Formal total synthesis of trichodiene *via* skeletal rearrangement of regioselective photochemical [2+2] cycloadducts from cyclohexene derivatives

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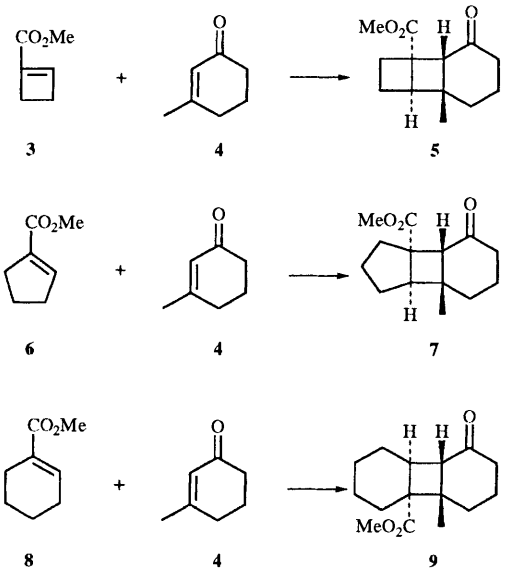
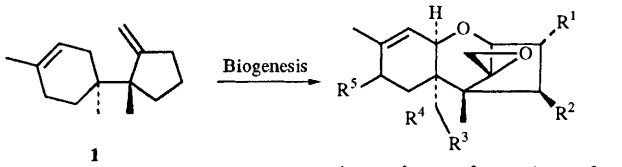
A formal total synthesis of trichodiene 1 is accomplished *via* the photochemical [2 + 2] cycloaddition of 3-methylcyclohex-2-enone with methyl cyclohex-1-enecarboxylate to give methyl (1α,2β,7β,8α)-2-methyl-6-oxotricyclo[6.4.0.0^{2,7}]dodecan-1-carboxylate, and its skeletal rearrangement to give a tricyclo[6.4.0.0^{2,6}]dodecene derivative. Cleavage of the central five-membered ring of the tricyclo[6.4.0.0^{2,6}]dodecene and modification of functional groups leads to the synthesis of trichodiene 1.

Introduction

Trichodiene **1**[1] is a bicyclic sesquiterpene which has been considered to be a common biogenetic precursor[2] of trichothecene-type mycotoxins, *e.g.*, trichodermol **2a**,[3] verrucarol **2b**,[4] anguidine **2c**[5] and deoxynivalenol **2d**.[6] These mycotoxins were also reported to show various biological activities.[7] One of the structural characteristics of tricothecene-type sesquiterpenes is their two contiguous asymmetric quaternary centres connecting the five- and one of the six-membered rings in the molecule. Although syntheses of trichodiene **1** have been reported by several groups,[8,9] it has been difficult to control the stereochemistry of the two contiguous chiral quaternary carbons whose C–C bond can rotate freely. We discovered the ring-size effect on [2+2] photochemical cycloaddition of enones with cyclic olefins,[10] in which the regioselectivity of the reaction was determined by the ring size of the cyclic olefins. In the photocycloaddition of 3-methylcyclohex-2-enone **4** with methyl cyclobut-1-enecarboxylate **3** or with methyl cyclopent-1-enecarboxylate **6**, the photoadduct has the head-to-head, *cis-transoid-cis* ring system **5**, or **7**, whereas the photocycloaddition of enone **4** with methyl cyclohex-1-enecarboxylate **8** gave regioselectively a head-to-tail, *cis-transoid-cis* photoadduct **9** which contains the two contiguous asymmetric quaternary carbons (Scheme 1). We report here a formal total synthesis of trichodiene **1** from the photoadduct **9** which has contiguous quaternary carbons of the same stereochemistry as those in trichodiene **1**.



Scheme 1 Ring-size effect on [2+2] photocycloaddition of enone with cyclic olefins

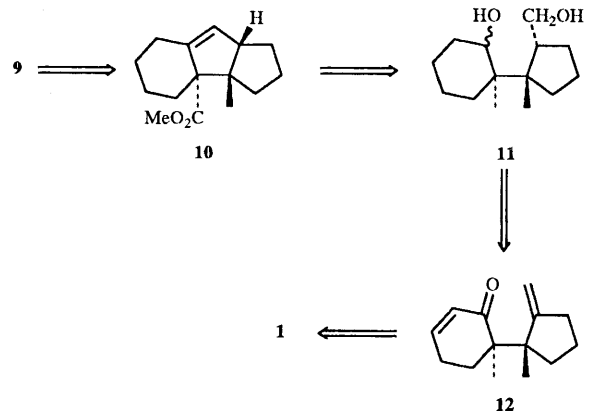


	R^1	R^2	R^3	R^4	R^5
2a	H	OH	H	H	H
2b	H	OH	OH	H	H
2c	OH	OAc	OAc	H	H
2d	OH	H	OH	OH	=O

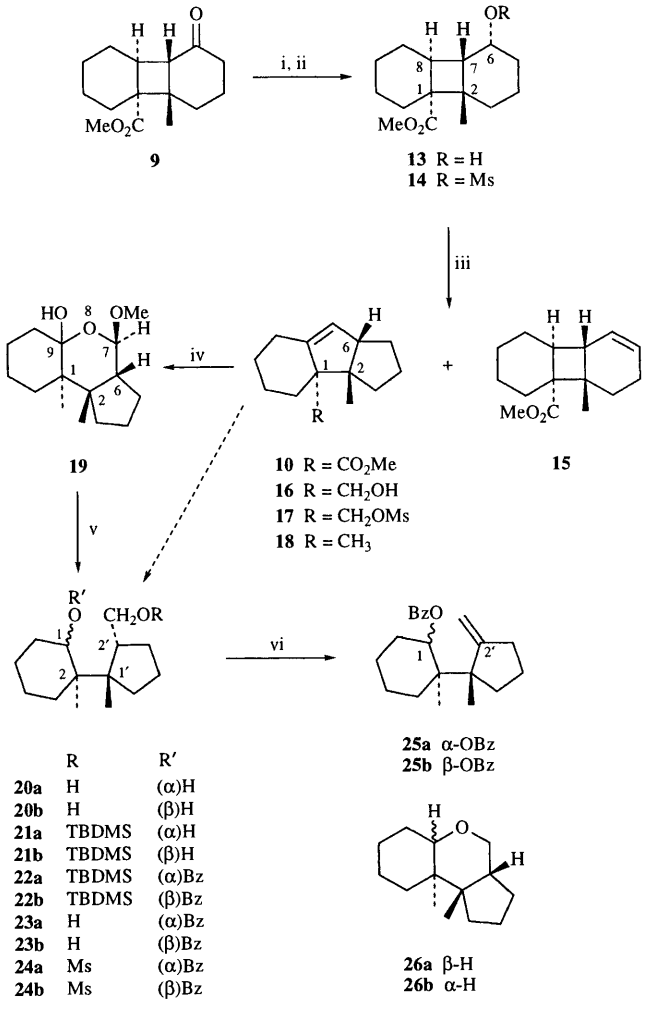
Results and discussion

We planned to synthesize trichodiene **1** from tricycle **9** *via* successive reactions for rearrangement of a tricyclo[6.4.0.0^{2,7}]dodecane to a tricyclo[6.4.0.0^{2,6}]dodecene **10**, transformation of the methyl ester into a methyl group, cleavage of the central five-membered ring to give compound **11**, and modification of functional groups, *via* compound **12** as summarised in Scheme 2.

