Pergamon

Tetrahedron 56 (2000) 6099–6113

TETRAHEDRON

Synthesis of Natural Oxygenated Monocarbocyclic Sesquiterpenoids from 6,7-Epoxygeranyl Acetate

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Received 15 March 2000; revised 19 May 2000; accepted 8 June 2000

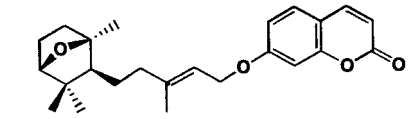
Abstract—Natural sesquiterpenes 5-(2′,5′-epoxy-2′,6′,6′-trimethyl)cyclohexyl-3-methyl-1-penten-3-ol (**5**), *cis*-3-[(*E*)-5′-hydroxy-3′-methyl-3′-pentenyl]-2,2-dimethyl-4-methylenecyclohexanol (elegansidiol) (**6**), 4-(5′-acetoxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-3-methyl-1-penten-3-ol (**7**) and 5-acetoxy-3-(3-hydroxy-3-methylpent-4-enyl)-2,4,4-trimethylcyclohex-2-enone (**8**) were prepared from 6,7-epoxygeranyl acetate (**9**), via (2′,5′-epoxy-2′,6′,6′-trimethyl)cyclohexylmethyl tosylate (**10**), for the first time. **5** is an intermediate in the synthesis of the sesquiterpene-coumarin ether (±)-farnesiferol C (**1**). The preparation of suitable intermediates for synthesising related natural farnesiferol B (**3**) and D (**4**) is also reported.

Introduction

Natural oxygenated monocarbocyclic terpenoids are not very common because biosynthetic processes usually involve polycyclization. These compounds have a bicyclic ether fragment, e.g. farnesiferol C (**1**)[1] or a cyclohexanol moiety, e.g. achilleol A (**2**)[2] and farnesiferol B (**3**) and D (**4**).[1] During the last few years the isolation of several monocarbocyclic compounds, such as **5**, **7**, **8**[3,4] and elegansidiol (**6**),[5] have been reported, which suggests that they could be more prevalent than it was presumed.

Several procedures have been described to create the bicyclic system of **1**. Mukaiyama et al. used a Diels–Alder asymmetric reaction to prepare (+)-farnesiferol C.[6] More recently, Demnitz et al. reported the formation of the 7-oxabicyclo[2.2.1]heptane ring system through an unexpected rearrangement in the Baeyer–Villiger oxidation of *trans*-3β-hydroxy-4,4,10β-trimethyl-9-decalone.[7] The present authors have reported the preparation of the same bicyclic ether system by selective electrophilic cyclization of 6,7-epoxygeranyl acetate (**9**); as well as the obtention of cyclohexanol type structures, such as elegansidiol (**6**), by the Lewis acid-mediated opening of the bicyclic ether.[5,8]

In this paper the synthesis of **5**, **7** and **8**, natural sesquiterpenes isolated from *Artemisia* species,[3,4] and elegansidiol (**6**), a constituent from *Santolina elegans*,[5] via selective electrophilic cyclization of 6,7-epoxygeranyl acetate (**9**) is reported.



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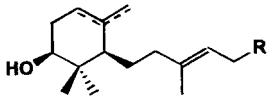

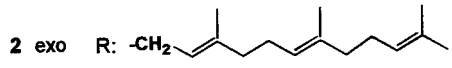

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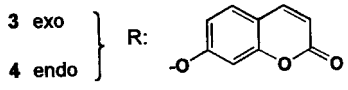
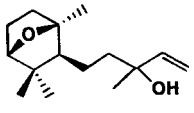


3 exo
4 endo
R:



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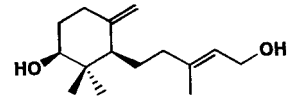

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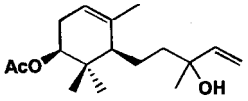

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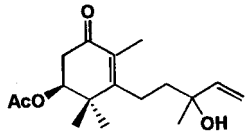

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Keywords: terpenes; cyclization.

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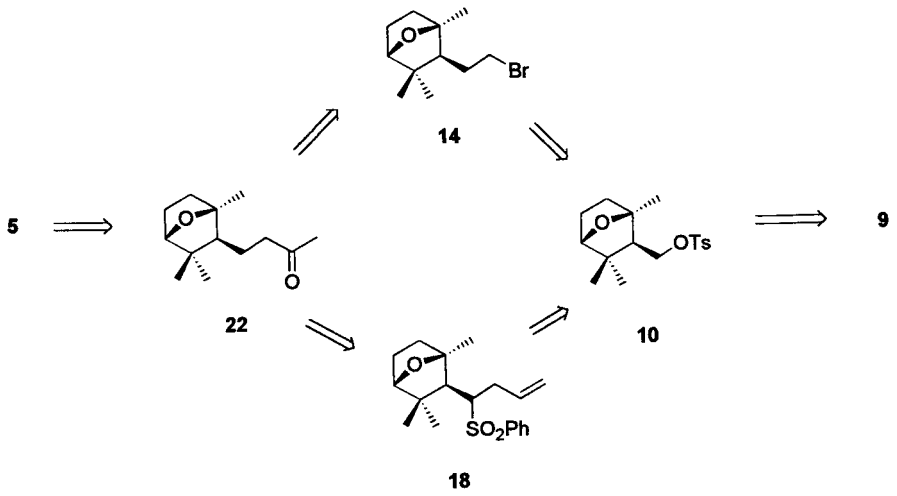


Scheme 1.

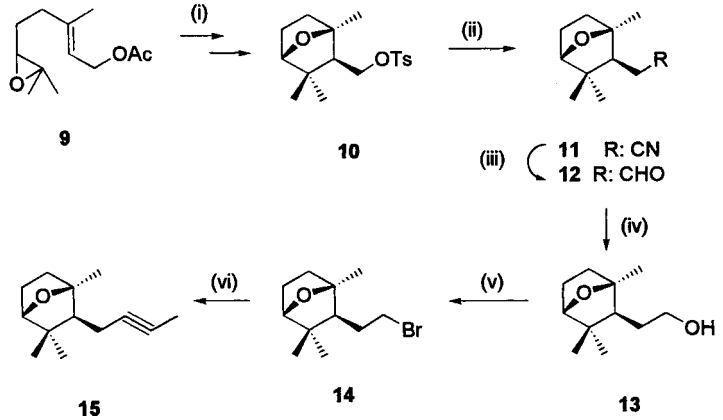
Results and Discussion

Two alternative routes to prepare the methylketone **22**, precursor of **5**, from the tosyl derivative **10**, which can be easily synthesised from **9**,[8] were proposed. In the first the side chain carbons are sequentially introduced (1C+2C), using cyanide and acetylide ions as synthons. In the second route these carbons are simultaneously introduced through an allyl halide (Scheme 1)

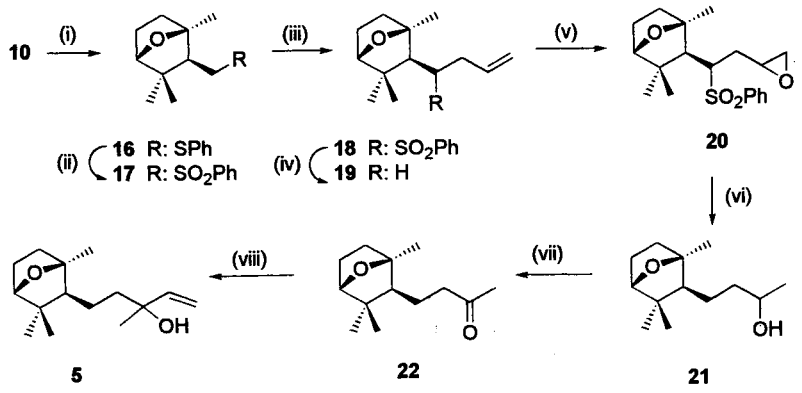
Heating of tosyl derivative **10** with KCN in DMSO yielded the nitrile **11**, which was reduced to the aldehyde **12** by treating with DIBAL at −80°C in toluene under argon. Further treatment with $NaBH_4$ afforded the alcohol **13**, which after treating with TsCl and LiBr gave the bromide **14**. The internal alkyne **15**, instead of the terminal one, was obtained when **14** was treated with lithium ethynyl–ethylenediamine complex (Scheme 2). ^{1}H NMR of **15** shows a triplet (J=2.5 Hz) at δ 1.74 due to the Me–C_3. The quaternary carbons of the acetylenic group appears at δ 75.8 and 79.5 in the ^{13}C NMR spectrum. Rearrangement of carbon–carbon triple bond from the C_3–C_4 to the C_2–C_3 position under basic conditions is a known process.[9] **15** could be converted into the methylketone **22** by regioselective hydroboration using bulky reagents.

The second route in Scheme 1 involves the reversal of the reactivity of the C_1 of the tosyl derivative **10**. Treatment of **10** with PhSH and KH afforded in quantitative yield the sulfide **16**, which was oxidised to the sulfone **17** with MCPBA. The allylsulfone **18** was obtained by treating **17** with BuLi and HMPA in THF and then with allyl bromide. Desulfonylation of **18** with 6% Na–Hg in a Na_2HPO_4 buffered solution yielded the allyl derivative **19**, besides significant amounts of the diene derived from the sulfone elimination (Scheme 3).

To prevent this problem an alternative route was established. This involves the introduction of the side chain oxygenated function, via epoxidation before reducing the sulfone group. Treatment of **18** with MCPBA at room temperature for 3 days yielded the epoxysulfone **20** as a diastereomeric mixture. The ^{1}H NMR spectrum of the crude shows signals due to three of the four possible isomers in a 3:1:1 ratio. These can be satisfactorily resolved by column chromatography. Treatment of **20** with $LiAlH_4$ under reflux allows the regioselective opening of the epoxide and simultaneous desulfonylation, affording the alcohol **21**. This was oxidised with Jones reagent to give **22**, which by treating with vinylmagnesium bromide gave **5**, which consists almost exclusively of an epimer. The



Scheme 2. (i) Ref. 8. (ii) KCN, DMSO, 135°C, 5 h (80%). (iii) DIBAL, Toluene, −80° to 0°C (70%). (iv) $NaBH_4$, MeOH, −10°C (70%). (v) TsCl, Py, DMAP, OEt_2, 0°C; LiBr, THF, 60°C (71%). (vi) LiCCH, EDA, DMSO, 2.5 h (57%).



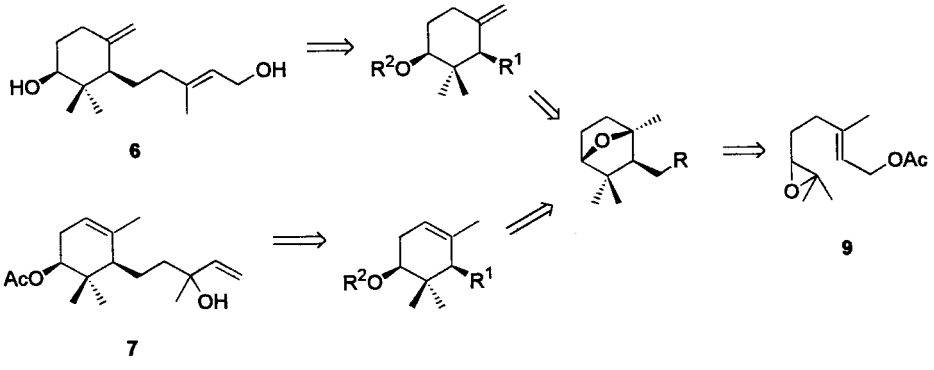
Scheme 3. (i) PhSH, KH, EtOH, reflux, 4 h (92%). (ii) MCPBA, CH_2Cl_2, 0°C (98%). (iii) BuLi, HMPA, THF, −78°C; $BrCH_2CH{=}CH_2$, rt, Ar, 12 h (77%). (iv) 6% Na–Hg, Na_2HPO_4, rt, 6 h (37%). (v) MCPBA, CH_2Cl_2, rt, 3 days (90%). (vi) $LiAlH_4$, THF, reflux, 80 h (98%). (vii) Jones, acetone, 0°C (89%). (viii) $BrMgCH{=}CH_2$, THF; $ClNH_4$, (85%).

spectroscopic properties of this compound were identical to those reported for the natural sesquiterpene[4] (Scheme 3). **5** had been previously reported as an intermediate in the synthesis of farnesiferol C (**1**).[1]

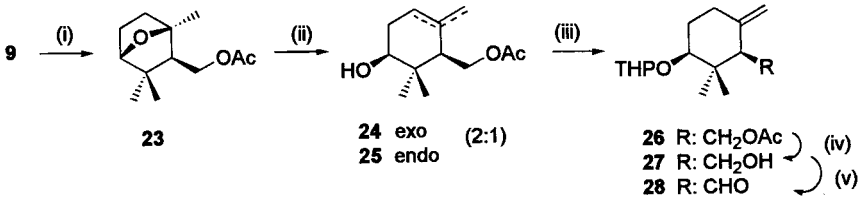
The synthesis of compounds **6** and **7** was planned through the cyclohexanol derivatives which result from the BBr_3-mediated opening of the corresponding bicyclic ether (Scheme 4).

The synthesis of **6** was first approached by condensation of a monocyclic synthon C_{10} with an acyclic synthon C_5. The elaboration of the C_{10} moiety was carried out through electrophilic cyclization of 6,7-epoxygeranyl acetate (**9**), on the basis of previous studies by the present authors.[8] Scheme 5 depicts the first synthetic approach using aldehyde **28** as the C_{10} electrophile synthon. The efficient cyclization of **9** to **23** and subsequent opening of the bicyclic ether in anhydrous conditions, which has been improved, led to a mixture of regiosomers **24** and **25** (ratio 2:1), the combined yield being higher than 60%. After isolation of the *exo* isomer and protection of the secondary hydroxyl group, transformation of **26** into **28** was achieved under standard conditions. Nevertheless, all the attempts to condense this aldehyde with nucleophiles such as 2-oxopropylidentriphenylphosphorane were unsuccessful. This difficulty has also been described in related structures,[10] and can be accounted for by considering the steric hindrance exerted on the aldehyde group by both the *gem*-dimethyl and the exocyclic double bond.

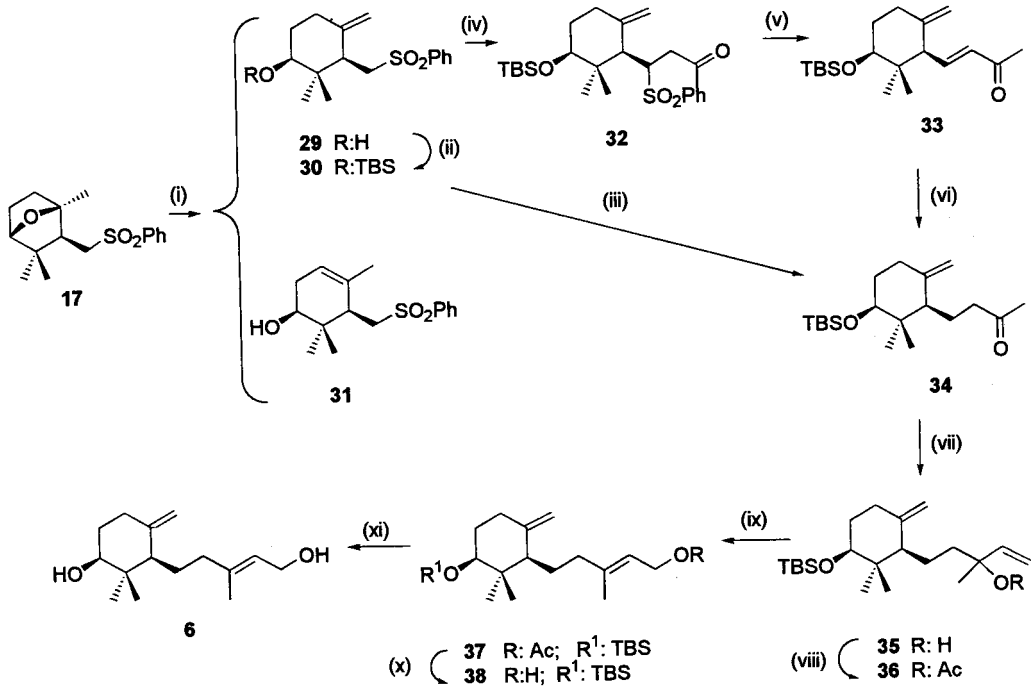
The sulfone **29** was therefore studied as a new C_{10} nucleophilic synthon. This sulfone was formed starting from the bicyclic ether **17**, which after treating with BBr_3 afforded a mixture of the regioisomers **29** and **31** (ratio 1:1), which were easily separated by column chromatography. After protecting the hydroxyl group of **29** as its *t*-butyldimethylsilylether, alkylation of the carbanion generated from **30** by



Scheme 4.



