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# SULPHONE-MEDIATED CYCLOBUTANONE TO α-ALKOXY-CYCLOPENTANONE RING EXPANSION REACTIONS; SCOPE, LIMITATIONS AND APPLICATIONS

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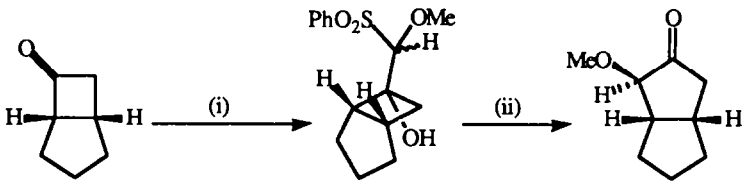
Abstract

The bicycloalkanones (1)-(3) were treated with the lithiated sulphone (4) to give the ring expanded α-methoxyketones (12), (14) and (16) generally as a mixture of epimers. The same bicycloalkanones furnished the α-benzyloxyketones (13), (15), and (17) on reaction with reagent (5). The ketone (3) reacted with the sulphone anion (6) to give, after Lewis acid treatment, the α-allyloxycyclopentanone derivatives (27a) and (27b) and one of these compounds (27b) was transformed into the ether (31). The bicycloheptanone (20) was converted into four ring-expanded products (22a), (22b), (24a) and (24b) and one of the compounds (24a) was used to synthesise the prostacyclin analogue (36). A brief study was made of the mechanism of the Lewis-acid catalysed rearrangement of the intermediate hydroxy sulphone to the ring-expanded compounds.

In 1987 Trost and Mikhail described a method for the conversion of cyclic ketones, particularly cyclobutanones and cyclopentanones, into their α-methoxylated ring expanded homologues.[1] The procedure involves treatment of a cycloalkanone such as the bicycloheptanone (1) with lithiated methoxymethyl phenyl sulphone (4) at -78 °C followed by rearrangement of the intermediate adduct (7) with diisobutylaluminium chloride to furnish the methoxybicyclooctanone (12b) (Scheme 1). The reaction proceeds with the expected[2] regioselectivity and high stereoselectivity for the thermodynamically more stable diastereoisomer.

Dedicated to Professor W. David Ollis on the occasion of his 65th birthday

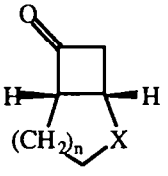



(1) (7) (12b)

Scheme 1. Reagents: i) $MeO\bar{C}HSO_2PhLi^+$ (4), -78°C;
ii) $^iBu_2AlCl$ overall yield 68% (reference 1)

We have investigated the potential of this new Trost reaction for the provision of novel prostaglandin analogues, using as starting materials a range of readily prepared cyclobutanone derivatives. In addition to examining the reaction of lithiated methoxymethyl phenyl sulphone (4), we have also investigated the lithiated benzyloxymethyl phenyl sulphone (5) and the lithiated allyloxymethyl phenyl sulphone (6).

The starting cyclobutanones (1)-(3),[3] and the sulphone reagent (4),[1] were prepared using literature procedures and the sulphones (5) and (6) were readily obtained by analogous reactions (see Experimental Section). The lithiation and addition reactions were carried out using *tert*-butyllithium in dimethoxyethane following Trost's procedure.[1] Trost and



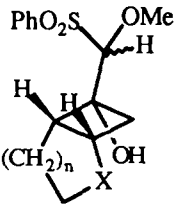

$PhSO_2CHOR^- Li^+$

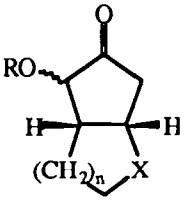
(1) n = 1, X = $CH_2$
(2) n = 2, X = $CH_2$
(3) n = 2, X = O

(4) R = Me
(5) R = $CH_2Ph$
(6) R = $CH_2CH{=}CH_2$

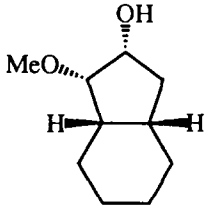
Mikhail reported that the intermediate hydroxy sulphones could be isolated and rearranged in a separate step although given the sensitivity of these intermediates the "one-pot" procedure outlined in Scheme 1 was preferred in their work. In a number of reactions in this present study we have compared the two procedures, maintaining the use of $^iBu_2AlCl$ as the Lewis

acid in both protocols, and the results are detailed in the Table.





(7) R = Me, n = 1, X = $CH_2$
(8) R = Me, n = 2, X = $CH_2$
(9) R = Me, n = 2, X = O
(10) R = $CH_2Ph$, n = 2, X = $CH_2$
(11) R = $CH_2Ph$, n = 2, X = O



(18)

(12a) R = Me, n = 1, X = $CH_2$, α-isomer
(12b) R = Me, n = 1, X = $CH_2$, β-isomer
(13a) R = $CH_2Ph$, n = 1, X = $CH_2$, α-isomer
(13b) R = $CH_2Ph$, n = 1, X = $CH_2$, β-isomer
(14a) R = Me, n = 2, X = $CH_2$, α-isomer
(14b) R = Me, n = 2, X = $CH_2$, β-isomer
(15a) R = $CH_2Ph$, n = 2, X = $CH_2$, α-isomer
(15b) R = $CH_2Ph$, n = 2, X = $CH_2$, β-isomer
(16a) R = Me, n = 2, X = O, α-isomer
(16b) R = Me, n = 2, X = O, β-isomer
(17a) R = $CH_2Ph$, n = 2, X = O, α-isomer
(17b) R = $CH_2Ph$, n = 2, X = O, β-isomer

Entry 1 in the Table is a repeat of the Trost and Mikhail reaction (Scheme 1) and it provided confirmation that the ketone (12b) is the only isolable reaction product, although in our hands the reaction proved unreliable with the yield, at best, a meagre 14%. The stereoselectivity of this reaction is noteworthy: other results in the Table indicate that the stereoselectivity of the process is dependant on the substrate and the reaction conditions. For example, carrying out the same reaction *via* the two-step protocol (entry 2) or repeating the one-pot reaction with reagent (5) (entry 3) resulted in a diastereomeric mixture of alkoxy ketones, (12a) and (12b) and (13a) and (13b) respectively, again in low overall yield. The α- and β-diastereomers (13a) and (13b) were distinguished by n.O.e. studies.

An extension of the study using bicyclo[4.2.0]heptanone (2) as a substrate provided a slightly different picture. Thus "one-pot" reactions with reagents (4) and (5) gave a diastereomeric mixture of alkoxy ketones (14) and (15) in low overall yield with the α-diastereomers predominating in each case (entries 4 and 6). A small amount (5%) of

hydroxy ether (18) was also isolated from the reaction shown in entry 4; the configuration of the hydroxyl group was confirmed by n.O.e. studies. In the corresponding two-step reaction (entries 5 and 7), the ring expansion proceeded much more efficiently but diastereomeric mixtures were obtained once again.

TABLE.

Reaction of Some Bicyclo[n.2.0]alkanones with Alkoxymethyl Phenyl Sulphones Anions.

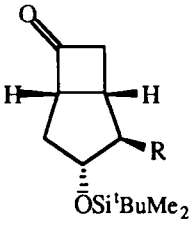
| Entry | Bicyclic ketone | Sulphone carbanion | 1 or 2 step reaction | Hydroxysulphone (diastereomeric ratio of adducts) | Product(s) (ratio of α:β epimers) | Yield(s) % |
|---|---|---|---|---|---|---|
| 1 | (1) | (4) | 1 | - | (12) 0:100 | 14 |
| 2 | (1) | (4) | 2 | (7) (66:34)[a] | (12) 25:75 | 41,51 |
| 3 | (1) | (5) | 1 | - | (13) 50:50 | 16 |
| 4 | (2) | (4) | 1 | - | (14) 60:40 | 30[b] |
| 5 | (2) | (4) | 2 | (8) (66:34)[a] | (14) 83:17 | 40,78 |
| 6 | (2) | (5) | 1 | - | (15) 70:30 | 19 |
| 7 | (2) | (5) | 2 | (10) (50:50) | (15) 44:56 | 77,94 |
| 8 | (3) | (4) | 1 | - | (16) 65:35 | 22 |
| 9 | (3) | (4) | 2 | (9) (50:50) | (16) 55:45 | 78,75 |
| 10 | (3) | (5) | 1 | - | (17) 80:20 | 20 |
| 11 | (3) | (5) | 2 | (11) (50:50) | (17) 61:39 | 71,76 |

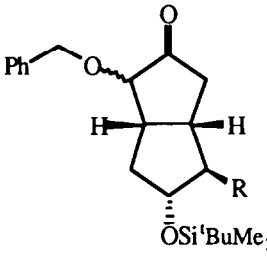
Footnotes a. The hydroxysulphones were formed as a 1:1 mixture of diastereomers inseparable from residual methoxymethyl phenyl sulphone. Purification was achieved by acetate formation,[4] chromatography and deesterification.[5]

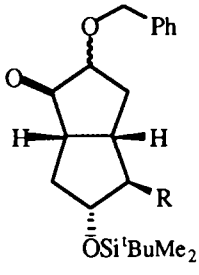
b. The alcohol (18) (5%) was also formed.

The behaviour of 2-oxabicyclo[4.2.0]octan-7-one (3) in the ring expansion reactions was investigated. Again the "one-pot" procedures (entries 8 and 10) gave the expected products as diastereomeric mixtures (16) and (17) in low yield with the α-isomers [(16a) and (17a)] predominating. The two step reactions (entries (9) and (11)) provided an opportunity to correlate the stereochemical relationship between the sulphone intermediates and the ring-expanded products. Treatment of the ketone (3) and the reagent (4) gave a 50:50 mixture of

hydroxy sulphones (9) (78%). Rearrangement of this mixture gave the methoxy ketones (16a) and (16b) (75%) in the ratio 55:45. The hydroxy sulphones were separated by chromatography and individually subjected to the rearrangement reaction. The less polar hydroxy sulphone diastereomer gave a 70:30 mixture of the α- (16a) and β-products (16b), whereas the more polar diastereomer gave a predominance (12% d.e.) of the β-isomer. Similar results were obtained with the hydroxybenzyloxy sulphones (11) with quantitative conversion to ring expanded products being obtained for both of the separated diastereomeric sulphones and high diastereo-selectivities (*ca.* 50% d.e.) observed for the formation of the α- (17a) and β-products (17b). Epimerisation of the α-isomer (17a) using DBU provided a mixture rich in the β-isomer (60% d.e.) suggesting that the β-isomer is thermodynamically favoured. This result suggests the alkoxy ketones may be prone to epimerisation during the basic work-up procedure thus affecting the product ratios. This possibility notwithstanding a clear correlation exists between the structure of the intermediate hydroxy sulphone and the predominant diastereomer of the rearranged alkoxy ketone.




