Spiroannulation by the [2,3]Sigmatropic Rearrangement *via* the Cyclic Allylsulfonium Ylide. A Stereoselective Synthesis of (+)-Acorenone B

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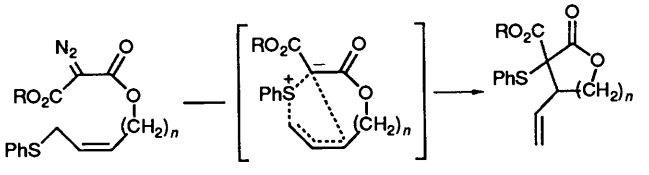
A spiroannulation reaction using the [2,3]sigmatropic rearrangement *via* a cyclic allylsulfonium ylide was developed and applied to the synthesis of (+)-acorenone B starting from (−)-perillaldehyde.

We have recently reported an attractive method for the synthesis of five- to eight-membered lactones from a variety of acyclic α-diazomalonates having an allylic sulfide function, by use of a [2,3]sigmatropic rearrangement *via* cyclic allylsulfonium ylides (eqn. 1).[1] This methodology has been extended to the efficient synthesis of spiro-fused five- to six-



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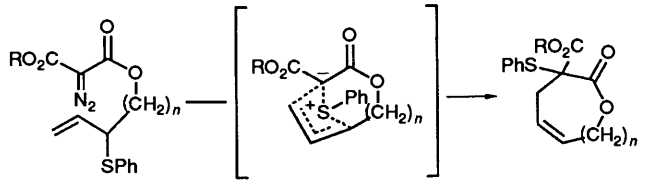
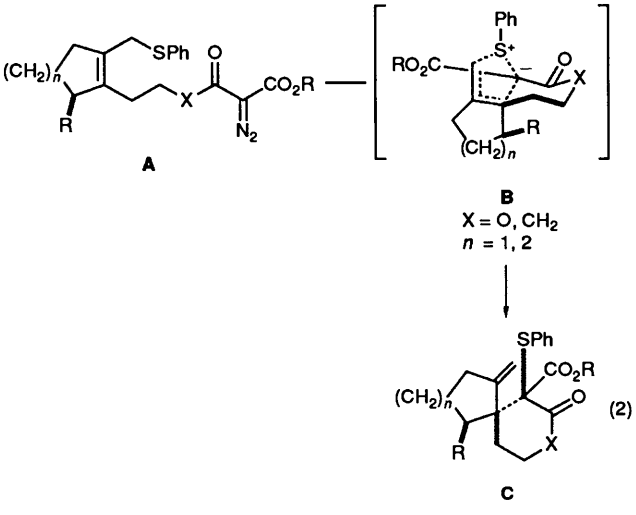


n = 1, 2

membered lactones having a spirocyclic centre at the β-position, starting from cycloalkenes vicinally substituted with a diazomalonyl and phenylthiomethyl functions at the double bond carbons (eqn. 2, X=O).[2] In the case when cycloalkenes **A** possess a β-keto-α-diazo ester group in the side chain in place of an α-diazomalonyl function, the above methodology would allow for spiroannulation,[3] giving the spiro carbocyclic compounds **C** possessing an exocyclic methylene group adjacent to the spirocyclic centre (eqn. 2, X=CH_2). Furthermore, provided that the diazo compound **A** has a bulky substituent (R) adjacent to the side chain, remarkable stereoselectivity would be expected for construction of the spirocyclic carbon skeleton, because the carbanion approaches the sulfonium reaction site from the less hindered side, away from the substituent, as seen in the transition state **B**.

To realise the above considerations in the natural product synthesis, acorane-type sesquiterpenes[4] possessing the spiro[4.5]decane nucleus with a bulky isopropyl unit adjacent to the spirocyclic centre are suitable as target molecules. Herein we show that starting with commercially available (−)-perillaldehyde **2**, a stereoselective synthesis of (+)-acorenone B **1**, antipodal to the natural (−)-acorenone B,[5] was accomplished by a strategy in which the key chemical transformation involves spiroannulation due to [2,3]sigmatropic rearrangement *via* the cyclic allyl sulfonium ylide.

A key-intermediate in this synthesis is β-keto-α-diazo ester **17**, and our synthesis began with conversion of **2** into the cyclopentenecarbaldehyde **8** by a well-established sequence of

