Studies on a New Route to (±)-Copaene and (±)-Ylangene

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Elaboration of the perhydroazulene ring system formed by the intramolecular cycloaddition of a dienyl-substituted 3-oxidopyrylium has generated key intermediates used in the total synthesis of the α- and β-series of the copaene and ylangene sesquiterpene hydrocarbons. During the synthesis of the β-series of compounds selective protection of an olefinic bond was achieved by thiol addition; protection in this manner preventing migration of the double bond from an exocyclic to endocyclic position during the perhydroazulene to decalone rearrangement.

The tricyclic sesquiterpene hydrocarbons copaene and ylangene have recently been chosen as targets to illustrate new synthetic methodology.[1] In the classical syntheses of the α- and β-series of copaenes and ylangenes compounds (**1**)—(**4**), both Heathcock *et al.*,[2] in 1966 and Corey and Watt, in 1973,[3] utilized as the key reaction an intramolecular, transannular elimination from an appropriately substituted, *cis*-fused decalone of the type (**5**), leading to the required tricyclic carbon framework (**6**). Our recent work on intramolecular cycloadditions to the 3-oxidopyrylium system has opened up a new route to *cis*-fused decalones[4] and in this paper we describe an efficient route to the key intermediates (**7**) and (**8**) used in the synthesis of the title sesquiterpene hydrocarbons.

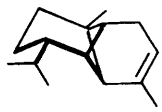
The retrosynthetic route we envisaged to compound (**7**) is shown in Scheme 1. The starting alcohol (**12**) was prepared by standard methods from furfuraldehyde. Thus chloroprene was metallated with magnesium and treated with ethylene oxide, using zinc chloride as a catalyst[5] to give the alcohol (**9**). Conversion of this alcohol into the corresponding bromide (**11**) was most efficiently achieved by prior formation of the methanesulphonate (**10**) and then reaction of this with lithium bromide in tetrahydrofuran (THF).[6] The bromide (**11**) only reacted with magnesium using the entrainment method with 1,2-dibromoethane,[7] but the Grignard reagent so formed reacted smoothly with furfuraldehyde to give the alcohol (**12**) in 60% yield. This route to the dienyl alcohol (**12**) was more than twice as efficient as the one we previously reported in the synthesis of (±)-bulnesene.[8]

The synthetic route followed is outlined in Scheme 2. Oxidation of the furan ring in the presence of the diene group was achieved chemoselectively[8] using singlet oxygen at −60 °C in a flow cell, with a mixture of Rose Bengal and Methylene Blue as sensitizer, whilst irradiating the mixture with a bank of fluorescent lamps. The intermediate ozonide was reduced, using dimethyl sulphide, until it gave a negative peroxide test, and was then worked up to afford the desired hydroxypyranones (**13**) as an epimeric mixture. Acetylation gave the acetate (**14**) and heating this in acetonitrile, using triethylamine as a base, gave the expected perhydroazulenone (**15**) as a single product; the overall yield from the alcohol (**12**) to the latter compound was 55%.

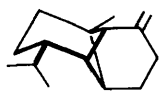
A chemoselective means for the conjugate reduction of the α,β-unsaturated ketone in the presence of the exocyclic methylene group was next required. The use of the 'Selectride' reagents (lithium or potassium tris-s-butylborohydride), which have been reported to effect such a reduction,[9] instead gave 1,2-reduction of the carbonyl group. However, use of diphenylsilane, catalysed by a palladium(0) system in the presence of zinc chloride[10] did give selective reduction of the enone at room temperature, to produce the required ketone (**18**) in 86% yield. Subsequent reaction of the ketone (**18**) with methylmagnesium iodide gave the tertiary alcohol (**17**) by stereoselective addition to the β-face of the molecule.[4]

The direct Lewis acid-catalysed rearrangement of the tertiary alcohol (**17**) to the required decalone (**16**) could not be effected,

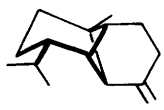
(**1**) α-copaene



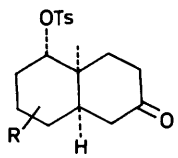
(**2**) α-ylangene



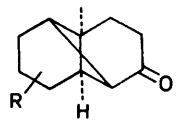
(**3**) β-copaene



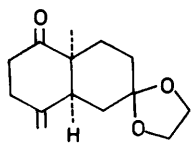
(**4**) β-ylangene



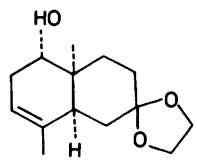
(**5**)



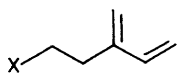
(**6**)



(**7**)



(**8**)