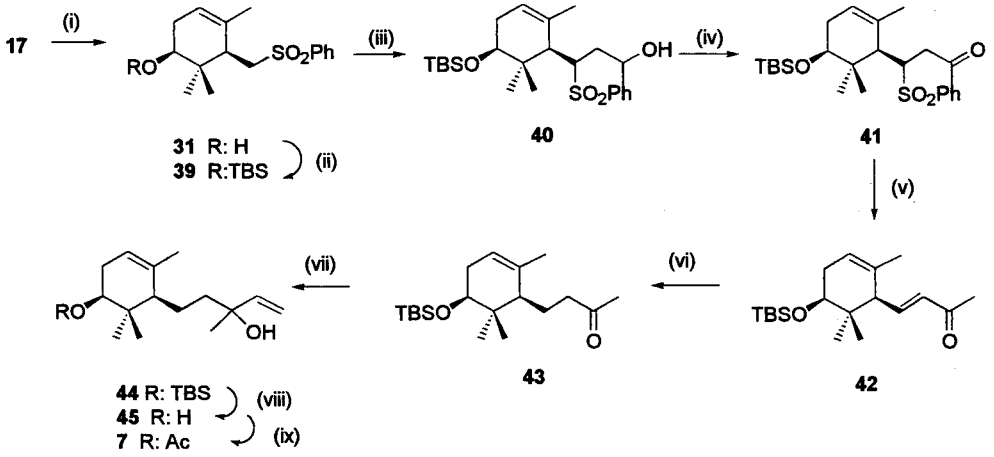
Scheme 5. (i) Ref. 8. (ii) BBr_3, CH_2Cl_2, rt, 10 min; Collidine, CH_2Cl_2 (72%). (iii) DHP, PPTS, CH_2Cl_2 rt, 6h (85%). (iv) 2N KOH-MeOH, rt, 12 h (90%). (v) PDC, CH_2Cl_2, rt, 24 h (80%).



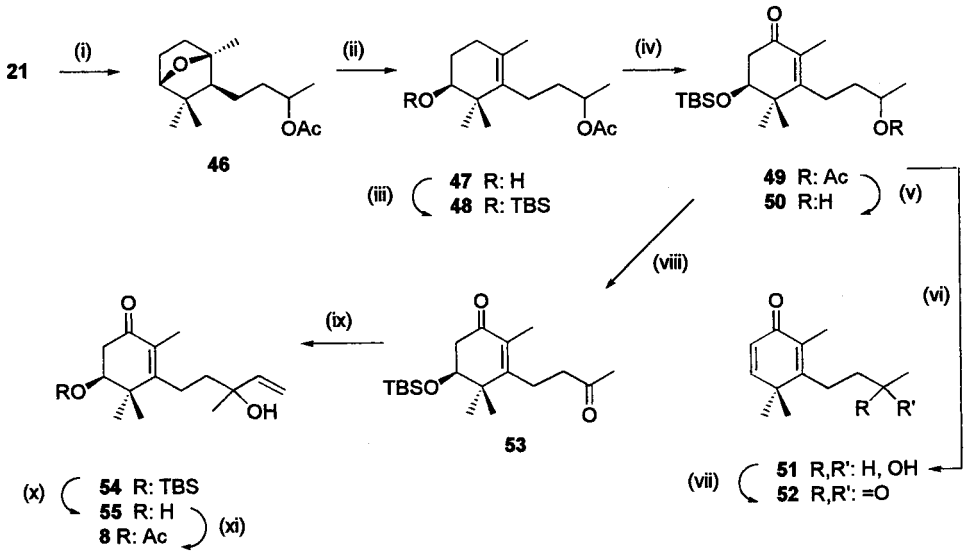
Scheme 6. (i) BBr_3, CH_2Cl_2, rt, 15 min; Collidine (82%). (ii) TBSCl, imidazole, DMF, DMAP. rt, 10 h (87%). (iii) (a) *n*-BuLi, THF, 0°C, 30 min; rt, 45 min. (b) propylene oxide, rt, 1 h; 65°C, 45 min. (c) 6% Na–Hg, Na_2HPO_4, EtOH, reflux, 6 h. (d) Jones, acetone, 0°C, 30 min (70% overall yield). (iv) (a) *n*-BuLi, THF, 0°C, 30 min; rt, 45 min. (b) propylene oxide, rt, 1 h; 65°C, 45 min. (c) Jones, acetone, 0°C, 30 min (82% from **30**). (v) Alumina, THF, rt, 2 h (95%). (vi) Raney Ni, THF, rt, 30 min (92%). (vii) BrMgCH=CH2, THF, 0°C, 30 min (95%). (viii) Ac_2O, Et_3N, DMAP, THF, reflux, 26 h (90%). (ix) $PdCl_2(CH_3CN)_2$, THF, rt, 45 min (95%). (x) KOH, MeOH, rt, 45 min (94%). (xi) TBAF, THF rt, 6 h 89%).

treatment with butyllithium was attempted with a C_5 allylic bromide, the tetrahydropyranyl derivative of 4-bromo-3-methyl-2(*E*)-butenol. Unfortunately, the use of the monocarbocycle as the nucleophile did not lead to a successful reaction. In fact, at room temperature starting materials remained unaltered and only decomposition of the allylic derivative was observed after heating (Scheme 6).

This task could only be accomplished by treatment of the sulfone anion with the much more stable propylene oxide at 65°C to give a β-hydroxysulfone which was converted into the ketone **34** following two alternative methods. The first involves the reduction of the sulfone group with sodium amalgam and further oxidation of the hydroxyl group with Jones reagent. In the second method oxidation of the hydroxyl group was first carried out, affording the ketosulfone **32**, which was transformed into **34** by using a new methodology developed by the present authors.[11] Column chromatography on alumina of **32** yielded the α,β-unsaturated ketone **33**, which was chemoselectively reduced with Raney Ni to give **34**. This ketone afforded the allylic alcohol **35** after being exposed to vinylmagnesium bromide. **35** is a suitable intermediate for synthesizing (±)-farnesiferol B (**3**).[1] Acetate **36** underwent allylic rearrangement after treatment with palladium dichloride bis acetonitrile to afford the carbon skeleton of elegansidiol. Saponification of the ester



Scheme 7. (i) BBr_3, CH_2Cl_2, rt, 1 h; Et_3N (87%). (ii) TBSCl, imidazole, DMF, DMAP, rt, 10 h (80%). (iii) (a) *n*-BuLi, THF, 0°C, 30 min; rt, 45 min. (b) propylene oxide, rt, 1 h; 65°C, 15 min (85%). (iv) Jones, acetone, 0°C, 30 min (90%). (v) Alumina, THF, rt, 4 h (98%). (vi) Raney Ni, THF, rt, 30 min (95%). (vii) BrMgCH=CH_2, THF, 0°C, 30 min (93%). (viii) TBAF, THF, rt, 4 h (81%). (ix) Ac_2O, Py, rt, 4 h (83%).



Scheme 8. (i) Ac_2O, Py, rt 6 h (95%). (ii) BBr_3, CH_2Cl_2, rt, 15 min; Collidine (89%). (iii) TBSCl, DMF, Imidazole, DMAP, rt, 44 h (95%). (iv) Na_2CrO_4, NaOAc, Ac_2O, AcOH, Benzene, 65°C, 3 h (88%).(v) K_2CO_3, MeOH, rt, 1 h (95%). (vi) 2 N KOH–MeOH, rt, 24 h (93%). (vii) Jones, acetone, 0°C. (viii) Jones, acetone, −15°C, 30 min (96%). (ix) $BrMgCH{=}CH_2$, THF, −15°C, rt, 45 min (87%). (x) TBAF, THF, 0°C, rt, 2 h (81%). (xi) Ac_2O, Py, rt, 1 h (93%).

group and fluoride-induced cleavage of the silyl ether completed the synthesis of **6**, whose spectroscopic properties were identical to those of the natural product.[5]

Sesquiterpene **7** was synthesised from sulfone **31**, which was obtained as the sole product when the BBr_3-induced opening of **17** was quenched with Et_3N, following a similar procedure to the above described for elegansidiol (**6**) (Scheme 7). **44** could be easily converted into (±)-farnesiferol D (**4**).[1] At this time it should be pointed out that the side chain carbon of endocyclic isomer **31** seems to be less hindered than that of exocyclic compound **29**. So, treatment of the mixture of anions derived from regioisomers **29**–**31** with allyl bromide afforded the alkylated *endo*-alkene, being **29** recovered unaltered. **44** was converted into the mixture of diastereomers **7** after removal of the *tert*-butyldimethylsilyl group and acetylation of the hydroxyl group. The spectroscopic properties of the major epimer were identical to those reported for the natural product.

Scheme 8 shows the synthetic sequence to **8**. It is based on the surprising behaviour of bicyclic ether **46** towards BrB_3, which underwent regioselective opening to give the cyclohexenol derivative **47**. Oxidation at C_5 was carried out after protecting the hydroxyl group as a *tert*-buthyldimethylsilyl ether. Treatment of **48** with Na_2CrO_4 yielded the enone **49**. This compound is very reactive towards elimination processes. When it was treated with 2N KOH–MeOH at room temperature dienone **51** was obtained as the only product. Its ^1H NMR spectrum shows two doublets (J=9.9 Hz) at δ 6.19 and 6.72 due to the olefinic protons. Oxidation of **51** with Jones reagent gave the diketone **52**, which exhibited a simple spectrum. Treatment of **49** with K_2CO_3 in MeOH afforded the alcohol **50**, which was oxidized with the Jones reagent at −15°C to give the diketone **53**. When **53** was treated with vinylmagnesium bromide in Et_2O at −15°C the allylic alcohol **54** was obtained. Deprotection of the silyl ether with TBAF gave the diol **55**, which after acetylation was converted into **8**, obtained as a mixture of diastereomers. The spectroscopic properties of **8** were identical to those of an authentic sample (Scheme 8).

In summary the monocarbocyclic terpenoids, **5**–**8**, have been synthesised from 6,7-epoxygeranyl acetate (**9**). The key step in the synthesis of cyclohexenol derivatives, as **6**–**8**, is the regioselective opening of the bicyclic ether with BBr_3. The course of this reaction seems to depend on the nature of the ether side chain as well as on the base used to quench the reaction. Thus, bicyclic ethers having a polar group at the carbon adjacent to the ring give mixtures of tri- and disubstituted alkenes, when collidine is used as base;[8] the use of the less hindered Et_3N affords the trisubstituted carbon–carbon double bond almost exclusively (Scheme 7). However, the tetrasubstituted alkene is obtained when the side chain is longer and the polar group is distant from the ring (Scheme 8).

Experimental

Melting points were determined with a Kofler hot stage melting point apparatus and are uncorrected. IR spectra were obtained on Perkin–Elmer Models 782 and 983G spectrometers with samples between sodium chloride plates or as potassium bromide pellets. Proton nuclear magnetic resonance spectra were taken on a Bruker AMX 300 (300 MHz), Bruker ARX 400 (400 MHz) and Bruker AMX 500 (500 MHz) spectrometers using $CDCl_3$, and CD_3COCD_3 as solvent and TMS or residual protic solvent $CHCl_3$ (δ_H=7.25 ppm) as internal reference, and the multiplicity of a signal is a singlet unless otherwise stated, when the following abbreviations are used: s, singlet; bs, broad singlet; d, doublet; bd, broad doublet; dd, double doublet; t, triplet; m, multiplet. ^{13}C NMR spectra were run on a Bruker AMX 300 (75 MHz), ARX 400 (100 MHz) and AMX 500 (125 MHz) instruments. Chemical shifts are in ppm (δ scale) and the coupling constants are in Hertz. Carbon

substitution degrees were established by DEPT pulse sequence. MS were recorded on a Hewlett–Packard 5988A spectrometer using an ionizing voltage of 70 eV. HRMS were obtained on a trisector WG AutoSpecQ spectrometer. For analytical TLC Merck silica gel 60G in 0.25 mm thick layers was used. Chromatographic separations were carried out by conventional column on Merck silica gel 60 (70–230 mesh) and by flash column on Merck silica gel 60 (230–400 mesh) using hexane–MeO^{t}Bu (H–E) mixtures of increasing polarity. Routinely, dry organic solvents were stored under argon, over freshly activated molecular sieves. Ether, benzene, and THF, were dried over sodium-benzophenone ketyl, HMPA from Na, dichloromethane over calcium hydride, and methanol from magnesium methoxide. Where necessary reactions were carried out under a nitrogen or argon atmosphere.

2-(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexyl acetonitrile (11). To a solution of **10** (0.7 g, 2.18 mmol) in dimethylsulfoxide (DMSO) (30 ml), was added 0.79 g of KCN (12.04 mmol) and the mixture was heated at 135°C for 5 h. The mixture was fractionated in H_2O–ether (100 ml) and extracted with ether (3×50 ml). The dried organic phases were evaporated and the residue was filtered through silica gel to afford 0.31 g of **11** (79%) as a colourless oil. IR (film): 2245(CN), 1024, 990 cm^{-1}. MS *m/z* (rel. int.): 179 [M$^+$] (6), 165 [M$^+$−N](8), 164 [M$^+$−Me](73). ^{1}H NMR ($CDCl_3$, 300 MHz): 3.79 (1H, d, *J*=5.5 Hz, H-5′), 2.30 (1H, dd, *J*=16.6, 7.2 Hz, H-2), 2.26 (1H, dd, *J*=16.6, 8.6 Hz, H-2), 1.95 (1H, ddd, *J*=12.7, 8.7, 4.5 Hz, H-3′), 1.80–1.50 (4H, m, H-3′, H-4′, H-6′), 1.38 (3H, s, Me–$C_{2'}$), 1.15 (3H, s, Me–$C_{6'}$), 1.09 (3H, s, Me–$C_{6'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 120.3 (1), 15.7 (2), 52.9 (1′), 85.9 (2′), 37.8 (3′), 25.9 (4′), 86.2 (5′), 45.1 (6′), 25.7 (7′), 23.3 (8′), 18.4 (9′). HREIMS *m/z* calcd for $C_{11}H_{17}ON$ M$^+$ 179.1310, found 179.1318.

2-(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexyl acetaldehyde (12). DIBAH (1 M in hexane, 20 ml, 20 mmol) was added to a solution of **11** (1.5 g, 8.37 mmol) in toluene (30 ml) at −78°C, and the whole mixture was slowly warmed to 0°C for 8 h, stirred at this temperature for an additional 5 h. 5% NH_4Cl solution (25 ml) was added to the mixture and then diluted with ether (100 ml). The organic layers were washed with 1 M HCl, sat. NaCl and dried. Concentration gave a crude which was directly purified by flash chromatography (H–E 8:2) to yield 1.07 g of the aldehyde **12** (70%), as a colourless oil, and 0.27 g (18%) of starting material. IR (film): 2722, 1724, 1022 cm^{-1}. MS *m/z* (rel. int.): 182 [M$^+$] (2), 167 [M$^+$−Me](8), 164 [M$^+$−H_2O](2). ^{1}H NMR ($CDCl_3$, 300 MHz): 9.83 (1H, t, *J*=1.3 Hz, H-1), 3.79 (1H, d, *J*=5.1 Hz, H-5′), 2.44 (1H, ddd, *J*=18.2, 7.5, 1.3 Hz, H-2), 2.42 (1H, ddd, *J*=18.2, 7.5, 1.3 Hz, H-2), 1.92 (1H, m, H-3′), 1.75–1.42 (4H, m), 1.29 (3H, s, Me–$C_{2'}$), 1.06 (3H, s, Me–$C_{6'}$), 0.91 (3H, s, Me–$C_{6'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 202.5 (1), 43.1 (2), 50.3 (1′), 86.2 (2′), 37.9 (3′), 26.2 (4′), 86.1 (5′), 44.7 (6′), 18.9 (7′), 24.7 (8′), 25.7 (9′). HREIMS *m/z* calcd for $C_{11}H_{18}O_2$ M$^+$ 182.1307, found 182.1295.

