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The Stereospecific Synthesis of *cis* and *trans* 1-Oxabicyclo[4,4,0]decanes and 9-Methoxycarbonyl-1-oxabicyclo[4,3,0]nonanes

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Abstract: The allylic sulphoxides **1b** and **1e** reacted with 1-pyrrolidinylcyclohexene and 2-ethoxycarbonyl cyclopentanone to yield the 2-substituted keto-sulphoxides **10** and **14** respectively, which on reduction followed by oxidation yielded in each case a mixture of *cis* and *trans* sulphones that were separated by column chromatography. Base induced cyclisation followed by reductive desulphurisation of the cyclised sulphones yielded the corresponding bicyclic compounds **6**, **7**, **8** and **9** in good yields. © 1999 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Functionalised allylic organosulphur molecules of the type **1** (a. Z = t-BuSO$_2$, Y= Br;[1] b. Z = PhSO, Y = Br ; c. Z = PhSO, Y = OTs ,[2] d. Z = PHSO, Y = OPh)[3] and **2**[4] are versatile reagents that have cosiderable potential in organic synthesis. We have used these alkenyl organosulphur reagents to construct prostanoids **3**[4] benzofurans **4**[3], and steroids **5**[5]. We now wish to report a new stereospecific approach to the synthesis of the oxybicyclic systems *cis* **6** , *trans* **7**, cis **8** and trans **9** using the allylic sulphoxides **1c** and **1e** (Z = PhSO, Y = OMs).

The 1-oxadecalins have been obtained by a variety of methods such as the cycloaddition reaction of 2-alkylidenecyclohexanone derivatives with vinyl ethers[6] , intramolecular condensation reactions of 2-alkynylcyclohexanones[7] , cyclisation of 2-(3-hydroxypropyl)cyclohexanols[8,9] and by the catalytic hydrogenation of chromans[10] and coumarins[11,12] as a mixture of the two isomers **6** and **7** which have then been separated. Oxidation of 3-cyclohexylpropanol with lead tetraacetate has been reported to yield, amongst other products, a mixture of *cis* and *trans* 1-oxadecalins[13].

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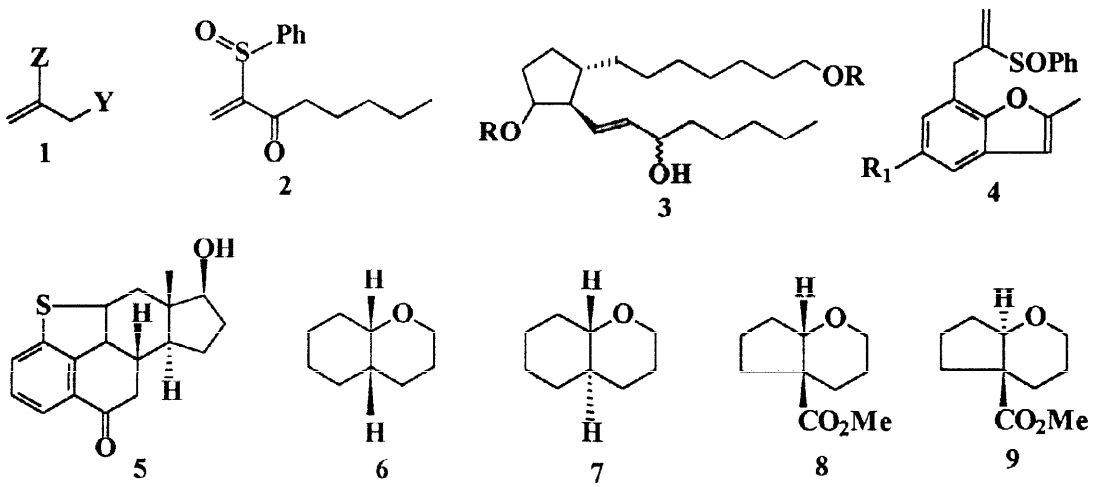
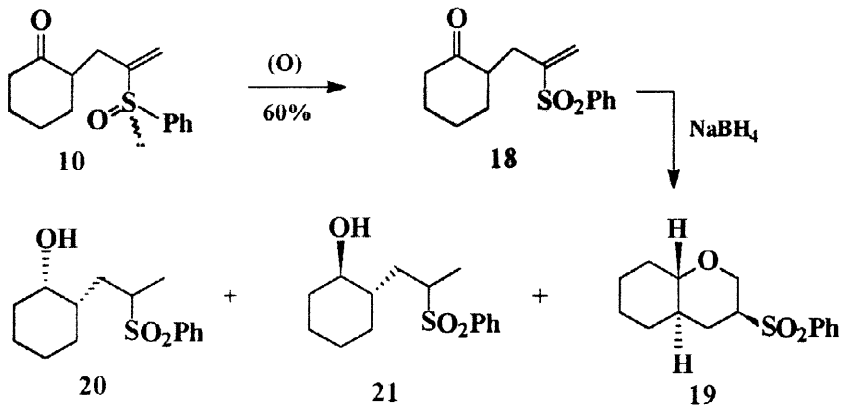


Compounds **8** and **9** are unprecedented in the literature. Our general and stereospecific approach to the synthesis of these bicyclic molecules **6**, **7**, **8** and **9** is based on the readily obtainable starting materials 1-pyrrolidinylcyclohexene, 2-ethoxycarbonylcyclopentanone and the synthons **1c** and **1e**

