Total Synthesis of (+)-Dihydrocompactin

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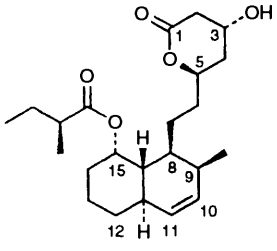
The total synthesis of (+)-dihydrocompactin **1** has been achieved by employing double Michael reaction of 3-(*tert*-butyldimethylsiloxy)-1-acetylcyclohexene **13** with methyl crotonate and the $TiCl_4$-promoted aldol condensation of the bis(trimethylsilyl enol ether) of methyl acetoacetate **7** as key reactions.

The major cause of death among other geriatric diseases in western countries is cardiac infarction or angina pectoris due to coronary sclerosis. Hypercholesterolaemia is one of the major factors causing such coronary heart disease. In fact, when the concentration of cholesterol exceeds the normal upper level (2.2 mg cm^{-3}), the rate of coronary heart disease increases with an increase in the concentration of cholesterol in blood.[1] Since, in human bodies, more than 70% of the total input of cholesterol is biosynthesized from acetyl-CoA in over twenty steps, control of biosynthesis of cholesterol in liver is substantial in order effectively to lower the concentration of cholesterol.[1] Compactin **2**, isolated from 6000 cultures of *Penicillium brevicompactum* by Sankyo[2] and at the same time by Beecham,[3] efficiently inhibits 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase), the rate-limiting enzyme in the biosynthesis. Later, a team from Merck isolated dihydrocompactin **1**[4] from *P. citrinum*, having comparable bioactivity as compactin **2** among other congeners.[5] Owing to their prominent bioactivity and intriguing structure, these compounds have attracted much attention as targets for synthetic study.[6] At the outset of these synthetic studies, the inter- or intra-molecular Diels–Alder reaction was a major key reaction for synthesis of the decalin portion. We delineate herein our new synthetic pathway toward the total synthesis of (+)-dihydrocompactin **1**,[7] demonstrating the synthetic utility of double Michael reactions[8] in constructing the decalin portion of compactin and its congeners.



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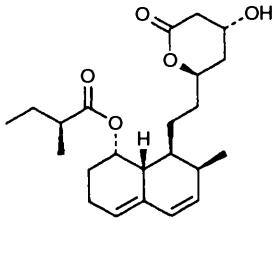

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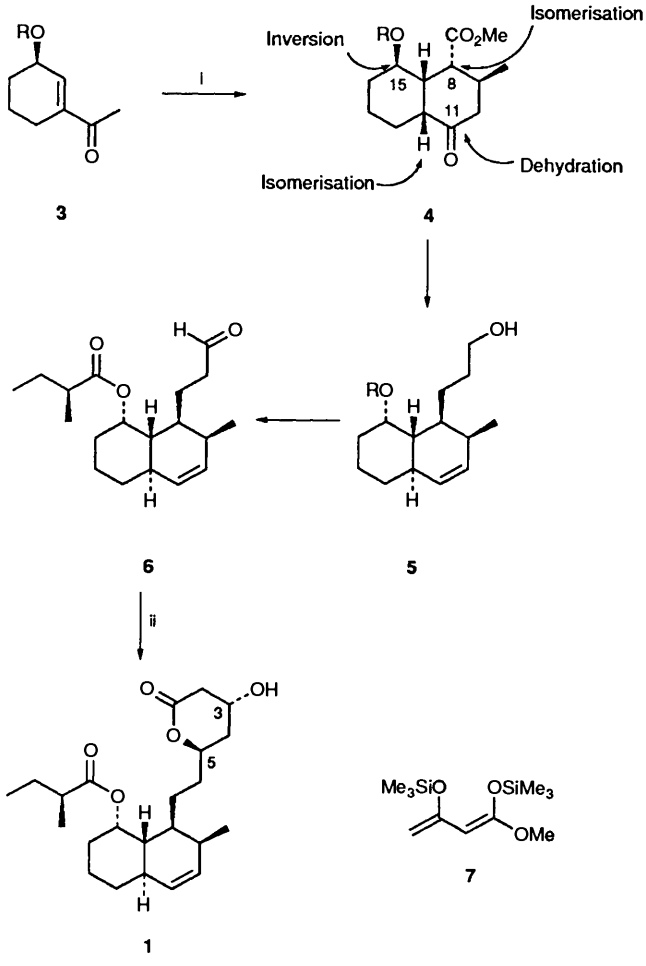
Results and Discussion

Synthetic Design.—The present synthesis is outlined in Scheme 1. A double Michael reaction of alkoxy(acetyl)cyclohexene **3** and methyl crotonate would give a decalone **4** as an initial product having *cis*-steroidal conformation with an equatorial ester group. Configurations of the methyl group at C-9† and the proton at C-15a are *syn*-diaxial which is the desired configuration for synthesis of dihydrocompactin **1**. After equilibration at C-8 and C-11a followed by inversion of configuration at C-15 and introduction of a double bond at C-10, elongation of the side chain from C-8 would give, after oxidation of the alcohol **5**, the aldehyde **6**. Addition of methyl acetoacetate or its equivalent[9] to the aldehyde **6** would furnish (+)-dihydrocompactin **1**.



Scheme 1 *Reagents:* i, $MeCH{=}CHCO_2Me$; ii. **7**

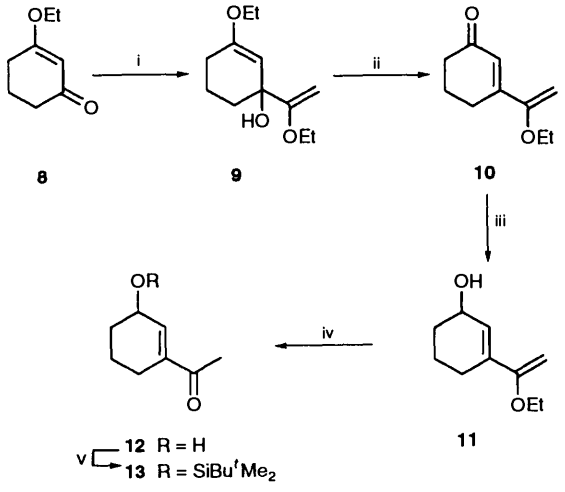
Synthesis of Starting Material.—1-Acetyl-3-hydroxycyclohexene [1-(3-hydroxycyclohex-1-enyl)ethanone] **12** was prepared by improving the procedure by Kraus[10] (Scheme 2). Addition of ethoxyvinyllithium to 3-ethoxycyclohex-2-enone **8** gave 1,2-adduct **9**. It was crucial at this point to quench the reaction with water. A solution of the adduct **9** in hexane–ethyl acetate was passed through a short column of silica gel to afford 3-(1-ethoxyvinyl)cyclohex-2-ene **10** in 93% overall yield. The

† Non-systematic numbering is used in this text, except in the Experimental section.

Table 1 Double Michael reaction of the enolate **14** with methyl crotonate

Entry	Additive	Yield (%) of ketones **16** and **17**
1	HMPA (2 mol equiv.)	85
2	HMPA (4 mol equiv.)	78
3	DMPU[a] (4 mol equiv.)	52
4	HMPA (4 mol equiv. and $HNPr^i_2$	28
5	None	24

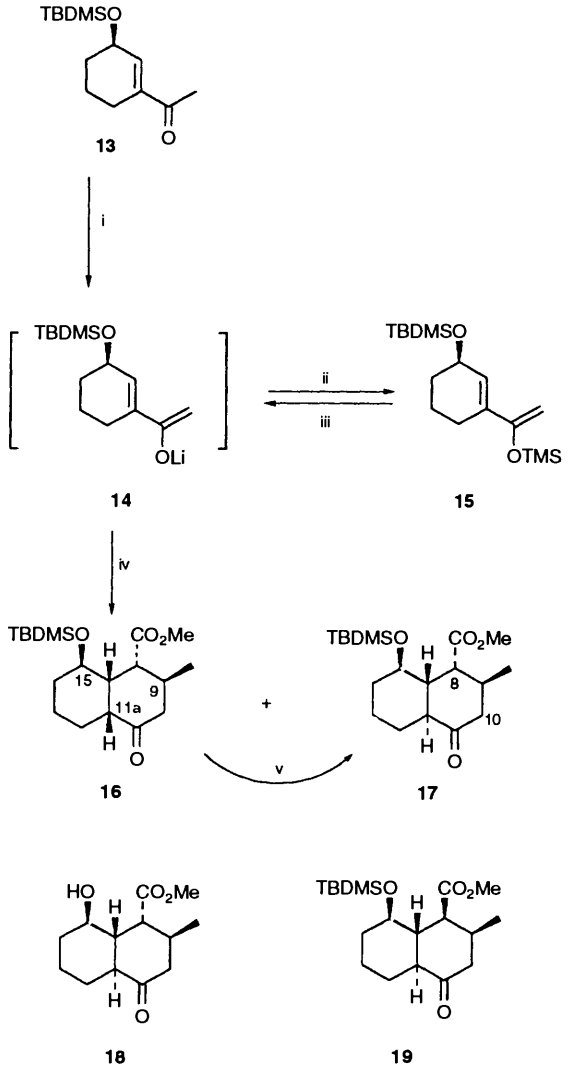
[a] DMPU = 1,3-Dimethylhexahydro-2-pyrimidone.



Scheme 2 *Reagents and conditions:* i, Bu'Li, ethyl vinyl ether, THF; ii, silica gel; iii, $CeCl_3 \cdot 7H_2O$, $NaBH_4$, MeOH; iv, PTSA·H_2O, reflux; v, $Bu'Me_2SiCl$, DMAP, DMF

resulting enone **10** was reduced with sodium boranuide (sodium borohydride, $NaBH_4$) in the presence of cerium chloride to give the alcohol **11** whose enol ether moiety was hydrolysed with toluene *p*-sulfonic acid (PTSA) in aq. acetone at reflux to furnish 1-acetyl-3-hydroxycyclohexene **12** in 67% overall yield. Attempted reduction of the enone **10** with lithium aluminium hydride (LAH) led only to the recovery of a fair amount of the enone **10**. The hydroxy group of the hydroxy(acetyl)cyclohexene **12** was protected as its *tert*-butyldimethylsilyl (TBDMS) ether to give the acetylcyclohexene **13** in 97% yield.

Double Michael Reaction.—Trimethylsilyl enol ether **15** was obtained in 83% yield by conventional procedure. Reaction of kinetic enolate **14**, generated from the trimethylsilyl (TMS) enol ether **15** by treatment with methyllithium, with methyl crotonate gave a mixture of two decalones **16** and **17** (Scheme 3). Since the yield was lower when the reaction mixture was warmed up to room temperature, the reaction was quenched at −20 °C. The best reproducible yield was obtained when two mole equivalents of hexamethylphosphoric triamide (HMPA) were added as a co-solvent (Table 1, entry 1). The presence of four mole equivalents of HMPA slightly decreased the yield (Table 1, entry 2). Kinetic enolate **14** directly generated from the acetylcyclohexene **13** by tereatment with lithium diisopropylamide (LDA) afforded a mixture of the decalones **16** and **17** in 28% yield (Table 1, entry 4). On the other hand, an attempt at Lewis acid-promoted double Michael reaction, namely the reaction of the trimethylsilyl enol ether **15** with methyl crotonate in the presence of titanium tetrachloride, gave no desired decalones.[8] Also, attempted Diels–Alder reaction of the trimethylsilyl enol ether **15** led to recovery of the

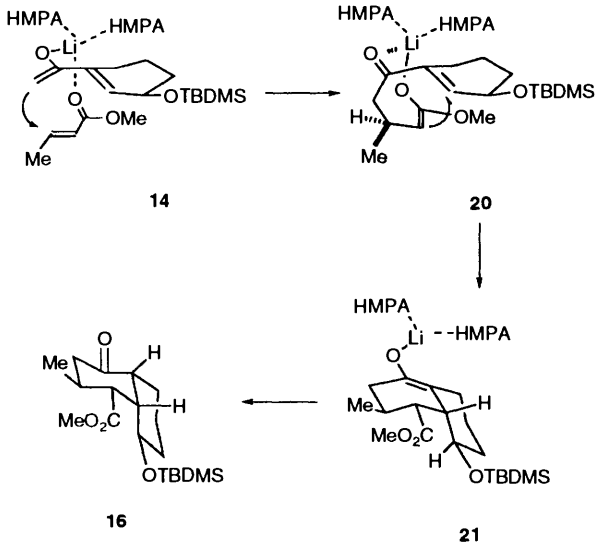


Scheme 3 *Reagents and conditions:* i, LDA, THF, −78 °C; ii, Me_3SiCl, −78 to 0 °C; iii, MeLi, THF, −78 °C; iv, methyl crotonate, HMPA, −78 to −20 °C; v, MeONa, MeOH, reflux, 2 h

acetylcyclohexene **13**. The decalones **16** and **17** thus obtained were separable by medium-pressure liquid chromatography (MPLC). The less polar, minor decalone was the *trans*-decalone **17** and the more polar, major decalone was the *cis*-decalone **16**. Treatment of a mixture of these decalones **16** and **17** with sodium methoxide resulted in isomerisation of the more polar decalone **16** into the less polar decalone **17** in 78% yield.

The relative stereochemistry of the *trans*-decalone **17** was assigned by NMR spectroscopy. The methine proton at δ 3.02 (t-like, J 2.1 Hz) was assigned to the proton at C-8. Since this signal had a long-range W-type coupling with a β-equatorial proton at C-10, orientation of the proton at C-8 was assigned to be β-equatorial. The signal at δ 2.98 (td, J 12.2 and 3.3 Hz) was assigned to the proton at C-11a. From these coupling constants, the ring juncture of decalone **17** was determined to be *trans*. Moreover, methylene protons at C-10 appeared at δ 2.71 (dd, J 13.6 and 5.9 Hz, α-axial H) and δ 2.09 (ddd, J 13.6, 2.3 and 1.4 Hz, β-equatorial H) as an AB-type quartet, indicating the axial nature of the secondary methyl group at C-9. Thus, three of the five requisite stereocentres in the decaline portion of dihydrocompactin **1**, C-9, C-11a and C-15a, were arranged in the decalone **17** by double Michael reaction followed by base-catalysed equilibration.