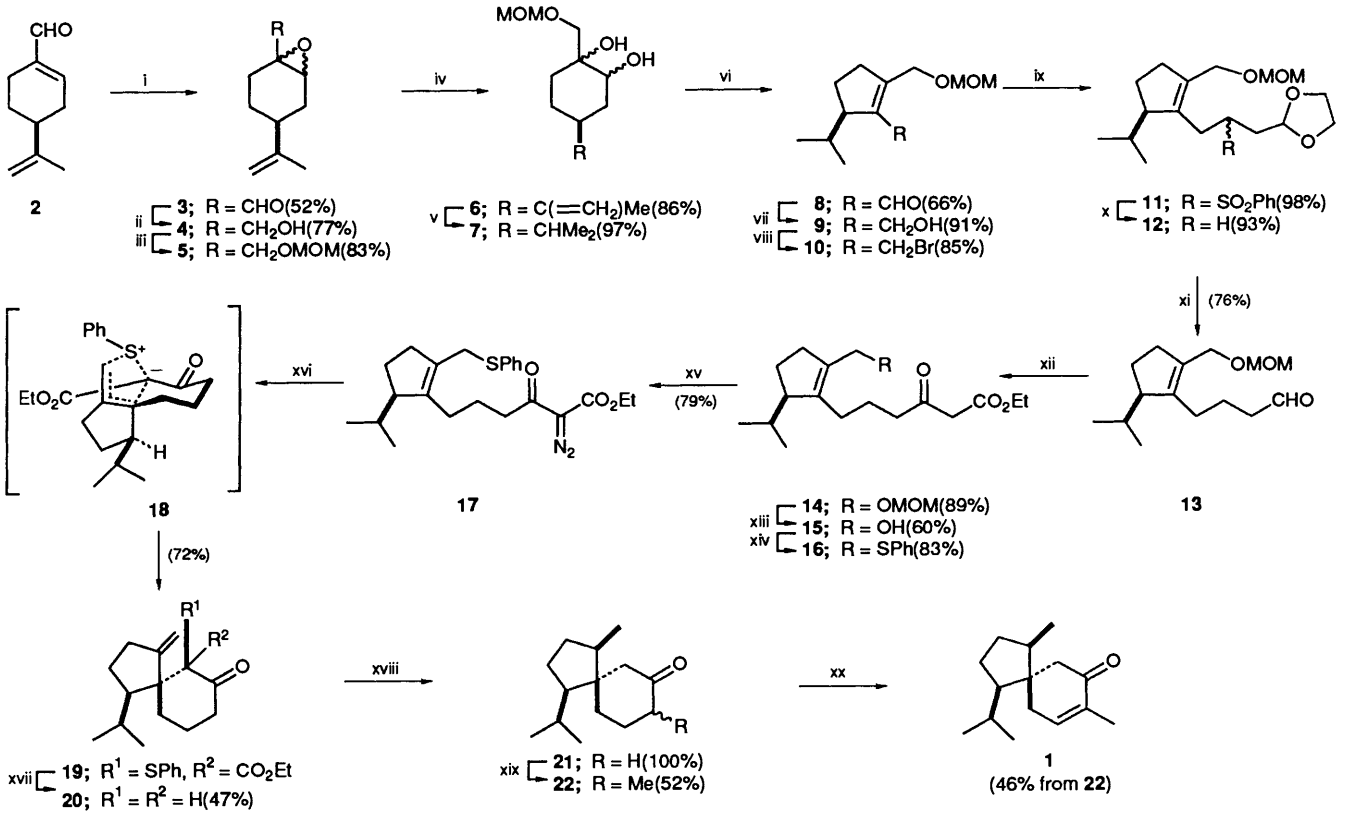


A **B** X = O, CH_2; n = 1, 2 **C** (2)

reactions for ring contraction.[5d,6] Transformation of **2** into diastereoisomeric (4*S*)-4-isopropylcyclohexane-1,2-diol **7** was carried out by a sequence of five conventional reactions (Scheme 1); oxidation of **2** with 30% H_2O_2 under aqueous basic conditions to give the epoxide **3**, reduction of a formyl group in **3** with sodium borohydride, protection of the resulting alcohol **4** to give the ether **5**, epoxide ring-opening of **5** with aqueous base to give the diastereoisomeric diol **6**, and hydrogenation of a double bond in **6** with formation of the desired **7**. Oxidative 1,2-diol cleavage of **7** followed by cyclisation upon exposure to piperidine in acetic acid provided the requisite **8** in good overall yield.

The compound **8** was then reduced by sodium borohydride to the allylic alcohol **9** which was converted into the corresponding bromide **10** by the phosphine–carbon tetrabromide[7] system. Treatment of **10** with the lithium salt of 3-ethylenedioxy-1-phenylsulfonylpropane[8] afforded the sulfone **11** in excellent yield, and reductive desulfurisation of **11** with sodium amalgam followed by selective deprotection of the resulting acetal **12** with pyridinium toluene-*p*-sulfonate in aqueous acetone gave the aldehyde **13** in good overall yield. Direct conversion of **13** into the β-keto ester **14** with ethyl diazoacetate in the presence of tin(II) chloride[9] followed by deprotection with dimethylboron bromide[10] gave the allylic alcohol **15**. Finally, the alcohol **15** was transformed to the key compound **17** with displacement of the hydroxy group to a phenylthio group, followed by treatment of the resulting sulfide **16** with tosyl azide.[11]

Construction of the spirocyclic carbon skeleton from **17** was readily performed under our standard reaction conditions,[1] wherein treatment with rhodium acetate (0.01 mol equiv.) in refluxing benzene produced the spiro ketone **19** in 72% yield. No isomer of **19** could be detected in spite of a careful inspection of the reaction mixture. Hereupon, it was demonstrated that this spiroannulation reaction proceeded in stereoselective fashion