RESULTS AND DISCUSSION

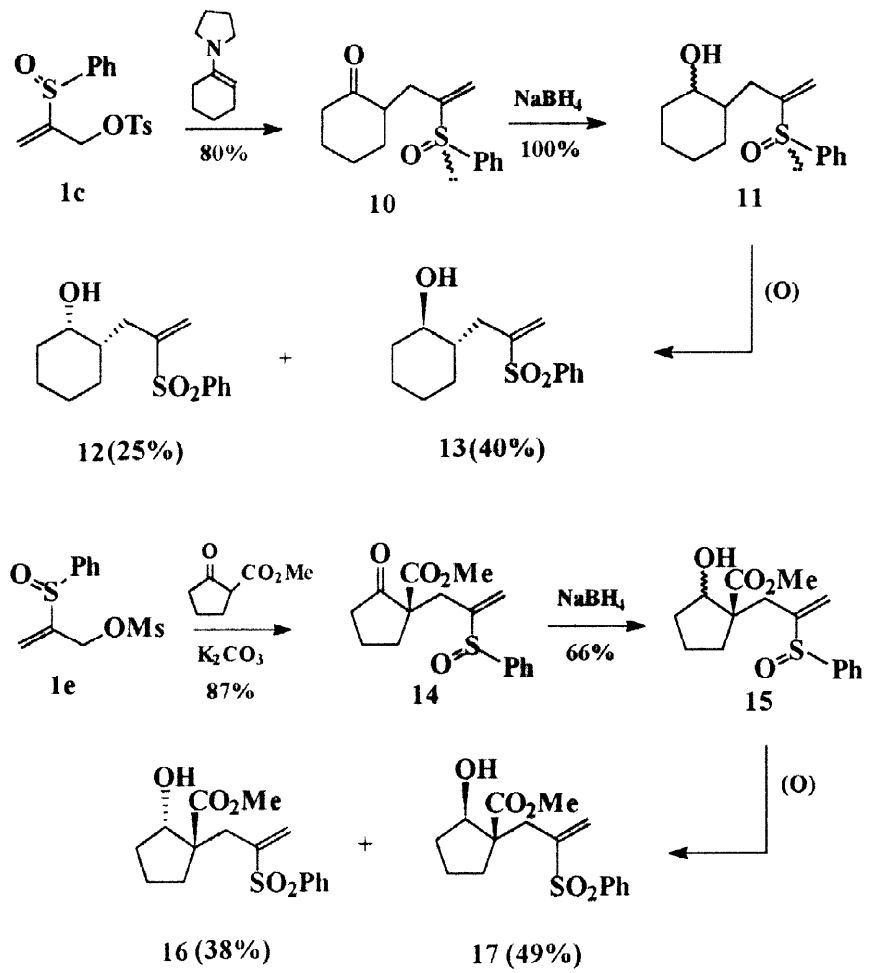
The tosylate **1c** and the mesylate **1e** were readily prepared in two steps from prop-2-yn-1-ol. The tosylate **1c** alkylated 1-pyrrolidinylcyclohexene in DCM to yield the ketone **10** in 50% purified yield. Similarly the adduct **14** was obtained as an inseparable mixture of diastereomers at sulphur in 87% purified yield by the alkylation of 2-ethoxycarbonylcyclopentanone with the mesylate **1e** in THF containing K_2CO_3. Our initial intention was to oxidise the alkenyl keto-sulphoxide **10** to the corresponding alkenyl keto-sulphone **18** and to reduce the latter compound to the epimeric hydroxy sulphones **12** and **13**. However, the sulphone **18** obtained by oxidation of the alkenyl keto-sulphoxide **10** with peroxydodecanoic acid, on reduction ($NaBH_4$ / ^iPrOH) did not give the anticipated products **12** and **13** but istead yielded a mixture of chromatographically very similar products, which after separation by careful chromatography, were shown to be compounds **19** (6%), **20** and **21** (69% combined yield) (Scheme 1).

The derivatives *cis* **20** and *trans* **21** which resulted from the conjugate addition of hydride ions to the olefinic bonds of the initially formed products **12** and **13** were shown by proton nmr to lack olefinic protons. We decided, therefore, to reverse the order in which we operated on the keto group and sulphoxide group, that is to reduce the ketone **10** to the alcohols **11** , then to oxidise the sulphoxide to the sulphones **12** and **13.** Thus reduction of the keto-sulphoxide **10** proceeded without conjugate reduction of the double bond to yield the expected racemic mixture of hydroxy alkenyl sulphoxides **11** (69% combined yield). Oxidation of **11** afforded the two sulphones **12** and **13**(92% combined yield) as a mixture which was separated by column chromatography into **12** (25%) and **13** (40%). Analogously, reduction of **14** ($NaBH_4$ / ^iPrOH) gave racemate **15** which on oxidation and separation yielded the sulphones **16** (38%) and **17**



Scheme 1

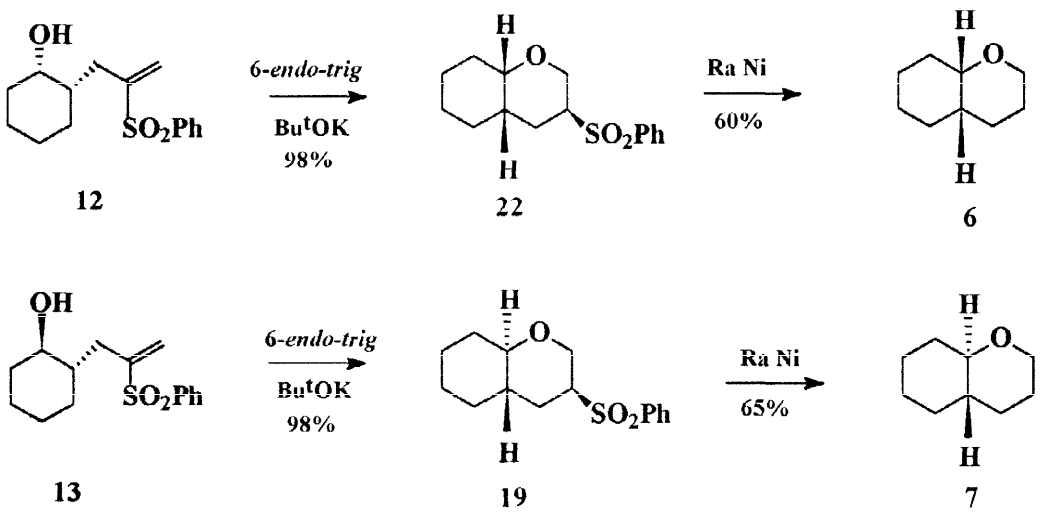
(49%) (Scheme 2). Evidently the reduction reactions of both precursors **10** and **14** were dominated by the sterically preferred formation of the *trans* products (*viz.* **13** and **17**). The configuration of the hydroxy groups (*cis* or *trans*) relative to the alkyl substituent at C-2 followed