(19) R = Br
(20) R = Bu$^n$

(21a)....R = Br, α-isomer.....(23a)
(21b)....R = Br, β-isomer.....(23b)
(22a)....R = $^n$Bu, α-isomer...(24a)
(22b)....R = $^n$Bu, β-isomer...(24b)

Experiments involving reaction of the carbanion (5) with the poly-substituted bicycloheptan-6-ones (19)[6] and (20)[7] revealed a more complex situation. Reaction of the protected bromohydrin (19) with the carbanion (5) gave four products which were separated and identified (by nmr spectroscopy) as the ketones (21a), (21b), (23a) and (23b) formed in the ratio 5:2:5:2 in 54% overall yield. The 2-butylbicycloheptanone (20) produced the ketone (22b) (35%), the ketone (24b) (19%) and the isomer (24a) (20%). All three compounds were obtained in a pure state and identified by nmr spectroscopy.

From the information generated to this point the following observations can be made:

(a) Trost-style ring expansions of cyclobutanone derivatives to the corresponding α-alkoxycyclopentanone derivatives rarely produced a single stereoisomer of the product.

(b) Isolation of the intermediate alcohol does not appear to significantly alter the stereochemical outcome of the ring expansion reaction.

(c) In general the nature of the sulphone used has little affect on the stereochemical outcome of the reaction.

(d) The presence of an oxygen atom in the larger ring of the bicyclic ketone does not affect the stereochemical outcome of the reaction.

(e) The size of the larger ring in the starting bicyclic ketone does appear to affect the stereochemical outcome of the ring expansion reaction.

(f) In general the two-step process is higher yielding than the one-pot reaction.

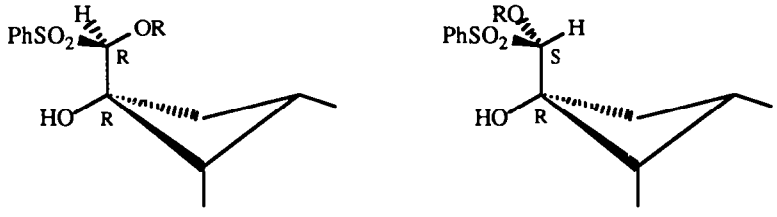
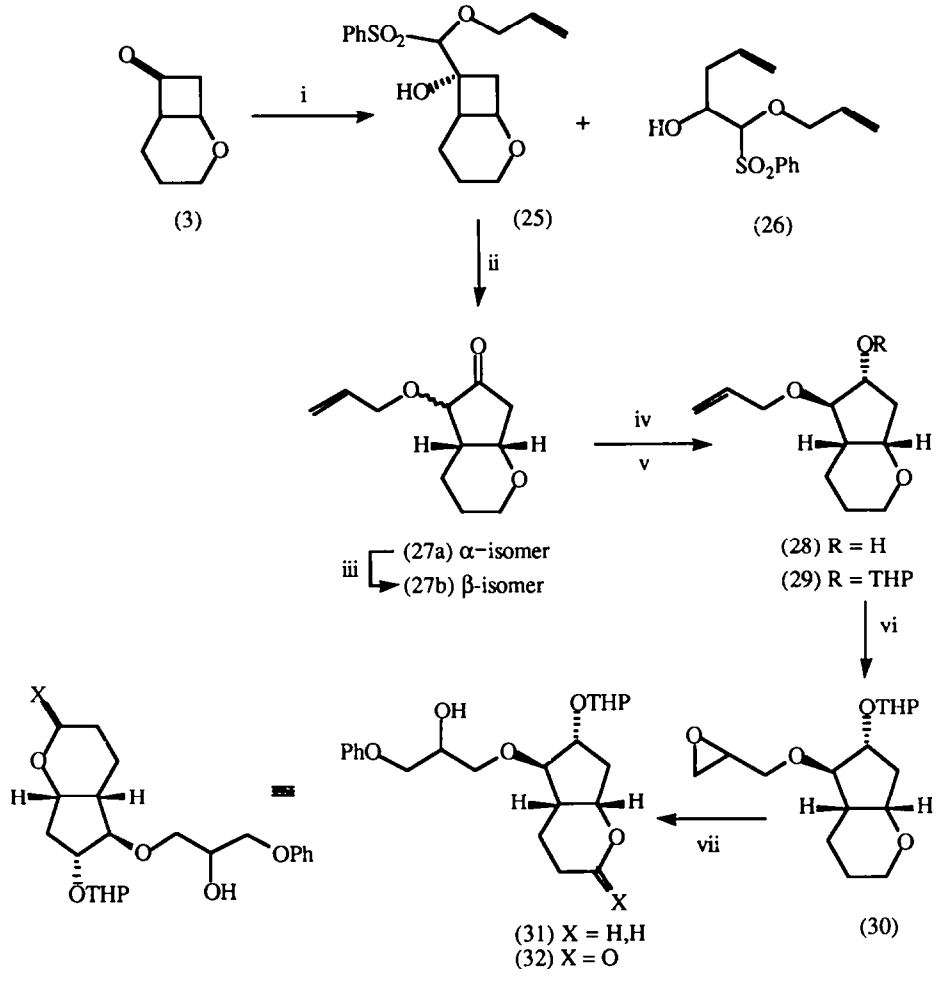



Figure 1

With regard to the mechanism of the reaction we can draw the following conclusions. In common with other nucleophiles the carbanions (4) and (5) attack the bicyclic ketones from the *exo*-face (for the hydroxy sulphones that were isolated and purified by chromatography detailed nmr experiments did indeed establish that the hydroxy group possessed the *endo* configuration). The hydroxy sulphones are thus formed as the *R,R* (*S,S*) and *S,R* (*R,S*) stereoisomers (Figure 1). The *R,R* stereoisomer, on activation of the sulphone group with di-*iso*-butylaluminium chloride, can give rise to the 3-*exo*-alkoxybicycloalkan-2-one and the 2-*endo*-alkoxybicycloalkan-3-one assuming an $S_N2$ reaction takes place at the *exo*-cyclic chiral centre. The *S,R*-stereoisomer can lead to only the 3-*endo*-alkoxybicycloalkan-2-one and the 2-*exo*-alkoxybicycloalkan-3-one by way of an $S_N2$ type reaction. However the reactions of the individual hydroxy sulphone stereoisomers with Lewis acid gave mixtures of products (*vide supra*) suggesting a considerable build up of

positive charge at the carbon centre bearing the electron-donating alkoxy group and non-synchronous migration of the C-C bond. From the data obtained from the rearrangements of the individual hydroxysulphones we believe the less polar of the sulphones (9) is the *S,R* (*R,S*)-stereoisomer, while the less polar of the sulphones (11) is the *R,R* (*R,R*)-stereoisomer: however this is a very tentative assignment.

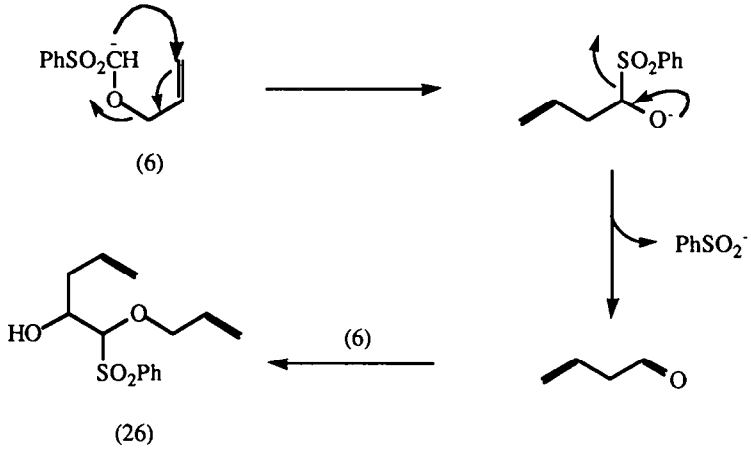



Reagents:

1) Anion (6); 26% (25), 39% (26). ii)$iBu_2AlCl$/DME; 79%. iii) DBU/$CH_2Cl_2$; 86%. iv) $NaBH_4$/$CeCl_3$EtOH; 85%. v) DHP/PPTS/$CH_2Cl_2$; 100%. vi) MCPBA/ $NaHCO_3$/$CH_2Cl_2$; 58%. vii) PhOH/$K_2CO_3$/MeCN; 75%.

Scheme 2.

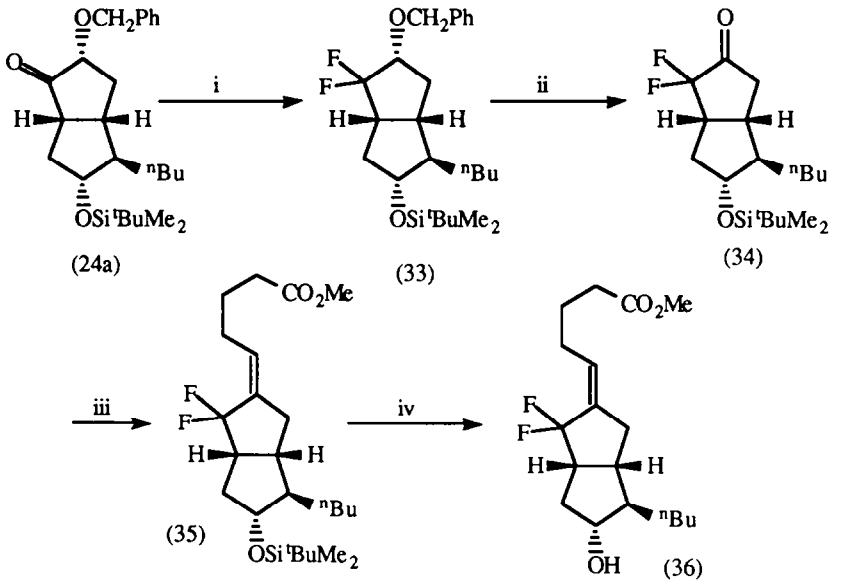
Thus, the Trost reaction under investigation often gives rise to mixtures of products which have to be separated by chromatography. Nevertheless compounds can be obtained by this methodology in sufficient quantities that they can be used as starting materials in organic synthesis. For example, a model study towards the synthesis of intermediates of 13-oxa-prostaglandins utilised this Trost reaction, as shown in Scheme 2. Allyloxymethyl phenyl sulphone was prepared from allyl alcohol.[8] Addition of the corresponding anion (6) to the ketone (3) gave a 26% yield of the required adduct (25) and a substantial amount of the alcohol (26). The by-product (26) presumably arises from initial Wittig rearrangement of the sulphone anion (6) to give but-3-enal, followed by addition of the sulphone anion (6) to this aldehyde to afford the alcohol (26) (Scheme 3). Wittig rearrangements of this type have been described in the literature.[9]




Scheme 3.