(**9**) X = OH
(**10**) X = OSO_2Me
(**11**) X = Br

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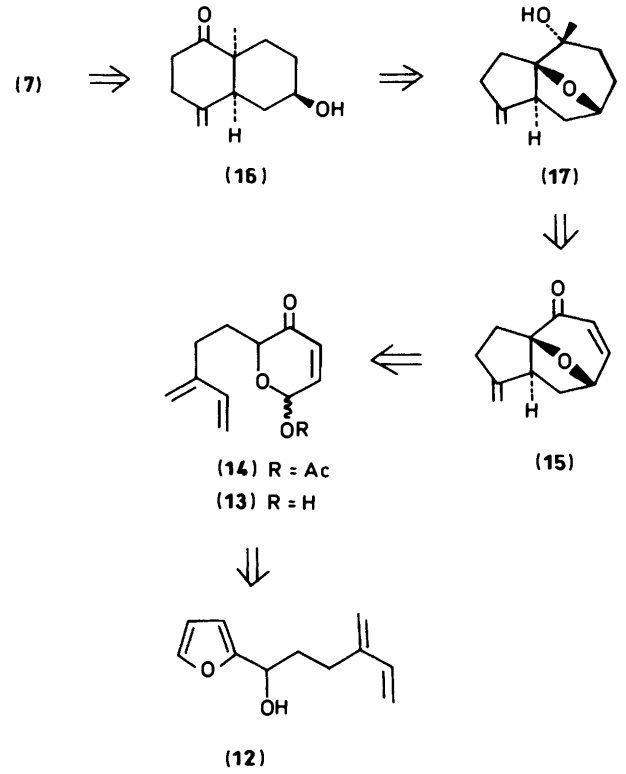


Scheme 1.

the isomeric compound (**20**) being isolated as the only product. By monitoring the reaction, using n.m.r. spectroscopy, it was established that Lewis acids, such as stannic chloride, initially catalysed a double-bond shift, to produce the endocyclic isomer (**19**) before rearrangement occurred. Further treatment of the isomer (**19**) with the catalyst effected a smooth rearrangement to the decalone (**20**); other acids gave similar results and in no case was any of the other isomer (**21**) detected. Presumably isomer (**21**) is less favoured since it imposes both ring strain on the bridged epoxy system and gives a sterically crowded double bond, with interference between the substituents at positions 7 and 8. All other attempts to effect the direct conversion of the alcohol (**26**) into the decalone (**16**) failed, including attempts using the preformed trifluoroacetate and methanesulphonate esters of the starting alcohol. A consolation of the observed, smooth migration of the double bond was the opening up of a route to the α-series of natural products, (**1**) and (**2**).

Oxidation of the alcohol (**20**) to the diketone (**22**) was effected with pyridinium chlorochromate and subsequent, selective acetal formation was achieved, using the catalysed trimethylsilyl triflate procedure of Hua and Wetzel,[11] to give the sterically less hindered monoacetal (**23**). Reduction of the remaining oxo group with sodium in propanol gave the thermodynamically more stable alcohol (**8**), identical in its physical properties to that described by Corey and Watt.[3]

The overall yield of the alcohol (**8**) from the alcohol (**12**) was 23%, which compares well with the overall 8% yield reported previously.[3]

Returning to the synthesis of the β-series of hydrocarbons, (**3**) and (**4**), it is evident that a means for preventing the migration of the exocyclic methylene group is required. This may be accomplished by appropriate masking of the olefinic bond, effecting the perhydroazulene to decalone rearrangement, and then releasing the olefinic bond. The use of either selenium or sulphur methodology was considered but since selenium is a Lewis base known to complex with Lewis acids[12] the use of sulphur reagents was explored.

Heating the alcohol (**17**) with thiophenol in the presence of a trace of the radical catalyst α,α-azoisobutyronitrile (AIBN) produced a 4:1 mixture of the epimeric adducts (**24**) and (**25**). The relative configuration of these adducts was assigned by 400 MHz n.m.r. spectroscopy. For the major isomer the coupling constant between 7-H at δ 2.82 and 8-H at δ 2.24 is 9.5 Hz, whereas for the minor isomer 7-H appeared at δ 2.38 with a coupling of 4.5 Hz to 8-H. The C-8 substituent in the major adduct (**24**) is in a pseudo-equatorial configuration in which 8-H and 7-H are eclipsed, leading to a large coupling constant, whereas in the minor isomer (**25**) the dihedral angle between these two protons approaches 120°, leading to a smaller coupling constant.

The mixture of sulphides was treated with boron trifluoride–diethyl ether in dichloromethane to produce the rearranged sulphides (**26**) and (**27**) respectively. Treatment of the mixture of latter sulphides with sodium metaperiodate in aqueous methanol gave a mixture of the corresponding sulphoxides, which were immediately processed by heating in refluxing xylene, in the presence of trimethyl phosphite as a sulphenic acid trap.[13] Elimination proceeded smoothly to give in 86% yield the exocyclic methylene compound (**16**), with no evidence for migration of the double bond into the ring.

