol) was added dropwise over 5 minutes to a stirred solution of the *syn*-dimethyl bromide **53** (2.9 g, 8.3 mmol) in THF (170 mL) at −90 °C and the resulting orange solution was then stirred at −78 °C for 1 hour. The aldehyde **54** (4.0 g, 16.5 mmol) was added in one portion and the resulting pale yellow solution was then stirred at −78 °C for 1 hour. Water (10 mL) was added and the mixture was then allowed to warm to room temperature. The mixture was poured into water (160 mL) and then extracted with ether (170 mL, 100 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 0.5% triethylamine and 66% diethyl ether in petroleum ether as eluent to give the *allylic alcohol* (2.8 g, 67%) as an inseparable 1 : 1 mixture of secondary alcohol epimers, as a pale yellow oil; data for the mixture of diastereoisomers, λ_{max} (EtOH)/nm (ε) 205 (8,500), 270 (12,800); ν_{max} (film)/cm^{-1} 3484, 1661, 1607, 1377, 1224, 1106, 1029, 836 and 776; δ_H (500 MHz, $CDCl_3$) 5.48–5.38 (2H, m, :C*H* and C*H*OH), 4.80 (1H, dd, *J* 9.2 and 4.6, OC*H*O), 4.48 (1H, d, *J* 10.4, O*H*), 4.25–3.96 (2H, m, OCH_2CH_3), 3.94–3.88 (2H, m, OCH_2CH_2O), 3.84–3.79 (2H, m, OCH_2CH_2O), 3.56–3.51 (2H, m, CH_2OTBS), 2.60 (0.5H, dd, *J* 7.0 and 4.7), 2.56 (0.5H, dd, *J* 7.3 and 4.6), 2.31–2.07 (2H, m), 1.97–1.94 (3H, m), 1.69 (1.5H, s, :CCH_3), 1.68 (1.5H, s, :CCH'_3), 1.64–1.36 (6H, m), 1.34 (1.5H, t, *J* 6.8, OCH_2CH_3), 1.32 (1.5H, t, *J* 6.8, $OCH_2CH'_3$), 1.02–1.00 (1H, m), 0.98 (1.5H, d, *J* 7.1, $CHCH_3$), 0.96 (1.5H, d, *J* 5.2, $CHCH'_3$), 0.93 (1.5H, s, CCH_3), 0.90 (1.5H, s, CCH'_3), 0.86 (9H, 2 × s, $C(CH_3)_3$ and $C(CH'_3)_3$), 0.01 (6H, 2 × s, $Si(CH_3)_2$) and $Si(CH'_3)_2$); δ_C (125 MHz, $CDCl_3$) 204.6 (s), 168.9 (s), 168.7 (s), 136.0 (s), 126.8 (d), 126.2 (d), 118.6 (s), 118.4 (s), 104.6 (d), 104.6 (d), 64.7 (t), 64.3 (d), 64.1 (d), 63.6 (t), 63.5 (t), 62.9 (t), 62.9 (t), 46.5 (t), 46.3 (s), 35.7 (t), 32.4 (d), 32.3 (d), 32.2 (d), 31.8 (d), 30.9 (t), 30.4 (t), 30.4 (t), 29.6 (t), 29.0 (t), 28.7 (t), 28.4 (t), 28.36 (t), 28.3 (t), 25.9 (q), 18.5 (q), 18.4 (q), 18.2 (q), 18.1 (q), 16.3 (q), 16.3 (q), 15.1 (q), 15.0 (q), 14.95 (q), 14.9 (q), −5.4 (q); *m*/*z* (FAB) 509.3282 (M^+ − H, $C_{28}H_{49}O_6Si$ requires 509.3298).

2-[(*E*)-6-(*tert*-Butyldimethylsilanyloxy)-1-methoxymethoxy-3-methylhex-2-enyl]-6-(2-[1,3]dioxolan-2-ylethyl)-5,6-dimethyl-3-ethoxycyclohex-2-enone 55b

Chloromethylmethyl ether (1.3 mL, 17 mmol) was added dropwise over *ca*. 1 minute to a stirred solution of a 1 : 1 mixture of diastereoisomers of the allylic alcohol **55a** (2.84 g, 5.6 mmol) and diisopropylethylamine (5.8 mL, 33 mmol) in dichloromethane (65 mL) at room temperature and the resulting yellow solution was then heated under reflux for 12 hours. The mixture was allowed to cool to room temperature and then poured into a saturated aqueous solution of sodium hydrogencarbonate (60 mL). The organic layer was separated and the aqueous layer was then extracted with dichloromethane (30 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 66% diethyl ether in petroleum ether as eluent to give the *MOM ether* (2.74 g, 89%) as a corresponding mixture of diastereoisomers, as a colourless oil; data for the mixture of diastereoisomers, ν_{max} (film)/cm^{-1} 1650, 1611, 1378, 1096, 1038, 836 and 776; δ_H (500 MHz, $CDCl_3$) 5.74–5.71 (1H, m, :C*H*), 5.66 (0.5H, d, *J* 8.5, C*H*OMOM), 5.65 (0.5H, d, *J* 8.5, C*H*′OMOM), 4.80 (1H, dd, *J* 4.7 and 4.7, OC*H*O), 4.59 (0.5H, d, *J* 6.5, OC*H*-(H)O), 4.58 (0.5H, d, *J* 6.5, OC*H*′(H)O), 4.51 (0.5H, d, *J* 6.5, OC(H)*H*O), 4.50 (0.5H, d, *J* 6.5, OC(H)*H*′O), 4.20–4.00 (2H, m, OCH_2CH_3), 3.93–3.88 (2H, m, OCH_2CH_2O), 3.84–3.77 (2H,

m, OCH_2CH_2O), 3.55 (2H, br. t, *J* 6.1, $TBSOCH_2$), 3.29 (3H, s, OCH_3), 2.62 (0.5H, dd, *J* 11.4 and 5.0, :CC*H*(H)), 2.59 (0.5H, dd, *J* 11.3 and 4.9, :CC*H′* (H)), 2.28 (1H, m, :CC(H)*H*), 2.15–2.09 (1H, m), 2.00–1.97 (3H, m, $:CCH_2$), 1.60 (3H, s, $:CCH_3$), 1.62–1.38 (6H, m), 1.35 (3H, t, *J* 7.0, OCH_2CH_3), 0.97 (1.5H, d, *J* 6.8, $CHCH_3$), 0.97 (1.5H, d, *J* 6.7, $CHCH'_3$), 0.91 (3H, s, CCH_3), 0.86 (9H, s, $C(CH_3)_3$), 0.01 (6H, s, $Si(CH_3)_2$); δ_C (125 MHz, $CDCl_3$) 200.6 (s), 170.4 (s), 170.4 (s), 137.0 (s), 136.8 (s), 124.6 (d), 124.6 (d), 117.7 (s), 117.5 (s), 104.8 (d), 104.5 (d), 93.8 (t), 66.3 (d), 66.2 (d), 64.7 (t), 63.4 (t), 62.9 (t), 54.9 (q), 46.3 (s), 46.3 (s), 35.7 (t), 32.2 (d), 32.0 (d), 31.0 (t), 30.9 (t), 30.8 (t), 29.4 (t), 28.5 (t), 28.4 (t), 25.9 (q), 18.5 (s), 18.3 (q), 18.2 (q), 16.4 (q), 15.3 (q), 15.2 (q), 15.1 (q), −5.3 (q); *m*/*z* (FAB) 493.3333 (M^+ − OMOM, $C_{28}H_{49}O_5Si$ requires 493.3349).

2-[(*E*)-6-(*tert*-Butyldimethylsilanyloxy)-1-methoxymethoxy-3-methylhex-2-enyl]-4-(2-[1,3]dioxolan-2-ylethyl)-4,5-dimethyl-3-hydroxymethylcyclohex-2-enone 56

A solution of trimethylsilylmethyl lithium (1.0 M in pentane, 3.4 mL, 3.4 mmol) was added dropwise over 5 minutes to a stirred solution of the diastereoisomeric MOM ether **55b** (1.74 g, 3.1 mmol) in diethyl ether (50 mL) at room temperature and the resulting yellow solution was then stirred at room temperature for 30 minutes. The mixture was poured into water (50 mL) and the separated aqueous layer was then extracted with ether (25 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave crude *β-hydroxysilane* as a yellow oil. A solution of the hydroxysilane in THF (10 mL) was added dropwise over 5 minutes to a stirred slurry of pentane washed KH (35% wt/wt oil dispersion, 0.80 g, 7.0 mmol) in THF (15 mL) at room temperature and the mixture was then stirred at room temperature for 2 hours. The mixture was diluted CAREFULLY with water (50 mL) and then extracted with ether (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave the crude *diene ether* as an orange oil. *m*-Chloroperoxybenzoic acid (56–86%, 1.3 g) was added portionwise to a stirred solution of the diene ether in ethanol (50 mL) at 0 °C and the mixture was then stirred at 0 °C for 30 minutes. The mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate (25 mL) and a 10% aqueous solution of sodium thiosulfate (25 mL), and then stirred vigorously at room temperature for 30 minutes. The majority of the solvent was removed *in vacuo* to leave an oily residue which was partitioned between water (25 mL) and ether (50 mL). The organic layer was separated and the aqueous layer was then extracted with ether (50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the *cyclohexenone* (0.18 g, 10%) as a single diastereoisomer, as a yellow oil; ν_{max} (film)/cm^{-1} 3484, 1670, 1096, 1034 and 837; δ_H (500 MHz, $CDCl_3$) 5.78 (1H, d, *J* 9.0, C*H*OMOM), 5.39–5.37 (1H, br. d, *J* 9.0, :C*H*), 4.87–4.84 (1H, m, OC*H*O), 4.68 (1H, d, *J* 6.5, OC*H*(H)OMe), 4.55 (1H, d, *J* 6.5, OC(H)*H*OMe), 4.47 (1H, dd, *J* 12.3 and 4.4, :CC*H*(H)OH), 4.22 (1H, dd, *J* 12.3 and 7.8, :CC(H)*H*OH), 3.99–3.93 (2H, m, OCH_2CH_2O), 3.86–3.82 (2H, m, OCH_2CH_2O), 3.54 (2H, t, *J* 6.5, CH_2OTBS), 3.33 (3H, s, OCH_3), 2.36–2.25 (2H, m, CH_2CO), 2.21–2.17 (1H, m), 2.05–2.02 (3H, m), 1.75 (3H, d, *J* 1.1, $:CCH_3$), 1.73–1.55 (10H, m), 1.38–1.18 (5H, m), 1.05 (3H, s, CCH_3), 0.95 (3H, d, *J* 6.7, $CHCH_3$), 0.88 (9H, s, $C(CH_3)_3$), 0.03 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$); δ_C (125 MHz, $CDCl_3$) 197.9 (s), 163.0 (s), 141.8 (s), 138.7 (s), 122.3 (d), 104.6 (d), 93.7 (t), 69.1 (d), 64.9 (t), 64.8 (t), 62.6 (t), 58.6 (t), 55.6 (q), 42.8 (s), 41.9 (t), 36.0 (t), 33.0 (d), 30.9 (t), 30.3 (t), 28.9 (t), 25.9 (q), 19.3 (q), 18.3 (s), 16.6 (q), 15.3 (q), −5.3 (q); *m*/*z* (FAB) 477.3000 (M^+ − H_2O − MOM, $C_{27}H_{45}O_5Si$ requires 477.3036).

3-[(*E*)-5-(*tert*-Butyldimethylsilanyloxy)-2-methylpent-1-enyl]-7-(2-[1,3]dioxolan-2-ylethyl)-6,7-dimethyl-3,5,6,7-tetrahydro-1*H*-isobenzofuran-4-one 57

Camphorsulfonic acid (5 mg, 0.02 mmol) was added in one portion to a stirred solution of the diastereoisomeric cyclohexenone **56** (0.24 g, 0.44 mmol) in dichloromethane (10 mL) at 0 °C and the solution was then stirred at 0 °C for 1 hour. The mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate (10 mL) and the organic layer was then separated. The aqueous layer was extracted with dichloromethane (10 mL) and the combined organics were dried over $MgSO_4$ and concentrated *in vacuo* to leave the crude *dihydrofuran* (0.24 g) as an inseparable 1 : 1 mixture of diastereoisomers, as a yellow oil; data for the mixture of diastereoisomers, ν_{max} (film)/cm^{-1} 1676, 1099, 835 and 775; δ_H (500 MHz, $CDCl_3$) 5.71–5.64 (1H, m, OC*H*), 5.08–5.04 (1H, m, :C*H*), 4.91–4.66 (3H, m, $:CCH_2O$ and OC*H*O), 3.99–3.93 (2H, m, OCH_2CH_2O), 3.90–3.84 (2H, m, OCH_2CH_2O), 3.60–3.53 (2H, m, CH_2OTBS), 2.35–2.28 (3H, m), 2.08–2.03 (2H, m), 1.82 (1.5H, s, $:CCH_3$), 1.81 (1.5H, d, *J* 1.0, $:CCH'_3$), 1.78–1.60 (6H, m), 1.59–1.48 (1H, m), 1.43–1.37 (1H, m), 1.11 (1.5H, s, CCH_3), 1.08 (1.5H, s, CCH'_3), 0.97–0.95 (3H, m, $CHCH_3$), 0.89 (4.5H, s, $C(CH_3)_3$), 0.88 (4.5H, s, $C(CH'_3)_3$), 0.04–0.03 (6H, 3 × s, $SiCH_3$); δ_C (125 MHz, $CDCl_3$) 194.1 (s), 193.8 (s), 166.7 (s), 166.4 (s), 140.6 (s), 140.3 (s), 136.5 (s), 136.1 (s), 123.3 (d), 122.7 (d), 103.9 (d), 81.4 (d), 81.3 (d), 73.1 (t), 72.9 (t), 65.0 (t), 65.0 (t), 62.6 (t), 43.3 (t), 42.8 (t), 38.9 (s), 38.8 (s), 35.8 (t), 35.8 (t), 35.4 (d), 34.6 (d), 30.7 (t), 30.63 (t), 30.6 (t), 30.5 (t), 29.0 (t), 29.0 (t), 25.9 (q), 19.8 (q), 19.5 (q), 18.3 (s), 16.7 (q), 14.5 (q), 14.2 (q), −5.3 (q); *m*/*z* (FAB) 421.2405 (M^+ − *t*Bu, $C_{23}H_{37}O_5Si$ requires 421.2410), which was used without further purification.

3-[(*E*)-5-(*tert*-Butyldimethylsilanyloxy)-2-methylpent-1-enyl]-7-(2-[1,3]dioxolan-2-ylethyl)-6,7-dimethyl-1,3,4,5,6,7-hexahydroisobenzofuran-4-ol 58a

A solution of diisobutylaluminium hydride (1.5 M in toluene, 0.30 mL, 0.45 mmol) was added dropwise over 5 minutes to a stirred solution of the diastereoisomeric enone **57** (235 mg, 0.44 mmol) in toluene (9 mL) at −78 °C and the yellow solution was then stirred at −78 °C for 1.5 hours. Methanol (1 mL) was added and the solution was then allowed to warm to room temperature. A saturated aqueous solution of Rochelles salt (10 mL) was added and the mixture was then stirred vigorously at room temperature for 1 hour. The organic layer was separated and the aqueous layer was then extracted with ether (10 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 60% diethyl ether in petroleum ether as eluent to give the *allylic β-alcohol* (103 mg, 45%) as a corresponding mixture of diastereoisomers, as a colourless oil; data for the mixture of diastereoisomers, ν_{max} (film)/cm^{-1} 3441, 1100 and 836; δ_H (400 MHz, $CDCl_3$) 5.63–5.57 (0.5H, m, OC*H*), 5.55–5.50 (0.5H, m, OC*H′*), 5.33–5.31 (0.5H, m, :C*H*), 5.08–5.06 (0.5H, m, :C*H′*), 4.80–4.77 (1H, m, OC*H*O), 4.65–4.47 (2H, m, $:CCH_2O$), 4.34 (0.5H, br. s, C*H*OH), 4.17 (0.5H, br. s, C*H′*OH), 3.98–3.89 (2H, m, OCH_2CH_2O), 3.86–3.77 (2H, m, OCH_2CH_2O), 3.60–3.56 (2H, m, CH_2OTBS), 2.09–2.03 (2H, m, $:CCH_2$), 1.88–1.80 (1H, m), 1.78 (1.5H, d, *J* 1.1, $:CCH_3$), 1.75 (1.5H, d, *J* 1.1, $:CCH'_3$), 1.67–1.44 (3H, m), 1.36–1.27 (2H, m), 0.96 (1.5H, s, CCH_3), 0.93 (1.5H, s, CCH'_3), 0.88 (4.5H, s, $C(CH_3)_3$), 0.87 (4.5H, s, $C(CH'_3)_3$), 0.04 (1.5H, s, $SiCH_3$), 0.03 (1.5H, s, $SiCH_3$), 0.02 (3H, s, $Si(CH'_3)_2$); δ_C (100 MHz, $CDCl_3$) 142.5 (s), 140.9 (s), 140.7 (s), 139.8 (s), 137.9 (s), 135.7 (s), 125.5 (d), 124.1 (d), 104.4 (d), 104.4 (d), 82.7 (d), 82.4 (d), 73.3 (t), 72.9 (t), 66.3 (d), 65.4 (d), 64.9 (t), 64.8 (t), 62.7 (t), 62.6 (t), 37.9 (t), 37.8 (s), 37.5 (s), 37.5 (t), 36.1 (t), 35.9 (t), 32.8 (d), 32.6 (d), 30.9 (t), 30.8 (t), 30.7 (t), 30.6 (t), 29.0 (t), 28.8 (t), 25.9

(q), 21.1 (q), 21.0 (q), 18.2 (s), 16.5 (q), 14.6 (q), 14.5 (q), −5.3 (q).

tert-Butyl-{(*E*)-5-[(1*R*,4*S*,5*R*,7*S*)-4-(2-[1,3]dioxolan-2-ylethyl)-4,5-dimethyl-7-methoxymethoxy-1,3,4,5,6,7-hexahydroisobenzofuran-1-yl]-4-methylpent-4-enyloxy}dimethylsilane 58b

Chloromethylmethyl ether (0.2 mL, 3 mmol) was added dropwise over *ca*. 1 minute to a stirred solution of the diastereoisomeric allylic alcohol **58a** (94 mg, 0.20 mmol) and diisopropylethylamine (0.7 mL, 4 mmol) in dichloromethane (2.5 mL) at room temperature and the resulting yellow solution was then stirred at room temperature for 5 hours. The mixture was diluted with dichloromethane (2.5 mL) and then poured into a saturated aqueous solution of sodium hydrogencarbonate (5 mL). The organic layer was separated and the aqueous layer was then extracted with dichloromethane (5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave an orange oil. The residue was purified by flash column chromatography on silica using 20–50% diethyl ether in petroleum ether as eluent to give: (i) the 1α-epimer (36 mg, 35%) (eluted first) as a colourless oil, ν_{max} (CH_2Cl_2)/cm^{-1} 1096, 1039 and 839; δ_H (500 MHz, $CDCl_3$) 5.61–5.58 (1H, m, OC*H*), 5.10 (1H, obs. dq, *J* 9.5 and 1.2, :C*H*), 4.82–4.80 (1H, m, OC*H*O), 4.65 (1H, d, *J* 6.7, OC*H*(H)O), 4.65–4.57 (2H, m, :CCH_2O), 4.55 (1H, d, *J* 6.7, OC(H)*H*O), 4.09–4.06 (1H, m, C*H*OMOM), 3.97–3.93 (2H, m, OCH_2CH_2O), 3.88–3.83 (2H, m, OCH_2CH_2O), 3.60 (2H, t, *J* 6.5, CH_2OTBS), 3.33 (3H, s, OCH_3), 2.07–2.03 (2H, m, :CCH_2), 1.97 (1H, ddd, *J* 12.6, 6.2 and 2.5), 1.81–1.77 (1H, ddd, *J* 12.6, 6.9 and 2.4), 1.76–1.75 (1H, m), 1.74 (3H, d, *J* 1.2, :CCH_3), 1.72–1.55 (8H, m), 0.96 (3H, s, CCH_3), 0.90–0.89 (12H, m, CHCH_3 + SiC(CH_3)$_3$), 0.05 (6H, s, Si(CH_3)$_2$); δ_C (125 MHz, $CDCl_3$) 142.2 (s), 140.6 (s), 137.0 (s), 124.8 (d), 104.9 (d), 96.5 (t), 82.8 (d), 73.7 (t), 72.4 (d), 65.3 (t), 65.2 (t), 63.2 (t), 55.7 (q), 37.8 (s), 36.4 (t), 35.9 (t), 33.1 (d), 31.5 (t), 31.1 (t), 29.3 (t), 26.3 (q), 21.3 (q), 18.7 (s), 16.8 (q), 15.0 (q), −4.9 (q); *m*/*z* (EI) 467.2817 (M^+-*t*Bu, $C_{25}H_{43}O_6Si$ requires 467.2829); and (ii) the 1β-epimer (59 mg, 57%) (eluted second) as a colourless oil, ν_{max} (film)/cm^{-1} 1255, 1100, 1039, 836 and 776; δ_H (360 MHz, $CDCl_3$) 5.28–5.44 (1H, m, OC*H*), 5.31 (1H, obs. dq, *J* 9.5 and 1.2, :C*H*), 4.81–4.78 (1H, m, OC*H*O), 4.62 (1H, ddd, *J* 12.2, 5.1 and 2.2, :CC*H*(H)O), 4.49 (1H, d, *J* 6.9, OC*H*(H)O), 4.48–4.44 (1H, m, :CC(H)*H*), 4.44 (1H, d, *J* 6.9, OC(H)*H*O), 4.23 (1H, br. s, C*H*OMOM), 3.97–3.90 (2H, m, OCH_2CH_2O), 3.88–3.81 (2H, m, OCH_2CH_2O), 3.59 (2H, t, *J* 6.5, CH_2OTBS), 3.31 (3H, s, OCH_3), 2.06–2.02 (2H, m, :CCH_2), 1.89 (1H, ddd, *J* 12.3, 6.0 and 2.5), 1.84–1.78 (1H, m), 1.73 (3H, d, *J* 1.2, :CCH_3), 1.68–1.53 (5H, m), 0.97 (3H, s, CCH_3), 0.89–0.87 (12H, m, CHCH_3 and SiC(CH_3)$_3$), 0.03 (6H, s, Si(CH_3)$_2$); δ_C (100 MHz, $CDCl_3$) 143.2 (s), 137.7 (s), 135.4 (s), 125.7 (d), 104.5 (d), 95.6 (t), 82.9 (d), 72.4 (t), 71.6 (d), 64.9 (t), 64.8 (t), 63.0 (t), 55.2 (q), 37.5 (s), 35.9 (t), 35.4 (t), 32.9 (d), 31.1 (t), 30.8 (t), 29.0 (t), 25.9 (q), 21.2 (q), 18.3 (s), 16.2 (q), 14.7 (q), −5.3 (q); *m*/*z* (EI) 524.3516 (M^+, $C_{29}H_{52}O_6Si$ requires 524.3533).