The photoadduct **9** from reaction of 3-methylcyclohex-2-enone **4** with methyl cyclohex-1-enecarboxylate **8** was transformed into 6α-alcohol **13** quantitatively by reduction with $NaBH_4$ in methanol (Scheme 3). The stereochemistry at C-6 of compound **13** was deduced from the nuclear Overhauser effect (NOE) between 6β-H (δ 3.75) and 7β-H (δ 2.24). The alcohol **13** was functionalised with methanesulfonyl chloride (MsCl) in pyridine to produce mesyl ester **14** in which the C–O bond of the mesyl group is anti-parallel with one of the C–C bonds in the cyclobutane ring. The skeletal rearrangement of compound **14** was then examined under various conditions, and afforded tricyclo[6.4.0.0^{2,6}]dodec-7-ene derivative **10**. When the mesyl derivative **14** was treated with HCO_2K in HCO_2H or potassium acetate in acetic acid the simple 1,2-elimination product **15** was predominantly obtained, whereas the yield of the ring-migration product **10** was 18.4 or 20.9%, respectively. Finally, the mesyl ester **14** was treated with AcOK in trifluoroacetic acid (TFA) to afford the rearranged compound **10** in moderate yield (50–60%) together with compound **15** (10–20%). The proof of the stereochemistry at C-6 of compound **10** was obtained from the NOE between 6β-H



Scheme 2 Synthetic plan for trichodiene



	R	R′
20a	H	(α)H
20b	H	(β)H
21a	TBDMS	(α)H
21b	TBDMS	(β)H
22a	TBDMS	(α)Bz
22b	TBDMS	(β)Bz
23a	H	(α)Bz
23b	H	(β)Bz
24a	Ms	(α)Bz
24b	Ms	(β)Bz

Scheme 3 *Reagents and conditions:* i, $NaBH_4$, MeOH; ii, MsCl, pyridine; iii, (a) AcOK, TFA; (b) $LiAlH_4$, Et_2O; (c) MsCl, pyridine, CH_2Cl_2; (d) $LiAlH_4$, Et_2O, reflux; iv, O_3, MeOH, −78 °C; then $NaBH_4$; v, (a) TBDMSCl, DIPEA, DMF; (b) BzCl, pyridine, CH_2Cl_2; (c) 1% HCl in 95% EtOH; (d) AcOH, aq. THF, 60 °C; (e) MsCl, pyridine, CH_2Cl_2; vi, DBU, toluene, reflux

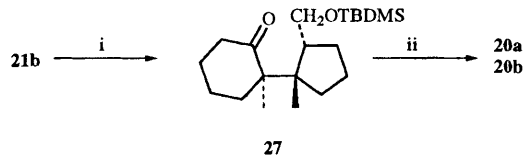
(δ 2.59) and 2β-Me (δ 1.13). The methyl ester of compound **10** was transformed into a methyl group by the following three-step reactions; reduction of the methyl ester **10** with $LiAlH_4$ (LAH) in diethyl ether, functionalisation of the alcohol **16** with MsCl and pyridine in CH_2Cl_2 to give mesyl ester **17** (80.8% from **10**), and finally hydride displacement of mesyl ester **17** with LAH in refluxing Et_2O. As the formation of a hydrocarbon **18** could be determined by ^1H NMR spectroscopy after separation with a short silica gel column (eluted with hexane), crude alkene **18** was used for the next reaction without further purification.

Ozonolysis of alkene **18** with ozone gas in MeOH at −78 °C, followed by reduction of the ozonide with $NaBH_4$ in MeOH, produced a hemiacetal **19** (43.1% from mesyl ester **17**), which may be formed by the reaction of an intermediate during ozonolysis of alkene **18** with MeOH, instead of the desired diols **20a** and **20b**. The stereochemistry at C-7 of compound **19** was deduced from the coupling constant of 7-H (δ 4.56, d, *J* 10 Hz) with 6-H (δ 2.57, m). Reduction of the hemiacetal **19** was achieved with LAH in Et_2O to give diols **20a** and **20b** in 51.1 and 45.2% yield, respectively. The stereochemistry at C-1 of compound **20a** was deduced from the NOE between 1β-H (δ 5.31) and 1′-Me (δ 1.00) of monobenzoates **23a**.

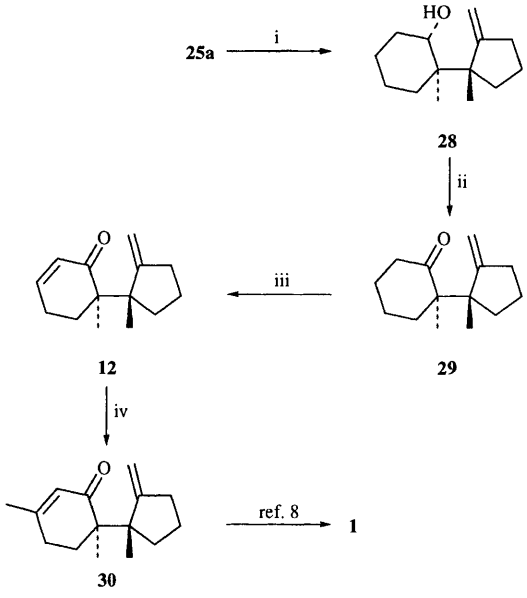
In order to form the *exo*-methylene moiety, functionalisation of the primary alcohol of diols **20a** and **20b** was examined with MsCl in pyridine and was found to give cyclic ethers **26a** and **26b**, instead of the corresponding monomesyl derivative, respectively. Hydroxy groups were thus protected as follows. Silylation of primary alcohols[11] **20a** and **20b** with *tert*-butyldimethylsilyl chloride (TBSCl) and diisopropylethylamine (DIPEA) in *N*,*N*-dimethylformamide (DMF), followed by esterification of the secondary alcohol groups of monosilyl ethers **21a** and **21b** with BzCl and pyridine in CH_2Cl_2 gave benzoates **22a** and **22b** in 94.6 and 79.9% yield, respectively. The removal of the silyl group from compound **22a** was carried out with 1% HCl in 95% EtOH (96.2%),[12] whereas deprotection of the silyl group of compound **22b** (in 90.2% yield) was carried out in AcOH–aq. tetrahydrofuran (THF),[13] necessitated by the insolubility of compound **22b** in EtOH. Reaction of benzoates **23a** and **23b** with MsCl and pyridine in CH_2Cl_2 gave mesyl esters **24a** and **24b** in 99.2 and 98.1% yields, respectively. Treatment of diesters **24a** and **24b** with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU)[14] in refluxing toluene afforded *exo*-methylene derivatives **25a** (91.3%) and **25b** (32.4%), respectively. The difference of yields between diastereoisomers **25a** and **25b** may be attributed to the steric hindrance of the benzoyl group which may disturb the nucleophilic attack of DBU at the 2′-position in the β-isomer **24b**.

Epimerisation of the secondary alcohol of the monosilyl ether **21b** was examined by two-step reactions as follows. Oxidation of compound **21b** with pyridinium chlorochromate (PCC)–alumina[15] in benzene gave the ketone **27** in 92.3% yield. Reduction of ketone **27** with LAH in dry Et_2O afforded the 1α-diol **20a** and 1β-diol **20b** in 48.6 and 44.8% yield respectively, with poor stereoselectivity (Scheme 4). The 1β-diol **20b** can be transformed into the 1α-diol **20a** by repeating these procedures.

With construction of the five-membered ring moiety of trichodiene **1** successfully accomplished, the modification of the functional groups in the cyclohexane ring of the intermediate **25a** was examined. Cleavage of the benzoyl group in **25a**, followed by oxidation of the product **28** with PCC–alumina[15] in CH_2Cl_2, gave the ketone **29**, which was converted into enone **12** by selenation at the α position of the ketone, using lithium diisopropylamide (LDA) in THF and benzeneselenenyl chloride (PhSeCl) in THF–hexamethylphosphoric triamide (HMPA), and subsequent elimination with H_2O_2 in CH_2Cl_2 (56.0%). Introduction of a methyl group at the β-position of enone **12** and re-introduction of the double bond was achieved by successive methylation with $(CH_3)_2CuLi$ in Et_2O, quenching of the resulting enolate anion with PhSeCl in Et_2O, and oxidation with H_2O_2 in CH_2Cl_2 to give enone **30** (42.9%) without separation of the intermediate. The ^1H and ^{13}C NMR, IR and mass spectra of compound **30** were identical with those of compound **30** as reported by Gilbert and Selliah.[8] As the synthesis of trichodiene **1** from compound **29** was published recently by the latter authors (Scheme 5),[8] this report constitutes another formal total synthesis of trichodiene **1**.