2-(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexyl ethanol (13). $NaBH_4$ (0.38 g, 10 mmol) was added to a solution of **12** (1.8 g, 9.9 mmol) in methanol (20 ml) at −10°C and the mixture was stirred at 0°C for 70 min. Then it was diluted with ether (100 ml), washed with water, sat. NaCl, and dried, to yield after concentration 1.26 g of **13** (70%) (colourless oil). IR (film): 3422 (OH), 2950, 2855, 1097 cm^{-1}. MS *m/z* (rel. int.): 184 [M$^+$] (1), 169 [M$^+$−Me](30), 166 [M$^+$−H_2O](2), 153 [M$^+$−Me–H_2O](20). ^{1}H NMR ($CDCl_3$, 300 MHz): 3.65 (1H, d, *J*=5.5 Hz, H-5′), 3.50 (2H, m, H-1), 1.90 (1H, ddd, *J*=12.6, 8.7, 4.5 Hz, H-3′), 1.68–1.35 (4H, m), 1.25 (3H, s, Me–$C_{2'}$), 0.96 (3H, s, Me–$C_{6'}$), 0.92 (3H, s, Me–$C_{6'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 62.4 (1), 31.0 (2), 51.8 (1′), 86.6 (2′), 38.7 (3′), 25.6 (4′), 85.9 (5′), 45.0 (6′), 18.7 (7′), 23.6 (8′), 25.7 (9′). HREIMS *m/z* calcd for $C_{11}H_{20}O_2$ M$^+$ 184.1463, found 184.1472.

2-(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexyl-1-bromoethane (14). To a stirred solution of **13** (1.125 g, 6.1 mmol) in THF (3 ml), pyridine (7 ml), dimethylamino pyridine (DMAP) (20 mg, 0.16 mmol) and TsCl (1.79 g, 8.65 mmol) were successively added at −5°C and the mixture was stirred at this temperature for 2 h 30 min. At the end of this period a solution of lithium bromide (2.62 g, 30.5 mmol) in THF (26 ml) was added, and the mixture was heated at 60°C for 2 h. After dilution with ether (100 ml), the mixture was successively washed with 5% $NaHSO_4$ solution, 5% $NaHCO_3$ solution, water, sat. NaCl and then dried. Concentration and chromatography (H–E 9:1) gave 1.07 g of **14** (71%) as a colourless oil. IR (film): 2925, 2850, 1085 cm^{-1}. MS *m/z* (rel. int.): 231, 233 [M$^+$−Me] (5, 5), 228(15), 230 [M$^+$−H_2O](1, 1), 167 [M$^+$−Br](3). ^{1}H NMR ($CDCl_3$, 300 MHz): 3.73 (1H, d, *J*=5.0 Hz, H-5′), 3.37 (2H, m, H-1), 2.75–2.36 (4H, m, H-3′, H-4′, H-6′), 1.98–1.84 (2H, m, H-2, H-3′), 1.31 (3H, s, Me–$C_{2'}$), 1.05 (3H, s, Me–$C_{6'}$), 0.99 (3H, s, Me–$C_{6'}$). HREIMS *m/z* calcd for $C_{11}H_{19}OBr$ M$^+$ 246.0619, found 246.0627.

1-(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexyl-2-butyne (15). A solution of lithium acetylide ethylenediamine complex (0.49 g, 5.08 mmol) in anhydrous DMSO (20 ml) was added to a solution of the bromide **14** (0.25 g, 1.02 mmol) in DMSO (20 ml). The whole was heated at 40°C and stirred for 2 h 30 min, then it was quenched with water (20 ml), and stirred for an additional 10 min. The mixture was extracted with ether (25 ml×4) and the combined extracts were washed with sat. NaCl, dried, and concentrated to give after cromatography of the crude (H–E 7:3) 0.11 g of **15** (57%) as a colourless oil. IR (film): 1086, 908 cm^{-1}. MS *m/z* (rel. int.): 192 [M$^+$] (7), 177 [M$^+$−Me](56), 162 [M$^+$−2Me](22) [M$^+$−H_2O–Me](10). ^{1}H NMR ($CDCl_3$, 300 MHz): 3.56 (1H, d, *J*=5.1 Hz, H-5′), 2.14 (2H, m, H-1), 1.90 (1H, ddd, *J*=12.6, 8.7, 4.5 Hz), 1.75–1.35 (4H, m), 1.74 (3H, t, *J*=2.5 Hz, Me-4), 1.31 (3H, s, Me–$C_{2'}$), 1.08 (3H, s, Me–$C_{6'}$), 1.07 (3H, s, Me–$C_{6'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 114.5 (1), 138.9 (2), 33.9 (3), 27.9 (4) 55.1 (1′), 86.7 (2′), 39.0 (3′), 25.8 (4′), 86.1 (5′), 45.3 (6′), 18.9 (7′), 23.4 (8′), 26.1 (9′). HREIMS *m/z* calcd for $C_{13}H_{20}O$ M$^+$ 192.1514, found 192.1522.

(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexylmethyl phenyl thioether (16). To a stirred suspension of KH (35% in oil, 1.45 g, 0.0126 mol) in ethanol (20 ml), thiophenol (1.33 g, 0.0126 mol) was added and the mixture was stirred for 15 min. Then a solution of **10** (1.95 g, 6.018 mmol) in

ethanol (5 ml) was added, and the whole was heated under reflux for 4 h. After removing the solvent, the residue was taken up into ether, and the insoluble material was removed by filtration. Concentration and column chromatography (H–E 8:2) afforded **16** (1.45 g, 92%) (colourless oil). IR (film): 2000, 1600, 1582, 1478, 1437, 1090, 937, 738, 690 cm^{-1}. MS *m/z* (rel. int.): 262 [M^+] (2), 153 [M^+-SPh] (100). ^1H NMR ($CDCl_3$, 300 MHz): 7.22 (5H, bs, Ph), 3.71 (1H, d, *J*=7.0 Hz, H-5′), 2.95 (1H, dd, *J*=12.0 and 7.0 Hz, H-1), 2.79 (1H, dd, *J*=15.0 and 12.0 Hz, H-1), 1.95–1.40 (5H, m), 1.32 (3H, s, Me-9′), 1.1 (3H, s, Me-8′), 1.05 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): 32.7 (1), 54.8 (1′), 86.8 (2′), 38.5 (3′), 25.7 (4′), 85.9 (5′), 45.7 (6′), 18.7 (7′), 22.9 (8′), 25.8 (9′), 137.6 (1″), 128.5 (2″), 128.8 (3″), 125.6 (4″), 128.8 (5″), 128.5 (6″). HREIMS *m/z* calcd for $C_{16}H_{22}OS$ M^+ 262.1391, found 262.1403.

(2′,5′-Epoxy-2′,6′,6′-trimethyl)cyclohexylmethyl phenyl sulphone (17). A solution of 85% *m*-chloroperbenzoic acid (MCPBA) (0.99 g, 5.72 mmol) in CH_2Cl_2 (12 ml) was slowly added at 0°C to a solution of **16** (0.6 g, 2.3 mmol) in CH_2Cl_2 (12 ml). After stirring at rt for 1 h, the mixture was concentrated, and the residue was taken up in $CHCl_3$ (50 ml), washed successively with sat. $NaHCO_3$ and brine (2×30 ml). The ethereal phase was dried over anh Na_2SO_4, filtered and evaporated under vacuum to give a crude mixture which after chromatography (H–E 1:9) yielded **17** (660 mg, 98%) as a colourless oil. IR (film): 2000, 1600, 1589, 1307, 1150, 1070, 938, 738, 690 cm^{-1}. MS *m/z* (rel. int.): 294 [M^+] (1), 153 [M^+-SO_2Ph](100), 135 [$M^+-SO_2Ph-H_2O$](43). ^1H NMR ($CDCl_3$, 300 MHz): 7.88 (2H, d, *J*=8.3 Hz, H-3″and 5″), 7.64 (1H, d, *J*=6.9 Hz, H-4″), 7.54 (2H, d, *J*=7.2 Hz, H-2″and 6″), 3.79 (1H, d, *J*=5.3 Hz, H-5′), 3.10 (2H, dd, *J*=4.5 and 1.5 Hz, H-1), 1.89 (2H, m), 1.70 (1H, m), 1.59 (1H, m), 1.47 (1H, m), 1.28 (3H, s, Me-9′), 1.08 (3H, s, Me-8′), 1.05 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): 55.1 (1), 49.9 (1′), 86.3 (2′), 38.5 (3′), 25.9(4′), 86.2 (5′), 45.6 (6′), 19.3 (7′), 24.7 (8′), 24.8 (9′), 140.2 (1″), 129.4 (2″), 127.9 (3″), 133.7 (4″), 127.9 (5″), 129.4 (6″). HREIMS *m/z* calcd for $C_{16}H_{22}O_3S$ M^+ 294.1289, found 294.1278.

4-(2′,5′-Epoxy-2′,6′,6′-trimethyl) cyclohexyl-4-phenyl-sulphonyl-1-butene (18). *n*-Butyl lithium (2.26 M in hexane, 11.3 ml, 2.94 mmol) and 5.2 ml of HMPA, was added to a solution of **17** (0.83 g, 2.82 mmol) in 30 ml of THF at −78°C, and the whole mixture was slowly warmed to 0°C and stirred for 1 h. A solution of allyl bromide (3.41 g, 0.028 mol) was added at −78°C to this mixture and stirred for 12 h. After addition of sat. NH_4Cl the mixture was diluted with ether (100 ml), washed with 5% HCl, water, sat. $NaHCO_3$, and sat. NaCl and the organic layer was dried. Concentration and chromatography (H–E 1:1) gave 0.73 g of **18** (77%) as a colourless oil. IR (film): 1639, 1584, 1303, 1146, 1085, 999, 918 cm^{-1}. MS *m/z* (rel. int.): 334 [M^+] (1), 193 [M^+-SO_2Ph](100), 175 [$M^+-SO_2Ph-H_2O$](30). ^1H NMR ($CDCl_3$, 300 MHz): 7.87 (2H, d, *J*=8.3 Hz, H-3″ and 5″), 7.62 (1H, d, *J*=6.9 Hz, H-4″), 7.54 (2H, dt, *J*=7.2 Hz, H-2″ and 6″), 5.44 (1H, ddd, *J*=17.1, 10.1 and 5.6 Hz, H-2), 4.87 (1H, dd, *J*=17.1 and 1.6 Hz, H-1*trans*), 4.80 (1H, dd, *J*=10.1 and 1.6 Hz, H-1*cis*), 3.81 (1H, d, *J*=4.9 Hz, H-5′), 2.85 (1H, dddd, *J*=7.5, 7.0, 5.7 and 1.4 Hz, H-4), 1.90–1.62 (5H, m), 1.55–1.38 (2H, m), 1.61 (3H, s, Me-9′), 0.92 (3H, s, Me-8′), 0.76 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): 116.8 (1), 135.9 (2), 41.2 (3), 66.3 (4), 53.9(1′), 87.3 (2′), 30.3 (3′), 25.7 (4′), 85.0 (5′), 47.9 (6′), 20.3 (7′), 24.9 (8′), 24.3 (9′), 139.1 (1″), 129.3 (2″-6″), 128.9 (3″-5″), 133.7 (4″). HREIMS *m/z* calcd for $C_{19}H_{26}O_3S$ M^+ 334.1602, found 334.1595.

4-(2′,5′-Epoxy-2′,6′,6′-trimethyl) cyclohexyl-1-butene (19). To a solution of the sulphone **18** (0.7 g, 2.095 mmol) in anhydrous ethanol (25 ml), Na_2HPO_4 (1.2 g, 8.38 mmol) and 6% Na–Hg (3.23 g, 8.43 mmol) was added and the whole was heated under reflux for 6 h. It was cooled to room temperature and the mixture poured into a 1 M HCl solution, and extracted with ether (4×25 ml). The combined extracts were washed with 10% $NaHCO_3$, water, sat. NaCl, and then dried. Concentration and chromatography (hexane–ether, 8:2) gave 0.15 g of **19** (36.9%) (colourless oil). IR (film): 3070, 1638, 1081, 1005, 995, 910, 909 cm^{-1}. MS *m/z* (rel. int.): 194 [M^+] (1), 179 [M^+-Me](5), 161 [M^+-Me-H_2O](4). ^1H NMR ($CDCl_3$, 300 MHz):, 4.97 (1H, ddt, *J*=16.7, 9.0, 6.6 Hz, H-2), 5.02 (1H, dq, *J*=16.7, 1.2 Hz, H-1*trans*), 4.97 (1H, dq, *J*=9.0, 1.2 Hz, H-1*cis*), 3.74 (1H, d, *J*=5.7 Hz, H-5′), 2.15–1.90 (m, 3H), 1.80–1.60 (m, 2H), 1.60–1.20 (m, 4H), 1.34 (3H, s, Me-9′), 1.07 (3H, s, Me-8′), 1.03 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): 114.5 (1), 138.9 (2), 33.9 (3), 27.9 (4), 55.1(1′), 86.7 (2′), 39.0 (3′), 25.8 (4′), 86.1 (5′), 45.3 (6′), 18.9 (7′), 23.4 (8′), 26.1 (9′). HREIMS *m/z* calcd for $C_{13}H_{22}O$ M^+ 194.1670, found 194.1681.

4-(2′,5′-Epoxy-2′,6′,6′-trimethyl) cyclohexyl-4-phenyl-sulphonyl-1,2-epoxybutene (20). A solution of allyl sulphone **18** (2.56 g, 8 mmol) and 85% *m*-chloroperbenzoic acid (MCPBA) (1.85 g, 10.4 mmol) in CH_2Cl_2 (50 ml), was stirred at room temperature for 77 h. After concentration, the residue was taken up into ether (150 ml) and washed successively with sat. $NaHCO_3$, sat. NaCl and dried. Concentration and chromatography (H–E 1:1) of the crude gave 1.3 g of the mixture of epoxysulphone **20a** and **20b** and 1.1 g of epoxysulphone **20c**, as colourless oils. **20a–c** IR (KBr): 1582, 1449, 1300, 1145, 1086, 876 cm^{-1}. **20a–c** MS *m/z* (rel. int.) of **20a–c**: 350. [M^+] (0.02), 209 [M^+-SO_2Ph](75), 161 [$M^+-SO_2Ph-H_2O$](12). **20a–b** ^1H NMR ($CDCl_3$, 300 MHz): Signals assignable to **20a** 3.76 (1H, d, *J*=4.9 Hz, H-5′), 3.73 (1H, dd, *J*=4.7 and 4.2 Hz, H-1), 3.41 (1H, d, *J*=10 Hz, H-4), 3.11 (1H, m, H-2), 2.52 (1H, dd, *J*=5.0 and 2.6 Hz, H-1), 2.12 (1H, dd, *J*=15.9 and 7.6 Hz, H-3), 1.87 (1H, s, H-1′), 1.60 (3H, s, Me-9′), 0.99 (3H, s, Me-8′), 0.60 (3H, s, Me-7′). Signals assignable to **20b**: 3.80 (1H, d, *J*=5.1 Hz, H-5′), 3.71 (1H, dd, *J*=10.3, 2.1 Hz, H-1), 2.42 (1H, dd, *J*=4.9, 2.4 Hz, H-1), 2.00 (1H, d, *J*=2.1 Hz, H-1′), 1.60 (3H, s, Me-9′), 0.99 (3H, s, Me-8′), 0.60 (3H, s, Me-7′). **20a–b** ^{13}C NMR ($CDCl_3$, 75 MHz): 41.3 (1), 63.2 (2), 47.8 (3), 51.0 (4), 53.9(1′), 86.9 (2′), 28.2 (3′), 25.5 (4′), 84.8 (5′), 47.7 (6′), 20.1 (7′), 24.2 (8′), 25.1 (9′) 138.5 (1″), 129.3 (2″-6″), 128.9 (3″-5″), 133.9 (4″). **20c** ^1H NMR ($CDCl_3$, 300 MHz): 3.80 (1H, d, *J*=5.0 Hz, H-5′), 3.20 (1H, d, *J*=8.8 Hz, H-4), 2.90 (1H, m, H-2), 2.75 (1H, ddd, *J*=15.9, 8.8, 3.6 Hz, H-3), 2.72 (1H, t, *J*=4.9 Hz, H-1), 2.60 (1H, dd, *J*=4.9, 2.6 Hz, H-1), 2.21 (1H, dd, *J*=15.9, 7.3 Hz, H-3), 1.54 (3H, s, Me-9′), 0.98 (3H, s, Me-8′), 0.73 (3H, s, Me-7′). ^{13}C NMR

($CDCl_3$, 75 MHz): 41.3 (1), 63.5 (2), 48.4 (3), 51.6 (4), 53.6 (1′), 86.8 (2′), 29.0 (3′), 25.4 (4′), 84.6 (5′), 47.6 (6′), 20.0 (7′), 23.6 (8′), 24.8 (9′) 138.4 (1″), 129.2 (2″-6″), 128.5 (3″-5″), 133.6 (4″). **20a–c** HREIMS *m/z* calcd for $C_{19}H_{26}O_4S$ M^+ 350.1551, found 350.1543.