3-[(1*R*,4*S*,5*R*,7*S*)-1-((*E*)-5-Hydroxy-2-methylpent-1-enyl)-4,5-dimethyl-7-methoxymethoxy-1,3,4,5,6,7-hexahydroisobenzofuran-4-yl]propionaldehyde 59

Camphorsulfonic acid (4 mg, 0.02 mmol) was added in one portion to a stirred solution of the 1α-epimer of the dioxolane **58b** (23 mg, 0.044 mmol) in THF (1 mL) and water (0.5 mL) at room temperature and the mixture was heated under reflux for 6 hours, then poured into a mixture of water (2 mL) and a saturated aqueous solution of sodium hydrogencarbonate (2.5 mL) and extracted with ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 25% diethyl ether in ethyl acetate as eluent to give the *hydroxy aldehyde* (11 mg, 68%) as a colourless oil; ν_{max} (film)/cm^{-1} 3427, 1722, 1148, 1101 and 1038; δ_H (500 MHz, $CDCl_3$) 9.78 (1H, t, *J* 1.3, C*H*O), 5.63–5.59 (1H, m, OC*H*), 5.13 (1H, dd, *J* 9.5 and 1.2, :C*H*), 4.66 (1H, d, *J* 6.7, OC*H*(H)O), 4.60–4.56 (1H, m, :CC*H*(H)O), 4.57 (1H, d, *J* 6.7, OC(H)*H*O), 4.50 (1H, ddd, *J* 12.1, 5.0 and 3.1, :CC(H)*H*O), 4.12–4.09 (1H, m, C*H*OMOM), 3.66 (2H, t, *J* 6.4, CH_2OH), 3.34 (3H, s, OCH_3), 2.44–2.37 (1H, m), 2.23–2.16 (1H, m), 2.12 (2H, t, *J* 7.7, :CCH_2), 1.99 (1H, ddd, *J* 12.2, 6.0 and 2.1), 1.84–1.64 (4H, m), 1.77 (3H, d, *J* 1.3, :CCH_3), 1.62–1.55 (3H, m), 1.00 (3H, s, CCH_3), 0.90 (3H, d, *J* 6.7Hz, CHCH_3); δ_C (125 MHz, $CDCl_3$) 201.5 (d), 140.9 (s), 140.4 (s), 137.6 (s), 124.6 (d), 96.1 (t), 82.3 (d), 73.2 (t), 71.7 (d), 62.5 (t), 55.4 (q), 39.4 (t), 37.4 (s), 36.0 (t), 35.4 (t), 32.9 (d), 30.7 (t), 28.2 (t), 20.8 (q), 16.4 (q), 14.7 (q); *m*/*z* (EI) 366.2415 (M^+, $C_{21}H_{34}O_5$ requires 366.2406).

Using an identical procedure to that described for the synthesis of **59**, the 1β-epimer of the dioxolane **58b** (42 mg, 0.080 mmol) in THF (2 mL) and water (1 mL) with CSA (9 mg) gave the corresponding epimeric hydroxy aldehyde*3-[(1S,4S,5R,7S)-1-((E)-5-hydroxy-2-methylpent-1-enyl)-4,5-dimethyl-7-methoxymethoxy-1,3,4,5,6,7-hexahydroisobenzofuran-4-yl]-propionaldehyde* (21 mg, 75%) as a colourless film; ν_{max} (film)/cm^{-1} 3418, 1722 and 1038; δ_H (500 MHz, $CDCl_3$) 9.78 (1H, s, C*H*O), 5.52–5.48 (1H, m, OC*H*), 5.36 (1H, app. dd, *J* 9.4 and 1.0, :C*H*), 4.66 (1H, ddd, *J* 12.2, 5.1 and 2.3, :CC*H*(H)O), 5.46 (1H, d, *J* 6.9, OC*H*(H)O), 4.50 (1H, d, *J* 6.9, OC(H)*H*O), 4.33 (1H, app. dt, *J* 12.2 and 3.0, :CC(H)*H*O), 4.30–4.27 (1H, m, C*H*OMOM), 3.65 (2H, t, *J* 6.3, CH_2OH), 3.33 (3H, s, OCH_3), 2.45–2.38 (1H, m, C*H*(H)CHO), 2.23–2.17 (1H, m, C(H)*H*-CHO), 2.15–2.11 (2H, m, :CCH_2), 1.93 (1H, ddd, *J* 12.3, 5.8 and 2.2), 1.77 (3H, d, *J* 1.2, :CCH_3), 1.84–1.53 (6H, m), 1.02 (3H, s, CCH_3), 0.91 (3H, d, *J* 6.8, CHCH_3); δ_C (125 MHz, $CDCl_3$) 201.4 (d), 142.1 (s), 138.0 (s), 136.4 (s), 126.0 (d), 95.4 (t), 82.9 (d), 72.4 (t), 71.4 (d), 62.7 (t), 55.3 (q), 39.5 (t), 37.6 (s), 36.3 (t), 35.2 (t), 33.2 (d), 30.4 (t), 28.3 (t), 21.2 (q), 16.1 (q), 14.8 (q); *m*/*z* (FAB) 365.2271 (M^+ − H, $C_{21}H_{33}O_5$ requires 365.2269).

(*E*)-5-[4-(3-Hydroxybutyl)-4,5-dimethyl-7-methoxymethoxy-1,3,4,5,6,7-hexahydroisobenzofuran-1-yl]-4-methylpent-4-en-1-ol 60

A solution of methylmagnesium chloride (3.0 M in THF, 0.032 mL, 0.11 mmol) was added dropwise over 1 minute to a stirred solution of the 1α-epimer of the aldehyde **59** (18 mg, 0.049 mmol) in THF (1 mL) at room temperature and the resulting suspension was then stirred at room temperature for 15 minutes. The mixture was poured into a saturated aqueous solution of ammonium chloride (1 mL) and water (4 mL) and then extracted with ether (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 50% diethyl ether in ethyl acetate as eluent to give the *diol* (13 mg, 68%) as an inseparable 1 : 1 mixture of secondary alcohol epimers, as a colourless oil; data for the mixture of diastereoisomers ν_{max} (film)/cm^{-1} 3410 and 1038; δ_H (500 MHz, $CDCl_3$) 5.61–5.59 (1H, m, OC*H*), 5.16 (0.5H, d, *J* 8.2, :C*H*), 5.15 (0.5H, d, *J* 8.2, :C*H*′), 4.66 (1H, d, *J* 6.8, OC*H*(H)O), 4.62–4.56 (2H, m, :CCH_2O), 4.57 (1H, d, *J* 6.8, OC(H)*H*O), 4.12–4.09 (1H, m, C*H*OMOM), 3.78–3.69 (1H, m, C*H*OH), 3.65 (2H, t, *J* 6.4, CH_2OH), 3.35 (3H, s, OCH_3), 2.11 (2H, t, *J* 7.6, :CCH_2), 1.97 (1H, ddd, *J* 12.6, 6.1 and 2.4), 1.84–1.78 (1H, m), 1.76 (3H, s, :CCH_3), 1.75–1.56 (8H, m), 1.20 (1.5H, d, *J* 6.1, CH(OH)CH_3), 1.19 (1.5H, d, *J* 6.1, CH(OH)CH'_3), 0.96 (3H, s, CCH_3), 0.89 (1.5H, d, *J* 6.9, CHCH_3), 0.88 (1.5H, d, *J* 6.9, CHCH'_3); δ_C (125 MHz, $CDCl_3$) 142.1 and 142.0 (s), 140.1 and 140.0 (s), 136.4 and 136.3 (s), 124.9 and 124.8 (d), 96.1 (t), 82.3 (d), 73.4 (t), 71.9 (d), 68.6 and 68.4 (d), 62.6 and 62.5 (t), 55.4 (q), 37.6 and 37.5 (s), 36.0 and 35.4 (t), 34.0 and 33.7 (t), 32.9 and 32.8 (t), 32.7 and 32.6 (d),

30.7 and 30.6 (t), 29.7 (t), 23.6 and 23.5 (q), 21.1 and 21.0 (q), 16.3 (q), 14.7 (q); *m/z* (FAB) 381.2643 ($M^+ - H$, $C_{22}H_{37}O_5$ requires 381.2641).

Using an identical procedure to that described for the synthesis of **60**, the 1β-epimer of the aldehyde **59** (28 mg, 0.077 mmol) in THF (2 mL) was treated with a solution of methylmagnesium chloride (3.0 M in THF, 0.1 mL, 0.3 mmol) to give *(E)-5-[(1S,4S,5R,7S)-4-(3-hydroxybutyl)-4,5-dimethyl-7-methoxymethoxy-1,3,4,5,6,7-hexahydroisobenzofuran-1-yl]-4-methylpent-4-en-1-ol* (22 mg, 75%) as an inseparable 1 : 1 mixture of secondary alcohol epimers, as a colourless oil; data for the mixture of diastereoisomers, ν_{max} (film)/cm^{-1} 3402 and 1038; δ_H (500 MHz, $CDCl_3$) 5.51–5.47 (1H, m, :CC*H*O), 5.36 (1H, app. dd, *J* 9.3 and 0.9, :C*H*), 4.66–4.62 (1H, m, :CC*H*-(H)O), 4.55 (1H, d, *J* 6.9, OC*H*(H)OMe), 4.49 (1H, d, *J* 6.9, OC(H)*H*OMe), 4.46 (0.5H, dt, *J* 12.2 and 3.1, :CC(H)*H*O), 4.40 (0.5H, dt, *J* 12.2 and 3.1, :CC(H)*H′*O), 4.27 (1H, br. s, C*H*OMOM), 3.76–3.68 (1H, m, C*H*OH), 3.64 (2H, t, *J* 6.2, CH_2OH), 3.33 (3H, s, OCH_3), 2.14–2.09 (2H, m, :CCH_2), 1.91 (1H, ddd, *J* 12.5, 5.9 and 2.5), 1.87–1.82 (1H, m), 1.77 (3H, d, *J* 1.0, :CCH_3), 1.74–1.58 (6H, m), 1.47–1.34 (3H, m), 1.19 (1.5H, d, *J* 6.1, CH(OH)CH_3), 1.18 (1.5H, d, *J* 6.1, CH(OH)-CH'_3), 0.98 (1.5H, s, CCH_3), 0.97 (1.5H, s, CCH'_3), 0.89 (1.5H, d, *J* 6.8, CHCH_3), 0.88 (1.5H, d, *J* 6.8, CHCH'_3); δ_C (125 MHz, $CDCl_3$) 143.3 and 143.2 (s), 137.7 (s), 135.2 and 135.2 (s), 126.3 (d), 95.3 (t), 82.84 and 82.81 (d), 72.5 (t), 71.7 (d), 68.6 and 68.4 (d), 62.7 (t), 55.3 (q), 37.7 (s), 36.3 (t), 35.3 (t), 34.2 and 33.9 (t), 33.1 and 32.9 (t), 32.8 (d), 30.4 (t), 23.6 (q), 21.5 and 21.4 (q), 16.1 (q), 14.7 (q); *m/z* (EI) 323.2226 ($M^+ - n$-PrOH, $C_{19}H_{31}O_4$ requires 323.2222).

(*E*)-5-[(1*R*,4*S*,5*R*,7*S*)-4,5-Dimethyl-7-methoxymethoxy-4-(3-oxobutyl)-1,3,4,5,6,7-hexahydroisobenzofuran-1-yl]-4-methylpent-4-enal 61

Dess–Martin periodinane (17 mg, 0.040 mmol) was added in one portion to a stirred solution of a 1 : 1 mixture of secondary alcohol epimers of the 1α-epimer of the diol **60** (7 mg, 0.018 mmol) in dichloromethane (1 mL) at 0 °C. The suspension was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature and stirred for a further 30 minutes. A saturated aqueous solution of sodium hydrogencarbonate (2.5 mL) and water (2.5 mL) were added followed by sodium thiosulfate (40 mg) and the mixture was then stirred vigorously for 1 hour. The organic layer was separated and the aqueous layer was then extracted with dichloromethane (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to leave a colourless film. The residue was purified by flash column chromatography on silica using 66% diethyl ether in pentane as eluent to give the *keto-aldehyde* (5 mg, 72%) as a colourless film; ν_{max} ($CDCl_3$)/cm^{-1} 1719, 1148 and 1037; δ_H (500 MHz, $CDCl_3$) 9.78 (1H, t, *J* 1.6, C*H*O), 5.61–5.58 (1H, m, OC*H*), 5.12 (1H, app. dd, *J* 9.4 and 1.1, :C*H*), 4.66 (1H, d, *J* 6.7, OC*H*(H)O), 4.57 (1H, app. dt, *J* 12.2 and 3.0, :CC*H*-(H)O), 4.56 (1H, d, *J* 6.7, OC(H)*H*O), 4.50 (1H, ddd, *J* 12.2, 5.0 and 3.0, :CC(H)*H*O), 4.09–4.06 (1H, m, C*H*OMOM), 2.61–2.56 (2H, m), 2.43–2.37 (3H, m), 2.17 (3H, s, COCH_3), 2.16–2.09 (1H, m), 1.99 (1H, ddd, *J* 12.4, 6.1 and 2.1), 1.77 (3H, d, *J* 1.1, :CCH_3), 1.70–1.65 (1H, m), 1.61–1.51 (3H, m), 0.98 (3H, s, CCH_3), 0.89 (3H, d, *J* 6.8, CHCH_3); δ_C (125 MHz, $CDCl_3$) 208.2 (s), 201.7 (d), 141.6 (s), 138.5 (s), 136.9 (s), 125.3 (d), 96.2 (t), 82.2 (d), 73.4 (t), 71.8 (d), 55.5 (q), 41.9 (t), 38.7 (t), 37.3 (s), 35.4 (t), 33.0 (d), 31.7 (t), 30.1 (q), 30.0 (t), 20.9 (q), 16.6 (q), 14.7 (q); *m/z* (FAB) 377.2319 ($M^+ - H$, $C_{22}H_{33}O_5$ requires 377.2328).

Using an identical procedure to that described for the synthesis of **61**, a 1 : 1 mixture of secondary alcohol epimers of the 1β-epimer of the diol **60** (10 mg, 0.036 mmol) in dichloromethane (1 mL) was treated with Dess–Martin periodinane (44 mg, 0.10 mmol) to give *(E)-5-[(1S,4S,5R,7S)-4,5-dimethyl-7-methoxymethoxy-4-(3-oxobutyl)-1,3,4,5,6,7-hexahydroisobenzofuran-1-yl]-4-methylpent-4-enal* (7 mg, 71%) as a colourless film; ν_{max} (film)/cm^{-1} 1715 and 1038; δ_H (500 MHz, $CDCl_3$) 9.82 (1H, t, *J* 1.6, C*H*O), 5.54–5.52 (1H, m, :CC*H*O), 5.39–5.37 (1H, app. dd, *J* 9.3 and 1.0, :C*H*), 4.68 (1H, ddd, *J* 12.2, 5.1 and 2.0, :CC*H*(H)O), 4.56 (1H, d, *J* 6.9, OC*H*(H)O), 4.50 (1H, d, *J* 6.9, OC(H)*H*O), 4.37 (1H, dt, *J* 12.2 and 3.1, :CC(H)*H*O), 4.30 (1H, br. s, C*H*OMOM), 3.36 (3H, s, OCH_3), 2.63–2.58 (2H, m), 2.45–2.39 (3H, m), 2.21–2.14 (1H, m), 2.18 (3H, s, C(O)CH_3), 1.96 (1H, ddd, *J* 12.3, 5.8 and 2.2), 1.82–1.72 (3H, m), 1.81 (3H, d, *J* 0.8, :CCH_3), 1.68–1.55 (3H, m), 1.04 (3H, s, CCH_3), 0.94 (3H, d, *J* 6.8, CHCH_3); δ_C (125 MHz, $CDCl_3$) 208.0 (s), 202.1 (d), 142.7 (s), 135.9 (s), 135.8 (s), 126.6 (d), 95.4 (t), 82.7 (d), 72.6 (t), 71.3 (d), 55.3 (q), 41.8 (t), 38.9 (t), 37.5 (s), 35.3 (t), 33.2 (d), 31.6 (t), 30.11 (q), 30.06 (t), 21.2 (q), 16.4 (q), 14.8 (q); *m/z* (FAB) 401.2340 ($M^+ + Na$, $C_{22}H_{34}O_5Na$ requires 401.2304).

Attempted cyclisation of the keto aldehyde 61

A solution of the keto aldehyde **61** (4 mg, 0.01 mmol) and *t*-BuOH (5 μl, 0.05 mmol) in THF (1.0 mL) was added dropwise over 12 hours to a stirred solution of SmI_2 (0.1 M in THF, 1.0 mL, 0.10 mmol), samarium powder (15 mg, 0.10 mmol) and HMPA (0.035 mL, 0.20 mmol) at −78 °C. The mixture was stirred at −78 °C for a further 4 hours and then allowed to warm to room temperature. The mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate (4 mL) and a saturated aqueous solution of Rochelles salt (4 mL) and then stirred vigorously at room temperature for 1 hour. The mixture was extracted with ethyl acetate (2 × 10 mL) and the combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave an orange film. The residue was purified by flash column chromatography on silica using 50–75% ethyl acetate in diethyl ether as eluent to give the tetrol **63** (2 mg) as a mixture of diastereoisomers; data for the mixture of diastereoisomers, δ_H (500 MHz, $CDCl_3$) 5.61–5.59 (1H, m, OC*H*), 5.16 (0.5H, d, *J* 8.2, :C*H*), 5.15 (0.5H, d, *J* 8.2, :C*H′*), 4.66 (1H, d, *J* 6.8, OC*H*(H)O), 4.62–4.56 (2H, m, :CCH_2O), 4.57 (1H, d, *J* 6.8, OC(H)*H*O), 4.12–4.09 (1H, m, C*H*OMOM), 3.78–3.69 (1H, m, C*H*OH), 3.65 (2H, t, *J* 6.4, CH_2OH), 3.35 (3H, s, OCH_3), 2.11 (2H, t, *J* 7.6, :CCH_2), 1.97 (1H, ddd, *J* 12.6, 6.1 and 2.4), 1.84–1.78 (1H, m), 1.76 (3H, s, :CCH_3), 1.75–1.56 (8H, m), 1.20 (1.5H, d, *J* 6.1, CH(OH)CH_3), 1.19 (1.5H, d, *J* 6.1, CH(OH)CH'_3), 0.96 (3H, s, CCH_3), 0.89 (1.5H, d, *J* 6.9, CHCH_3), 0.88 (1.5H, d, *J* 6.9, CHCH'_3).

