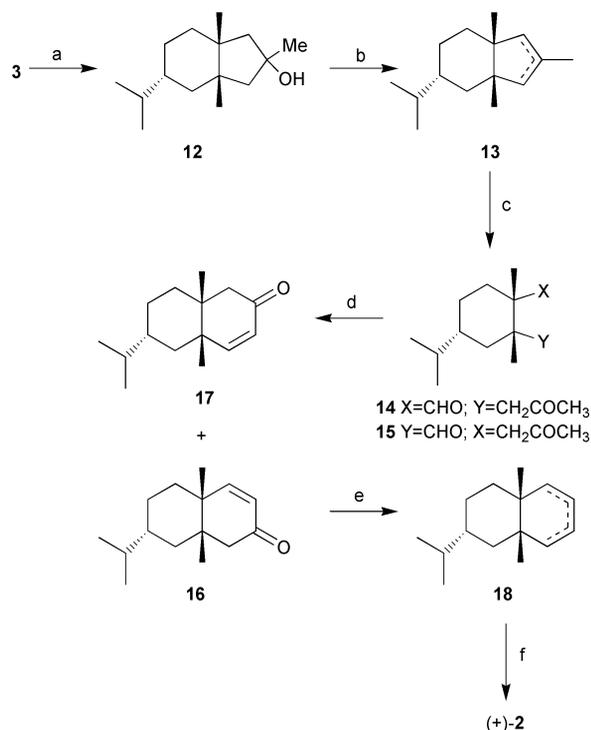


Scheme 2 Reagents and yields: a) ref. 8; b) LAH, 95%; c) $\text{CH}_3\text{C}(\text{OEt})_3$, EtCO_2H ; KOH; 63%; d) $(\text{COCl})_2$; CH_2N_2 ; 75%; e) CuSO_4 , 76%; f) Li, liq. NH_3 , 76%; g) H_2 , Pd-C, 98%.

centre. Thus, thermal activation of a solution of the allyl alcohol **6**, triethyl orthoacetate and a catalytic amount of propionic acid in a sealed tube for 5 days, furnished the ester **9**, which on alkaline hydrolysis generated the acid **5**. The stereochemistry at the newly created quaternary centre rests secured from the well established stereospecificity of the Claisen rearrangement. Reaction of the acid **5** with oxalyl dichloride in benzene followed by treatment of the resulting acid chloride with an excess of ethereal diazomethane furnished the diazo ketone **10** in 75% yield. Anhydrous copper(II) sulfate-catalysed decomposition of the diazo ketone **10** in refluxing cyclohexane, using a tungsten lamp, led to the intramolecular insertion of the resultant ketocarbenoid into the ring olefinic moiety in a regio- and stereospecific manner,¹² resulting in the formation of the cyclopropyl ketone **4** in 76% yield, whose structure was established from its spectral data. The *cis* stereochemistry of the ring junction was a consequence of the insertion of the ketocarbenoid from the preferred *syn* face of the olefin. Treatment of the cyclopropyl ketone **4** with lithium in liquid ammonia furnished the ketone **11** in 76% yield, in a highly regioselective manner. The regioselectivity in the cyclopropane cleavage can be readily explained, as it is well established that in cyclopropyl ketones the cyclopropane bond which possesses maximum overlap with the p-orbital of the carbonyl system will be cleaved preferentially.¹³ Hydrogenation of the isopropenyl double bond in the enone **11** using 10% Pd/C as the catalyst in methanol at one atmosphere of hydrogen furnished the saturated ketone **3** in 98% yield.