Scheme 4 *Reagents and conditions:* i, PCC-alumina, benzene; ii, $LiAlH_4$, Et_2O



Scheme 5 *Reagents and conditions:* i, $LiAlH_4$, Et_2O; ii, PCC-alumina, CH_2Cl_2; iii, (a) LDA, THF, −78 °C; (b) PhSeCl, HMPA, THF; (c) H_2O_2, pyridine, CH_2Cl_2; iv, (a) Me_2CuLi, Et_2O, 0 °C; (b) PhSeCl, Et_2O; (c) H_2O_2, pyridine, CH_2Cl_2

Experimental

NMR spectra were measured on a JEOL JNM-EX-270 spectrometer at 270 (^1H) and 68 (^{13}C) MHz for samples in $CDCl_3$ containing tetramethylsilane as internal standard. *J*-Values are in Hz. IR and UV spectra were measured on a JASCO IR-810 infrared spectrometer and a JASCO UVDEC-460 spectrometer, respectively. Mass spectra were recorded on a JEOL JMS-SX-102A spectrometer. Mps were measured on a MEL-TEMP (Laboratory Device) and are uncorrected; TLC was carried out on Kiesel-gel GF_{254} (0.25 mm thickness). Silica gel 60 (70–230 mesh ASTM) was used for column chromatography.

Methyl (1α,2β,7β,8α)-2-methyl-6-oxo-tricyclo[6.4.0.0^{2,7}]-dodecane-1-carboxylate 9

A toluene solution (50 cm^3) of 3-methylcyclohex-2-enone **4** (2.2 g, 20 mmol) and methyl cyclohex-1-enecarboxylate **8** (2.8 g, 20 mmol) was irradiated through a Pyrex glass vessel at −5 °C for 5 days under nitrogen, using a 100 W high-pressure Hg lamp. The reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography over silica gel [eluted with hexane–ethyl acetate (5:1)] to give the *photoadduct* **9** (3.0 g, 60.0%) as an oil (Found: M^+, 250.1568. $C_{15}H_{22}O_3$ requires *M*, 250.1569); ν_{max}(neat)/cm^{-1} 2940, 2862, 1721, 1693, 1450, 1430, 1302, 1240, 1220, 1151 and 1029; δ_H 3.72 (3 H, s, CO_2Me), 2.96 (1 H, ddd, *J* 11, 5 and 2, 8-H), 2.50 (1 H, d, *J* 11, 7-H), 2.43–2.25 (2 H, m), 2.06–1.86 (2 H, m), 1.79–1.49 (6 H, m), 1.45–1.25 (2 H, m), 1.14 (3 H, s, 2-Me) and 1.08–0.90 (2 H, m); δ_C 212.1, 176.0, 51.4, 50.4, 49.8, 45.1, 38.4, 37.0, 31.6, 27.7, 23.7, 21.8, 21.4, 21.3 and 20.7; *m/z* 250 (M^+, 7%), 218 (7), 190 (13), 152 (18), 140 (26), 112 (18) and 111 (100).

Methyl (1α,2β,6α,7β,8α)-6-hydroxy-2-methyltricyclo[6.4.0.0^{2,7}]-dodecane-1-carboxylate 13

A mixture of the photoadduct **9** (3.0 g, 12 mmol) and $NaBH_4$ (684 mg, 18 mmol) in MeOH (50 cm^3) was stirred at 0 °C for 4 h, and was then poured into brine. The mixture was extracted with ethyl acetate and the organic layer was washed with brine, dried ($MgSO_4$), and evaporated to afford compound **13** (3.02 g, 99.9%) as an oil (Found: M^+, 252.1767. $C_{15}H_{24}O_3$ requires *M*, 252.1725); ν_{max}(neat)/cm^{-1} 3430br, 2925, 2850, 1722, 1445, 1300, 1243, 1220, 1152, 1042 and 1020; δ_H 3.75 (1 H, ddd, *J* 11.5, 6 and 6, 6-H), 3.66 (3 H, s, CO_2Me), 2.73 (1 H, ddd, *J* 11.5, 2.5 and 2.5, 8-H), 2.24 (1 H, dd, *J* 11.5 and 6, 7-H), 2.01–1.52 (7 H, m), 1.47–0.90 (7 H, m) and 1.06 (3 H, s, 2-Me); δ_C 177.0, 69.0, 51.1, 49.9, 43.4, 42.1, 32.6, 31.1, 31.0, 27.9, 25.4, 22.1, 21.8, 20.9 and 20.4; *m/z* 252 (M^+, 3%), 193 (3), 175 (5), 141 (100) and 112 (20).

Methyl (1α,2β,6α,7β,8α)-2-methyl-6α-methylsulfonyloxy-tricyclo[6.4.0.0^{2,7}]dodecane-1-carboxylate 14 .

To a solution of the alcohol **13** (3.02 g, 11.98 mmol) in pyridine (15 cm^3) was added methanesulfonyl chloride (3 cm^3, 38.76 mmol) dropwise. The solution was stirred at ambient temperature for 18 h, then was diluted with brine (external cooling). The solution was extracted with ethyl acetate and the organic layer was washed successively with aq. 10% HCl, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated to give *mesyl ester* **14** (3.95 g, 99.9%) as yellow crystals, mp 89–90 °C (Found: M^+, 330.1485. $C_{16}H_{26}O_5S$ requires *M*, 330.1501); ν_{max}(KBr)/cm^{-1} 3850, 2933, 1718, 1444, 1350, 1225, 1160, 931 and 889; δ_H 4.80 (1 H, ddd, *J* 11.5, 6 and 6, 6-H), 3.66 (3 H, s, CO_2Me), 3.00 (3 H, s, OSO_2Me), 2.81 (1 H, ddd, *J* 11.5, 3 and 2.5, 8-H), 2.42 (1 H, dd, *J* 11.5 and 6, 7-H), 2.05–1.92 (2 H, m), 1.83–1.52 (7 H, m), 1.45–0.91 (5 H, m) and 1.08 (3 H, s, 2-Me); δ_C 176.4, 80.0, 51.2, 49.9, 44.4, 40.1, 38.6, 31.9, 31.6, 28.5, 27.7, 24.6, 21.8, 21.7, 20.6 and 20.3; *m/z* 330 (M^+, 35%), 235 (48), 175 (98) and 141 (100).

Methyl (1α,2β,6β)-2-methyltricyclo[6.4.0.0^{2,6}]dodec-7-ene-1-carboxylate 10

A solution of the mesyl ester **14** (3.9 g, 11.82 mmol) and AcOK (11.6 g, 118.2 mmol) in TFA (30 cm^3) was stirred at ambient temperature for 14 h and the mixture was then poured into brine and extracted with ethyl acetate. The extracts were washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was separated by column chromatography on silica gel [hexane–ethyl acetate (30:1)] to give the rearranged compound **10** (1.48 g, 53.5%) and isomer **15**. Compound **10** was a pale yellow oil (Found: M^+, 234.1579. $C_{15}H_{22}O_2$ requires *M*, 234.1620); ν_{max}(neat)/cm^{-1} 3036, 2950, 2860, 1728, 1442, 1250, 1220, 1148, 1089 and 1002; δ_H 5.20 (1 H, m, 7-H), 3.70 (3 H, s, CO_2Me), 2.59 (1 H, m, 6-H), 2.40–2.22 (3 H, m), 1.93–1.02 (11 H, m) and 1.13 (3 H, s, 2-Me); δ_C 175.9, 144.1, 127.7, 64.2, 56.1, 54.7, 51.0, 38.4, 35.3, 30.6, 28.7, 28.4, 25.3, 24.4 and 21.7; *m/z* 234 (M^+, 87%), 202 (48), 175 (100), 141 (25), 133 (22), 131 (20) and 105 (34).