The reaction pathway of the present double Michael reaction was explained as follows (Scheme 4). Methyl crotonate

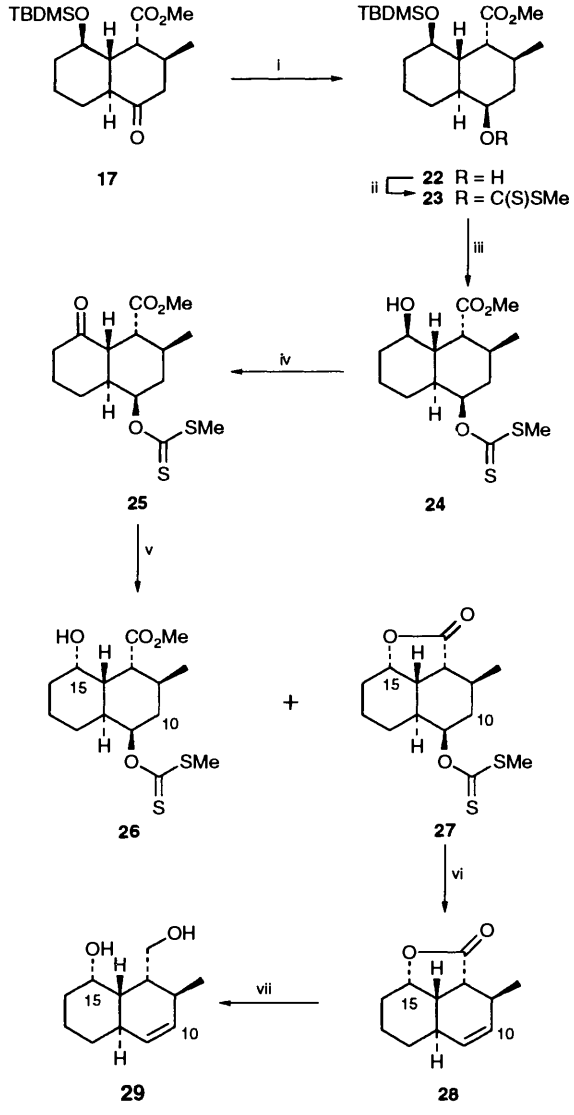


Scheme 4

approached the kinetic enolate **14** of the 1-acetylcyclohexene **13** from the α-face, avoiding steric crowding from the *tert*-butyldimethylsiloxy group. After coordination of the lithium cation of the enolate **14** with the oxygen of the carbonyl group of methyl crotonate and two molecules of HMPA, the first Michael reaction occurred at the *re*-face of the α,β-unsaturated ester. In this instance, methyl crotonate reacted in the *s-cis* conformation. The subsequent second Michael reaction proceeded from the *si*-face of the enone moiety of the enolate **20** to give enolate **21** having an equatorial ester group. Intervention of chelation structures through a double Michael pathway was supported by the result that addition of two mole equivalents of HMPA gave the highest yield (Table 1, entry 1). When axial protonation of the intermediate **21** occurred, the decalone **16** having *cis*-steroidal conformation was obtained as an initial product.[8] Contrary to the various attempts to trap intermediate enolate **20**, a single Michael adduct was not isolated, probably because the second intramolecular Michael addition was fast. It is worthy of note that 1,6-remote stereocontrol was realized in this double Michael reaction, because configuration of C-3 of the 1-acetylcyclohexene **13** was transferred to the stereochemistry of the methyl group at C-9 in the product. Similar stereochemical aspects were observed in the reaction of the enolate **14** with methyl α-bromocrotonate.[11]

The base-catalysed isomerisation of a mixture of decalones **16** and **17** afforded the decalone **17** having a *trans*-junction. Against our earlier expectation, the ester group of the *trans*-decalone **17** stayed in the axial orientation even after prolonged heating with sodium methoxide. Many attempts at isomerisation at C-8 with strong base failed. The stereochemical stabilities of the related decalones **16**, **17**, **18** and **19** were unveiled by molecular mechanics calculations.[12] The initial double Michael product, *cis*-decalone **16**, was 5.19 kcal mol^{-1}* more unstable than the *trans*-decalone **17** which is 3.51 kcal mol^{-1} more stable than the *trans*-decalone **19** having an equatorial ester. Steric repulsion between methoxycarbonyl and *tert*-butyldimethylsiloxy groups destabilised the decalone **19** having an equatorial methoxycarbonyl group, because the van der Waals repulsion was larger in the decalone **19** than in the decalone **17** in these calculations. However, treatment of sterically less congested hydroxy ester **18** with base resulted in decomposition of compound **18**. Prior to inversion of configuration of the C-8 substituent, functional group manipulations at C-11 and 15 were investigated.

Inversion of Configuration of C-15 *and Introduction of Double Bond at* C-10.—The carbonyl group at C-11 of the decalone **17** was reduced with $NaBH_4$ to give predominantly β-axial alcohol **22** whose configuration was desired for selective introduction of double bond between C-10 and -11 by *syn*-elimination (Scheme 5). The resulting β-hydroxy group of the alcohol **22** was



Scheme 5 *Reagents and conditions:* i, $NaBH_4$, MeOH, 0 °C; ii, BuLi, CS_2, MeI, THF, −50 to −25 °C; iii, TBAF, THF; iv, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; v, $NaBH_4$, MeOH, −60 °C; vi, 1-methylnaphthalene, 210 °C, 1.5 h; vii, LAH, Et_2O

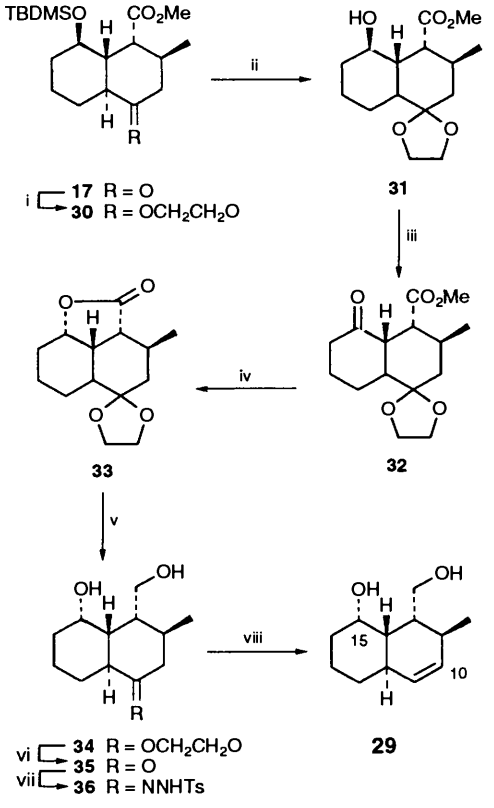
protected as a xanthate ester by sequential treatment with butyllithium, carbon disulfide and iodomethane to give xanthate **23** in 72% yield (overall in two steps). Deprotection of the *tert*-butyldimethylsiloxy group with tetrabutylammonium fluoride (TBAF) followed by Swern oxidation[13] of the alcohol **24** afforded keto ester **25** in 82% overall yield. Among the reducing agents tested, $NaBH_4$ gave the best result at −60 °C to give α-alcohol **26**, a part of which cyclised to lactone **27** upon warming to room temperature. The selectivity of the $NaBH_4$ reduction was lower when the reduction was conducted after introduction of the double bond at C-10. The presence of sp^3 carbons in the decalin structure was required to control the stereochemistry of reduction of carbonyl group at C-15.

* 1 cal = 4.184 J.

Attempted Mitsunobu inversion[14] at C-15 resulted in recovery or decomposition of starting material depending on reaction conditions, probably because of steric hindrance imposed by the axial ester group at C-8.

The double bond at C-10 was introduced by pyrolysis of the xanthate ester **26**. Heating a solution of the xanthate ester **26** in 1-methylnapthalene at 210 °C led to complete consumption of compound **26** to give the lactone **28**. Pyrolysis in another solvent or without a solvent under reduced pressure resulted in recovery of a fair amount of starting material. Since 1-methylnaphthalene and the lactone **28** were difficult to separate due to the higher boiling point of the former and similar chromatographic behaviour, after dilution with diethyl ether, the resulting lactone **28** was reduced *in situ* with LAH to give diol **29** in 80% yield (overall in three steps).

Alternatively, the Shapiro reaction[15] was tested to introduce the double bond at C-10 (Scheme 6). As noted above, the



Scheme 6 *Reagents and conditions:* i, $(CH_2OH)_2$, benzene, PTSA, reflux; ii, TBAF, THF; iii, PCC, molecular sieves 4Å, CH_2Cl_2; iv, $NaBH_4$, MeOH, −78 °C to room temperature; v, LAH, THF; vi, PTSA·H_2O, aq. EtOH, reflux; vii, $TsNHNH_2$, MeOH, aq. HCl; viii, MeLi, TMEDA, 40 °C

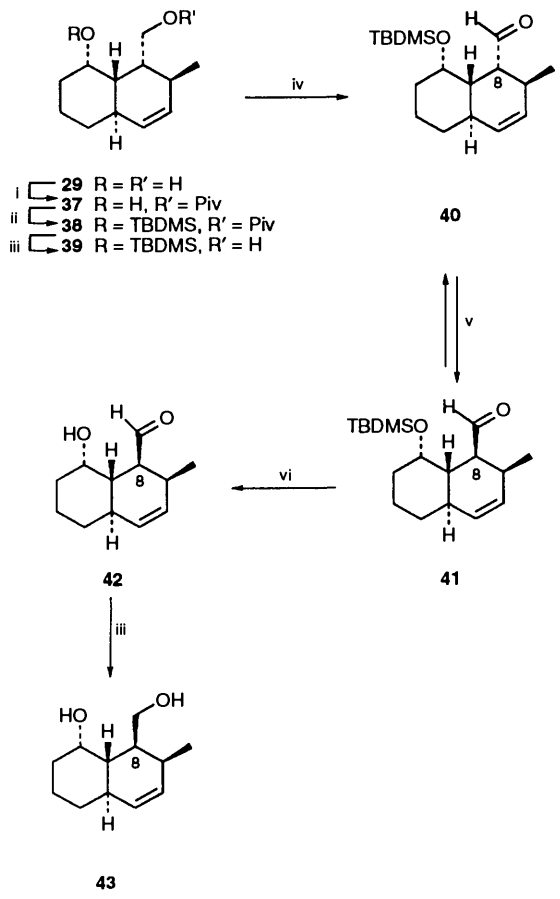
absence of sp^2 carbons in the decalin moiety is required for selective reduction of carbonyl group at C-15. Thus, inversion of configuration of the C-15 substituent was at first carried out. Protection of the carbonyl group at C-11 as a ketal (**30**), followed by deprotection of the *tert*-butyldimethylsilyl ether with TBAF gave hydroxy ester **31**, which was oxidised by pyridinium chlorochromate (PCC) to provide keto ester **32** in 55% yield (overall in 3 steps). Reduction of the keto ester **32** with $NaBH_4$ at −78 °C gave lactone **33** quantitatively. Reduction of the lactone **33** with LAH followed by hydrolysis of the ketal moiety in intermediate diol **34** furnished hydroxy ketone **35** in 67% yield (overall in two steps). The hydroxy ketone **35** was then transformed into hydrazone **36** which was treated with large excess of methyllithium at 40 °C to give the diol **29** in 61% yield (overall in two steps). However a synthetic sequence *via* pyrolysis of xanthate ester was superior, because the final Shapiro reaction was rather capricious, leading to recovery of the hydrazone **36**.

Equilibration at C-8.—Control of stereochemistry at C-8 was effected by base-catalysed equilibration of aldehyde **40** (Scheme 7). Selective protection of the primary alcohol of diol **29** as a pivalate **37** and then the secondary alcohol as a *tert*-butyldimethylsilyl ether (compound **38**), followed by deprotection of the pivaloyl group with LAH afforded the alcohol **39** in 85% yield (overall in three steps). The alcohol **39** was transformed into aldehyde **40** in 80% yield by Swern oxidation. Isomerisation of the aldehyde **40** was investigated under base catalysis. Among bases examined (potassium carbonate, potassium carbonate–18-crown-6, potassium carbonate–ultrasound, caesium carbonate, potassium *tert*-butoxide or sodium hydride), potassium carbonate in methanol[6d] gave reproducible results with good recovery of both starting aldehyde **40** (42%) and desired isomeric aldehyde **41** (55%) enabling ease of recycling. The relative stereochemistry of the isomeric aldehyde **41** was assigned to be β-equatorial from the coupling constants of the proton at C-8 which appeared at δ 2.84 (ddd, J 11.2, 5.8 and 2.5 Hz). Furthermore, after deprotection of the *tert*-butyldimethylsilyl group of the aldehyde **41**, the resulting hydroxy aldehyde **42** was reduced with LAH to give diol **43** which was identical with the sample kindly supplied by Prof. Funk.[16] According to molecular mechanics calculations,[12] the β-equatorial aldehyde **41** was 0.81 kcal mol^{-1} more stable than the α-axial aldehyde **40** and the population of both aldehydes **41** and **40** was calculated to be 58:42, in good agreement with the experimental data.

Elongation of Side Chain and Optical Resolution of Alcohol **47**.—The bridge which connects the decalin and lactonic portions in our target molecule **1** was installed by the Horner–Emmons reaction (Scheme 8). Condensation of the aldehyde **41** with a large excess of 'triethyl phosphonoacetate' and sodium hydride in the presence of HMPA under reflux provided the *E*-unsaturated ester **44** in 95% yield. The double bond at C-6 was selectively reduced with magnesium[17] in methanol to afford a mixture of methyl and ethyl esters **45** which was reduced with LAH to give alcohol **46** in 85% yield (2 steps).

The alcohol **46** was deprotected with aq. hydrogen fluoride to give crystalline diol **47** in 92% yield. Selective esterification of the primary alcohol of the diol **47** was accomplished (*R*)-(−)-*O*-methylmandelic acid[15] in the presence of dicyclohexylcarbodiimide (DCC) to give in 85% yield a mixture of diastereoisomers **48** and **49**, which were easily separated by MPLC. Less polar diastereoisomer **48** had an optical rotational value of $+33 \times 10^{1}$ deg cm^2 g^{-1}, and more polar diastereoisomer **49** had $[\alpha]_D$ -102×10^{-1} deg cm^2 g^{-1}. When the hydroxy groups at C-15 of the mandelates **48** and **49** were protected as a *tert*-butyldimethylsilyl ether, baseline separation of the diastereoisomers was not observed in MPLC. The hydroxy group at C-15 of the alcohol **48** was protected as its (*S*)-2-methylbutyric ester to give the diester **50**, which was selectively hydrolysed to provide the alcohol **51** in 93% yield (overall yield in 2 steps).

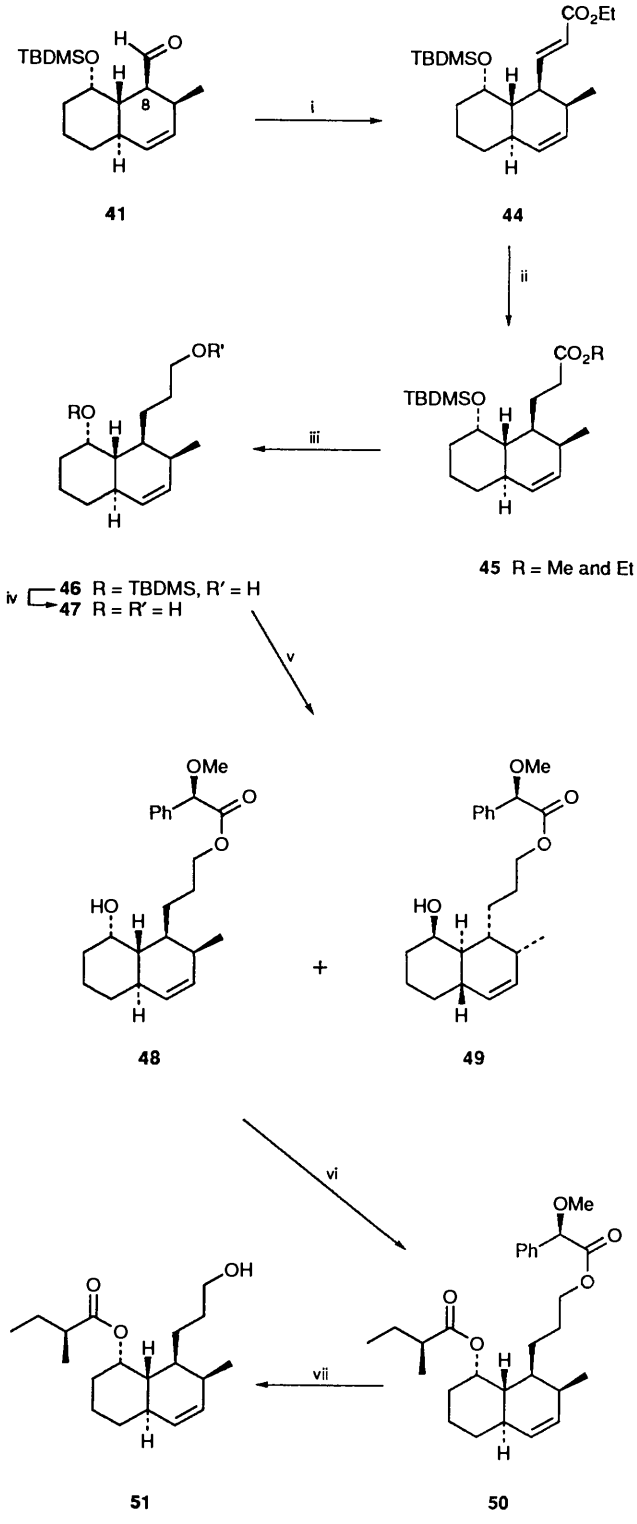
Determination of Absolute Stereochemistry of Decalin Portion.—The absolute stereochemistry of the decalin **51** derived from the less polar diastereoisomer **48** having the positive optical rotational value was determined by the exciton chirality method[18] (Scheme 9). Osmium tetraoxide *cis*-dihydroxylation selectively occurred from the α face of the alcohol **51** probably due to steric hindrance of the axial methyl group at C-9 to give the triol **52** in 70% yield. The primary alcohol of the resulting triol **52** was selectively protected with pivaloyl