3-((1*S*,6*R*)-3-Bromo-1,6-dimethyl-4-ethoxy-2-oxocyclohex-3-enyl)propionaldehyde 64a

Bis(acetonitrile)dichloropalladium(II) (0.14 g, 0.54 mmol) was added in one portion to a stirred solution of the *syn*-dimethyl dioxolane **53** (3.7 g, 10.6 mmol) in acetone (1000 mL) at room temperature and the resulting yellow solution was then stirred at room temperature in the dark for 2 hours. The mixture was filtered through silica and then the solvent was evaporated *in vacuo* to leave an orange oil. The oil was dissolved in dichloromethane (10 mL), then filtered through silica and the residue was washed with ether (3 × 50 mL). The combined organic solutions were concentrated *in vacuo* to leave a pale yellow oil which was purified by flash column chromatography on silica using 60–66% diethyl ether in petroleum ether as eluent to give the *aldehyde* (1.9 g, 52%) as a yellow oil; λ_{max} (EtOH)/nm (ε) 274 (13,500); ν_{max} (film)/cm^{-1} 1719, 1657, 1587, 1247 and 1024; δ_H (360 MHz, $CDCl_3$) 9.71 (1H, t, *J* 1.3, C*H*O), 4.24–4.14 (2H, m, OCH_2), 2.74 (1H, dd, *J* 17.8 and 5.0), 2.42 (1H, dd, *J* 17.8 and 9.8), 2.36–2.23 (3H, m), 2.21–2.11 (1H, m), 1.68–1.61 (1H, m), 1.41 (3H, t, *J* 7.1, OCH$_2$CH_3), 1.01 (3H, d, *J* 6.8, CHCH_3), 0.99 (3H, s, CCH_3); δ_C (90 MHz, $CDCl_3$) 201.8 (d), 195.2 (s), 170.2 (s), 104.5 (s), 101.9 (d), 64.9 (t), 47.7 (s), 38.9 (t),

32.3 (t), 27.2 (t), 18.3 (q), 15.0 (q), 14.8 (q); *m/z* (EI) 302.0521 (M^+, $C_{13}H_{19}O_3Br$ requires 302.0518).

(5*R*,6*S*)-2-Bromo-5,6-dimethyl-3-ethoxy-6-(3-oxobutyl)cyclohex-2-enone 64b

A solution of methylmagnesium chloride (3.0 M in THF, 2.1 mL, 6.3 mmol) was added dropwise over 5 minutes to a stirred solution of the aldehyde **64a** (1.9 g, 5.5 mmol) in THF (60 mL) at 0 °C and the mixture was then stirred at 0 °C for 30 minutes. The mixture was poured into water (60 mL) and then extracted with ether (2 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 50–75% diethyl ether in petroleum ether as eluent to give *(5R,6S)-2-bromo-5,6-dimethyl-3-ethoxy-6-(3-hydroxybutyl)cyclohex-2-enone* (1.2 g, 66%) as an inseparable 1 : 1 mixture of secondary alcohol epimers, as a viscous colourless oil; data for the mixture of diastereoisomers, (Found: C, 52.5; H, 7.4; Br, 25.2. $C_{14}H_{23}BrO_3$ requires C, 52.7; H, 7.3; Br, 25.0%); λ_{max} (EtOH)/nm (ε) 274 (15,900); ν_{max} (film)/cm^{-1} 3440, 1657, 1585, 1247 and 1027; δ_H (360 MHz, $CDCl_3$) 4.24–4.11 (2H, m, OCH_2), 3.71–3.63 (1H, m, $CHOH$), 2.73 (0.5H, dd, *J* 9.6 and 4.9, :CC*H*(H)), 2.68 (0.5H, dd, *J* 9.6 and 4.9, :CC*H*′(H)), 2.42 (0.5H, d, *J* 10.1, :CC(H)*H*), 2.37 (0.5H, d, *J* 10.1, :CC(H)*H*′), 2.26–2.17 (1H, m, $CHCH_3$), 2.09–1.99 (2H, m, $CH(OH)CH_2$), 1.41 (3H, t, *J* 7.0, OCH_2CH_3), 1.13 (3H, d, *J* 6.2, $CH(OH)CH_3$), 1.01 (1.5H, d, *J* 6.8, $CHCH_3$), 1.00 (1.5H, d, *J* 6.8, $CHCH'_3$), 0.96 (1.5H, s, CCH_3), 0.95 (1.5H, s, CCH'_3); δ_C (90 MHz, $CDCl_3$) 196.4 (s), 196.2 (s), 170.4 (s), 170.1 (s), 102.2 (s), 102.1 (s), 68.0 (d), 67.5 (d), 64.8 (t), 64.8 (t), 48.3 (s), 48.1 (s), 33.6 (t), 33.4 (t), 32.3 (t), 32.0 (d), 31.8 (d), 31.3 (t), 30.9 (t), 23.3 (q), 23.2 (q), 18.7 (q), 18.5 (q), 15.0 (q), 14.8 (q), 14.7 (q); *m/z* (EI) 319.0900 (M^+ + H, $C_{14}H_{24}O_3Br$ requires 319.0909).

Dess–Martin periodinane (1.9 g, 4.4 mmol) was added in one portion to a stirred solution of a 1 : 1 mixture of diastereoisomers of the alcohol (1.2 g, 3.6 mmol) in dichloromethane (35 mL) at 0 °C and the resulting suspension was then stirred at 0 °C for 30 minutes. The mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate (35 mL), sodium thiosulfate (3.8 g) was then added in one portion and the mixture was stirred vigorously at room temperature for 1 hour. The organic layer was separated and the aqueous layer was then extracted with dichloromethane (35 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a residue which crystallised to give the *ketone* (1.2 g, 99%) as a colourless solid; mp. 98–100 °C (diethyl ether); (Found: C, 52.8; H, 6.8. $C_{14}H_{21}BrO_3$ requires C, 53.0; H, 6.7%); λ_{max} (EtOH)/nm (ε) 275 (11,800); ν_{max} (CH_2Cl_2)/cm^{-1} 1715, 1660, 1592 and 1036; δ_H (360 MHz, $CDCl_3$) 4.24–4.12 (2H, m, OCH_2), 2.75 (1H, dd, *J* 17.8 and 5.0, :CC*H*(H)), 2.45–2.34 (2H, m, :CC(H)*H* and C(O)C*H*(H)), 2.26–2.09 (3H, m, C(O)C(H)*H*, $CHCH_3$ and CC*H*(H)), 2.11 (3H, s, $COCH_3$), 1.70–1.62 (1H, m, CC(H)*H*), 1.42 (3H, t, *J* 7.0, OCH_2CH_3), 1.01 (3H, d, *J* 6.9, $CHCH_3$), 0.99 (3H, s, CCH_3); δ_C (90 MHz, $CDCl_3$) 208.5 (s), 195.4 (s), 170.0 (s), 101.9 (s), 64.8 (t), 47.7 (s), 38.4 (t), 32.6 (d), 32.4 (t), 29.8 (q), 29.1 (t), 18.3 (q), 15.0 (q), 14.9 (q); *m/z* (EI) 317.0762 (M^+ + H, $C_{14}H_{22}O_3Br$ requires 317.0752).

(5*R*,6*S*)-2-Bromo-5,6-dimethyl-3-ethoxy-6-(3-methylbut-3-enyl)cyclohex-2-enone 65

A solution of *n*-butyllithium (2.5 M in hexanes, 1.6 mL, 4.1 mmol) was added dropwise over 5 minutes to a stirred slurry of methyltriphenylphosphonium bromide (1.6 g, 4.5 mmol) in ether (35 mL) at room temperature. The bright yellow coloured mixture was stirred at room temperature for 30 minutes, then cooled to −78 °C, and treated dropwise over 5 minutes with a solution of the ketone **64b** (1.1 g, 3.4 mmol) in THF (5 mL). The mixture was stirred at −78 °C for 1 hour, then at room temperature for 1 hour, diluted with ether (35 mL) and filtered through florisil. The residue was washed with ether (2 × 50 mL) and then the combined organic extracts were concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 5–20% diethyl ether in petroleum ether as eluent to give the *alkene* (0.47 g, 44%) as a colourless solid; mp. 97–98 °C (ether–petrol); (Found: C, 57.3; H, 7.6; Br, 25.2. $C_{15}H_{23}BrO_2$ requires C, 57.2; H, 7.4; Br, 25.4%); λ_{max} (EtOH)/nm (ε) 274 (20,200); ν_{max} (CH_2Cl_2)/cm^{-1} 1661, 1593 and 1030; δ_H (360 MHz, $CDCl_3$) 4.67 (2H, br. s, :CH_2), 4.25–4.13 (2H, m, OCH_2), 2.72 (1H, dd, *J* 17.5 and 4.8, :CC*H*(H)), 2.42 (1H, dd, *J* 17.5 and 9.6, :CC(H)*H*), 2.30–2.25 (1H, m), 2.16–2.08 (1H, m), 1.85–1.79 (2H, m), 1.72 (3H, s, :CCH_3), 1.47–1.40 (1H, m), 1.43 (3H, t, *J* 7.0, OCH_2CH_3), 1.03 (3H, d, *J* 6.8, $CHCH_3$), 0.99 (3H, s, CCH_3); δ_C (90 MHz, $CDCl_3$) 195.6 (s), 169.7 (s), 145.9 (s), 109.6 (t), 102.4 (s), 64.7 (t), 48.3 (s), 33.9 (t), 32.4 (t), 32.1 (t), 32.0 (d), 22.4 (q), 18.6 (q), 15.1 (q), 14.9 (q); *m/z* (CI) 315.0944 (M^+ + H, $C_{15}H_{24}BrO_2$ requires 315.0960).

(*E*)-3-Methylhept-2,6-dien-1-al 66

N-bromosuccinimide (18.1 g, 100 mmol) was added portionwise over 10 minutes to a stirred solution of geranylacetate (21.4 mL, 100 mmol) in THF (225 mL) and water (100 mL) and the mixture was then stirred at room temperature for 30 minutes. A solution of potassium hydroxide (11.2 g, 200 mmol) in water (50 mL) was added dropwise over 10 minutes and the mixture was then stirred at room temperature for 1 hour. The mixture was poured into a saturated aqueous solution of ammonium chloride (300 mL) and then extracted with ether (2 × 250 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a pale yellow oil. The crude epoxide was partitioned between THF (125 mL) and water (125 mL) and then a 60% aqueous solution of perchloric acid (1 mL) was added in one portion. The resulting homogeneous solution was stirred at room temperature for 15 minutes, and then potassium periodate (23.0 g, 100 mmol) was added portionwise over 5 minutes. The mixture was stirred vigorously at room temperature for 30 minutes, then poured into water (250 mL) and extracted with ether (2 × 250 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a colourless oil. The residue was purified by flash column chromatography on silica using 5–20% diethyl ether in petroleum ether as eluent to give the acetic acid (*E*)-3-methyl-6-oxohex-2-enyl ester (11.1 g, 65%) as a colourless oil; (Found: C, 63.3; H, 8.5. $C_9H_{14}O_3$ requires C, 63.5; H, 8.3%); ν_{max} (film)/cm^{-1} 1732, 1235 and 1024; δ_H (360 MHz, $CDCl_3$) 9.79 (1H, t, *J* 1.6, C*H*O), 5.39–5.35 (1H, m, :C*H*), 4.59 (2H, d, *J* 7.0, CH_2OAc), 2.59 (2H, m, CH_2CHO), 2.39 (2H, t, *J* 7.5, CH_2C:), 2.06 (3H, s, C(O)CH_3), 1.73 (3H, br. s, :CCH_3); δ_C (90 MHz, $CDCl_3$) 201.6 (d), 171.0 (s), 139.9 (s), 119.3 (d), 61.0 (t), 41.6 (t), 31.4 (t), 20.9 (q), 16.5 (q); *m/z* (EI) 126.0681 (M^+ − H − C(O)Me, $C_7H_{10}O_2$ requires 126.0681).

Potassium *t*-butoxide (7.1 g, 63 mmol) was added portionwise over 1 minute to a stirred slurry of methyltriphenylphosphonium bromide (23.0 g, 64 mmol) in THF (130 mL) at room temperature and the resulting bright yellow mixture was then stirred at room temperature for 1 hour. The mixture was added dropwise *via* cannula over 30 minutes to an ice-cooled solution of the above aldehyde (9.0 g, 53 mmol) in THF (130 mL) and the viscous mixture was then stirred at 0 °C for 10 minutes. The mixture was poured into a saturated aqueous solution of ammonium chloride (300 mL) and then extracted with ether (2 × 250 mL). The combined organics were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 5% diethyl ether in petroleum ether as eluent to give acetic acid (*E*)-3-methylhepta-2,6-dienyl ester (8.3 g, 93%) as a colourless oil; (Found: C, 71.6; H, 9.9. $C_{10}H_{16}O_2$ requires C,

71.4; H, 9.6%); ν_{max} (film)/cm^{-1} 1741, 1232, 1024 and 912; δ_H (360 MHz, $CDCl_3$) 5.80 (1H, ddt, *J* 17.0, 10.2 and 6.3, H_2C:C*H*), 5.36 (1H, tq, *J* 7.1 and 1.2, :C*H*), 5.06–4.94 (2H, m, :CH_2), 4.59 (2H, d, *J* 7.1, CH_2OAc), 2.23–2.10 (4H, m, CH_2CH_2), 2.06 (3H, s, COCH_3), 1.71 (3H, d, *J* 1.2, :CCH_3); δ_C (90 MHz, $CDCl_3$) 171.0 (s), 141.6 (s), 138.0 (d), 118.6 (d), 114.7 (t), 61.3 (t), 38.8 (t), 31.8 (t), 21.0 (q), 16.4 (q); *m*/*z* (EI) 109.1012 (M^+ − OAc, C_8H_{13} requires 109.1017).

Potassium carbonate (13.5 g, 98 mmol) was added in one portion to a stirred solution of the acetate (8.3 g, 49 mmol) in methanol (100 mL) at room temperature and the mixture was then stirred at room temperature for 30 minutes. The solvent was evaporated *in vacuo* to leave a colourless gum which was then partitioned between ether (250 mL) and water (250 mL). The separated aqueous layer was extracted with ether (100 mL) and the combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave the corresponding alcohol (5.1 g, 82%) as a pale yellow oil; (Found: C, 75.6; H, 11.5. $C_8H_{14}O$ requires C, 76.1; H, 11.2%); ν_{max} (film)/cm^{-1} 3340, 1668, 1640, 995 and 910; δ_H (360 MHz, $CDCl_3$) 5.79 (1H, ddt, *J* 17.0, 10.3 and 6.3, H_2C:C*H*), 5.41 (1H, m, :C*H*), 5.04–4.93 (2H, m, H_2C:), 4.14 (2H, d, *J* 6.9Hz, CH_2OH), 2.21–2.08 (4H, m, CH_2CH_2), 1.67 (3H, s, :CCH_3); δ_C (90 MHz, $CDCl_3$) 139.0 (s), 138.2 (d), 123.6 (d), 114.6 (t), 59.2 (t), 38.7 (t), 31.9 (t), 16.1 (q); *m*/*z* (EI) 109.1017 (M^+ − OH, C_8H_{13} requires 109.1017), which was used without further purification.

Manganese dioxide (2.8 g, 32 mmol) was added portionwise over 5 minutes to a solution of the above alcohol (2.0 g, 0.16 mmol) in dichloromethane (40 mL) at room temperature; the slurry was then stirred at room temperature for 2 hours. The mixture was filtered through Celite and the residue was then washed with dichloromethane (6 × 25 mL). The solvent was removed *in vacuo* to leave a yellow oil which was purified by flash column chromatography on silica using 5% diethyl ether in petroleum ether as eluent to give the aldehyde (1.4 g, 73%) as a pale yellow oil; ν_{max} (film)/cm^{-1} 1676, 1640, 1611, 1442, 1194 and 993; δ_H (360 MHz, $CDCl_3$) 10.00 (1H, d, *J* 8.0, C*H*O), 5.89 (1H, br. d, *J* 8.0, :C*H*), 5.84–5.73 (1H, m, H_2C:C*H*), 5.09–5.00 (2H, m, H_2C:), 2.35–2.24 (4H, m, CH_2CH_2), 2.17 (3H, d, *J* 1.3, :CCH_3); δ_C (90 MHz, $CDCl_3$) 191.2 (d), 163.0 (s), 136.8 (d), 127.6 (d), 115.7 (t), 39.7 (t), 31.1 (t), 17.6 (q); *m*/*z* (EI) 124.0891 (M^+, $C_8H_{12}O$ requires 124.0888), which was used immediately.

5,6-Dimethyl-3-ethoxy-2-((*E*)-1-hydroxy-3-methylhepta-2,6-dienyl)-6-(3-methylbut-3-enyl)cyclohex-2-enone 67a

A solution of *tert*-butyllithium (1.5 M in pentane, 2.8 mL, 4.2 mmol) was added dropwise over 5 minutes to a stirred solution of the bromide **65** (0.47 g, 1.5 mmol) in THF (30 mL) at −78 °C, and the bright yellow solution was then stirred at −78 °C for 30 minutes. The aldehyde **66** (0.50 g, 4.0 mmol) was added, in one portion, and the resulting pale yellow solution was then stirred at −78 °C for 15 minutes. Water (5 mL) was added and the mixture was then allowed to warm to room temperature. The mixture was poured into water (30 mL) and then extracted with ether (2 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 0.5% triethylamine and 50% diethyl ether in petroleum ether as eluent to give the *allylic alcohol* (0.41 g, 76%) as an inseparable 1 : 1 mixture of secondary alcohol epimers, as a pale yellow oil; data for the mixture of diastereoisomers, λ_{max} (EtOH)/nm (ε) 270 (14,000); ν_{max} (film)/cm^{-1} 1639, 1609, 1377, 1232 and 1020; δ_H (360 MHz, $CDCl_3$) 5.83–5.70 (1H, m, H_2C:C*H*), 5.55–5.40 (2H, m, C*H*OH and :C*H*), 5.01–4.87 (2H, m, H_2C:CH), 4.68 (2H, 2 × s, C:CH_2), 4.55 (0.5H, d, *J* 10.7, O*H*), 4.54 (0.5H, d, *J* 10.2, O*H*), 4.15–3.99 (2H, m, OCH_2), 2.65–2.56 (1H, m), 2.35–1.95 (9H, m), 1.90–1.76 (2H, m), 1.73 (3H, d, *J* 1.1, :CCH_3), 1.72 (1.5H, d, *J* 1.3, :CCH_3), 1.71 (1.5H, d, *J* 1.2, :CCH_3), 1.37 (1.5H, t, *J* 7.0, OCH$_2$CH_3), 1.35 (1.5H, t, *J* 7.0, OCH$_2$CH_3), 1.00 (1.5H, d, *J* 6.7, CHCH_3), 0.99 (1.5H, d, *J* 6.4, CHCH_3), 0.96 (1.5H, s, CCH_3), 0.93 (1.5H, s, CCH_3); δ_C (90 MHz, $CDCl_3$) 205.0 (s), 204.9 (s), 168.8 (s), 168.7 (s), 146.1 (s), 146.0 (s), 138.5 (d), 135.6 (s), 135.5 (s), 127.2 (d), 126.7 (d), 118.7 (s), 118.6 (s), 114.2 (t), 114.2 (t), 109.6 (t), 109.5 (t), 64.4 (d), 64.2 (d), 63.6 (t), 63.6 (t), 46.8 (s), 46.6 (s), 38.8 (t), 33.7 (t), 32.6 (d), 31.8 (d), 32.2 (t), 32.0 (t), 30.4 (t), 30.4 (t), 22.5 (q), 18.4 (q), 18.3 (q), 16.4 (q), 15.3 (q), 15.1 (q); *m*/*z* (FAB) 343.2669 (M^+ − OH, $C_{23}H_{35}O_2$ requires 343.2637).