Scheme 2

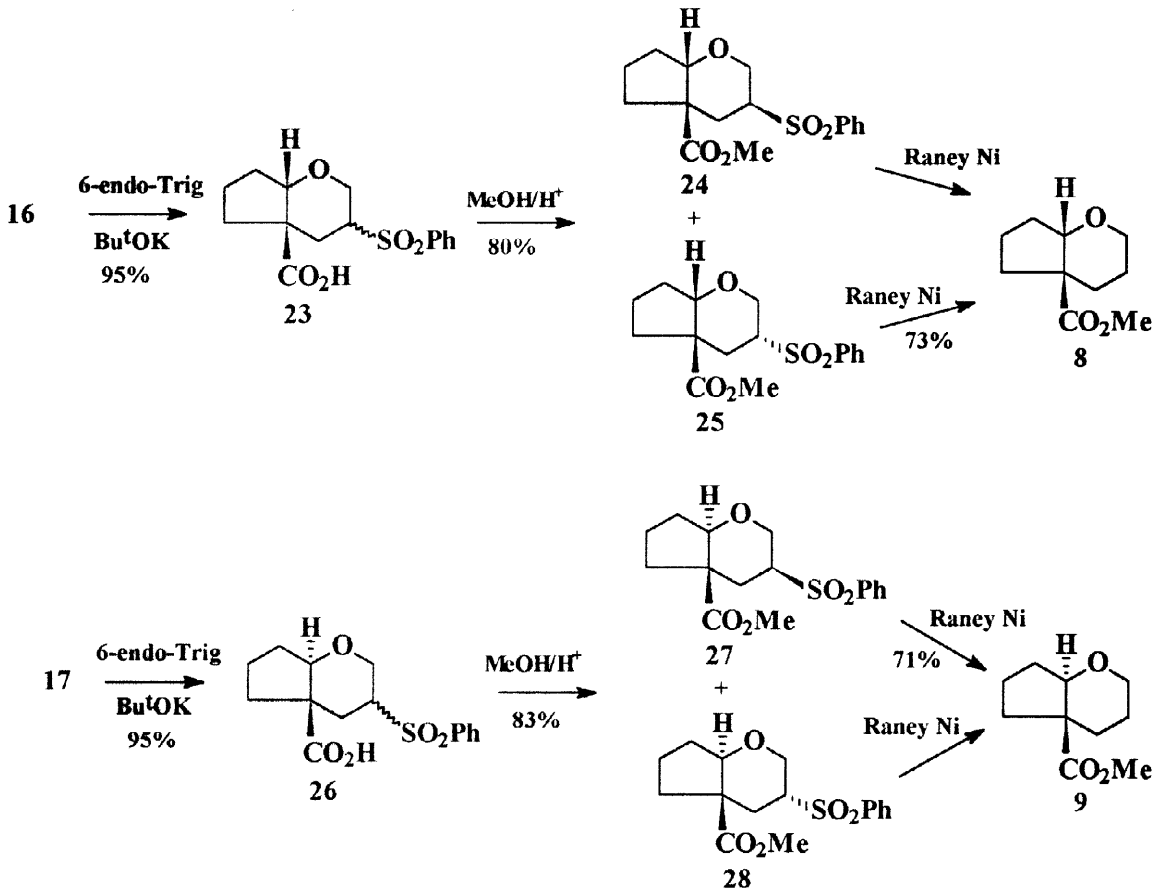
from the ^{1}H-NMR spectral characteristics of the geminal proton at C-1 . Use was made of the criteria that axial protons resonate at higher field than equatorial protons and signals due to axial protons are significantly broader than those due to equatorial protons[14]. In assigning configuration in this way an assumption was made about the preferred conformation of the molecule. It was assumed that alkyl substituents at C-2 always adopted the equatorial orientation. This is most probably valid since the conformational preference of the hydroxy group (2.9 kJ mol^{-1}) is appreciably less than that of alkyl groups roughly comparable in size to that of the alkyl substituent at C-2 (*viz.* the conformational preference of the propyl group is 9 kJmol^{-1}) [15] . This criterion was also applied to five membered rings in which the substituents actually exist in pseudo-axial and pseudo-equatorial dispositions rather than pronounced axial and equatorial dispositions as in six membered rings.

The hydroxy sulphones **12**, **13**, **16** and **17** readily underwent cyclisation by the 6-*endo-trig* process[16] to give the cyclic adducts **19**, **22**, **23** and **26** respectively in 95-98% yields. However, in the case of the sulphones **16** and **17** the ring closure reactions gave rise to the formation of carboxylic acids **23** and **26** as reaction products, presumably by transesterification of the intermediate methyl ester products to the t-butyl esters which on subsequent work-up hydrolysed to the corresponding acids **23** and **26**. Esterification of the crude products **23** and **26** in acidic methanol afforded after chromatographic separation a pair of the bicyclic esters: *cis* **24** and **25** and *trans* **27** and **28** respectively (Schemes 3 and 4).



Scheme 3

That the compound pairs *cis* (**24** and **25**) and *trans* (**27** and **28**) were stereoisomers at C-3 was established by proton nmr as well as by reductive desulphurisation, in which each pair of compounds yielded a single product (see later). Thus in the *cis* pair of compounds **24** and **25**, the one in which the C-3 (H_D) proton resonated at δ 3.34 was assigned the configuration **24**, whilst



Scheme 4

the one in which the C-3 (H_D) resonated at δ 3.46 was allocated the configuration **25**. Moreover, the large coupling between (H_B) and (H_D) (J = 11 Hz) in the NMR spectrum of **24** was consistent with an antiperiplanar relationship between them and hence an axial orientation for (H_D) (Fig.1). Likewise for the *trans* compounds **27** and **28**, the proton (H_D) resonated high field at δ 3.33 in the NMR spectrum of **27** and the large coupling between (H_B) and (H_D) (J = 11Hz) was consistent with an anti-periplanar relationship between them and hence an axial orientation for (H_D). The bicyclic adduct in which the proton (H_D) resonated low field at δ 3.45 was assigned the structure **28**. The proton assignments for (H_A), (H_B), (H_C), and (H_D) in all the compounds **22- 25, 27** and **28** (Fig. 1) were based on appropriate spin decoupling experiments. That the phenylsulphonyl group at C-3 had adopted the thermodynamically more favourable equatorial orientation in both cyclic adducts *cis* **22** and *trans* **19** was clear from their proton NMR spectra. Thus the NMR of **19** showed the proton (H_D) at C-3 as a triplet of triplets (J = 12 and 3.6 Hz) indicative of an axial relationship with each of the protons (H_B) and (H_F). The bridgehead proton (H_C) at C-9 appeared as a triplet of doublets indicating that it was axially orientated and coupled in an antiperiplanar relationship with the C-10 proton (H_G) and the axial proton at C-8 (J = 12 Hz) (Fig 1). Finally,

reductive desulphurisation (Raney Ni / ethanol) of the sulphones *cis* **22** and *trans* **19** yielded the corresponding parent 1-oxadecalins *cis* **6** (60% yield) and *trans* **7** (65% yield) respectively.