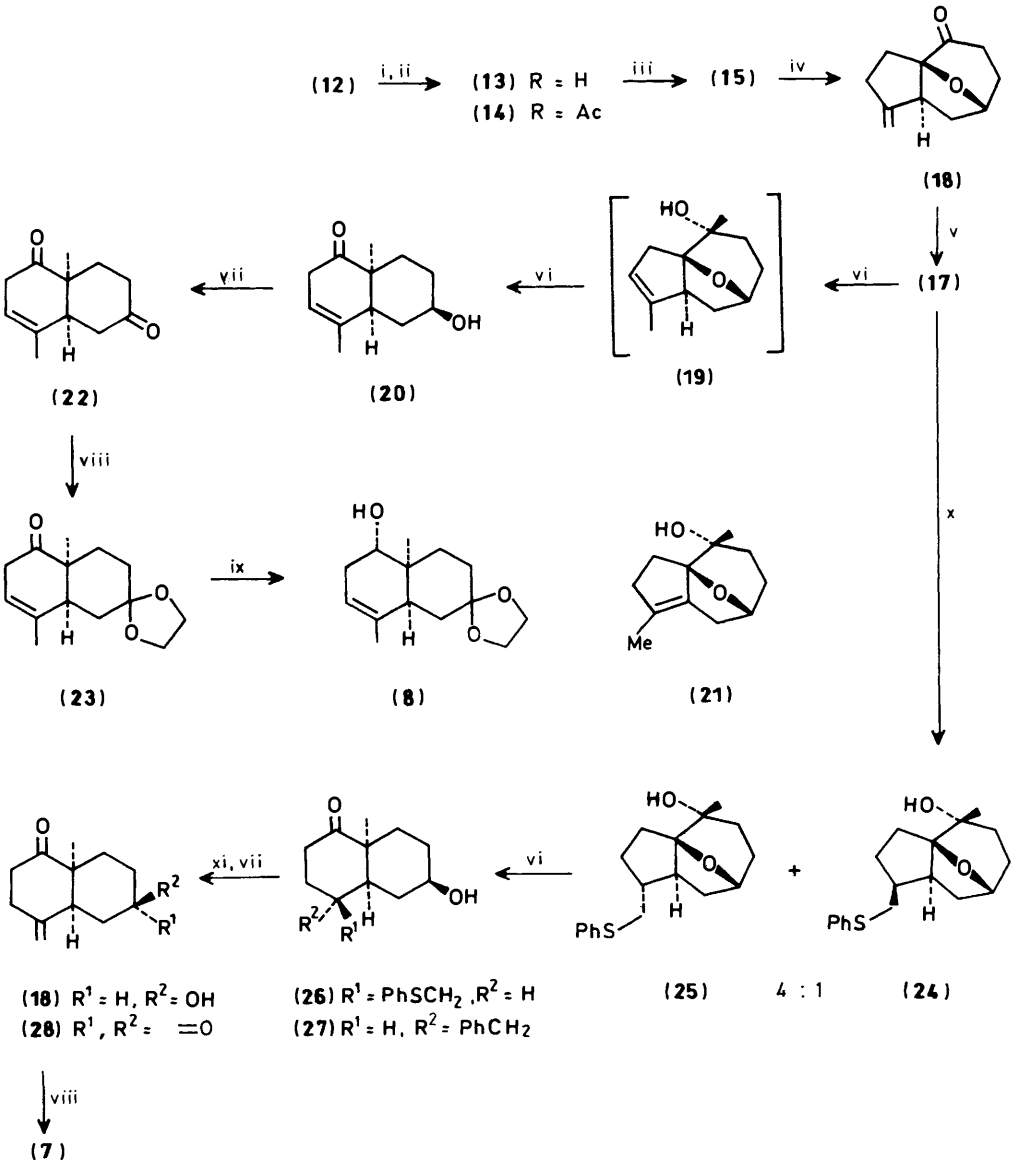
After oxidation to the diketone, selective acetalisation of the unencumbered ketone group was again achieved using the trimethylsilyl triflate-catalysed exchange reaction. The product (**7**) was identical with that described previously;[3] the overall yield from the ketone (**12**) was 16% compared to a literature process of 7% as described by Corey and Watt.[3] Since the acetals (**7**) and (**8**) have been converted to the α- and β-series of copaenes and ylangenes (**1**) and (**4**), the above represents a formal route to these compounds.

Experimental

M.p.s were determined on a Kofler block and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 1420 Ratio Recording spectrophotometer either as solutions in chloroform, Nujol mulls or, for liquids, as films. Proton n.m.r. spectra were recorded on Varian EM360A (60 MHz), Perkin-Elmer R32 (90 MHz), Jeol FX90Q (90 MHz) or Bruker AM400 (400 MHz) spectrometers. Chemical shifts are quoted in p.p.m. relative to tetramethylsilane as internal reference, for solutions in deuteriochloroform. Mass spectra were obtained using a Kratos MS25 instrument and accurate mass determinations were obtained using an AEI-Kratos MS9/50 instrument. Microanalytical determinations were performed by the University of Leeds, School of Chemistry, Microanalytical Laboratory.

All chiral compounds were obtained as racemates. T.l.c. was carried out on aluminium or glass plates precoated with Merck Kieselgel 60 GF_{254}. Column chromatography was carried out on either MN-Kieselgel 60, 230—400 mesh (Camlab) or Kieselgel 60G (Merck); columns were generally packed and run under pressure. Solvents were dried and distilled by standard methods before use.[14] Light petroleum refers to the fraction of boiling range 40—60 °C and ether refers to diethyl ether throughout. Solutions of organic compounds from extractions were generally dried over anhydrous sodium sulphate before being filtered and evaporated under reduced pressure on a rotary evaporator. Dry nitrogen was generally employed as the atmosphere for most reactions. Ethanol was removed from chloroform by passing the solvent through an activated, basic alumina column.