2-[(*E*)-1-(*tert*-Butyldimethylsilanyloxy)-3-methylhepta-2,6-dienyl]-5,6-dimethyl-3-ethoxy-6-(3-methylbut-3-enyl)cyclohex-2-enone 67b

tert-Butyldimethylsilyl triflate (0.32 mL, 1.40 mmol) was added dropwise over 1 minute to a stirred solution of a 1 : 1 mixture of diastereoisomers of the alcohol **67a** (0.38 g, 1.1 mmol) and diisopropylethylamine (0.92 mL, 5.3 mmol) in dichloromethane (11 mL) at 0 °C, and the mixture was stirred at 0 °C for 10 minutes, then allowed to warm to room temperature and diluted with dichloromethane (10 mL). The mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate (25 mL) and the separated aqueous layer was then extracted with dichloromethane (20 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 5% diethyl ether in petroleum ether as eluent to give the *silyl ether* (0.41 g, 82%) as a corresponding mixture of diastereoisomers, as a pale yellow oil; data for the mixture of diastereoisomers, λ_{max} (EtOH)/nm (ε) 267 (13,600); ν_{max} (film)/cm^{-1} 1641, 1613, 1375, 1235, 1059 and 836; δ_H (360 MHz, $CDCl_3$) 5.85–5.73 (2H, m, H_2C:C*H* and :C*H*), 5.69 (0.5H, d, *J* 7.9, C*H*OTBS), 5.68 (0.5H, d, *J* 7.9, C*H*′OTBS), 5.01–4.87 (2H, m, CH:CH_2), 4.67 (1H, 2 × s, C:CH_2), 4.66 (1H, s, C:CH'_2), 4.12–4.00 (2H, m, OCH_2), 2.58 (0.5H, dd, *J* 17.1 and 4.3), 2.57 (0.5H, dd, *J* 17.1 and 4.8), 2.31–1.96 (8H, m), 1.86–1.78 (2H, m), 1.74 (1.5H, s, :CCH_3), 1.72 (1.5H, s, :CCH_3), 1.56 (3H, s, :CCH_3), 1.38 (1.5H, t, *J* 7.0, OCH$_2$CH_3), 1.37 (1.5H, t, *J* 7.0, OCH$_2$CH_3), 0.99 (1.5H, d, *J* 6.1, CHCH_3), 0.98 (1.5H, d, *J* 6.2, CHCH_3), 0.93 (1.5H, s, CCH_3), 0.90 (1.5H, s, CCH_3), 0.85 (4.5H, s, C(CH_3)$_3$), 0.84 (4.5H, s, C(CH'_3)$_3$), 0.02 (1.5H, s, SiCH_3), 0.01 (1.5H, s, SiCH_3), −0.03 (1.5H, s, SiCH_3), −0.04 (1.5H, s, SiCH_3); δ_C (90 MHz, $CDCl_3$) 200.3 (s), 200.2 (s), 146.6 (s), 146.5 (s), 138.8 (d), 131.9 (s), 129.6 (d), 129.5 (d), 121.1 (s), 114.1 (t), 109.3 (t), 63.6 (d), 63.5 (d), 63.1 (t), 46.5 (s), 46.4 (s), 38.8 (t), 38.7 (t), 34.0 (t), 33.7 (t), 32.4 (d), 31.9 (d), 32.2 (t), 30.9 (t), 30.8 (t), 25.9 (q), 22.6 (q), 22.6 (q), 18.4 (q), 18.4 (q), 18.1 (s), 16.3 (q), 15.4 (q), 15.3 (q), −4.6 (q), −4.6 (q); *m*/*z* (EI) 474.3547 (M^+, $C_{29}H_{50}O_3Si$ requires 474.3529).

(5*R*,6*S*)-2-Bromo-5,6-dimethyl-3-ethoxy-6-((*E*/*Z*)-3-methylocta-3,7-dienyl)cyclohex-2-enone 70

A solution of *n*-butyllithium (2.5 M in hexanes, 1.8 mL, 4.5 mmol) was added dropwise over 5 minutes to a stirred slurry of 4-pentenyltriphenylphosphonium bromide **69** (2.0 g, 4.9 mmol) in ether (40 mL) at room temperature and the bright orange mixture was then stirred at room temperature for 30 minutes. The mixture was cooled to −78 °C and then a solution of the ketone **64b** (1.2 g, 3.8 mmol) in THF (5 mL) was added dropwise over 5 minutes. The mixture was stirred at −78 °C for 1 hour and then at room temperature for 1 hour. The mixture was diluted with ether (40 mL), filtered through florisil and then the residue was washed with ether (2 × 50 mL). The combined organic solutions were concentrated *in vacuo* to leave a yellow oil which was purified by flash column chromatography on silica using 5–20% diethyl ether in petroleum ether as eluent to give the *diene* (0.81 g, 58%) as an inseparable 1 : 1 mixture of the *E* and *Z* isomers, as a pale yellow oil; data for the mixture of

isomers, (Found: C, 62.0; H, 8.2; Br, 21.4. $C_{19}H_{29}BrO_2$ requires C, 61.8; H, 7.9; Br, 21.6%); λ_{max} (EtOH)/nm (ε) 274 (16,000); ν_{max} ($CHCl_3$)/cm^{-1} 1661 and 1592; δ_H (360 MHz, $CDCl_3$) 5.85–5.76 (1H, m, H_2C:C*H*), 5.13–5.04 (1H, m, :C*H*), 5.03–4.91 (2H, m, :CH_2), 4.26–4.14 (2H, m, OCH_2), 2.74 (0.5H, dd, *J* 17.5 and 4.5), 2.69 (0.5H, dd, *J* 17.5 and 4.5), 2.43 (0.5H, dd, *J* 17.5 and 3.4), 2.38 (0.5H, dd, *J* 17.5 and 4.5), 2.32–2.24 (1H, m), 2.12–1.98 (5H, m), 1.92–1.74 (2H, m), 1.69 (1.5H, d, *J* 1.2, :CCH_3), 1.60 (1.5H, d, *J* 0.9, :CCH'_3), 1.42 (3H, t, *J* 7.0, OCH_2CH_3), 1.05 (1.5H, d, *J* 6.8, CHCH_3), 1.02 (1.5H, d, *J* 6.8, CHCH_3), 0.98 (1.5H, s, CCH_3), 0.97 (1.5H, s, CCH'_3); δ_C (90 MHz, $CDCl_3$) 195.6 (s), 195.5 (s), 169.6 (s), 169.5 (s), 138.6 (d), 138.6 (d), 135.6 (s), 135.5 (s), 124.4 (d), 123.7 (d), 114.4 (t), 114.3 (t), 102.4 (s), 102.4 (s), 64.7 (t), 48.4 (s), 48.3 (s), 34.4 (t), 34.1 (t), 33.9 (t), 33.8 (t), 32.4 (t), 32.3 (t), 32.0 (d), 31.9 (d), 27.3 (t), 27.1 (t), 26.3 (t), 23.3 (q), 18.6 (q), 18.6 (q), 16.0 (q), 15.1 (q), 14.9 (q), 14.9 (q); *m*/*z* (FAB) 369.1441 (M^+ + H, $C_{19}H_{30}BrO_2$ requires 369.1429).

5,6-Dimethyl-3-ethoxy-2-(1-hydroxyallyl)-6-((*E*/*Z*)-3-methylocta-3,7-dienyl)cyclohex-2-enone 71a

A solution of *tert*-butyllithium (1.5 M in pentane, 4.0 mL, 6.0 mmol) was added dropwise over 5 minutes to a stirred solution of a 1 : 1 mixture of the *E* and *Z* isomers of the bromide **70** (0.81 g, 2.2 mmol) in THF (44 mL) at −78 °C and the bright yellow solution was then stirred at −78 °C for 30 minutes. Acrolein (0.40 mL, 6.0 mmol) was added in one portion and the resulting pale yellow solution was then stirred at −78 °C for 15 minutes. Water (5 mL) was added and the mixture was then allowed to warm to room temperature. The mixture was poured into water (35 mL) and then extracted with ether (2 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a pale yellow oil. The residue was purified by flash column chromatography on silica using 0.5% triethylamine and 20–50% diethyl ether in petroleum ether as eluent to give the *allylic alcohol* (0.58 g, 76%) as an inseparable 1 : 1 mixture of secondary alcohol epimers and *E* and *Z* isomers, as a colourless oil; data for the mixture of isomers, λ_{max} (EtOH)/nm (ε) 204 (9,800), 266 (13,900); ν_{max} (film)/cm^{-1} 3421, 1638, 1608, 1378 and 1234; δ_H (360 MHz, $CDCl_3$) 6.09–5.96 (1H, m, H_2C:C*H*), 5.88–5.80 (1H, m, H_2C:C*H*), 5.28–5.13 (3H, m, C*H*OH, :C*H* and CHO*H*), 5.06–4.83 (4H, m, :CH_2 and :CH_2), 4.19–4.05 (2H, m, OCH_2), 2.68–2.62 (1H, m), 2.40–2.24 (2H, m), 2.10–1.74 (8H, m), 1.72 (1.5H, 2 × br. s, :CCH_3), 1.63 (1.5H, 2 × br. s, :CCH'_3), 1.43–1.36 (3H, m, OCH_2CH_3), 1.08–1.02 (3H, m, CHCH_3), 0.99 (1.5H, 2 × s, CCH_3), 0.95 (1.5H, s, CCH_3); δ_C (90 MHz, $CDCl_3$) 204.8 (s), 204.8 (s), 204.7 (s), 204.7 (s), 169.7 (s), 169.6 (s), 140.2 (d), 140.2 (d), 139.8 (d), 138.8 (d), 138.7 (d), 138.7 (d), 138.6 (d), 135.8 (s), 135.7 (s), 135.6 (s), 135.5 (s), 124.4 (d), 124.3 (d), 123.7 (d), 123.5 (d), 117.0 (s), 116.9 (s), 116.8 (s), 114.4 (t), 114.4 (t), 114.3 (t), 114.3 (t), 112.9 (t), 112.9 (t), 112.8 (t), 68.6 (d), 68.6 (d), 68.4 (d), 63.8 (t), 63.7 (t), 47.1 (s), 46.9 (s), 46.8 (s), 46.7 (s), 34.2 (t), 34.1 (t), 34.1 (t), 33.9 (t), 33.9 (t), 33.6 (t), 33.3 (t), 32.6 (d), 32.5 (d), 31.7 (d), 31.7 (d), 30.4 (t), 27.4 (t), 27.2 (t), 26.6 (t), 26.4 (t), 23.3 (q), 18.4 (q), 18.3 (q), 18.3 (q), 18.2 (q), 16.1 (q), 16.1 (q), 15.3 (q), 15.1 (q); *m*/*z* (EI) 328.2407 (M^+ − H_2O, $C_{22}H_{32}O_2$ requires 328.2402).

2-[1-(*tert*-Butyldimethylsilanyloxy)allyl]-5,6-dimethyl-3-ethoxy-6-((*E*/*Z*)-3-methylocta-3,7-dienyl)cyclohex-2-enone 71b

tert-Butyldimethylsilyl triflate (0.46 mL, 2.0 mmol) was added dropwise over 1 minute to a stirred solution of the diastereoisomeric allylic alcohol **71a** (0.58 g, 1.8 mmol) and diisopropylethylamine (1.5 mL, 8.6 mmol) in dichloromethane (17 mL) at 0 °C and the mixture was then stirred at 0 °C for 30 minutes. The mixture was allowed to warm to room temperature, then diluted with dichloromethane (23 mL) and poured into a saturated aqueous solution of sodium hydrogencarbonate (40 mL). The organic layer was separated and the aqueous layer was then extracted with dichloromethane (20 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated *in vacuo* to leave a yellow oil. The residue was purified by flash column chromatography on silica using 5% diethyl ether in petroleum ether as eluent to give the *silyl ether* (0.66 g, 86%) as a corresponding mixture of diastereoisomers, as a colourless oil; data for the mixture of isomers, (Found: C, 73.1; H, 10.7. $C_{28}H_{48}O_3Si$ requires C, 73.0; H, 10.5%); λ_{max} (EtOH)/nm (ε) 202 (10,800), 265 (12,700); ν_{max} (film)/cm^{-1} 1640, 1612, 1380, 1239 and 836; δ_H (360 MHz, $CDCl_3$) 6.15–6.05 (1H, m, H_2C:C*H*), 5.86–5.78 (1H, m, H_2C:C*H*), 5.49–5.45 (1H, m, C*H*OTBS), 5.18–5.08 (2H, m, HC:CH_2), 5.05–4.89 (3H, m, :C*H* and HC:CH_2), 4.11–3.98 (2H, m, OCH_2), 2.61–2.54 (1H, m), 2.32–2.16 (2H, m), 2.10–1.74 (7H, m), 1.71 (0.75H, d, *J* 1.1, :CCH_3), 1.70 (0.75H, d, *J* 1.1, :CCH_3), 1.62 (0.75H, d, *J* 1.1, :CCH_3), 1.60 (0.75H, d, *J* 1.0, :CCH_3), 1.35 (1.5H, t, *J* 7.1, OCH_2CH_3), 1.34 (1.5H, t, *J* 7.0, OCH_2CH_3), 1.31–1.26 (1H, m), 0.93–0.90 (3H, m, CHCH_3), 0.88 (1.5H, 2 × s, CCH_3 and CCH_3), 0.87 (1.5H, 2 × s, CCH_3 and CCH_3), 0.86 (4.5H, s, C(CH_3)$_3$), 0.85 (4.5H, s, C(CH_3)$_3$), 0.03 (3H, s, Si(CH_3)$_2$), −0.04 (1.5H, s, Si(CH'_3)$_2$), −0.05 (1.5H, s, Si(CH''_3)$_2$); δ_C (90 MHz, $CDCl_3$) 200.6 (s), 200.5 (s), 200.2 (s), 170.6 (s), 170.4 (s), 170.3 (s), 141.0 (s), 141.0 (s), 140.7 (s), 140.6 (s), 138.8 (d), 138.7 (d), 136.1 (d), 136.1 (d), 136.0 (d), 135.9 (d), 124.1 (d), 124.0 (d), 123.4 (d), 123.3 (d), 119.6 (d), 119.5 (d), 114.4 (t), 114.4 (t), 114.3 (t), 111.7 (t), 67.2 (d), 66.9 (d), 66.8 (d), 63.3 (t), 46.6 (s), 46.5 (s), 46.4 (s), 46.3 (s), 34.4 (t), 34.2 (t), 34.0 (t), 33.9 (t), 33.7 (t), 32.2 (d), 31.8 (d), 31.6 (d), 31.0 (t), 30.9 (t), 27.4 (t), 27.18 (t), 27.15 (t), 26.5 (t), 26.4 (t), 25.9 (q), 23.4 (q), 23.3 (q), 18.4 (q), 18.4 (q), 18.4 (q), 18.1 (s), 16.2 (q), 16.1 (q), 15.4 (q), 15.4 (q), 15.2 (q), 15.2 (q), 15.1 (q), −4.7 (q), −4.7 (q), −4.9 (q), −5.0 (q); *m*/*z* (CI) 460.3334 (M^+, $C_{28}H_{48}O_3Si$ requires 460.3373).

(3*E*,7*E*)-2-(*tert*-Butyldimethylsilanyloxy)-14-ethoxy-8,11,12-trimethylbicyclo[9.3.1]pentadeca-1(14),3,7-trien-15-one 72

A solution of the Grubbs′ ruthenium pre-catalyst (74 mg, 0.091 mmol) in dichloromethane (5 mL) was added dropwise over 10 hours to a refluxing solution of the diastereoisomeric diene **71b** (245 mg, 0.53 mmol) and the ruthenium pre-catalyst (37 mg, 0.05 mmol) in dichloromethane (180 mL). The mixture was heated under reflux for a further 5 hours and then allowed to cool to room temperature. The solvent was removed *in vacuo* to leave an orange residue which was purified by flash column chromatography on silica using 5–10–20% diethyl ether in petroleum ether as eluent to give: (i) a less polar isomer (48 mg, 22%) (eluted first) as a colourless oil, ν_{max} (film)/cm^{-1} 1644, 1614, 1380, 1226 and 833; δ_H (500 MHz, $CDCl_3$) 5.45 (1H, dd, *J* 14.8 and 9.2, CHOTBSC:*H*), 5.38 (1H, d, *J* 9.2, C*H*OTBS), 5.14 (1H, ddd, *J* 14.8, 11.2 and 2.6, HC:C*H*CH_2), 4.72–4.70 (1H, m, :C*H*), 4.15 (1H, dq, *J* 9.6 and 7.1, OC*H*(H)CH_3), 3.95 (1H, dq, *J* 9.6 and 7.1, OC(H)*H*CH_3), 2.50–2.46 (1H, m), 2.39–2.17 (3H, m), 2.08–2.01 (1H, m), 1.93–1.82 (3H, m), 1.59 (3H, br. s, :CCH_3), 1.37 (3H, t, *J* 7.1, OCH_2CH_3), 0.94 (3H, d, *J* 6.7, CHCH_3), 0.87 (9H, s, SiC(CH_3)$_3$), 0.85 (3H, s, CCH_3), 0.01 (3H, s, SiCH_3), 0.00 (3H, s, SiCH_3); δ_C (90 MHz, $CDCl_3$) 199.7 (s), 168.9 (s), 135.5 (s), 132.2 (d), 129.2 (d), 124.3 (d), 121.1 (s), 70.3 (d), 63.2 (t), 45.8 (s), 34.7 (t), 31.3 (t), 30.5 (t), 27.7 (t), 26.2 (q), 18.8 (q), 18.3 (s), 15.4 (q), 15.2 (q), 15.1 (q), −4.6 (q); *m*/*z* (FAB) 432.3097 (M^+, $C_{26}H_{44}O_3Si$ requires 432.3060); and (ii) a more polar isomer (10 mg, 5%) (eluted second) as a yellow oil, δ_H (360 MHz, $CDCl_3$) 5.97 (1H, dd, *J* 15.9 and 7.1, CH(OTBS)C:*H*), 5.32 (1H, d, *J* 7.1, C*H*OTBS), 5.12 (1H, dt, *J* 15.9 and 6.6, HC:C*H*CH_2), 4.75–4.72 (1H, m, :C*H*), 4.09–3.99 (2H, m, OCH_2), 2.69 (1H, dd, *J* 17.5 and 5.0), 2.24 (1H, dd, *J* 17.5 and 7.3), 2.11–2.06 (3H, m), 2.02–1.90 (3H, m), 1.52 (3H, br. s, :CCH_3), 1.37 (3H, t, *J* 7.0, OCH_2CH_3), 0.96 (3H, d, *J* 6.9, CHCH_3), 0.91 (3H, s, CCH_3), 0.85 (9H, s, SiC(CH_3)$_3$), 0.02 (3H, s, SiCH_3), −0.02 (3H, s, SiCH_3); δ_C (90 MHz, $CDCl_3$) 199.4 (s),

165.5 (s), 137.6 (d), 135.3 (s), 125.3 (d), 124.7 (d), 122.6 (s), 66.6 (d), 63.1 (t), 46.8 (s), 34.5 (d), 34.1 (t), 32.5 (t), 30.3 (t), 29.7 (t), 26.5 (t), 26.0 (q), 19.1 (q), 18.2 (s), 15.9 (q), 15.6 (q), 15.3 (q), −4.5 (q), −4.6 (q); *m*/*z* (EI) 375.2362 ($M^+ - t$Bu, $C_{22}H_{35}O_3Si$ requires 375.2355).