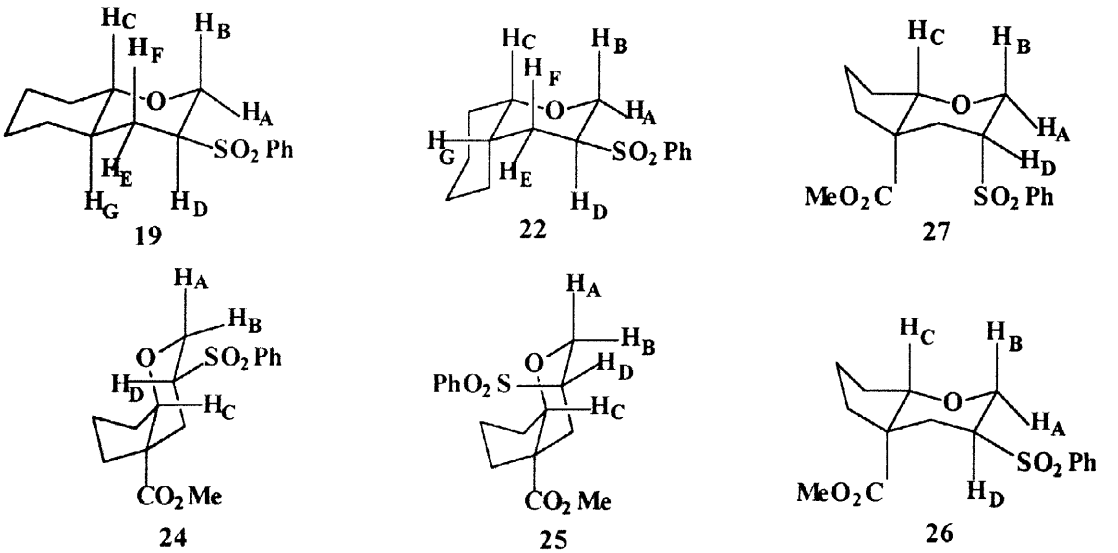


Fig. 1

Similarly, desulphurisation of the two sulphones *cis* **24** and *cis* **25** afforded the *cis* heterocycle **8** (70% yield). Likewise the reductive removal of the phenylsulphonyl group from the precursors *trans* **27** and *trans* **28** provided the parent ester *trans* **9** (73% yield). The fact that both compounds **24** and **25** yielded one product and likewise both **27** and **28** yielded also one product proved that the stereochemistry in each of the compound in the pairs (**24** and **25**) and (**27** and **28**) differed at C-3 only, as was earlier confirmed from their proton NMR spectra. The proton NMR spectra of the 1-oxadecalins showed that the signals due to the proton at C-9 in the *cis* isomer **6** was narrower ($W_{1/2}$ = 8 Hz) and at lower field (3.58 ppm) than that due to the C-9 proton in the *trans* isomer **7** (2.90 ppm, $W_{1/2}$ = 22 Hz), which was indicative of its equatorial orientation (with respect to the cyclohexane ring) in the former and its axial orientation in the latter. No such dramatic changes in the chemical shifts of the bridgehead protons at C-8 were observed in the *cis* and *trans* 1-oxahydrindanes **8** and **9**.

CONCLUSION

A general method for the stereoselective synthesis of the bicyclic systems *cis* and *trans* 1-oxadecalins **6** and **7** and 9-methoxycarbonyl-1-oxahydrindanes **8** and **9** from readily obtainable and reactive organosulphur reagents **1c** and **1e** has been successfully demonstrated.

EXPERIMENTAL

General Methods. Mps are uncorrected and were determined on a Kofler hot stage micro melting point apparatus. Infrared spectra were measured on either a Pekin-Elmer model 137 or

157G or 457 double beam spectrophotometer as solutions in chloroform unless otherwise stated. ^{1}H-NMR spectra were recorded in $CDCl_3$ using either Perkin-Elmer R-34 (220 MHz) or Brucker 360 MHz or 400 MHz spectrometers. ^{13}C-NMR spectra (^{1}H-coupled and decoupled) were recorded in $CDCl_3$ using a JEOL PFT-100 spectrometer. Chemical shifts (δ) are in ppm downfield from tetramethylsilane as internal standard, *J* values are given in Hz. Mass spectra were recorded with AEI M12 mass spectrometer. Analytical GLC was performed on Perkin-Elmer F11 instrument and preparative GLC was performed on Pye 105 with a FID detector and employing a glass column of 2.13m length and internal diameter (9.5mm) packed with 7% OV17 by weight on 60-80 mesh chromosorb G or W with N_2 as carrier gas. Column chromatography was performed using the short path technique with Whatman silica gel SOTLC without additives. Microanalyses were performed by the University of Sheffield microanalytical laboratory. All solvents were dried and distilled by standard techniques. All organic solutions were dried over anhydrous $MgSO_4$ unless othrwise stated. Light petroleum refers to the fraction boiling in the range 40-60°C. All the 1-oxadecalin and 1-oxahydrindane derivatives were obtained as racemic modifications. For clarity the steroid convention α and β is used for the naming of 1-oxahydrindane derivatives to designate the orientation of the substituents and configuration at ring junctions.

2-Phenylsulphinyl-3-methanesulphonyloxyprop-1-ene (1e)

A solution of methanesulphonyl chloride (0.69 g, 0.47 mL, 6.02 mmol) in DCM (3 mL) was added dropwise over 10 min. to a stirred mixture of 2-phenylsulphinyl-3-hydroxyprop-1-ene[2] (1.0g, 5.50 mmol) and Et_3N (0.84 g, 1.15 mL, 8.28 mmol) in DCM (25 mL) at -15°C. After that the reaction mixture was allowed to warm to 0°C, diluted with DCM and washed with ice cold water, cold dilute HCl, saturated $NaHCO_3$ solution and brine respectively. The organic phase after drying over anhydrous Na_2SO_4 was evaporated to give an oil which was purified by column chromatography (ether) to afford pure compound **1e** as a pale-brown oil (0.79g, 55%); ν_{max} (neat)/cm^{-1} 1351 and 1174 (OSO_2), 1041 (SO); δ_H 2.85 (3H, s, OSO_2CH_3), 4.69 (2H, AB system, *J* 13, OCH_2), 6.68 (1H, s, HC=C, *trans* to SOPh), 6.33 (1H, s, HC=C, *cis* to SOPh), 7.48-7.57 (3H, m, Ph), 7.61-7.73 (2H, m, Ph); m/z 260 (M^+); Found: C, 46.4; H, 4.85; S, 24.8. $C_{10}H_{12}O_4S_2$ requires C, 46.15; H, 4.6; S, 24.6 %.

Cis-(9SR),(10SR)-1-Oxabicyclo[4,4,0]decane (6)

To a solution of the cyclic adduct **22** (956 mg, 3.41 mmol) in EtOH (20 mL) was added Raney nickel (10 g) and the resultant mixture was stirred and refluxed under nitrogen for 9 h. The cooled reaction mixture was filtered through hyflo supercell at the pump and washed with more ethanol. The ethanol was removed by distillation using a 40 cm fractionating column leaving a colourless residue which still contained a little ethanol. Examination of the residue by TLC (petroleum ether: ether 12:1) revealed two visual products (R_f 0.74; 0.97). Analysis by GLC (6' Harflex) showed a major peak (t_R ,12 min, 60%) and two minor peaks (t_R, 16.5 min, 3%; t_R, 17.5 min, 2%). The compound (t_R, 12 min) was isolated by preparative GLC (7' Harflex, 60-190°C) as a colourless liquid and identified as the *cis* 1-oxadecalin **6**; δ_H 1.11-1.98 (13H, m, aliphatic ring), 3.40-3.62 (2H, m, axial 2-H, 9-H), 4.02 (1H, m, equatorial 2-H); GCMS: m/z 140 (M^+); Found

C, 77.35;H, 11.6. $C_9H_{16}O$ requires C, 77.1; H, 11.4%.