4-(2′,5′-Epoxy-2′,6′,6′-trimethyl) cyclohexyl-2-butanol (21). To a cold (0°C) solution of epoxysulphone **20** (2.4 g, 7 mmol)) in THF (42 ml) lithium aluminium hydride (2.68 g, 6 mmol) was added under argon atmosphere. The reaction mixture was stirred for 72 h at room temperature and further 12 h under reflux. This mixture was diluted with ether (100 ml), and poured into water-ice. The mixture was filtered, and the ether layer separated and successively washed with sat. NaCl and dried. Concentration and chromatography (hexane–ether, 6:4) gave 1.47 g of **21a–b** (98%) (colourless oil). IR (film): 3406, 2871, 1071, 938 cm^{-1}. MS *m/z* (rel. int.): 212 [M^+] (4), 197 [M^+-Me](19), 123 [$M^+-C_5H_{11}O$](18), 43 [$M^+-C_2H_3O^+$] (100). ^{1}H NMR ($CDCl_3$, 300 MHz): 1.70–1.15 (18H, m). Signals assignable to **21a**: 3.75 (1H, m, H-2), 3.69 (1H, d, *J*=5.3 Hz, H-5′), 1.31 (3H, s, Me-9′), 1.19 (3H, d, *J*=4.1 Hz, Me-1), 1.04 (3H, s, Me-8′), 0.99 (3H, s, Me-7′).^{13}C NMR ($CDCl_3$, 75 MHz): 19.9 (1), 68.4 (2), 39.6 (3), 23.5 (4), 56.1(1′), 86.8 (2′), 39.1 (3′), 25.6 (4′), 86.1 (5′), 39.7 (6′), 18.9 (7′), 23.3 (8′), 26.1 (9′). Signals assignable to **21b**: 3.75 (1H, m, H-2), 3.69 (1H, d, *J*=5.3 Hz, H-5′), 1.31 (3H, s, Me-9′), 1.20 (3H, d, *J*=4.1 Hz, Me-1), 1.04 (3H, s, Me-8′), 0.99 (3H, s, Me-7′).^{13}C NMR ($CDCl_3$, 75 MHz): 19.9 (1), 68.3 (2), 39.4 (3), 23.6 (4), 55.9(1′), 86.7 (2′), 39.0 (3′), 25.6 (4′), 86.1 (5′), 39.7 (6′), 18.9 (7′), 23.4 (8′), 26.1 (9′). HREIMS *m/z* calcd for $C_{13}H_{24}O_2$ M^+ 212.1776, found 212.1785.

4-(2′,5′-Epoxy-2′,6′,6′-trimethyl) cyclohexyl-2-butanone (22). A 3 M solution of Jones reagent (0.1 ml) was added dropwise to a stirred solution of **21** (0.35 g, 2 mmol) in acetone (15 ml) at 0°C, and the mixture stirred at room temperature for 30 min. It was diluted with water (10 ml) and extracted with ether (3×20 ml). The combined layers were washed with sat. NaCl (5×20 ml) and dried. Concentration gave 0.31 g of **22** (89%) (colourless oil). IR (film): 2960, 2850, 1715, 1083 cm^{-1}. MS *m/z* (rel. int.): 210 [M^+] (1), 195 [M^+-Me](6), 152 [$M^+-C_3H_6O^+$](14), 43 [$M^+-C_2H_3O^+$] (100). ^{1}H NMR ($CDCl_3$, 300 MHz):3.76 (1H, d, *J*=5.4 Hz, H-5′), 2.45 (2H, m, H-3), 2.17 (3H, s, Me–COO), 1.93 (1H, ddd, *J*=12.5, 6.8, 4.5 Hz, H-3′), 1.80–1.40 (6H, m), 1.37 (3H, s, Me-9′), 1.08 (3H, s, Me-8′), 1.04 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): 30.2 (1), 208.7 (2), 43.9 (3), 21.7 (4), 55.5(1′), 86.7 (2′), 39.0 (3′), 25.9 (4′), 86.2 (5′), 45.3 (6′), 19.0 (7′), 23.6 (8′), 26.3 (9′). HREIMS *m/z* calcd for $C_{13}H_{22}O_2$ M^+ 210.1619, found 210.1627.

5-(2′,5′-Epoxy-2′,6′,6′-trimethyl) cyclohexyl-3-methyl-1-penten-3-ol (5). A 1 M solution of vinylmagnesium bromide in THF (0.95 ml) was added to a stirred solution of **22** (0.15 g, 0.63 mmol) in THF (4 ml) at 0°C, and the whole was stirred at 10°C for 20 min, and then quenched with sat. NH_4Cl. The mixture was extracted with ether (3×15 ml) and the combined extracts were washed with sat. NaCl and dried. Concentration and column chromatography (hexane–ether, 7:3) gave 0.14 g of **5** (85%) (colourless oil). IR (film): 3440, 3085, 1708, 1637, 1071, 918 cm^{-1}. MS *m/z* (rel. int.): 238 [M^+] (1), 195 [M^+-Me] (9), 220 [M^+-H_2O] (1), 205 [M^+-H_2O-Me] (9), 43 [$M^+-C_2H_3O^+$] (100). ^{1}H NMR ($CDCl_3$, 300 MHz): 5.90 (1H, dd, *J*=17.4, 10.8 Hz, H-2), 5.20 (1H, d, *J*=17.4 Hz, H-1), 5.05 (1H, d, *J*=10.8 Hz, H-1), 3.70 (1H, d, *J*=5.4 Hz, H-5′), 1.90 (1H, m), 1.68 (1H, m), 1.60–1.20 (6H, m), 1.28 (3H, s, Me-3), 1.31 (3H, s, Me-9′), 1.15 (1H, m), 1.03 (3H, s, Me-8′), 0.99 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): 111.9 (1), 145.1 (2), 73.6 (3), 42.5 (4), 21.9 (5), 56.2(1′), 86.8 (2′), 39.0 (3′), 25.8 (4′), 86.1 (5′), 45.4 (6′), 19.0 (7′), 23.4 (8′), 26.2 (9′). HREIMS *m/z* calcd for $C_{15}H_{26}O_2$ M^+ 238.1933, found 238.1920.

3-Acetyloxymethyl-2,2-dimethyl-4-methylenecyclohexanol (24) and 3-acetyloxymethyl-2,2,4-trimethylcyclohex-4-enol (25). To a stirred solution of **23** (1.27 g, 0.69 mmol) in dry CH_2Cl_2 (100 ml) a solution of freshly distilled BBr_3 (1.62 g, 6.46 mmol) in dry CH_2Cl_2 (25 ml) was added dropwise. After stirring at room temperature under nitrogen for 10 min, the mixture was added to a 1 M solution of distilled collidine in CH_2Cl_2 (25 ml). The mixture was washed with 1 M HCl (3×50 ml) and saturated $NaHCO_3$ (3×50 ml). Organic layers were dried over anh. Na_2SO_4 and evaporated affording a crude (1.10 g), which after column chromatography (H–E 1:1) yielded 0.91 g (72%) of a mixture of regioisomers **24**and **25** (ratio 2:1). Compounds **24** and **25** were further separated by $AgNO_3–SiO_2$ 1:5 column chromatography. **24** (colourless oil) IR (film): 3462, 1646, 1736, 1236 cm^{-1}. MS: *m/z* (%)=153 (2), 137 (7), 123 (10), 119 (31), 107 (18), 93 (23), 57(6), 43(100). ^{1}H NMR (300 MHz): 4.86 (1H, bs, H-9), 4.60 (1H, bs, H-9), 4.36 (1H, dd, *J*=11.3, 9.1 Hz, H-1′), 4.30 (1H, dd, *J*=11.3, 4.3 Hz, H-1), 2.38 (1H, ddd, *J*=11.5, 5.6, 4.9 Hz, H-1), 2.20–2.02 (2H, m), 1.99 (3H, s, MeCOO), 1.85 (1H, m), 1.70 (1H, s, OH), 1.55 (1H, m), 1.04 (3H, s, Me-7), 0.82 (3H, s, Me-8). ^{13}C NMR (75 MHz): 76.6 (1), 39.3 (2), 50.7 (3), 145.6 (4), 31.1 (5), 31.4 (6), 17.4 (7), 20.1 (8), 109.9 (9), 62.2 (1′), 171.3 (Me*C*OO), 21.1 (*Me*COO). HREIMS *m/z* calcd for $C_{12}H_{20}O_3$ M^+ 212.1412, found 212.1421. **25** (colourless oil) IR (film): 3474, 1670, 1738, 1240 cm^{-1}. MS: *m/z* (rel. int.): 153 (6), 137 (26), 119(34), 107(51), 81 (50), 57(16), 43(100). ^{1}H NMR (300 MHz): 5.38 (1H, bs, H-5), 4.44 (1H, dd, *J*=11.8, 4.2 Hz, H-′1), 4.14 (1H, dd, *J*=11.8, 4.2 Hz, H-1′), 3.43 (1H, t, *J*=5.4 Hz, H-1), 2.28 (1H, m, H-1), 2.10–1.90 (2H, m, H-4), 2.04 (3H, s, MeCOO), 1.70 (3H, bs, Me-9), 1.00 (3H, s, Me-8), 0.95 (3H, s, Me-7). ^{13}C NMR (75 MHz): 73.5 (1), 37.2 (2), 48.4 (3), 136.6 (4), 120.7 (5), 29.7 (6), 22.4 (7), 26.8 (8), 19.4 (9), 62.6 (1′), 170.7 (Me*C*OO), 21.2 (*Me*COO). HREIMS *m/z* calcd for $C_{12}H_{20}O_3$ M^+ 212.1412, found 212.1408.

(2′,2′-Dimethyl-3′-tetrahydropyranyloxy-6′-methylene)-cyclohexylmethyl acetate (26). To a solution of **25** (0.38 g, 1.77 mmol) in dry CH_2Cl_2 (10 ml) was added a solution of freshly prepared pyridinium *p*-toluenesulphonate (PPTS) (45 mg, 0.177 mmol) in dry CH_2Cl_2 (7 ml) and then dihydropyran (DHP) (0.22 g, 2.65 mmol) and the mixture was stirred at room temperature for 5 h 30 min under argon. After evaporating the solvent the residue was diluted with Et_2O (60 ml) and the organic phase was washed with brine (3×25 ml), dried over anh. Na_2SO_4 and evaporated to yield a crude (0.54 g), which after column chromatography (H–E

9:1) afforded **26** (0.44 g, 85%) as a colourless oil. IR (film): 3005, 2942, 1738, 1675, 1230, 1201, 1154, 1117, 1078 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 4.80 (1H, bs, H-9′), 4.71 (1H, t, *J*=3.0 Hz, H-2″), 4.60 (1H, bs, H-9′), 4.58 (1H, m, H-2″), 4.44 (1H, dd, *J*=11.7, 4.5 Hz, H-1), 4.40 (1H, dd, *J*=11.7, 4.5 Hz), 3.90 (2H, m, H-6″), 3.50 (1H, dd, *J*=4.0, 4.5 Hz, H-3′), 3.45 (2H, m, H-6″), 3.26 (1H, dd, *J*=3.0, 4.5 Hz, H-3′), 1. 98 (3H, s, MeCO), 1.01 (3H, s, Me–$C_{2'}$), 1.00 (3H, s, Me–$C_{2'}$), 0.95 (3H, s, Me–$C_{2'}$), 0.89 (3H, s, Me–$C_{2'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 63.1, 62.5 (1), 52.2, 51.9 (1′), 39.2, 38.5 (2′), 84.4, 77.3 (3′), 29.7 (4′), 31.2 (5′), 146.2, 146.1 (6′), 27.5, 26.6 (7′), 21.5, 21.1 (8′), 110.6, 110.3 (9′), 101.6, 94.5 (2″), 30.7 (3″), 29.7 (4″), 25.5, 25.3 (5″), 63.3, 62.2 (6″), 171.0 (CO), 21.0, 20.5 (MeCO). HREIMS *m/z* calcd for $C_{17}H_{28}O_4$ M^+ 296.1987, found 296.1976.

(2′,2′-Dimethyl-3′-tetrahydropyranyloxy-6′-methylene)-cyclohexylmethanol (27). 3N KOH in MeOH (8 ml) was added to a solution of **26** (0.36 g, 1.21 mmol) in MeOH (15 ml) and the mixture was refluxed for 2 h. After evaporation of the solvent the crude was dissolved in Et_2O (60 ml) and the organic phase was washed with H_2O (4×30 ml), dried over anh. Na_2SO_4 and evaporated to yield a crude (0.3 g), which was chromatographed on silica gel (H–E 6:4) to give **27** (0.27 g, 91%) as a colourless oil. IR (film): 3449, 1645, 117, 814 cm^{-1}. EIMS *m/z* (rel. int.): 254 [M^+] (1), 169 [M^+−THP] (1), 153 [M^+−THPO] (4), 85 [THP] (100). ^1H NMR ($CDCl_3$, 300 MHz): 4.87 (1H, bs, H-9′), 4.69 (1H, m, H-2″), 4.68 (1H, bs, H-9′), 4.57 (1H, t, *J*=3.6 Hz, H-2″), 3.86 (1H, m, H-1), 3.80 (2H, m, H-6″), 3.58 (1H, ddd, *J*=14.8, 7.4, 3.8 Hz, H-1), 3.46 (1H, t, *J*=4.3 Hz, H-3′), 3.43 (2H, m, H-6″), 3.25 (1H, t, *J*=3.8 Hz, H-3′), 1.07 (3H, s, Me–$C_{2'}$), 0.98 (3H, s, Me–$C_{2'}$), 0.94 (3H, s, Me–$C_{2'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 62.4, 62.2 (1), 55.9, 55.8 (1′), 38.6, 37.9 (2′), 83.6, 76.7 (3′), 30.5, 30.4 (4′), 30.8, 30.7 (5′), 147.2, 147.1 (6′), 101.2, 93.8 (2″), 29.1 (3″), 195., 191. (4″), 25.3, 24.7 (5″), 61.3, 61.0 (6″). HREIMS *m/z* calcd for $C_{15}H_{26}O_3$ M^+ 254.1882, found 254.1895.