7-Methyl-4,6,7,8-tetrahydrobenzo[1,3]dioxin-5-one 73a

A solution of 5-methylcyclohexane-1,3-dione (8.0 g, 63.7 mmol) in dichloromethane (400 mL) was added dropwise *via* cannula over 5 hours to a stirred solution of *s*-trioxane (34.4 g, 382 mmol) and boron trifluoride diethyl etherate (24.5 mL, 191 mmol) in dichloromethane (1.1 L) at room temperature. The mixture was stirred for 21 hours, then quenched with a saturated aqueous solution of $NaHCO_3$ (1 L) and stirred vigorously for 90 minutes. The separated aqueous phase was extracted with dichloromethane (3 × 200 mL) and the combined organic extracts were washed with brine (1 L), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash vacuum chromatography on silica using 20–40% diethyl ether in petroleum ether as eluent to give the *dioxin* (10.0 g, 93%) as a colourless oil, which crystallised on storage at 4 °C; mp 34–35 °C; ν_{max} (film)/cm^{-1} 2956, 2872, 1710, 1634 and 1223; δ_H (360 MHz, $CDCl_3$) 5.19 (1H, d, *J* 5.5, OC*H*HO), 5.07 (1H, d, *J* 5.5, OCH*H*O), 4.43 (2H, br. s, CH_2O), 2.44 (1H, d, *J* 3.0, C*H*HCO), 2.40 (1H, d, *J* 3.7, CH*H*CO), 2.26–2.03 (3H, m, CH_2C=C and C*H*), 1.08 (3H, d, *J* 6.3, CH_3CH); δ_C (90 MHz, $CDCl_3$) 196.3 (C=O), 169.6 (CO*C*=C), 111.3 (COC=*C*), 91.5 (O*C*H_2O), 62.9 (*C*H_2O), 44.8 (*C*H_2C=O), 35.7 (*C*H_2C=C), 28.4 (CH_3*C*H), 21.0 (*C*H_3CH); *m*/*z* (EI) 168.0793 (M^+, 45%, $C_9H_{12}O_3$ requires 168.0786), 152 (73), 137 (35), 124 (45), 110 (30), 96 (100) and 82 (57).

syn- and *anti*-6,7-Dimethyl-4,6,7,8-tetrahydrobenzo[1,3]dioxin-5-ones 73b

Diisopropylamine (4.6 mL, 33 mmol) was added dropwise over 1 minute to a stirred solution of *n*-butyllithium (2.5 M in hexane, 12.0 mL, 30 mmol) in THF (100 mL) at 0 °C and the mixture was stirred at 0 °C for 15 minutes. The solution was allowed to warm to room temperature over 30 minutes, then cooled to −78 °C, and a solution of the dioxin **73a** (5.0 g, 30 mmol) in THF (100 mL) was added dropwise *via* cannula over 15 minutes. The mixture was stirred at −78 °C for 1 hour, then methyl iodide (4.6 mL, 71 mmol) was added dropwise over 5 minutes and the mixture was allowed to warm to room temperature over 16 hours. The mixture was quenched with water (150 mL) and the separated aqueous phase was extracted with diethyl ether (3 × 100 mL). The combined organic extracts were washed with brine (200 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20–40% diethyl ether in petroleum ether as eluent to give: (i) the *syn-dimethyl dioxin* (2.55 g, 47%) (eluted first) as a colourless oil; (Found: C, 65.6; H, 7.6. $C_{10}H_{14}O_3$ requires C, 65.9; H, 7.7%); ν_{max} (film)/cm^{-1} 2967, 2874, 1632 and 1221; δ_H (360 MHz, $CDCl_3$) 5.17 (1H, d, *J* 5.5, OC*H*HO), 5.07 (1H, d, *J* 5.5, OCH*H*O), 4.46–4.36 (2H, m, CH_2O), 2.43 (1H, dd, *J* 17.6 and 4.6, C*H*HC=C), 2.21 (1H, ddt, *J* 17.6, 10.0 and 2.4, CH*H*C=C), 1.99 (1H, dq, *J* 10.5 and 6.5, CH_3C*H*), 1.93–1.84 (1H, m, CH_3C*H*), 1.14 (3H, d, *J* 6.6, CH_3CH), 1.09 (3H, d, *J* 6.4, CH_3CH); δ_C (90 MHz, $CDCl_3$) 198.2 (C=O), 168.3 (CO*C*=C), 110.6 (COC=*C*), 91.3 (O*C*H_2O), 63.0 (*C*H_2O), 46.9 (*C*HC=O), 35.4 (*C*H_2C=C), 34.4 (CH_3*C*H), 19.7 (*C*H_3CH), 12.4 (*C*H_3CH); *m*/*z* (EI) 182.0947 (M^+, 71%, $C_{10}H_{14}O_3$ requires 182.0943), 152 (73), 137 (33), 124 (38), 96 (100) and 82 (34); and (ii) the *anti-dimethyl dioxin* (2.55 g, 47%) as a colourless oil; ν_{max} (film)/cm^{-1} 2967, 2931, 2876, 1634 and 1231; δ_H (360 MHz, $CDCl_3$) 5.15 (1H, d, *J* 5.5, OC*H*HO), 5.12 (1H, d, *J* 5.5, OCH*H*O), 4.42 (2H, t, *J* 2.0, *CH*$_2$*O*), 2.48–2.29 (3H, m, CH_3C*H* and CH_2C=C), 2.24 (1H, ddt, *J* 17.1, 7.6 and 2.0, CH_3C*H*), 1.06 (3H, d, *J* 7.1, CH_3CH), 1.00 (3H, d, *J* 6.6, CH_3CH); δ_C (90 MHz, $CDCl_3$) 199.7 (C=O), 168.2 (CO*C*=C), 110.0 (COC=*C*), 91.4 (O*C*H_2O), 62.9 (*C*H_2O), 44.8 (*C*HC=O), 33.1 (*C*H_2C=C), 31.4 (CH_3*C*H), 15.9 (*C*H_3CH), 11.0 (*C*H_3CH); *m*/*z* (EI) 182.0950 (M^+, 95%, $C_{10}H_{14}O_3$ requires 182.0943), 152 (51), 137 (38), 124 (47), 109 (46), 96 (100) and 82 (32).

tert-Butyl-((*E*)-4-iodo-3-methylbut-3-enyloxy)dimethylsilane 80

The vinyl iodide **80** was prepared according to a modification of the method of Negishi and co-workers.[35,43] Trimethylaluminium (2.0 M in hexane, 100 mL, 200 mmol) was added dropwise over 20 minutes to a stirred solution of zirconocene dichloride (7.4 g, 25.5 mmol) in dichloromethane (300 mL) at −10 °C. The mixture was stirred at −10 °C for 10 minutes and then a solution of 3-butyn-1-ol (4.6 g, 65.7 mmol) in dichloromethane (15 mL) was added dropwise cautiously over 15 minutes. **Caution: the addition results in a rapid increase in pressure.** The stirred mixture was allowed to warm to room temperature over 22 hours, then cooled to −30 °C and treated dropwise *via* cannula with a solution of iodine (30.0 g, 118 mmol) in THF (65 mL) over 20 minutes. The brown coloured solution was allowed to warm to 0 °C over 40 minutes and then quenched cautiously with methanol (15 mL) and a saturated aqueous solution of Rochelle's salt (400 mL). The resulting mixture was allowed to warm to room temperature and then stirred vigorously for 10 hours. The mixture was filtered through a pad of celite and then the separated aqueous phase was extracted with dichloromethane (3 × 100 mL). The combined organic extracts were sequentially washed with 2M sodium hydroxide solution (100 mL) and brine (200 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 35–50% diethyl ether in pentane as eluent to give the vinyl iodide (11.4 g, 81%) as a colourless oil; ν_{max} (film)/cm^{-1} 3298, 3058, 2938, 1616, 1272 and 1047; δ_H (360 MHz, $CDCl_3$) 6.02 (1H, m, C=C*H*I), 3.72 (2H, t, *J* 6.3, HOCH_2), 2.48 (2H, dt, *J* 6.3 and 1.0, HOCH$_2$CH_2), 1.88 (3H, d, *J* 1.1, CH_3C=CHI), 1.46 (1H, br. s, O*H*); δ_C (90 MHz, $CDCl_3$) 144.5 (*C*=CHI), 76.8 (C=*C*HI), 60.1 (HO*C*H_2), 42.4 (HOCH$_2$*C*H_2), 23.8 (*C*H_3C=CHI).

tert-Butyldimethylsilyl chloride (2.85 g, 18.9 mmol) was added in portions to a stirred solution of the vinyl iodide (2.97 g, 14.0 mmol), 4-dimethylaminopyridine (0.17 g, 1.4 mmol), and triethylamine (4.1 mL, 29.4 mmol) in dichloromethane (88 mL) at 0 °C. The mixture was allowed to warm to room temperature over 70 hours and then washed with a saturated aqueous solution of $NaHCO_3$ (40 mL). The separated aqueous phase was extracted with dichloromethane (3 × 30 mL) and the combined organic extracts were washed with brine (35 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 10% diethyl ether in pentane as eluent to give the silyl ether (4.5 g, 98%) as a colourless oil; ν_{max} (film)/cm^{-1} 2952, 2856, 1618, 1255 and 1103; δ_H (360 MHz, $CDCl_3$) 5.94 (1H, t, *J* 1.0, C=C*H*I), 3.69 (2H, t, *J* 6.6, SiOCH_2), 2.42 (2H, dt, *J* 6.6 and 1.0, SiOCH$_2$CH_2), 1.86 (3H, d, *J* 1.0, CH_3C=CHI), 0.89 (9H, s, SiC(CH_3)$_3$), 0.05 (6H, s, Si(CH_3)$_2$); δ_C (90 MHz, $CDCl_3$) 145.2 (*C*=CHI), 76.3 (C=*C*HI), 61.3 (SiO*C*H_2), 42.6 (SiOCH$_2$*C*H_2), 25.9 (SiC(*C*H_3)$_3$), 24.2 (*C*H_3C=CH), 18.2 (SiC(CH$_3$)$_3$), −5.4 (Si(*C*H_3)$_2$); *m*/*z* (CI) 327.0641 (MH^+, 32%, $C_{11}H_{24}$OISi requires 327.0629), 311 (40), 286 (100), 269 (49), 256 (25), 239 (19), 199 (30), 187 (42) and 132 (22).

(4-Iodobut-1-ynyl)trimethylsilane 81

The alkynyl iodide **81** was prepared according to a modification of the method of Pattenden and Teague.[44] *n*-Butyllithium (2.5 M in hexane, 80.4 mL, 201 mmol) was added dropwise *via* cannula over 20 minutes to a stirred solution of 3-butyn-1-ol (6.7 g, 96 mmol) in THF (300 mL) at −78 °C. The mixture was stirred at −78 °C for 1 hour, then chlorotrimethylsilane (29.5 mL, 232 mmol) was added dropwise over 5 minutes and

the mixture was stirred at −78 °C for 30 minutes. The mixture was allowed to warm to 0 °C over 1 hour, then quenched by cautious addition of water (100 mL) and allowed to warm to room temperature. The separated aqueous phase was extracted with diethyl ether (2 × 100 mL) and the combined organic extracts were concentrated *in vacuo*. The residue was dissolved in diethyl ether (200 mL) and washed sequentially with 2 M hydrochloric acid (100 mL), a saturated aqueous solution of $NaHCO_3$ (2 × 200 mL), and brine (200 mL). The organic extract was dried over $MgSO_4$ and concentrated *in vacuo*. Triphenylphosphine (28.9 g, 110 mmol) and imidazole (12.4 g, 183 mmol) were added to a stirred solution of the residue in dichloromethane (450 mL) and the mixture was then cooled to 0 °C. Iodine (27.9 g, 110 mmol) was added in portions over 10 minutes and the resulting mixture was stirred at 0 °C for 5 hours. The mixture was diluted with water (300 mL) and the separated aqueous phase was extracted with pentane (2 × 100 mL). The combined organic extracts were washed with brine (200 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using petroleum ether as eluent to give the iodide (21.9 g, 91%) as a colourless oil (Found: C, 33.3; H, 5.0. Calc. for $C_7H_{13}ISi$: C, 33.3; H, 5.2%); ν_{max} (film)/cm^{-1} 2958, 2175 and 1249; δ_H (360 MHz, $CDCl_3$) 3.22 (2H, t, *J* 7.5, ICH_2), 2.80 (2H, t, *J* 7.5, ICH_2CH_2), 0.17 (9H, s, $Si(CH_3)_3$); δ_C (90 MHz, $CDCl_3$) 105.0 (C≡*C*TMS), 86.8 (*C*≡CTMS), 25.0 (ICH_2CH_2), 1.0 (ICH_2CH_2), −0.1 ($Si(CH_3)_3$).

(*E*)-8-(*tert*-Butyldimethylsilanyloxy)-6-methyl-1-trimethylsilanyloct-5-en-1-yne 82

The enyne **82** was prepared according to a modification of the method of Negishi and co-workers.[35] A solution of the iodide **81** (4.2 g, 16.6 mmol) in diethyl ether (50 mL) was added dropwise *via* cannula over 15 minutes to a stirred solution of *tert*-butyllithium (1.5 M in pentane, 21.0 mL, 31.5 mmol) in diethyl ether (30 mL) at −78 °C. The solution was stirred at −78 °C for 90 minutes and then a solution of anhydrous zinc chloride (3.0 g, 22.1 mmol), pre-weighed in a glove bag under an atmosphere of argon, in THF (40 mL) was added dropwise *via* cannula over 5 minutes. The mixture was allowed to warm to 0 °C over 1 hour and then added dropwise *via* cannula over 5 minutes to a stirred mixture of *tetrakis*(triphenylphosphine)-palladium(0) (0.4 g, 0.4 mmol) and the vinyl iodide **80** (3.7 g, 11.3 mmol) at 0 °C. The mixture was allowed to warm to room temperature over 15 hours and then quenched with water (70 mL). The separated aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 0–2% diethyl ether in pentane as eluent to give the olefin (3.5 g, 94%) as a colourless oil; ν_{max} (film)/cm^{-1} 2956, 2928, 2857, 2176, 1472, 1250 and 1097; δ_H (360 MHz, $CDCl_3$) 5.20 (1H, br. t, *J* 5.7, C=C*H*), 3.67 (2H, t, *J* 7.1, $SiOCH_2$), 2.23–2.19 (6H, m, 3 × CH_2), 1.64 (3H, d, *J* 1.2, CH_3C=CH), 0.90 (9H, s, $SiC(CH_3)_3$), 0.15 (9H, s, $Si(CH_3)_3$), 0.05 (6H, s, $Si(CH_3)_2$); δ_C (90 MHz, $CDCl_3$) 133.7 (*C*=CH), 124.5 (C=*C*H), 107.3 (C≡*C*Si), 84.3 (*C*≡CSi), 62.4 ($SiOCH_2$), 43.0 ($SiOCH_2CH_2$), 27.4 (C=CHCH_2), 25.9 ($SiC(CH_3)_3$), 20.2 (CH_2C≡C), 18.3 ($SiC(CH_3)_3$), 16.6 (CH_3C=CH), 0.1 ($Si(CH_3)_3$), −5.3 ($Si(CH_3)_2$); *m*/*z* (EI) 267.1600 (M^+ − ^{t}Bu, 9%, $C_{14}H_{27}OSi_2$ requires 267.1597), 179 (18) and 73 (100).

(*E*)-3-Methyloct-3-en-7-yn-1-ol 83

Tetra-*n*-butylammonium fluoride trihydrate (32.2 g, 102 mmol) was added in one portion to a stirred solution of the silyl ether **82** (9.90 g, 30.5 mmol) in THF (250 mL) at 0 °C and the resulting mixture was allowed to warm to room temperature over 3 hours. The reaction was quenched with a saturated aqueous solution of NH_4Cl (75 mL), then diluted with diethyl ether (150 mL) and the separated aqueous phase was extracted with diethyl ether (3 × 75 mL). The combined organic extracts were washed with brine (120 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 50% diethyl ether in pentane as eluent to give the *alcohol* (3.84 g, 91%) as a colourless oil; ν_{max} (film)/cm^{-1} 3288, 2933, 2116, 1668 and 1043; δ_H (360 MHz, $CDCl_3$) 5.29 (1H, br. t, *J* 5.8, C=C*H*), 3.67 (2H, t, *J* 6.1, $HOCH_2$), 2.31–2.23 (6H, m, 3 × CH_2), 1.95 (1H, t, *J* 2.4, C≡C*H*), 1.67 (3H, d, *J* 0.7, CH_3C=CH), 1.60 (1H, br. s, O*H*); δ_C (90 MHz, $CDCl_3$) 133.2 (*C*=CH), 126.0 (C=*C*H), 84.2 (*C*≡CH), 68.5 (C≡*C*H), 59.8 ($HOCH_2$), 42.6 ($HOCH_2CH_2$), 26.9 (C=CHCH_2), 18.8 (CH_2C≡C), 15.8 (CH_3C=CH); *m*/*z* (EI) 138.1045 (M^+, 1%, $C_9H_{14}O$ requires 138.1041), 105 (20), 99 (24), 81 (100), 69 (27) and 55 (28).

(3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dien-1-ol 84

Trimethylaluminium (2.0 M in hexane, 4.80 mL, 9.54 mmol) was added dropwise over 15 minutes to a stirred solution of zirconocene dichloride (0.46 g, 1.6 mmol) in dichloromethane (20 mL) at −5 °C. The mixture was stirred at −5 °C for 40 minutes and then a solution of the alcohol **83** (0.44 g, 3.2 mmol) in dichloromethane (20 mL) was added dropwise *via* cannula over 10 minutes. The stirred mixture was allowed to warm to room temperature over 15 hours, then cooled to −25 °C, and a solution of iodine (1.61 g, 6.36 mmol) in THF (10.6 mL) was added dropwise *via* cannula over 5 minutes. The brown coloured solution was allowed to warm to 0 °C over 1 hour and then quenched by the cautious addition of methanol (6 mL) followed by 2 M hydrochloric acid (10 mL). The separated aqueous phase was extracted with dichloromethane (3 × 10 mL) and the combined organic extracts were washed with brine (25 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 40% diethyl ether in pentane as eluent to give the *vinyl iodide* (0.81 g, 91%) as a colourless oil (Found: C, 43.2; H, 6.0. $C_{10}H_{17}IO$ requires C, 42.9; H, 6.1%); ν_{max} (film)/cm^{-1} 3622, 2939, 1715 and 1050; δ_H (360 MHz, $CDCl_3$) 5.88 (1H, app. sextet, *J* 1.0, C=C*H*I), 5.17 (1H, br. t, *J* 6.8, C=C*H*), 3.66 (2H, t, *J* 6.1, $HOCH_2$), 2.27–2.15 (6H, m, 3 × CH_2), 1.84 (3H, d, *J* 1.0, CH_3C=CHI), 1.63 (3H, d, *J* 0.4, CH_3C=CH), 1.40 (1H, br. s, O*H*); δ_C (90 MHz, $CDCl_3$) 147.6 (*C*=CHI), 132.3 (*C*=CH), 126.4 (C=*C*H), 74.9 (C=*C*HI), 60.0 ($HOCH_2$), 42.6 ($HOCH_2CH_2$), 39.3 (CH_2C=CHI), 26.2 (C=CHCH_2), 23.8 (CH_3C=CHI), 15.7 (CH_3C=CH); *m*/*z* (FAB) 279.0241 (M^+ − H, 10%, $C_{10}H_{16}IO$ requires 279.0246), 153 (31), 138 (22), 121 (18), 107 (43), 97 (25), 93 (38), 79 (24), 73 (100) and 57 (46).

(1*E*,5*E*)-1,8-Diiodo-2,6-dimethylocta-1,5-diene 85

Triphenylphosphine (3.91 g, 14.9 mmol) and imidazole (1.77 g, 26.0 mmol) were added to a stirred solution of the alcohol **84** (3.48 g, 12.4 mmol) in dichloromethane (78 mL) and the mixture was cooled to 0 °C. Iodine (3.78 g, 14.9 mmol) was added in portions over 10 minutes and the resulting mixture was allowed to warm to room temperature over 22 hours. The mixture was washed with a saturated aqueous solution of $Na_2S_2O_3$ (70 mL) and the separated aqueous phase was extracted with pentane (3 × 70 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20% diethyl ether in pentane as eluent to give the *homoallylic iodide* (4.80 g, 99%) as a colourless oil; ν_{max} (film)/cm^{-1} 3052, 2910, 2850, 1616, 1442, 1375 and 1267; δ_H (360 MHz, $CDCl_3$) 5.90 (1H, app. sextet, *J* 1.1, C=C*H*I), 5.16 (1H, tq, *J* 6.9 and 1.2, C=C*H*), 3.22 (2H, t, *J* 7.5, ICH_2), 2.53 (2H, t, *J* 7.5, ICH_2CH_2), 2.26 (2H, t, *J* 7.4, CH_2C=CHI), 2.15 (2H, dt, *J* 7.6 and 6.9, C=CHCH_2), 1.85 (3H, d, *J* 1.1, CH_3C=CHI), 1.61 (3H, br. s, CH_3C=CH); δ_C (90 MHz, $CDCl_3$) 147.4 (*C*=CHI), 134.4 (*C*=CH), 126.0

(C=*C*H), 75.1 (C=*C*HI), 43.6 (ICH$_2$*C*H$_2$), 39.1 (*C*H$_2$C=CHI), 26.2 (C=CH*C*H$_2$), 23.9 (*C*H$_3$C=CHI), 15.3 (*C*H$_3$C=CH), 4.9 (I*C*H$_2$); *m/z* (EI) 263.0292 (M$^+$ − I, 78%, $C_{10}H_{16}I$ requires 263.0297) and 81 (100).