3-*Methylenepent*-4-*en*-1-*ol* (**9**).—Methyl iodide (0.3 ml, 0.93 mmol) was added to magnesium turnings (9 g, 0.4 mol) in THF



Scheme 2. *Reagents:* i, $^1O_2$ then Me_2S; ii, Ac_2O, pyridine; NEt_3, CH_3CN, reflux; iv, Ph_2SiH_2, $ZnCl_2$, $(Ph_3P)_4Pd$; v, MeMgI; vi, Lewis acid; vii, pyridinium chlorochromate; viii, $(Me_3SiOCH_2)_2$, TMS triflate; ix, Na, Pr^iOH; x, PhSH, AIBN; xi, $NaIO_4$ then heat, xylene, $P(OMe)_3$

(20 ml) and the mixture heated to activate the metal surface. Zinc chloride (0.5 g, 3.67 mmol) was then added, followed by THF (300 ml). 2-Chlorobutadiene (55.2 ml, 50% solution in xylene; 0.28 mol) was added dropwise to the mixture at 60 °C and the whole heated at this temperature for a further 1 h after addition. The reaction mixture was cooled to room temperature and copper(I) iodide (1 g, 5.25 mmol) added. After cooling the mixture to −50 °C a precooled solution of ethylene oxide (30 ml, 0.6 mol) in THF (60 ml) was added at such a rate as to maintain the temperature below −50 °C. After a further 0.5 h the reaction was allowed to warm to room temperature and stirred for a further 2 h before quenching with saturated aqueous NH_4Cl. The mixture was extracted with ether (3 × 200 ml), and the extracts washed with brine and dried. The solvent was evaporated off, the residue filtered through silica, using ether–light petroleum as solvent, and the product distilled to give the alcohol (20.6 g, 75%), b.p. 68—71 °C 22 mmHg, $\nu_{max.}$ 3 340, 2 950, 1 595, 1 045, and 900 cm^{-1}.

5-Bromo-3-methylenepent-1-ene (**11**).—Methanesulphonyl chloride (17.4 ml, 0.22 mol) was added dropwise to a stirred solution of the alcohol (**9**) (20 g, 0.20 mol) and triethylamine (57 ml, 0.41 mol) in dichloromethane (250 ml) at −30 °C. The reaction mixture was allowed to warm to 0 °C, poured into water (150 ml), the organic phase was isolated, and the aqueous phase was extracted with dichloromethane (2 × 150 ml). The combined organic phases were dried and evaporated to give the crude methanesulphonate (**10**) (33.4 g, 93%); $\nu_{max.}$(film) 2 980, 1 595, 1 355, 1 175, and 960 cm^{-1}. The crude methanesulphonate (33 g) and anhydrous lithium bromide (30 g, 0.345 mol) were heated in THF (300 ml) at reflux for 1.5 h, and the mixture was cooled and poured into water (200 ml) before being extracted with ether (2 × 200 ml). The organic extract was washed with saturated aqueous sodium hydrogen carbonate (100 ml) and brine (100 ml) before drying and evaporation of solvent. The residue was distilled to give the title bromide (22.5 g, 69%), b.p. 54—56 °C/25 mmHg; $\nu_{max.}$ 3 090, 1 595, 1 260, 1 210, 990, and

905 cm^{-1}; δ 2.80 (2 H, t, *J* 6 Hz, CH_2C=), 3.50 (2 H, t, *J* 6 Hz, CH_2Br), 5.0—5.4 (4 H, m, olefinic H), and 6.35 (1 H, dd, *J* 11, 17 Hz, vinylic H).

1-(2-*Furyl*)-4-*methylenehex*-5-*en*-1-*ol* (**12**).—The bromide (**11**) (12.53 g, 0.078 mol) and 1,2-dibromoethane (7.5 ml, 0.087 mol) in THF (30 ml) were slowly added to magnesium turnings (6 g, 0.25 mol) in THF (200 ml) at reflux. The mixture was refluxed for a further 1 h, cooled to 0 °C, and furfuraldehyde (6.5 ml, 0.08 mol) in THF (20 ml) was added. The reaction mixture was stirred at room temperature for 0.5 h, quenched with saturated aqueous ammonium chloride (150 ml), and the aqueous phase was extracted with ether (3 × 150 ml). The ether extracts were washed with aqueous sodium hydrogen carbonate, dried, evaporated, and the residue chromatographed on silica gel, using 1:1 ether–light petroleum as eluant, to give the *title alcohol* (8.17 g, 59%), b.p. 95 °C/2 mmHg; $\nu_{max.}$(film) 3 380, 1 595, 1 010, and 900 cm^{-1}; δ 1.6—2.5 (5 H, m, CH_2 and OH), 4.70 (1 H, m, C*H*OH), 5.0—5.3 (4 H, m vinylic H), 6.2—6.55 (3 H, m, vinyl and furyl H) and 7.36 (1 H, m, furyl H) (Found: C, 74.0; H, 8.0. $C_{11}H_{14}O_2$ requires C, 74.1; H, 7.9%).