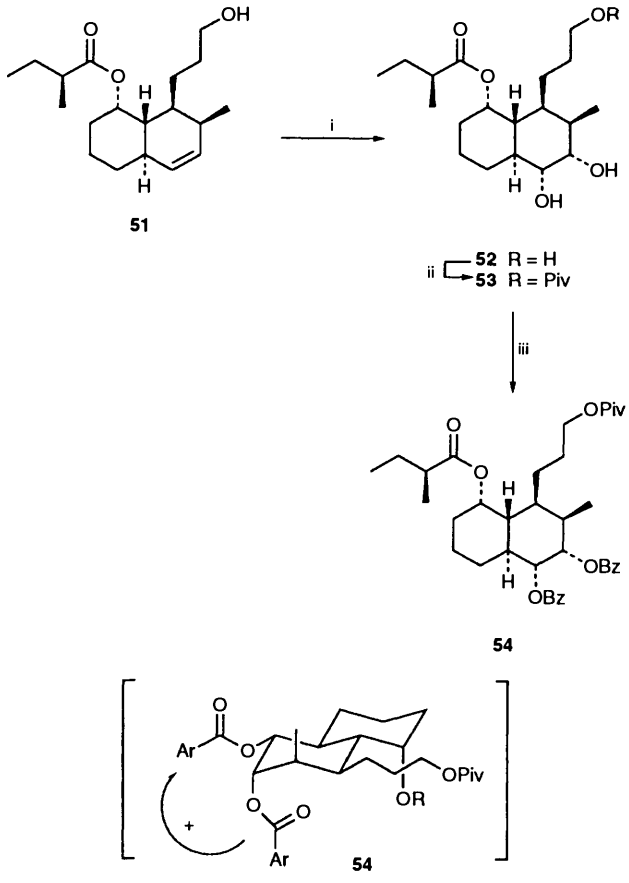
Scheme 7 *Reagents:* i, pivaloyl chloride, pyridine; ii, TBDMSOTf, Et_3N, CH_2Cl_2; iii, LAH, Et_2O; iv, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; v, K_2CO_3, MeOH; vi, HF–pyridine complex, MeCN

chloride to afford the pivalate **53** in 56% yield. Benzoylation of diol **53** provided, in 71% yield, the dibenzoate **54** whose CD spectrum exhibited first positive ($\Delta\varepsilon$ +20.8 at 238 nm) and second negative ($\Delta\varepsilon$ −13.9 at 220 nm) Cotton effects. Since the chirality of the two benzoate chromophores was positive, absolute configurations at C-10 and 11 were unambiguously determined to be 10*S* and 11*R* respectively. Thus, the absolute stereochemistry of the less polar diastereoisomer **48** having a positive optical rotational value, was established as depicted in Scheme 9 and had the correct absolute stereochemistry for (+)-dihydrocompactin **1** synthesis.

Synthesis of (+)-*Dihydrocompactin and Determination of the Absolute Stereochemistry of its Lactonic Portion.*—Swern oxidation of the alcohol **51** gave the aldehyde **6** in 97% yield (Scheme 10). The requisite functional groups for construction of the lactonic portion of (+)-dihydrocompactin **1** was introduced by aldol condensation of the bis(trimethylsilyl enol ether) of methyl acetoacetate, compound **7**. Thus, the reaction of the aldehyde **6** with compound **7** in the presence of titanium tetrachloride at −90 °C afforded an inseparable epimeric mixture of aldol adducts **55** and **56**, which were reduced with $NaBH_4$ in the presence of diethylmethoxyborane[19] to give an inseparable isomeric mixture of *syn*-diols **56** and **57** (40%) and the corresponding boronates **59** and **60** (19%) (overall in two steps). High *syn* selectivity of the reduction was verified after subsequent lactonisation. Finally, treatment of the mixture of diols **57** and **58** with HF–pyridine complex in acetonitrile completed in 70% yield, the total synthesis of (+)-dihydrocompactin **1** {$[\alpha]_D$ +127 × 10^{-1} cm^2 g^{-1} (*c* 0.12, $CHCl_3$) (lit.,[6a] +128° in $CHCl_3$)} and (+)-3,5-epidihydrocompactin **61** {$[\alpha]_D$ +120 × 10^{-1} deg cm^2 g^{-1} (*c* 0.22, $CHCl_3$)} (1.7:1 ratio) which were separable by MPLC. It was unfortunate that the spectral data (^1H and ^{13}C NMR, IR, mass, optical rotation) of both compounds **1** and **61** were identical with those of authentic (+)-dihydrocompactin **1** (except for the CD spectra). Less polar compound **61** exhibited only a negative Cotton effect ($\Delta\varepsilon$ −1.52 at 220 nm), whereas the more polar (+)-dihydro-



Scheme 8 *Reagents and conditions:* i, NaH, $(EtO)_2P(O)CH_2CO_2Et$, HMPA, THF, reflux; ii, Mg, MeOH, 0 °C; iii, LAH, ether; iv, aq. HF, MeCN; v, (*R*)-(−)-*O*-methylmandelic acid, DCC, DMAP; vi, MPLC separation; then (*S*)-2-methylbutanoic anhydride, DMAP, CH_2Cl_2, 40 °C; vii, KOH, MeOH



Scheme 9 *Reagents:* i, NMO, OsO_4, aq. Bu^{t}OH; ii, pivaloyl chloride, pyridine; iii, benzoyl chloride, DMAP, pyridine

compactin **1** exhibited both first positive ($\Delta\varepsilon$ +0.2 at 242 nm) and second negative ($\Delta\varepsilon$ −1.3 at 212 nm) Cotton effects.

In order to determine the absolute stereochemistry of the 3-hydroxy-δ-lactonic moiety, the exciton chirality method was employed (Scheme 11).[20] To this end, the less polar lactone **61** was transformed into its 1,3-dibenzoate **68** after the following protection–deprotection sequence. Protection of the hydroxy group at C-3 of compound **61** gave the tetrahydropyran-2-yl (THP) ether **62** in 79% yield. Reduction of the THP ether **62** with LAH (to give triol **63**) followed by selective protection of the primary alcohol with *tert*-butyldiphenylsilyl chloride (TBDPSCl) afforded diol **64** in 40% (overall yield in two steps). Acetylation of the diol **64** gave quantitatively the diacetate **65**, whose *tert*-butyldiphenylsiloxy group was deprotected with TBAF to give the alcohol **66** quantitatively. Deprotection of the THF ether (to give diol **67**) followed by *p*-bromobenzoylation furnished 1,3-bis(bromobenzoate) **68** in 41% (overall yield in two steps). Since the CD spectrum of the bis(bromobenzoate) **68** exhibited first positive ($\Delta\varepsilon$ +5.46 at 252 nm) and second negative ($\Delta\varepsilon$ −2.18 at 236 nm) Cotton effects, the absolute stereochemistry at C-3 of the bis(bromobenzoate) **68** was determined to be *R*. Since the two hydroxy groups at C-3 and -5 of the compound **68** were *syn* to each other, the absolute stereostructure at C-5 was established to be *S*. Thus, it was concluded that the more polar isomer had the correct absolute stereochemistry of (+)-dihydrocompactin **1**.

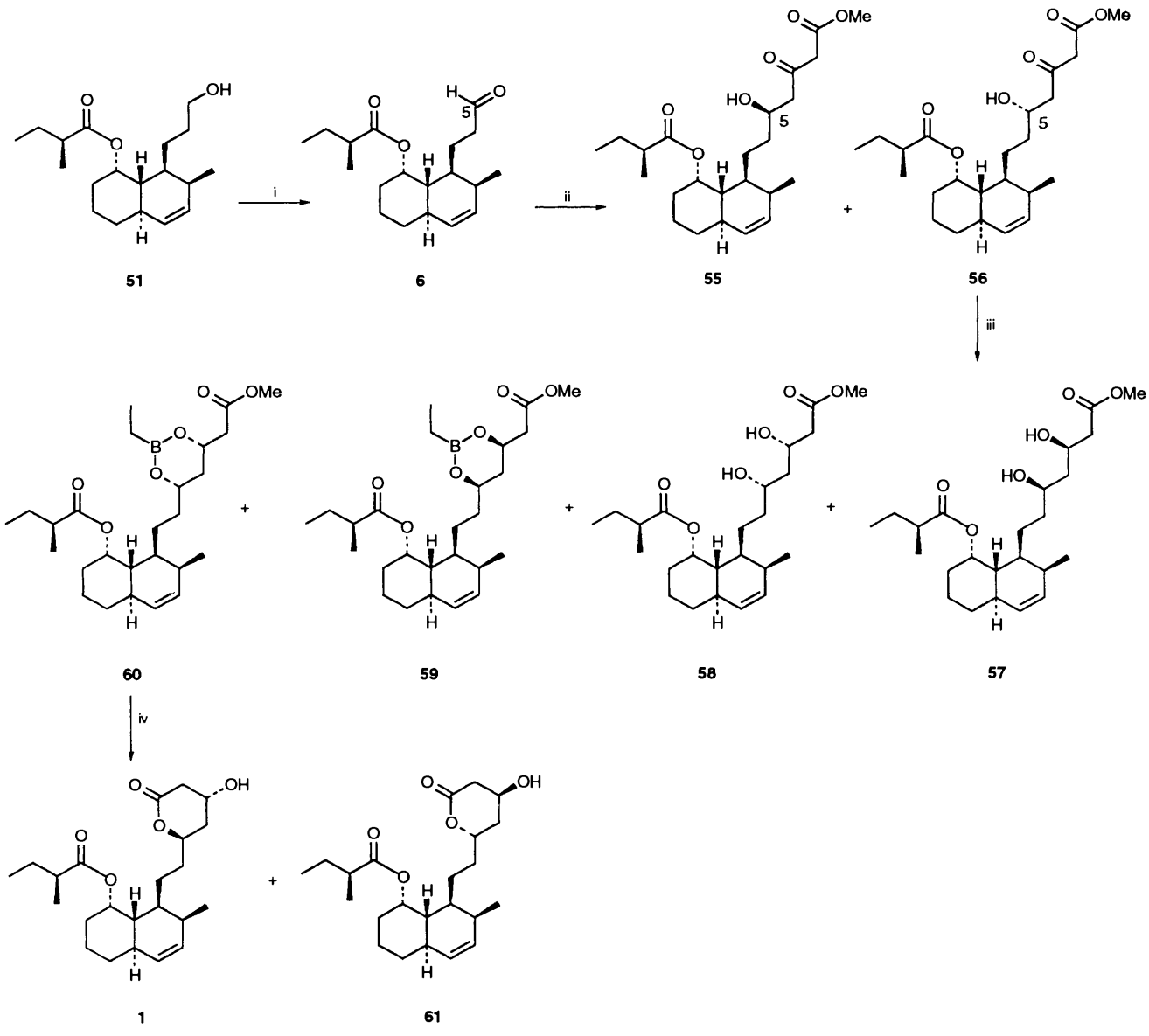
Experimental

All m.p.s were determined with a Mitamura Riken hot-stage apparatus and are uncorrected. IR spectra were recorded on a JASCO A-3 or FT/IR-8300 spectrophotometer for solutions in tetrachloromethane unless otherwise indicated. ^{1}H NMR spectra were obtained for solutions in deuteriochloroform with Bruker AM 600 (600 MHz), Bruker CXP-300 (300 MHz), Bruker AC 250 (250 MHz) and JEOL-PMX 60 (60 MHz) instruments with tetramethylsilane as internal standard. *J*-Values are given in Hz. Mass spectra were run on a JEOL JMS-DX300 spectrometer with a JMA-3500 data system. Specific rotations, $[\alpha]_D$, were determined on a JASCO DIP-370 polarimeter for solutions in chloroform, and are given in 10^{-1} deg cm^2 g^{-1}. CD spectra were measured on a JASCO J-400X spectrophotometer. UV spectra were obtained on a JASCO UVDEC-505 spectrophotometer. MPLC was carried out on a JASCO PRC-50 instrument with a silica gel-packed column. High-pressure liquid chromatography (HPLC) was performed on a Waters ALC/GPC 244. Microanalyses were carried out in the microanalytical laboratory of this Institute. Ether refers to diethyl ether. Anhydrous sodium sulfate was used for drying organic extracts. Tetrahydrofuran (THF) was distilled from LAH before use. Upon typical work-up, the product was extracted with solvent (2 × 20 cm^3 for 1–10 mmol-scale reaction). The organic layer was washed with water once and brine once. After being dried over sodium sulfate, the solvent was evaporated off under reduced pressure.

3-(1-*Ethoxyvinyl*)*cyclohex*-2-*enone* **10**.[10]—To a stirred solution of ethoxyethene (25.6 cm^3, 268 mmol) in anhydrous THF (100 cm^3) was added *tert*-BuLi (1.5 mol dm^3 solution in hexane; 140 cm^3, 210 mmol) at −78 °C under nitrogen. After being stirred at −78 °C for 45 min and 0 °C for 15 min, the solution was cooled again at −78 °C. A solution of 3-ethoxycyclohex-2-enone **8** (23.5 g, 168 mmol) in THF (50 cm^3) was added over a period of 5 min. The resulting solution was stirred at that temperature for 15 min, and at 0 °C for 45 min. The reaction was quenched by addition of wet ether (100 cm^3). The organic layer was washed with water and brine. The aqueous layer was extracted with ether (100 cm^3 × 2) and the combined organic layer was washed with water and brine. After evaporation of the extract, flash column chromatography provided the enone **10**[10] (25.87 g, 93%); δ(60 MHz) 1.33 (3 H, t, *J* 7, Me), 1.72–2.75 (6 H, m), 3.82 (2 H, q, *J* 7, MeC*H*$_2$O), 4.40 (1 H, d, *J* 3, methylene), 4.64 (1 H, d, *J* 3, methylene) and 6.43 (1 H, br s, 2-H); *m*/*z* 166 (M$^+$, 69%), 138 (57), 137 (36), 110 (100), 95 (36), 68 (87) and 43 (29) (Found: M$^+$, 166.0989. Calc. for $C_{10}H_{14}O_2$: M, 166.0992).

1-(3-*Hydroxycyclohex*-1-*enyl*)*ethane* **12**.—To a stirred solution of the enone **10** (5.52 g, 33 mmol) and $CeCl_3 \cdot 7H_2O$ (1.26 g, 3.3 mmol) in methanol (35 cm^3) was added $NaBH_4$ (1.26 g, 33 mmol) portionwise at 0 °C. After being stirred at 0 °C for 1 h and at room temperature for 10 min, the resulting solution was poured into water. The aqueous layer was extracted with ether (100 cm^3 × 2) and the combined organic layer was washed with water and brine. Evaporation of the extract left 3-(1-ethoxyvinyl)cyclohex-2-enol **11**[10] (4.97 g), which was used without purification; ν_{max}/cm^{-1} 3620, 3600–3100, 1680, 1285 and 1065; δ(60 MHz) 1.33 (3 H, t, *J* 7, Me), 1.2–2.5 (7 H, m), 3.79 (2 H, q, *J* 4, C*H*$_2$Me), 4.07 (1 H, d, *J* 2, methylene), 4.25 (2 H, d, *J* 2, methylene and 1-H) and 6.1 (1 H, m, 2-H); *m*/*z* 168 (M$^+$, 33%), 140 (50), 112 (100), 95 (54), 84 (66), 67 (45) and 41 (38).