Lewis acid mediated ring expansion of the alcohol (25) gave a 2:1 mixture of the ketones (27a) and (27b) (79%); this mixture was converted into solely the β-isomer (27b) by DBU-catalysed epimerisation. Cerium(III) chloride assisted sodium borohydride reduction of the ketone (27b) gave the alcohol (28) (85%) (contaminated with *ca.* 10% of the 3 *exo*-ol). This alcohol was protected as the tetrahydropyranyl ether (29). Alkene epoxidation and phenol opening of the intermediate oxirane (30) afforded the desired alcohol (31).

Further work in this area aimed at the preparation of the potentially important prostanoid synthon (32), is currently under investigation in these laboratories.




Reagents: i) $Et_2NSF_3/CH_2Cl_2/0°C \Rightarrow$ r.t.; 74%. ii) 1. $Na/NH_3(l)/-78°C$; 2. $COCl_2/DMSO/CH_2Cl_2$; 40%. iii) 1. $Ph_3P{=}CH(CH_2)_3CO_2^-K^+/THF$; 2. $CH_2N_2/Et_2O$; 30%. iv) $Bu_4NF/THF$; 100%.

Scheme 4.

In the synthesis of an interesting prostacyclin analogue the ketone (24a) was converted into the difluorocompound (33) using diethyl-aminosulphur trifluoride (DAST) (74%).[10] (Scheme 4). Debenzylation (sodium in liquid ammonia) and oxidation (oxalyl chloride and dimethylsulphoxide) furnished the ketone (34) in 40% overall yield. Rapid addition of the ketone (34) to the Wittig reagent formed from 4-carboxybutyltriphenylphosphonium bromide and potassium *tert*-butoxide followed by treatment with diazomethane furnished the olefin (35) (20%). The Z-geometry of the alkene unit was confirmed by n.O.e. experiments which showed a "through-space" interaction between the proton on the double bond and the adjacent methylene group in the five-membered ring. Treatment of the ester (35) with fluoride ion gave the prostaglandin-$I_2$ analogue (36).

Interestingly, treatment of the β-benzyloxyketone (24b) with DAST gave the fluoroether (37), presumably by an intramolecular desilylation process involving the activated DAST complex (Figure 2). The chemistry of tricyclic compounds of type (37) is under investigation in these laboratories.[11]

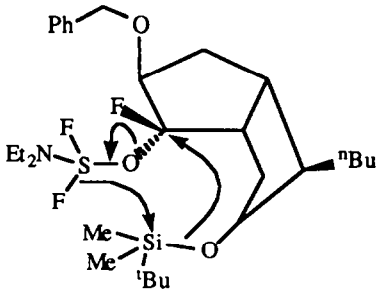
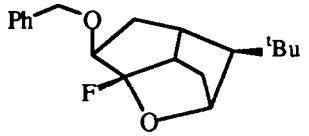



Figure 2




(37)

## Experimental

The ketones (1-3),[3] (19)[6] and (20)[7] and the sulphone (4)[1,12] were prepared by the methods described in the literature. All reactions were carried out under nitrogen using standard techniques for exclusion of moisture. The standard work-up procedure involved addition of ammonium chloride solution to the reaction mixture, followed by extraction of the two phase mixture with the specified solvent. The combined organic extracts were washed with a saturated brine solution, dried ($MgSO_4$), filtered and concentrated *in vacuo* to yield the crude product.

Anhydrous 1,2-dimethoxyethane (DME) and dimethylformamide (DMF) were obtained by storage of the commercial product over activated 4Å molecular sieves under a nitrogen atmosphere for 24h before use. The DME was filtered through alumina on to activated 4Å molecular sieves under a nitrogen atmosphere directly before use. Oil free sodium hydride was prepared by stirring a slurry of the commercially available 60% sodium hydride suspension with anhydrous hexane under a nitrogen atmosphere for 10 min. The solvent was removed by syringe leaving the reagent ready for use. Anhydrous acetonitrile and methanol were obtained by distillation of the commercial products from potassium carbonate in an atmosphere of nitrogen. In each case the distillate was stored over activated 4Å molecular sieves. Anhydrous hexane, dichloromethane, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and dihydropyran (DHP) were obtained by distillation of the respective compounds on to activated 4Å molecular sieves under a nitrogen atmosphere. Anhydrous ether was obtained by storage of the distilled commercial product over sodium wire.

M.p.s were determined using a Gallenkamp apparatus and are uncorrected. I.r. spectra were recorded using a liquid film on a Perkin Elmer 357 spectrometer. $^1H$ and $^{13}C$ n.m.r.

spectra were obtained on a Brücker WM250 spectrometer using $CDCl_3$ as solvent and $Me_4Si$ as internal standard. Flash chromatography[13] was performed on Merck Kieselgel 9385 silica gel using predistilled solvents. All g.l.c. separations were performed on a Perkin Elmer 8500 machine using a 10m x 0.22mm fused silica capillary column.

[[(Phenylmethoxy)methyl]thio]benzene.- Potassium *tert* -butoxide (2.87 g, 25.24 mmol) was added to a stirred solution of thiophenol (2.62 ml, 25.24 mmol) in dry DMF (25 ml) at 20 °C under a nitrogen atmosphere. After stirring for 1h, a solution of benzylchloromethyl ether (1.90 ml, 13.77 mmol) in dry DMF (25 ml) was added. The reaction mixture was stirred for 2h, then standard work-up using ether as solvent yielded a yellow oil (4.04 g). Purification by flash chromatography [60 mm column, petroleum ether (b.p. 40-60 °C) as eluant] yielded the title compound as a colourless oil (3.12 g, 99%); (Found: C, 73.1; H, 6.2; S, 14.1. $C_{14}H_{14}OS$ requires C, 73.0; H, 6.1; S, 13.9%); $\nu_{max}$ ($CHBr_3$) 1590 (Ph), 1067 (COC, ether) and 740 $cm^{-1}$ (Ph); $\delta_H$ 4.70 (2H, s, $OC\underline{H_2}Ph$), 5.04 (2H, s, $SC\underline{H_2}O$) and 7.20-7.53 (10H, m, S<u>Ph</u> and $CH_2$<u>Ph</u>).

[[(Phenylmethoxy)methyl]sulphonyl]benzene.- A solution of oxone (12.79 g, 20.81 mmol) in water (60 ml) was added to a stirred solution of [[(phenylmethoxy)methyl] thio]benzene (3.08 g, 13.37 mmol) in methanol (30 ml) at 0-5 °C. The resultant slurry was stirred at 0-5 °C for 1h and 20 °C for 3h. The reaction mixture was extracted with ether (3 x 100 ml) and the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield an off-white wax (3.31 g). Purification by flash chromatography [60 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:3) as eluant] yielded the title compound as a white solid (3.03 g, 88%), m.p. 68-71 °C; (Found: C, 63.8; H, 5.4; S, 12.1. $C_{14}H_{14}O_3S$ requires C, 64.1; H, 5.48; S, 12.2%); $\nu_{max}$ ($CHBr_3$) 1150 ($SO_2$), 1075 (COC, ether) and 750 $cm^{-1}$ (Ph); $\delta_H$ 4.57 (2H, s, $OC\underline{H_2}Ph$), 4.90 (2H, s, $OC\underline{H_2}SO_2Ph$) and 7.23-8.00 (10H, m, $SO_2Ph$ and $CH_2$<u>Ph</u>).

(1α,5α)-6-Acetoxy-6-[methoxy(phenylsulphonyl)methyl]bicyclo-[3.2.0]heptane.- *Tert* -butyl lithium (1.7M in hexane, 1.76 ml, 2.99 mmol) was added to a stirred solution of the sulphone (4) (557 mg, 2.99 mmol) in dry DME (10 ml) at -78 °C under a nitrogen atmosphere. After 1h a solution of the ketone (1) (300 mg, 2.70 mmol) in dry DME (6 ml) was added and the reaction mixture was stirred at -78 °C for 2h. Standard work-up using dichloromethane as solvent yielded a pale yellow oil (960 mg) which was purified by flash chromatography [30 mm column, ether:petroleum ether (b.p. 40-60

°C) (3:2) as eluant] to give a mixture of the alcohol (7) and the sulphone as a pale yellow oil (760 mg).

Acetic anhydride (0.31 ml, 3.21 mmol) was added to a stirred solution of the impure alcohol (7) and 4-dimethylaminopyridine (536 mg, 4.37 mmol) in dry dichloromethane (12 ml) under a nitrogen atmosphere. The resultant solution was stirred at 20 °C for 3.5h, methanol (10 ml) was added and the reaction mixture was concentrated *in vacuo* to yield an orange oil (1.35 g). Purification by flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:3) as eluant] yielded the title compound as a colourless oil (400 mg, 42%); (Found: C, 60.5; H, 6.5. $C_{17}H_{22}O_5S$ requires C, 60.3; H, 6.55%); $\nu_{max}$ ($CHBr_3$) 1740 (ester), 1305 and 1144 $cm^{-1}$ ($SO_2$); $\delta_H$ 1.14-1.83 (8H, m, 1-H, 2 x 2-H, 2 x 3-H, 2 x 4-H and 5-H), 2.08 and 2.13 (3H, 2 x s, 6-OAc diastereomers), 2.30-2.40 (2H, m, 2 x 7-H), 3.59 and 3.69 (3H, 2 x s, OMe diastereomers), 5.00 and 5.20 (1H, s, OCHS diastereomers) and 7.60-7.93 (5H, m, $SO_2Ph$).

(1α,5α)-6-[Methoxy(phenylsulphonyl)methyl]bicyclo[3.2.0]heptan-6-ol (7).- A solution of the above acetate (371 mg, 1.02 mmol) in dry ether (20 ml) was added over 5 min. to a stirred suspension of lithium aluminium hydride (42 mg, 1.02 mmol) in dry ether (8 ml) at -10 °C under a nitrogen atmosphere. The reaction mixture was stirred at -10 °C for 45 min., then standard work-up using ether as solvent yielded a colourless oil (369 mg). Purification by flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant] yielded the title compound as a colourless oil (315 mg, 97%); $\nu_{max}$ ($CHBr_3$) 3496 (OH) and 1135 $cm^{-1}$ ($SO_2$); $\delta_H$ 1.27-2.53 (10H, m, 1-H, 2 x 2-H, 2 x 3-H, 2 x 4-H, 5-H and 2 x 7-H), 3.09 (1H, d, J3Hz, 6-OH), 3.61 and 3.69 (3H, 2 x s, MeO diastereomers), 4.20 and 4.24 (1H, 2 x s, OCHS diastereomers) and 7.54-8.01 (5H, m, $SO_2Ph$).