Trans (9SR),(10SR)-1-Oxabicyclo[4,4,0]decane (7)

In a similar manner to above sulphone **19** (403 mg, 1.44 mmol) and Raney nickel (5 g) in EtOH (20 mL) after refluxing for 10 h gave a residue which on TLC (petroleum ether: ether 12:1) consisted of two visual spots (R_f 0.80, 0.98).GLC analysis (6' Harflex) showed a major peak (t_R 12 min, 65%) which was isolated by preparative GLC as a colourless liquid and identified as the *trans* 1-oxadecalin 7; δ_H 1.08-2.0 (13H, m, aliphatic ring), 2.82-2.98 (1H, broad m, 9-H), 3.45 (1H, td, *J* 2, 11, axial 2-H), 3.98 (1H, qd, *J* 11, 2, equatorial 2-H); GCMS: m/z 140 (M^+); Found C, 77.35; H, 11.6. $C_9H_{16}O$ requires C, 77.1; H, 11.4%.

9β-Methoxycarbonyl-8β-1-oxabicyclo[4,3,0]nonane (8)

In a similar manner to above the sulphone **24** or **25** (290 mg, 0.90 mmol) in ethanol (20 mL) containing Raney nickel (3 g) after an overnight reflux under argon yielded an oil which on purification by GLC (7' OV, 150°C) afforded ester **8** as a colourless oil (t_R 9.5 min, 120 mg, 73%); ν_{max} (neat)/cm^{-1} 1722 (CO); δ_H 1.34-2.20 (10H, m, aliphatic ring), 3.42 (1H, dt, *J* 11, 2, axial 2-H), 3.67 (3H, s, OMe), 3.87 (1H, m, equatorial 2-H), 4.10 (1H, d, *J* 3, 8-H); HRMS Found: M^+, 184.1105 $C_{10}H_{16}O_3$ requires M^+, 184.1099.

9β-Methoxycarbonyl-8α-1-oxabicyclo[4,3,0]nonane (9)

Similarly the sulphone **27** or **28** (320 mg, 0.99 mmol) in ethanol (20 mL) containing Raney nickel (4 g) after an overnight reflux under argon yielded an oil which was purified by GLC (7' OV, 150°C) to give ester **9** as a colourless oil (t_R 7.4 min, 129 mg, 71%); ν_{max} (neat)/cm^{-1} 1722 (C=O); δ_H 1.38-2.14 (10H, m, aliphatic ring), 3.38 (1H, dt, *J* 11, 2, axial 2-H), 3.66 (3H, s, OMe), 3.86 (1H, m, equatorial 2-H), 4.08 (1H, d, *J* 3, 8-H); HRMS Found: M^+, 184.1110 $C_{10}H_{16}O_3$ requires M^+, 184.1099.

2-(2'-Phenylsulphinylprop-2'-enyl)cyclohexanone (10)

To a stirred solution of 2-phenylsulphinyl-3-ρ-toluenesulphonyloxyprop-1-ene **1c**[2] (20.28 g, 60.4 mmol) in dry DCM (150 mL) was added dropwise 1-pyrrolidinyl cyclohexene (9.10 g, 60.4 mmol). After the addition was complete and the exothermic reaction had subsided, stirring was continued for 1.75 h. The solvent was evaporated and to the residue was added MeOH (150 mL) and H_2O (10 mL) and refluxed on a steam bath for 3.5 h. After evaporation of MeOH the residue was neutralised with dil.HCl. Normal ether work-up gave crude product **10** as a dark brown oil (12.68g, 80%) which was purified by column chromatography using ether to afford pure product **10** as a light brown oil (7.90g, 50%); ν_{max} (neat)/cm^{-1} 1712 (CO), 1045 , 1080 (SO); δ_H 1.10-2.42 (9H, m, aliphatic ring), 2.43-2.71 (2H, m, allylic CH_2), 5.63 (1H, d, *J* 4.8 , CH=C trans to SOPh), 6.11 (1H, s, CH=C cis to SOPh), 7.46-7.55 (3H, m, Ph), 7.58-7.68 (2H, m, Ph); m/z 263 (M^++1); Found: C, 68.4; H, 6.75, S, 12.4. $C_{15}H_{18}O_2S$ requires C, 68.75; H, 6.9; S, 12.2 %.

Cis-(1RS)-1α-Hydroxy-2α- (2'-phenylsulphonylprop-2'-enyl)cyclohexane (12) and trans-(1RS)-1β-Hydroxy-2α-(2'-phenylsulphonylprop-2'-enyl)cyclohexane (13)

To a stirred solution of sulphoxide **10** (6.97 g, 26.6 mmol) in ^{i}PrOH (280 mL) was added sodium borohydride (3.0 g, 79.8 mmol). After stirring overnight the solvent was removed on the rotary evaporator and to the residue was added water (5 mL) followed by the dropwise addition of 2M aq.HCl to destroy the excess sodium borohydride. After adding benzene, the residual mixture was refluxed under a Dean-Stark water separator until all the water had been transferred. The benzene solution was evaporated to yield a mixture of the hydroxy vinyl sulphoxides **11** as an oil (7.0 g, quantitative yield) which showed as three spots on TLC (ether, Rf 0.78, 0.46 and 0.37). To a well cooled and stirred solution of the crude mixture **11** (7.0 g, 26.6 mmol) in DCM (150 mL) was added peroxydodecanoic acid (83% pure, 7.2 g, 27.7 mmol) and the mixture stirred overnight at RT. After evaporation, the residue was passed through a column of alumina using ether to give an oil (6.8 g, 92%) which showed two spots on TLC (ether-light petroleum, 4:1). Elution of the mixture on a column of silica yielded firstly the *cis* hydroxy sulphone **12** as a white solid (1.8g, 25%) which was recrystallised (ether-light petroleum), mp 68-69°C; ν_{max} ($CHCl_3$)/cm^{-1} 3600 (OH, hydrogen bonded), 3520 (OH, non-hydrogen bonded), 1154, 1136, 1078 (SO_2); δ_H 1.05-1.85 (9H, m, aliphatic ring), 2.03 (1H,s, OH), 1.95-2.20 (1H, m, allylic), 2.26-2.48 (1H, m, allylic), 3.83 (1H, broad s, 1-H), 5.80 (1H, s, *trans* >C=CH), 6.43 (1H, s, *cis* >C=CH), 7.48-7.70 (3H, m, Ph), 7.88 (2H, d, *J* 7.2, Ph); m/z 279, 262 (M-OH); Found: C, 64.6; H, 7.3; S, 11.4. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.15; S, 11.4%; followed by secondly the *trans* hydroxy sulphone **13** as an oil (3.0 g, 40%); ν_{max} (neat)/ cm^{-1} 3595 (OH, hydrogen bonded), 3519 (OH, non-hydrogen bonded), 1078 ,1135 (SO_2); δ_H 0.95-1.80 (8H, m, aliphatic ring), 1.96 (2H, dd, *J* 4.8,9.6, allylic and 2-H), 2.04 (1H, broad s, OH), 2.81 (1H, broad m, allylic), 3.05-3.23 (1H, broad m, 1-H), 5.78 (1H, s, *trans* >C=CH), 6.42 (1H, s, *cis* >C=CH), 7.5-7.7 (3H, m, Ph), 7.91 (2H, d, *J* 7.2, Ph); m/z 280 (M^+), 263 (M^+-OH); Found: C, 64.5; H, 7.4; S, 11.2. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.1; S, 11.4%.