6-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-6,7-dimethyl-4,6,7,8-tetrahydrobenzo[1,3]dioxin-5-one 74

Diisopropylamine (1.3 mL, 9.3 mmol) was added dropwise over 1 minute to a stirred solution of *n*-butyllithium (2.5 M in hexane, 3.5 mL, 8.8 mmol) in THF (25 mL) at 0 °C. The solution was stirred at 0 °C for 20 minutes, then cooled to −78 °C, and a solution of a 1 : 1 mixture of diastereoisomers of the enone **73b** (1.6 g, 8.8 mmol) in THF (5 mL) was added dropwise *via* cannula over 3 minutes. The mixture was stirred at −78 °C for 2 hours and then DMPU (5.3 mL, 44 mmol) was added dropwise over 5 minutes. The mixture was stirred at −78 °C for 25 minutes, then a solution of the iodide **85** (2.3 g, 5.9 mmol) in THF (10 mL) was added dropwise *via* cannula over 3 minutes and the mixture was allowed to warm to room temperature over 4 days. The mixture was quenched with a saturated aqueous solution of NH_4Cl (20 mL), then diluted with water (10 mL), and the separated aqueous phase was extracted with diethyl ether (4 × 20 mL). The combined organic extracts were washed with brine (50 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 10% diethyl ether in pentane as eluent to give the *ketone* (2.0 g, 76%) as an inseparable 3 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a viscous, colourless oil; data for the *syn*-dimethyl isomer, (Found: C, 54.4; H, 6.6. $C_{20}H_{29}O_3I$ requires C, 54.1; H, 6.6%); ν_{max} (film)/cm^{-1} 2962, 2928, 2874, 1640 and 1223; δ_H (360 MHz, $CDCl_3$) 5.85 (1H, app. sextet, *J* 1.1, C=C*H*I), 5.17 (1H, d, *J* 5.5, OC*H*HO), 5.09 (1H, d, *J* 5.5, OCH*H*O), 5.06 (1H, tq, *J* 6.6 and 1.1, C=C*H*), 4.45–4.38 (2H, m, CH_2O), 2.42–2.20 (5H, m, CH$_3$C*H*, CH_2C=CHI and CHCH_2), 2.10 (2H, dt, *J* 7.5 and 6.9, C=CHCH_2), 2.01 (1H, ddd, *J* 13.3, 11.9 and 4.6, CH*H*C=CH), 1.94–1.85 (1H, m, C*H*HC=CH) 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.80–1.70 (1H, m, C(4°)–CH*H*), 1.61 (3H, br. s, CH_3C=CH), 1.34 (1H, ddd, *J* 13.4, 11.9 and 5.0, C(4°)–C*H*H), 1.00 (3H, d, *J* 6.2, CH_3CH), 0.98 (3H, s, CH_3–C(4°)); δ_C (90 MHz, $CDCl_3$) 200.8 (*C*=O), 167.4 (COC=*C*), 147.8 (*C*=CHI), 136.4 (*C*=CH), 122.9 (C=*C*H), 110.0 (CO*C*=C), 91.3 (O*C*H$_2$O), 74.7 (C=*C*HI), 63.1 (*C*H$_2$O), 47.2 (*C*(4°)–C=O), 39.4 (CH*C*H$_2$), 34.1 (C(4°)–*C*H$_2$), 33.8 (*C*H$_2$C=CH), 32.7 (*C*H$_2$C=CHI), 32.0 (CH$_3$*C*H), 26.2 (C=CH*C*H$_2$), 23.9 (*C*H$_3$C=CHI), 18.6 (*C*H$_3$–C(4°)), 16.0 (*C*H$_3$C=CH), 14.9 (*C*H$_3$CH); *m/z* (ES) 445.1235 (MH$^+$, 100%, $C_{20}H_{30}O_3I$ requires 445.1240).

2-Hydroxymethyl-4-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-3-(4-methoxybenzyloxymethyl)-4,5-dimethylcyclohex-2-enone 75a

n-Butyllithium (2.5 M in hexane, 4.2 mL, 10.5 mmol) was added dropwise over 5 minutes to a stirred solution of the tributyl-(4-methoxybenzyloxymethyl)-stannane[45] (4.89 g, 11.1 mmol) in diethyl ether (12.3 mL) at −78 °C. The solution was stirred at −78 °C for 70 minutes and then a solution of a 3 : 1 mixture of diastereoisomers of the ketone **74** (1.10 g, 2.47 mmol) in toluene (49.0 mL) was added dropwise over 5 minutes. The mixture was allowed to warm to −25 °C over 5 hours, then quenched with a saturated aqueous solution of NH_4Cl (40 mL) and allowed to warm to room temperature overnight. The separated aqueous phase was extracted with diethyl ether (3 × 40 mL), and the combined organic extracts were concentrated *in vacuo*. The residue was diluted with THF (40 mL), then treated with 2M hydrochloric acid (20 mL) and stirred at room temperature for 40 minutes. The mixture was neutralised with a saturated aqueous solution of K_2CO_3 (30 mL), and the separated aqueous phase was then extracted with diethyl ether (3 × 40 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 50–60% diethyl ether in pentane as eluent to give the *hydroxyketone* (0.96 g, 69%) as an inseparable 2 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a colourless oil; data for the *syn*-dimethyl isomer, ν_{max} (film)/cm^{-1} 3474, 2933, 1666, 1612, 1249 and 1035; δ_H (360 MHz, $CDCl_3$) 7.27 (2H, d, *J* 8.2, 2 × Ar*H*), 6.89 (2H, dd, *J* 8.2 and 1.2, 2 × Ar*H*), 5.85 (1H, br. s, C=C*H*I), 5.02 (1H, dd, *J* 12.9 and 6.7, C=C*H*), 4.51 (2H, s, ArCH_2), 4.41–4.33 (2H, m, CH_2OH), 4.18 (1H, d, *J* 10.8, OC*H*HC=C), 4.10 (1H, d, *J* 10.8, OCH*H*C=C), 3.81 (3H, s, OCH_3), 2.98 (1H, br. s, O*H*), 2.52–2.28 (2H, m, CH_2C=CHI), 2.22 (1H, d, *J* 6.6, CHCH*H*), 2.20 (1H, d, *J* 5.8, CHC*H*H), 2.14–2.05 (3H, m, CH$_3$C*H* and C=CHCH_2), 1.92 (2H, t, *J* 8.4, CH_2C=CH), 1.83 (3H, br. s, CH_3C=CHI), 1.73–1.51 (2H, m, C(4°)–CH_2), 1.56 (3H, br. s, CH_3C=CH), 1.04 (3H, s, CH_3–C(4°)), 0.96 (3H, d, *J* 6.6, CH_3CH); δ_C (90 MHz, $CDCl_3$) 200.2 (*C*=O), 160.4 (*C*=CC=O), 159.5 (Ar–*C*(4°)), 147.6 (*C*=CHI), 138.0 (Ar–*C*(4°)), 136.0 (*C*=CH), 129.7 (Ar–*C*H), 129.1 (C=*C*C=O), 123.4 (C=*C*H), 113.9 (Ar–*C*H), 74.8 (C=*C*HI), 73.3 (Ar*C*H$_2$O), 66.1 (O*C*H$_2$C=C), 57.5 (*C*H$_2$OH), 55.3 (O*C*H$_3$), 42.5 (*C*H$_2$C=CHI), 41.6 (*C*(4°)–C=C), 39.3 (CH*C*H$_2$), 37.5 (CH$_3$*C*H), 34.7 (*C*H$_2$C=CH), 34.0 (C(4°)–*C*H$_2$), 26.1 (C=CH*C*H$_2$), 23.9 (*C*H$_3$C=CHI), 16.1 (*C*H$_3$C=CH), 15.9 (*C*H$_3$–C(4°)), 15.5 (*C*H$_3$CH); *m/z* (ES) 589.1811 (M$^+$ + Na, 100%, $C_{28}H_{39}O_4INa$ requires 589.1791).

4-Nitrobenzoic acid 3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-3,4-dimethyl-6-oxocyclohex-1-enylmethyl ester 75b

4-Nitrobenzoyl chloride (1.70 g, 9.15 mmol) was added to a stirred solution of 4-dimethylaminopyridine (74.5 mg, 0.61 mmol), triethylamine (2.00 mL, 14.3 mmol), and a 2 : 1 mixture of diastereoisomers of the alcohol **75a** (1.73 g, 3.05 mmol) in dichloromethane (60 mL) at −25 °C. The mixture was allowed to warm to 0 °C over 90 minutes and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 40–50% diethyl ether in pentane as eluent to give the *ester* (2.18 g, 99%) as a corresponding mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a colourless oil; data for the *syn*-dimethyl isomer, ν_{max} (film)/cm^{-1} 2935, 1724, 1676 and 1610; δ_H (360 MHz, $CDCl_3$) 8.19 (2H, dd, *J* 8.2 and 1.0, 2 × Ar*H*), 8.05 (2H, ddd, *J* 8.2, 2.6 and 1.0, 2 × Ar*H*), 7.18 (2H, dd, *J* 8.4 and 1.3, 2 × Ar*H*), 6.89 (2H, dd, *J* 8.4 and 2.1, 2 × Ar*H*), 5.85 (1H, app. sextet, *J* 1.1, C=C*H*I), 5.23 (1H, d, *J* 11.6, C*H*HOPNB), 5.17 (1H, d, *J* 11.6, CH*H*OPNB), 5.03 (1H, dd, *J* 12.5 and 6.4, C=C*H*), 4.46 (2H, s, ArCH_2), 4.25 (1H, d, *J* 10.5, OC*H*HC=C), 4.20 (1H, d, *J* 10.5, OCH*H*C=C), 3.76 (3H, s, OCH_3), 2.63–2.35 (2H, m, CH_2C=CHI), 2.22 (1H, d, *J* 7.0, CHCH*H*), 2.18 (1H, d, *J* 5.3, CHC*H*H), 2.15–2.09 (3H, m, CH$_3$C*H* and C=CHCH_2), 1.98–1.93 (2H, m, CH_2C=CH), 1.83 (3H, br. s, CH_3C=CHI), 1.75–1.60 (2H, m, C(4°)–CH$_2$), 1.58 (3H, br. s, CH_3C=CH), 1.28 (3H, s, CH_3–C(4°)), 1.06 (3H, d, *J* 6.8, CH_3CH); δ_C (90 MHz, $CDCl_3$) 197.7 (*C*=O), 164.5 (O*C*=O), 164.2 (*C*=CC=O), 159.3 (Ar–*C*(4°)OCH$_3$), 150.3 (Ar–*C*(4°)NO$_2$), 147.5 (*C*=CHI), 135.9 (Ar–*C*(4°)), 135.6 (Ar–*C*(4°)), 132.9 (*C*=CH), 130.7 (Ar–*C*H), 129.5 (Ar–*C*H), 129.2 (C=*C*C=O), 123.5 (C=*C*H), 123.3 (Ar–*C*H), 113.7 (Ar–*C*H), 74.8 (C=*C*HI), 73.3 (Ar*C*H$_2$O), 66.2 (O*C*H$_2$C=C), 59.0 (*C*H$_2$OPNB), 55.1 (O*C*H$_3$), 42.9 (*C*(4°)–C=C), 42.0 (*C*H$_2$C=CHI), 39.3 (CH*C*H$_2$), 37.3 (CH$_3$*C*H), 34.3 (*C*H$_2$C=CH), 34.1 (C(4°)–*C*H$_2$), 26.1 (C=CH*C*H$_2$), 24.2 (*C*H$_3$–C(4°)), 23.9 (*C*H$_3$C=CHI), 16.1 (*C*H$_3$C=CH), 15.9 (*C*H$_3$CH); *m/z* (ES) 738.1828 (M$^+$ + Na, 100%, $C_{35}H_{42}INO_7Na$ requires 738.1904).

4-Nitrobenzoic acid (3*S*,4*S*,6*R*)-6-hydroxy-3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-3,4-dimethylcyclohex-1-enylmethyl ester 76

Cerium trichloride heptahydrate (1.70 g, 4.58 mmol) was added to a stirred solution of the diastereoisomeric enone **75b** (2.18 g, 3.05 mmol) in dichloromethane (15.2 mL) and methanol (15.2 mL) at −78 °C. The mixture was stirred at −78 °C for

15 minutes, then sodium borohydride (0.23 g, 6.1 mmol) was added, and the resulting mixture was allowed to warm to −60 °C over 2 hours. The mixture was quenched with a saturated aqueous solution of NH_4Cl (25 mL), then allowed to warm to room temperature and diluted with water (70 mL). The separated aqueous phase was extracted with dichloromethane (3 × 80 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20–40% diethyl ether in pentane as eluent to give: (i) 4-nitrobenzoic acid (3*S*,4*R*,6*S*)-6-hydroxy-3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-3,4-dimethylcyclohex-1-enylmethyl ester, the *anti-dimethyl 6a-alcohol* (0.57 g, 26%) (eluted first) as a colourless oil, ν_{max} (film)/cm^{-1} 3434, 2965, 2932, 2862, 1722, 1609 and 1274; δ_H (360 MHz, $CDCl_3$) 8.23 (2H, dd, *J* 7.0 and 2.0, 2 × Ar*H*), 8.12 (2H, dd, *J* 7.0 and 2.0, 2 × Ar*H*), 7.24 (2H, dd, *J* 6.7 and 2.1, 2 × Ar*H*), 6.89 (2H, dd, *J* 6.7 and 2.1, 2 × Ar*H*), 5.84 (1H, app. sextet, *J* 1.1, C=C*H*I), 5.27 (1H, d, *J* 12.1, C*H*HOPNB), 5.11 (1H, d, *J* 12.1, CH*H*OPNB), 5.00 (1H, t, *J* 6.4, C=C*H*), 4.48 (1H, d, *J* 11.4, ArC*H*H), 4.44 (1H, d, *J* 11.4, ArCH*H*), 4.33 (1H, dd, *J* 8.0 and 7.9, C*H*OH), 4.03 (2H, s, OCH_2C=C), 3.78 (3H, s, OCH_3), 2.21–2.17 (2H, m, CH_2C=CHI), 2.10 (2H, app. quartet, *J* 7.3, C=CHCH_2), 2.03–1.88 (3H, m, CH_2C=CH and CHC*H*H), 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.69–1.51 (3H, m, C(4°)–C*H*H, CHCH*H* and CH_3C*H*), 1.56 (3H, br. s, CH_3C=CH), 1.40 (1H, dt, *J* 13.3 and 4.0, C(4°)–CH*H*), 1.04 (3H, s, CH_3–C(4°)), 1.04 (3H, d, *J* 6.0, CH_3CH); δ_C (90 MHz, $CDCl_3$) 165.0 (O*C*=O), 159.2 (Ar–*C*(4°)OCH$_3$), 150.4 (Ar–*C*(4°)NO$_2$), 147.7 (*C*=CHI), 143.8 (C=*C*CHOH), 136.8 (Ar–*C*(4°)), 135.7 (Ar–*C*(4°)), 135.7 (*C*=CH), 130.7 (Ar–*C*H), 129.9 (*C*=CCHOH), 129.5 (Ar–*C*H), 123.4 (Ar–*C*H), 122.8 (C=*C*H), 113.7 (Ar–*C*H), 74.8 (C=*C*HI), 72.9 (Ar*C*H$_2$O), 67.9 (*C*HOH), 65.8 (O*C*H$_2$C=C), 63.0 (*C*H$_2$OPNB), 55.2 (O*C*H$_3$), 41.2 (*C*(4°)–C=C), 39.4 (*C*H$_2$C=CHI), 37.4 (CH*C*H$_2$), 36.8 (CH_3*C*H), 36.5 (*C*H$_2$C=CH), 34.6 (C(4°)–*C*H$_2$), 26.2 (C=CH*C*H$_2$), 25.9 (*C*H$_3$–C(4°)), 23.9 (*C*H$_3$C=CHI), 16.5 (*C*H$_3$CH), 16.1 (*C*H$_3$C=CH); *m*/*z* (ES) 740.2098 (M$^+$ + Na, 100%, $C_{35}H_{44}INO_7Na$ requires 740.2060); and (ii) the *syn-dimethyl 6β-alcohol* (1.11 g, 51%) (eluted second) as a colourless oil, ν_{max} (film)/cm^{-1} 3606, 2929, 2856, 1723, 1611 and 1274; δ_H (360 MHz, $CDCl_3$) 8.24 (2H, d, *J* 8.6, 2 × Ar*H*), 8.12 (2H, d, *J* 8.6, 2 × Ar*H*), 7.25 (2H, d, *J* 8.4, 2 × Ar*H*), 6.83 (2H, d, *J* 8.4, 2 × Ar*H*), 5.84 (1H, br. s, C=C*H*I), 5.23 (1H, d, *J* 12.3, C*H*HOPNB), 5.12 (1H, d, *J* 12.3, CH*H*OPNB), 4.98 (1H, t, *J* 6.6, C=C*H*), 4.48 (1H, d, *J* 11.3, ArC*H*H), 4.44 (1H, d, *J* 11.3, ArCH*H*), 4.31 (1H, dd, *J* 9.8 and 6.1, C*H*OH), 4.13 (1H, d, *J* 10.6, OC*H*HC=C), 3.92 (1H, d, *J* 10.6, OCH*H*C=C), 3.78 (3H, s, OCH_3), 2.21–2.17 (2H, m, CH_2C=CHI), 2.09 (2H, app. quartet, *J* 7.1, C=CHCH_2), 1.92–1.87 (1H, m, C*H*HC=CH), 1.85–1.78 (2H, m, CH_3C*H* and CHC*H*H), 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.58–1.51 (2H, m, C(4°)–C*H*H, and CHCH*H*), 1.54 (3H, br. s, CH_3C=CH), 1.51–1.38 (2H, m, CH*H*C=CH and C(4°)–CH*H*), 0.95 (3H, s, CH_3–C(4°)), 0.91 (3H, d, *J* 6.8, CH_3CH); δ_C (90 MHz, $CDCl_3$) 164.8 (O*C*=O), 159.2 (Ar–*C*(4°)OCH$_3$), 150.4 (Ar–*C*(4°)NO$_2$), 147.6 (*C*=CHI), 143.7 (C=*C*CHOH), 136.7 (Ar–*C*(4°)), 136.4 (Ar–*C*(4°)), 135.8 (*C*=CH), 130.7 (Ar–*C*H), 129.9 (*C*=CCHOH), 129.5 (Ar–*C*H), 123.4 (Ar–*C*H), 122.7 (C=*C*H), 113.7 (Ar–*C*H), 74.7 (C=*C*HI), 72.7 (Ar*C*H$_2$O), 68.2 (*C*HOH), 65.7 (O*C*H$_2$C=C), 63.0 (*C*H$_2$OPNB), 55.2 (O*C*H$_3$), 42.1 (*C*(4°)–C=C), 39.4 (*C*H$_2$C=CHI), 36.6 (*C*H$_2$C=CH), 35.3 (C(4°)–*C*H$_2$), 34.4 (CH*C*H$_2$), 31.0 (CH_3*C*H), 26.1 (C=CH*C*H$_2$), 23.9 (*C*H$_3$C=CHI), 20.8 (*C*H$_3$–C(4°)), 16.2 (*C*H$_3$C=CH), 16.0 (*C*H$_3$CH); *m*/*z* (ES) 740.2039 (M$^+$ + Na, 100%, $C_{35}H_{44}INO_7Na$ requires 740.2060).

[(3*S*,4*R*,6*S*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-6-methoxymethoxy-3,4-dimethylcyclohex-1-enyl]methanol 77

Chloromethyl methyl ether (105 μL, 1.38 mmol) was added dropwise over 30 seconds to a stirred solution of diisopropylethylamine (360 μL, 2.07 mmol), tetra-*n*-butylammonium iodide (51 mg, 0.14 mmol), and the 6β-epimer of the alcohol **76** (99 mg, 0.14 mmol) in dichloromethane (2 mL) at 0 °C and the mixture was stirred for 15 minutes, and then allowed to warm to room temperature over 19 hours. The mixture was diluted with methanol (1 mL), then treated with potassium hydroxide (30 mg, 0.54 mmol) and stirred at room temperature for 12 hours. The mixture was diluted with water (4 mL) and the separated aqueous phase was extracted with dichloromethane (2 × 2 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 30–40% diethyl ether in pentane as eluent to give the *alcohol* (61 mg, 73%) as a viscous, colourless oil; δ_H (360 MHz, $CDCl_3$) 7.28–7.25 (2H, m, 2 × Ar*H*), 6.89–6.85 (2H, m, 2 × Ar*H*), 5.84 (1H, m, C=C*H*I), 4.98 (1H, br. t, *J* 6.8, C=C*H*), 4.82 (1H, d, *J* 6.8, OC*H*HOCH$_3$), 4.71 (1H, d, *J* 6.8, OCH*H*OCH$_3$), 4.47 (2H, s, ArCH_2), 4.31–4.27 (2H, m, C*H*OCH$_2$ and C*H*HOH), 4.10 (1H, d, *J* 12.1, CH*H*OH), 4.01–3.95 (2H, m, OCH_2C=C), 3.80 (3H, s, OCH_3), 3.43 (3H, s, OCH_3), 3.11 (1H, br. s, O*H*), 2.21–1.45 (11H, m, 5 × CH_2 and CH_3C*H*), 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.54 (3H, s, CH_3C=CH), 0.89 (3H, obs. d, CH_3CH), 0.88 (3H, s, CH_3–C(4°)); δ_C (90 MHz, $CDCl_3$) 159.2 (s), 147.7 (s), 141.5 (s), 141.0 (s), 136.6 (s), 129.7 (s), 129.6 (d), 122.4 (d), 113.7 (d), 95.8 (t), 75.8 (d), 74.7 (d), 72.9 (t), 66.1 (t), 59.8 (t), 55.7 (q), 55.2 (q), 41.4 (s), 39.4 (t), 35.2 (t), 34.2 (t), 33.6 (t), 30.9 (d), 26.2 (t), 23.9 (q), 21.3 (q), 16.2 (q), 16.0 (q); *m*/*z* (ES) 635.2167 (M$^+$ + Na, 100%, $C_{30}H_{45}IO_5Na$ requires 635.2209).