A solution of compound **11** (4.97 g) and PTSA (300 mg) in acetone (30 cm^3)–water (10 cm^3) was heated under reflux for 3 h. After being cooled to room temperature, the solution was extracted with ethyl acetate (50 cm^3 × 2) and the organic layer was washed with water and brine. Evaporation of the extract followed by column chromatography gave the *ketone* **12** (3.09 g, 67% in two steps); ν_{max}/cm^{-1} 3600–3000, 1675, 1235 and 1080; δ(60 MHz) 1.1–2.23 (6 H, m), 2.3 (3 H, s, Ac), 3.43–4.63 (2 H, m, 3-H and OH) and 6.68–6.88 (1 H, m, 2-H); *m*/*z* 140 (M$^+$, 54%), 97 (100),



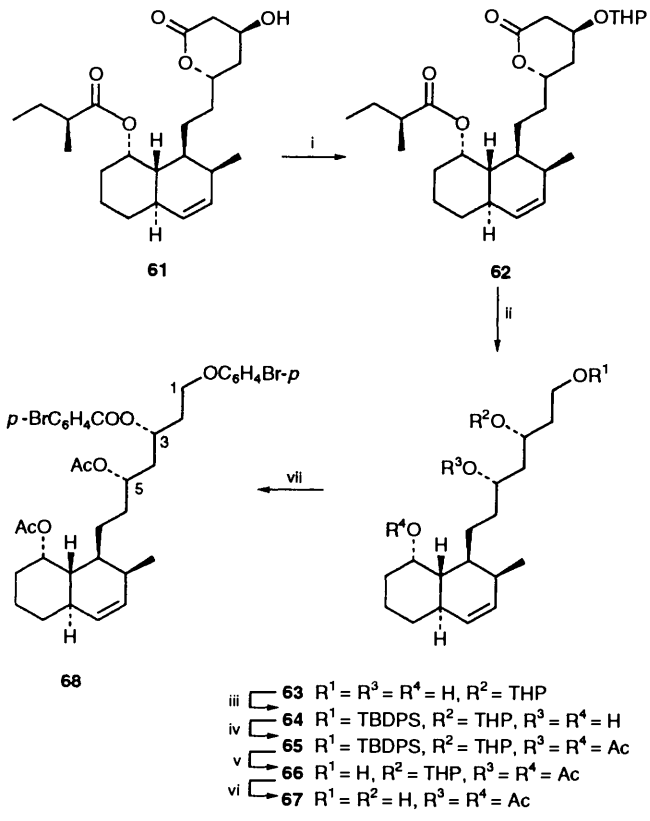
Scheme 10 *Reagents and conditions:* i, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; ii, $TiCl_4$, bis(trimethylsilyl enol ether) **7**, CH_2Cl_2, −78 °C; iii, Et_2BOMe, $NaBH_4$, MeOH, −78 °C; iv, HF–pyridine complex, MeCN

79 (27), 69 (30) and 43 (86) (Found: M^+, 140.0839. $C_8H_{12}O_2$ requires M, 140.0838).

1-[3-(tert-*Butyldimethylsiloxy*)*cyclohex*-1-*enyl*]*ethanone* **13**.—To a stirred solution of the alcohol **12** (6.19 g, 44.5 mmol) in dichloromethane (20 cm^3) were added dimethyl formamide (20 cm^3, triethylamine (10.1 cm^3), 4-(dimethylamino)pyridine (DMAP) 114.3 mg) and TBDMSCl (11.1 g, 66.8 mmol) successively at room temperature. After being stirred overnight, the resulting solution was poured into water. The organic layer was extracted with ether (50 cm^3 × 2) and the combined ether layer was washed with water and brine. Evaporation of the extract followed by Kugelrohr distillation (150 °C at 0.4 mmHg) afforded the *siloxy compound* **13** (10.95 g, 97%); ν_{max}/cm^{-1} 1675, 1472, 1463, 1095 and 1034; δ(60 MHz) 0.15 (6 H, s, Me_2Si), 0.95 (9 H, s, Bu^t), 1.23–2.23 (6 H, m), 2.32 (3 H, s, Ac), 4.27–4.57 (1 H, m, 1-H) and 6.53–6.7 (1 H, m, 2-H); *m*/*z* 254 (M^+, 4%), 198 (23), 197 (100) and 75 (38) (Found: M^+, 254.1704. $C_{14}H_{26}O_2Si$ requires M, 254.1704).

3-(tert-*Butyldimethylsiloxy*)-1-(1-*trimethylsiloxyvinyl*)*cyclohexene* **15**.—A solution of LDA was prepared from diisopropylamine (3.9 cm^3, 27.8 mmol) and BuLi (1.66 mol dm^3 solution in hexane; 15.4 cm^3, 25.5 mmol) at 0 °C under nitrogen. After being stirred for 10 min, the resulting solution was cooled at −78 °C and a solution of the acetylcyclohexene **13** (5.91 g, 23.3 mmol) in THF (25 cm^3) was added. The mixture was stirred for 30 min and TMSCl (382 cm^3, 30 mmol) was added. The reaction mixture was allowed to warm from −78 °C to ambient temperature overnight. The reaction was quenched by addition of aq. ammonium chloride. The aqueous layer was extracted with ether (50 cm^3 × 2) and the combined ether layer was washed with water and brine. After evaporation of the extract, the residue was passed through a short column of silica gel. Kugelrohr distillation (105 °C, 0.1–0.05 mmHg) provided the disiloxy compound **15** (6.3 g, 83%); ν_{max}/cm^{-1} 1668, 1598, 1278, 1254, 1098, 1071 and 1011; δ(60 MHz) 0.08 (6 H, s, Me_2Si). 0.18 (9 H, s, Me_3Si), 0.9 (9 H, s, Bu^t), 1.15–2.31 (6 H, m), 4.17–4.44 (3 H, m, methylene and 1-H) and 5.94–6.11 (1 H, m, 2-H).

Methyl (1R*,2S*,4aR*,8R*,8aS*)-8-tert-*Butyldimethylsiloxy*)-2-*methyl*-4-*oxodecahydronaphthalene*-1-*carboxylate* **16**.—To a stirred solution of the disiloxy compound **15** (314 mg, 0.96



Scheme 11 *Reagents and conditions:* i, dihydropyran, PPTS, CH_2Cl_2; ii, LAH, Et_2O; iii, TBDPSCl, DMAP, DMF, Et_3N; iv, acetic anhydride, DMAP, pyridine; v, TBAF, THF; vi, PPTS, aq. EtOH, reflux; vii, *p*-promobenzoyl chloride, DMAP, pyridine

mmol) in THF (5 cm^3) was added MeLi (1 mol dm^3 solution in ether; 1.1 cm^3, 1.1 mmol) at −78 °C. After being stirred at −78 °C for 20 min and at room temperature for 1.5 h, the mixture was treated with a solution of HMPA (0.35 cm^3, 2 mmol) and methyl crotonate (0.16 cm^3, 1.42 mmol) in THF (2 cm^3) at −78 °C. The resulting solution was allowed to warm to −20 °C and the reaction was quenched by addition of aq. ammonium chloride. The product was extracted with ether and the ether layer was washed with water and brine. Evaporation of the extract followed by MPLC [eluent hexane–ethyl acetate (5:1)] afforded a mixture of the keto ester **16** and **17**. The keto ester **16** was separated by HPLC; δ(300 MHz) 0.05 (6 H, s, Me_2Si), 0.85 (9 H, s, Bu^t), 1.17 (3 H, d, *J* 5.5, Me), 1.2–1.33 (2 H, m), 1.49–1.65 (2 H, m), 1.84–2.01 (2 H, m), 2.08–2.19 (2 H, m), 2.08–2.19 (2 H, m), 2.33–2.73 (4 H, m), 3.47 (1 H, td, *J* 10.1 and 3.5, 3-H) and 3.67 (3 H, s, MeO); *m/z* 297 (M^+ − Bu^t, 100%), 298 (26), 297 (100) and 89 (16) (Found: M^+ − Bu^t, 297.1521. $C_{15}H_{25}O_4Si$ requires *m/z*, 297.1521).

Methyl (1R*,2S*,4aS*,8R*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-4-*oxodecahydronaphthalene*-1-*carboxylate* **17**.—To a stirred solution of sodium methoxide prepared from sodium (222 mg, 9.64 mmol) and anhydrous methanol (6 cm^3) was added a solution of a mixture of keto esters **16** and **17** (1.95 g, 5.5 mmol) in methanol (10 cm^3) under nitrogen. The resulting solution was heated under reflux for 2 h and poured into cold aq. HCl. The product was extracted with ether (50 cm^3 × 2) and the organic layer was washed with water and brine. After evaporation of the extract, the residue was treated with a solution of diazomethane in ether and purified by column chromatography on silica gel [eluent hexane–ethyl acetate 6:1)] to give the *keto ester* **17** (1.51 g, 78%) (Found: C, 64.2; H, 9.9. $C_{19}H_{34}O_4Si$ requires C, 64.2; H, 9.7%); ν_{max}/cm^{-1} 1732, 1713, 1256, 1210 and 1191; δ(600 MHz) 0.04 (6 H, s, Me_2Si), 0.88 (9 H, s, Bu^t), 1.05 (3 H, d, *J* 7.2, Me), 1.12–1.28 (3 H, m), 1.68–1.77 (3 H, m), 1.9–1.95 (2 H, m), 2.09 (1 H, ddd, *J* 13.6, 2.3 and 1.4, 3β-H), 2.71 (1 H, dd, *J* 13.6 and 5.9, 3α-H), 2.98 (1 H, td, *J* 12.2 and 3.3, 4a-H), 3.02 (1 H, $w_{\frac{1}{2}}$ 8.5, 1-H), 3.71 (3 H, s, MeO) and 3.81 (1 H, td, *J* 10.2 and 4.4, 8-H).

Methyl (1R*,2S*,4R*,4aS*,8R*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-4-*hydroxy*-2-*methyldecahydronaphthalene*-1-*carboxylate* **22**.—To a stirred solution of the keto ester **17** (1.12 g, 3.16 mmol) in methanol (10 cm^3) was added $NaBH_4$ (143.5 mg, 3.79 mmol) portionwise at 0 °C under nitrogen. After being stirred at room temperature for 1 h, the reaction was quenched by addition of aq. ammonium chloride. The product was extracted with ethyl acetate and the organic layer was washed with water and brine. Evaporation of the extract under reduced pressure followed by MPLC purification of the residue afforded the alcohol **22** (902.4 mg, 80%); ν_{max}/cm^{-1} 3520, 1730 and 1145; δ(60 MHz) 0.03 (6 H, s, Me_2Si), 0.88 (9 H, s, Bu^t), 1.3 (3 H, d, *J* 7.2, Me), 2.1–2.53 (12 H, m), 2.83–3.0 (1 H, m, 1-H), 3.59 (3 H, s, MeO) and 3.67–3.97 (2 H, m, 4- and 8-H); *m/z* 299 (M^+ − Bu^t, 100%), 249 (25), 147 (39) and 89 (28) (Found: M^+ − Bu^t, 299.1677. $C_{15}H_{27}O_4Si$ requires *m/z*, 299.1678).

Methyl (1R*,2S*,4R*, 4aS*, 8R*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-4-[(*methylsulfanyl*)*thiocarbonyloxy*]-*decahydronaphthalene*-1-*carboxylate* **23**.—To a stirred solution of the alcohol **22** (1.42 g, 3.98 mmol) in THF (14 cm^3) was added BuLi (1.66 mol dm^3 solution in hexane; 3.6 cm^3, 5.98 mmol) at −50 °C under nitrogen. After being stirred for 15 min, carbon disulfide (475 mm^3, 7.89 mmol) at −30 °C and iodomethane (495 mm^3, 7.97 mmol) at −25 °C were added. The resulting solution was stirred for 30 min and the reaction was quenched by addition of aq. ammonium chloride. The product was extracted with ethyl acetate (30 cm^3 × 2) and the combined organic layer was washed with water and brine. Evaporation of the extract under reduced pressure followed by column chromatography [eluent hexane–ethyl acetate (6:1)] gave the xanthate **23** (1.59 g, 90%); m.p. 85.5–86 °C; ν_{max}/cm^{-1} 1730, 1462, 1230 and 1217; δ(60 MHz) 0.33 (6 H, s, Me_2Si), 0.99 (9 H, s, Bu^t), 1.19 (3 H, d, *J* 7.2, Me), 1.01–2.07 (11 H, m), 2.57 (3 H, s, MeS), 2.90–3.07 (1 H, m, 1-H), 3.62 (4 H, s, MeO and 8-H) and 5.66–5.88 (1 H, m, 4-H); *m/z* 431 (M^+ − Me, 10%), 365 (29), 341 (16), 315 (16) and 207 (100) (Found: M^+ − Bu^t, 389.1278. $C_{17}H_{29}O_4S_2Si$ requires *m/z*, 389.1276).

Methyl (1R*,2S*,4R*,4aS*,8R*,8aS*)-8-*Hydroxy*-2-*methyl*-4-[(*methylsulfanyl*)*thiocarbonyloxy*]*decahydronaphthalene*-1-*carboxylate* **24**.—A solution of the siloxy compound **23** (883 mg, 1.86 mmol) and TBAF (1 mol dm^3 solution in THF; 14.9 cm^3, 14.9 mmol) in THF (11 cm^3) was stirred at room temperature overnight under nitrogen. The solution was poured into water and the product was extracted with ethyl acetate. The organic layer was washed with water and brine and the ethyl acetate was removed under reduced pressure. MPLC separation of the residue provided the alcohol **24** (535.1 mg, 87%); ν_{max}/cm^{-1} 3603, 3300–3650, 1732, 1435 and 1326; δ(60 MHz) 1.16 (3 H, d, *J* 7.2, Me), 1.1–2.37 (12 H, m), 2.55 (3 H, s, MeS), 2.93–3.1 (1 H, br d), 3.13–3.57 (1 H, br, OH), 3.67 (3 H, s, MeO) and 5.73–5.9 (1 H, m, 4-H); *m/z* 225 (20), 147 (100), 105 (31) and 91 (22) (Found: M^+ − MeSCSO, 225.1492. $C_{13}H_{21}O_3$ requires *m/z*, 225.1492).

Methyl (1R*,2S*,4R*,4aS*,8aS*)-2-*Methyl*-4-[(*methylsulfanyl*)*thiocarbonyloxy*]-8-*oxodecahydronaphthalene*-1-*carboxylate* **25**.—To a stirred solution of oxalyl dichloride (135 mm^3, 1.59 mmol) in dichloromethane (0.5 cm^3) was added a solution of dimethyl sulfoxide (DMSO) (110 mm^3, 1.59 mmol) at

−78 °C under nitrogen. After the mixture had been stirred for 10 min, a solution of the alcohol **24** (335 mg, 1 mmol) in dichloromethane (4 cm^3) was added and the mixture was stirred for 30 min. Then, triethylamine (0.5 cm^3, 3.7 mmol) was added and the resulting white suspension was warmed to −25 °C. The reaction was quenched by addition of water and the product was extracted with ethyl acetate. Evaporation of the extract under reduced pressure followed by MPLC purification [eluent hexane–ethyl acetate (3 : 1)] gave the *keto ester* **25** (318 mg, 95%; m.p. 93.5–94.5 °C (Found: C, 54.8; H, 6.3; S, 19.2. $C_{15}H_{22}O_4S_2$ requires C, 54.5; H, 6.7; S, 19.4%); ν_{max}/cm^{-1} 1734, 1716, 1436 and 1326; δ(60 MHz) 1.17 (3 H, d, *J* 7.3, Me), 1.48–2.59 (9 H, m), 2.59 (3 H, s, MeS), 2.67–3.07 (3 H, m), 3.66 (3 H, d, MeO) and 5.77–5.97 (1 H, m, 4-H).