(1α,3aβ,6aβ) and (1α,3aα,6aα)-Perhydro-1-methoxy-1(1H)-pentalenone (12a) and (12b).- A solution of diisobutylaluminium chloride (1.09 ml, 3.74 mmol) in dry DME (6 ml) was added to a stirred solution of the alcohol (7) (194 mg, 0.61 mmol) in dry DME (10 ml) at -78 °C under a nitrogen atmosphere. The solution was allowed to warm to 0 °C over 3h. Sodium bicarbonate solution (8%, 30 ml) was slowly added and the aqueous phase was extracted with ether (3 x 20 ml). The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield an opaque gum (180 mg). Purification by flash chromatography [25 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:3) as eluant] yielded the β-methoxy isomer (12b) as a colourless oil (34 mg, 38%); $\nu_{max}$ ($CHBr_3$) 1742

$cm^{-1}$ (ketone); $\delta_H$ 1.30-2.13 (6H, m, 2 x 4-H, 2 x 5-H and 2 x 6-H), 2.43-2.73 (4H, m, 2 x 3-H, 3a-H and 6a-H), 3.36-3.46 (1H, m, 1-H) and 3.51 (3H, s, OMe). Further elution gave the α-methoxy isomer (12a) as a colourless oil (12 mg, 13%); $\nu_{max}$ ($CHBr_3$) 1727 $cm^{-1}$ (ketone); $\delta_H$ 1.42-1.97 (6H, m, 2 x 4-H, 2 x 5-H and 2 x 6-H), 2.20-3.00 (4H, m, 2 x 3-H, 3a-H and 6a-H), 3.48 (3H, s, 1-OMe) and 4.07 (1H, d, J8Hz, 1-H).

'One-pot' conversion of the ketone (1) to (1α,3aα,6aα)-perhydro-1-methoxy-2(1H)-pentalenone (12b).- *tert* -Butyl lithium (1.7M in hexane, 1.72 ml, 2.94 mmol) was added to a stirred solution of the metoxymethyl phenyl sulphone (548 mg, 2.94 mmol) in dry DME (17 ml) at -78 °C under a nitrogen atmosphere. The solution was stirred at -78 °C for 1h, then a solution of the ketone (1) (308 mg, 2..68 mmol) in dry DME (11 ml) was added and stirring was continued for a further 70 min. A solution of diisobutyl-aluminium chloride (3.14 ml, 16.08 mmol) in dry DME (15 ml) was added and the reaction mixture was allowed to warm to 0 °C over 3h. Sodium bicarbonate solution (8%, 30 ml) was added and the aqueous phase was extracted with ether (3 x 40 ml). The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield a pale brown oil (206 mg). Purification by flash chromatography [40 mm column, ether:petroleum ether (b.p. 40-60 °C) 2:3 as eluant] yielded the title compound as a colourless oil (46 mg, 14%). The compound was identical to the sample previously described according to i.r. and n.m.r. analysis.

'One-pot' conversion of the ketone (1) to (1α,3aβ,6aβ) and (1α,3aα,6aα)-perhydro-1-(phenylmethoxy)-2(1H)-pentalenone (13a) and (13b).- Following the 'one-pot'; procedure described for the preparation of compound (12b), the ketone (1) (300 mg, 2.72 mmol) and the sulphone (5) (740 mg, 2.82 mmol) gave the β-isomer (13b) as a colourless oil (53 mg, 8%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant]; $\nu_{max}$ ($CHBr_3$) 1740 $cm^{-1}$ (ketone); $\delta_H$ 1.26-2.13 (6H, m, 2 x 4-H, 2 x 5-H and 2 x 6-H), 2.50-2.90 (4H, m, 2 x 3-H, 3a-H and 5a-H), 3.58 (1H, d, J6Hz, 1-H), 4.59-4.89 (1H, d and 1H, d, J12Hz, $OC\underline{H}_2Ph$ AB system) and 7.24-7.42 (5H, m, $CH_2\underline{Ph}$). Further elution gave the α-isomer (13a) as a colourless oil (52 mg, 8%); $\nu_{max}$ ($CHBr_3$) 1744 $cm^{-1}$ (ketone); $\delta_H$ 1.51-2.03 (6H, m, 2 x 4-H, 2 x 5-H and 2 x 6-H), 2.46-2.83 (4H, m, 2 x 3-H, 3a-H and 6a-H), 4.16 (1H, d, J8Hz, 1-H), 4.65-4.80 (1H, d and 1H, d, J10Hz, $OC\underline{H}_2Ph$ AB system) and 7.29-7.39 (5H, m, $CH_2\underline{Ph}$).

'One-pot' conversion of the ketone (2) into (1α,3aβ,7aβ) and (1α,3aα,7aα)-perhydro-1-methoxy-2H-inden-2-one (14a) and (14b).-
Following the 'one-pot' procedure described for the preparation of compound (12b), the ketone (2) (250 mg, 2.01 mmol) and the sulphone (4) (411 mg, 2.21 mmol) gave the β-isomer (14b) as a colourless oil (40 mg, 12%) after flash chromatography [15 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:3) as eluant]; $\nu_{max}$ ($CHBr_3$) 1732 $cm^{-1}$ (ketone); $\delta_H$ 0.80-1.80 (8H, m, 2 x 4-H, 2 x 5-H, 2 x 6-H and 2 x 7-H), 2.08-2.38 (4H, m, 2 x 3-H, 3a-H and 7a-H), 3.53-3.56 (1H, d, J8Hz, 1-H) and 3.58 (3H, s, 1-OMe); $\delta_c$ 83.00 (1-C), 58.75 (1-OMe), 42.22 (3-C), 40.87 (7a-C), 31.22 (3a-C) and 29.10, 24.72, 23.85 and 21.32 (4-C, 5-C, 6-C and 7-C). N.B. The signal for the ketone (2-C) was too weak to be observed. Further elution gave the α-isomer (14a) as a colourless oil (65 mg, 18%); $\nu_{max}$ ($CHBr_3$) 1729 $cm^{-1}$ (ketone); $\delta_H$ 0.87-1.80 (8H, m, 2 x 4-H, 2 x 5-H, 2 x 6-H and 2 x 7-H), 2.10-2.30 (2H, m, 2 x 3-H), 2.37-2.45 (2H, m, 3a-H and 7a-H), 3.47 (3H, s, 1-OMe) and 3.85 (1H, d, J6Hz, 1-H); $\delta_c$ 216.01 (2-C), 88.79 (1-C), 58.31 (1-OMe), 38.21 (7a-C), 35.82 (3-C), 28.63 (3a-C) and 26.52, 24.07, 21.52 and 20.07 (4-C, 5-C, 6-C and 7-C). Continued elution gave the alcohol (18) as a colourless oil (15 mg, 5%); $\nu_{max}$ ($CHBr_3$) 3605 and 3539 $cm^{-1}$ (OH); $\delta_H$ 0.80-2.10 (12H, m, 2 x 3-H, 3a-H, 2 x 4-H, 2 x 5-H, 2 x 6-H, 2 x 7-H and 7a-H), 2.73 (1H, d, J2Hz, 2-OH), 3.45 (3H, s, 1-OMe), 3.46-3.54 (1H, m, 1-H) and 4.15-4.27 (1H, m, 2-H); $\delta_c$ 84.80 (1-C), 70.32 (2-C), 58.11 (1-OMe), 40.11 (7a-C), 35.51 (3-C), 32.64 (3a-C) and 26.66, 24.99, 21.95 and 20.89 (4-C, 5-C, 6-C and 7-C).

(1α,2α,3aβ,7aβ)-Perhydro-1-methoxy-1H-inden-2-ol (18).- Cerium (III) chloride heptahydrate (75 mg, 0.23 mmol) was added to a stirred solution of the ketone (14a) (38 mg, 0.23 mmol) in methanol (5 ml) at 0-5 °C. After 2 min. sodium borohydride (10 mg, 0.23 mmol) was added. The reaction mixture was stirred at 0-5 °C for 10 min., brine (5 ml) was added and the aqueous phase was extracted with ether (3 x 10 ml). The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield a colourless oil (48 mg). Purification by flash chromatography [10 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant] yielded the title compound as a colourless oil (36 mg, 92%). This sample was identical to the above compound according to i.r. and n.m.r. analysis.

(1α,6α)-7-Acetoxy-7-[methoxy(phenylsulphonyl)methyl]bicyclo-[4.2.0]octane- Following the procedure described for the preparation of the acetate of the alcohol (7), the sulphone (4) (720 mg, 3.87 mmol), the ketone (2) and acetic anhydride (0.33 ml, 3.42 mmol) gave the title

compound as a white wax (550 mg, 45%) after flash chromatography [40 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:3) as eluant]; $\nu_{max}$ ($CHBr_3$) 1733 (ester) and 1302 $cm^{-1}$ ($SO_2$); $\delta_H$ 1.10-2.01 (10H, m, 1-H, 2 x 2-H, 2 x 3-H, 2 x 4-H, 2 x 5-H and 6-H), 2.07 and 2.09 (3H, 2 x s, 7-OAc diastereomers), 2.15-2.30 (2H, m, 2 x 8-H), 3.53 (3H, s, MeO), 5.01 and 5.18 (1H, 2 x s, OCHS diastereomers) and 7.60-7.91 (5H, m, $SO_2Ph$).

(1α,6α)-7-[Methoxy(phenylsulphonyl)methyl]bicyclo[4.2.0]octan-7-ol (8).- Following the procedure described for the preparation of compound (7), the above ester (170 mg, 0.49 mmol) and lithium aluminium hydride (20 mg, 0.49 mmol) gave the title compound as a white wax (133 mg, 88%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant]; $\nu_{max}$ ($CHBr_3$) 3482 $cm^{-1}$ (OH); $\delta_H$ 1.15-2.10 (12H, m, 1-H, 2 x 2-H, 2 x 3-H, 2 x 4-H, 2 x 5-H, 6-H and 2 x 8-H), 2.85 (1H, br.s, 7-OH), 3.50 (3H, s, OMe), 4.28 and 4.31 (1H, 2 x s, OCHS diastereomers) and 7.52-7.93 (5H, m, $SO_2Ph$).

(1α,3aβ,7aβ) and (1α,3aα,7aα)-Perhydro-1-methoxy-2H-inden-2-one (14a) and (14b).- Following the procedure described for the preparation of compounds (12a) and (12b), the alcohol (8) (107 mg, 0.33 mmol) and diisobutylaluminium chloride (0.61 ml, 2.10 mmol) gave the title compounds as a straw coloured oil (43 mg, 78%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:3) as eluant]. The isomer ratio [(14a):(14b) = 83:17] was determined by $^1H$ n.m.r. integrations of the 1-OMe protons of each isomer. All other spectroscopic details were consistent with the compounds previously described.