Compound **15** was an oil (Found: M^+, 234.1626); ν_{max}(neat)/cm^{-1} 3020, 2930, 2860, 1725, 1457, 1448, 1302, 1247, 1223, 1209, 1154, 1128, 1092 and 1032; δ_H 5.74 and 5.73 (1 H each, each m, olefinic), 3.66 (3 H, s, CO_2Me), 2.24 (1 H, ddd, *J* 10, 5 and 4, 8-H), 2.24 (1 H, m, 7-H), 2.05–1.94 (3 H, m), 1.68–1.51 (6 H, m), 1.46–1.25 (2 H, m) and 1.04 (3 H, s, 2-Me); δ_C 176.7, 128.8, 127.1, 51.0, 49.4, 41.0, 40.2, 38.7, 29.1, 28.1, 24.0, 22.3, 21.8, 21.2 and 19.4; *m/z* 234 (M^+, 3), 229 (1), 202 (1), 175 (11), 152 (2), 141 (14), 105 (6) and 94 (100).

{(1α,2β,6β)-2-Methyltricyclo[6.4.0.0^{2,6}]dodec-7-en-1-yl}-methanol 16

To a cooled solution of compound **10** (1.48 g, 6.32 mmol) in dry Et_2O (40 cm^3) was added LAH (600 mg, 15.8 mmol). The mixture was stirred at ambient temperature for 40 h. A small amount of ethyl acetate was added carefully to the cooled

mixture to quench the excess of LAH. The mixture was poured into aq. 5% HCl and extracted with ethyl acetate. The extracts were washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed over silica gel [hexane–ethyl acetate (12:1)] to afford the *alcohol* **16** (1.06 g, 81.4%) as crystals, mp 58–59 °C (Found: M^+, 206.1658. $C_{14}H_{22}O$ requires *M*, 206.1671); ν_{max}(KBr)/cm^{-1} 3400br, 3020, 2950, 2858, 1470, 1440, 1018, 992 and 825; δ_H 5.17 (1 H, m, 7-H), 3.95 and 3.71 (2 H, AB_q, *J* 12, CH_2OH), 2.52 (1 H, m), 2.22 (1 H, m), 2.05–1.58 (9 H, m), 1.42–1.10 (4 H, m) and 1.07 (3 H, s, 2-Me); δ_C 145.8, 126.7, 62.7, 56.9, 54.5, 54.4, 36.8, 31.6, 31.0, 29.2, 27.6, 26.2, 24.1 and 22.3; *m/z* 206 (M^+, 18%), 176 (42), 175 (100), 147 (30), 133 (26), 131 (24) and 105 (43).

{(1α,2β,6β)-2-Methyltricyclo[6.4.0.0^{2,6}]dodec-7-en-1-yl}methyl methanesulfonate 17

To a solution of alcohol **16** (1.06 g, 5.14 mmol) in pyridine (3 cm^3, 37.1 mmol) and CH_2Cl_2 (5 cm^3) was added methanesulfonyl chloride (1.2 cm^3, 15.5 mmol) dropwise. After being stirred at ambient temperature for 16 h, the solution was diluted with ice-cooled brine. The mixture was extracted with ethyl acetate. The organic extract was washed successively with aq. 10% HCl, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated to give *mesyl ester* **17** (1.45 g, 99.3%) as a yellow oil (Found: M^+, 284.1419. $C_{15}H_{24}O_3S$ requires *M*, 284.1446); ν_{max}(neat)/cm^{-1} 3030, 2945, 2867, 1445, 1352, 1173, 941 and 830; δ_H 5.20 (1 H, m, 7-H), 4.68 and 4.20 (2 H, AB_q, *J* 10, CH_2OMs), 3.02 (3 H, s, OSO_2Me), 2.59 (1 H, m), 2.26 (1 H, m), 2.10–1.55 (9 H, m), 1.47–1.10 (4 H, m) and 1.08 (3 H, s, 2-Me); δ_C 143.8, 128.3, 69.9, 56.1, 54.8, 52.9, 37.2, 36.6, 32.0, 30.0, 29.3, 27.3, 25.5, 22.5 and 21.8; *m/z* 284 (M^+, 8%), 220 (11), 202 (10), 188 (70), 175 (100), 145 (58), 131 (50) and 105 (40).

(1α,2β,6β)-1,2-Dimethyltricyclo[6.4.0.0^{2,6}]dodec-7-ene 18

A mixture of mesyl ester **17** (1.45 g, 5.11 mmol) and LAH (580 mg, 15.3 mmol) in dry Et_2O (50 cm^3) was heated to reflux for 38 h under argon. After work-up as described for compound **16**, the product was separated by a short column of silica gel (eluted with hexane) to give the hydrocarbon **18** (620 mg) as a crude, pale yellow oil; δ_H 5.01 (1 H, m, 7-H), 2.54 (1 H, m, 6-H), 2.24–1.02 (14 H, m) and 0.98 and 0.94 (3 H each, each s, 1- and 2-Me).

(1α,2β,6β)-7β-Methoxy-1,2-dimethyl-8-oxatricyclo[7.4.0.0^{2,6}]-tridecan-9-ol 19

Ozone gas was introduced into a MeOH (60 cm^3) solution of crude hydrocarbon **18** (620 mg) at −78 °C until a blue colour persisted. Excess of ozone was expelled with a stream of argon, the solution was treated with $NaBH_4$ (500 mg, 13.2 mmol), and was then stirred for 4 h at ambient temperature. The solution was then extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a silica gel column [hexane–ethyl acetate (10:1)] to afford the *hemiacetal* **19** (589 mg, 43.1% from **18**) as crystals, mp 95–96 °C (Found: M^+, 254.1879. $C_{14}H_{26}O_2$ requires *M*, 254.1882); ν_{max}(KBr)/cm^{-1} 3400, 2930, 2850, 1441, 1400, 1372, 1160, 1100, 1075, 1018, 980, 940 and 870; δ_H 4.56 (1 H, d, *J* 10, 7-H), 3.46 (3 H, s, OMe), 2.57 (1 H, m, 6-H), 1.93–1.12 (14 H, m) and 1.05 and 0.82 (3 H each, each s, 1- and 2-Me); δ_C 101.1, 99.6, 56.2, 49.7, 47.0, 40.0, 38.5, 33.7, 33.0, 25.0, 22.7, 21.9, 21.5, 20.2 and 15.8; *m/z* 254 (M^+, 14%), 236 (10), 222 (98), 172 (20), 135 (87),121 (70) and 112 (100).