Methyl (1R*,2S*,4R*,4aS*,8S*,8aS*)-8-*Hydroxy*-2-*methyl*-4-[(*methylsulfanyl*)*thiocarbonyloxy*]*decahydronaphthalene*-1-*carboxylate* **26** *and* (2aR*,3S*,5R*,5aS*,8aS*,8bS*)-3-*Methyl*-5-[(*methylsulfanyl*)*thiocarbonyloxy*]*decahydro*-1-*oxaacenaphthen*-2-*one* **27**.—To a stirred solution of the keto ester **25** (303.7 mg, 0.919 mmol) in methanol (10 cm^3) was added $NaBH_4$ (51 mg, 1.46 mmol) at −60 °C under nitrogen. The resulting solution was stirred for 3 h at that temperature and at 0 °C for 30 min. The reaction was quenched by addition of aq. ammonium chloride. The product was extracted with ethyl acetate and the combined organic layer was washed with water and brine. Evaporation of the extract under reduced pressure by MPLC purification [eluent hexane–ethyl acetate (5 : 1)] afforded a mixture of the *hydroxy ester* **26** and the *lactone* **27** (289.3 mg). A part of the mixture was separated by HPLC. The hydroxy ester **26** had m.p. 109.5–110 °C (Found: C, 54.1; H, 7.2; S, 19.1. $C_{15}H_{24}O_4S_2$ requires C, 54.0; H, 7.6; S, 19.2%); ν_{max}/cm^{-1} 3629, 3400–3600, 1724, 1458 and 1435; δ(60 MHz) 1.13 (3 H, d, *J* 7.2, Me), 1.4–2.4 (13 H, m), 2.57 (3 H, s, MeS), 3.63 (3 H, s, MeO), 3.87–4.08 (1 H, m, 8-H) and 5.73–5.93 (1 H, m, 4-H); *m/z* 225 (M^+ − MeSCSO, 13%), 207 (39), 147 (100), 105 (31) and 91 (23). The lactone **27** had (Found: C, 55.8; H, 6.7; S, 21.0. $C_{14}H_{20}O_3S_2$ requires C, 56.0; H, 6.7; S, 21.3%); ν_{max}/cm^{-1} 1781, 1741, 1296, 1251 and 1218; δ(60 MHz) 1.19 (3 H, d, *J* 7.2, Me), 2.1–2.57 (12 H, m), 2.57 (3 H, s, MeS), 4.4–4.62 (1 H, m, 8a-H) and 5.67–5.97 (1 H, m, 5-H).

(2aR*,3S*,5aR*,8aS*,8bS*)-3-*Methyl*-3,3a,5a,6,7,8,8a,8b-*octahydro*-1-*oxaacenaphthen*-2-*one* **28**.—A stirred solution of the mixture of the hydroxy ester **26** and the lactone **27** (289.3 mg) in 1-methylnaphthalene (8 cm^3) was heated at 210 °C for 1.5 h. Without work-up, the solution was subjected to the next reaction. A part of the solution was purified by MPLC to obtain spectroscopic data of the *lactone* **28**; m.p. 36.5–38 °C (Found: C, 75.0; H, 8.3%; M^+, 192.1151. $C_{12}H_{16}O_2$ requires C, 75.0; H, 8.4%; M, 192.1150); ν_{max}/cm^{-1} 1781, 1629, 1457 and 1449; δ(60 MHz) 1.23 (3 H, d, *J* 7.2, Me), 1.0–2.9 (10 H, m), 4.4–4.63 (1 H, m, 8a-H) and 5.33–5.87 (2 H, m, olefinic H); *m/z* 192 (M^+, 9%), 147 (99), 105 (100) and 91 (42).

(1R*,2S*,4aR*,8S*,8aS*)-8-*Hydroxy*-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene*-1-*methanol* **29**.—To a solution of the lactone **28** in 1-methylnapthalene obtained in the previous experiment was added anhydrous ether (10 cm^3) at 0 °C. Powdered LAH (73.6 mg, 1.94 mmol) was added and the suspension was stirred at room temperature for 1 h. The reaction was quenched at 0 °C with a small amount of water. After removal of aluminium hydroxide by filtration, the solvents were evaporated off under reduced pressure. Column chromatography (eluent ethyl acetate) gave the *diol* **29** (144.5 mg, 80% in two steps); m.p. 134–136 °C (Found: C, 73.1; H, 10.2. $C_{12}H_{20}O_2$ requires C, 73.4; H, 10.3%); ν_{max}/cm^{-1} 3500–3100; δ(60 MHz) 1.08 (3 H, d, *J* 7.2, Me), 2.23–2.67 (12 H, m), 3.37 (1 H, dd, *J* 10.8 and 2.4, CH*H*OH), 3.63 (1 H, d, *J* 10.8, C*H*HOH), 3.84–4.03 (1 H, br s, 8-H) and 5.47–5.3 (2 H, br s, olefinic H); *m/z* 178 ($M^+ - H_2O$, 7%), 147 (89), 105 (100) and 91 (27).

Methyl (1R*,2S*,4aS*,8R*,8aS*)-8-(tert-*Butyldimethylsilyoxy*)-2-*methyl*-4-*oxodecahydronaphthalene*-1-*carboxylate Ethylene Ketal* **30**.—A solution of the keto ester **17** (1.27 g, 3.58 mmol), PTSA (135 mg) and ethylene glycol (3 cm^3) in anhydrous benzene (20 cm^3) was heated under reflux under a Dean–Stark water separator. Aliquots were taken and the reaction was monitored by IR spectroscopy. After the mixture had been heated for 4 h, additional PTSA (100 mg) and ethylene glycol (2 cm^3) were added and reflux was continued overnight. After being cooled to room temperature, the mixture was poured into aq. sodium hydrogen carbonate and the product was extracted with ethyl acetate. The organic layer was washed with brine and evaporated to dryness to give the ketal **30**; ν_{max}/cm^{-1} 1740, 1470, 1380, 1260, 1160 and 1085; δ(60 MHz) 0.06 (6 H, s, Me_2Si), 0.87 (9 H, s, Bu^t), 1.22 (3 H, d, *J* 7, Me), 1.5–2.7 (12 H, m), 3.63 (3 H, s, MeO) and 3.93 (5 H, br s, OCH_2CH_2O and 8-H); *m/z* 367 (M^+ − OMe, 3%), 342 (30), 341 (100), 207 (6) and 113 (24) (Found: $M^+ - Bu^t$, 341.1783. $C_{17}H_{29}O_5Si$ requires *m/z*, 341.1784).

Methyl (1R*,2S*,4aS*,8R*,8aS*)-8-*Hydroxy*-2-*methyl*-4-*oxodecahydronaphthalene*-1-*carboxylate Ethylene Ketal* **31**.—To a solution of the crude ketal **30** in THF (10 cm^3) was added TBAF (7 cm^3). After being stirred overnight, the resulting solution was heated at 60 °C with additional TBAF (2 cm^3) for 1.5 h. The product was extracted with ethyl acetate and the organic layer was washed with brine. Evaporation of the mixture followed by column chromatography afforded the *alcohol* **31** (800 mg, 79% in two steps); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600, 1725, 1160, 1100 and 905; δ(60 MHz) 1.15 (3 H, d, *J* 8, Me), 1.2–2.8 (11 H, m), 2.9 (1 H, br d, *J* 4, 1-H), 3.3 (1 H, br, OH), 3.7 (3 H, s, OMe), and 3.93 (5 H, br s, OCH_2CH_2O and 8-H); *m/z* 284 (M^+, 3%), 253 (4), 186 (8), 169 (25), 115 (45), 113 (100) and 86 (40) (Found: M^+, 284.1625. $C_{15}H_{24}O_5$ requires M, 284.1624).

Methyl (1R*,2S*,4aS*,8aS*)-2-*Methyl*-4,8-*dioxodecahydronapthalene*-1-*carboxylate* 4-(*Ethylene Ketal*) **32**.—To a stirred mixture of PCC (580 mg, 2 mmol) and ground molecular sieves 4 Å (120 mg) in dichloromethane (5 cm^3) was added a solution of the alcohol **31** (145 mg, 0.51 mmol) in dichloromethane (3 cm^3). After being stirred for 2.5 h, the resulting mixture was passed through a short column of silica gel. Evaporation of the mixture followed by MPLC separation provided the *keto ester* **32** (100 mg, 69%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1740, 1710, 1440, 1375, 1240, 1160, 1105 and 1080; δ(60 MHz) 1.17 (3 H, d, *J* 7, Me), 1.4–3.0 (11 H, m), 2.9 (1 H, br d, *J* 4), 3.66 (3 H, s, MeO) and 3.93 (4 H, br s, OCH_2CH_2O); *m/z* 252 (M^+, 3%), 251 (6), 184 (33), 113 (100), 99 (11) and 86 (55) (Found: M^+, 282.1467. $C_{15}H_{22}O_5$ requires M, 282.1467).

(2aR*,3S*,5aS*,8aS*,8bS*)-3-*Methyldecahydro*-1-*oxaacenaphthene*-2,5-*dione* 5-(*Ethylene Ketal*) **33**.—To a stirred solution of the keto ester **32** (276 mg, 0.98 mmol) in methanol (5 cm^3) was added $NaBH_4$ (73 mg, 2 mmol) at −78 °C. The resulting solution was stirred overnight with gradual warming to room temperature. The solution was poured into water and the product was extracted with ethyl acetate. Evaporation of the mixture left the pure *lactone* **33** (250 mg, quantitative); $\nu_{max}(CHCl_3)/cm^{-1}$ 1770, 1170, 1140 and 975; δ(60 MHz) 1.18 (3 H, d, *J* 6, Me), 1.2–2.77 (12 H, m), 3.9 (4 H, br s, OCH_2CH_2O), and 4.5 (1 H, br s, 8-H); *m/z* 252 (M^+, 2%), 224 (5), 113 (100), 87 (20), 86 (36) and 69 (10) (Found: M^+, 252.1362. $C_{14}H_{20}O_4$ requires M, 252.1362).

(3S*,4R*,4aS*,5S*,8aS*)-5-*Hydroxy*-4-(*hydroxymethyl*)-3-*methyldecahydronaphthalen*-1-*one Ethylene Ketal* **34**.—To a stirred solution of the lactone **33** (410 mg, 1.63 mmol) in THF (6 cm^3) was added LAH (92 mg, 2.5 mmol) at 0 °C. The resulting slurry was stirred at room temperature for 2 h and the reaction was quenched by careful addition of aq. ammonium chloride. Filtration followed by evaporation of the mixture left an oil, which was purified by column chromatography to give the *ketal* **34** (310 mg, 74%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600, 3350, 1450, 1380, 1150, 1110, 1080 and 980; δ(60 MHz) 1.15 (3 H, d, *J* 7, Me), 1.2–2.2 (12 H, m), 3.93 (4 H, br s, OCH_2CH_2O), 3.37–4.2 (3 H, m, CH_2OH and 5-H) and 4.6 (2 H, br, OH); *m/z* 256 (M^+, 0.8%), 194 (12), 169 (18), 123 (18), 113 (100) and 86 (14) (Found: M^+, 256.1674. $C_{14}H_{24}O_4$ requires M, 256.1674).

(3S*,4R*,4aS*,5S*,8aS*)-5-*Hydroxy*-4(*hydroxymethyl*)-3-*methyldecahydronaphthalen*-1-*one* **35**.—A solution of the ketal **34** (310 mg, 1.21 mmol) and a catalytic amount of PTSA·H_2O in 80% aq. ethanol (10 cm^3) was heated under reflux for 4.5 h. After being cooled to room temperature, the solution was poured into aq. sodium hydrogen carbonate and the product was extracted with ethyl acetate. Evaporation of the extract followed by column chromatography provided the *ketone* **35** (234 mg, 91%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600, 3300, 1700, 1450, 1175, 1010 and 910; δ(60 MHz) 0.98 (3 H, d, *J* 6, Me), 1.2–3.1 (12 H, m), 3.6–4.3 (3 H, m, CH_2OH and 5-H) and 4.53 (2 H, br, OH); *m/z* 212 (M^+, 75%), 194 (97), 163 (85), 124 (66), 122 (86), 97 (90), 81 (76), 79 (73), 69 (75), 67 (62) and 41 (100) (Found: M^+ 212.1414. $C_{12}H_{20}O_3$ requires M, 212.1415).

(1R*,2S*,4aR*,8S*,8aS*)-8-*Hydroxy*-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalenemethanol* (*Alternative Preparation*) **29**.—A solution of the ketone **35** (57 mg, 0.27 mmol) and toluene-*p*-sulfonohydrazide (70 mg, 0.37 mmol) in methanol (0.5 cm^3) with a drop of hydrochloric acid was stored in a freezer (−20 °C) overnight. The solvent was removed under reduced pressure to give (3*S**,4*R**,4a*S**,5*S**,8a*S**)-5-hydroxy-4-(hydroxymethyl)-3-decahydronaphthalen-1-one toluene-*p*-sulfonylhydrazone **36**; δ(60 MHz) 0.77 (3 H, d, *J* 7, Me), 1.0–2.5 (12 H, m), 2.4 (3 H, s, tolyl Me), 2.5–3.3 (2 H, br, OH), 3.3–4.0 (3 H, m, CH_2OH and 5-H), 5.4 (1 H, s, NH), 7.24 (2 H, B part of AB-type quartet, *J* 8, ArH) and 7.74 (2 H, A part of AB-type quartet, *J* 8, ArH); *m/z* 265 (15), 207 (86), 156 (64), 147 (26), 139 (25), 91 (100) and 79 (21).

To a stirred solution of crude hydrazone **36** in tetramethylethylenediamine (TMEDA) (3.5 cm^3) was added MeLi (1.05 mol dm^3 solution in ether; 2 cm^3, 2 mmol) at 0 °C and the resulting solution was heated at 40 °C for 1 h. The reaction was quenched by addition of aq. ammonium chloride and the products were extracted with ethyl acetate. Evaporation of the extract followed by MPLC separation of the residue gave the recovered hydrazone **36** (34 mg, 33%) and the diol **29** (32 mg, 61%).

[(1R*,2S*,4aR*,8S*,8aS*)-8-*Hydroxy*-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene*-1-*yl*]*methyl Pivalate* **37**.—To a stirred solution of the diol **36** (771.8 mg, 3.93 mmol) in anhydrous pyridine (8 cm^3) was added pivaloyl chloride (957 mm^3, 7.77 mmol) at 0 °C under nitrogen. The reaction mixture was stirred at room temperature for 1 h and the reaction was quenched by addition of ice. The product was extracted with ethyl acetate and the organic layers were washed with water and brine. Evaporation of the extract followed by column chromatography [eluent hexane–ethyl acetate (5:1)] provided the crude *pivalate* **37** (1.24 g) which was used for the next reaction without purification. A part of the residue was purified by MPLC for spectral data of product **37**; m.p. 57.5–59.5 °C (Found: C, 73.1; H, 10.1. $C_{17}H_{28}O_3$ requires C, 72.8; H, 10.1%); ν_{max}/cm^{-1} 3628, 3500–3300, 1739, 1730, 1480 and 1369; δ(60 MHz) 1.03 (3 H, d, *J* 6.6, Me), 1.18 (9 H, s, Bu^t), 1.30–2.52 (11 H, m), 3.93–4.1 (1 H, m), 3.86 (1 H, dd, *J* 11 and 8.1, 7-H), 4.69 (1 H, dd, *J* 11 and 4.5, 7-H) and 5.36–5.48 (2 H, m, olefinic H).