For the hydrindanone-to-decalin ring expansion, an oxidative cleavage and aldol condensation sequence was contemplated, Scheme 3. Treatment of the ketone **3** with methylmagnesium iodide in diethyl ether provided the *tert*-alcohol **12** as a mixture of diastereomers, which on treatment with a catalytic amount of toluene-*p*-sulfonic acid (PTSA) in benzene generated the expected mixture of the olefins **13** in a 3:2 regioisomeric ratio. No attempt was made to separate the isomers of the olefin **13** as both the isomers will lead to (+)-valerane **2**. Ozonolysis of the



Scheme 3 Reagents and yields: a) MeMgI , 85%; b) PTSA, 98%; c) O_3/O_2 ; PPh_3 ; 83%; d) 1 M NaOH - MeOH , 60%; e) $\text{BF}_3 \cdot \text{Et}_2\text{O}$, NaBH_3CN , 89%; f) H_2 , 10% Pd-C, 84%.

mixture of olefins **13** in methanol-methylene dichloride (1:5) at -70°C , followed by reductive work-up of the ozonide with triphenylphosphine furnished a mixture of keto aldehydes **14** and **15**. Intramolecular aldol condensation of the mixture of keto aldehydes **14** and **15** in tetrahydrofuran (THF) using 1 M potassium hydroxide in methanol furnished a $\approx 2:1$ mixture of the regioisomeric enones **16** and **17**. For the deoxygenation of the enones **16** and **17** an ionic hydrogenation, employing a combination of sodium cyanoborohydride and boron trifluoride-diethyl ether,¹⁴ was chosen. Thus, refluxing a solution of a mixture of the enones **16** and **17** in dry THF with sodium cyanoborohydride and boron trifluoride-diethyl ether, as anticipated, furnished a regioisomeric mixture of the olefins **18** in 89% yield. Finally, hydrogenation of the mixture of olefins **18** in methanol using 10% Pd/C as the catalyst at one atmosphere pressure of hydrogen furnished (+)-valerane **2**, $[\alpha]_D^{26} +88$ (*c* 0.5, CHCl_3) [lit.,⁴ⁱ $+76$ (*c* 5, CHCl_3)]. The ^1H and ^{13}C NMR spectral data of (+)-valerane **2** obtained in this study were found to be identical with those reported^{5j} in the literature.

To overcome the regiochemical problems, an alternative strategy was explored, Scheme 4. It was anticipated that intramolecular cyclopropanation of the diazo ketone derived from the acid **19** would generate the tricyclic ketone **20**, which could be transformed into valerane **2** via reductive cyclopropane ring cleavage, catalytic hydrogenation, and reductive deoxygenation of the resulting valerane-3-one. The acid **19** could be generated by homologation of the γ,δ -unsaturated aldehyde **21**, which could be obtained from the ester **9**.

The synthetic sequence is depicted in Scheme 5. Reduction of the ester **9** with LAH furnished the primary alcohol **22**, which on oxidation with PCC and silica gel furnished the aldehyde **21**. Reaction of the aldehyde **21** with methoxymethylene(triphenyl)phosphorane followed by treatment of the resulting Wittig product **23** with Jones reagent in acetone generated the acid **19** in 60% overall yield. The structure of the acid **19** was established from the spectral data of the corresponding methyl ester **19a**,[‡] obtained via diazomethane esterification. Reaction of the

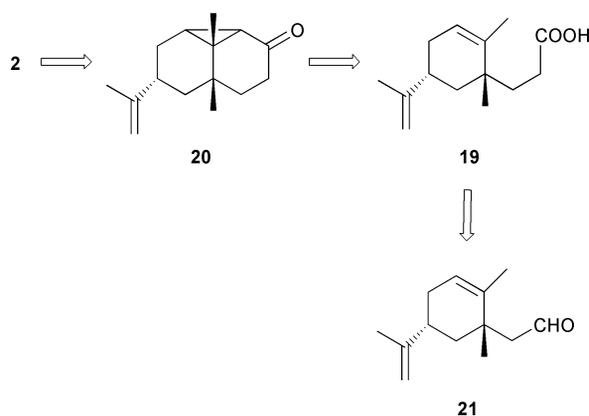
[‡] Subsequently, the ester **19a** was also obtained by photolysis (Hanovia 450 W medium pressure mercury vapour lamp, pyrex filter) of the diazo ketone **10** in methanol for 15 min, in 75% yield.