(1α)-2β-(2α-Hydroxymethyl-1β-methylcyclopentyl)-2α-methylcyclohexanol 20a and (1β)-2β-(2α-hydroxymethyl-1β-methylcyclopentyl)-2α-methylcyclohexanol 20b

To a solution of hemiacetal **19** (585 mg, 2.30 mmol) in cooled, dry Et_2O (30 cm^3) was added LAH (260 mg, 6.85 mmol). The mixture was stirred at ambient temperature for 20 h. After work-up as described for compound **16**, the products were separated by chromatography on a silica gel column [hexane–ethyl acetate (2:1)] to give epimeric diols **20a** (266 mg, 51.1%) and **20b** (235 mg, 45.2%) respectively, as crystalline solids. *Diol* **20a**, mp 106–107 °C (Found: M^+, 226.1949. $C_{14}H_{26}O_2$ requires *M*, 226.1933); ν_{max}(KBr)/cm^{-1} 3340br, 2940, 2867, 1448, 1373, 1055, 1043 and 992; δ_H 4.42 (1 H, br, OH), 3.93 (1 H, dd, *J* 10.5 and 8, 1-H), 3.78 (1 H, dd, *J* 11 and 4, CH_2OH), 3.34 (1 H, dd, *J* 11 and 4, CH_2OH), 2.12–1.95 (2 H, m), 1.84–1.10 (14 H, m) and 1.06 and 1.03 (3 H each, each s, 2- and 1′-Me); δ_C 72.9, 65.5, 53.9, 51.2, 44.1, 34.2, 33.1, 31.9, 30.8, 24.9, 23.4, 21.0, 20.3 and 12.2; *m/z* 226 (M^+, 1%), 208 (54), 149 (30), 135 (40), 123 (75) and 112 (100).

Compound **20b** mp 120–121 °C (Found: M^+, 226.1917); ν_{max}(KBr)/cm^{-1} 3340br, 2940, 2888, 1452, 1380, 1310, 1252, 1145, 1016 and 968; δ_H 3.93 (1 H, dd, *J* 10 and 3, CH_2OH), 3.77 (1 H, m, 1-H), 3.22 (1 H, dd, *J* 10 and 10, CH_2OH), 1.95–1.08 (16 H, m) and 1.04 (3 H each, each s, 2- and 1′-H); δ_C 73.1, 64.7, 52.8, 52.3, 41.4, 32.7, 30.1, 27.8, 25.1, 22.1, 21.4, 21.3, 19.6 and 17.9; *m/z* 226 (M^+, 3%), 208 (84), 182 (30), 149 (42), 135 (90), 123 (90) and 112 (100).

(1α,2β,6β,9β)-1,2-Dimethyl-8-oxatricyclo[7.4.0.0^{2,6}]tridecane 26a

To a solution of diol **20a** (20 mg, 0.088 mmol) and CH_2Cl_2 (1 cm^3)–pyridine (0.01 cm^3, 0.12 mmol) was added methanesulfonyl chloride (8 μg, 0.1 mmol) dropwise. After being stirred at 0 °C for 2 h, the solution was diluted with ice-cooled brine. The mixture was extracted with ethyl acetate. The organic extract was treated as described for compound **17** to give *compound* **26a** (13 mg, 71.0%) as an oil (Found: M^+, 208.1831. $C_{14}H_{24}O$ requires *M*, 208.1827); ν_{max}(neat)/cm^{-1} 2940, 2875, 1468, 1450, 1372 and 1120; δ_H 3.83 (1 H, dd, *J* 11 and 2, 7-H), 3.78 (1 H, dd, *J* 12 and 4, 9-H), 3.23 (1 H, dd, *J* 11 and 4.5, 7-H), 1.99–1.25 (13 H, m), 1.08–0.62 (2 H, m) and 1.09 and 1.01 (3 H each, each s, 1- and 2-Me); δ_C 78.4, 67.3, 49.0, 45.2, 38.7, 36.8, 31.9, 31.5, 27.5, 25.3, 24.9, 23.2, 20.7 and 14.8; *m/z* 208 (M^+, 98%), 193 (23), 179 (12), 165 (13), 151 (10), 139 (14), 123 (30), 113 (58) and 112 (100).

(1α,2β,6β,9α)-1,2-Dimethyl-8-oxatricyclo[7.4.0.0^{2,6}]tridecane 26b

The diol **20b** (20 mg) gave compound **26b** (15 mg, 81.9%) by the procedure described for its isomer **26a**. *Compound* **26b** was obtained as an oil (Found: M^+, 208.1829); ν_{max}(neat)/cm^{-1} 2940, 2865, 1468, 1462, 1384 and 1105; δ_H 3.66 (1 H, dd, *J* 11.5 and 6.5, 7-H), 3.41 (1 H, br s, 9-H), 3.09 (1 H, dd, *J* 11.5 and 11.5, 7-H), 2.00–1.01 (15 H, m) and 0.82 and 0.79 (3 H each, each s, 1- and 2-Me); δ_C 75.8, 69.4, 47.9, 41.9, 35.8, 29.91, 28.61, 27.8, 25.3, 21.4, 20.0, 19.8, 19.7 and 16.5; *m/z* 208 (M^+, 100%), 193 (61), 179 (28), 165 (29), 149 (22), 139 (17), 123 (61), 113 (50) and 112 (100).

(1α)-2β-[2α-(*tert*-Butyldimethylsiloxymethyl)-1β-methylcyclopentyl]-2α-methylcyclohexanol 21a

To a solution of diol **20a** (266 mg, 1.18 mmol) in DMF (5 cm^3) was added DIPEA (0.22 cm^3, 2.4 mmol) and TBDMSCl (266 mg, 1.76 mmol) and the mixture was stirred at ambient temperature for 3 h. An excess of water was added to the solution, which was extracted with hexane. The extracts were washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on silica gel [hexane–ethyl acetate (15:1)] to give the *monosilylated ether* **21a** (391 mg, 97.7%) as an oil (Found: M^+, 340.2841. $C_{20}H_{40}O_2Si$ requires *M*, 340.2798); ν_{max}(neat)/cm^{-1} 3440br, 2935, 2860, 1470, 1382, 1253, 1056, 835 and 773; δ_H 3.90 (1 H, dd, *J* 10 and 8, $CH_2OTBDMS$), 3.74 (1 H, m, 1-H), 3.50 (1 H, dd, *J* 10 and 5, CH_2OTBS), 2.93 (1 H, br s, 1-OH), 2.08–1.05 (15 H, m), 1.01 (6 H, s, 2- and 1′-Me), 0.89 (9 H, s, $OSiMe_2Bu^t$) and 0.05 and 0.04 (3 H each, each s, $OSiMe_2Bu^t$); δ_C 73.0, 66.2, 53.6, 51.6, 44.1, 34.2, 33.4, 32.0, 29.9, 25.9, 25.0,

23.6, 21.2, 20.4, 18.3, 12.9 and −5.5; *m/z* 340 (M^+, 2%), 283 (22), 265 (12), 227 (40), 191 (84), 169 (98), 149 (27), 135 (80), 123 (99), 109 (100) and 105 (100).

(1β)-2β-[2α-(*tert*-Butyldimethylsiloxymethyl)-1β-methylcyclopentyl]-2α-methylcyclohexanol 21b

The diol **20b** (220 mg, 0.97 mmol) gave the monosilyl ether **21b** (317 mg, 95.8%) by the procedure described for compound **21a**. *Silyl ether* **21b** was obtained as a crystalline solid, mp 55–56 °C (Found: M^+, 340.2812); ν_{max}(KBr)/cm^{-1} 3340br, 2950, 2860, 1468, 1383, 1250, 1145, 1120, 1050, 993, 880, 834 and 772; δ_H 3.79–3.70 (2 H, m, 1-H and CH_2OTBDMS), 3.31 (1 H, dd, *J* 9 and 9, CH_2OTBDMS), 1.93–1.12 (14 H, m), 1.01 and 0.98 (3 H each, each s, 2- and 1′-Me), 0.88 (9 H, s, $OSiMe_2Bu^t$) and 0.03 (6 H, s, $OSiMe_2Bu^t$); δ_C 73.1, 65.0, 52.4, 52.1, 41.5, 32.9, 30.1, 27.7, 26.0, 25.3, 22.2, 21.5, 21.4, 19.6, 18.3, 18.0, −5.2 and −5.3; *m/z* 340 (M^+, 1%), 307 (1), 283 (13), 265 (7), 258 (4), 227 (41), 191 (76), 169 (75), 149 (34), 135 (85), 123 (81), 109 (100) and 105 (100).