[(1R*,2S*,4aR*,8S*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalen*-1-*yl*]*methyl Pivalate* **38**.—To a stirred solution of the pivalate **37** (1.24 g) in anhydrous dichloromethane (15 cm^3) were added triethylamine (3.7 cm^3, 27.4 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBDMSOTf) (1.81 cm^3, 8.84 mmol) at 0 °C under nitrogen. After being stirred at room temperature for 1 h, the reaction mixture was poured into water. The product was extracted with ethyl acetate (30 cm^3 × 2) and the solvents were evaporated off under reduced pressure. The residue was used for the next reaction without further purification. A part of the residue was purified by MPLC for spectral data of product **38**; m.p. 69.5–70.5 °C; ν_{max}/cm^{-1} 1726, 1479, 1471, 1463 and 1284; δ(60 MHz) 0.04 (6 H, s, Me_2Si), 0.91 (9 H, s, Bu^t), 1.02 (3 H, d, *J* 6, Me), 1.17 (9 H, s), 1.27–2.87 (10 H, m), 3.86 (1 H, t, *J* 10.8, CH*H*O), 3.93–4.1 (1 H, m), 4.58 (1 H, dd, *J* 10.8 and 3, C*H*HO) and 5.34–5.45 (2 H, m, olefinic H); *m/z* 395 (M^+ + 1, 0.2%), 337 (9), 161 (100), 160 (35), 159 (82), 119 (38) and 57 (36) (Found: M^+, 394.291. $C_{23}H_{42}O_3Si$ requires M, 394.2903).

(1R*,2S*,4aR*,8S*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene*-1-*methanol* **39**.—To a stirred solution of the pivalate **38** in anhydrous ether (20 cm^3) was added LAH (149 mg, 3.9 mmol) at 0 °C and the resulting suspension was stirred at room temperature for 1 h. The reaction was quenched by addition of a small amount of water at 0 °C. After filtration of aluminium hydroxide, the ether was evaporated off and the residue was chromatographed on silica gel [eluent hexane–ethyl acetate (5:1)] to give the *alcohol* **39** (1.04 g, 85% in three steps); m.p. 67.5–68 °C (Found: C, 69.7; H, 11.2. $C_{18}H_{34}O_2Si$ requires C, 69.6; H, 11.0%); ν_{max}/cm^{-1} 3642, 3600–3200, 1471 and 1463; δ(60 MHz) 0.13 (6 H, s, Me_2Si), 0.92 (9 H, s, Bu^t), 1.04 (3 H, d, *J* 6.6, Me), 1.16–2.6 (11 H, m), 4.0–4.13 (1 H, m, 8-H), 3.35 (1 H, dd, *J* 10.8 and 8.4, CH*H*OH), 4.12 (1 H, dd, *J* 10.8 and 5.4, C*H*HOH) and 5.34–5.47 (2 H, m, olefinic H).

(1R*,2S*,4aR*,8S*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene*-1-*carbaldehyde* **40**.—To a stirred solution of oxalyl dichloride (776 mm^3, 9.17 mmol) in dichloromethane (15 cm^3) was added a solution of DMSO (631 mm^3, 9.17 mmol) in dichloromethane (5 cm^3) at −78 °C under nitrogen. Then, a solution of the alcohol **39** (1.89 g, 6.1 mmol) in dichloromethane (15 cm^3) was added. After the mixture had been stirred for 30 min, triethylamine (4.13 cm^3, 30.6 mmol) was added and the resulting solution was warmed to −25 °C. The reaction was quenched by addition of aq. ammonium chloride and the product was extracted with ethyl acetate. The combined extracts were washed with water and brine. Evaporation of the extract followed by column chromatography on silica gel [eluent hexane–ethyl acetate (20:1)] gave the *aldehyde* **40** (1.5 g, 80%); m.p. 63–64 °C (Found: C, 70.1; H, 10.4. $C_{18}H_{32}O_2Si$ requires C, 70.1; H, 10.5%); ν_{max}/cm^{-1} 1718, 1098 and 1074; δ(300 MHz) 0.05 (6 H, s, Me_2Si), 0.88 (9 H, s, Bu^t), 1.09 (3 H, d, *J* 7.1, Me), 1.4–1.68 (4 H, m), 1.7–1.96 (4 H, m), 2.14 (1 H, br s), 2.68–2.76 (1 H, m, 1-H), 3.98–4.05 (1 H, m, 8-H), 5.48–5.57 (2 H, m, olefinic H) and 9.85 (1 H, d, *J* 4.7, CHO).

(1S*,2S*,4aR*,8S*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene*-1-*carbaldehyde* **41**.—A solution of the aldehyde **40** (14.0 mg, 0.045 mmol) and potassium carbonate (52.1 mg, 0.38 mmol) in anhydrous methanol was stirred at room temperature overnight under

nitrogen. After addition of aq. ammonium chloride, the product was extracted with ether (10 cm^3 × 2) and the extracts were washed with water and brine. Evaporation of the extract followed by MPLC separation [eluent hexane–ethyl acetate (20:1)] afforded the more polar recovered aldehyde **40** (8.5 mg, 41.7%) and the less polar *equatorial aldehyde* **41** (11.3 mg, 55.4%) which had m.p. 39–40 °C (Found: C, 70.0; H, 10.6%); ν_{max}/cm^{-1} 1725, 1472, 1254 and 1075; δ(300 MHz) 0.05 (3 H, s, Me_2Si), 0.07 (3 H, s, Me_2Si), 0.92 (9 H, s, Bu^t), 0.97 (3 H, d, *J* 7, Me), 1.01–1.88 (9 H, m), 2.84 (1 H, ddd, *J* 11.2, 5.8 and 2.5, 1-H), 4.33–4.4 (1 H, m, 8-H), 5.48 (1 H, br d, *J* 9.8, 4-H), 5.58 (1 H, ddd, *J* 9.8, 4.4 and 2.7, 3-H) and 9.82 (1 H, d, *J* 2.5, CHO).

(1S*,2S*,4aR*,8S*,8aS*)-8-*Hydroxy*-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene*-1-*methanol* **43**.[16]—To a stirred solution of the aldehyde **41** (14 mg, 0.045 mmol) in acetonitrile (1.5 cm^3) was added hydrogen fluoride–pyridine complex (2.5 cm^3, 2.5 mmol) at room temperature under nitrogen. After being stirred for 15 min, the reaction mixture was quenched by addition of aq. sodium hydrogen carbonate. The product was extracted with ethyl acetate (10 cm^3 × 2) and the extracts were washed with water and brine. Evaporation of the extracts followed by MPLC purification (eluent ethyl acetate) provided (1*S**,2S*,4a*R**,8*S**,8a*S**)-8-hydroxy-2-methyl-1,2,4a,5,6,7,8,8a-octahydronaphthalene-1-carbaldehyde **42** (6.8 mg, 77.6%), which was subjected to LAH (10 mg) reduction in anhydrous ether (2 cm^3) at 0 °C. After being stirred for 5 min, the reaction mixture was quenched by addition of a small amount of water. Evaporation of the mixture followed by MPLC purification gave the diol **43**[16] (6.1 mg, 69%); m.p. 118–120 °C (Found: C, 73.4; H, 10.1. Calc. for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3); ν_{max}/cm^{-1} 3630, 3600–3200, 1457 and 1034; δ(300 MHz) 0.81 (3 H, d, *J* 7, Me), 1.0–2.01 (9 H, m), 2.25–2.4 (3 H, m), 3.66 (1 H, dd, *J* 10 and 2.9, CH*H*OH), 3.77 (1 H, t, *J* 10, C*H*HOH), 4.18–4.19 (1 H, m, 8-H), 5.35 (1 H, d *J* 9.6, olefinic H) and 5.51 (1 H, ddd, *J* 9.6, 4.4 and 2.5, olefinic H); *m/z* 178 ($M^+ - H_2O$, 5%), 147 (100) and 105 (92).

Ethyl(1′S*,2′S*,4a′R*,8′S*,8a′S*)-(E)-8′-(tert-*Butyldimethylsiloxy*)-2′-*methyl*-(1′,2′,4a′,5′,6′,7′,8′,8a′-*octahydronaphthalene*-1′-*prop*-2-*enoate* **44**.—Sodium hydride (55%; 68 mg, 1.7 mmol) was washed with anhydrous hexane three times under nitrogen. After evaporation of the mixture under reduced pressure, anhydrous THF (3 cm^3) was added. To this stirred suspension was added triethyl phosphonoacetate [$(EtO)_2P(=O)CH_2CO_2Et$] (510 mm^3, 0.174 mmol) at 0 °C. After the mixture had been stirred for 20 min, a solution of the aldehyde **41** (53.6 mg, 0.174 mmol) and HMPA (1.5 cm^3, 8.7 mmol) in THF (5 cm^3) was added and the resulting mixture was heated under reflux for 3 h. The reaction was quenched by addition of aq. ammonium chloride and the product was extracted with ethyl acetate (10 cm^2 × 2). The extracts were washed with water and brine and evaporated to dryness under reduced pressure. MPLC purification [eluent hexane–ethyl acetate (30:1)] afforded the *unsaturated ester* **44** (62.6 mg, 95%); m.p. 61–62 °C (Found: C, 69.6; H, 10.1. $C_{22}H_{38}O_3Si$ requires C, 69.8; H, 10.1%); ν_{max}/cm^{-1} 1720, 1652, 1472, 1462 and 1253; δ(90 MHz) 0.05 (6 H, s, Me_2Si), 0.92–1.04 (11 H, m), 1.36 (3 H, t, *J* 7, *Me*CH_2O), 1.3–1.98 (9 H, m), 2.16–2.84 (2 H, m), 3.92–4.04 (1 H, m, 8′-H), 4.28 (2 H, q, *J* 7.3, MeCH_2O), 5.48–5.62 (2 H, m, olefinic H), 5.92 (1 H, d, *J* 15.8, 2′-H) and 7 (1 H, dd, *J* 15.6 and 10.8, olefinic H).

Ethyl and Methyl (1S*,2S*,4aR*,8S*,8aS*)-8-(tert-*Butyldimethylsiloxy*)-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalenepropanoate* **45**.—A mixture of Mg (337 mg, 13.9 mmol) in anhydrous methanol (10 cm^3) was stirred at room temperature under nitrogen until effervescence of gas was observed. Then, a solution of the unsaturated ester **44** (175.3 mg, 0.463 mmol) in methanol (5 cm^3) was added at 0 °C and the mixture was stirred at 0 °C overnight. The reaction was quenched by addition of aq. ammonium chloride and the product was extracted with ethyl acetate. The organic layers were washed with water and brine. Evaporation of the mixture followed by MPLC purification [eluent hexane–ethyl acetate (5:1)] gave a mixture of ethyl and methyl esters (174.2 mg) **45** which was used for the next reaction without further separation. The methyl ester **45** had ν_{max}/cm^{-1} 1740, 1471, 1437 and 1254; δ(300 MHz) 0.08 (6 H, s, Me_2Si), 0.82 (3 H, d, *J* 7, Me), 0.88 (9 H, s, Bu^t), 0.9–1.06 (1 H, m), 1.26–1.84 (8 H, m), 1.98–2.42 (5 H, m), 3.67 (3 H, s, MeO), 4.15 (1 H, br s, 8-H), 5.37–5.4 (1 H, m, olefinic H) and 5.55 (1 H, ddd, *J* 9.7, 4.4 and 2.9, olefinic H); *m/z* 309 ($M^+ - Bu^t$, 100%), 234 (34), 159 (29), 147 (36) and 75 (18) (Found: $M^+ - Bu^t$, 309.1885. $C_{17}H_{29}O_3Si$ requires *m/z*, 309.1885).

(1′S*,2′S*,4a′R*,8′S*,8a′S*)-8′-(tert-*Butyldimethylsiloxy*)-2′-*methyl*-1′,2′,4a′,5′,6′,7′,8′,8a′-*octahydronaphthalene*-1′-*propanol* **46**.—To a stirred solution of a mixture of ethyl and methyl esters **45** (174.2 mg) in anhydrous ether (3 cm^3) was added LAH (35 mg, 0.92 mmol) at 0 °C and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched by addition of water, and aluminium hydroxide was removed by filtration. Evaporation of the mixture followed by MPLC purification gave the *alcohol* **46** (133.6 mg, 85% in two steps) (Found: C, 70.9; H, 11.1. $C_{20}H_{38}O_2Si$ requires C, 71.0; H, 11.3%); ν_{max}/cm^{-1} 1720, 1652, 1472, 1462 and 1253; δ(300 MHz) 0.07 (3 H, s, MeSi), 0.08 (3 H, s, MeSi), 0.83 (3 H, d, *J* 7, Me), 0.89 (9 H, s, Bu^t), 0.93–1.15 (3 H, m), 1.23–1.52 (4 H, m), 1.53–1.87 (6 H, m), 2.21–2.39 (2 H, m), 3.58–3.73 (2 H, m, 1-H_2), 4.16–4.2 (1 H, m, 8′-H), 5.36–5.46 (1 H, olefinic H) and 5.57 (1 H, ddd, *J* 9.4, 4.7 and 2.7, olefinic H); *m/z* 337 ($M^+ - 1$, 0.3%), 281 (11), 206 (41), 189 (74), 147 (100), 133 (24), 105 (54) and 75 (40).

(1′S*,2′S*,4a′R*,8′S*,8a′S*)-8′-*Hydroxy*-2′-*methyl*-1′,2′,4a′,5′,6′,7′,8′,8a′-*octahydronaphthalene*-1′-*propanol* **47**.—To a stirred solution of the siloxy compound **46** (462.8 mg, 1.34 mmol) in acetonitrile (15 cm^3) was added aq. hydrogen fluoride (46.5%; 4 cm^3) at 0 °C and the resulting solution was stirred at room temperature for 1 h. The reaction was quenched by addition of aq. sodium hydrogen carbonate and extraction with ethyl acetate followed by evaporation of the extract left an oil, which was purified by MPLC (eluent ethyl acetate) to give the *diol* **47** (283 mg, 92%); m.p. 128–130 °C (Found: C, 74.8; H, 10.7. $C_{14}H_{24}O_2$ requires C, 75.0; H, 10.8%); ν_{max}/cm^{-1} 3615, 3600–3200, 1447 and 1236; δ(300 MHz) 0.84 (3 H, d, *J* 7.1, Me), 0.93–1.25 (3 H, m), 1.39–1.93 (11 H, m), 2.15–2.38 (2 H, m), 3.61–3.71 (2 H, m, 1-H_2), 4.16 (1 H, br s, 8′-H), 5.39 (1 H, br d, *J* 9.7, olefinic H) and 5.56–5.65 (1 H, m, olefinic H).