(2′,2′-Dimethyl-3′-tetrahydropyranyloxy-6′-methylene)-cyclohexylcarboxaldehyde (28). Pyridinium dichromate (PDC) (0.55 g, 1.47 mmol) was added to a solution of **27** in dry CH_2Cl_2 (5 ml) and the mixture was stirred at room temperature under argon for 24 h. Then it was diluted with Et_2O (50 ml), filtered and evaporated to yield a crude (0.25 g) which by column chromatography (H–E 95:5) gave **28** (0.22 g, 90%) (colourless oil). IR (film): 2740, 1714, 1645, 1118, 815 cm^{-1}. EIMS *m/z* (rel. int.): 252 [M^+] (1), 234 [M^+−H_2O] (1), 151 [M^+−THPO] (2). ^1H NMR ($CDCl_3$, 300 MHz): 9.86 (1H, d, *J*=3.5 Hz, H-1), 9.85 (1H, d, *J*=3.5 Hz, H-1), 4.99 (1H, bs, H-9′), 4.81 (1H, t, *J*=3.3 Hz, H-2″), 4.74 (2H, bs, H-9′), 4.67 (1H, t, *J*=3.3 Hz, H-2″), 3.85 (2H, m, H-6″), 3.58 (1H, t, *J*=2.5 Hz, H-6″), 3.52 (2H, m, H-6″), 3.40 (1H, t, *J*=3.4 Hz, H-3′), 2.56 (1H, dd, *J*=8.7, 3.0 Hz, H-1′), 1.26 (3H, s, Me–$C_{2'}$), 1.11 (3H, s, Me–$C_{2'}$), 1.00 (3H, s, Me–$C_{2'}$), 0.96 (3H, s, Me–$C_{2'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 202.3, 202.1 (1), 66.3 (1′), 40.6, 29.9 (2′), 82.7, 81.0 (3′), 28.4, 28.2 (4′), 30.9, 30.7 (5′), 142.9, 142.8 (6′), 24.0, 23.8 (7′), 26.8 26.3 (8′), 113.6, 113.5 (9′), 101.7, 101.3 (2″), 30.4, 29.0 (3″), 19.7, 19.5 (4″), 25.9, 25.5 (5″), 62.6, 62.5 (6″). HREIMS *m/z* calcd for $C_{15}H_{24}O_3$ M^+ 252.1725, found 252.1713.

Treatment of 28 with 2-oxopropylidenetriphenylphosphorane

A mixture of **28** (0.4 g, 1.6 mmol) and the phosphorane (0.57 g, 1.8 mmol) was refluxed in toluene (15 ml) overnight. After cooling the mixture was passed through a silica-gel column, and the eluate was evaporated affording compound **26** unaltered.

Treatment of 17 with BBr_3

Synthesis of 2,2-dimethyl-4-methylene-3-phenylsulphonylmethylcyclohexanol (29) and 2,2,4-trimethyl-3-phenylsulphonylmethylcyclohex-4-enol (31). To a stirred solution of **17** (0.5 g, 1.7 mmol) in dry CH_2Cl_2 a solution of BBr_3 (0.52 g, 2.4 mmol) in CH_2Cl_2 (4 ml) was added dropwise. After stirring at room temperature under argon for 15 min, the mixture was added to a 1 M solution of collidine in CH_2Cl_2 (5 ml), diluted with $CHCl_3$ (75 ml) and successively washed with 5% $NaHSO_4$ (4×25 ml), 5% $NaHCO_3$ (3×25 ml) and brine (4×25 ml). The organic phase was dried over anh. Na_2SO_4 and the solvent evaporated to afford a crude that by column chromatography (MeOH–E 1:9) gave **29** (0.20 g) and **31** 0.21 g) (82%). **29** (colourless oil) IR (film): 3530, 2935, 2856, 1651, 1495, 1469, 1446, 1145, 1024, 895 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): 7.88 (2H, d, *J*=7.1 Hz, H-3″, H-5″), 7.66–7.50 (3H, m, H-2″, H-4″, H-6″), 4.78 (1H, s, H-9), 4.62 (1H, s, H-9), 3.59 (1H, dd, *J*=15.1, 9.6 Hz, CH–SO_2Ph), 3.45 (1H, dd, *J*=7.1, 3.6 Hz, H-1), 3.37 (1H, dd, *J*=15.1, 2.1 Hz, CH–SO_2Ph), 2.45 (1H, d, *J*=9.6, 2.1 Hz, H-3), 2.27 (1H, ddd, *J*=13.2, 8.4, 4.9 Hz, H-5), 1.92 (1H, ddd, *J*=13.2, 7.7, 4.9 Hz, H-5), 1.76 (1H, m), 1.50 (1H, m), 0.92 (3H, s, Me–C_2), 0.79 (3H, s, Me–C_2). ^{13}C NMR ($CDCl_3$, 75 MHz): 75.6 (1), 39.9 (2), 46.3 (3), 144.5 (4), 31.3 (5), 29.2 (6), 26.0 (7), 19.1 (8), 111.5 (9), 57.0 (1′), 144.5 (1″), 129.1 (2″, 6″), 128.2 (3″, 5″), 133.3 (4″). HRFABMS *m/z* calcd for $C_{16}H_{22}O_3S$ $(M+Na)^+$ 317.1187, found 317.1196. **31** (colourless oil) IR (film): 3445, 3065, 2960, 1585, 1500, 1471, 1446, 1145, 1085, 1001, 916, 893, 880, 835 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 7.92 (2H, d, *J*=7.1, H-2″, H-6″), 7.65–7.50 (3H, m, H-3″, H-4″, H-5″), 5.26 (1H,bs, H-5), 3.81 (1H, dd, *J*=15.6, 3.6 Hz, CH–SO_2Ph), 3.50 (1H, t, *J*=4.4 Hz, H-1), 3.21 (1H, bs, OH), 3.00 (1H, dd, *J*=15.6, 4.5 Hz, CH–SO_2Ph), 2.32 (1H, d, *J*=18.4 Hz, H-6), 1.98 (1H, d, *J*=18.4 Hz, H-6), 1.71 (3H, bs, Me–C_4), 0.96 (3H, s, Me–C_2), 0.88 (3H, s, Me–C_2). ^{13}C NMR ($CDCl_3$, 75 MHz): 73.0 (1), 36.6 (2), 41.6 (3), 134.1 (4), 118.7 (5), 23.2 (6), 21.2 (7), 25.6 (8), 25.6 (9), 55.1 (1′), 140.0 (1″), 129.1 (2″, 6″), 127.9 (3″, 5″), 133.4 (4″). HRFABMS *m/z* calcd for $C_{16}H_{22}O_3S$ $(M+Na)^+$ 317.1187, found 317.1196.

(3′-*tert*-Butyldimethylsilyloxy-2′,2′-dimethyl-6′-methylene)cyclohexylmethyl phenyl sulphone (30). *tert*-Butyldimethylsilyl chloride (1.08 g, 7.2 mmol) and imidazole (0.5 g, 7.3 mmol) were added to a solution of **29** (1.32 g, 4.5 mmol) in DMF (15 ml) and the mixture was stirred for 10 h at room temperature. Then it was fractionated in ether (100 ml)–brine (100 ml), and the organic phase was washed with 1N HCl (3×25 ml), 5% $NaHCO_3$ (3×25 ml) and brine

(4×25 ml). The ethereal solution was dried over anh. Na_2SO_4 and evaporated to give a crude mixture, that after column chromatography (H–E 7:3) afforded **30** (1.55 g, 87%) as a colourless oil. IR (film): 2957, 2924, 2856, 1668, 1490, 1450, 1080, 1026, 885 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 7.87 (2H, d, J=8.3 Hz, H-2″, H-6″), 7.57 (1H, t, J=6.9 Hz, H-4″), 7.48 (2H, t, J=7.2 Hz, H-3″, H-5″), 4.71 (1H, s, H-9), 4.65 (1H, s, H-9), 3.66 (1H, dd, J=7.5, 6.0 Hz, CH-SO_2Ph), 3.48 (1H, dd, J=7.0, 2.5 Hz, H-1), 3.40 (1H, dd, J=7.5, 2.0 Hz, CH–SO_2Ph), 0.84 (6H, s, Me–C_2), 0.80 (9H, s, Me–C–Si), −0.02 (6H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 56.1 (1), 46.7 (1′), 145.1 (6′), 30.9 (5′), 30.9 (4′), 75.9 (3′), 39.8 (2′), 25.8 (7′), 25.9 (8′), 112.3 (9′), 140.5 (1″), 128.9 (2″, 6″), 128.1 (3″, 5″), 133.3 (4″), −4.8 (*Me*–Si), −4.5 (*Me*–Si), 18.1 (Me–*C*–Si), 25.7 (*Me*–C–Si). HRFABMS *m/z* calcd for $C_{22}H_{36}O_3SSi$ $(M+Na)^+$ 431.2052, found 431.2043.

Treatment of anion derived from 30 with 4-bromo-3-methyl-2(*E*)-butenol

A 2.3 M solution of *n*-BuLi in hexane (0.3 ml) was added under argon to a stirred solution of **30** (0.25 g, 0.61 mmol) and HMPA (1.3 ml) in dry THF at −78°C and the mixture was allowed to warm to 0°C and further stirred for 1 h. Then a solution of the allylic bromide (0.80 g, 3.23 mmol) in dry THF (5 ml) was added and the mixture was stirred at room temperature for 12 h. It was diluted with ether (100 ml) and the organic phase was washed with 1 M HCl (3×25 ml), 5% $NaHCO_3$ (3×25 ml) and brine (3×50 ml), and dried over anh. Na_2SO_4 and evaporated, affording a residue which consists of unaltered starting materials.

Synthesis of 4-(3′-*tert*-butyldimethylsilyloxy-2,2′-dimethyl-6′-methylene)cyclohexyl-2-butanone (34) from 30. *Method A:* To a solution of *n*-butyllithium (1.8 M in hexane, 1.5 ml, 2.8 mmol) in THF (10 ml) cooled at 0° was added HMPA (3 ml) and then a solution of sulphone **30** (0.99 g, 2.42 mmol) in THF (20 ml) under argon atmosphere. The mixture was stirred for 30 min at 0°C and it was allowed to warm to room temperature and stirred for 45 min. Then 0.5 ml (7.26 mmol) of propylene oxide was added, the mixture stirred at the same temperature for 1 h and further heated at 65° for an additional 45 min. Then sat. aqueous NH_4Cl (3 ml) and ether (100 ml) was added and the organic solution was successively washed with 2N HCl (3×30 ml) and brine (3×50 ml), dried over anh. Na_2SO_4 and the solvent evaporated to afford 0.85 g of crude.

6% Na–Hg (0.79 g, 2.1 mmol) was added under argon to a solution of the above crude (0.25 g) and disodium hydrogen phosphate (0.29 g, 2.1 mmol) in EtOH cooled at −10°. The mixture was stirred under reflux for 4 h, and then sat. aqueous NH_4Cl (20 ml) was added and the mixture extracted with OEt_2 (3×30 ml). The organic phase was washed with sat. aqueous $NaHCO_3$ (3×30 ml) and H_2O (3×40 ml), dried over anh. Na_2SO_4 and evaporated to give 150 mg of crude.

Jones reagent (0.03 ml) was added to a solution of the crude (0.15 g, 0.46 mmol) in acetone (7 ml) cooled at 0°C and the mixture was stirred at this temperature for 30 min. H_2O (5 ml) was added and the mixture was extracted with OEt_2 (3×30 ml). The organic phase was washed with brine (3×30 ml), dried over anh. Na_2SO_4 and the solvent evaporated to give 140 mg of methylketone **34** (95%).

Method B: **4-(3′-*tert*-Butyldimethylsilyloxy-2,2′-dimethyl-6′-methylene)cyclohexyl-4-phenylsulphonyl-2-butanone (32).** Jones reagent (0.02 ml) was added to a solution of the crude (0.1 g, 0.21 mmol), resulting of the reaction of anion derived from **30** with propylene oxide, in acetone (5 ml) cooled at 0°, and the mixture was stirred at this temperature for 20 min. Following the same procedure described for the synthesis of **34**, 95 mg of sulphonylketone **32** (95%) was obtained as a colourless oil. IR (film): 3020, 2950, 2920, 2854, 1720, 1490, 1450, 1300, 1145, 1080, 950, 830 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): Signals corresponding to the major diastereoisomer: 7.87 (2H, d, J=8.6 Hz, $PhSO_2$), 7.63–7.45 (3H, m, $PhSO_2$), 5.07 (1H, s, H-9′), 5.03 (1H, s, H-9′), 4.45 (1H, dt, J=8.0, 2.1 Hz, H-4), 3.32 (1H, dd, J=7.2, 3.2 Hz, H-3′), 3.22 (2H, m, H-3), 2.83 (1H, bs, H-1′), 2.28 (1H, m, H-5′α), 2.11 (1H, m, H-5′β), 2.08 (3H, s, H-1), 1.69 (1H, m, H-4′β), 1.50 (1H, m, H-4′α), 0.87 (3H, s, Me–$C_{2'}$), 0.81 (9H, s, Me_3C–Si), 0.67 (3H, s, Me–$C_{2'}$), 0.00 (6H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 29.5 (1), 203.5 (2), 39.9 (3), 59.5 (4), 47.3 (1′), 40.3 (2′), 76.2 (3′), 31.1 (4′), 30.2 (5′), 142.4 (6′), 19.8 (7′), 26.9 (8′), 115.1 (9′), 128.5 (3″, 5″), 128.7 (2″, 6″), 133.2 (4″), 139.3 (1″), 25.6 (*Me*–C–Si), −5.0 (*Me*–Si), −4.9 (*Me*–Si), 17.8 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{25}H_{40}O_4SSi$ $(M+Na)^+$ 487.2314, found 487.2325.

4-(3′-*tert*-Butyldimethylsilyloxy-2,2′-dimethyl-6′-methylene)cyclohexyl-3-buten-2-one (33). Aluminium oxide (10 g, 9.8 mmol) was added to a solution of **32** (0.15 g, 0.32 mmol) in THF (15 ml) and the mixture was stirred for 2 h. Then it was filtered and the solvent was evaporated, affording 0.095 g (95%) of **33** (colourless oil). IR (film): 2957, 2930, 2850, 1697, 1670, 1610, 1468, 1080, 1000, 875 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 7.08 (1H, dd, J=15.9, 9.7 Hz, H-4), 5.99 (1H, d, J=15.9 Hz, H-3), 4.80 (1H, s, H-9′), 4.56 (1H, s, H-9′), 3.44 (1H, dd, J=7.6, 3.6 Hz, H-3′), 2.57 (1H, bd, J=9.7 Hz, H-1′), 2.23 (3H, s, H-1), 1.80–1.50 (4H, m, H-4′, H-5′), 0.89 (9H, s, Me_3C–Si), 0.86 (Me–$C_{2'}$), 0.85 (3H, s, Me–$C_{2'}$), 0.05 (6H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 27.7 (1), 197.5 (2), 133.4 (3), 147.6 (4), 56.9 (1′), 40.3 (2′), 76.6 (3′), 31.3 (4′), 30.2 (5′), 148.2 (6′), 26.9 (7′), 27.1 (8′), 110.4 (9′), 26.0 (*Me*–C–Si), −4.8 (*Me*–Si), −4.2 (*Me*–Si), 18.1 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{19}H_{34}O_2Si$ $(M+Na)^+$ 345.2226, found 345.2218.

4-(3′-*tert*-Butyldimethylsilyloxy-2,2′-dimethyl-6′-methylene)cyclohexyl-2-butanone (34). 1.4 g of an aqueous suspension of Raney Nickel was added to a stirred solution of **33** (0.15 g, 0.465 mmol) in THF (6 ml) and the mixture was further stirred at room temperature for 30 min. Then it was diluted with OEt_2 and filtered through silicagel and the solvent was evaporated to yield 0.138 g of **34** (92%) as a colourless oil. IR (film): 2960, 2930, 2856, 1718, 1473, 1251, 109, 1006, 835 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 4.80 (1H, bs, H-9′), 4.48 (1H, bs, H-9′), 3.38 (1H, dd, J=7.1, 3.6 Hz, H-5′), 2.44 (1H, ddd, J=17.1, 7.4, 7.1 Hz, H-3), 2.30 (1H, m, H-5′α), 2.21 (1H, ddd, J=17.1, 8.1, 4.6 Hz, H-3), 2.08 (3H, s, H-1), 1.96 (1H, m, H-5′β), 1.84

(1H, m, H-4′α), 1.65 (1H, m, H-4), 1.60 (1H, m, H-1′), 1.51 (2H, m, H-4, H-4′β), 0.91 (3H, s, Me–$C_{2'}$), 0.88 (9H, s, Me_3C–Si), 0.81 (3H, s, Me–$C_{2'}$), 0.02 (6H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 27.0 (1), 209.7 (2), 43.2 (3), 20.9 (4), 52.3 (1′), 40.4 (2′), 76.8 (3′), 20.7 (4′), 32.0 (5′), 148.1 (6′), 21.9 (7′), 25.9 (8′), 109.1 (9′), 26.0 (*Me*–C–Si), −4.9 (*Me*–Si), −4.1 (Me–Si), 17.8 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{19}H_{34}O_2Si$ $(M+Na)^+$ 345.2226, found 345.2232.