Scheme 1 *Reagents and conditions:* i, 30% H_2O_2, aq. NaOH; ii, $NaBH_4$; iii, methoxymethyl chloride; iv, 15% KOH, dimethyl sulfoxide (DMSO); v, H_2, 10% Pd–C; vi, $Pb(OAc)_4$, then piperidine, AcOH; vii, $NaBH_4$, $CeCl_3$; viii, CBr_4, Ph_3P; ix, BuLi, 1-phenylsulfonyl-3-ethylenedioxypropane; x, Na(Hg); xi, pyridinium toluene-*p*-sulfonate, aq. acetone; xii, N_2CHCO_2Et, $SnCl_2$; xiii, Me_2BBr; xiv, PhSSPh, Bu_3P; xv, TsN_3; xvi, $Rh_2(OAc)_4$, PhH, reflux; xvii, Na(Hg), then NaCl, aq. DMSO; xviii, H_2, PtO_2; xix, lithium diisopropylamide, MeI; xx, Br_2, then LiBr, Li_2CO_3

predicated by our aforementioned considerations to give **19** as the only product *via* the transition state **18**. The stereochemistry of the two substituents, a phenylthio and ethoxycarbonyl group in **19** was surmised, as depicted, on the basis of the favourable conformation of the transition state **18**, whereas the stereostructure of **19** was chemically confirmed by derivation to the target acorenone B **1** (*vide infra*).

The phenylthio and ethoxycarbonyl groups in **19** were removed by reductive desulfurisation with sodium amalgam in methanol and by deethoxycarbonylation with NaCl in aqueous dimethyl sulfoxide,[12] respectively, giving the spiro ketone **20**. Hydrogenation of **20** over platinum(IV) oxide proceeded in exclusive attack of the hydride at the face of the double bond opposite the isopropyl group to give the known compound, noracorenone **21**[5a] stereoselectively.

Finally, transformation of **21** to acorenone B **1** was accomplished according to the reported procedure[5a] with a slight modification; (i) regioselective methylation of the lithium enolate of **21** with methyl iodide; (ii) bromination of the resulting ketone **22** followed by dehydrobromination with formation of (+)-acorenone B **1**, $[\alpha]_D^{23}$ +17.3 (*c* 0.15, $CHCl_3$). The spectroscopic data (IR, ^1H NMR and MS) of the synthetic (+)-**1** were in good agreement with those of (−)-acorenone B except for the sign of the specific rotation $[\alpha]_D^{22}$ −17.3 (*c* 0.45, $CHCl_3$).[5i]

The one-step spiroannulation described above would be practically useful for the synthesis of spiro carbocyclic compounds of this type, because of its simplicity, mild reaction conditions and high yield.

Experimental

IR spectra were obtained with a JASCO IR/FT-8300 spectrophotometer. ^1H NMR spectra were recorded on a JEOL FX90 spectrometer, *J* values are given in Hz. [α] Values are given in units of 10^{-1} deg cm^2 g^{-1}. Dry tetrahydrofuran (THF) was obtained by distillation over sodium benzophenone ketyl. Other organic solvents were purified and dried by using standard procedures. All reactions were carried out under dry N_2 or Ar atmosphere with use of standard procedures for the exclusion of moisture. Extracts obtained on aqueous workup of the reaction mixtures were washed successively with water and brine, and dried using $MgSO_4$, unless otherwise stated. Column and flash column chromatography were performed on 70–230 and 230–400 mesh silica gel (Merck), respectively, and Kieselgel GF_{254} was employed for preparative thin-layer chromatography (TLC). Solvents for elution are shown in parentheses.

Epoxidation of Compound **2**.—To a stirred mixture of (−)-perillaldehyde **2** (751 mg, 5.00 mmol), H_2O_2 (30%; 1.5 cm^3, 15.0 mmol) and MeOH (10 cm^3) was added, dropwise at 0 °C, a solution of NaOH (6 mol dm^{-3}; 0.4 cm^3, 2.5 mmol). After being stirred for an additional 30 min at room temp., the reaction mixture was diluted with water and extracted with ether. An oily residue, obtained by evaporation, was chromatographed on silica gel (hexane–AcOEt, 10:1) to give 4-*isopropenyl*-1,2-*epoxycyclohexanecarbaldehyde* **3** (431 mg, 52%) as an oil, (Found: C, 72.2; H, 8.5. $C_{10}H_{14}O_2$ requires C, 72.3; H, 8.5%); ν_{max}(film)/cm^{-1} 3080vw, 1726vs and 890; δ_H(90 MHz; $CDCl_3$) 1.69 (3 H, s, CH_3), 1.0–2.8 (7 H, m), 3.51 (1 H, br s, CHO), 4.6–4.8 (2 H, m, $=CH_2$) and 8.85 (1 H, s, CHO).

Reduction of Compound **3** *with Sodium Borohydride*.—To a stirred solution of **3** (431 mg, 2.59 mmol) in MeOH (8 cm^3) was added, at 0 °C, sodium borohydride (49 mg, 1.30 mmol). After being stirred for 30 min, the reaction mixture was quenched by addition of aqueous NH_4Cl, and the product was extracted with

CH_2Cl_2. Concentration followed by purification of the oily residue by column chromatography on silica gel (hexane–AcOEt, 1:1) afforded (*4-isopropenyl-1,2-epoxycyclohexan-1-yl)methanol* **4** (335 mg, 77%) as an oil, (Found: C, 71.0; H, 9.5. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%); ν_{max}(film)/cm^{-1} 3424vs, 3080vw, 1038 and 888; δ_H($CDCl_3$) 1.0–2.4 (7 H, m), 1.70 (3 H, s, CH_3), 3.36 (1 H, br s, CHO), 3.5–3.8 (2 H, br m, CH_2O) and 4.6–4.8 (2 H, br s, $=CH_2$).