(1α)-2β-[2α-(*tert*-Butyldimethylsiloxymethyl)-1β-methylcyclopentyl]-2α-methylcyclohexyl benzoate 22a

To a solution of the monosilyl ether **21a** (390 mg, 1.15 mmol) and pyridine (0.28 cm^3) in CH_2Cl_2 (3 cm^3) was added benzoyl chloride (0.2 cm^3, 1.74 mmol) dropwise. The solution was stirred at ambient temperature for 15 h and then an excess of water was added to the solution. The mixture was extracted with ethyl acetate. The organic extract was washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a silica gel column [hexane–ethyl acetate (25:1)] to yield *benzoate* **22a** as an oil (Found: M^+, 444.3061. $C_{27}H_{44}O_3Si$ requires *M*, 444.3060); ν_{max}(neat)/cm^{-1} 3060, 2945, 2860, 1714, 1600, 1468, 1450, 1268, 1107, 1065, 832, 772 and 705; λ_{max}(hexane)/nm 228; δ_H 8.03–7.39 (5 H, m, ArH), 5.30 (1 H, dd, *J* 10.5 and 4.5, 1-H), 3.87 (1 H, dd, *J* 9 and 4, CH_2OTBDMS), 3.67 (1 H, dd, *J* 9 and 7, CH_2OTBDMS), 1.99–1.13 (15 H, m), 1.25 and 0.99 (3 H each, each s, 2- and 1′-H), 0.88 (9 H, s, $OSiMe_2Bu^t$) and 0.05 and 0.01 (3 H each, each s, $OSiMe_2Bu^t$); δ_C 165.8, 132.7, 131.2, 129.5, 128.3, 76.8, 65.1, 52.9, 52.2, 42.7, 34.1, 33.5, 28.5, 28.2, 26.0, 24.6, 24.0, 21.2, 20.6, 18.3, 15.7, −5.3 and −5.4; *m/z* 444 (M^+, 1%), 265 (14), 227 (22), 191 (37), 180 (33), 179 (99), 169 (30), 135 (26), 109 (76) and 105 (100).

(1β)-2β-[2α-(*tert*-Butyldimethylsiloxymethyl)-1β-methylcyclopentyl]-2α-methylcyclohexyl benzoate 22b

The monosilyl ether **21b** (313 mg, 0.92 mmol) gave the benzoate **22b** (341 mg, 83.4%) as a crystalline solid by the procedure described for compound **22a**. *Compound* **22b** had mp 87–88 °C (Found: M^+, 444.3043); ν_{max}(KBr)/cm^{-1} 3070, 2940, 2858, 1712, 1470, 1275, 1256, 1118, 1069, 935, 877, 835, 775 and 708; λ_{max}(hexane)/nm 224; δ_H 8.13–7.14 (5 H, m, ArH), 5.17 (1 H, m, 1-H), 3.81 (1 H, dd, *J* 9.5 and 3.5, CH_2OTBDMS), 3.37 (1 H, dd, *J* 9.5 and 9.5, CH_2OTBDMS), 2.18–1.20 (14 H, m), 1.16 and 0.86 (3 H each, each s, 2- and 1′-Me), 0.91 (9 H, s, $OSiMe_2Bu^t$) and 0.06 (6 H, s, $OSiMe_2Bu^t$); δ_C 165.3, 132.8, 131.1, 129.7, 128.4, 76.3, 64.9, 52.2, 52.1, 41.0, 32.2, 28.8, 26.6, 26.0, 25.2, 22.2, 21.3, 20.4, 18.3, 17.6, −5.2 and −5.3; *m/z* 444 (M^+, 6%), 410 (1), 387 (2), 281 (7), 265 (6), 227 (18), 191 (52), 179 (100), 169 (20), 135 (15) and 105 (80).

(1α)-2β-(2α-Hydroxymethyl-1β-methylcyclopentyl)-2α-methylcyclohexyl benzoate 23a

Conc. aq. HCl (0.3 cm^3) was added dropwise to a solution of silyl ether **22a** (491 mg, 1.11 mmol) in 95% EtOH (10 cm^3). After being stirred at ambient temperature for 30 min, the mixture was poured into brine, and extracted with ethyl acetate. The extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was subjected to chromatography on a silica gel column [hexane–ethyl acetate (4:1)] to afford the *monoalcohol* **23a** (351 mg, 96.2%) as an oil (Found: M^+, 330.2183. $C_{21}H_{30}O_3$ requires *M*, 330.2195); ν_{max}(neat)/cm^{-1} 3450br, 2940, 2875, 1708, 1600, 1449, 1312, 1275, 1110, 1022, 753 and 710; λ_{max}(EtOH)/nm 232; δ_H 8.07–7.40 (5 H, m, ArH), 5.31 (1 H, dd, *J* 10 and 4.5, 1-H), 4.12 (1 H, dd, *J* 10 and 4, CH_2OH), 3.43 (1 H, dd, *J* 10 and 10, CH_2OH), 1.98–1.22 (15 H, m), 1.19 (3 H, s, 2-Me) and 1.00 (3 H, s, 1′-Me); δ_C 165.9, 132.9, 131.0, 129.4, 128.5, 76.6, 64.7, 53.4, 52.4, 42.7, 34.1, 32.9, 28.5, 27.5, 24.5, 23.6, 21.1, 20.2 and 16.1; *m/z* 330 (M^+, 1%), 312 (2), 208 (13), 190 (7), 149 (10), 123 (21) and 105 (100).

(1β)-2β-(2α-Hydroxymethyl-1β-methylcyclopentyl)-2α-methylcyclohexyl benzoate 23b

A solution of the siloxy benzoate **22b** (337 mg, 0.76 mmol) in THF (3 cm^3), water (1 cm^3) and AcOH (1 cm^3) was stirred at 50–60 °C for 2 h. An excess of water was added to the solution which was then extracted with ethyl acetate. The extracts were washed successively with aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed over silica gel [hexane–ethyl acetate (4:1)] to afford the *monoalcohol* **23b** (226 mg, 90.2%) as a crystalline solid, mp 88–89 °C (Found: M^+, 330.2196); ν_{max}(KBr)/cm^{-1} 3300br, 2945, 2880, 1708, 1448, 1310, 1270, 1096, 1020 and 710; λ_{max}(EtOH)/nm 226; δ_H 8.13–7.41 (5 H, m, ArH), 5.15 (1 H, m, 1-H), 3.98 (1 H, dd, *J* 10 and 3, CH_2OH), 3.26 (1 H, dd, *J* 10 and 10, CH_2OH), 2.18–1.20 (14 H, m) and 1.16 and 0.87 (3 H each, each s, 2- and 1′-Me); δ_C 165.3, 132.8, 130.9, 129.7, 128.4, 76.2, 64.5, 52.6, 52.2, 40.9, 32.1, 28.9, 26.5, 25.5, 22.1, 21.3, 21.2, 20.3 and 17.5; *m/z* 330 (M^+, 15%), 312 (41), 256 (38), 217 (24), 208 (59), 190 (35), 175 (24), 149 (65), 137 (77), 123 (94) and 105 (100).