4-(3′-*tert*-Butyldimethylsilyloxy-2,2′-dimethyl-6′-methylene)cyclohexyl-3-methyl-1-penten-3-ol (35). 1 M vinylmagnesium bromide in THF (1 ml) was added to a solution of **34** (0.3 g, 0.926 mmol) in THF (20 ml) at 0°C and the mixture was stirred at this temperature for 30 min; then sat. NH_4Cl solution (1 ml) was added and the mixture was diluted with OEt_2 (50 ml). The organic phase was washed with H_2O (3×30 ml), brine (3×30 ml), dried over anh. Na_2SO_4 and the solvent evaporated to give a residue, which was chromatographed on silicagel (H–E 8:2) affording 0.31 g (95%) of **35** (colourless oil). IR (film): 2955, 2925, 1653, 1558, 1541, 1508, 885, 833 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): 5.90 (1H, dd, *J*=17.3, 10.7 Hz, H-2), 5.18 (1H, dd, *J*=173, 1.5 Hz, H-1), 5.02 (1H, dd, *J*=10.7, 1.5 Hz, H-1), 4.79 (1H, d, *J*=2.1 Hz, H-9′), 4.55 (1H, d, *J*=2.1 Hz, H-9′), 3.38 (1H, dd, *J*=6.7, 3.5 Hz, H-3′), 2.33 (1H, m, H-5′), 1.91 (1H, ddd, *J*=12.2, 7.6, 4.7 Hz, H-5′), 1.73 (1H, ddd, *J*=13.1, 8.4, 4.5 Hz, H-4), 1.70–1.50 (6H, m), 1.21 (3H, s, Me–C_3), 0.89 (9H, s, Me_3C–Si), 0.82 (3H, s, Me–$C_{2'}$), 0.81 (Me–$C_{2'}$), 0.05 (3H, s, Me–Si), 0.04 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 111.6 (1), 145.4 (2), 73.6 (3), 41.9 (4), 21.0 (5), 28.1 (Me–C_3), 53.1 (1′), 40.5 (2′), 76.9 (3′), 32.1 (4′), 29.7 (5′), 148.4 (6′), 25.9 (7′), 27.4 (8′), 118.9 (9′), 26.0 (*Me*–C–Si), −4.8 (*Me*–Si), −4.1 (*Me*–Si), 18.1 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{21}H_{40}O_2Si$ $(M+Na)^+$ 375.2695, found 375.2703.

Acetylation of 35

Synthesis of 4-(3′-*tert*-butyldimethylsilyloxy-2′,2′-dimethyl-6′-methylene)cyclohexyl-3-methyl-1-penten-3-yl acetate (36). Acetic anhydride (1 ml), triethylamine (2 ml) and dimethylaminopyridine (50 mg) was added to a solution of **35** (0.25 g, 0.71 mmol) in THF (20 ml) and the mixture was stirred under reflux for 26 h. It was diluted with Et_2O (80 ml) and washed with 2N HCl (3×30 ml), sat. $NaHCO_3$ (3×30 ml) and brine (3×30 ml). After drying the organic phase over anh. Na_2SO_4, the solvent was evaporated to give, after chromatography on silicagel (H–E 9:1), 0.25 g (90%) of **36** as a colourless oil. IR (film): 2960, 2856, 1741, 1508, 1473, 1259, 1095, 1022, 835 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 5.96 (1H, dd, *J*=17.6, 10.9 Hz, H-2), 5.10 (1H, dd, *J*=17.6, 1.3 Hz, H-1), 5.09 (1H, dd, *J*=10.9, 1.3 Hz, H-1), 4.78 (1H, s, H-9′), 4.53 (1H, s, H-9′), 3.37 (1H, dd, *J*=6.4, 3.5 Hz, H-3′), 2.33 (2H, m, H-5′), 1.92 (3H, s, AcO), 1.85–1.50 (8H, m), 1.50 (3H, s, Me–C_3), 0.88 (9H, s, Me_3C–Si), 0.86 (3H, s, Me–$C_{2'}$), 0.81 (Me–$C_{2'}$), 0.03 (3H, s, Me–Si), 0.02 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 113.1 (1), 142.1 (2), 83.4 (3), 39.7 (4), 20.8 (5), 23.6 (Me–C_3), 53.1 (1′), 40.4 (2′), 76.8 (3′), 32.0 (4′), 29.6 (5′), 148.4 (6′), 25.9 (7′), 27.3 (8′), 109.1 (9′), 26.0 (*Me*–C–Si), −4.9 (*Me*–Si), −4.1 (*Me*–Si), 18.1 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{23}H_{42}O_3Si$ $(M+Na)^+$ 417.2801, found 417.2814.

4-(3′-*tert*-Butyldimethylsilyloxy-2,2′-dimethyl-6′-methylene)cyclohexyl-3-methyl-2-penten-1-yl acetate (37). Palladium (II) chloride bis acetonitrile complex (20 mg, 0.77 mmol) was added under argon atmosphere to a solution of **36** (0.25 g, 0.634 mmol) in THF (10 ml) and the mixture was stirred at room temperature for 45 min. The crude obtained after evaporating the solvent was filtered through silicagel to give 0.237 g (95%) of **37** (colourless oil). IR (film): 2955, 2932, 1739, 1640, 1095, 1020, 835 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 5.31 (1H, t, *J*=7.1 Hz, H-2), 4.57 (2H, d, *J*=7.1 Hz, H-1), 4.78 (1H, bs, H-9′), 4.54 (1H, bs, H-9′), 3.37 (1H, dd, *J*=7.1, 3.6 Hz, H-3′), 2.32 (1H, m, H-5′), 2.04 (3H, s, AcO), 1.92 (1H, ddd, *J*=12.4, 7.2, 4.3 Hz, H-4), 1.80–1.55 (7H, m), 1.67 (3H, s, Me–C_3), 0.90 (3H, s, Me–$C_{2'}$), 0.88 (9H, s, Me_3C–Si), 0.78 (Me–$C_{2'}$), 0.03 (3H, s, Me–Si), 0.02 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 61.6 (1), 117.8 (2), 142.2 (3), 38.8 (4), 24.7 (5), 16.6 (Me–C_3), 52.4 (1′), 40.4 (2′), 76.9 (3′), 32.1 (4′), 29.7 (5′), 148.3 (6′), 25.8 (7′), 27.1 (8′), 108.8 (9′), 26.0 (*Me*–C–Si), −4.7 (*Me*–Si), −4.1 (*Me*–Si), 18.1 (Me–*C*–Si), 171.0 (Me*C*OO), 22.0 (*Me*COO). HRFABMS *m/z* calcd for $C_{23}H_{42}O_3Si$ $(M+Na)^+$ 417.2801, found 417.2810.

4-(3′-*tert*-Butyldimethylsilyloxy-2′,2′-dimethyl-6′-methylene)cyclohexyl-3-methyl-2-pentenol (38). 2N KOH in methanol (2 ml) was added to a solution of **37** (0.2 g, 0.507 mmol) in methanol (6 ml) and the mixture was stirred for 45 min. After evaporating the solvent, the crude was fractionated in Et_2O (50 ml)–H_2O (10 ml), and the organic phase was washed with brine (3×30 ml), dried over anh. Na_2SO_4 and the solvent concentrated to afford 0.17 g (94%) of **38** as a colourless oil. IR (film): 3560, 2960, 2925, 2856, 1645, 1097, 1022, 804 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 5.38 (1H, t, *J*=6.9 Hz, H-2), 4.80 (1H, s, H-9′), 4.54 (1H, s, H-9′), 4.12 (2H, d, *J*=6.9 Hz, H-1), 3.37 (1H, dd, *J*=7.2, 3.6 Hz, H-5′), 2.34 (1H, ddd, *J*=12.3, 7.5, 4.7 Hz, H-5′), 1.90 (1H, ddd, *J*=12.9, 8.3, 4.3 Hz, H-4), 1.80–1.45 (7H, m), 1.65 (3H, s, Me–C_3), 0.91 (3H, s, Me–$C_{2'}$), 0.87 (9H, s, Me_3C–Si), 0.78 (Me–$C_{2'}$), 0.03 (3H, s, Me–Si), 0.02 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 59.4 (1), 123.0 (2), 141.8 (3), 38.9 (4), 24.9 (5), 16.4 (Me–C_3), 52.4 (1′), 40.5 (2′), 77.1 (3′), 32.2 (4′), 29.5 (5′), 148.3 (6′), 25.9 (7′), 27.1 (8′), 108.7 (9′), 26.0 (*Me*–C–Si), −4.8 (*Me*–Si), −4.1 (*Me*–Si), 18.2 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{21}H_{40}O_2Si$ $(M+Na)^+$ 375.2695, found 375.2701.

Elegansidiol (*cis*-3-[(*E*)-5-hydroxy-3-methyl-3-pentenyl]-2,2-dimethyl-4-methylenecyclohexanol) (6). Tetrabutylammonium fluoride (0.1 g, 0.34 mmol) was added to a solution of **39** (0.1 g, 0.25 mmol) in THF (10 ml) and the mixture was stirred at room temperature for 6 h. After evaporating the solvent, the crude was chromatographed on silicagel (H–E 4:6) to yield 54 mg (89%) of **6** (colourless oil). IR (film): 3384, 2930, 2852, 1717, 1645, 1449, 1379, 1261, 1183, 1082, 1023, 890 cm^{-1}. EIMS *m/z* 238 [M^+], (1), 220 (8), 205 (35), 187 (27), 175 (24), 159 (18), 134 (27), 119 (45), 107 (62), 96 (100), 81 (64), 67 (44), 55 (54), 43 (85), 41 (83). ^{1}H NMR (300 MHz, $CDCl_3$): 5.40 (1H, tq, *J*=6.9, H-4′), 4.88 (1H, bs, 1H, H-9), 4.60 (1H, bs, H-9), 4.15 (2H, d, *J*=6.9 Hz, H-5′), 3.42 (1H, dd, *J*=9.6, 4.2 Hz, H-1), 2.32 (1H, dt, *J*=13.1, 4.4 Hz, H-5α), 2.10 (1H, m, H-2′), 2.00–1.85 (m, 2H, H-5β, H-6β), 1.75 (1H, m, H-2′),

1.68 (3H, s, Me–$C_{3'}$), 1.65 (2H, m, H-3, H-1′), 1.50 (2H, m, H-6α, H-1′), 1.03 (3H, s, Me-8), 0.73 (s, 3H, Me-7). ^{13}C NMR (75 MHz, $CDCl_3$): 77.2 (1), 40.4 (2), 51.2 (3), 147.1 (4), 32.7 (5), 32.0 (6), 26.0 (7), 16.2 (8), 108.3 (9), 23.8 (1′), 38.7 (2′), 140.1 (3′), 123.1 (4′), 59.3 (5′), 15.7 (Me–$C_{3'}$). HRFABMS *m/z* calcd for $C_{15}H_{27}O_2$ $(M+H^+)$ 239.201105, found 239.201432.

2,2,4-Trimethyl-3-phenylsulphonylmethylcyclohex-4-enol (31). To a stirred solution of **17** (0.42 g, 1.44 mmol) in dry CH_2Cl_2 a solution of BBr_3 (0.44 g, 2.04 mmol) in CH_2Cl_2 (4 ml) was added dropwise. After stirring at room temperature under argon for 15 min, the mixture was added to 5 ml of Et_3N, diluted with $CHCl_3$ (75 ml) and was successively washed with 5% $NaHSO_4$ (4×25 ml), 5% $NaHCO_3$ (3×25 ml) and brine (4×25 ml). The organic phase was dried over anh. Na_2SO_4 and the solvent evaporated to afford **31** (0.37 g, 82%).

Treatment of 31 with TBSCl

Synthesis of (5′-*tert*-butyldimethylsilyloxy-2′,2′,6′-trimethyl)cyclohex-2′-enylmethyl phenyl sulphone (39). *tert*-Butyldimethylsilyl chloride (0.75 g, 5.04 mmol) and imidazole (0.35 g, 5.11 mmol) was added to a solution of **31** (0.92 g, 3.15 mmol) in DMF (10 ml) and the mixture was stirred for 10 h at room temperature. Then it was fractionated in ether (70 ml)–brine (70 ml), and the organic phase was washed with 1N HCl (3×20 ml), 5% $NaHCO_3$ (3×20 ml) and brine (4×20 ml). The ethereal solution was dried over anh. Na_2SO_4 and evaporated to give a crude, that after column chromatography (H–E 7:3) afforded **39** (1.42 g, 80%) as a colourless oil. IR (film): 2950, 2920, 2860, 1620, 1500, 1440, 1095, 1015, 870 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.93 (2H, d, *J*=7.1 Hz, H-2″, H-6″), 7.67–7.53 (3H, m, H-3″, H-4″, H-5″), 5.24 (1H, bs, H-3′), 3.95 (1H, dd, *J*=15.6, 3.5 Hz, H-1), 3.46 (1H, t, *J*=4.1 Hz, H-5′), 2.93 (1H, dd, *J*=15.6, 4.5 Hz, H-1), 2.39 (1H, bs, H-1′), 2.23 (1H, bs, *J*=18.2 Hz, H-4′), 1.97 (1H, bd, *J*=18.2 Hz, H-4′), 1.73 (3H, s, Me–$C_{2'}$), 0.98 (3H, s, Me–$C_{6'}$), 0.89 (3H, s, Me–$C_{6'}$), 0.75 (9H, s, Me–C–Si), 0.05 (3H, s, Me–Si), −0.05 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 57.9 (1), 41.8 (1′), 134.5 (2′), 118.5 (3′), 32.3 (4′), 74.2 (5′), 37.1 (6′), 26.0 (7′), 25.7 (8′), 22.5 (9′), 140.6 (1″), 129.2 (2″, 6″), 128.0 (3″, 5″), 133.4 (4″), 25.7 (*Me*–C–Si), −5.0 (*Me*–Si), −4.4 (*Me*–Si), 17.8 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{22}H_{36}O_3SSi$ $(M+Na)^+$ 431.2052, found 431.2064.

4-(5′-*tert*-Butyldimethylsilyloxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-4-phenylsulphonyl-2-butanol (40). A solution of **39** (2.0 g, 4.9 mmol) and HMPA (5 ml) in THF (35 ml) was added under argon atmosphere to a solution of *n*-butyllithium (1.8 M in hexane, 2.8 ml, 5.2 mmol) in THF (20 ml) cooled at 0°C and the mixture was stirred at this temperature for 30 min and it was allowed to warm to room temperature and stirred for 45 min. Then propylene oxide (0.7 ml, 14.6 mmol) was added and the mixture was stirred at room temperature for 1 h and heated at 65°C for an additional 15 min. Following the same work-up used for **30**, 1.94 g (85%) of **40** was obtained as a mixture of diastereomers. Colourless oil. IR (film): 3570, 2958, 2931, 1630, 1471, 1253, 1083, 1008, 835 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.96 (2H, d, *J*=8.6 Hz, Ph), 7.68–7.54 (3H, m, Ph), 5.44 (1H, bs, H-3′), 3.88 (1H, m, H-2), 3.69 (1H, d, *J*=6.3 Hz, H-4), 3.29 (1H, dd, *J*=7.3, 5.8 Hz, H-5′), 2.47 (1H, bs, H-1′), 2.27 (1H, ddd, *J*=17.7, 9.2, 8.5 Hz, H-3), 2.05 (1H, m, H-4′), 1.97 (1H, m, H-4′), 1.87 (1H, bd, *J*=17.7 Hz, H-3), 1.66 (3H, s, Me–C_3), 1.18 (3H, d, *J*=5.9 Hz, H-1), 0.82 (9H, s, Me_3C–Si), 0.64 (3H, s, Me–$C_{2'}$), 0.38 (Me–$C_{2'}$), −0.03 (3H, s, Me–Si), −0.05 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 25.7 (1), 67.3 (2), 35.7 (3), 64.7 (4), 48.7 (1′), 139.7 (2′), 124.3 (3′), 32.2 (4′), 74.4 (5′), 39.3 (6′), 24.5 (7′), 24.7 (8′), 22.5 (9′), 138.5 (1″), 129.6 (2″), 129.3 (3″), 132.4 (4″), 26.0 (*Me*–C–Si), −4.7 (*Me*–Si), −4.1 (*Me*–Si), 18.1 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{25}H_{42}O_4SSi$ $(M+Na)^+$ 489.2471, found 489.2480.