Reaction of Compound **4** *and Chloromethyl Methyl Ether.*—A mixture of **4** (334 mg, 1.99 mmol), diisopropylethylamine (3 cm^3), and chloromethyl methyl ether (320 mg, 3.98 mmol) was stirred at 0 °C for 4 h, and then at room temp. for 10 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed successively with 3 mol dm^{-3} HCl, water, and brine, and dried. Concentration left an oil which was purified by column chromatography on silica gel (hexane–AcOEt, 3:1) to give *4-isopropenyl-1-(methoxymethoxymethyl)-1,2-epoxycyclohexane* **5** (351 mg, 83%) as an oil, (Found: C, 68.0; H, 9.4. $C_{12}H_{20}O_3$ requires C, 67.9; H, 9.5%); ν_{max}(film)/cm^{-1} 3082vw, 1110, 960, 919 and 889; δ_H($CDCl_3$) 1.70 (3 H, s, $=CCH_3$), 1.0–2.2 (7 H, m), 3.20 (1 H, s, CHO), 3.36 (3 H, s, OCH_3), 3.52 (2 H, s, CH_2O), 4.62 (2 H, s, OCH_2O) and 4.70 (2 H, m, $=CH_2$).

Epoxide Ring-opening of Compound **5**.—A mixture of **4** (6.54 g, 30.8 mmol), KOH (15%; 205 cm^3, 616 mmol) and DMSO (100 cm^3) was stirred at 110 °C overnight. After cooling, the reaction mixture was carefully neutralised with conc. HCl in an ice–water bath, and extracted with a mixed solvent (ether–CH_2Cl_2, 3:1). Evaporation followed by purification of the oily residue by flash column chromatography on silica gel gave *4-isopropenyl-1-(methoxymethoxymethyl)cyclohexane-1,2-diol* **6** (6.08 g, 86%) as an oil (Found: C, 62.1; H, 9.9. $C_{12}H_{22}O_4$ requires C, 62.5; H, 9.6%); ν_{max}(film)/cm^{-1} 3446vs, 3050vw, 1045 and 888; δ_H($CDCl_3$) 1.73 (3 H, s, $=CCH_3$), 1.2–2.6 (9 H, m), 3.40 (3 H, s, OCH_3), 3.46 and 3.74 (1 H, d, *J* 10.8 each, CH_2O), 3.83 (1 H, br s, C*H*OH), 4.66 (2 H, s, OCH_2O) and 4.72 (2 H, m, $=CH_2$).

Hydrogenation of Compound **6**.—A mixture of **6** (5.59 g, 24.3 mmol), 10% Pd–C (560 mg) and MeOH (120 cm^3) was stirred over H_2 at a pressure (3 kg cm^{-2}) overnight. The reaction mixture was filtered through a short silica gel column and the filtrate was concentrated. Purification of the oily residue by column chromatography on silica gel (hexane–AcOEt, 1:1) afforded *4-isopropyl-1-(methoxymethoxymethyl)cyclohexane-1,2-diol* **7** (5.50 g, 97%) as an oil, (Found: C, 62.0; H, 10.4. $C_{12}H_{24}O_4$ requires C, 62.0; H, 10.4%), ν_{max}(film)/cm^{-1} 3446vs, 1110 and 1046; δ_H($CDCl_3$) 0.85 (6 H, d, *J* 7.2, isopropyl CH_3), 1.0–2.0 (10 H, m), 3.36 (3 H, s, OCH_3), 3.38 and 3.74 (1 H, d, *J* 10.8 each, CH_2O), 3.78 (1 H, m, C*H*OH) and 4.64 (2 H, s, OCH_2O).

(5R)-5-*Isopropyl-2-(methoxymethoxymethyl)cyclopent-1-enecarbaldehyde* **8**.—To a stirred solution of **7** (502 mg, 2.18 mmol) in benzene (10 cm^3) was added portionwise at room temp. lead tetracetate (1.53 g, 3.27 mmol). After brief stirring for 15 min, the reaction mixture was filtered through a short alumina column (neutral, grade V) with ether. The filtrate was concentrated to leave an oil (464 mg).