(1α,6α)-7-(Phenylmethoxy)(phenylsulphonyl)methyl]bicyclo[4.2.0]octan-7-ol (10).- *tert*-Butyl lithium (1.7 M in hexane, 0.98 ml, 1.67 mmol) was added to a stirred solution of [[(phenylmethoxy0methyl]sulphonyl]benzene (438 mg, 1.67 mmol) in dry DME (8 ml)) at -78 °C under a nitrogen atmosphere. After 50 min. a solution of the ketone (2) (200 mg, 1.61 mmol) in dry DME (5 ml) was added, and the reaction mixture was stirred at -78 °C for a further 30 min. Standard work-up, using ether as solvent, yielded a white wax (660 mg). After purification of the crude product by flash chromatography [30 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant] a small quantity of sulphone remained. This was removed by trituration with hexane, the hexane being concentrated *in vacuo* to yield the title compound as a colourless gum (481 mg, 77%); $\nu_{max}$ ($CHBr_3$) 3552 (OH) and 1300 $cm^{-1}$ ($SO_2$); $\delta_H$ 1.00-2.15 (12H, m, 1-H, 2 x 2-H, 2 x 3-H, 2 x 4-H, 2 x 5-H, 6-H and 2 x 8-H), 2.54 (1H, br.s, 7-OH), 4.53 (1H, s, OCHS), 4.76 and 5.00 (1H, d and 1H, d, J11Hz, $OCH_2Ph$ AB system) and 7.20-8.00 (10H, m, $SO_2Ph$ and $CH_2Ph$).

(1α,3aβ,7aβ) and (1α,3aα,7aα)-Perhydro-1-(phenylmethoxy)-2H-inden-2-one (15a) and (15b).- Following the procedure described for the preparation of compounds (12a) and (12b), the alcohol (10) (123 mg, 0.32 mmol) and diisobutylaluminium chloride (0.,55 ml, 1.90 mmol) gave the β-isomer (15b) as a colourless oil (41 mg, 53%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:3) as eluant]; (Found: C, 78.6; H, 8.5. $C_{16}H_{20}O_2$ requires C, 78.7; H, 8.3%; $\nu_{max}$ ($CHBr_3$) 1740 $cm^{-1}$ (ketone); $\delta_H$ 1.06-1.80 (8H, m, 2 x 4-H, 2 x 5-H, 2 x 6-H and 2 x 7-H), 2.07 (1H, m, 3-Hα (1)), 2.15-2.35 (2H, m, 3a-H and 7a-H), 2.43 (1H, d, J8Hz, 3-Hβ (1)), 3.95 (1H, d, J6Hz, 1-H), 4.70 and 4.99 (1H, d and 1H, d, J12Hz, 1-OC$H_2$Ph AB system) and 7.24-7.40 (5H, m, $CH_2$Ph). Further elution gave the α-isomer (15a) as a colourless oil (32 mg, 41%); $\nu_{max}$ ($CHBr_3$) 1744 $cm^{-1}$ (ketone); $\delta_H$ 0.86-1.40 (8H, m, 2 x 4-H, 2 x 5-H, 2 x 6-H and 2 x 7-H), 2.14-2.43 (4H, m, 2 x 3-H, 3a-H and 7a-H), 3.77 (1H, d, J7Hz, 1-H), 4.65-4.80 (1H, d and 1H, d, J10Hz, OC$H_2$Ph AB system) and 7.30-7.40 (5H, m, $CH_2$Ph).

'One-pot' conversion of the ketone (2) to (1α,3aβ,7aβ) and (1α,3aα,7aα)-Perhydro-1-(phenylmethoxy)-2H-inden-2-one (15a) and (15b).- Following the 'one-pot' procedure described for the preparation of compound (12b), the ketone (2) (130 mg, 1.05 mmol) and the sulphone (5) (304 mg, 1.16 mmol) gave the title compounds as a colourless oil (48 mg, 19%) after flash chromatography [30 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:3) as eluant]. The isomer ratio [(15a):(15b) = 70:30] was determined by $^1H$ n.m.r. integration of the 1-H protons of each isomer. All other spectroscopic details were consistent with the compounds previously described.

(1α,6α)-7-[Methoxy(phenylsulphonyl)methyl]-2-oxabicyclo[4.2.0]octan-7-ol (9).- Following the procedure described for the preparation of compound (10), the ketone (3) (400 mg, 3.18 mmol) and the sulphone (4) (644 mg, 3.46 mmol) gave the title compound as an opaque oil (771 mg, 78%) after flash chromatography [40 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:1) as eluant]; $\nu_{max}$ ($CHBr_3$) 3508 (OH), 1301 ($SO_2$) and 1075 $cm^{-1}$ (COC); $\delta_H$ 1.35-2.07 (5H, m, 2 x 4-H, 2 x 5-H and 6-H), 2.18-2.30 (1H, m, 8-Hα (1)), 2.45-2.70 (2H, m, 8-Hβ (1) and 7-OH), 3.33-3.42 (1H, m, 3-Hβ (1)), 3.56 and 3.60 (3H, 2 x s, OMe diastereomers), 3.75-3.88 (1H, m, 3-Hα (1)), 4.00-4.10 (1H, m, OCHS), 4.15 (1H, d, J20Hz, 1-H) and 7.56-7.95 (5H, m, $SO_2$Ph). The two diastereomers were separated by flash chromatography and each isomer was subjected to the ring expansion conditions described for

compounds (12a) and (12b). The less polar diastereomer was assigned diastereomer 1 and the more polar diastereomer was assigned diastereomer 2.

(4aα,5β,7aα) and (4aα,5α,7aα)-Perhydro-5-methoxy-cyclopenta[b]pyran-6-one (16a) and (16b).- Following the procedure described for the preparation of compounds (12a) and (12b), the alcohol (9) (110 mg, 0.35 mmol) and diisobutylaluminium chloride (0.45 ml, 2.31 mmol) gave the β-methoxy isomer (16b) as a straw coloured oil (20 mg, 34%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:1) as eluant]; $\nu_{max}$ ($CHBr_3$) 1748 $cm^{-1}$ (ketone); $\delta_H$ 1.47-1.61 (2H, m, 2 x 3-H), 1.78-1.97 (2H, m, 2 x 4-H), 2.00-2.12 (1H, m, 4a-H), 2.36 (1H, d, J20Hz, 7-Hα (1)), 2.44 (1H, dd, J5Hz and 12Hz, 7-Hβ (1)), 3.48 (1H, dt, J2Hz and 12Hz, 2-Hβ (1)), 3.70 (3H, s, 5-OMe), 3.91-4.01 (1H, m, 2-Hα (1)), 4.06 (1H, d, J10Hz, 5-H) and 4.09 (1H, t, J4Hz, 7a-H). Further elution gave the α-methoxy isomer (16a) as a colourless oil (24 mg, 41%); $\nu_{max}$ ($CHBr_3$) 1746 $cm^{-1}$ (ketone); $\delta_H$ 1.43-1.90 (4H, m, 2 x 3-H and 2 x 4-H), 2.36-2.55 (3H, m, 2 x 7-H and 4a-H), 3.55 (3H, s, 5-OMe), 3.57-3.61 (1H, m, 2-Hβ (1)), 3.66 (1H, d, J7Hz, 5-H), 3.70-3.78 (1H, m, 2-Hα (1)) and 4.30-4.38·(1H, m, 7a-H).

Ring expansion of diastereomer 1 and diastereomer 2 of (1α,6α)-7-[methoxy(phenylsulphonyl)methyl]-2-oxabicyclo[4.2.0]octan-7-ol (9).-Using the procedure described above, diastereomer 1 (160 mg, 0.48 mmol) was ring expanded to give two products (16a) and (16b) as a colourless oil (55 mg, 67%). The isomer ratio [(16a):(16b) = 70:30] was determined by $^1H$ n.m.r. integration of the OMe protons of each isomer. Similarly, ring expansion of diastereomer 2 (84 mg, 0.27 mmol) provided the ring expansion products (30 mg, 65%) in the ratio (16a):(16b) = 44:56. In each case all other spectroscopic details were consistent with the compounds previously described.

'One-pot' conversion of the ketone (3) to (4aα,5β,7aα) and (4aα,5α,7aα)-perhydro-5-methoxy-cyclopenta[b]pyran-6-one (16a) and (16b).- Following the 'one-pot' procedure described for the preparation of compound (12b), the ketone (3) (218 mg, 1.73 mmol) and the sulphone (4) (322 mg, 1.73 mmol) gave the title compound as a colourless oil (62 mg, 22%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:1) as eluant]. The isomer ratio [(16a):(16b) = 65:35] was determined by $^1H$ n.m.r. integration of the 5-OMe protons of each isomer. All other spectroscopic details were consistent with the compounds previously described

(1α,6α)-7-[(Phenylmethoxy)(phenylsulphonyl)methyl]-2-oxabicyclo-[4.2.0]octan-7-ol (11).- Following the procedure described for the preparation of compound (10), the ketone (3) (204 mg, 1.60 mmol) and the sulphone (5) (459 mg, 1.75 mmol) gave the title compound as a colourless gum (444 mg, 71%) after flash chromatography [30 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:1) as eluant]; (Found: C, 64.9; H, 6.4; S, 8.0. $C_{21}H_{24}O_5S$ requires C, 64.8; H, 6.5; S, 8.2%); $\nu_{max}$ ($CHBr_3$) 3500 (OH), 1600 (Ph), 1500 (Ph) and 1145 $cm^{-1}$ ($SO_2$); $\delta_H$ 1.25-2.20 (6H, m, 2 x 4-H, 2 x 5-H, 6-H and 8-Hα (1)), 2.39-2.50 (1H, m, 8-Hβ (1)), 3.03 (1H, s, 7-OH), 3.20-3.35 (1H, m, 3-Hβ (1)), 3.72-3.76 ((1H, m, 3-Hα (1)), 3.88-3.97 (1H, m, 1-H), 4.37 (1H, s, 7-OCHS), 4.72 and 4.95 (1H, d and 1H, d, J10Hz, $OCH_2Ph$ AB system) and 7.25-7.40 (10H, m, $SO_2Ph$ and $CH_2Ph$). The two diastereomers were separated by flash chromatography and each isomer was subjected to the ring expansion conditions described for compounds (12a) and (12b). The less polar diastereomer was assigned diastereomer 1 and the more polar diastereomer was assigned diastereomer 2.