(3*S*,4*R*,6*S*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-2-(4-methoxybenzyloxymethyl)-6-methoxymethoxy-3,4-dimethylcyclohex-1-enecarbaldehyde 78

Dess–Martin periodinane (63 mg, 0.15 mmol) was added to a stirred solution of pyridine (24 μL, 0.30 mmol) and the alcohol **77** (61 mg, 0.10 mmol) in dichloromethane (1.5 mL) at 0 °C. The mixture was stirred at 0 °C for 90 minutes, then allowed to warm to room temperature and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 30% diethyl ether in petroleum ether as eluent to give the *aldehyde* (60 mg, 99%) as a viscous, colourless oil; ν_{max} ($CHCl_3$)/cm^{-1} 2938, 2887 and 1679; δ_H (360 MHz, $CDCl_3$) 10.00 (1H, s, C*H*O), 7.26–7.23 (2H, m, 2 × Ar*H*), 6.90–6.86 (2H, m, 2 × Ar*H*), 5.84 (1H, m, C=C*H*I), 4.98 (1H, br. t, *J* 6.8, C=C*H*), 4.87 (1H, d, *J* 6.9, OC*H*HOCH$_3$) 4.64 (1H, d, *J* 6.9, OCH*H*OCH$_3$), 4.52–4.48 (3H, m, ArCH_2 and C*H*OCH$_2$), 4.20 (2H, s, OCH_2C=C), 3.81 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 2.21–1.96 (5H, m, 2 × CH_2 and C*H*H), 1.84–1.51 (6H, m, 2 × CH_2, CH*H* and CH_3C*H*), 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.54 (3H, s, CH_3C=CH), 1.01 (3H, s, CH_3–C(4°)), 0.93 (3H, d, *J* 6.8, CH_3CH); δ_C (90 MHz, $CDCl_3$) 193.7 (d), 159.3 (s), 157.1 (s), 147.7 (s), 139.7 (s), 136.1 (s), 129.5 (d), 122.9 (d), 113.8 (s), 113.8 (d), 97.5 (t), 74.7 (d), 72.9 (t), 71.8 (d), 63.9 (t), 55.7 (q), 55.3 (q), 42.2 (s), 39.4 (t), 35.3 (t), 34.1 (t), 33.8 (t), 30.8 (d), 26.2 (t), 23.9 (q), 20.5 (q), 16.1 (q), 15.8 (q); *m*/*z* (ES) 633.2045 (M$^+$ + Na, 100%, $C_{30}H_{43}IO_5Na$ requires 633.2053).

(3*E*,7*E*)-(2*R*,11*S*,12*R*,14*S*)- and (3*E*,7*E*)-(2*S*,11*S*,12*R*,14*S*)-15-(4-methoxybenzyloxymethyl)-14-methoxymethoxy-4,8,11,12-tetramethylbicyclo[9.3.1]pentadeca-1(15),3,7-trien-2-ols 79a and 79b

Nickel chloride (1.2 mg, 0.01 mmol) and chromium chloride (23 mg, 0.23 mmol) were added sequentially to a stirred solution of the aldehyde vinyl iodide **78** (23 mg, 0.04 mmol) in DMSO (3.6 mL) at room temperature in a glove bag under an atmosphere of argon. The mixture was diluted with THF (1.2 mL), then removed from the glove bag and stirred under a positive pressure of argon for 16 hours. The mixture was diluted with hexane (2 mL), then cooled to 0 °C and quenched cautiously with serine (1.0 M in a saturated aqueous solution of $NaHCO_3$, 15 mL). The mixture was stirred vigorously and

allowed to warm to room temperature over 1 hour. The separated aqueous phase was extracted with diethyl ether (4 × 3 mL) and the combined organic extracts were washed with brine (2 × 20 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 30–50% diethyl ether in pentane as eluent to give: (i) the *α-alcohol* **79a** (4.5 mg, 25%) (eluted first) as a colourless oil, δ_H (360 MHz, $CDCl_3$) 7.30–7.27 (2H, m, 2 × Ar*H*), 6.91–6.87 (2H, m, 2 × Ar*H*), 5.28 (1H, br. d, *J* 8.0, C=C*H*CHOH), 5.08–5.04 (1H, br. d, *J* 8.0, C=CHC*H*OH), 4.96–4.94 (1H, br. s, O*H*), 4.86 (1H, d, *J* 7.0, OC*H*HOCH$_3$), 4.75–4.70 (2H, m, OCH*H*OCH$_3$ and C=C*H*), 4.54 (1H, d, *J* 11.1, ArC*H*H), 4.42 (1H, d, *J* 11.1, ArCH*H*), 4.22 (1H, dd, *J* 10.8 and 1.4, OC*H*HC=C), 3.95 (1H, dd, *J* 9.0 and 6.7, C*H*OCH$_2$), 3.81 (3H, s, OCH_3), 3.74 (1H, d, *J* 10.8, OCH*H*C=C), 3.45 (3H, s, OCH_3), 2.40–1.48 (11H, m, 5 × CH_2 and CH$_3$C*H*), 1.74 (3H, d, *J* 0.7, CH_3C=CH), 1.51 (3H, s, CH_3C=CH), 0.86 (3H, s, CH_3–C(4°)), 0.85 (3H, obs. d, CH_3CH); δ_C (90 MHz, $CDCl_3$) 159.5 (s), 142.6 (s), 141.4 (s), 133.0 (s), 132.7 (s), 130.3 (d), 129.0 (s), 128.2 (d), 127.7 (d), 113.8 (d), 96.0 (t), 76.5 (d), 72.8 (t), 68.2 (d), 67.4 (t), 55.9 (q), 55.3 (q), 41.8 (s), 36.3 (t), 34.6 (t), 33.6 (t), 33.0 (t), 29.9 (d), 25.8 (t), 21.2 (q), 18.1 (q), 15.7 (q), 15.4 (q); and (ii) the *β-alcohol* **79b** (5.0 mg, 27%) (eluted second) as a colourless oil, δ_H (360MHz, $CDCl_3$) 7.33–7.31 (2H, m, 2 × Ar*H*), 6.91–6.89 (2H, m, 2 × Ar*H*), 5.60 (1H, d, *J* 10.7, C=CHC*H*OH), 5.28 (1H, br. d, *J* 10.7, C=C*H*CHOH), 5.01 (1H, br. s, O*H*), 4.89 (1H, d, *J* 7.0, OC*H*HOCH$_3$), 4.82–4.74 (2H, m, C=C*H* and C*H*OCH$_2$), 4.73 (1H, d, *J* 7.0, OCH*H*OCH$_3$), 4.47 (2H, s, ArCH_2), 3.82 (3H, s, OCH_3), 3.66 (1H, dd, *J* 11.2 and 1.2, OC*H*HC=C), 3.50 (1H, d, *J* 11.2, OCH*H*C=C), 3.46 (3H, s, OCH_3), 2.47–2.32 (1H, m, C*H*H), 2.14–1.50 (10H, m, 4 × CH_2, C*H* and CH$_3$C*H*), 1.60 (3H, d, *J* 1.1, CH_3C=CH), 1.44 (3H, s, CH_3C=CH), 0.88 (3H, s, CH_3–C(4°)), 0.85 (3H, d, *J* 6.8, CH_3CH); δ_C (90 MHz, $CDCl_3$) 159.3 (s), 141.2 (s), 138.4 (s), 135.5 (s), 132.5 (s), 130.3 (s), 129.8 (d), 128.1 (d), 127.5 (d), 113.8 (d), 94.7 (t), 75.6 (d), 72.7 (t), 69.8 (d), 65.6 (t), 56.7 (q), 55.3 (q), 41.1 (s), 38.4 (t), 34.6 (t), 33.4 (t), 31.8 (t), 30.2 (d), 26.9 (t), 21.0 (q), 16.1 (q), 15.8 (q), 15.1 (q); *m/z* (ES) 507.3067 (M^+ + Na, 100%, $C_{30}H_{44}O_5Na$ requires 507.3086).

2-Hydroxymethyl-4-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-4,5-dimethylcyclohex-2-enone 86a

Diisobutylaluminium hydride (1.5 M in toluene, 1.5 mL, 2.2 mmol) was added dropwise over 2 minutes to a stirred solution of a 3 : 1 mixture of diastereoisomers of the ketone **74** (450 mg, 1.0 mmol) in toluene (12 mL) at −70 °C. The mixture was stirred at −70 °C for 15 minutes and then quenched by cautious addition of a saturated aqueous solution of Rochelle's salt (20 mL). The resulting mixture was allowed to warm to room temperature and then stirred vigorously for 15 hours. The separated aqueous phase was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with brine (30 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was diluted with THF (20 mL), then treated with 2M hydrochloric acid (10 mL) and stirred at room temperature for 10 minutes. The mixture was diluted with diethyl ether (10 mL) and neutralised with a saturated aqueous solution of K_2CO_3 (10 mL), and the separated aqueous phase was then extracted with diethyl ether (2 × 10 mL). The combined organic extracts were washed with brine (30 mL), and then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 50% diethyl ether in pentane as eluent to give the *hydroxyketone* (400 mg, 96%) as an inseparable 2.5 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a colourless oil; data for the *syn*-dimethyl isomer, ν_{max} ($CHCl_3$)/cm^{-1} 3610, 2925, 1666 and 1602; δ_H (360 MHz, $CDCl_3$) 6.61 (1H, s, C*H*=CCH$_2$O), 5.86 (1H, m, C=C*H*I), 5.07 (1H, br. t, *J* 7.0, C=C*H*CH$_2$), 4.23 (2H, s, CH_2OH), 2.50 (1H, br. s, O*H*), 2.40–2.32 (2H, m, CH_2), 2.27–1.42 (9H, m, 4 × CH_2 and CH$_3$C*H*), 1.83 (3H, d, *J* 0.9, CH_3C=CHI), 1.60 (3H, s, CH_3C=CH), 1.00 (3H, s, CH_3–C(4°)), 0.94 (3H, d, *J* 6.6, CH_3CH); δ_C (90 MHz, $CDCl_3$) 200.8 (s), 156.1 (d), 147.6 (s), 136.2 (s), 135.8 (s), 123.3 (d), 74.8 (d), 61.9 (t), 42.2 (t), 39.3 (t), 39.0 (s), 38.2 (t), 34.3 (t), 33.9 (d), 26.1 (t), 23.9 (q), 19.5 (q), 16.2 (q), 15.2 (q); *m/z* (ES) 439.1139 (M^+ + Na, 100%, $C_{19}H_{29}IO_2Na$ requires 439.1110).

4-Nitrobenzoic acid 3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-3,4-dimethyl-6-oxocyclohex-1-enylmethyl ester 86b

4-Nitrobenzoyl chloride (0.47 g, 2.52 mmol) was added to a stirred solution of 4-dimethylaminopyridine (21 mg, 0.17 mmol), triethylamine (0.47 mL, 3.37 mmol), and a 2.5 : 1 mixture of diastereoisomers of the alcohol **86a** (0.70 g, 1.68 mmol) in dichloromethane (17 mL) at −25 °C. The mixture was allowed to warm to 0 °C over 2 hours and then filtered through a pad of silica and washed with 50% diethyl ether in petroleum ether. The filtrate was concentrated *in vacuo* to leave the *ester* (0.90 g, 95%) as an inseparable 2.5 : 1 mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a viscous, pale yellow oil; data for the *syn*-dimethyl isomer, ν_{max} (film)/cm^{-1} 2963, 1728, 1678 and 1529; δ_H (360 MHz, $CDCl_3$) 8.30–8.26 (2H, m, 2 × Ar*H*), 8.21–8.18 (2H, m, 2 × Ar*H*), 6.82 (1H, s, C*H*=CCH$_2$OPNB), 5.84 (1H, app. sextet, *J* 1.1, C=C*H*I), 5.07–5.01 (3H, m, C=C*H*CH$_2$ and CH_2OPNB), 2.46–1.44 (11H, m, 5 × CH_2 and CH$_3$C*H*), 1.82 (3H, d, *J* 1.1, CH_3C=CHI), 1.58 (3H, br. s, CH_3C=CH), 1.04 (3H, s, CH_3–C(4°)), 0.97 (3H, d, *J* 6.6, CH_3CH); δ_C (90 MHz, $CDCl_3$) 179.7 (s), 164.2 (s), 159.1 (d), 150.4 (s), 147.4 (s), 135.6 (s), 135.4 (s), 132.0 (s), 130.7 (d), 123.4 (d), 123.3 (d), 74.8 (d), 62.5 (t), 41.9 (t), 39.3 (t), 39.2 (s), 38.1 (t), 34.4 (t), 33.2 (d), 26.0 (t), 23.8 (q), 19.4 (q), 16.1 (q), 15.1 (q); *m/z* (ES) 588.1223 (M^+ + Na, 100%, $C_{26}H_{32}INO_5Na$ requires 588.1225).

4-Nitrobenzoic acid (3*S*,4*R*,6*S*)-6-hydroxy-3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-3,4-dimethylcyclohex-1-enylmethyl ester 87a

Cerium trichloride heptahydrate (380 mg, 1.02 mmol) was added to a stirred solution of a 2.5 : 1 mixture of diastereoisomers of the enone **86b** (580 mg, 1.02 mmol) in dichloromethane (4 mL) and methanol (11 mL) at −30 °C. The mixture was stirred at −30 °C for 10 minutes, then sodium borohydride (60 mg, 1.57 mmol) was added, and the mixture was stirred at −30 °C for 30 minutes. The mixture was quenched with a saturated aqueous solution of NH_4Cl (5 mL), then allowed to warm to room temperature and diluted with water (10 mL). The separated aqueous phase was extracted with dichloromethane (3 × 3 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 15–30% diethyl ether in pentane as eluent to give: (i) the *anti-dimethyl alcohol* (140 mg, 24%) (eluted first) as a pale yellow oil, and (ii) the *syn-dimethyl 6β-alcohol* (320 mg, 55%) (eluted second) as a pale yellow oil, ν_{max} (film)/cm^{-1} 3436, 2959, 1724 and 1529; δ_H (360 MHz, $CDCl_3$) 8.31–8.27 (2H, m, 2 × Ar*H*), 8.23–8.20 (2H, m, 2 × Ar*H*), 5.85 (1H, m, C=C*H*I), 5.63 (1H, br. s, C*H*=CCH$_2$O), 5.22 (1H, d, *J* 12.1, C*H*HOPNB), 5.03 (1H, br. t, *J* 6.9, C=C*H*CH$_2$), 4.72 (1H, d, *J* 12.1, CH*H*-OPNB), 4.31 (1H, br. dd, *J* 8.2 and 7.2, C*H*OH), 2.29 (1H, br. s, O*H*), 2.27–2.07 (4H, m, 2 × CH_2), 1.96–1.83 (2H, m, CH_2), 1.82 (3H, d, *J* 1.0, CH_3C=CHI), 1.81–1.71 (2H, m, CH_2), 1.60–1.30 (3H, m, CH_2 and CH$_3$C*H*), 1.57 (3H, d, *J* 0.4, CH_3C=CH), 0.89 (3H, d, *J* 6.8, CH_3CH), 0.89 (3H, s, CH_3–C(4°)); δ_C (90 MHz, $CDCl_3$) 165.0 (s), 150.6 (s), 147.6 (s), 140.6 (d), 136.4 (s), 135.6 (s), 134.3 (s), 130.8 (d), 123.5 (d), 122.8 (d), 74.7 (d), 67.6 (d), 66.8 (t), 39.4 (t), 38.5 (s), 38.5 (t), 37.2 (t), 34.4 (t), 32.2 (d), 26.2 (t), 23.9 (q), 21.6 (q), 16.2 (q), 15.5 (q); *m/z* (ES) 590.1340 (M^+ + Na, 100%, $C_{26}H_{34}INO_5Na$ requires 590.1379).

4-Nitrobenzoic acid (3*S*,4*R*,6*S*)-3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-6-methoxymethoxy-3,4-dimethylcyclohex-1-enylmethyl ester 87b

Chloromethyl methyl ether (140 μL, 1.84 mmol) was added dropwise over 30 seconds to a stirred solution of diisopropylethylamine (640 μL, 3.69 mmol), tetra-*n*-butylammonium iodide (98 mg, 0.26 mmol), and the 6β-epimer of the alcohol **87a** (150 mg, 0.26 mmol) in dichloromethane (3 mL) at 0 °C and the mixture was stirred for 10 minutes, and then allowed to warm to room temperature over 13 hours. The mixture was diluted with water (4 mL) and the separated aqueous phase was extracted with dichloromethane (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 15–20% diethyl ether in petroleum ether as eluent to give the *ether* (141 mg, 87%) as a pale yellow oil; ν_{max} ($CHCl_3$)/cm^{-1} 2939, 1723 and 1530; δ_H (360 MHz, $CDCl_3$) 8.30–8.27 (2H, m, 2 × Ar*H*), 8.23–8.19 (2H, m, 2 × Ar*H*), 5.83 (1H, m, C=C*H*I), 5.65 (1H, br. s, C*H*=CCH_2O), 5.03 (1H, d, *J* 12.2, CC*H*HOPNB), 5.01 (1H, br. t, *J* 6.9, C=C*H*CH_2), 4.80 (1H, d, *J* 12.2, CCH*H*OPNB), 4.77 (1H, d, *J* 6.9, OC*H*HOCH$_3$), 4.65 (1H, d, *J* 6.9, OCH*H*OCH$_3$), 4.30 (1H, br. dd, *J* 6.7 and 8.7, C*H*OCH_2), 3.35 (3H, s, OCH_3), 2.21–1.86 (6H, m, 3 × CH_2), 1.83–1.69 (2H, m, CH_2), 1.81 (3H, d, *J* 0.9, CH_3=CHI), 1.59–1.27 (3H, m, CH_2 and CH_3CH), 1.55 (3H, s, CH_3C=CH), 0.89 (3H, d, *J* 6.7, CH_3CH), 0.89 (3H, s, CH_3–C(4°)); δ_C (90 MHz, $CDCl_3$) 164.3 (s), 150.5 (s), 147.6 (s), 140.2 (d), 136.4 (s), 135.8 (s), 132.6 (s), 130.6 (d), 123.5 (d), 122.8 (d), 95.8 (t), 74.7 (d), 73.4 (d), 66.4 (t), 55.6 (q), 39.3 (t), 38.5 (t), 38.2 (s), 34.3 (t), 34.3 (t), 32.0 (d), 26.2 (t), 23.9 (q), 21.5 (q), 16.1 (q), 15.6 (q); *m*/*z* (ES) 634.1657 (M^+ + Na, 100%, $C_{28}H_{38}INO_6Na$ requires 634.1642).

(3*S*,4*R*,6*S*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-6-methoxymethoxy-3,4-dimethylcyclohex-1-enecarbaldehyde 88a

Potassium carbonate (152 mg, 1.10 mmol) was added to a stirred solution of the ester **87b** (134 mg, 0.22 mmol) in dichloromethane (1.5 mL) and methanol (1.5 mL) at room temperature. The mixture was stirred vigorously for 80 minutes, then diluted with water (4 mL) and the separated aqueous phase was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20–50% diethyl ether in petroleum ether as eluent to give the *alcohol* (100 mg, 99%) as a colourless oil; ν_{max} (film)/cm^{-1} 3514, 2933 and 1602; δ_H (360 MHz, $CDCl_3$) 5.85 (1H, m, C=C*H*I), 5.46 (1H, br. s, C*H*=CCH_2O), 5.03 (1H, br. t, *J* 7.0, C=C*H*CH_2), 4.78 (1H, d, *J* 6.7, OC*H*HOCH$_3$), 4.68 (1H, d, *J* 6.7, OCH*H*OCH$_3$), 4.30 (1H, br. dd, *J* 8.3 and 6.4, C*H*OCH_2), 4.13 (1H, d, *J* 12.2, C*H*HOH), 4.08 (1H, d, *J* 12.2, CH*H*OH), 3.42 (3H, s, OCH_3), 2.52 (1H, br. s, O*H*), 2.23–2.07 (4H, m, 2 × CH_2), 1.93–1.65 (4H, m, 2 × CH_2), 1.82 (3H, d, *J* 1.0, CH_3=CHI), 1.60–1.25 (3H, m, CH_2 and CH_3CH), 1.57 (3H, s, CH_3C=CH), 0.87 (3H, d, *J* 6.7, CH_3CH), 0.86 (3H, s, CH_3–C(4°)); δ_C (90 MHz, $CDCl_3$) 147.7 (s), 137.5 (d), 136.8 (s), 136.5 (s), 122.6 (d), 95.9 (t), 75.7 (d), 74.7 (d), 65.1 (t), 55.7 (q), 39.4 (t), 38.5 (t), 37.9 (s), 34.4 (t), 34.2 (t), 32.2 (d), 26.2 (t), 23.9 (q), 21.7 (q), 16.2 (q), 15.6 (q); *m*/*z* (ES) 485.1571 (M^+ + Na, 100%, $C_{21}H_{35}IO_3Na$ requires 485.1529).