A mixture of the above oil, piperidine (0.2 cm^3), AcOH (0.2 cm^3) and benzene (15 cm^3) was stirred at 55 °C for 3.5 h. After cooling, the reaction mixture was washed successively with 3 mol dm^{-3} HCl, aqueous $NaHCO_3$, water, and brine, and dried. Evaporation followed by purification of an oily residue by column chromatography on silica gel (hexane–AcOEt, 4:1) afforded the *title compound* **8** (293 mg, 63%) as an oil, $[\alpha]_D^{18}$ −2.73 (*c* 1.76, $CHCl_3$) (Found: C, 67.6; H, 9.6. $C_{12}H_{21}O_3$ requires C, 67.9; H, 9.5%); ν_{max}(film)/cm^{-1} 1672 and 1050; δ_H($CDCl_3$) 0.68 and 0.90 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.65–2.0 (2 H, m, $=CCH_2CH_2$), 2.05–2.33 (1 H, m, =CCH), 2.4–2.75 (2 H, m, $=CCH_2CH_2$), 3.38 (3 H, s, OCH_3), 4.53 (2 H, s with fine splittings, $=CCH_2O$), 4.66 (3 H, s, OCH_2O) and 10.09 (1 H, s, CHO).

[(5R)-5-*Isopropyl-2-(methoxymethoxymethyl)cyclopent-1-enyl]methanol* **9**.—To a stirred suspension of **8** (565 mg, 2.66 mmol) and cerium chloride heptahydrate (991 mg, 2.66 mmol) in propan-2-ol (10 cm^3) was added at room temp. sodium borohydride (101 mg, 2.66 mmol) followed by water (0.5 cm^3). After stirring for an additional 15 min, the reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed successively with aqueous AcOH, water, and brine, and dried. The oily residue obtained by evaporation was chromatographed on silica gel (hexane–AcOEt, 2:1) to give the *title compound* **9** (519 mg, 91%) as an oil, $[\alpha]_D^{18}$ −21.7 (*c* 1.73, $CHCl_3$); ν_{max}(film)/cm^{-1} 3605vw, 3450vs and 1040; δ_H($CDCl_3$) 0.70 and 0.92 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.5–2.5 (5 H, m), 2.8 (1 H, br s, OH), 3.36 (3 H, s, OCH_3), 4.0–4.4 (4 H, m, CH_2OH, CH_2O) and 4.60 (2 H, s, OCH_2O).

4-(5R)-[5-*Isopropyl-2-(methoxymethoxymethyl)cyclopent-1-enyl]butanal Ethylene Acetal* **12**.—To a stirred solution of **9** (1.03 g, 4.80 mmol) and carbon tetrabromide (3.18 g, 9.60 mmol) in THF (5 cm^3) was added dropwise at 0 °C a solution of triphenylphosphine (2.52 g, 9.60 mmol) in THF (5 cm^3).[7] The reaction temperature gradually rose to 10 °C and stirring was continued for an additional 15 min. Water was added and the product extracted with a mixed solvent (ether–CH_2Cl_2, 3:1). Evaporation followed by purification of the residue by column chromatography on silica gel (hexane–AcOEt, 10:1) afforded *2-bromomethyl-3-isopropyl-1-(methoxymethoxymethyl)cyclopent-1-ene* **10** (1.13 g, 85%) as an oil, δ_H($CDCl_3$) 0.68 and 0.94 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.5–2.2 (3 H, m, =CCH, $=CCH_2CH_2$), 2.2–2.6 (2 H, m, $=CCH_2CH_2$), 3.36 (3 H, s, OCH_3), 3.90 and 4.25 (2 H, d, *J* 10.0, OCH_2), 4.18 (2 H, s, CH_2Br) and 4.60 (2 H, s, OCH_2O).

To a stirred solution of 3-ethylenedioxy-1-phenylsulphonylpropane[8] (390 mg, 1.61 mmol) in THF (6.2 cm^3) and HMPA (1.6 cm^3) was added dropwise at −70 °C a solution of BuLi in hexane (1.59 mol dm^{-3}; 1.01 cm^3, 1.61 mmol). After stirring for 1.5 h, a solution of **10** (149 mg, 0.54 mmol) in THF (3 cm^3) was added, and stirring was continued for an additional 15 min. Water was added and the product was extracted with a mixed solvent (ether–CH_2Cl_2, 3:1). Evaporation followed by purification of the oily residue by column chromatography on silica gel provided 4-[(5R)-5-*isopropyl-2-(methoxymethoxymethyl)-cyclopent-1-enyl]-3-phenylsulphonylbutanal ethylene acetal* **11** (231 mg, 98%) as an oil (Found: C, 63.0; H, 7.7. $C_{23}H_{34}O_6S$ requires C, 63.0; H, 7.3%), ν_{max}(film)/cm^{-1} 1310 and 1150; δ_H($CDCl_3$) 0.45–0.84 (6 H, m, isopropyl CH_3), 1.1–2.7 (9 H, m), 3.28 (3 H, s, OCH_3), 3.3 (1 H, m, CHS), 3.81 (2 H, s, OCH_2), 3.8–4.0 (4 H, m, OCH_2CH_2O), 4.57 (2 H, s, OCH_2O), 4.9–5.15 (1 H, m, OCHO) and 7.4–8.0 (5 H, m, Ph).