2β-Ethoxycarbonyl-2α -(2'-phenylsulphinylprop-2'-enyl)cyclopentanone (14)

Potassium carbonate (1.8 g, 12.8 mmol) was added to a vigorously stirred mixture of 2-ethoxy carbonyl- cyclopentanone (4.0 g, 25.6 mmol) and the mesylate **1e** (7.3 g, 28.1 mmol) in THF (50 mL). The resulting mixture was stirred overnight and subjected to normal ether-work-up to yield an oily residue which was chromatographed (ether:light petroleum, 1:1) to give pure compound **14** as an oil (7.1 g, 87%); ν_{max} (neat)/cm^{-1} 1752 (CO), 1628 (C= C), 1048 (SO); δ_H 1.14-1.26 (3H, td, *J* 7, OCH_2), 1.78-2.66 (7H, m, ring CH_2 and allylic CH), 2.84 (1H, d, *J* 15, allylic CH of AB system), 4.06-4.24 (2H, q, *J* 7, OCH_2), 5.67 (0.35H, s, HC=C, *trans* to SOPh), 5.69 (0.65H, s, HC=C, *trans* to SOPh), 6.20 (0.35H, s, HC=C, *cis* to SOPh), 6.23 (0.65H, s, HC=C, *cis* to SOPh), 7.43-7.55 (3H, m, Ph), 7.60-7.73 (2H, m, Ph); m/z 320 (M^+); Found: C, 63.9; H, 6.5; S, 10.0. $C_{17}H_{20}O_4S$ requires C, 63.8; H, 6.3; S, 10.0 %.

1α-Hydroxy-2β-ethoxycarbonyl-2α-(2'-phenylsulphonylprop-2'-enyl)cyclopentane (16) and 1β-Hydroxy-2β-ethoxycarbonyl-2α-(2'-phenylsulphonylprop-2'-enyl) cyclopentane (17)

Sodium borohydride (1.2 g, 31.6 mmol) was added to a stirred solution of the keto-sulphoxide **14** (4.0 g, 12.5 mmol) in EtOH (50 mL) maintained at 0°C and the resulting mixture stirred for 2 h allowing it to warm to RT. The solvent was evaporated and the residue was partitioned between ether and sat. NaCl solution. A normal ether work-up afforded the mixture of hydroxy alkenyl sulphoxides **15** as an oil which showed up as four overlapping spots on TLC (ether). To the crude mixture **15** in DCM (50 mL) at 0°C was added m-chloroperbenzoic acid (2.1 g, 12.2 mmol) and stirred for 2 h. The reaction mixture, after dilution with DCM and washing with sat. $NaHCO_3$ solution, was dried and evaporated to yield an oil which according to TLC (ether-light petroleum, 1:1) consisted of two products. Column chromatography afforded firstly the hydroxy sulphone **16** as an oil (1.6 g, 38%); ν_{max} (neat)/ cm^{-1} 3490 (OH), 1721 (CO), 1300, 1161 (SO_2); δ_H 1.14 (3H, t, *J* 7, Me), 1.45-2.30 (6H, m, aliphatic ring), 2.72 (2H, AB system, *J* 17, allylic), 3.32 (1H, broad s, 2-H), 4.08 (2H, q, *J* 7, O-CH_2-), 4.38 (1H, m, 1-H), 5.80(1H, s, *trans* >C=CH), 6.43 (1H, s, *cis* >C=CH), 7.50-7.74 (3H, m, Ph), 7.95-7.85 (2H, m, Ph); m/z 338 (M^+); Found: C, 60.5; H, 6.7; S, 9.45. $C_{17}H_{22}O_5S$ requires C, 60.35; H, 6.5; S, 9.45%; followed by the hydroxy sulphone **17** as an oil (2.1 g, 49%); ν_{max} (neat)/cm^{-1} 3496 (OH), 1718 (CO), 1310, 1160 (SO_2); δ_H 1.14 (3H, t, *J* 7, Me), 1.40-2.46 (7H, m, aliphatic ring and allylic), 2.85 (1H, d, *J* 7, allylic), 3.28 (1H, broad, OH), 3.99 (1H, t, *J* 5, 1-H) 4.11 (2H, q, *J* 7, O-CH_2-), 5.82 (1H, s, *trans* >C=CH), 6.44 (1H, s, *cis* >C=CH), 7.72-7.50 (3H, m, Ph), 7.83-7.94 (2H, m, Ph); m/z 338 (M^+); Found: C, 60.4; H, 6.5; S, 9.3. $C_{17}H_{22}O_5S$ requires C, 60.35; H, 6.5; S, 9.45%.

2-(2'-Phenylsulphonylprop-2'-enyl)cyclohexanone (18)

To a well cooled solution of sulphoxide **10** (4.50 g, 17.4 mmol) in dry DCM (90 mL) was added peroxydodecanoic acid (83% pure, 5.0 g) and the mixture stirred at RT for 2 h. After evaporation of the solvent the residue was chromatographed on a column of alumina (Et_2O) to yield compound **18** as an oil (2.70 g, 60%) which crystallised on keeping. Recrystallisation (Et_2O/light petroleum) afforded pure sulphone **18** (2.31g, 51%), mp 73.5-74.5°C; ν_{max} ($CHCl_3$)/cm^{-1} 1708 (CO), 1160, 1140, 1083 (SO_2); δ_H 1.10-2.50 (9H, m, ring CH), 2.54-2.96 (2H, m, allylic CH_2), 5.78 (1H, s, CH=C *trans* to SO_2Ph), 6.40 (1H, s, CH=C *cis* to SO_2Ph), 7.45-7.68 (3H, m, Ph), 7.80-7.97 (2H, m, Ph); δ_C {H^1} 211.14 (s, CO), 148.04 (s, olefinic carbon bearing SO_2Ph), 138.75 (s, Ar carbon adjacent to SO_2-), 133.48 (d, *para* Ar carbon), 129.17 (d, *ortho* and *meta* Ar carbons), 128.20 (d, *ortho* and *meta* Ar carbons), 125.95 (t, primary olefinic carbon), 48.72 (d, tertiary carbon adjacent to CO), 42.17 (t, allylic), 33.79 (t, aliphatic C-6), 25.12-30.03 (remaining aliphatics); m/z 279 (M^++1); Found: C, 64.4; H, 6.6; S, 11.7 %. $C_{15}H_{18}O_3S$ requires C, 64.7; H, 6.5; S, 11.5 %.