6-*Hydroxy*-2-(3-*methylenepent*-4-*enyl*)-6H-*pyran*-3(2H)-*one* (**13**).—The furyl alcohol (**12**) (8.12 g, 45.6 mmol) was dissolved in dichloromethane (400 ml) and methanol (200 ml) with Rose Bengal (10 mg) and methylene blue (10 mg) as sensitisers. Oxygen was bubbled through the solution which was irradiated at −60 °C in an apparatus containing a central cooled well (acetone–solid CO_2) and outer vacuum jacket, with four 2 ft, 40 W fluorescent tubes until t.l.c. showed the complete disappearance of starting material (2 h). The solution was then decanted into dimethyl sulphide (6.8 ml, 93 mmol), warmed to room temperature, and stirred until the test for peroxides was negative (0.75 h). The solvent was evaporated off under reduced pressure and the residue filtered through silica, using 1:1 ether–light petroleum as solvent, to give the *title compound* (7.29 g, 82%) as a viscous oil; $\nu_{max.}$ 3 400, 1 690, 1 595, 1 100, 1 040, and 905 cm^{-1}; δ 1.8—2.5 (5 H, m), 4.1 and 4.7 (1 H, m, 2-H), 5.0—5.4 (4 H, m, vinylic H), 5.7 (1 H, m, 6-H), 6.0—6.6 (2 H, m, vinylic H and 4-H), and 6.9 and 6.95 (1 H, d, *J* 10 Hz, 5-H) (Found: M^+, 194.094 18. $C_{11}H_{14}O_3$ requires *M*, 194.094 29).

6-*Acetoxy*-2-(3-*methylenepent*-4-*enyl*)-6H)-*pyran*-3(2H)-*one* (**14**).[8]—A solution of the hydroxypyranone (**13**) (7.09 g, 36.6 mmol) and pyridine (4.3 ml, 52.7 mmol) in dichloromethane (200 ml) was treated with acetyl chloride (2.9 ml, 40.7 mmol) at 0 °C for 12 h. The resulting precipitate was removed by filtration and the supernatant washed with brine (2 × 70 ml), dried, and the solvent evaporated off. The crude product was chromatographed on silica, eluting with 1:2 ether–light petroleum, to give the title acetate (7.72 g, 90%) as a mixture of epimers. An analytical sample was prepared by distillation, b.p. 105 °C/0.5 mmHg; $\nu_{max.}$ 1 760, 1 690, 1 595, 1 220, and 930 cm^{-1}; δ 1.8—2.6 (4 H, m), 2.1 (3 H, s, Ac), 4.25 and 4.5 (1 H, m), 5.0—5.4 (4 H, m, vinylic H), 6.1—6.4 (3 H, m), and 6.8 and 6.9 (1 H, m, vinylic H). (Found: C, 66.2; H, 6.4. Calc. for $C_{13}H_{16}O_4$: C, 66.1; H, 6.8%).

1β,5β-*Epoxy*-8-*methylene*-1β,7α-*bicyclo*[5.3.0]*dec*-3-*en*-2-*one* (**15**).[8,*]—The acetate (**14**) (7.61 g, 32.2 mmol) and triethylamine (18 ml) were heated in refluxing acetonitrile (250 ml) for 16 h. The solvent was evaporated off and the residue chromatographed on silica, using 1:2 ether–light petroleum as eluant, to give the title cycloadduct (4.2 g, 74%) as a pale yellow oil. An analytical sample was prepared by distillation, b.p. 100 °C/0.8 mmHg; $\nu_{max.}$ 2 940 and 1 690 cm^{-1}; δ 1.80 (1 H, dd, *J* 7.7 and 12.4 Hz, 6α-H), 2.05 (1 H, ddd, *J* 5.5, 6.8, and 12.1 Hz, 6β-H), 2.32 (1 H, dd, *J* 9.3 and 12.0 Hz, CH), 2.47 (2 H, m, CH_2), 2.63 (1 H, m, CH), 2.92 (1 H, m, CH), 4.83 (1 H, m, vinyl H), 4.89 (1 H, dd, *J* 4.4 and 6.7 Hz, 5-H), 5.00 (1 H, m, vinyl H), 5.98 (1 H, d, *J* 9.7 Hz, 3-H), and 7.17 (1 H, dd, *J* 4.4 and 9.8 Hz, 4-H) (Found: C, 75.1; H, 7.0. Calc. for $C_{11}H_{12}O_2$: C, 75.0; H, 6.9%).

1β,5β-*Epoxy*-8-*methylene*-1β,7α-*bicyclo*[5.3.0]*decan*-2-*one* (**18**).—Tetrakis(triphenylphosphine)palladium(0) (46 mg, 0.04 mmol) was added to a solution of the cycloadduct (**15**) (420 mg, 2.39 mmol), diphenylsilane (530 mg, 2.88 mmol), and zinc chloride (33 mg, 0.24 mmol) in dry chloroform (15 ml) (previously filtered through a neutral alumina column) and the mixture was stirred at room temperature for 6 h, then filtered through a short silica gel column using dichloromethane as eluant. The crude product was purified by chromatography, using 1:3 ether–light petroleum as eluant, to give the *title compound* (366 mg, 86%) as a colourless oil. A sample was distilled (90 °C, 1 mmHg) to give $\nu_{max.}$ 2 950, 1 720, 1 120, and 885 cm^{-1}; δ 1.81 (2 H, m, CH_2), 2.16 (1 H, m, CH), 2.25—2.53 (6 H, m), 2.61 (1 H, m, CH), 3.02 (1 H, m, CH), 4.66 (1 H, t, *J* 5.7 Hz, 5-H), 4.83 (1 H, m, vinyl H), and 4.96 (1 H, m, vinyl H) (Found: C, 74.1; H, 7.9. $C_{11}H_{14}O_2$ requires C, 74.1; H, 7.9%).