To a stirred suspension of 6% sodium amalgam (23.8 g, 62.1 mmol) and sodium hydrogen phosphate (3.52 g, 24.8 mmol) in MeOH (50 cm^3) was added, at room temp., a solution of **11** (2.63 g, 6.01 mmol) in MeOH (20 cm^3). After being stirred for 30 min, the reaction mixture was quenched by addition of aqueous NH_4Cl, and the resulting mixture was filtered through a small bed of Celite 545. The filtrate was extracted with a mixed solvent (ether–CH_2Cl_2, 3:1) and concentrated. The oily residue obtained was chromatographed on silica gel (hexane–AcOEt, 4:1) to give the *title compound* **12** (1.63 g, 91%) as an oil, $[\alpha]_D^{18}$ −3.19 (*c* 1.91, $CHCl_3$) (Found: C, 68.0; H, 10.4. $C_{17}H_{30}O_4$ requires C, 68.4; H, 10.1%); ν_{max}($CHCl_3$)/cm^{-1} 1150 and 1050;

$\delta_H(CDCl_3)$ 0.66 and 0.92 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.3–2.8 (12 H, m), 3.36 (3 N, s, OCH_3), 3.80–4.00 (4 H, m, OCH_2CH_2O), 4.10 (2 H, s, $=CCH_2O$), 4.58 (2 H, s, OCH_2O) and 4.84 (1 H, t, *J* 3.6, OCHO).

4-[(5R)-5-*Isopropyl*-2-(*methoxymethoxymethyl*)*cyclopent*-1-*enyl*]*butanal* **13**.—A mixture of **12** (1.03 g, 3.45 mmol), water (20 cm^3) and acetone (20 cm^3) was refluxed for 4 h. After cooling, the reaction mixture was diluted with aqueous $NaHCO_3$ and extracted with a mixed solvent (ether–CH_2Cl_2, 3:1). Evaporation followed by purification by column chromatography on silica gel gave the *title compound* **13** (710 mg, 81%) as an oil, $[\alpha]_D^{17}$ −3.87 (*c* 0.57, $CHCl_3$) (Found: C, 71.0; H, 10.4. $C_{15}H_{26}O_3$ requires C, 70.8; H, 10.3%); ν_{max}(film)/cm^{-1} 2725vw, 1732 and 1050; $\delta_H(CDCl_3)$ 0.66 and 0.92 (3 H, d, *J* 7.2, isopropyl CH_3), 1.5–2.8 (12 H, m), 3.36 (3 H, s, OCH_3), 4.10 (2 H, s, $=CCH_2O$), 4.60 (2 H, s, OCH_2O) and 9.76 (1 H, t, *J* 1.8, CHO).

Ethyl 6-[(5R)-5-*Isopropyl*-2-(*methoxymethoxymethyl*)*cyclopent*-1-*enyl*]-3-*oxohexanoate* **14**.—To a stirred suspension of ethyl diazoacetate[9] (0.51 cm^3, 4.83 mmol) and tin(II) chloride (61 mg, 0.32 mmol) in CH_2Cl_2 (10 cm^3) was added dropwise, at room temp., a solution of **13** (820 mg, 3.22 mmol) in CH_2Cl_2 (16 cm^3) over a period of 15 min. After stirring for 1.5 h, the reaction mixture was poured into brine and extracted with ether. Concentration followed by purification by column chromatography on silica gel (hexane–AcOEt, 3:1) afforded the *title compound* **14** (970 mg, 89%) as an oil, $[\alpha]_D^{17}$ −5.75 (*c* 0.65, $CHCl_3$) (Found: C, 67.3; H, 9.8. $C_{19}H_{32}O_5$ requires C, 67.0; H, 9.5%); ν_{max}(film)/cm^{-1} 1742, 1718 and 1040; $\delta_H(CDCl_3)$ 0.64 and 0.90 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.26 (3 H, t, *J* 7.2, OCH_2CH_3), 1.50–2.9 (12 H, m), 3.36 (3 H, s, OCH_3), 3.42 (2 H, s, $COCH_2CO$), 4.08 (2 H, s, $=CCH_2O$), 4.20 (2 H, q, *J* 7.2, OCH_2CH_3) and 4.59 (2 H, s, OCH_2O).

Ethyl 6-[(5R)-5-*Isopropyl*-2-(*phenylthiomethyl*)*cyclopent*-1-*enyl*]-3-*oxohexanoate* **16**.—To a stirred solution of **14** (154 mg, 0.45 mmol) in CH_2Cl_2 (5 cm^3) was added at −78 °C a solution of dimethylboron bromide[10] in CH_2Cl_2 (1.93 mol dm^{-3}; 0.47 cm^3, 0.91 mmol) over a period of 15 min, and stirring was continued for an additional 10 min. The reaction mixture was poured into a well-stirred mixture of THF (4 cm^3) and aqueous saturated $NaHCO_3$ (2 cm^3), and the resulting mixture was stirred at room temp. for an additional 15 min, and then extracted with ether. Evaporation followed by purification of the residue by preparative TLC (hexane–ether, 2:1) afforded *ethyl* 6-[5*R*]-2-*hydroxymethyl*-5-*isopropylcyclopent*-1-*enyl*]-3-*oxohexanoate* **15** (164 mg, 60%) as an oil (Found: C, 69.0; H, 9.4. $C_{17}H_{28}O_4$ requires C, 68.9; H, 9.5%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3605, 3540, 1745 and 1718; $\delta_H(CDCl_3)$ 0.66 and 0.92 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.28 (3 H, t, *J* 7.2, OCH_2CH_3), 1.5–3.0 (12 H, m), 3.44 (2 H, s, $COCH_2CO$) and 4.00–4.4 (4 H, m, $=CCH_2OH$, OCH_2CH_3).