Trans-(3SR),(9SR),(10SR)-3β-Phenylsulphonyl-1-oxabicyclo[4,4,0]decane (19)

To a solution of *trans* hydroxy vinyl sulphone **13** (572 mg, 2.04 mmol) in dry ^tBuOH 24 mL) was added ^tBuOK (228 mg, 2.04 mmol) and the mixture was heated under N_2 at 56°C for 2.5 h. The solvent was evaporated and the residue acidified with aq. 2M HCl. Normal ether work-up gave

the crude product which was purified by column chromatography (ether-light petroleum, 3:1) to give pure **19** as a white solid (560 mg, 98%) and recrystallised (ether-light petroleum), mp 74-75.5°C. ν_{max} ($CHCl_3$)/cm^{-1} 1140, 1076 (SO_2); δ_H 0.95-1.95 (10H, m, aliphatic ring), 2.04 (1H, broad dq, *J* 12, 2.4, equatorial 4-H), 2.76-2.89 (1H, broad dt, *J* 9.8, 3, 9-H), 3.19-3.36 (1H, tt, *J* 12.2, 3.6, 3-H), 3.54 (1H, t, *J* 10.6, axial 2-H), 4.14 (1H, dq, *J* 9.8, 2.4, equatorial 2-H), 7.53-7.70 (3H, m, Ph), 7.50 (2H,d, *J* 7.2, Ph); δ_C {^1H} 24.70-31.85 (aliphatic), 40.77 (t, 4-C), 60.85 (d, 9-C), 65.83 (t, 2-C), 81.54 (d, 3-C), 133.84,128.56, 129.23 (d, Ph), 137.42 (s, Ph); m/z 280 (M^+); Found: C, 64.5; H, 7.4; S, 11.2. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.1; S, 11.4%.

Cis-(3SR),(9SR),(10SR)-3β-Phenylsulphonyl-1-oxabicyclo[4,4,0]decane (22)

Similar to **19** above treatment of the corresponding *cis* alkenyl sulphone **12** (524 mg, 1.87 mmol) with Bu^tOK (210 mg, 1.87 mmol) in ^{t}BuOH (22 mL) afforded crude **22** (532 mg, >100%) which was chromatographed (ether-light petroleum, 3:1) to give pure product **22** as a white solid (515.5 mg, 98%) that recrystallised (ether-light petroleum), mp 92-95°C; ν_{max} ($CHCl_3$)/cm^{-1} 1083, 1070 (SO_2); δ_H 1.12-1.43 (5H, m, aliphatic ring), 1.45-1.58 (1H, qd, axial 5-H),1.64-1.76 (2H, m, 8-H), 1.79-1.87 (1H, m, 10-H), 1.89-2.03 (2H, AB system, 4-H), 3.34-3.43 (1H, m, 3-H), 3.46 (1H, d, *J* 2, 9-H), 3.52 (1H, t, *J* 11, axial 2-H), 4.09 (1H, dd, *J* 11,2, equatorial 2-H), 7.63-7.70 (3H, m, Ph), 7.78-7.90 (2H, m, Ph); δ_C {^1H} 19.96-31.25 (t, aliphatic ring), 34.34 (d, 10-C), 59.48 (d, 9-C), 69.56 (t, 2-C), 75.17 (d, 3-C), 129.17,129.56 (d, Ph), 133.94 (d, Ph), 137.42 (s, Ph); m/z 281(M^++1); Found: C, 64.3; H, 7.4;S, 11.3. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.1; S,11.4%.

3αβ-Phenylsulphonyl-9β-carboxy-8β-1-oxabicyclo[4,3,0]nonane (23)

By the above procedure the hydroxy sulphone **16** (540 mg, 1.59 mmol) in dry ^{t}BuOH (8 mL) containing ^{t}BuOK (207 mg, 1.86 mmol) produced crude acid **23** as a solid (471mg, 95%) which was recrystallised ($^iPr_2O$-DCM) to give pure **23** as white needles, mp 184.5-185.5°C; ν_{max} ($CHCl_3$)/cm^{-1} 3655-3020 (OH), 1703 (CO), 1302, 1144 (SO_2); δ_H 1.65-2.14 (6H, m, aliphatic ring), 2.31 (2H, d, *J* 10.5, 4-H), 3.34 (1H, m, 3-H), 3.49 (1H, t, *J* 11, axial 2-H), 4.01 (1H, d, *J* 4, 8-H), 4.09 (1H, m, equatorial 2-H), 7.60 (2H, m, Ph), 7.72 (1H, m, Ph), 7.87 (2H, m, Ph); m/z 310 (M^+); Found: C, 58.1; H, 6.1; S, 10.45. $C_{15}H_{18}O_5S$ requires C, 58.05; H, 5.8; S, 10.3%.

3αβ-Phenylsulphonyl-9β-carboxy-8α-1-oxabicyclo[4,3,0]nonane (26)

Similar **23** to above the hydroxy sulphone **17** (495 mg, 1.47 mmol) and ^{t}BuOK (183 mg, 1.62 mmol) in dry ^{t}BuOH (8 mL) produced **26** (432 mg, 95%) as a solid which was recrystallised ($^iPr_2O$-DCM) to give pure **26** as white needles, mp 182.5-183.5°C; ν_{max} ($CHCl_3$)/cm^{-1} 3655-3020 (OH), 1697 (CO), 1303, 1144 (SO_2); δ_H 1.62-2.16 (6H, m, aliphatic ring), 2.33 (2H, d, *J* 10, 4-H), 3.35 (1H, m, 3-H), 3.50 (1H, t, *J* 11, axial 2-H), 4.01 (1H, d, *J* 4, 8-H), 4.09 (1H, m, equatorial 2-H), 7.63 (2H, m, Ph), 7.72 (1H, m, Ph), 7.89 (2H, m, Ph); Found: C, 57.85; H, 5.8; S, 10.3. $C_{15}H_{18}O_5S$ requires C, 58.05; H, 5.8; S, 10.3%.

3β-Phenylsulphonyl-9β-methoxycarbonyl-8β-1-oxabicyclo[4,3,0]nonane (24) and 3α-Phenylsulphonyl-9β-methoxycarbonyl-8β-1-oxabicyclo[4,3,0]nonane (25)