(4aα,5β,7aα) and (4aα,5α,7aα)-Perhydro-5-(phenylmethoxy)cyclopenta-[b]-pyran-6-one (17a) and (17b).- Following the procedure described for the preparation of compounds (12a) and (12b), the alcohol (11) (190 mg, 0.49 mmol) and diisobutylaluminium chloride (0.61 ml, 3.12 mmol) gave the β-isomer (17b) as a colourless oil (34 mg, 28%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant]; (Found: C, 72.9; H, 7.4. $C_{15}H_{18}O_3$ requires C, 73.1; H, 7.4%); $\nu_{max}$ ($CHBr_3$) 1749 (ketone), 1600 (Ph), 1495 (Ph) and 1060 $cm^{-1}$ (COC, ether); $\delta_H$ 1.36-1.48 (2H, m, 2 x 3-H), 1.77-1.96 (2H, m, 2 x 4-H), 2.08 (1H, m, 4a-H), 2.36 (1H, d, J20Hz, 7-Hα (1)), 2.48 (1H, dd, J5Hz and 14Hz, 7-Hβ (1)), 3.42 (1H, dt, J3Hz and 12Hz, 2-Hβ (1)), 3.87 (1H, m, 2-Hα (1)), 4.03 (1H, t, J5Hz, 7a-H), 4.12 (1H, d, J8Hz, 5-H),. 4.73 and 5.08 (1H, d and 1H, d, J10Hz, 5-$OCH_2Ph$ AB system) and 7.30-7.40 (5H, m, Ph). Further elution gave the α-isomer (17a) as a colourless oil (58 mg, 48%); $\nu_{max}$ ($CHBr_3$) 1748 (ketone), 1600 (Ph), 1490 (Ph) and 1060 $cm^{-1}$ (COC, ether); $\delta_H$ 1.40-1.90 (4H, m, 2 x 3-H and 2 x 4-H), 2.40 (2H, m, 7-Hβ (1) and 4a-H), 2.57 (1H, dd, J5Hz and 15Hz, 7-Hα (1)), 3.57 (1H, m, 2-Hβ (1)), 3.75 (1H, m, 2-Hα (1)), 3.78 (1H, d, J8Hz, 5-H), 4.28 (1H, m, 7a-H), 4.69-4.91 (1H, d and 1H, d, J10Hz, 5-$OCH_2Ph$ AB system) and 7.30-7.40 (5H, m, Ph).

Ring expansion of diastereomer 1 and diasteromer 2 of (1α,6α)-7-[(phenylmethoxy)(phenylsulphonyl)methyl]-2-oxabicyclo[4.2.0]octan-7-ol (11).- Using the procedure described above, diastereomer 1 (44 mg, 0.11 mmol) was ring expanded to give the two ring expansion products (17a) and (17b) as a colourless oil (27 mg, 100%). The isomer ratio [(17a):(17b) = 26:74] was determined by g.l.c. analysis. Similarly, ring expansion of diasteromer 2 (54 mg, 0.14 mmol) provided the ring expansion products (34 mg, 100%) in the ratio (17a):(17b) = 79:21. In each case all other spectroscopic details were consistent with the compounds previously described.

'One-pot' conversion of the ketone (3) to (4aα,5β,7aα) and (4aα,5α,7aα)-perhydro-5-(phenylmethoxy)cyclopenta[b]pyran-6-one (17a) and (17b).- Following the 'one-pot' procedure described for the preparation of compound (12b), the ketone (3) (191 mg, 1.52 mmol) and the sulphone (5) (459 mg, 1.75 mmol) gave the title compound as a colourless oil (76 mg, 20%) after flash chromatography [50 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant]. The isomer ratio [(17a):(17b) = 82.18] was determined by $^1$H n.m.r. integration of the benzylic methylene AB system of (17b) and 7a-H of (17a). All other spectroscopic details were consistent with the compounds previously described.

Isomerisation of a mixture of (4aα,5β,7aα) and (4aα,5α,7aα)-perhydro-5-(phenylmethoxy) cyclopenta[b]pyran-6-ol (17a) and (17b).- One drop of DBU was added to a stirred solution of the epimers (17a) and (17b) (31 mg, g.l.c. ratio (17a):(17b) = 79:21) in dry dichloromethane (3 ml) at 20 °C under a nitrogen atmosphere. The resultant solution was stirred for 5.5h then concentrated *in vacuo* to yield predominantly the β-isomer (17b) by g.l.c. analysis (31 mg, 100%, (17a):(17b) = 21.79). Repeating the reaction using predominantly the β-isomer (17b) (g.l.c. ratio (17a):(17b) = 3:97), caused no change in the isomer ratio, and the β-isomer (17b) was recovered (g.l.c. ratio (17a):(17b) = 3:97).

Ring expansion of the ketone (20).- The sulphone (5) (6.23 g) was stirred in dry (DME) (5 ml) at -60 °C under nitrogen.*tert* -Butyllithium (1.7M in hexane) (1.39 ml) was added dropwise and the resulting deep red mixture was stirred at -60 °C for 10 minutes. The mixture was transferred by cannula to a solution of the ketone (20) (0.70 g) in dry DME (5 ml) at -78 °C under nitrogen. After 20 min. di-*iso*-butylaluminium chloride (2.2 ml) was added. The mixture was stirred for 2.5h at -78 °C, then poured into a 500 ml conical flask immersed in an ice-bath. The reaction flask was rinsed with ethyl acetate. The reaction

mixture was quenched by dropwise addition of saturated aqueous sodium hydrogencarbonate. The white solid was filtered off and washed with ethyl acetate. The combined organic fractions were washed with saturated brine and dried ($MgSO_4$). After removing the drying agent, the solvent was evaporated *in vacuo* and the residue was chromatographed over silica using ether/petroleum ether (40-60 °C) (ratio 1:6) to afford, in the first fractions, the ketone (24a) (200 mg); $\delta_H$ 0.00 (6H, s, $Si(C\underline{H}_3)_2$), 0.9 (12H, m, 4 x $C\underline{H}_3$), 1.3 (7H, m, 3 x $CH_2$ and 4-H), 1.62 (1H, m, 6-H), 2.2 (1H, m, 6-H), 2.32 (2H, m, 2 x 3-H), 2.38 (2H, m, 3a-H and 6a-H), 3.9 (2H, m, 2-H and 5-H), 4.82 and 4.6 (2H, 2 x d, $OC\underline{H}_2Ph$ AB doublet), 7.3 (5H, m, Ph); (Found: $M^+ + NH_4$, 434.3101. $C_{25}H_{40}O_3Si$ requires M + $NH_4$, 434.3110). The second compound eluted from the column was the ketone (24b) (180 mg); $\delta_H$ 0.1 (6H, s, $Si(C\underline{H}_3)_2$), 0.9 (9H, s, $C(C\underline{H}_3)_3$), 0.93 (3H, t, $CH_2C\underline{H}_3$), 1.3 (6H, m, 3 x $C\underline{H}_2$), 1.6 (1H, m, 4-H), 1.9 (1H, m, 6-H), 2.1 (3H, m, 6-H and 2 x 3-H), 2.4 (1H, dm, J9.5Hz, 3a-H), 2.65 (1H, ddd, J9.5, 9.5 and 3.2 Hz, 6a-H), 3.88 (1H, ddd, J 4.5, 3.2, and 3.2 Hz, 5-H),. 4.20 (1H, t, J7.8Hz, 2-H), 4.82 and 4.6 (2H, 2 x d, $OC\underline{H}_2Ph$), 7.3 (5H, m, Ph); (Found: $M^+ + NH_4$ 434.3096. $C_{25}H_{40}O_3Si$ requires M + $NH_4$, 434.3102). Final fractions contained the ketone (22b) (335 mg); $\delta_H$ 0.1 (6H, 2 x s, $Si(C\underline{H}_3)_2$), 0.9 (12H, m, 4 x $C\underline{H}_3$), 1.3 (7H, m, 4-H and 3 x $C\underline{H}_2$), 1.5 (2H, m, 2 x 6-H), 1.95 (2H, m, 2 x 3-H), 2.30 (1H, m, 3a-H), 2.5 (1H, m, 6a-H), 3.85 (1H, m, 5-H), 4.1 (1H, m, 1-H), 4.72 (2H, m, $OC\underline{H}_2Ph$), 7.3 (5H, m, Ph). (Found: $M^+ + NH_4$, 434.3096. $C_{25}H_{40}O_3Si$ requires M + $NH_4$ 434.3102).

Ring expansion of the ketone (19).- The reaction was carried out as described for the ketone (20) using [[(phenylmethoxy)methyl]sulphonyl)benzene (130 mg), *tert* -butyllithium (0.29 ml), the ketone (19) (160 mg) and di-*iso* -butyl-aluminium chloride (0.58 ml) to afford a residue which was chromatographed over silica using ether and petroleum ether (40-60 °C) (1:9) to give in the first fractions the ketone (23b) (14 mg); $\delta_H$ ($CDCl_3$) 0.1 (6H, 2 x s, $Si(C\underline{H}_3)_2$), 0.85 (9H, s, $SiC(C\underline{H}_3)_3$), 2.2 (2H, m, 2 x 6-H), 2.5 (2H, m, 2 x 3-H), 3.30 (2H, m, 3a-H and 6a-H), 3.78 (1H, m, 5-H), 3.9 (1H, d, 4-H), 3.94 (1H, t, 2-H), 4.65 (2H, 2 x d, $OC\underline{H}_2Ph$), 7.35 (5H, m, Ph). (Found: $M^+$ 364.0888. Calculated for $C_{15}H_{27}O_3SiBr$, M, 364.0911). Next eluted was the ketone (21a) (36 mg). $\delta_H$ 0.1 (6H, 2 x s, $Si(C\underline{H}_3)_2$), 0.9 (9H, s, $C(C\underline{H}_3)_3$), 1.6 (1H, m, 6-H), 2.4 (1H, m, 6-H), 2.7-2.6 (2H, m, 2 x 3-H), 2.82 (1H, dm, J3Hz, 6a-H), 3.15 (1H, dddd, J 11.0, 5.2, 3.0 and 3.0 Hz, 3a-H), 3.8 (1H, d, J5.2Hz, 1-H), 3.9 (1H, dd, J 3.1 and 3.0 Hz, 4-H), 4.35 (1H, ddd, J 5.3, 3.2, and 3.1 Hz, 5-H), 4.7 (2H, 2 x d, $OC\underline{H}_2Ph$), 7.3 (5H, m, ArH). (Found: $M^+$, 364.0880. $C_{15}H_{27}O_3SiBr$ requires M,