A mixture of **15** (15 mg, 0.08 mmol), diphenyl disulphide (44 mg, 0.20 mmol), tributylphosphine (62.5 mm^3, 0.25 mmol) and THF (1 cm^3) was stirred at 55 °C for 2 h, and diluted with water, and then extracted with CH_2Cl_2. The oily residue obtained by concentration was chromatographed on silica gel (hexane–AcOEt, 10:1) to give the *title compound* **16** (16 mg, 83%) as an oil, $[\alpha]_D^{17}$ −6.23 (*c* 0.77, $CHCl_3$) (Found: 71.2; H, 8.4. $C_{23}H_{32}O_3S$ requires C, 71.1; H, 8.3%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1743, 1717, 1650, 1585 and 695; $\delta_H(CDCl_3)$ 0.54 and 0.86 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.26 (3 H, t, *J* 7.2, OCH_2CH_3), 1.5–2.8 (12 H, m), 3.40 (2 H, s, $COCH_2CO$), 3.62 (2 H, br m, $=CCH_2S$), 4.20 (2 H, q, *J* 7.2, OCH_2CH_3) and 7.10–7.50 (5 H, m, Ph).

Ethyl 2-*Diazo*-6-[(5R)-5-*isopropyl*-2-(*phenylthiomethyl*)*cyclopent*-1-*enyl*]-3-*oxohexanoate* **17**.—A mixture of **16** (16 mg, 0.04 mmol), tosyl azide[11] (40 mg, 0.21 mmol), triethylamine (21 mg, 0.21 mmol) and MeCN (1 cm^3) was stirred at 45 °C for 2 d. Water was added and the product was extracted with ether. The combined extracts were washed successively with water, aqueous K_2CO_3, 3 mol dm^{-3} HCl, water, and brine, and dried. Evaporation followed purification by preparative TLC (hexane–AcOEt, 20:1) gave the *title compound* **17** (14 mg, 83%) as an oil, $[\alpha]_D^{25}$ −11.73 (*c* 1.66, $CHCl_3$); (Found: C, 66.8; H, 7.5; N, 6.5; S, 7.4. $C_{23}H_{30}N_2O_3S$ requires C, 66.6; H, 7.3; N, 6.7; S, 7.7%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2147, 1722, 1719, 1655, 1595 and 698; $\delta_H(CDCl_3)$ 0.54 and 0.88 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.32 (3 H, t, *J* 7.2, OCH_2CH_3), 1.50–3.00 (12 H, m), 3.64 (2 H, dd, *J* 19.8, 12.6, $=CCH_2S$), 4.30 (2 H, q, *J* 7.2, OCH_2CH_3) and 7.0–7.45 (5 H, m, Ph).

Ethyl (1R,5R,6R)-1-*Isopropyl*-4-*methylene*-7-*oxo*-6-(*phenylthio*)*spiro*[4.5]*decane*-6-*carboxylate* **19**.—A mixture of **17** (76 mg, 0.18 mmol), rhodium acetate (0.8 mg, 1.83 × 10^{-3} mmol), and benzene (7.6 cm^3) was stirred at room temp. for 15 min, then at 85 °C for 30 min, meanwhile the medium changed from purple to yellow. After cooling, the mixture was filtered through a short silica gel column with the aid of AcOEt. Evaporation followed by purification by preparative TLC (hexane–AcOEt, 15:1) gave the *title compound* **19** (51 mg, 72%) as an oil, $[\alpha]_D^{18}$ −3.37 (*c* 0.58, $CHCl_3$) (Found: C, 71.4; H, 7.7; S, 8.3. $C_{23}H_{30}O_3S$ requires C, 71.4; H, 7.8; S, 8.3%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1718, 1702, 1231 and 895; $\delta_H(CDCl_3)$ 0.80 and 0.88 (3 H, d, *J* 7.2 each, isopropyl CH_3), 1.02 (3 H, t, *J* 7.2, OCH_2CH_3), 1.50–3.22 (12 H, m), 3.40–4.0 (2 H, m, OCH_2CH_3), 4.68 and 5.18 (1 H, br s with fine splittings each, $=CH_2$) and 7.1–7.70 (5 H, m, Ph).

(1R,5R)-1-*Isopropyl*-4-*methylenespiro*[4.5]*decan*-7-*one* **20**.—To a stirred suspension of 6% sodium amalgam (94 mg, 0.25 mmol) and sodium hydrogen phosphate (28 mg, 0.20 mmol) in MeOH (0.3 cm^3) was added, at room temp., a solution of **19** (19 mg, 0.05 mmol) in MeOH (0.3 cm^3). After being stirred for 30 min, the reaction mixture was poured into well-stirred aqueous NH_4Cl and extracted with a mixed solvent (ether–CH_2Cl_2, 3:1). Evaporation left an oil (9 mg).