1β,5β-*Epoxy*-2β-*methyl*-8-*methylene*-1β,7α-*bicyclo*[5.3.0]-*decan*-2α-*ol* (**17**).—The ketone (**18**) (1.13 g, 6.35 mmol) in ether (20 ml) was added to a stirred solution of methylmagnesium iodide [prepared from iodomethane (0.8 ml, 12.9 mmol) and magnesium turnings (0.34 g, 14 mmol)] in ether (50 ml) at 0 °C. The reaction mixture was stirred for 1.5 h at room temperature then poured into saturated aqueous ammonium chloride (50 ml). The aqueous phase was extracted with ether (3 × 50 ml) and the combined organic extracts dried and evaporated. The crude product was chromatographed on silica gel using 1:2 ether–light petroleum as eluant to afford the *title alcohol* (1.16 g, 94%), m.p. (hexane) 69—70 °C; $\nu_{max.}$ 3 450, 2 945, 1 650, 1 135, and 1 010 cm^{-1}; δ 1.36 (3 H, s, 2-Me), 1.2—2.8 (11 H, m), 3.20 (1 H, m, CH), 4.45 (1 H, m, 5-H), 4.82 (1 H, br s, vinyl H), and 4.95 (1 H, br s, vinyl H) (Found: C, 74.4; H, 9.5; $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%).

1β,5β-*Epoxy*-2β-*methyl*-8-[(*phenylthio*)*methyl*]-1β,7α-*bicyclo*[5.3.0]*decan*-2α-*ols* (**24**) *and* (**25**).—Azoisobutyronitrile (10 mg, 0.06 mmol) was added in portions over 4 h to a refluxing mixture of the alcohol (**17**) (0.646 g, 3.33 mmol) and freshly distilled thiophenol (1.4 ml, 17.5 mmol) in carbon tetrachloride (2 ml). After a further 2 h at reflux the reaction mixture was cooled and the solvent and excess of thiophenol evaporated off under reduced pressure. Chromatography of the residue on silica gel, using 1:8 acetone–light petroleum as eluant gave a 1:4 mixture of the *title sulphides* (0.794 g, 78%) as a solid, together with some of the recovered starting alcohol (0.114 g, 18%). A sample of the sulphides was recrystallised as a mixture from ether–hexane, m.p. 132—135 °C; $\nu_{max.}$ 3 600, 2 940, 1 435, 1 030, and 710 cm^{-1}; δ [400 MHz, major, β-isomer (**24**)] 1.32 (3 H, s, Me), 1.35—2.15 (11 H, m), 2.24 (1 H, m, 8-H), 2.82 (1 H, ddd, *J* 6.5, 9, and 9.5 Hz, reduces to dd, *J* 6.5 and 9 Hz on irradiation of 8-H signal at δ 2.24; 7-H), 2.93 (1 H, dt, *J* 8.5 and 12.5 Hz, reduces to d, *J* 12.5 Hz on irradiation of 8-H signal at δ 2.24; 8′-H), 3.00 (1 H, dd, *J* 7, 12.5 Hz, reduces to d, *J* 12.5 Hz on irradiation of 8-H signal at δ 2.24; 8′-H), 4.35 (1 H, m, 5-H), and 7.13—7.34 (5 H, m, ArH); δ [400 MHz, minor, α-isomer (**25**)] 1.32 (3 H, s, Me), 1.35—2.15 (12 H, m), 2.38 (1 H, ddd, *J* 4.5, 7.5, and 9 Hz, 7-H), 2.92 (1 H, dd, *J* 7 and 12.5 Hz, 8′-H), 3.01 (1 H, dd, *J* 7 and 12.5 Hz, 8′-H), 4.43 (1 H, m, 5-H), and 7.13—7.34 (5 H, m, ArH (Found: C, 70.8; H, 7.9; S, 10.7. $C_{18}H_{24}O_2S$ requires C, 71.0; H, 7.9; S, 10.5%).

* α-Groups are assigned as those in which the substituent is on the opposite side of the carbon framework compared with the epoxy bridge, β-substituents being on the same side.

Rearrangement of the Alcohol (**17**).—Tin tetrachloride (0.06 ml, 0.51 mmol) was added to a stirred solution of the alcohol (50 mg, 0.26 mmol) in dichloromethane (2 ml) at 0 °C. After 1 h at room temperature the reaction mixture was poured into water (10 ml) and extracted with ether (4 × 15 ml). The combined extracts were dried, the solvent evaporated off, and the residue chromatographed on silica gel, using 2:1 ether–light petroleum as eluant, to afford 8β-*hydroxy*-1α,5-*dimethyl*-1α,6α-*bicyclo*[4.4.0]*dec*-4-*en*-2-*one* (**20**) (37 mg, 74%), m.p. (ether–hexane) 83–84 °C; $\nu_{max.}$ 3 400, 1 940, 1 710, 1 450, 1 060, and 730 cm^{-1}; δ 1.12 (3 H, s, 1-Me), 1.4—2.6 (8 H, m), 1.80 (3 H, s, 5-Me), 2.85 (2 H, m, 3-H), 3.55 (1 H, m, 8-H), and 5.40 (1 H, m, 4-H) (Found: C, 74.2; H, 9.3. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%).

Rearrangement of the starting alcohol was followed by n.m.r. spectroscopy in $CDCl_3$; the methylene peaks at δ 4.82 and 4.95 disappeared whilst a peak appeared at δ 5.4 and a methyl signal at δ 1.8 (vinylic methyl) before the disappearance of the other methyl group (δ 1.3). On prolonged standing the latter signal also disappeared, being replaced by a new methyl group at δ 1.1 as the skeletal rearrangement occurred.