4-(5′-*tert*-Butyldimethylsilyloxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-4-phenylsulphonyl-2-butanone (41). Jones reagent (0.1 ml) was added to a solution of **40** (0.5 g, 1.07 mmol) in acetone (20 ml) cooled at 0°C and the mixture was stirred at this temperature for 30 min. Following the same procedure described for **32**, 0.45 g (90%) of **41** was obtained as a colourless oil. IR (film): 3015, 2955, 2926, 2856, 1724, 1492, 1448, 1186, 1084, 970, 835 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 7.88 (2H, d, *J*=7.5 Hz, Ph), 7.55 (3H, m, Ph), 5.47 (1H, bs, H-3′), 4.43 (1H, d, *J*=9.4 Hz, H-4), 3.36 (1H, t, *J*=5.4 Hz, H-5′), 3.23 (1H, dd, *J*=18.9, 9.4 Hz, H-3), 2.74 (1H, bs, H-1′), 2.71 (1H, d, *J*=18.9 Hz, H-3), 2.04 (3H, s, MeCOO), 2.20–1.95 (2H, m, H-4′), 1.85 (3H, s, Me–$C_{2'}$), 0.79 (9H, s, Me_3C–Si), 0.73 (3H, s, Me–$C_{6'}$), 0.59 (3H, s, Me–$C_{6'}$), −0.03 (3H, s, Me–Si), −0.05 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 29.7 (1), 203.6 (2), 40.6 (3), 59.3 (4), 46.2 (1′), 132.5 (2′), 123.4 (3′), 32.4 (4′), 74.2 (5′), 39.0 (6′), 24.5 (7′), 26.5 (8′), 18.6 (9′), 139.9 (1″), 129.0 (2″), 128.7 (3″), 133.5 (4″), 26.0 (*Me*–C–Si), −4.6 (*Me*–Si), −4.4 (*Me*–Si), 18.3 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{25}H_{40}O_4SSi$ $(M+Na)^+$ 487.2314, found 487.2302.

4-(5′-*tert*-Butyldimethylsilyloxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-3-buten-2-one (42). Aluminium oxide (3 g, 29.4 mmol) was added to a solution of **41**(0.5 g, 1.08 mmol) in THF (50 ml) and the mixture was stirred at room temperature for 4 h. Following the same procedure described for **33**, 0.34 g (98%) of **42** (colourless oil) was obtained. IR (film): 2957, 2930, 2856, 1697, 1676, 1618, 1471, 1084, 1005, 880 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 6.83 (1H, dd, *J*=16.1, 10.5 Hz, H-4), 6.00 (1H, d, *J*=16.1 Hz, H-3), 5.38 (1H, bs, H-3′), 3.48 (1H, t, *J*=5.1 Hz, H-5′), 2.37 (1H, d, *J*=10.5 Hz, H-1′), 2.25 (3H, s, H-1), 2.25 (1H, bd, *J*=17.6 Hz, H-4′), 2.05 (1H, bd, *J*=17.6 Hz, H-4′), 1.54 (3H, bs, Me–$C_{2'}$), 0.88 (9H, s, Me_3C–Si), 0.86 (3H, s, Me–$C_{6'}$), 0.85 (3H, s, Me–$C_{6'}$), −0.03 (3H, s, Me–Si), −0.04 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 26.6 (1), 198.3 (2), 133.6 (3), 150.3 (4), 55.1 (1′), 131.9 (2′), 119.9 (3′), 32.4 (4′), 74.2 (5′), 37.9 (6′), 22.8 (7′), 26.5 (8′), 21.1 (9′), 26.0 (*Me*–C–Si), −4.7 (*Me*–Si), −4.3 (*Me*–Si), 18.2 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{19}H_{34}O_2Si$ $(M+Na)^+$ 345.2226, found 345.2237.

4-(5′-*tert*-Butyldimethylsilyloxy-2′,6′,6′-trimethyl)cyclohex-2′enyl-2-butanone (43). An aqueous Raney Nickel suspension (2.4 g) was added to a stirred solution of **42**

(0.3 g, 0.93 mmol) in THF (10 ml) and the mixture was further stirred at room temperature for 30 min. Following the same procedure described for **34**, 0.28 g (95%) of **43** was obtained. Colourless oil. IR (film): 2960, 2930, 2856, 1734, 1618, 1471, 1257, 1107, 887 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 5.24 (1H, bs, H-3′), 3.39 (1H, dd, *J*=8.1, 5.7 Hz, H-5′), 2.62 (1H, ddd, *J*=16.3, 10.6, 5.5 Hz, H-3), 2.41 (1H, ddd, *J*=15.9, 10.2, 5.5 Hz, H-3), 2.12 (3H, s, H-1), 2.10–1.90 (2H, m, H-4′), 1.70–1.25 (3H, m, H-4, H-1′), 1.65 (3H, s, Me–$C_{2'}$), 0.91 (3H, s, Me–$C_{6'}$), 0.87 (9H, s, Me_3C–Si), 0.78 (3H, s, Me–$C_{6'}$), 0.01 (6H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 30.0 (1), 202.4 (2), 45.2 (3), 22.3 (4), 49.1 (1′), 135.6 (2′), 119.9 (3′), 32.5 (4′), 75.1 (5′), 38.7 (6′), 22.6 (7′), 25.9 (8′), 16.7 (9′), 26.2 (*Me*–C–Si), −4.8 (*Me*–Si), −4.1 (*Me*–Si), 18.1 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{19}H_{36}O_2Si$ $(M+Na)^+$ 347.2382, found 347.2391.

4-(5-*tert*-Butyldimethylsilyloxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-3-methyl-1-penten-3-ol (44). 1 M solution of vinylmagnesium bromide in THF (3.2 ml) was added to a solution of **43** (0.7 g, 2.16 mmol) in THF (50 ml) cooled at 0°C and the mixture was stirred at this temperature for 30 min. Following the same procedure described for **35**, 0.7 g (93%) of **44** was obtained as a colourless oil. IR (film): 3480, 2962, 2930, 2856, 1471, 1085, 1000, 885, 770 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 5.92 (1H, dd, *J*=16.3, 10.7 Hz, H-2), 5.20 (1H, d, *J*=16.3 Hz, H-1), 5.19 (1H, bs, H-3′), 5.06 (1H, d, *J*=10.7 Hz, H-1), 3.40 (1H, dd, *J*=8.1, 5.6 Hz, H-5′), 2.10–1.90 (2H, m, H-4′), 2.00 (1H, m, H-4′), 1.70–1.30 (5H, m, H-4, H-5, H-1′), 1.67 (3H, s, Me–$C_{2'}$), 1.29 (3H, s, Me–C_3), 0.90 (3H, s, Me–$C_{6'}$), 0.87 (9H, s, Me_3C–Si), 0.78 (3H, s, Me–$C_{6'}$), 0.06 (3H, s, Me–Si), 0.01 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 111.8 (1), 145.1 (2), 73.6 (3), 44.7 (4), 22.8 (5), 27.6 (*Me*–C_3), 49.9 (1′), 136.6 (2′), 118.9 (3′), 32.6 (4′), 75.2 (5′), 38.8 (6′), 22.6 (7′), 25.9 (8′), 16.5 (9′), 26.0 (*Me*–C–Si), −4.8 (*Me*–Si), −4.1 (*Me*–Si), 18.1 (Me–*C*–Si). HRFABMS *m/z* calcd for $C_{21}H_{40}O_2Si$ $(M+Na)^+$ 375.2695, found 375.2684.

5-(5′-Hydroxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-3-methyl-1-penten-3-ol (45). Tetrabutylammonium fluoride (0.13 g, 0.43 mmol) was added to a solution of **44** (0.14 g, 0.40 mmol) in THF (10 ml) and the mixture was stirred at room temperature for 6 h. 76 mg (81%) of **45** was obtained following the same procedure described for **38**. Colourless oil. IR (film): 3481, 2965, 2930, 2850, 1471, 1255, 1088, 1004, 918, 835, 758 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 5.94 (1H, dd, *J*=18.6, 10.7 Hz, H-2), 5.24 (1H, bs, H-3′), 5.22 (1H, dd, *J*=18.6 Hz, 1.2H, H-1), 5.08 (1H, dd, *J*=10.7, 1.2 Hz, H-1), 3.47 (1H, dd, *J*=8.1, 5.5 Hz, H-5′), 2.21 (1H, m, H-4′), 1.99 (1H, m, H-4′), 1.75–1.30 (5H, m, H-4, H-5, H-1′), 1.71 (3H, bs, Me–$C_{2'}$), 1.30 (3H, s, Me–C_3), 0.98 (3H, s, Me–$C_{6'}$), 0.85 (3H, s, Me–$C_{6'}$). ^{13}C NMR ($CDCl_3$, 75 MHz): 112.0 (1), 145.1 (2), 73.6 (3), 44.6 (4), 22.7 (5), 26.0 (Me–C_3), 49.7 (1′), 136.9 (2′), 118.6 (3′), 31.9 (4′), 75.0 (5′), 38.6 (6′), 22.4 (7′), 25.6 (8′), 16.5 (9′). HRFABMS *m/z* calcd for $C_{15}H_{26}O_2$ $(M+Na)^+$ 261.1830, found 261.1819.

5-(5′-Acetoxy-2′,6′,6′-trimethyl)cyclohex-2′-enyl-3-methyl-1-penten-3-ol (7). Acetic anhydride (1 ml) was added to a solution of **45** (60 mg, 0.252 mmol) in pyridine (3 ml) and the mixture was stirred at room temperature for 4 h. After work-up as for alcohol **35**, 58 mg (83%) of **7** was obtained as a colourless oil. IR (film): 3488, 2960, 2850, 1725, 1445, 1255, 1030, 1000, 918, 83, 760 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 5.91 (1H, dd, *J*=17.5, 10.7 Hz, H-2), 5.20 (1H, dd, *J*=17.5, 1.1 Hz, H-1), 5.05 (1H, dd, *J*=10.7 Hz, 1.1H, H-1), 5.08 (1H, dd, *J*=10.7, 1.2 Hz, H-1), 4.65 (1H, t, *J*=6.4 Hz, H-5′), 2.25 (1H, dd, *J*=18.0, 6.4 Hz, H-4′), 2.00 (1H, dd, *J*=18.0, 6.4 Hz, H-4′), 1.99 (3H, s, OAc), 1.72 (1H, m, H-4), 1.70 (3H, bs, Me-9′), 1.67 (1H, m, H-5), 1.50 (1H, m, H-4), 1.28 (1H, m, H-5), 1.25 (3H, s, Me–C_3), 0.98 (3H, s, Me-7′), 0.85 (3H, s, Me-8′). ^{13}C NMR ($CDCl_3$, 75 MHz): 111.7 (1), 145.0 (2), 73.7 (3), 44.1 (4), 22.6 (5), 27.8 (Me–C_3), 49.5 (1′), 136.8 (2′), 117.3 (3′), 28.8 (4′), 76.5 (5′), 36.7 (6′), 25.5 (7′), 18.7 (8′), 22.8 (9′), 171.0 (Me*C*OO), 20.9 (*Me*COO). HRFABMS *m/z* calcd for $C_{17}H_{28}O_3$ $(M+Na)^+$ 303.1936, found 303.1942.

Acetate of 4-(2′,5′-epoxy-2′,6′,6′-trimethyl)cyclohexyl-2-butyl (46). Acetic anhydride (5 ml) was added to a solution of **21** (1.3 g, 6.13 mmol) in pyridine (10 ml), and the mixture was stirred at room temperature for 6 h. Then it was diluted with ether (100 ml), and washed with 2N HCl, sat. $NaHCO_3$, water, sat. NaCl and dried. Concentration gave 1.47 g of **46** (95%) as a mixture of diastereomers. Colourless oil. IR (film): 2874, 1736, 1060, 951 cm^{-1}. MS *m/z* (rel. int.): 254. $[M^+]$ (2), 239 $[M^+-Me]$(8), 180 $[M^+-C_3H_7O_2]$(11), 43 $[M^+-C_2H_3O^+]$(100). ^1H NMR ($CDCl_3$, 300 MHz): 1.73–1.14 (18H, m). Signals assignable to **46a**: 4.90 (1H, m, H-2), 3.70 (1H, d, *J*=5.4 Hz, H-5′), 2.02 (3H, s, Me–COO), 1.30 (3H, s, Me-9′), 1.20 (3H, d, *J*=6.0 Hz, Me-2), 1.04 (3H, s, Me-8′), 0.98 (3H, s, Me-7′). Signals assignable to **46b**: 4.90 (1H, m, H-2), 3.70 (1H, d, *J*=5.4 Hz, H-5′), 2.03 (3H, s, Me–COO), 1.30 (3H, s, Me-9′), 1.20 (3H, d, *J*=6.0 Hz, Me-2), 1.06 (3H, s, Me-8′), 0.99 (3H, s, Me-7′). ^{13}C NMR ($CDCl_3$, 75 MHz): Signals assignable to **46a**: 19.9 (1), 71.3 (2), 36.1 (3), 23.4 (4), 55.8(1′), 86.7 (2′), 39.0 (3′), 25.8 (4′), 86.1 (5′), 45.2 (6′), 18.9 (7′), 23.4 (8′), 26.1 (9′), 170.8 (OAc), 21.4 (*Me*–COO). Signals assignable to **46b**: 19.8 (1), 71.2 (2), 36.1 (3), 23.4 (4), 55.6(1′), 86.7 (2′), 38.9 (3′), 25.8 (4′), 86.2 (5′), 45.2 (6′), 18.9 (7′), 23.2 (8′), 26.2 (9′), 170.8 (OAc), 21.4 (*Me*–COO). HRFABMS *m/z* calcd for $C_{15}H_{26}O_3$ $(M+Na)^+$ 277.1780, found 277.1768.

3-(3′-Acetoxybutyl)-2,2,4-trimethylcyclohex-3-enol (47). To a stirred solution of **46** (1.04 g, 4.1 mmol) in dry CH_2Cl_2 (45 ml), a 1 M solution of BBr_3 in CH_2Cl_2 (4.9 ml) was added dropwise at 0°C. After stirring for 15 min at room temperature a 1 M solution of collidine in CH_2Cl_2 (13.1 ml) was added at 0°C and the mixture stirred for 15 min at room temperature. Then, it was diluted with $CHCl_3$ (90 ml) and washed with 5% $NaHSO_4$ (2×125 ml), 10% $NaHCO_3$ (2×100 ml) and brine (2×100 ml). The organic phase was dried over anh. Na_2SO_4 and the solvent evaporated to afford a crude reaction that by column chromatography (H–E 1:1) yielded **47** (927 mg, 89%) as a colourless oil. IR (film): 3450, 2974, 1734, 1244 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): 4.87 (1H, tq, *J*=6.2 Hz, H-3′), 3.45 (1H, dd, *J*=9.3, 2.9 Hz, H-1), 2.10–1.90 (4H, m, H-5, H-1′), 2.25 (1H, m, H-4′), 2.02 (3H, s, MeCO), 1.80 (1H, m), 1.70–1.50 (3H, m), 1.58 (3H, s, Me-9), 1.21 (3H, d, *J*=6.2 Hz, Me-4′), 1.03 (3H, bs, Me-8), 0.97 (3H, s, Me-7).

^{13}C NMR ($CDCl_3$, 75 MHz): 75.9 (1), 40.1 (2), 126.6 (3), 135.0 (4), 29.6 (5), 26.6 (6), 21.4 (7), 26.2 (8), 19.4 (9), 24.5 (1′), 36.4 (2′), 71.4 (3′), 19.8 (4′), 170.9 (Me*C*OO), 21.7 (*Me*COO). HRFABMS *m/z* calcd for $C_{15}H_{26}O_3$ $(M+Na)^+$ 277.1780, found 277.1779.