A mixture of the above oil, saturated brine (20 mm^3), and DMSO (0.2 cm^3) was heated at 130 °C for 2 h.[12] After cooling, the mixture was diluted with water and extracted with ether. Evaporation followed by purification by preparative TLC (hexane–AcOEt, 10:1) gave the *title compound* **20** (5 mg, 70%) as an oil, $[\alpha]_D^{18}$ +3.32 (*c* 0.31, $CHCl_3$) (Found: C, 81.7; H, 10.6. $C_{14}H_{22}O$ requires C, 81.5; H, 10.7%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1702, 1649cw, 897 and 886; $\delta_H(CDCl_3)$ 0.87 and 0.97 (3 H, d, *J* 5.4 each, isopropyl CH_3), 1.05–2.70 (14 H, m) and 4.62 and 4.82 (1 H, t, *J* 1.8 each, $=CH_2$).

Hydrogenation of Compound **20**.—A solution of **20** (5 mg, 0.02 mmol) in AcOEt (0.6 cm^3) was hydrogenated in the presence of PtO_2 (1 mg) for 15 h. The reaction mixture was diluted with CH_2Cl_2 and filtered through a short silica gel column. Evaporation of the filtrate provided oily (1R,5R)-1-*isopropyl*-4-*methylspiro*[4.5]*decan*-7-*one* **21** (5 mg, quantitative), whose TLC and HPLC analyses indicated it to be homogeneous, $[\alpha]_D^{20}$ +4.59 (*c* 0.33, $CHCl_3$); [HRMS(EI), Found: M^+, 208.1827. $C_{14}H_{24}O$ requires *M*, 208.1826]; $\nu_{max}(CHCl_3)/cm^{-1}$ 1702; $\delta_H(CDCl_3)$ 0.80–1.02 (9 H, m, isopropyl CH_3, $CHCH_3$), 1.05–2.05 (11 H, m) and 2.05–2.60 (4 H, m).

(+)-*Acorenone B* **1**.—To a stirred LDA solution [prepared from a solution of BuLi in hexane (1.64 mol dm^{-3}; 80 mm^3, 0.13 mmol) and diisopropylamine (16.5 mg, 0.16 mmol) in THF (0.3 cm^3)], was added at −40 °C a solution of **21** (14 mg, 0.07 mmol) in THF (0.2 cm^3), and stirring was continued for an additional 1 h at −30 °C. The reaction mixture was recooled to −50 °C,

HMPA (64 mm^3) followed by methyl iodide (8 mm^3, 0.13 mmol) was added with stirring, and the reaction temperature was gradually raised to 0 °C over a period of 1 h. The reaction mixture was quenched by addition of aqueous NH_4Cl and the product was extracted with ether. Evaporation followed by purification by preparative TLC (hexane–AcOEt, 15:1) gave diastereoisomeric 1-*isopropyl*-4,8-*dimethylspiro*[4.5]*decan*-7-*one* **22** (8 mg, 52%) as an oil, [HRMS(EI), Found: M^+, 222.1984. $C_{15}H_{26}O$ requires *M*, 222.1982]; ν_{max}(film)/cm^{-1} 1713; $\delta_H(CDCl_3)$ 0.87–1.20 (12 H, m, isopropyl CH_3, two $CHCH_3$), 1.22–2.05 (12 H, m) and 2.05–2.70 (2 H, m).

To a stirred solution of **22** (7 mg, 0.03 mmol) in CH_2Cl_2 (0.1 cm^3) was added, at 0 °C, a solution of Br_2 in CH_2Cl_2 (0.07 mol dm^{-3}; 1 cm^3, 0.07 mmol), and stirring was continued for an additional 6 h at 0 °C. The reaction mixture was quenched by addition of aqueous $NaHCO_3$ and the product was extracted with a mixed solvent (ether–CH_2Cl_2, 3:1). The combined extracts were washed successively with aqueous $Na_2S_2O_3$, water and brine, and dried. Evaporation afforded an oil (8 mg), ν_{max}(film)/cm^{-1} 1714.

A mixture of the above oil, Li_2CO_3 (5 mg), LiBr (5 mg) and DMF (0.2 cm^3) was heated at 130 °C with stirring for 20 min. After cooling, the reaction mixture was diluted with water and the product was extracted with ether. Evaporation followed by purification by preparative TLC (hexane–AcOEt, 15:1) gave (+)-acorenone B **1** (3 mg, 46%) as an oil, $[\alpha]_D^{23}$ +17.3 (*c* 0.15, $CHCl_3$); [HRMS(EI) Found: M^+, 220.1827, $C_{15}H_{24}O$ requires *M*, 220.1826]. The spectroscopic data of the synthetic (+)-(**1**) (^1H NMR, IR and MS) were identical with those of the synthetic (−)-[5i] and (±)-(**1**).[5a,c] **1**: δ_H(600 MHz; $CDCl_3$) obtained with Bruker AM-600; 0.77 (3 H, d, *J* 6.79, $CHCH_3$), 0.86 and 0.94 (3 H, d, *J* 6.61 each, isopropyl CH_3), 1.08–1.70 (7 H, m), 1.76 (3 H, s, $=CCH_3$), 2.06 and 2.29 (1 H, d with fine splittings, *J* 20 each, $=CHCH_2$), 2.24 and 2.70 (1 H, d, *J* 16.6 each, $COCH_2$) and 6.65 (1 H, m, =CH).

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