Rearrangement of the Sulphides (**24**) *and* (**25**).—Boron trifluoride–diethyl ether (0.03 ml, 0.24 mmol) was added dropwise to a stirred mixture of the sulphides (60 mg, 0.20 mmol) in dichloromethane (2 ml) at 0 °C and the mixture left at room temperature for 4 h, before being worked up in the manner described above. Chromatography on silica gel, using 2:1 ether–light petroleum as eluant, gave, in order of elution, the 5α-epimer (**27**) (9 mg, 15%) as a viscous oil, $\nu_{max.}$ 3 610, 2 930, 1 700, 1 580, 1 435, 1 040, 710, and 690 cm^{-1}; δ 1.03 (1 H, m, 6-H), 1.21 (3 H, s, 1-Me), 1.28—1.85 (7 H, m), 2.18 (2 H, m), 2.23—2.54 (3 H, m), 3.02 (1 H, dd, *J* 7, 13 Hz, reduces to d, *J* 13 Hz on irradiation at δ 2.18; 5′-H), 3.19 (1 H, dd, *J* 6, 13 Hz, reduces to d, *J* 13 Hz, on irradiation at δ 2.18; 5′-H), 3.76 (1 H, m, 8-H), and 7.15—7.40 (5 H, m, ArH); *m/z* 304 (M^+, 100%), 176 (74), 123 (94), 110 (95), 93 (47), and 55 (52) (Found: M^+ 304.148 69. $C_{18}H_{24}O_2S$ requires 304.149 69). The β-epimer (**26**) followed 33 mg, 55%), again as a viscous oil, $\nu_{max.}$ 3 480, 2 940, 1 700, 1 580, 1 440, 1 060, 740, and 690 cm^{-1}; δ 0.98 (1 H, m, 6-H), 1.12 (3 H, s, 1-Me), 1.30—1.85 (6 H, m), 2.01 (2 H, m), 2.27 (2 H, m), 2.54 (2 H, m), 2.88 (2 H, d, *J* 7 Hz, 5′-H), 3.58 (1 H, m, 8-H), and 7.15—7.40 (5 H, m, ArH); *m/z* 304 (M^+, 96%), 123 (100), 110 (98), 93 (55), and 55 (97) (Found: M^+ 304.149 63).

8β-*Hydroxy*-1α-*methyl*-5-*methylene*-1α,6α-*bicyclo*[4.4.0]-*decan*-2-*one* (**16**).—Sodium periodate (165 mg, 0.77 mmol) in the minimum volume of water (0.5 ml) was added dropwise to a stirred solution of the sulphides (**26**) and (**27**) (229 mg, 0.75 mmol) in methanol (4 ml) at 0 °C. The mixture was stirred at room temperature for 16 h, then filtered; the precipitate was washed with methanol (10 ml) and the filtrate evaporated to dryness under reduced pressure to afford the crude sulphoxides (212 mg, 88%), $\nu_{max.}$($CHCl_3$) 3 610, 3 010, 1 700, 1 040, 715, and 695 cm^{-1}. The crude sulphoxide mixture was immediately dissolved in xylene (8 ml) with trimethyl phosphite (0.16 ml, 1.36 mmol) and the solution heated to reflux for 17 h. The reaction mixture was cooled and poured directly onto a silica gel column. Elution with 2:1 ether–light petroleum afforded the *title olefin* (110 mg, 86%) as a colourless solid, m.p. (ether–hexane) 72—74 °C, $\nu_{max.}$ 3 610, 2 940, 1 700, 1 055, and 905 cm^{-1}; δ 0.92 (1 H, m), 1.11 (3 H, s, 1-Me), 1.2—2.0 (6 H, m), 2.2—2.8 (5 H. m), 3.63 (1 H, m, 8-H), and 4.90 (2 H, m, vinylic H) (Found: C, 73.9; H, 9.3. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%).

Oxidation of the Alcohols (**18**) *and* (**20**).—The alcohols were separately oxidised by the following method. Freshly prepared pyridinium chlorochromate[15] (200 mg, 0.93 mmol) was added in a single portion to a mixture of the oxo alcohol (110 mg, 0.57 mmol) and crushed 3 Å molecular sieves (150 mg) in dichloromethane (3 ml) at room temperature. After being stirred for 2 h the reaction mixture was diluted with ether (20 ml) and filtered through a short silica gel column, using ether as eluant. The crude product was purified by chromatography, using 1:1 ether–light petroleum as eluant, to give the diketone. 1α,5-*Dimethyl*-1α,6α-*bicyclo*[4.4.0]*dec*-4-*en*-2,8-*dione* (**22**) (85 mg, 78%) was obtained as a colourless solid, m.p. 94—96 °C; $\nu_{max.}$ 2 970, 1 710, 1 430, and 1 080 cm^{-1}; δ 1.24 (3 H, s, 1-Me), 1.42 (1 H, m), 1.78 (3 H, br s, 5-Me), 1.93 (1 H, t, *J* 14 Hz), 2.24 (1 H, m), 2.4 (1 H, dd, *J* 4 and 13.5 Hz), 2.52—2.65 (3 H, m), 2.86 (1 H, m, 3-H), 3.02 (1 H, m, 3-H), and 5.46 (1 H, m, 4-H) (Found: C, 75.0; H, 8.5. $C_{12}H_{16}O_2$ requires C, 75.0; H, 8.4%). 1α-*Methyl*-5-*methylene*-1α,6α-*bicyclo*[4.4.0]*decane*-2,8-*dione* (**28**) (103 mg, 95%) was obtained as a colourless solid, m.p. (ether–hexane) 80—81 °C; $\nu_{max.}$ 2 960, 1 705, 1 425, and 910 cm^{-1}; δ 1.24 (3 H, s, 1-Me), 1.80—2.50 (5 H, m), 2.51—2.78 (6 H, m), 4.95 (1 H, br s, CH_2=), and 4.99 (1 H, br s, CH_2=) (Found: C, 75.0; H, 8.5).