Treatment of 47 with TBSCl

TBSCl (0.17 g, 1.13 mmol), imidazole (0.08 g, 1.13 mmol) and catalytic amount DMAP was added to a solution of **47** (0.18 g, 0.71 mmol) in anh. DMF (20 ml) and the mixture stirred at room temperature for 44 h. Then it was diluted with Et_2O and washed with 1N HCl (4×50 ml), 5% $NaHCO_3$ (4×50 ml) and brine (2×50 ml). The ethereal phase was dried over anh. Na_2SO_4, filtered and evaporated under vacuum to give a crude which after chromatography (H–E 9:1) yielded **48** (1.07 g, 95 %). Colourless oil. IR (film): 2969, 1745, 1242 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 4.89 (1H, tq, *J*=6.3 Hz, H-3′), 3.44 (1H, dd, *J*=7.4, 2.3 Hz, H-4), 2.04 (3H, s, AcO), 2.01–1.90 (4H, m, H-6, H-1′), 1.70–1.50 (4H, m, H-5, H-2′), 1.56 (3H, s, Me–C_1), 1.25 (3H, s, Me–C_3), 1.23 (3H, d, *J*=6.3 Hz, H-4′), 0.91 (3H, s, Me–C_3), 0.89 (9H, s, *Me*–C–Si), 0.05 (3H, s, *Me*–Si), 0.04 (3H, s, *Me*–Si). HRFABMS *m/z* calcd for $C_{21}H_{40}O_3Si$ $(M+Na)^+$ 391.2644, found 391.2649.

3-(3′-Acetoxybutyl)-5-*t*-butyldimethylsilyloxy-2,4,4-trimethylcyclohex-2-enone (49). To a solution of **48** (0.4 mg, 1.09 mmol) in dry benzene (14 ml), Na_2CrO_4 (1.4 g, 8.6 mmol), NaOAc (1.06 g, 12.8 mmol), Ac_2O (4.2 ml) and glacial AcOH (1.8 ml) was added and the reaction mixture stirred at 65°C for 3 h. Then it was poured into ice and extracted with Et_2O (3×75 ml). The organic layer was washed with 5% $NaHCO_3$ (3×75 ml) and brine (3×50 ml), dried and evaporated affording a crude which after column chromatography (H–E 8:2), gave 366 mg of **49** (88%) as a colourless oil. IR (film): 2957, 2858, 1738, 1671, 1242, 1111 cm^{-1}. MS *m/z* (rel. int.): 383 [M+1] (70), 325 (15), 251 (91), 191 (100). ^{1}H NMR ($CDCl_3$, 300 MHz): 4.95 (1H, tq, *J*=6.2 Hz, H-3′), 3.76 (1H, dd, *J*=10.0, 4.8 Hz, H-5), 2.60 (1H, dd, *J*=16.7, 4.7 Hz, H-6), 2.49 (1H, dd, *J*=16.7, 10.4 Hz, H-6), 2.25 (2H, m, H-1′), 2.06 (3H, s, AcO), 1.76 (3H, s, Me-9), 1.67 (2H, m, H-2′), 1.26 (3H, d, *J*=6.3 Hz, Me-4′), 1.15 (3H, s, Me-8), 1.08 (3H, s, Me-7), 0.87 (9H, s, *t*-BuSi), 0.04 (3H, s, Me–Si), 0.03 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 75 MHz): 197.6 (1), 131.4 (2), 162.9 (3), 42.8 (4), 74.3 (5), 43.4 (6), 20.6 (7), 24.8 (8), 11.4 (9), 26.6 (1′), 34.6 (2′), 70.9 (3′), 19.9 (4′), −4.0 (*Me*–Si), −4.9 (*Me*–Si), 18.1 (Me–C–Si), 25.8 (*Me*–C–Si), 21.4 (*Me*–CO), 170.8 (Me–*CO*). HRFABMS *m/z* calcd for $C_{21}H_{38}O_4Si$ $(M+Na)^+$ 405.2432, found 405.2437.

Treatment of 49 with 2N KOH–MeOH

Preparation of 3-(3′-hydroxybutyl)-2,4,4-trimethylcyclohexa-2,5-dienone (51). To a solution of **49** (50 mg, 0.13 mmol) in MeOH, a 2N KOH–MeOH solution (2 ml) was added and the mixture stirred at room temperature for 24 h. After evaporating it was diluted with H_2O (10 ml) and extracted with Et_2O (3×30 ml). The combined organic phases were washed with brine (3×30 ml), dried over anh. Na_2SO_4, filtered and evaporated to afford a crude, which after chromatography (H–E 2:8) yielded **51** (25 mg, 93%). Colourless oil. IR (film): 3460, 2950, 2862, 1668, 1160, 1070 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): 6.72 (1H, d, *J*=9.9 Hz), 6.19 (1H, d, *J*=9.9 Hz), 3.88 (1H, tq, *J*=6.1 Hz, H-3′), 2.52 (1H, m, H-1′), 2.30 (1H, m, H-1′), 1.88 (3H, s, Me–C_4), 1.23 (3H, d, *J*=6.1 Hz, H-4′), 1.22 (6H, s, Me–C_4). HRFABMS *m/z* calcd for $C_{13}H_{20}O_2$ $(M+Na)^+$ 253.1807, found 253.1803.

Reaction of 51 with Jones reagent

Preparation of 3-(3′-oxobutyl)-2,4,4-trimethylcyclohexa-2,5-dienone (52). Jones reagent was added dropwise to a solution of **51** (25 mg) cooled at 0°C and the mixture stirred for 15 min. After work-up as for alcohol **21**, **52** (20 mg) was obtained as a colourless oil. IR (film): 2962, 2931, 2858, 1716, 1660, 1628, 1604, 1471, 1371, 1257, 1163, 1089, 881 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): 6.71 (1H, d, *J*=9.9 Hz, H-5), 6.16 (1H, d, *J*=9.9 Hz, H-6), 2.58 (4H, s, H-1′, H-2′), 2.16 (3H, s, H-4′), 1.84 (3H, s, Me–C_2), 1.20 (6H, s, Me–C_4).^{13}C NMR ($CDCl_3$, 100 MHz): 186.1 (1), 132.2 (2), 160.3 (3), 40.6 (4), 156.8 (5), 125.8 (6), 24.2 (7), 25.9 (8), 11.3 (9), 23.8 (1′), 42.1 (2′), 206.9 (3′), 29.7 (4′). HRFABMS *m/z* calcd for $C_{13}H_{18}O_2$ $(M+Na)^+$ 229.1204, found 229.1215.

5-*t*-Butyldimethylsilyloxy-3-(3-hydroxybutyl)-2,4,4-trimethylcyclohex-2-enone (50). K_2CO_3 (145 mg, 1.05 mmol) was added to a solution of **49** (300 mg, 0.78 mmol) and the reaction mixture stirred for 1 h. After evaporating it was diluted with H_2O (10 ml) and extracted with Et_2O (3×30 ml). The combined organic phases were washed with brine (3×30 ml), dried over anh. Na_2SO_4, filtered and evaporated to afford a crude, which after chromatography (H–E 7:3) gave 254 mg of **50** (95%). Colourless oil. IR (film): 3450, 2958, 2857, 1665, 1112 cm^{-1}. ^{1}H NMR (CD_3COCD_3, 500 MHz): 3.86 (1H, tq, *J*=6.1 Hz, H-3′), 3.75 (1H, dd, *J*=10.0, 4.7 Hz, H-5), 2.59 (1H, dd, *J*=16.8, 4.7 Hz, H-6), 2.48 (1H, dd, *J*=16.8, 10.0 Hz, H-6), 2.45–2.20 (2H, m, H-1′), 1.76 (3H, s, Me-9), 1.59 (2H, m, H-2′), 1.23 (3H, d, *J*=6.1 Hz, Me-4′), 1.16 (3H, s, Me-8), 1.08 (3H, s, Me-7), 0.86 (9H, s, *t*-Bu–Si), 0.04 (3H, s, Me–Si), 0.03 (3H, s, Me–Si). ^{13}C NMR (CD_3COCD_3, 125 MHz): 197.8 (1), 131.0 (2), 163.9 (3), 42.8 (4), 74.3 (5), 43.4 (6), 19.8 (7), 24.8 (8), 11.5 (9), 27.0 (1′), 37.8 (2′), 68.4 (3′), 19.8 (4′), −4.0 (*Me*–Si), −4.9 (*Me*–Si), 18.1 (Me–*C*–Si), 25.9 (*Me*–C–Si). HRFABMS *m/z* calcd for $C_{19}H_{36}O_3Si$ $(M+Na)^+$ 363.2332, found 363.2331.

5-*t*-Butyldimethylsilyloxy-3-(3′-oxobutyl)-2,4,4-trimethylcyclohex-2-enone (53). To a stirred solution of **50** (250 mg, 0.73 mmol) in acetone (8 ml), Jones reagent (0.3 ml) was added dropwise at −15°C and the mixture was further stirred for 30 min at this temperature. After work-up as for alcohol **21**, **53** (238 mg, 96%) was obtained as a colourless oil. IR (film): 2957, 2858, 1738, 1671, 1242, 1111 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): 3.89 (1H, dd, *J*=9.4, 4.5 Hz, H-5), 2.68–2.41 (4H, m, H-6, H-2′), 2.13 (3H, s, *Me*–CO), 2.05 (2H, m, H-1′), 1.68 (3H, s, Me-9), 1.19 (3H, s, Me-8), 1.11 (3H, s, Me-7), 0.89 (9H, s, *t*-Bu–Si), 0.09 (6H, s, Me–Si).^{13}C NMR (CD_3COCD_3, 100 MHz): 196.3 (1), 131.6 (2), 162.3 (3), 43.3 (4), 75.5 (5), 43.8 (6), 21.2 (7), 25.1 (8), 11.3 (9), 24.7 (1′), 42.2 (2′), 206.0 (3′), 29.6(4′), −4.0 (*Me*–Si), −4.8 (*Me*–Si), 18.5 (Me–*C*–Si),

26.2 (*Me*–C–Si). HRFABMS *m/z* calcd for $C_{19}H_{34}O_3Si$ $(M+Na)^+$ 361.2173, found 361.2174.

5-*t*-Butyldimethylsilyloxy-3-(3-hydroxy-3-methylpent-4-enyl)-2,4,4-trimethylcyclohex-2-enone (54). Vinylmagnesium bromide (1 M in THF, 1 ml, 1 mmol) was added to a stirred solution of **53** (200 g, 0.591 mmol) in THF (8 ml) at 0°C, and the whole was stirred at 0°C for 45 min. After work-up as for ketone **22**, **54** (188 mg, 87%) was obtained. Colourless oil. IR (film): 3426, 2929, 2856, 1655, 878 cm^{-1}.[1] ^1H NMR ($CDCl_3$, 400 MHz): 5.94 (1H, dd, *J*=17.5, 10.8 Hz, H-4′), 5.26 (1H, d, *J*=17.3 Hz, H-5′ *trans*), 5.13 (1H, d, *J*=10.7 Hz, H-5′ *cis*), 3.76 (1H, dd, *J*=10.0, 4.8 Hz, H-5), 2.61 (1H, dd, *J*=16.8, 4.8 Hz, H-6), 2.51 (1H, dd, *J*=16.8, 10.0 Hz, H-6), 2.30 (2H, m, H-1′), 1.73 (3H, s, Me-9), 1.70–1.60 (2H, m, H-2′), 1.33 (3H, s, Me–$C_{3'}$), 1.16 (3H, s, Me-8), 1.08 (3H, s, Me-7), 0.87 (9H, s, *t*-Bu–Si), 0.05 (3H, s, Me–Si), 0.04 (3H, s, Me–Si). ^{13}C NMR ($CDCl_3$, 100 MHz): 196.3 (1), 131.3 (2), 162.3 (3), 42.9 (4), 75.5 (5), 43.9 (6), 21.4 (7), 25.3 (8), 11.4 (9), 25.9 (1′), 41.3 (2′), 72.8 (3′), 146.3 (4′), 111.9 (5′), −4.0 (*Me*–C–Si), −4.8 (*Me*–Si), 18.2 (Me–*C*–Si), 28.3 (*Me*–C_3'), 25.9 (*Me*–C–Si). HRFABMS *m/z* calcd for $C_{21}H_{38}O_3Si$ $(M+Na)^+$ 389.2489, found 389.2487.

5-Hydroxy-3-(3′-hydroxy-3′-methylpent-4′-enyl)-2,4,4-trimethylcyclohex-2-enone (55). TBAF (158 mg, 0.5 mmol) was added at 0°C to a solution of **54** (150 mg, 0.41 mmol) in THF (5 ml) and the mixture stirred at room temperature for 2 h. The crude was diluted with Et_2O (25 ml) and the organic phase washed with brine (3×10 ml), dried and evaporated to yield **55** (83 mg, 81%) as a colourless oil. IR (film): 3402, 2929, 1653, 803 cm^{-1}. MS *m/z* (rel. int.): 253 [M+1] (30), 235 (25), 217 (37), 149 (51). ^1H NMR ($CDCl_3$, 300 MHz): 5.95 (1H, dd, *J*=17.3, 10.7 Hz, H-4′), 5.28 (1H, d, *J*=17.3 Hz, H-5′ *trans*), 5.15 (1H, d, *J*=10.7 Hz, H-5′ *cis*), 3.83 (1H, dd, *J*=9.2, 4.2 Hz, H-5), 2.72 (1H, dd, *J*=16.9, 4.1 Hz, H-6), 2.55 (1H, dd, *J*=16.9 and 9.2 Hz, H-6), 2.30 (2H, m, H-1′), 1.77 (3H, s, Me-9), 1.71–1.60 (2H, m, H-2′), 1.34 (3H, s, Me–$C_{3'}$), 1.15 (3H, s, Me-8), 0.87 (3H, s, Me-7). ^{13}C NMR ($CDCl_3$, 75 MHz): 196.9 (1), 131.5 (2), 163.8 (3), 43.5 (4), 74.0 (5), 43.5 (6), 20.9 (7), 25.2 (8), 11.5 (9), 25.8 (1′), 41.3 (2′), 72.2 (3′), 146.8 (4′), 111.9 (5′), 28.4 (*Me*–$C_{3'}$). HRFABMS *m/z* calcd for $C_{15}H_{25}O_3$ $(M+Na)^+$ 253.1807, found 253.1803.

5-Acetoxy-3-(3′-hydroxy-3′-methylpent-4′-enyl)-2,4,4-trimethylcyclohex-2-enone (8). Acetic anhydride (1 ml) was added to a solution of **55** (50 mg, 0.198 mmol) in pyridine (2 ml), and the mixture was stirred at room temperature for 1 h. After work-up as for alcohol **35**, **8** was obtained (54 mg, 93%). Colourless oil. IR (film): 3470, 1735, 1663, 924 cm^{-1}. MS *m/z* (rel. int.): 295 [M+1] (1), 235 (20), 220 (13), 149 (55). ^1H NMR ($CDCl_3$, 300 MHz): 5.91 (1H, dd, *J*=17.3, 10.7 Hz, H-4′), 5.27 (1H, d, *J*=17.3 Hz, H-5′ *trans*), 5.12 (1H, d, *J*=10.7 Hz, H-5′ *cis*), 5.04 (1H, dd, *J*=7.7 and 4.0 Hz, H-5), 2.75 (1H, dd, *J*=16.9 and 4.1 Hz, H-6), 2.54 (1H, dd, *J*=16.9 and 7.8 Hz, H-6), 2.30 (2H, m, H-1′), 2.03 (3H, s, Me–OAc), 1.77 (3H, s, Me-9), 1.75–1.65 (2H, m, H-2′), 1.34 (3H, s, Me–$C_{3'}$), 1.17 (3H, s, Me-8), 1.15 (3H, s, Me-7). ^{13}C NMR ($CDCl_3$, 75 MHz): 195.7 (1), 131.3 (2), 162.1 (3), 40.5 (4), 75.7 (5), 39.1 (6), 25.1 (7), 21.8 (8), 11.6 (9), 25.1 (1′), 39.9 (2′), 73.3 (3′), 143.9 (4′), 112.6 (5′), 28.1 (*Me*–$C_{3'}$), 170.5 (Me*C*OO), 21.1 (*Me*COO). HRFABMS *m/z* calcd for $C_{17}H_{26}O_4$ $(M+Na)^+$ 317.1729, found 317.1736.

Acknowledgements

We should like to thank the CICYT (Projet PB 98-1365) for financial support.

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