(1α)-2α-Methyl-2β-(1β-methyl-2α-methylsulfonyloxymethylcyclopentyl)cyclohexyl benzoate 24a

To a solution of the monoalcohol **23a** (350 mg, 1.06 mmol) and pyridine (0.3 cm^3, 3.7 mmol) in CH_2Cl_2 (3 cm^3) was added dropwise methanesulfonyl chloride (0.2 cm^3, 2.58 mmol). After being stirred at ambient temperature for 14 h, the mixture was treated as described for compound **17**. Removal of the solvent gave the *mesyl ester* **24a** (429 mg, 99.2%) as a yellow oil (Found: M^+, 408.1941. $C_{22}H_{32}O_5S$ requires *M*, 408.1970); ν_{max}(neat)/cm^{-1} 3060, 2940, 2878, 1736, 1710, 1449, 1352, 1332, 1270, 1173, 1105, 934 and 713; λ_{max}(EtOH)/nm 227; δ_H 8.07–7.42 (5 H, m, ArH), 5.34 (1 H, dd, *J* 10.5 and 5, 1-H), 4.73 (1 H, m, CH_2OMs), 4.07 (1 H, dd, *J* 10 and 8.5, CH_2OMs), 2.79 (3 H, s, OSO_2Me), 1.98–1.20 (15 H, m) and 1.19 and 1.07 (3 H each, each s, 2- and 1′-Me); δ_C 165.9, 132.9, 130.9, 129.6, 128.6, 76.4, 71.9, 52.9, 49.6, 42.9, 37.3, 34.2, 32.8, 28.3, 28.0, 24.4, 23.5, 20.9, 19.7 and 15.6; *m/z* 408 (M^+, 1%), 313 (13), 312 (10), 217 (95), 190 (78), 175 (35), 149 (26), 135 (26), 121 (49) and 105 (100).

(1β)-2α-Methyl-2β-(1β-methyl-2α-methylsulfonyloxymethylcyclopentyl)cyclohexyl benzoate 24b

The monoalcohol **23b** (225 mg, 0.68 mmol) gave the mesyl ester **24b** (273 mg, 98.1%) by the method described for isomer **24a**. *Compound* **24b** was isolated as a yellow oil (Found: M^+, 408.1940); ν_{max}(neat)/cm^{-1} 3070, 2980, 2940, 2865, 1734, 1703, 1600, 1450, 1353, 1270, 1170, 1112, 996, 938 and 714; λ_{max}(EtOH)/nm 227; δ_H 8.12–7.43 (5 H, m, ArH), 5.16 (1 H, m, 1-H), 4.59 (1 H, dd, *J* 9 and 2.5, CH_2OMs), 3.90 (1 H, dd, *J* 10.5 and 9, CH_2OMs), 3.03 (3 H, s, OSO_2Me), 2.20–1.22 (14 H, m) and 1.18 and 0.91 (3 H each, each s, 2- and 1′-Me); δ_C 165.1, 132.9, 130.8, 129.6, 128.5, 75.9, 71.8, 52.9, 49.0, 40.8, 37.7, 32.0, 29.1, 26.4, 25.2, 21.9, 21.2, 20.9, 20.1 and 17.6; *m/z* 408 (M^+, 1%), 386 (1), 368 (2), 341 (1), 313 (10), 312 (10), 256 (3), 217 (53), 190 (72), 175 (21), 121 (21) and 105 (100).

(1α)-2α-Methyl-2β-(1β-methyl-2-methylenecyclopentyl)cyclohexyl benzoate 25a

A solution of mesyl ester **24a** (425 mg, 1.04 mmol) and DBU (0.8 cm^3, 5.35 mmol) in toluene (15 cm^3) was heated to reflux for 72 h under argon. The reaction mixture was cooled to room temperature, diluted with aq. 5% HCl, and then extracted with hexane. The organic extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a silica gel column [hexane–ethyl acetate (30:1)] to give compound **25a** (297 mg, 91.3%) as a crystalline solid, mp 60–61 °C (Found: M^+, 312.2097. $C_{21}H_{28}O_2$ requires *M*, 312.2089); ν_{max}(KBr)/cm^{-1} 3070, 2945, 2863, 1714, 1640, 1450, 1312, 1270, 1105, 1067, 1023, 884 and 710; λ_{max}(hexane)/nm 228; δ_H 8.07–7.39 (5 H, m, ArH), 5.25 (1 H, dd, *J* 10.5 and 5, 1-H), 4.97 and 4.83 (1 H each, each m, olefinic), 2.35–1.12 (14 H, m) and 1.32 and 1.08 (3 H each, each s, 2- and 1′-Me); δ_C 165.5, 160.4, 132.7, 131.0, 129.6, 128.4, 106.7, 77.8, 51.1, 42.4, 38.7, 37.5, 32.6, 28.2, 26.6, 24.7, 23.2, 21.4 and 13.2; *m/z* 312 (M^+, 1%), 217 (50), 216 (33), 190 (69), 175 (31), 161 (11), 147 (10), 121 (20) and 105 (100).

(1β)-2α-Methyl-2β-(1β-methyl-2-methylenecyclopentyl)cyclohexyl benzoate 25b

The mesyl ester **24b** (270 mg, 0.66 mmol) gave compound **25b** (67 mg, 32.4%) by the method described for isomer **25a**. *Compound* **25b** was an oil (Found: M^+, 312.2091); ν_{max}(neat)/cm^{-1} 3070, 2945, 2865, 1712, 1600, 1448, 1267, 1170, 1106, 1065, 1021 and 710; λ_{max}(hexane)/nm 229; δ_H 8.13–7.38 (5 H, m, ArH), 5.30 (1 H, m, 1-H), 4.96 and 4.76 (1 H each, each m, olefinic), 2.35–0.80 (14 H, m) and 1.08 and 1.07 (3 H each, each s, 2- and 1′-Me); δ_C 165.7, 160.2, 132.8, 131.2, 129.7, 128.3, 107.5, 74.6, 50.6, 41.7, 38.7, 37.8, 28.0, 27.3, 25.7, 23.3, 21.3, 20.2 and 18.8; *m/z* 312 (M^+, 4%), 217 (56), 190 (65), 175 (13), 161 (5), 147 (4), 133 (4), 121 (5) and 105 (100).

2β-[2α-(*tert*-Butyldimethylsiloxymethyl)-1β-methylcyclopentyl]-2α-methylcyclohexanone 27

PCC on alumina (1 g, 0.93 mmol) was added to a solution of the monosilyl ether **21b** (48 mg, 0.14 mmol) in benzene (5 cm^3). The mixture was then stirred at ambient temperature for 6 h, after which Et_2O was added. The solid residue was removed by filtration and washed with Et_2O. The organic phase was concentrated and the residue was chromatographed on a silica gel column [hexane–ethyl acetate (30:1)] to give the *ketone* **27** (44 mg, 92.3%) as an oil (Found: M^+, 338.2628. $C_{20}H_{38}O_2Si$ requires *M*, 338.2641); ν_{max}(neat)/cm^{-1} 2950, 2860, 1700, 1471, 1458, 1380, 1252, 1070, 833 and 772; δ_H 3.35 (1 H, dd, *J* 9.5 and 4.5, C*H*$_2$OTBDMS), 3.21 (1 H, dd, *J* 9.5 and 9.5, C*H*$_2$OTBDMS), 2.60–2.23 (3 H, m), 2.00–1.51 (11 H, m), 1.26 (1 H, m), 1.18 and 0.94 (3 H each, each s, 2- and 1′-Me), 0.87 (9 H, s, OSiMe$_2$*Bu*^{t}) and 0.02 (6 H, s, OSi*Me*$_2$Bu^t); δ_C 215.7, 66.1, 52.5, 51.7, 50.9, 40.0, 35.2, 35.1, 29.0, 26.3, 26.0, 25.4, 22.2, 21.9, 21.4, 18.3 and −5.22; *m/z* 338 (M^+, 1%), 323 (5), 282 (59), 281 (59), 241 (5), 226 (6), 199 (72), 189 (46), 169 (100), 131 (20) and 112 (38).