364.0911). Later fractions contained the ketone (23a) (35 mg). $\delta_H$ 0.1 (6H, s, Si($C\underline{H}_3$)$_2$), 0.9 (9H, s, SiC($C\underline{H}_3$)$_3$), 1.95 (1H, dm, J11.5Hz, 3-H), 2.18 (1H, ddm, J 14 and 2 Hz, 6-H), 2.42 (1H, ddm, J 14 and 4.4 Hz, 6-H), 2.52 (1H, dm, J11.4Hz, 3-H), 2.85 (1H, ddd, J 10, 10 and 2 Hz, 6a-H), 3.0 (1H, ddd, J 10, 9 and 9 Hz, 3a-H), 3.5 (1H, dd, J 1.5 and 1.4 Hz, 4-H), 4.1 (1H, ddd, J 11, 9 and 2 Hz, 2-H), 4.35 (1H, dd, J 4.4 and 1.4 Hz, 5-H), 4.85 and 4.60 (2H, 2 x d, O$C\underline{H}_2$Ph), 7.32 (5H, m, Ph). (Found: $M^+$ 364.0880. $C_{15}H_{27}O_3SiBr$ requires M 364.0911). In the final fractions was contained the isomer (21b) (13 mg) $\delta_H$ 0.1 (6H, s, Si($C\underline{H}_3$)$_2$), 0.9 (9H, s, C($C\underline{H}_3$)$_3$), 1.9 (1H, dm, J14.5Hz, 6-H), 2.25 (1H, ddd, J 14.5, 6 and 5 Hz, 6-H), 2.38 (1H, d, J12Hz, 3-H), 2.5 (1H, ddm, J 12 and 1.6 Hz, 3-H), 2.95 (1H, dd, J 8.5 and 5.3 Hz, 3a-H), 3.1 (1H, dm, J8.5Hz, 6a-H), 3.8 (1H, dd, J 3.5 and 3.5 Hz, 4-H), 4.04 (1H, dd, J 8.5 and 1.6 Hz, 1-H), 4.4 (3H, m, 5-H and O$C\underline{H}_2$Ph), 7.32 (5H, m, Ph). (Found: $M^+$ 364.0880. $C_{15}H_{27}O_3SiBr$ requires M, 364.0911).

[[(2-Propenyloxy)methyl]sulphonyl]benzene.- A solution of allyl alcohol (1.17 ml, 17.22 mmol) in dry DME (50 ml) was added dropwise into a stirred suspension of oil free sodium hydride (827 mg, 34.43 mmol) in dry DME (25 ml) at 20 °C under a nitrogen atmosphere. The reaction mixture was cooled to 0-5 °C and sodium iodide (2.84 g; 18.93 mmol) followed by (chloromethyl) phenyl sulphide (2.54 g, 18.93 mmol) was added. Stirring was continued for 7h, then standard work-up using ether as solvent yielded the crude sulphide as an orange oil (3.70 g). The residue was dissolved in methanol (45 ml) and the resultant solution was cooled to 0-5 °C. A solution of oxone (19.65 g, 31.99 mmol) in water (90 ml) was added and the slurry was stirred at 0-5 °C for 5h. The reaction mixture was extracted with ether (3 x 40 ml), and the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield a yellow oil (4.14 g). Purification by flash chromatography [50 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant] yielded the title compound as a pale yellow oil (2.30 g, 64%); (Found: C, 56.3; H, 5.7; S, 15.0. $C_{10}H_{12}O_3S$ requires C, 56.6; H, 5.7; S, 15.1%); $\nu_{max}$ ($CHBr_3$) 1590 (Ph) and 1170 $cm^{-1}$ ($SO_2$); $\delta_H$ 4.24 (2H, d, J6Hz, $C\underline{H}_2CH{=}CH_2$), 4.44 (2H, s, O$C\underline{H}_2$S), 5.09-5.20 (2H, m, $C\underline{H}_2{=}CH$), 5.60-5.75 (1H, m, $C\underline{H}{=}CH_2$) and 7.40-7.85 (5H, M, $SO_2$Ph).

(1α,6α)-7-[(Phenylsulphonyl)(2-propenyloxy)methyl]-2-oxabicyclo-[4.2.0]octan-7-ol (25).- Following the procedure described for the preparation of compound (10), the ketone (3) (606 mg, 4.81 mmol) and the sulphone (6) (1.22 g, 5.77 mmol) gave the title compound as a pale yellow oil (420 mg, 26%) after flash chromatography [40 mm column, ether:petroleum ether

(b.p. 40-60 °C) (2:1) as eluant]; (Found: C. 60.7; H, 6.9; S, 9.3. $C_{17}H_{22}O_5S$ requires C, 60.4; H, 6.6; S, 9.5%); $\nu_{max}$ ($CHBr_3$) 3450 $cm^{-1}$ (OH); $\delta_H$ 1.30-2.05 (6H, m, 2 x 4-H, 2 x 5-H, 6-H and 8-Hα (1)), 2.15-2.40 (1H, m, 8-Hβ (1)), 3.10-3.57 (2H, m, 3-Hβ (1) and 7-OH), 3.72-4.44 (5H, m, 1-H, 3-Hα (1), 7-OCHS and $CH_2CH{=}CH_2$), 5.20-5.30 (2H, m, $CH_2{=}CH$), 5.68-5.85 (1H, m, $CH{=}CH_2$) and 7.50-7.95 (5H, m, $SO_2Ph$). Further elution gave the alcohol (26) as a yellow oil (303 mg, 39%). (Found: C, 59.4; H, 6.6; S, 11.0. $C_{14}H_{18}O_4S$ requires C, 59.6; H, 6.4; S, 11.3%); $\nu_{max}$ ($CHBr_3$) 3510 (OH) and 1140 $cm^{-1}$ ($SO_2$); $\delta_H$ 2.10 (1H, d,, J7Hz, OH), 2.15-2.45 (2H, m, $CH_2CHOH$), 4.15-4.48 (4H, m, $HOCHCHSO_2Ph$ and $OCH_2CH$), 5.07-5.32 (4H, m, $CH_2{=}CHx2$), 5.70-5.93 (2H, m,, $CH_2{=}CHx2$) and 7.52-7.93 (5H, m, $SO_2Ph$),

(4aα,5β,7aα) and (4aα,5α,7aα)-Perhydro-5-(2-propenyloxy)-cyclopenta[b]pyran-6-one (27a) and (27b).- Following the procedure described for the preparation of compounds (12a) and (12b), the sulphone (25) (65 mg, 0.19 mmol) and diisobutyl aluminium chloride (0.22 ml, 1.15 mmol) gave the β-isomer (27b) as a colourless oil (8 mg, 22%) after flash chromatography [10 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:1)) as eluant]; $\nu_{max}$ ($CHBr_3$) 1745 (ketone) and 1055 $cm^{-1}$ (COC, ether); $\delta_H$ 1.45-1.52 (2H, m, 2 x 3-H), 1.70-1.90 (2H, m, 2 x 4-H), 2.02-2.11 (1H, m, 4a-H), 2.34 (1H, d, J20Hz, 7-Hα (1)), 2.48 (1H, dd, J5Hz and 20Hz, 7-Hβ (1)), 3.40-3.52 (1H, m, 2-Hβ (1)), 3.90-4.57 (5H, m, 2-Hα (1), 5-H, 7a-H and 5-$OCH_2$), 5.20-5.47 (2H, m, $CH_2{=}CH$) and 5.85-6.00 (1H, m, $CH{=}CH_2$). Further elution gave the α-isomer (27a) as a colourless oil (21 mg, 57%); $\nu_{max}$ ($CHBr_3$) 1750 (ketone) and 1060 $cm^{-1}$ (COC, ether); $\delta_H$ 1.40-1.93 (4H, m, 2 x 3-H and 2 x 4-H), 2.34-2.60 (3H, m, 2 x 7-H and 4a-H), 3.53-3.85 (3H, m, 2 x 2-H and 5-H), 4.07-4.20 (1H, m, 7a-H), 4.27-4.40 (2H, m, 5-$OCH_2$), 5.15-5.37 (2H, m, $CH_2{=}CH$) and 5.85-6.00 (1H, m, $CH{=}CH_2$).

Isomerisation of (4aα,5β,7aα)-perhydro-5-(2-propenyl)cyclopenta-[b]pyran-6-one (27a).- The α-isomer (27a) (165 mg, 0.84 mmol) was isomerised using the procedure described for compounds (17a) and (17b) to give the β-isomer (27b) as a colourless oil (140 mg, 86%), which was identical to the sample previously described according to i.r. and n.m.r. analysis.

(4aα,5α,6β,7aα)-Octahydro-5-(2-propenyloxy)cyclopenta[b]pyran-6-ol (28).- Following the procedure described for the preparation of compound (20), the ketone (27a) (120 mg, 0.61 mmol), sodium borohydride (76 mg, 1.83 mmol) and cerium (III) chloride heptahydrate (198

mg, 0.61 mmol) gave the title compound as a colourless oil (100 mg, 85%) after flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:1) as eluant]. (Found: C, 66.4; H, 9.3. $C_{11}H_{18}O_3$ requires C, 66.6; H, 9.15%); $\nu_{max}$ ($CHBr_3$) 3450 $cm^{-1}$ (OH); $\delta_H$ 1.66-2.17 (7H, m, 2 x 3-H, 2 x 4-H, 4a-H and 2 x 7-H), 2.56 (1H, d, J10Hz, 6-OH), 3.27-3.40 (1H, m, 2-Hβ (1)), 3.80-4.25 (6H, m, 2-Hα (1), 5-H, 6-H, 7a-H and 5-$OCH_2$), 5.15-5.47 (2H, m, $CH_2CH$) and 5.85-6.01 (1H, m, $CH{=}CH_2$).

(4aα,5α,6β,7aα)-Perhydro-5-(2-propenyloxy-6-[(tetrahydro-2H-pyran-2-yl)oxy]cyclopenta[b]pyran (29).- DHP (0.08 ml, 0.88 mmol) was added to a stirred solution of the alcohol (28) (87 mg, 0.44 mmol) and pyridinium-4-toluenesulphonate (1 mg) in dry dichloromethane (6 ml) at 0-5 °C under a nitrogen atmosphere. The solution was stirred at 0-5 °C for 1.5h and at 20 °C for 20h. The reaction mixture was washed with sodium bicarbonate solution (8%, 10 ml), brine (10 ml), dried ($MgSO_4$) and concentrated *in vacuo* to yield a yellow oil (360 mg). Purification by flash chromatography [30 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:2) as eluant] yielded the title compound as a colourless oil (125 mg, 100%); $\nu_{max}$ ($CHBr_3$) 1065 $cm^{-1}$ (COC, ether); $\delta_H$ 1.45-2.00 (12H, m, 2 x 3-H, 4a-H, 2 x 4-H, 7-Hα (1) and THP aliphatic $CH_2$), 2.25-2.52 (1H, m, 7-Hβ (1)), 3.30-3.58 (3H, m, 2-Hβ (1) and THP ($OCH_2CH_2$)), 3.70-4.28 (6H, m, 2-Hα (1), 5-H, 6-H, 7a-H and 5-$OCH_2$), 4.65 and 4.73 (0.5H, m and 0.5H, m, THP-OCHO diastereomers), 5.15-5.35 (2H, m, $CH_2{=}CH$) and 5.85-6.02 (1H, m, $CH{=}CH_2$).