Resolution of Racemic (1′S*,2′S*,4a′R*,8′S*,8a′S*)-8′-*Hydroxy*-2′-*methyl*-1′,2′,4a′,5′,6′,7′,8′,8a′-*octahydronaphthalene*-1′-*propanol* **47**.—To a stirred solution of racemic diol **47** (109.5 mg, 0.485 mol) in anhydrous dichloromethane (4 cm^3) were added (*R*)-*O*-methylmandelic acid (87.1 mg, 0.534 mmol), DCC (114.5 mg, 0.485 mmol) and a catalytic amount of DMAP under nitrogen. After being stirred overnight, the mixture was treated with water. The product was extracted with ethyl acetate and the extracts were washed with water and brine. Evaporation of the extracts followed by MPLC separation [eluent hexane–ethyl acetate (3:1)] provided, in order of elution (1′*S*,2′*S*,4a′*R*,8′*S*,8a′*S*)-3-(8′-hydroxy-2′-methyl-1′,2′,4a′,5′,6′,7′,8′,8a′-octahydronaphthalen-1′-yl)propyl (*R*)-*O*-methylmandelate **48** (66.7 mg, 37%) and (1′*R*,2′*R*,4a′*S*,8′*R*,8a′*R*)-3-(8′-hydroxy-2′-methyl-1′,2′,4a′,5′,6′,7′,8′,8a′-octahydronaphthalen-1′-yl)propyl (*R*)-*O*-methylmandelate **49** (86 mg, 48%). The less polar mandelate **48** had $[\alpha]_D$ +32.9 (*c* 0.557); ν_{max}/cm^{-1} 3619, 3463,

1743, 1455, 1390, 1250 and 1212; δ(300 MHz) 0.73 (3 H, d, *J* 7, Me), 0.9–1.05 (4 H, m), 1.2 (1 H, br s, OH), 1.4–1.8 (8 H, m), 2.1–2.2 (2 H, m), 3.41 (3 H, s, MeO), 3.93 (1 H, s, 8'-H), 4.1–4.3 (2 H, m, 1-H_2), 4.77 (1 H, s, MeOC*H*Ph), 5.37 (1 H, d, *J* 9.8, olefinic H), 5.5 (1 H, br s, olefinic H) and 7.4–7.5 (5 H, m, ArH); *m/z* 354 ($M^+ - H_2O$, 17%), 188 (30), 145 (22), 121 (100) and 105 (20) (Found: $M^+ - H_2O$, 354.2195. $C_{23}H_{30}O_3$ requires *m/z*, 354.2195). The more polar mandelate **49** had m.p. 69–71 °C; $[\alpha]_D$ −101.5 (*c* 0.86); ν_{max}/cm^{-1} 3619, 3467, 1743, 1456, 1388, 1232 and 1114; δ(300 MHz) 0.73 (3 H, d, *J* 7.2, Me), 0.8–1.1 (4 H, m), 1.3–1.9 (9 H, m), 2.1–2.2 (2 H, m), 3.41 (3 H, s, MeO), 3.95 (1 H, br s, 8'-H), 4.17 (2 H, t, *J* 6.1, 1-H_2), 4.77 (1 H, s, MeOC*H*Ph), 5.36 (1 H, d, *J* 9.8, olefinic H), 5.55 (1 H, br s, olefinic H) and 7.3–7.5 (5 H, m, ArH); *m/z* CI (CH_4) 373 ($M^+ + 1$, 1%), 355 (9), 189 (100), 187 (18) and 121 (18) (Found: $M^+ - H_2O$, 354.2192).

(1'S,2'S,4a'S,8'S,8a'S)-3-{2'-*Methyl*-8'-[(S)-2-*methylbutanoyloxy*]-1',2',4a',5',6',7',8',8a'-*octahydronaphthalen*-1'-*yl*}*propyl* (R)-O-*Methylmandelate* **50**.—A solution of the mandelate **48** (195 mg, 0.53 mmol), (*S*)-2-methylbutanoic anhydride (212 mm^3, 1.06 mmol) and DMAP (100 mg) in dichloromethane (4 cm^3) was heated at 40 °C for 30 min. The reaction mixture was poured into water and the product was extracted with ether. The extracts were washed with water and brine. Evaporation of the extract left the diester **50**, which was used without purification; ν_{max}/cm^{-1} 1753, 1729, 1456, 1186 and 1172; δ(60 MHz) 0.69 (3 H, d, *J* 7, Me), 0.87 (3 H, t, *J* 7.4, *Me*CH_2), 1.08 (3 H, d, *J* 6.8, *Me*CH), 0.8–3.8 (9 H, m), 3.39 (3 H, s, OMe), 4.07 (2 H, br t, CH_2CH_2O), 4.72 (1 H, s, MeC*H*), 5.08 (1 H, br s, 8'-H), 5.3–5.7 (2 H, olefinic H) and 7.4 (5 H, br, ArH); *m/z* 456 (M^+, 0.7%), 354 (7), 188 (15), 121 (100) and 57 (18) (Found: $M^+ - C_5H_{10}O_2$, 354.2195. $C_{15}H_{22}O$ requires *m/z*, 354.2195).

(1S,4aR,7S,8S,8aS)-8-(3'-*Hydroxypropyl*)-7-*methyl*-1,2,3,4,4a,7,7,8a-*octahydronaphthalen*-1-*yl* (S)-2-*Methylbutanoate* **51**.—To a stirred solution of the crude diester **50** in methanol (2 cm^3) was added a methanolic solution of potassium hydroxide (0.1 mol dm^3 solution; 10 cm^3, 1 mmol), and the resulting solution was stirred overnight at room temperature. The solution was poured into water and neutralised with dil. HCl. The product was extracted with ethyl acetate. Evaporation of the extract followed by MPLC purification [eluent hexane–ethyl acetate (5:1)] gave the hydroxy ester **51** (151.5 mg, 93%); m.p. 37.5–38.5 °C; $[\alpha]_D$ +133 (*c* 0.624); ν_{max}/cm^{-1} 3638, 3600–3400, 1727, 1458, 1383 and 1187; δ(300 MHz) 0.84 (3 H, d, *J* 7, Me), 0.91 (3 H, t, *J* 7.4, *Me*CH_2), 1.15 (3 H, d, *J* 6.8, *Me*CH), 1.15 (3 H, d, *J* 6.8), 1.0–1.83 (11 H, m), 1.9–2.07 (1 H, m), 2.22–2.45 (3 H, m), 3.5–3.73 (2 H, m, 3'-H_2), 5.09–5.25 (1 H, m, 8-H), 5.36–5.49 (1 H, m, olefinic H) and 5.55–5.7 (1 H, m, olefinic H); *m/z* CI (CH_4) 309 ($M^+ + 1$, 3%), 207 (100), 189 (87) and 71 (19) (Found: $M^+ - C_5H_{10}O_2$, 206.1678. $C_{14}H_{22}O$ requires *m/z*, 206.1671).

(1S,4aR,7S,8S,8aS)-8-(2'-*Formylethyl*)-7-*methyl*-1,2,3,4,4a,7,8,8a-*octahydronaphthalen*-1-*yl* (S)-2-*Methylbutanoate* **6**.—To a stirred solution of oxalyl dichloride (117 mm^3, 1.38 mmol) in anhydrous dichloromethane (2 cm^3) was added a solution of DMSO (95 mm^3, 1.38 mmol) in dichloromethane (0.5 cm^3) at −78 °C under nitrogen. After being stirred for 10 min, the mixture was treated with a solution of the alcohol **51** (142 mg, 0.46 mmol) in dichloromethane (2 cm^3) and was then stirred for 30 min. Triethylamine (497 mm^3, 3.68 mmol) was added and reaction was quenched at −25 °C by addition of aq. ammonium chloride. The product was extracted with ethyl acetate. Evaporation of the extract under reduced pressure followed by column chromatography [eluent hexane–ethyl acetate (20:1)] gave the aldehyde **6** (136.6 mg, 97%); $[\alpha]_D$ +138.8 (*c* 0.533); ν_{max}/cm^{-1} 1731, 1460, 1185 and 1067; δ(300 MHz) 0.82 (3 H, d, *J* 7, Me), 0.9 (3 H, t, *J* 7.4, *Me*CH_2), 1.15 (3 H, d, *J* 6.8, *Me*CH), 0.7–2.6 (17 H, m), 5.1–5.3 (1 H, m, 8-H), 5.37–5.6 (2 H, m, olefinic H) and 9.6–9.7 (1 H, m, CHO); *m/z* 307 ($M^+ + 1$, 3%), 205 (89), 187 (100), 159 (15) and 85 (18) (Found: $M^+ - C_5H_{10}O_2$, 204.1513. $C_{14}H_{20}O$ requires *m/z*, 204.1513).

Methyl (5R)-5-*Hydroxy*-7-{(1'S,2'S,4a'R,8'S,8a'S)-2'-*methyl*-8'-[(S)-2-*methylbutanoyloxy*]-1',2',4a',5',6',7',8',8a'-*octahydronaphthalen*-1'-*yl*}-3-*oxoheptanoate* **55** *and Methyl* (5S)-5-*Hydroxy*-7-{(1'S,2'S,4a'R,8'S,8a'S)-2'-*methyl*-8'-[(S)-2-*methylbutanoyloxy*]-1',2',4a',5',6',7',8',8a'-*octahydronaphthalen*-1'-*yl*}-3-*oxoheptanoate* **56**.—To a stirred solution of the aldehyde **6** (85 mg, 0.28 mmol) in anhydrous dichloromethane (3 cm^3) was added a solution of $TiCl_4$ (1 mol dm^3 in dichloromethane; 0.65 cm^3, 0.65 mmol) at −90 °C under nitrogen. After the mixture had been stirred for 15 min, a solution of bistrimethylsiloxy compound **7** (179.9 mg, 0.691 mmol) in dichloromethane (1 cm^3) was added and the resulting solution was allowed to warm to −50 °C. The reaction was quenched by addition of water and the product was extracted with ethyl acetate. The extracts were washed with water and brine and evaporated to dryness to give an epimeric mixture of the aldol adducts **55** and **56** (149 mg); ν_{max}/cm^{-1} 3600–3200, 1752, 1725, 1657, 1631, 1240 and 1187; δ(300 MHz) 0.82 (d, *J* 6.9) and 0.83 (d, *J* 6.8) (3 H total, 2'-Me), 0.91 (3 H, t, *J* 7.4, *Me*CH_2), 1.14 (3 H, d, *J* 6.9, *Me*CH), 1.0–1.89 (13 H, m), 1.91–2.08 (1 H, m), 2.14–2.44 (3 H, m), 2.51–2.81 (3 H, m), 3.5 (2 H, s, 2-H_2), 3.75 (3 H, s, MeO), 3.93–4.08 (1 H, m, 5-H), 5.11–5.18 (1 H, m, 8'-H), 5.34–5.45 (1 H, m, olefinic H) and 5.26–5.64 (1 H, m, olefinic H); *m/z* 320 ($M^+ - C_5H_{10}O_2$, 15%), 162 (63), 160 (49), 147 (55), 145 (100) and 57 (99) (Found: $M^+ - C_5H_{10}O_2$, 320.1988. $C_{19}H_{28}O_4$ requires *m/z*, 320.1988).

Methyl (3R,5R)-3,5-*Dihydroxy*-7-{(1'S,2'S,4a'R,8'S,8a'S)-2'-*methyl*-8'-[(S)-2-*methylbutanoyloxy*]-1',2',4a',5',6',7',8',8a'-*octahydronaphthalen*-1'-*yl*}*heptanoate* **57** *and Methyl* (3S,5S)-3,5-*Dihydroxy*-7-{(1'S,2'S,4a'R,8'S,8a'S)-2'-*methyl*-8'-[(S)-2-*methylbutanoyloxy*]-1',2',4a',5',6',7',8',8a'-*octahydronaphthalen*-1'-*yl*}*heptanoate* **58**.—To a stirred solution of the epimeric mixture of keto esters **55** and **56** (149 mg) in anhydrous THF (3 cm^3)–methanol (0.75 cm^3) was added Et_2BOMe (1 mol dm^3 solution in THF; 0.34 cm^3, 0.34 mmol) at −78 °C under nitrogen and the resulting solution was stirred at room temperature for 15 min. Sodium boranuide (53 mg, 1.4 mmol) was added at −78 °C and the solution was allowed to warm to room temperature. The reaction was quenched by addition of acetic acid and the product was extracted with ethyl acetate. Evaporation of ethyl acetate followed by MPLC separation gave a mixture of the boronates **59** and **60** (52 mg, 40% in 2 steps) and a mixture of the *syn* diols **57** and **58** (23.1 mg, 19.3% in two steps) in order of elution. The mixture of the boronates **59** and **60** had ν_{max}/cm^{-1} 1741, 1728, 1460, 1400, 1383 and 1332; δ(300 MHz) 0.63 (2 H, q, *J* 7.5, MeCH_2B), 0.83 (3 H, d, *J* 7.4, 2'-Me), 0.91 (3 H, t, *J* 7.5, *Me*CH_2B), 1.14 (3 H, d, *J* 7, *Me*CH), 1.0–1.48 (18 H, m), 1.9–2.1 (2 H, m), 2.23–2.37 (2 H, m), 2.44 (1 H, dd, *J* 15.4 and 6.2, 4-H), 2.6 (1 H, dd, *J* 15.5 and 7.1, 4-H), 3.71 (3 H, s, MeO), 3.8–3.97 (1 H, m, 3- or 5-H), 4.3–4.43 (1 H, m, 5- or 3-H), 5.1–5.2 (1 H, m, 8'-H), 5.37–5.43 (1 H, m, olefinic H) and 5.56–5.67 (1 H, m, olefinic H); *m/z* 462 (M^+, 31%), 461 ($M^+ - 1$, 10), 361 (45), 360 (51), 288 (24), 287 (100), 162 (31), 160 (26) and 147 (24). The mixture of *syn* diols **57** and **58** had ν_{max}/cm^{-1} 3503, 1717, 1457, 1439 and 1216; δ(300 MHz) 0.82 (3 H, d, *J* 7, 2'-Me), 0.91 (3 H, t, *J* 7, *Me*CH_2), 1.14 (3 H, d, *J* 6.9, *Me*CH), 0.83–1.83 (18 H, m), 1.9–2.07 (1 H, m), 2.2–2.43 (3 H, m), 2.47–2.55 (1 H, m), 3.72 (3 H, s, MeO), 3.8–3.9 (1 H, m, 5-H), 4.2–4.33 (1 H, m, 3-H), 5.1–5.23 (1 H, m, 8'-H), 5.37–5.47 (1 H, m, olefinic H) and 5.55–5.67 (1 H, m, olefinic H).

Dihydrocompactin **1** *and* 3,5-*Epidihydrocompactin* **61**.—To a stirred solution of a mixture of *syn* diols **57** and **58** (23.1 mg, 0.054 mmol) in acetonitrile (1 cm^3) was added HF–pyridine complex (1 cm^3) at room temperature under nitrogen. After being stirred for 1 h, the reaction mixture was quenched by addition of aq. sodium hydrogen carbonate. The product was extracted with ethyl acetate (20 cm^3 × 2) and the extracts were washed with water and brine. Evaporation of the extracts under reduced pressure followed by repeated MPLC gave the less polar 3,5-epidihydrocompactin **61** (5.5 mg, 26%) and the more polar dihydrocompactin **1** (9.3 mg, 44%). The less polar 3,5-epidihydrocompactin **61** had m.p. 107.5–108.5 °C; $[\alpha]_D$ +120 (*c* 0.222); λ_{max}(EtOH)/nm 220 ($\Delta\varepsilon$ −1.52); ν_{max}/cm^{-1} 3600–3400, 1728, 1458, 1385 and 1246; δ*(300 MHz) 0.84 (3 H, d, *J* 6.9, 9-Me), 0.91 (3 H, t, *J* 7.4, *Me*CH_2), 1.15 (3 H, d, *J* 7.1, *Me*CH), 1.0–1.3 (3 H, m), 1.33–1.83 (12 H, m), 2.1–1.9 (2 H, m), 2.23–2.47 (3 H, m), 2.57–2.65 (1 H, m), 2.75 (1 H, dd, *J* 17.6 and 4.9, 2-H), 4.39 (1 H, br s, 3-H), 4.63–4.7 (1 H, m, 5-H), 5.16 (1 H, br s, 15-H), 5.41 (1 H, br d, *J* 9.8, olefinic H) and 5.57–5.63 (1 H, m, olefinic H); *m/z* CI (CH_4) 394 (M^+ + 2, 3%), 393 (M^+ + 1, 14), 291 (48), 274 (22), 273 (100), 189 (44), 187 (14) and 145 (13) (Found: $M^+ - C_5H_{10}O_2$, 290.1882. $C_{18}H_{26}O_3$ requires *m/z*, 290.1882). The more polar dihydrocompactin **1** had m.p. 80.5–82 °C; $[\alpha]_D$ +127 (*c* 0.119); λ_{max}(EtOH)/nm 242 ($\Delta\varepsilon$ +0.2) and 212 ($\Delta\varepsilon$ −1.3); ν_{max}/cm^{-1} 3600–3400, 1728, 1458, 1385 and 1246; δ*(300 MHz) 0.85 (3 H, d, *J* 7, 9-Me), 0.91 (3 H, t, *J* 7.5, *Me*CH_2), 1.15 (3 H, d, *J* 7, *Me*CH), 1.0–2.1 (17 H, m), 2.2–2.47 (3 H, m), 2.57–2.65 (1 H, m), 2.74 (1 H, dd, *J* 17.6 and 4.9, 2-H), 4.38 (1 H, br s, 3-H), 4.57–4.73 (1 H, m, 5-H), 5.18 (1 H, br s, 15-H), 5.41 (1 H, br d, *J* 9.8, olefinic H) and 5.57–5.63 (1 H, m, olefinic H); *m/z* CI (CH_4) 394 (M^+ + 2, 23%), 393 (M^+ + 1, 67), 291 (80), 273 (100), 189 (39), 187 (25) and 145 (13) (Found: $M^+ - C_5H_{10}O_2$, 290.1882).