Acetal Formation of the Diketones (**22**) *and* (**28**).—*Ketone* (**22**). 1,2-Bis(trimethylsilyloxy)ethane (0.47 ml, 1.9 mmol) was added to a stirred solution of the diketone (347 mg, 1.8 mmol) and trimethylsilyl trifluoromethanesulphonate (0.01 ml, 0.05 mmol) in dichloromethane (5 ml) at −78 °C. After 4 h at this temperature the reaction was quenched by the addition of dry pyridine (0.1 ml) and warmed to room temperature. The reaction mixture was poured into saturated aqueous sodium hydrogen carbonate (25 ml) and extracted with ether (3 × 30 ml), the organic extracts dried, and the solvent evaporated off. The crude reaction product was chromatographed on silica gel, using 1:2 ether–light petroleum as eluant, to give 1α,5-*dimethyl*-2-*oxo*-1α,6α-*bicyclo*[4.4.0]*dec*-4-*en*-8-*one ethylene acetal* (**23**) (404 mg, 95%) as a crystalline solid. A sample was distilled (110 °C, 0.4 mmHg) to give m.p. 38—39 °C; $\nu_{max.}$ 2 940, 1 710, and 1 085 cm^{-1}; δ 1.13 (1 H, t, *J* 14 Hz), 1.14 (3 H, s, 1-Me), 1.30 (1 H, dt, *J* 4.5 and 14 Hz), 1.63 (2 H, m), 1.78 (3 H, m, 5-Me), 1.88 (1 H, ddd, *J* 3, 4, and 14 Hz), 2.27 (2 H, m), 2.74 (1 H, m, *J* 2.5 and 23 Hz, 3-H), 2.91 (1 H, m, *J* 2.5 and 23 Hz, 3-H), 3.92 (4 H, m, acetal H), and 5.37 (1 H, m, 4-H) (Found: C, 71.0; H, 8.5. $C_{14}H_{20}O_3$ requires C, 71.1; H, 8.5%).

Ketone (**28**). In a similar manner to the foregoing ketone compound (**28**) (50 mg, 0.26 mmol) was treated with 1,2-bis-(trimethylsilyloxy)ethane (0.07 ml, 0.29 mmol) using trimethylsilyl trifluoromethanesulphonate (0.002 ml) as catalyst. On this scale some unchanged starting diketone (9 mg, 18%) was recovered with the required acetal (47 mg, 76%). After distillation (110 °C, 0.2 mmHg) this was isolated as a solid, m.p. 92—94 °C (lit.,[3] 93—94 °C); $\nu_{max.}$ 2 960, 1 700, 1 650, 1 175, 1 090, and 910 cm^{-1}; δ 1.14 (3 H, s, 1-Me), 1.24 (1 H, m), 1.55—1.75 (4 H, m), 2.23—2.34 (2 H, m), 2.48—2.67 (4 H, m), 3.93 (4 H, m, acetal H), 4.91 (1 H, m, vinylic H), and 4.94 (1 H, m, vinylic H) (Found: C, 71.1; H, 8.5).

Reduction of the Oxo-acetal (**23**).—Sodium metal (900 mg, 39 mmol) was added to the ketone (96 mg, 0.41 mmol) in refluxing propan-2-ol (12 ml) and the mixture was heated to reflux for 1 h, during which time the sodium was consumed. After cooling, water was added, and the mixture was diluted with ether (100 ml). The mixture was washed with water (4 × 40 ml), dried, and the solvent evaporated off. The crude product was chromatographed on silica gel, using 2:1 ether–light petroleum as eluant, to give 2α-hydroxy-1α,5-dimethyl-1α,6α-bicyclo[4.4.0]dec-4-en-8-one ethylene acetal (**8**) (93 mg, 96%) as a colourless viscous oil;[3] $\nu_{max.}$ 3 450, 3 940, 1 100, and 750 cm^{-1}; δ 0.87 (3 H, s, 1-Me), 1.24 (1 H, br s, OH), 1.32—1.73 (5 H, m), 1.65 (3 H, m, 5-Me), 1.85—2.04 (4 H, m), 2.39 (1 H, ddd, *J* 3, 7, and 18 Hz, 3β-H), 3.95

(4 H, m, acetal H), 4.07 (1 H, dd, *J* 7 and 9 Hz, 2β-H), and 5.19 (1 H, m, 4-H) (Found: C, 70.4; H, 9.5. Calc. for $C_{14}H_{22}O_3$: C, 70.6; H, 9.3%).

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