(1α)-2β-(2α-Hydroxymethyl-1β-methylcyclopentyl)-2α-methylcyclohexanol 20a and (1β)-2β-(2α-hydroxymethyl-1β-methylcyclopentyl)-2α-methylcyclohexanol 20b (alternative preparation)

LAH (20 mg, 0.53 mmol) was added to an ice-cooled solution of the ketone **27** (40 mg, 0.12 mmol) in dry Et_2O (5 cm^3). After being stirred at ambient temperature for 10 h, the mixture was treated as usual. The products were separated by chromatography on a silica gel column [hexane–ethyl acetate (2:1)] to give the diols **20a** (13 mg, 48.6%) and **20b** (12 mg, 44.8%) as crystals.

(1α)-2α-Methyl-2β-(1β-methyl-2-methylenecyclopentyl)cyclohexanol 28

LAH (100 mg, 2.64 mmol) was added to an ice-cooled solution of benzoate **25a** (295 mg, 0.95 mmol) in dry Et_2O (15 cm^3). The mixture was stirred at ambient temperature for 8 h. After the usual procedures, the product was purified by chromatography on a silica gel column [hexane–ethyl acetate (20:1)] to afford the *alcohol* **28** (182 mg, 92.5%) as crystals, mp 42–43 °C (Found: M^+, 208.1834. $C_{14}H_{24}O$ requires *M*, 208.1827); ν_{max}(KBr)/cm^{-1} 3310br, 3075, 2930, 2864, 1640, 1473, 1445, 1360, 1140, 1058, 1046, 941 and 878; δ_H 4.97 and 4.87 (1 H each, each m, olefinic), 3.78 (1 H, dd, *J* 11.5 and 4.5, 1-H), 2.41–2.14 (4 H, m), 1.80–0.82 (10 H, m) and 1.17 and 1.02 (3 H each, each s, 2- and 1′-Me); δ_C 161.8, 106.6, 74.4, 51.2, 43.3, 38.9, 37.7, 32.6, 32.2, 26.2, 25.1, 23.2, 21.5 and 11.9; *m/z* 208 (M^+, 14%), 190 (27), 175 (21), 147 (10), 135 (12), 121 (54), 112 (100) and 113 (100).

2α-Methyl-2β-(1β-methyl-2-methylenecyclopentyl)cyclohexanone 29

PCC on alumina (4 g, 3.71 mmol) was added to a solution of the alcohol **28** (180 mg, 0.87 mmol) in CH_2Cl_2 (5 cm^3). The mixture was stirred at ambient temperature for 3 h. The solid residue was removed by filtration and washed with Et_2O. The organic phase was concentrated and the residue was chromatographed on a silica gel column [hexane–ethyl acetate (15:1)] to give *ketone* **29** (157 mg, 88.1%) as an oil (Found: M^+, 206.1656. $C_{14}H_{22}O$ requires *M*, 206.1671); ν_{max}(neat)/cm^{-1} 3075, 2945, 2863, 1700, 1638, 1461, 1445, 1362, 1115, 1050 and 880; δ_H 4.93 and 4.81 (1 H each, each m, olefinic), 2.52–2.20 (4 H, m), 1.98–1.30 (10 H, m) and 1.25 and 1.20 (3 H each, each s, 2- and 1′-Me); δ_C 215.6, 160.5, 106.5, 54.1, 49.4, 39.9, 38.9, 38.4, 33.9, 25.5, 25.1, 23.4, 20.9 and 19.3; *m/z* 206 (M^+, 19%), 191 (8), 177 (8), 163 (10), 152 (10), 135 (9), 121 (20) and 112 (100).

6α-Methyl-6β-(1β-methyl-2-methylenecyclopentyl)cyclohex-2-enone 12

To a solution of LDA [prepared from diisopropylamine (0.3 cm^3, 2.13 mmol) and butyllithium (1.1 cm^3 of a 1.68 mol dm^{-3} solution, 1.85 mmol) in dry THF (5 cm^3)] was added a solution of the ketone **29** (155 mg, 0.75 mmol) in dry THF (4 cm^3) at −78 °C under argon. The mixture was stirred at −78 °C for 20 min and then a solution of benzeneselenenyl chloride (220 mg, 1.15 mmol) and HMPA (0.1 cm^3) in dry THF (0.5 cm^3) was added to the mixture *via* a cannula. The mixture was stirred at −78 °C for an additional 1 h and quenched at the same temperature with aq. 3% HCl. The reaction mixture was allowed to warm to room temperature and was then extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), and evaporated. The yellow residue was dissolved in CH_2Cl_2 (5 cm^3) and treated with 30% H_2O_2 (0.5 cm^3) in the presence of pyridine (0.5 cm^3). After being stirred at ambient temperature for 1 h, the solution was partitioned between Et_2O and water. The organic solution was washed successively with aq. 3% HCl and saturated aq. $NaHCO_3$, dried ($MgSO_4$), and evaporated. The residue was chromatographed on a silica gel column [hexane–ethyl acetate (40:1)] to give the *enone* **12** (86 mg, 56.0%) as an oil (Found: M^+, 204.1484. $C_{14}H_{20}O$ requires *M*, 204.1514); ν_{max}(neat)/cm^{-1} 3078, 3035, 2955, 2870, 1668, 1642, 1461, 1433, 1380, 1290, 1218, 1070, 882 and 815; λ_{max}(EtOH)/nm 226; δ_H 6.87 (1 H, m, 3-H), 5.84 (1 H, ddd, *J* 10, 2.5 and 1.5, 2-H), 4.93 and 4.83 (1 H each, each m, olefinic), 2.48–1.38 (10 H, m) and 1.33 and 1.23 (3 H each, each s, 2- and 1′-Me); δ_C 204.2, 160.5, 147.4, 130.3, 106.3, 49.9, 49.4, 39.0, 38.4, 30.1, 26.0, 23.4, 23.3 and 17.2; *m/z* 204 (M^+, 14%), 189 (1), 175 (1), 161 (1), 144 (3), 121 (5) and 110 (100).

3,6α-Dimethyl-2β-(1β-methyl-2-methylenecyclopentyl)cyclohex-2-enone 30

Methyllithium (2.6 cm^3 of a 1.2 mol dm^{-3} solution, 3.12 mmol) was added to a mixture of CuI (360 mg, 1.89 mmol) and dry Et_2O (5 cm^3) at 0 °C under argon. To the mixture was added a solution of the enone **12** (85 mg, 0.42 mmol) in dry Et_2O (4 cm^3) and the mixture was stirred at 0 °C for 4 h. A solution of

benzeneselenenyl chloride (120 mg, 0.63 mmol) in dry Et_2O (0.5 cm^3) was added to the solution *via* a cannula. After being stirred at 0 °C for an additional 1 h, the mixture was poured into saturated aq. NH_4Cl, and extracted with Et_2O. The extracts were washed successively with saturated aq. NH_4Cl and brine, dried ($MgSO_4$), and evaporated. The residue was subjected to oxidation and work-up as described for compound **12**. The product was separated by chromatography on a silica gel column [hexane–ethyl acetate (35:1)] to give the *enone* **30** (39 mg, 42.9%) as an oil (Found: M^+, 218.1676. $C_{15}H_{22}O$ requires *M*, 218.1671); ν_{max}(neat)/cm^{-1} 3075, 2950, 2870, 1662, 1640, 1433, 1375, 1306, 1210, 1070 and 983; λ_{max}(EtOH)/nm 233; δ_H 5.69 (1 H, s, 2-H), 4.91 and 4.81 (1 H each, each m, olefinic), 2.42–1.94 (6 H, m), 1.89 (3 H, s, 3-Me), 1.88–1.38 (4 H, m) and 1.32 and 1.19 (3 H each, each s, 2- and 1′-Me); δ_C 204.2, 160.7, 159.0, 127.2, 106.2, 49.4, 48.5, 39.0, 38.4, 30.3, 28.4, 26.1, 23.8, 23.4 and 17.4; *m*/*z* 218 (M^+, 13%), 188 (3), 175 (6), 173 (3), 145 (3), 131 (3), 124 (100) and 109 (28).

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