Determination of Absolute Stereostructure of Decalin Portion.—(1S,4aS,5R,6S,7R,8S.8aR)-5,6-*Dihydroxy*-8-(3′-*hydroxypropyl*)-7-*methyldecahydronaphthalen*-1-*yl* (S)-2-*methylbutanoate* **52**. To a stirred solution of the octahydronaphthalene **51** (30.5 mg, 0.1 mmol) in THF (1.5 cm^3) were added *N*-methylmorpholine *N*-oxide (NMO) monohydrate (33.9 mg, 0.25 mmol), *tert*-butyl alcohol (1 cm^3), water (0.1 cm^3) and osmium tetraoxide (11.6 mg, 0.046 mmol) successively. The resulting solution was stirred overnight at room temperature and the reaction was quenched by addition of aq. sodium hydrogen sulfate. The product was extracted with ethyl acetate (20 cm^3 × 2) and the extracts were washed with water and brine. Evaporation of the extracts under reduced pressure followed by MPLC (eluents ethyl acetate) gave the triol **52** (23.7 mg, 70%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3629, 1718, 1458, 1220 and 1052; δ(90 MHz) 0.83 (3 H, d, *J* 7.4, 2-Me), 0.91 (3 H, t, *J* 7.3, *Me*CH_2), 1.16 (3 H, d, *J* 6.8, *Me*CH), 1.26–1.95 (15 H, m), 2.04–2.21 (5 H, m), 3.40 (1 H, dd, *J* 10.4 and 3, 5-H), 3.58 (2 H, t, *J* 5.6, 3′-H_2), 3.78 (1 H, t, *J* 3, 6-H) and 5.17 (1 H, br, 1-H).

(1′S,2′R,3′S,4′R,4a′,8′S,8a′R)-3′-{3′,4′-*Dihydroxy*-2′-*methyl*-8′-[(S)-2-*methylbutanoyloxy*]*decahydronaphthalen*-1′-*yl*}*propyl pivalate* **53**. To a stirred solution of the triol **52** (14.7 mg, 0.043 mmol) in anhydrous pyridine (1 cm^3) was added pivaloyl chloride (30 mm^3, 0.24 mmol) at 0 °C and the resulting solution was stirred at room temperature for 20 min under nitrogen. The reaction was quenched by addition of ice and the product was extracted with ethyl acetate. The organic layer was washed with brine. Evaporation of the extract followed by MPLC purification afforded the pivalate **53** (10.3 mg, 56%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3567, 1719, 1289 and 1162; δ(90 MHz) 0.83 (3 H, d, *J* 7.2, 2′-Me), 0.91 (3 H, t, *J* 7.2, *Me*CH_2), 1.15 (3 H, d, *J* 5.9, *Me*CH), 1.18 (9 H, s, Bu^t), 1.22–2.04 (19 H, m), 3.41 (1 H, dd, *J* 10.5 and 2.9, 4′-H), 3.79 (1 H, t, *J* 2.9, 3′-H), 3.96 (2 H, t, *J* 5.4, 1-H_2) and 5.12 (1 H, br, 8′-H).

(1′S,2′R,3′S,4′R,4a′S,8′S,8a′R)-3-{3′,4′-*Dibenzoyloxy*-2′-[(S)-2-*methylbutanoyloxy*]*decahydronapthalen*-1′-*yl*}*propyl pivalate* **54**. A solution of the diol **53** (10.3 mg, 0.024 mmol) in anhydrous pyridine (1.6 cm^3) was stirred with benzoyl chloride (35 mm^3, 0.3 mmol) and DMAP (4.2 mg) at room temperature overnight under nitrogen. The reaction was quenched by addition of ice and the product was extracted with ethyl acetate. Evaporation of the extract followed by MPLC purification gave the dibenzoate **54** (10.7 mg, 71%); λ_{max}(EtOH)/nm 229 (ε/dm^3 mol^{-1} cm^{-1} 24 600); λ_{max}(EtOH)/nm 238 ($\Delta\varepsilon$ +20.8) and 222 ($\Delta\varepsilon$ −13.9); $\nu_{max}(CHCl_3)/cm^{-1}$ 1719, 1452, 1285 and 1120; δ(90 MHz) 0.94 (3 H, d, *J* 7.3, 2′-Me), 1.09 (3 H, t, *J* 7.4, *Me*CH_2), 1.18 (9 H, s, Bu^t), 1.24 (3 H, d, *J* 6.8, *Me*CH), 1.5–2.52 (17 H, m), 3.93–4.08 (2 H, m, 1-H_2), 5.17 (2 H, dd, *J* 11.4 and 2.8, 4′- and 8′-H), 5.5 (1 H, t, *J* 3.1, 3′-H), 7.32–7.62 (5 H, m, aromatic) and 7.85–8.16 (5 H, m, ArH); *m/z* 635 (M^+ + 1, 11%), 513 (20), 411 (100), 289 (61), 187 (46), 105 (36) and 57 (14).

Determination of Absolute Stereostructure of Lactonic Portion.—3,5-*Epidihydrocompactin* 3-O-*tetrahydropyranyl derivative* **62**. To a stirred solution of 3,5-epidihydrocompactin **61** (19.1 mg, 0.049 mmol) in anhydrous dichloromethane (2 cm^3) were added dihydropyran (35 mm^3, 0.38 mmol) and pyridinium toluene-*p*-sulfonate (PPTS) (7.5 mg, 0.03 mmol) at 0 °C and the resulting solution was stirred at room temperature overnight under nitrogen. The solution was poured into 50% aq. sodium chloride and the product was extracted with ethyl acetate. Evaporation of the extract followed by MPLC purification provided the tetrahydropyranyl derivative **62** (17.3 mg, 79%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720, 1457, 1256 and 1034; δ*(90 MHz) 0.84 (3 H, d, *J* 9-Me), 0.91 (3 H, t, *J* 7.2, *Me*CH_2), 1.15 (3 H, d, *J* 7, *Me*CH), 1.4–2.5 (25 H, m), 2.6–2.76 (2 H, m), 3.47–3.64 (1 H, m, OCHOC*H*H[CH_2]$_3$), 3.75–3.93 (1 H, m, OCHOCH-*H*[CH_2]$_3$), 4.24–4.34 (1 H, m, 3-H), 4.55–4.69 (2 H, m, 5-H and OC*H*O[CH_2]$_4$), 5.14 (1 H, br s, 15-H), 5.39 (1 H, d, *J* 9.9, olefinic H) and 5.52–5.74 (1 H, m, olefinic H).

(3R,5S)-7-[(1′S,2′S,4a′R,8′S,8a′S)-8′-*Hydroxy*-2′-*methyl*-1′,2′,4a′,5′,6′,7′,8′,8a′-*octahydronaphthalen*-1-*yl*]-3-(*tetrahydropyran*-2-*yloxy*)*heptane*-1,5-*diol* **63** *and its* 1-O-(tert-*butyl-diphenylsilyl*) *derivative* **64**. To a stirred solution of the tetrahydropyranyl compound **62** in anhydrous ether (2 cm^3) was added LAH (18.2 mg, 0.48 mmol) at 0 °C and the resulting slurry was stirred at room temperature for 6.5 h under nitrogen. The reaction was quenched by addition of a small amount of water. Evaporation of the extract gave crude (3R,5S)-7-[(1′*S*,2′*S*,4a′*R*,8′*S*,8a′*S*)-8′-hydroxy-2′-methyl-1′,2′,4a′,5′,6′,7′,8′,8a′-octahydronaphthalen-1′-yl]-3-(tetrahydropyran-2-yloxy)heptane-1,5-diol **63** (21.1 mg), which was used without purification.

To a stirred solution of the triol **63** (21.1 mg) in DMF (1 cm^3) were added triethylamine (30 mm^3, 0.22 mmol), DMAP (7.6 mg, 0.062 mmol) and TBDPSCl (45 mm^3, 0.17 mmol) and the resulting solution was stirred at room temperature overnight under nitrogen. The reaction was quenched by addition of water and the product was extracted with ethyl acetate. Evaporation of the extract followed by MPLC purification afforded the siloxy compound **64** (9.3 mg, 40% in two steps); $\nu_{max}(CHCl_3)/cm^{-1}$ 3467, 1428, 1112 and 1031; δ*(90 MHz) 0.82 (3 H, d, *J* 7, 9-Me), 1.05 (9 H, s, Bu^t), 1.54–2.33 (25 H, m), 3.32–3.49 (1 H, m), 3.66–4.01 (5 H, m, 3-, 5-, 8-H and OCHOCH_2[CH_2]$_3$), 4.10–4.19 (2 H, m, 1-H_2), 4.56–4.7 (1 H, m, OC*H*O[CH_2]$_4$), 5.38 (1 H, d, *J* 10.8, olefinic H), 5.52–5.7 (1 H, m, olefinic H), 7.35–7.42 (5 H, m, ArH) and 7.61–7.72 (5 H, m, ArH).

(1S,2S,4aR,8S,8aS)-8-*Acetoxy*-1-[(3′S,5′R)-3′-*acetoxy*-7′-

* Non-systematic numbering is used in this part. See text.

(tert-*butyldiphenylsiloxy*-5'-(*tetrahydropyran*-2-*yloxy*)*heptyl*]-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene* **65**. To a stirred solution of the siloxy compound **64** (9.3 mg, 0.015 mmol) in anhydrous pyridine (1 cm^3) were added acetic anhydride (40 mm^3, 0.42 mmol) and DMAP (2.4 mg, 0.02 mmol) and the resulting solution was stirred at room temperature overnight under nitrogen. Without aqueous work-up, the product was isolated by preparative TLC (PLC) [silica gel; developer hexane–ethyl acetate (1:1)] to give the diacetate **65** (10.5 mg, 100%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1724, 1375, 1254 and 1112; δ*(90 MHz) 0.8 (3 H, d, *J* 6.8, 9-Me), 1.04 (9 H, s, Bu^t), 1.16–1.97 (20 H, m), 2.01 (3 H, s, Ac), 2.03 (3 H, s, Ac), 2.08–2.37 (4 H, m), 3.3–3.5 (1 H, m, 3-H), 3.65–4.02 (4 H, m, 1-H_2 and $OCHOCH_2[CH_2]_4$), 4.58–4.64 (1 H, m, $OCHO[CH_2]_4$), 4.87–5.04 (1 H, m, 5-H), 5.12 (1 H, br s, 8-H), 5.37 (1 H, d, *J* 9.9, olefinic H), 5.53–5.68 (1 H, m, olefinic H), 7.28–7.49 (5 H, m, ArH) and 7.59–7.74 (5 H, m, ArH).

(1S,2S,4aR,8S,8aS)-8-*Acetoxy*-1-[(3'S,5'R)-3'-*acetoxy*-7'-*hydroxy*-5'-(*tetrahydropyran*-2-*yloxy*)*heptyl*]-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene* **66**. To a solution of the acetate **65** (10.5 mg, 0.015 mmol) in THF (1 cm^3) was added TBAF (80 mm^3, 0.08 mmol) and the resulting solution was stirred at room temperature overnight under nitrogen. Without aqueous work-up, the product was isolated by PLC [silica gel; hexane–ethyl acetate (1:3)] to give the alcohol **66** (7.5 mg, 100%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3503, 1724, 1375 and 1253; δ*(90 MHz) 0.81 (3 H, d, *J* 7, 9-Me), 0.93–1.98 (21 H, m), 2.048 (3 H, s, Ac), 2.053 (3 H, s, Ac), 2.1–2.38 (4 H, m), 3.36–4.03 (5 H, m, 1-H_2, 3-H and $OCHOCH_2[CH_2]_3$), 4.48–4.72 (1 H, m, $OCHO[CH_2]_4$), 4.82–5.04 (1 H, m, 5-H), 5.15 (1 H, br s, 8-H), 5.38 (1 H, d, *J* 9.6, olefinic H) and 5.51–5.7 (1 H, m, olefinic H).

(1S,2S,4aR.8S,8aS)-8-*Acetoxy*-1-[(3'S,5'S)-3'-*acetoxy*-5'5',7'-*bis*(p-*bromobenzoyloxy*)*heptyl*]-2-*methyl*-1,2,4a,5,6,7,8,8a-*octahydronaphthalene* **68**. A solution of the alcohol **66** (7.5 mg, 0.015 mmol) and PPTS (5.5 mg, 0.022 mmol) in 10% aq. ethanol (3 cm^3) was heated under reflux for 5 h. Without aqueous work-up, the product was isolated by PLC (silica gel; ethyl acetate) to give (1*S*,2*S*,4a*R*,8*S*,8a*S*)-8-acetoxy-1-[(3'S,5'S)-3'-acetoxy-5',7'-dihydroxyheptyl]-2-methyl-1,2,4a,5,6,7,8,8a-octahydronaphthalene **67** (5.8 mg).

To a solution of the diol **67** (5.8 mg) in anhydrous pyridine (0.5 cm^3) were added DMAP (3.1 mg, 0.025 mmol) and *p*-bromobenzoyl chloride (61.1 mg, 0.28 mmol) and the resulting solution was stirred at room temperature overnight under nitrogen. Without aqueous work-up, the product was isolated by PLC [silica gel; hexane–ethyl acetate (1:1)] followed by MPLC purification [eluent hexane–ethyl acetate (4:1)] to afford the bis-*p*-bromobenzoate **68** (4.6 mg, 41% in two steps); λ_{max}(EtOH)/nm 242 (ε/dm^{-3} mol^{-1} cm^{-1} 34 300); λ_{max}(EtOH)/nm 252 ($\Delta\varepsilon$ +5.46) and 236 ($\Delta\varepsilon$ −2.18); $\nu_{max}(CHCl_3)/cm^{-1}$ 1724, 1591, 1269 and 1103; δ*(90 MHz) 0.76 (3 H, d, *J* 7.3, 9-Me), 0.83–1.76 (16 H, m), 1.91 (3 H, s, Ac), 1.95 (3 H, s, Ac), 2.18–2.27 (3 H, m), 4.13 (1 H, m, 8-H), 4.42 (1 H, m, 5-H), 4.9–5.3 (2 H, m, olefinic H), 5.37 (1 H, br d, *J* 8.4, 1-H), 5.53–5.6 (1 H, m, 3-H), 7.49–7.56 (4 H, m, ArH) and 7.78–7.87 (4 H, ArH); *m*/*z* 702 ($M^+ - CH_3CO_2H$, 12%), 440 (7), 300 (39), 240 (50), 185 (79), 160 (100), 146 (78), 105 (69) and 43 (51).

* Non-systemic numbering is used in this part. See text.

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