(4aα,5α,6β,7aα)-Perhydro-5-(oxiranylmethoxy)-6-[(tetrahydro-2H-pyran-2-yl)oxy]cyclopenta[b]pyran (30).- *Meta* -chloroperbenzoic acid (223 mg, 1.29 mmol) was added to a stirred suspension of the alkene (29) (121 mg, 0.43 mmol) and sodium bicarbonate (127 mg, 1.51 mmol) in dry dichloromethane (3 ml) at 0-5 °C under a nitrogen atmosphere. The suspension was stirred at 0-5 °C for 2h and 20 °C for 21h. Sodium hydroxide solution (2M, 20 ml) was added and the aqueous phase was extracted with ether (3 x 15 ml). The combined extracts were washed with sodium bisulphite solution (1.5M, 10 ml) and brine (10 ml), dried ($MgSO_4$) and concentrated *in vacuo* to yield a pale yellow oil (117 mg). Purification by flash chromatography [15 mm column, ether:petroleum ether (b.p. 40-60 °C) (1:1)) as eluant] yielded the title compound as a colourless oil (70 mg, 58%). (Found: C, 64.2; H, 8.5. $C_{16}H_{26}O_5$ requires C, 64.4; H, 8.8%); $\nu_{max}$ ($CHBr_3$) 1065 $cm^{-1}$ (COC, ether); $\delta_H$ 1.35-2.00 (12H, m, 2 x 3-H, 2 x 4-H, 4a-H, 7-Hα (1) and THP aliphatic $CH_2$),

2.25-2.52 (1H, m, 7-Hβ (1)), 2.60-2.70 (1H, m, CH-C$\underline{H}_2$), 2.79-2.86 (1H, $CH_2$, m, CH-C$\underline{H}_2$), 3..10-3.23 (1H, m, C$\underline{H}$-$CH_2$), 3.30-3.40 (1H, m, 2-Hβ (1)), 3.45-4.30 (8H, m, 2-Hα (1), 5-H, 6-H, 7a-H, THP-OC$\underline{H}_2CH_2$ and 5-$OCH_2$) and 4.63 and 4.70 (0.5H, m and 0.5H, m, THP-OC$\underline{H}$O diastereomers).

(4aα,5α,6β,7aα)-1-[[Perhydro-6-[(tetrahydro-2H-pyran-2-yl)oxy]-cyclopenta[b]pyran-5-yl]oxy]-3-phenoxy-2-propanol (31).- Phenol (44 mg, 0.42 mmol) and potassium carbonate (58 mg, 0.42 mmol) were added to a stirred solution of the epoxide (30) (42 mg, 0.14 mmol) in dry acetonitrile (3 ml) at 20 °C under a nitrogen atmosphere. The resultant suspension was stirred under mild reflux for 48h. The reaction mixture was diluted with dichloromethane (10 ml) and washed with water (20 ml) and brine (20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to yield a colourless oil (70 mg). Purification by flash chromatography [20 mm column, ether:petroleum ether (b.p. 40-60 °C) (2:1) as eluant] yielded the title compound as a colourless oil (41 mg, 75%). (Found: C, 67.1; H, 8.4. $C_{22}H_{32}O_6$ requires C, 67.3; H, 8.2%); $\nu_{max}$ ($CHBr_3$) 3490 (OH), 1600 (Ph), 1500 (Ph) and 1040 $cm^{-1}$ (COC, ether); $\delta_H$ 1.34-1.95 (12H, m, 2 x 3-H, 2 x 4-H, 4a-H, 7-Hα (1) and THP aliphatic $CH_2$), 2.27-2.50 (1H, m, 7-Hβ (1)), 2.97 (1H, d, J3Hz, OH), 3.56-4.27 (12H, m, 2-H, 5-H, 6-H, 7a-H, THP-OC$\underline{H}_2CH_2$, C$\underline{H}_2$OPh, C$\underline{H}$OH and OC$\underline{H}_2$CHOH),. 4.56 and 4.62 (0.5H, m and 0.5H, m, THP-OC$\underline{H}$O diastereomers) and 6.90-7.30 (5H, m, OPh).

(2α,3aα,4β,5α,6aα)-Perhydro-2-benzyl-4-butyl-1,1-difluoro-5-*tert* -butyldimethyl silyloxypentalene (33).- The ketone (24a) (0.89 g) was dissolved in dry dichloromethane (26 ml) at 0 °C under nitrogen. Diethylaminosulphur trifluoride (1.5 ml) was added dropwise. The mixture was warmed to room temperature and stirred for 24h. Dichloromethane (30 ml) was added and the organic phase was washed with saturated aqueous sodium hydrogencarbonate (2 x 10 ml), and water (3 x 10 ml) and then dried ($MgSO_4$). The drying agent was removed and the solvent evaporated and the residue was chromatographed over silica using ether/ethyl acetate (1:20) as eluent to give the title compound (33) $\delta_H$ 0.1 (6H, s, Si($C\underline{H}_3$)$_2$) 0.9 (12H, m, 4 x $C\underline{H}_3$ ), 1.15 (1H, m, H-4), 1.4-1.2 (6H, m, 3 x $C\underline{H}_2$), 1.6 (2H, m, 2 x 6-H), 2.5-1.9 (4H, m, 2 x 3-H, 3a-H and 6a-H), 3.8 (1H, m, 5-H), 3.95 (1H, dd, J14, 7 and 7Hz, 2-H), 4.8-4.6 (2H, 2 x d, OC$\underline{H}_2$Ph). (Found: $M^+ + NH_4$ 456.3110. $C_{25}H_{40}O_2SiF_2$ requires M + $NH_4$ 456.3111).

3aα,4β,5α,6aα-Perhydro-4-butyl-1,1-difluoro-5-*tert* -butyldimethyl-silyloxy-2(1H)-pentalenone (34).- The difluorocompound (33) (130 mg) in dry ether (10 ml) was added to liquid ammonia (30 ml) at -78 °C. The mixture was stirred under nitrogen and sodium was added portionwise to establish a permanent blue colour. The solution was stirred for 10 min. whereupon ammonium chloride was added to discharge the blue colour. The ammonia was evaporated by warming the flask to room temperature. Diethyl ether (50 ml) was added and the mixture was stirred for 10 min. The solid was filtered off and washed with ether. The combined organic phases were evaporated and the crude product was chromatographed over silica using ether/petroleum ether 40-60 °C (ratio 1:3) as eluent to give the *endo* -alcohol (56 mg). (Found: $M^+ + H$, 349.2378. $C_{18}H_{35}O_2SiF_2$ requires M + H, 349.2382). Oxalyl chloride (44 ml) was stirred in dry dichloromethane (1.2 ml) under an atmosphere of nitrogen. Dimethyl-sulphoxide (74 ml) in dry dichloromethane (0.22 ml) was added dropwise. The resultant mixture was stirred at -60 °C for 5 min. The *endo* -alcohol (150 mg) in dry dichloromethane (0.44 ml) was added dropwise and the mixture was stirred for 45 min. at -60 °C. Dry triethylamine (0.3 ml) was added and the mixture was warmed to room temperature. Water (2 ml) was added and the two phases were separated. The aqueous layer was extracted with ether (2 x 20 ml). The combined organic fractions were washed with brine (10 ml) and dried over magnesium sulphate. The solvent was evaporated (after removing the drying agent) and the crude product was chromatographed over silica (eluent, ether/petroleum ether (40-60 °C), ratio 1:4) to furnish the fluoroketone (34) (110 mg). $\delta_H$ 0.1 (6H, 2 x s, $Si(C\underline{H}_3)_2$), 0.9 (9H, s, $C(C\underline{H}_3)_3$), 0.93 (3H, t, $CH_2C\underline{H}_3$), 1.3 (6H, m, 3 x $CH_2$), 1.78 (1H, m, 4-H), 2.1 (2H, m, 2 x 3-H), 2.68-2.15 (3H, m, 3a-H and 2 x 6-H), 2.9 (1H, m, 6a-H) and 4.0 (1H, m, 5-H). Found: $M^+ + NH_4$ 364.2472. $C_{18}H_{32}O_2SiF_2$ requires M+ $NH_4$ 364.2481).

Wittig Reaction on the Compound (34).- The fluoroketone (34) (40 mg) in dry tetrahydrofuran (2 ml) was added to a stirred mixture of 4-carboxybutyltriphenyl phosphonium bromide (250 mg) and potassium *tert* -butoxide (141 mg) at room temperature under an atmosphere of nitrogen. The mixture was stirred for 2.5h and refluxed for 3.5h, cooled and acidified with 2NHCl. Water (5 ml) was added and the mixture was extracted with ether (3 x 20 ml). The combined organic extracts were washed with brine (2 x 20 ml), dried ($MgSO_4$) and evaporated. The crude product was treated with diazomethane in ether. The ether was evaporated and the residue was chromatographed over silica (using ether and petroleum ether (40-60 °C), ratio 1:10 as eluent) to afford the methyl ester (35) (15 mg).

$\delta_H$ 0.1 (6H, 2 x s, Si($C\underline{H}_3$)$_2$), 0.9 (12H, 4 x $C\underline{H}_3$), 1.3 (6H, m, 3 x $CH_2$), 2.42-1.5 (13H, m), 2.95 (1H, m), 3.68 (3H, s, OCO$C\underline{H}_3$), 3.72 (1H, m, C$\underline{H}$O), 5.5 (1H, m, =C$\underline{H}$). (Found: $M^+ + NH_4$ 362.3214. $C_{24}H_{42}O_3F_2Si$ requires M + $NH_4$ 362.3213).

Synthesis of the Prostanoid (36).- The methyl ester (35) (10 mg) was stirred with dry tetrahydrofuran (2 ml) and tetrabutylammonium fluoride (1.1M, 0.04 ml) at room temperature under nitrogen for 15h. The solvent was evaporated and the product was chromatographed over silica, using ethyl acetate/petroleum ether (40-60 °C) (ratio 2:3) as eluent, to give the prostanoid (36) (4 mg). $\delta_H$ 0.93 (3H, t, $CH_2C\underline{H}_3$), 2.3-1.15 (20H, m), 3.68 (3H, s, $CO_2CH_3$), 3.75 (1H, m, CHO), 5.55 (1H, m, =CH). (Found: $M^+ + NH_4$, 348.2357. $C_{18}H_{28}O_3F_2$ requires M + $NH_4$, 348.2362).

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