To a stirred solution of the crude carboxylic acid **23** obtained from sulphone **16** (1.2 g, 3.55 mmol) in the above described manner, in dry MeOH (10 mL) was added concentrated H_2SO_4 (1drop) and the resulting mixture refluxed overnight. The solvent was evaporated and the residue partitioned between ether and H_2O. The organic phase was washed with sat. $NaHCO_3$ solution, dried (Na_2SO_4) and evaporated to yield an oil which was chromatographed (light petroleum-ether, 3:2) to afford firstly the ester **24** (405 mg, 35%) as a solid. Recrystallisation (ether-light petroleum) produced **24** as white needles, mp 107-108°C; ν_{max} ($CHCl_3$)/cm^{-1} 1725 (CO), 1300, 1145 (SO_2); δ_H 1.56-2.13 (6H, m, aliphatic ring), 2.27 (2H, d, *J* 10, 4-H), 3.34 (1H, m, 3-H), 3.49 (1H, dt, *J* 11,1.5, axial 2-H), 3.70 (3H, s, OMe), 4.00 (1H, d, *J* 4, 8-H), 4.06 (1H, m, equatorial 2-H), 7.59 (2H, m, Ph), 7.70 (1H, m, Ph), 7.87 (2H, m, Ph); m/z, 324 (M^+); Found: C, 59.2; H, 6.2; S, 9.85. $C_{16}H_{20}O_5S$ requires C, 59.25; H, 6.15; S, 9.9%; further elution afforded the isomeric ester ester **25** as a white solid (320 mg, 28%); ν_{max} ($CHCl_3$)/cm^{-1} 1725 (CO), 1302, 1145 (SO_2); δ_H 1.58-1.93 (6H, m, aliphatic ring), 2.03 (1H, m, axial 4-H), 2.32 (1H, dd, *J* 13,7, equatorial 4-H), 3.46 (1H, m, 3-H), 3.64 (1H, dd, *J* 13,7, axial 2-H), 3.65 (3H, s, OMe), 4.20 (1H, t, *J* 7, 8-H), 4.15 (1H, dd, *J* 13,7, equatorial 2-H), 7.60 (2H, m, Ph), 7.68 (1H, m, Ph), 7.80 (2H, m, Ph); m/z 324 (M^+); Found: C, 59.2; H, 6.2; S, 9.9 $C_{16}H_{20}O_5S$ requires C, 59.25; H, 6.15, S, 9.9%.

3β-Phenylsulphonyl-9β-methoxycarbonyl-8α-1-oxabicyclo[4,3,0]nonane (27) and 3α-Phenylsulphonyl-9β-methoxycarbonyl-8α-1-oxabicyclo[4,3,0]nonane (28)

The crude acid **26** obtained from the precursor **17** (1.60 g, 4.73 mmol) was esterified in dry MeOH (10 mL) containing a drop of conc. H_2SO_4 in the above described manner to give after chromatography firstly the ester **27** (660 mg, 43%) as a white solid which recrystallised (ether-light petroleum) as white needles, mp 98-99°C; ν_{max} ($CHCl_3$)/cm^{-1} 1725 (CO), 1305, 1148 (SO_2); δ_H 1.58-2.14 (6H, m, aliphatic ring), 2.29 (2H, d, *J* 10, 4-H), 3.33 (1H, m, 3-H), 3.50 (1H, dt, *J* 11, 1, axial 2-H), 3.70 (3H, s, OMe), 4.01 (1H, d, *J* 4, 8-H), 4.06 (1H, m, equatorial 2-H), 7.59 (2H,m, Ph), 7.69 (1H, m, Ph), 7.86 (2H, m, Ph); m/z 324 (M^+); Found: C, 59.4; H, 6.2; S, 9.8 $C_{16}H_{20}O_5S$ requires C, 59.25; H, 6.15; S, 9.9%; further elution gave the isomeric ester **28** (390 mg, 26%); ν_{max} ($CHCl_3$)/cm^{-1} 1725 (CO), 1304, 1145 (SO_2); δ_H 1.62-1.94 (6H, m, aliphatic ring), 2.03 (1H, m, , axial 4-H), 2.31 (1H, dd, *J* 13,5, equatorial 4-H), 3.45 (1H, m, 3-H), 3.66 (3H, s, OMe), 3.67(1H, dd, *J* 13, 7, axial 2-H), 4.16 (1H, dd, *J* 13,7, equatorial 2-H), 4.22 (1H, t, *J* 6, 8-H), 7.60 (2H,m, Ph), 7.71 (1H, m, Ph), 7.91 (2H, m, Ph); m/z 324 (M^+); Found: C, 59.4; H, 6.4; S, 9.8. $C_{16}H_{20}O_5S$ requires C, 59.25;H, 6.15; S, 9.9%.

Reduction of 2-(2'-Phenylsulphonylprop-2'-enyl)cyclohexanone (18) with sodium borohydride:

To a stirred solution of keto-sulphone **18** (2.85 g, 10.2 mmol) in ^iPrOH was added $NaBH_4$ (1.45 g, 38.4 mmol) and the mixture after overnight stirring was acidified with aq.HCl. Benzene was added and the mixture was heated under azeotropic reflux using a Dean-Stark apparatus to remove all the water after which it was filtered . Evaporation of the solvent yielded a residue

(3.15 g, > quantitative yield) which according to TLC (ether-light petroleum, 3:1) showed four products of very close R_f values. The residue was chromatographed to give firstly adduct *trans* **19** (171 mg, 6%) which was identical with the sample previously reported; followed by compound *cis* **20** (316 mg, 11%); ν_{max} ($CHCl_3$)/cm^{-1} 3440 (OH), 1078, 1180 (SO_2); δ_H 1.0 (3H, d, *J* 7.2 ,Me), 0.90-2.06 (11H, m, 9 ring H's and 1'-H), 3.10-4.0 (3H, m, OH, 1-H and 2'-H), 7.42-7.72 (3H, m, Ph), 7.94 (2H, m, Ph); m/z 280 (M^+-2); Found: C, 64.2;H, 7.4; S, 11.6. $C_{15}H_{22}O_3S$ requires C, 63.8;H, 7.8; S, 11.35%; followed by an inseparable mixture of compounds *cis* **20** and *trans* **21** (1.26g, 44%) as a solid mp 90-92°C, ν_{max} ($CHCl_3$)/cm^{-1} 3500 (OH), 1080, 1135 (SO_2); δ_H 1.25 (3H, dd, *J* 6.8,2.5, Me), 1.06-1.96 (10H, m, ring H's and 1'-H), 2.08-2.32 (1H, m, 2-H), 2.47 (1H, sharp s, OH), 3.08-3.30 (1H, m, *trans* isomer 0.5H 1-H, 0.5H 2'-H), 3.64 (0.5H, m, *cis* isomer 2'-H), 3.80 (0.5H, bm, *cis* isomer 1-H), 7.50-7.70 (3H, m, Ph), 7.88 (2H, m, Ph); m/z 283 (M^++1), 282 (M^+); Found: C, 63.55;H, 7.75; S, 11.3. $C_{15}H_{22}O_3S$ requires C, 63.8; H, 7.8; S, 11.35%; followed by the isomeric *trans* product **21** (397 mg, 14%) as a solid mp 90-92°C; ν_{max} ($CHCl_3$)/cm^{-1} 3510 (OH), 1083, 1138 (SO_2); δ_H 1.23 (3H, fine d, *J* 6.8, Me), 1.10-1.39 (5H, m, ring H's), 1.55-2.0 (6H, m, 1'-H, 2-H and ring H's), 1.97 (1H, s, OH), 3.09-3.28 (2H, m, axial 1-H and 2'-H), 7.50-7.70 (3H, m, Ph), 7.88 (2H, m, Ph) ; m/z 280 (M^+-2); Found: C, 63.7; H, 8.0; S, 11.2. $C_{15}H_{22}O_3S$ requires C, 63.8; H, 7.8; S, 11.35%.

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