Dess–Martin periodinane (42 mg, 0.10 mmol) was added to a stirred solution of pyridine (19 μL, 0.23 mmol) and the alcohol (36 mg, 0.08 mmol) in dichloromethane (2 mL) at 0 °C. The mixture was stirred at 0 °C for 40 minutes, then allowed to warm to room temperature and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 50% diethyl ether in petroleum ether as eluent to give the *aldehyde* (36 mg, 99%) as a colourless oil; ν_{max} (film)/cm^{-1} 2943, 2725, 1690 and 1640; δ_H (360 MHz, $CDCl_3$) 9.48 (1H, s, *CH*O), 6.54 (1H, d, *J* 1.1, C*H*=CCHO), 5.86 (1H, m, C=C*H*I), 5.05 (1H, br. t, *J* 7.0, C=C*H*CH_2), 4.94 (1H, d, *J* 6.9, OC*H*HOCH$_3$), 4.70 (1H, d, *J* 6.9, OCH*H*OCH$_3$), 4.46 (1H, app. t, *J* 7.8, C*H*OCH_2), 3.43 (3H, s, OCH_3), 2.23–1.89 (6H, m, 3 × CH_2), 1.83 (3H, d, *J* 1.0, CH_3=CHI), 1.77–1.41 (5H, m, 2 × CH_2 and CH_3CH), 1.58 (3H, s, CH_3C=CH), 1.02 (3H, s, CH_3–C(4°)), 0.93 (3H, d, *J* 6.7, CH_3CH); δ_C (90 MHz, $CDCl_3$) 193.0 (d), 160.2 (d), 147.6 (s), 140.8 (s), 135.8 (s), 123.2 (d), 97.3 (t), 74.8 (d), 70.8 (d), 55.7 (q), 39.3 (t), 38.3 (t), 38.3 (s), 34.6 (t), 34.2 (t), 31.9 (d), 26.2 (t), 23.9 (q), 20.6 (q), 16.2 (q), 15.4 (q); *m*/*z* (ES) 483.1379 (M^+ + Na, 100%, $C_{21}H_{33}IO_3Na$ requires 483.1372).

(3*E*,7*E*)-(2*R*,11*S*,12*R*,14*S*)-14-Methoxymethoxy-4,8,11,12-tetramethylbicyclo[9.3.1]pentadeca-1(15),3,7-trien-2-ol 91

Nickel chloride (2.5 mg, 0.02 mmol) and chromium chloride (71 mg, 0.57 mmol) were added sequentially to a stirred solution of the aldehyde vinyl iodide **88a** (44 mg, 0.10 mmol) in DMSO (11 mL) at room temperature in a glove bag under an atmosphere of argon. The mixture was removed from the glove bag, and then stirred under a positive pressure of argon for 42 hours, and then diluted with ethyl acetate (1.5 mL) and hexane (1.5 mL). The mixture was cooled to 15 °C and then quenched cautiously with serine (1.0 M in a saturated aqueous solution of $NaHCO_3$, 10 mL). The mixture was stirred vigorously for 20 minutes, then allowed to warm to room temperature and diluted with water (2 mL). The separated aqueous phase was extracted with ethyl acetate–hexane (1 : 1, 3 × 5 mL) and the combined organic extracts were washed with brine (2 × 20 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 35% diethyl ether in pentane as eluent to give the *bicyclic alcohol* (20 mg, 63%) which crystallised from pentane as a colourless solid; mp 78–80 °C; ν_{max} ($CDCl_3$)/cm^{-1} 3391, 2932 and 1612; δ_H (500 MHz, $CDCl_3$) 6.33 (1H, s, C*H*=CCHOH), 5.33 (1H, d, *J* 7.5, C=C*H*CHOH), 5.12 (1H, m, C=C*H*CH_2), 4.87 (2H, m, C*H*OH and OC*H*HOCH$_3$), 4.71 (1H, d, *J* 7.0, OCH*H*OCH$_3$), 4.36 (1H, app. t, *J* 7.5, C*H*OCH_2), 3.86 (1H, br. s, O*H*), 3.45 (3H, s, OCH_3), 2.43–2.22 (3H, m, CH_2 and C*H*H), 2.14–2.02 (3H, m, CH_2 and CH*H*), 1.89–1.85 (1H, m, C*H*H), 1.71–1.60 (1H, m, C*H*H), 1.52 (3H, s, CH_3C=CH), 1.49–1.44 (2H, CH*H* and CH_3CH), 1.42 (3H, d, *J* 1.1, CH_3C=CH), 1.22–1.16 (1H, m, CH*H*), 0.90 (3H, s, CH_3–C(4°)), 0.87 (3H, d, *J* 6.4, CH_3CH); δ_C (125 MHz, $CDCl_3$) 136.7 (s), 136.6 (d), 136.3 (s), 135.2 (s), 127.9 (d), 126.7 (d), 95.0 (t), 77.6 (d), 69.8 (d), 55.9 (q), 39.5 (t), 39.1 (s), 38.2 (d), 36.6 (t), 34.8 (t), 34.6 (t), 25.6 (t), 19.6 (q), 15.7 (q), 15.4 (q), 15.2 (q); *m*/*z* (ES) 398.2673 (M^+ + Na + CH_3CN, 100%, $C_{23}H_{37}NO_3Na$ requires 398.2671).

2-Hydroxymethyl-4-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-3,4,5-trimethylcyclohex-2-enone 89a

Methyllithium (1.6 M in diethyl ether, 610 μL, 0.98 mmol) was added dropwise over 2 minutes to a stirred solution of a 3 : 1 mixture of diastereoisomers of the ketone **74** (290 mg, 0.65 mmol) in toluene (9 mL) at −78 °C. The mixture was allowed to warm to −20 °C over 4 hours, then quenched with water (5 mL), followed by a saturated aqueous solution of NH_4Cl (5 mL), and allowed to warm to room temperature. The separated aqueous phase was extracted with diethyl ether (2 × 10 mL), and the combined organic extracts were concentrated *in vacuo*. The residue was diluted with THF (10 mL), then treated with 2M hydrochloric acid (5 mL) and stirred at room temperature for 10 minutes. The mixture was diluted with diethyl ether (10 mL) and neutralised with a saturated aqueous solution of K_2CO_3 (10 mL), and the separated aqueous phase was then extracted with diethyl ether (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 40–50% diethyl ether in petroleum ether as eluent to give the *hydroxyketone* (253 mg, 90%) as

an inseparable mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a colourless oil; data for the *syn*-dimethyl isomer, ν_{max} ($CHCl_3$)/cm^{-1} 3610, 2942 and 1651; δ_H (360 MHz, $CDCl_3$) 5.86–5.85 (1H, m, C=C*H*I), 5.06 (1H, br. t, *J* 6.9, C=C*H*), 4.43–4.33 (2H, m, CH_2OH), 2.55–1.54 (11H, m, 5 × CH_2 and CH_3CH), 1.99 (3H, s, CH_3C=C), 1.84 (3H, d, *J* 1.1, CH_3C=CHI), 1.60 (3H, s, CH_3C=CH), 1.03 (3H, s, CH_3–C(4°)), 0.97 (3H, d, *J* 6.5, CH_3CH); δ_C (90 MHz, $CDCl_3$) 199.9 (s), 164.8 (s), 147.5 (s), 135.8 (s), 135.1 (s), 123.2 (d), 74.8 (d), 58.1 (t), 42.9 (s), 41.6 (t), 39.3 (t), 35.3 (t), 34.2 (t), 32.7 (d), 26.1 (t), 23.8 (q), 19.3 (q), 16.1 (q), 15.5 (q), 15.5 (q); *m*/*z* (ES) 453.1236 (M^+ + Na, 100%, $C_{20}H_{31}IO_2Na$ requires 453.1267).

4-Nitrobenzoic acid 3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-2,3,4-trimethyl-6-oxocyclohex-1-enylmethyl ester 89b

4-Nitrobenzoyl chloride (112 mg, 0.60 mmol) was added to a stirred solution of 4-dimethylaminopyridine (6 mg, 0.05 mmol), triethylamine (130 μL, 0.93 mmol), and the diastereoisomeric alcohol **89a** (200 mg, 0.47 mmol) in dichloromethane (5 mL) at −45 °C. The mixture was allowed to warm to 0 °C over 2 hours and then filtered through a pad of silica and washed with 25% diethyl ether in petroleum ether. The filtrate was concentrated *in vacuo* to leave the *ester* (245 mg, 91%) as an inseparable mixture of the *syn*- and *anti*-dimethyl diastereoisomers, as a pale yellow oil; data for the *syn*-dimethyl isomer, ν_{max} ($CHCl_3$)/cm^{-1} 2942, 1723, 1667, 1610 and 1530; δ_H (360 MHz, $CDCl_3$) 8.27–8.24 (2H, m, 2 × Ar*H*), 8.16–8.12 (2H, m, 2 × Ar*H*), 5.84–5.83 (1H, m, CH_3C=C*H*I), 5.22–5.14 (2H, m, CH_2OPNB), 5.07–5.00 (1H, m, C=C*H*), 2.62–1.54 (11H, m, 5 × CH_2 and CH_3CH), 2.06 (3H, s, CH_3C=C), 1.80 (3H, d, *J* 1.0, CH_3C=CHI), 1.58 (3H, s, CH_3C=CH), 1.08 (3H, s, CH_3–C(4°)), 0.99 (3H, d, *J* 6.8, CH_3CH); δ_C (90 MHz, $CDCl_3$) 196.5 (s), 168.9 (s), 164.5 (s), 150.4 (s), 147.4 (s), 135.8 (s), 135.6 (s), 131.0 (s), 130.6 (d), 123.5 (d), 123.4 (d), 74.8 (d), 59.1 (t), 43.5 (s), 41.4 (t), 39.3 (t), 35.5 (t), 34.3 (t), 32.8 (d), 26.0 (t), 23.8 (q), 19.4 (q), 16.2 (q), 16.1 (q), 15.5 (q); *m*/*z* (ES) 602.1398 (M^+ + Na, 100%, $C_{27}H_{34}INO_5Na$ requires 602.1379).

4-Nitrobenzoic acid (3*S*,4*R*,6*S*)-6-hydroxy-3-((3*E*,7*E*)-8-iodo-3,7-dimethylocta-3,7-dienyl)-2,3,4-trimethylcyclohex-1-enylmethyl ester 90a

Cerium trichloride heptahydrate (170 mg, 0.45 mmol) was added to a stirred solution of the diastereoisomeric enone **89b** (260 mg, 0.45 mmol) in dichloromethane (2.5 mL) and methanol (2.5 mL) at −50 °C. The mixture was stirred at −50 °C for 10 minutes, then sodium borohydride (34 mg, 0.90 mmol) was added, and the mixture was stirred at −50 °C for 30 minutes. The mixture was quenched with a saturated aqueous solution of NH_4Cl (3 mL), then allowed to warm to room temperature and diluted with water (3 mL). The separated aqueous phase was extracted with dichloromethane (3 × 5 mL) and the combined organic extracts were then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 35–45% diethyl ether in petroleum ether as eluent to give the *alcohol* (93 mg, 70%) as a colourless oil; data for the *syn*-dimethyl 6β-alcohol, ν_{max} ($CHCl_3$)/cm^{-1} 3620, 2936, 1720 and 1609; δ_H (360 MHz, $CDCl_3$) 8.28–8.25 (2H, m, 2 × Ar*H*), 8.20–8.16 (2H, m, 2 × Ar*H*), 5.83 (1H, m, CH_3C=C*H*I), 5.18 (1H, d, *J* 12.1, C*H*HOPMB), 5.02 (1H, d, *J* 12.1, CH*H*OPMB), 4.96 (1H, br. t, *J* 6.6, C=C*H*), 4.33 (1H, br. dd, *J* 6.8 and 8.1, C*H*OH), 2.20–1.43 (11H, m, 5 × CH_2 and CH_3CH), 1.81 (3H, d, *J* 1.0, CH_3C=CHI), 1.77 (3H, d, *J* 1.6, CH_3C=C), 1.54 (3H, s, CH_3C=CH), 0.92 (3H, s, CH_3–C(4°)), 0.90 (3H, d, *J* 6.9, CH_3CH); δ_C (90 MHz, $CDCl_3$) 164.9 (s), 150.4 (s), 147.5 (s), 144.7 (s), 136.4 (s), 135.8 (s), 131.1 (s), 130.6 (d), 123.5 (d), 122.7 (d), 74.7 (d), 68.8 (d), 63.1 (t), 42.3 (s), 39.3 (t), 36.8 (t), 34.9 (t), 34.2 (t), 30.9 (d), 26.1 (t), 23.8 (q), 20.4 (q), 16.1 (q), 16.0 (q), 14.2 (q).

[(3*S*,4*R*,6*S*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-6-methoxymethoxy-2,3,4-trimethylcyclohex-1-enyl]methanol 90b

Chloromethyl methyl ether (85 μL, 1.12 mmol) was added dropwise over 20 seconds to a stirred solution of diisopropylethylamine (340 μL, 1.92 mmol), tetra-*n*-butylammonium iodide (59 mg, 0.16 mmol), and the 6β-epimer of the alcohol **90a** (93 mg, 0.16 mmol) in dichloromethane (2 mL) at 0 °C and the mixture was stirred for 10 minutes, and then allowed to warm to room temperature over 16 hours. The mixture was diluted with water (4 mL) and the separated aqueous phase was extracted with dichloromethane (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was diluted with dichloromethane (2 mL), then filtered through a pad of silica and washed thoroughly with dichloromethane. The filtrate was concentrated *in vacuo* to leave the crude *ester*. The residue was dissolved in dichloromethane (0.8 mL) and methanol (0.8 mL), then cooled to 0 °C and treated with potassium carbonate (100 mg, 0.70 mmol). The mixture was stirred at 0 °C for 5 minutes, then allowed to warm to room temperature over 22 hours. The mixture was diluted with water (4 mL) and dichloromethane (2 mL), and the separated aqueous phase was extracted with dichloromethane (2 × 4 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 20–35% diethyl ether in petroleum ether as eluent to give the *alcohol* (57 mg, 75%) as a colourless oil; ν_{max} (film)/cm^{-1} 3470 and 2934; δ_H (360 MHz, $CDCl_3$) 5.85 (1H, m, C=C*H*I), 5.02 (1H, br. t, *J* 6.7, C=C*H*), 4.82 (1H, d, *J* 6.8, OC*H*HOCH$_3$), 4.69 (1H, d, *J* 6.8, OCH*H*OCH$_3$), 4.29–4.24 (2H, m, C*H*OCH$_2$ and C*H*HOH), 4.06 (1H, d, *J* 11.8, CH*H*OH), 3.43 (3H, s, OCH_3), 2.60 (1H, br. s, O*H*), 2.27–2.07 (4H, m, 2 × CH_2), 1.92–1.43 (7H, m, 3 × CH_2 and CH_3CH), 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.73 (3H, d, *J* 1.8, CH_3C=C), 1.57 (3H, s, CH_3C=CH), 0.91 (3H, s, CH_3–C(4°)), 0.89 (3H, d, *J* 6.9, CH_3CH); δ_C (90 MHz, $CDCl_3$) 147.7 (s), 141.6 (s), 136.6 (s), 133.0 (s), 122.6 (d), 95.5 (t), 77.3 (d), 74.7 (d), 61.2 (t), 55.8 (q), 41.7 (s), 39.3 (t), 34.6 (t), 34.2 (t), 33.6 (t), 30.7 (d), 26.2 (t), 23.9 (q), 20.6 (q), 16.1 (q), 16.1 (q), 13.5 (q); *m*/*z* (ES) 499.1695 (M^+ + Na, 100%, $C_{22}H_{37}IO_3Na$ requires 499.1685).

(3*S*,4*R*,6*S*)-3-((3*E*,7*E*)-8-Iodo-3,7-dimethylocta-3,7-dienyl)-6-methoxymethoxy-2,3,4-trimethylcyclohex-1-enecarbaldehyde 88b

Dess–Martin periodinane (31 mg, 0.07 mmol) was added to a stirred solution of pyridine (12 μL, 0.14 mmol) and the alcohol **90b** (23 mg, 0.05 mmol) in dichloromethane (1 mL) at 0 °C. The mixture was stirred at 0 °C for 40 minutes, then allowed to warm to room temperature and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 22% diethyl ether in pentane as eluent to give the *aldehyde* (23 mg, 99%) as a colourless oil; ν_{max} (film)/cm^{-1} 2941, 2749, 1674 and 1614; δ_H (360 MHz, $CDCl_3$) 10.09 (s, 1H, C*H*O), 5.85 (1H, m, C=C*H*I), 5.02 (1H, br. t, *J* 6.9, C=C*H*), 4.89 (1H, d, *J* 7.1, OC*H*HOCH$_3$), 4.67 (1H, d, *J* 7.1, OCH*H*OCH$_3$), 4.47 (1H, app. t, *J* 7.5, C*H*OCH$_2$), 3.40 (3H, s, OCH_3), 2.24–1.99 (5H, m, 2 × CH_2 and C*H*H), 2.11 (3H, d, *J* 1.5, CH_3C=C), 1.88–1.48 (6H, m, 2 × CH_2, CH*H* and CH_3CH), 1.83 (3H, d, *J* 1.0, CH_3C=CHI), 1.58 (3H, s, CH_3C=CH), 1.02 (3H, s, CH_3–C(4°)), 0.93 (3H, d, *J* 6.7, CH_3CH); δ_C (90 MHz, $CDCl_3$) 192.7 (d), 161.1 (s), 147.6 (s), 136.2 (s), 136.0 (s), 123.1 (d), 99.4 (t), 74.8 (d), 72.2 (d), 55.7 (q), 43.2 (s), 39.4 (t), 35.0 (t), 34.1 (t), 33.9 (t), 30.6 (d), 26.1 (t), 23.8 (q), 20.0 (q), 16.1 (q), 16.0 (q), 13.4 (q); *m*/*z* (ES) 497.1533 (M^+ + Na, 100%, $C_{22}H_{35}IO_3Na$ requires 497.1529).

(3*E*,7*E*)-(2*R*,11*S*,12*R*,14*S*)-14-Methoxymethoxy-4,8,11,12,15-pentamethylbicyclo[9.3.1]pentadeca-1(15),3,7-trien-2-ol 92

Nickel chloride (1.6 mg, 0.01 mmol) and chromium chloride (36 mg, 0.29 mmol) were added sequentially to a stirred

solution of the aldehyde vinyl iodide **88b** (23 mg, 0.05 mmol) in DMSO (7 mL) at room temperature in a glove bag under an atmosphere of argon. The mixture was removed from the glove bag, and then stirred under a positive pressure of argon for 65 hours, and then diluted with ethyl acetate (1.5 mL) and hexane (1.5 mL). The mixture was cooled to 15 °C and then quenched cautiously with serine (1.0 M in a saturated aqueous solution of $NaHCO_3$, 10 mL). The mixture was stirred vigorously for 15 minutes, and then allowed to warm to room temperature. The separated aqueous phase was extracted with ethyl acetate–hexane (1 : 1, 4 × 5 mL) and the combined organic extracts were washed with brine (2 × 20 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica using 25–35% diethyl ether in pentane as eluent to give the *bicyclic alcohol* (11 mg, 62%), as a 3 : 1 mixture of the α- and β-alcohol epimers, as a colourless oil. The diastereoisomers were separated by flash column chromatography on silica using 10% diethyl ether and 20–30% dichloromethane in pentane as eluent to give the *α-alcohol* (7 mg, 41%) as a colourless oil; data for the α-alcohol isomer, δ_H (500 MHz, $CDCl_3$) 5.57 (1H, br. d, *J* 9.5, C=C*H*CHOH), 5.09 (1H, d, *J* 9.5, C*H*OH), 4.80 (1H, d, *J* 7.0, OC*H*HOCH$_3$), 4.78–4.74 (1H, m, C=C*H*), 4.73 (1H, d, *J* 7.0, OCH*H*OCH$_3$), 4.04–4.00 (1H, m, C*H*OCH$_2$), 3.46 (3H, s, OCH_3) 2.37–1.28 (11H, m, 5 × CH_2 and CH$_3$C*H*), 1.86 (3H, d, *J* 1.6, CH_3C=C), 1.69 (3H, s, CH_3C=CH), 1.63 (3H, s, CH_3C=CH), 0.89 (3H, s, CH_3–C(4°)), 0.84 (3H, d, *J* 6.9, CH_3CH); δ_C (125 MHz, $CDCl_3$) 144.4 (s), 135.6 (s), 134.0 (s), 132.9 (s), 127.8 (d), 126.0 (d), 95.1 (t), 77.4 (d), 69.0 (d), 55.9 (q), 42.1 (s), 36.4 (t), 34.2 (t), 33.6 (t), 32.0 (t), 30.4 (d), 25.6 (t), 21.7 (q), 18.0 (q), 16.4 (q), 15.7 (q), 15.7 (q); *m/z* (ES) 371.2523 (M^+ + Na, 100%, $C_{22}H_{36}O_3Na$ requires 371.2562).

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