acid **19** with oxalyl dichloride generated the corresponding acid chloride, which on treatment with an excess of ethereal diazomethane furnished the diazo ketone **24**. Reaction of the diazo ketone **24** with anhydrous copper(II) sulfate and copper in refluxing cyclohexane, as anticipated, furnished the tricyclic ketone **20**, in 51% overall yield from the acid **19**, *via* stereo- and regioselective insertion of the resulting keto carbenoid in the cyclohexene double bond. Lithium in liquid ammonia-mediated regioselective reductive cyclopropane ring cleavage transformed the tricyclic ketone **20** into (+)-valer-11-en-3-one **25**, which on hydrogenation employing 10% Pt on carbon as the catalyst furnished (+)-valeran-3-one **26**. Reaction of the ketone **26** with ethane-1,2-dithiol and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in benzene generated the dithioketal **27** in 95% yield. Desulfurisation of the dithioketal **27** with Raney nickel in refluxing ethanol furnished (+)-valerane **2**, $[\alpha]_{\text{D}}^{25} +72$ (*c* 1, CHCl_3) [lit.^{4f} +76 (*c* 5, CHCl_3)], which exhibited ^1H and ^{13}C NMR spectra identical with those of the authentic sample.

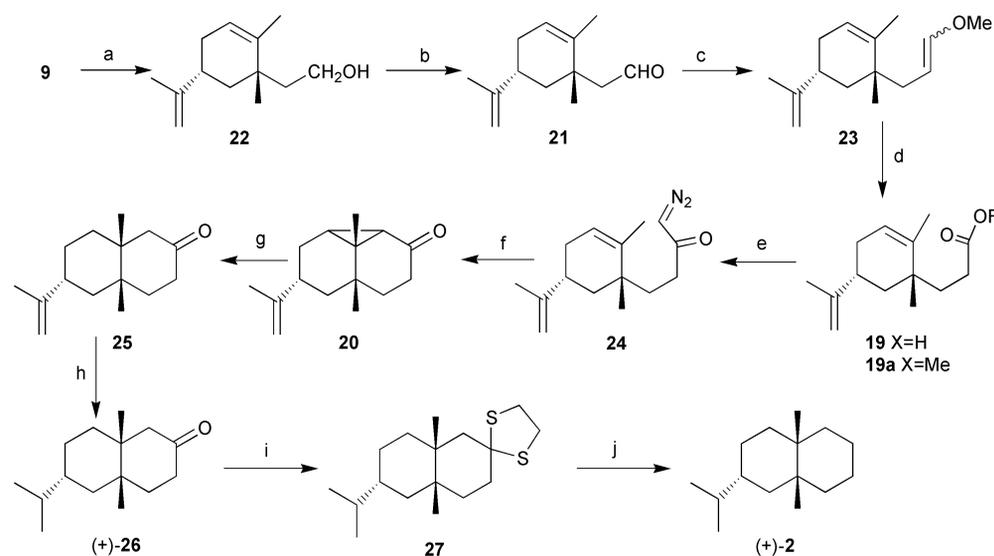
In conclusion, two routes for the enantiospecific total synthesis of (+)-valerane **2** starting from (*R*)-carvone have been achieved. The two quaternary carbon atoms were created in a highly regio- and stereoselective manner employing an ortho-ester Claisen rearrangement and intramolecular diazo ketone cyclopropanation reaction, respectively.

Experimental

Mps were recorded using a Tempo melting point apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer 781 and Hitachi 270-50 spectrophotometers. ^1H (90, 200, 270, 300



Scheme 4



Scheme 5 Reagents and yields: a) LiAlH_4 , 90%; b) PCC, 95%; c) $\text{MeOCH}=\text{PPh}_3$; d) Jones reagent, 60% from **21**; e) i) $(\text{COCl})_2$; ii) CH_2N_2 ; f) $\text{Cu}-\text{CuSO}_4$, 51% from acid **19**; g) $\text{Li}-\text{liq. NH}_3$, 55%; h) H_2 , 10% Pt-C, 98%; i) $(\text{CH}_2\text{SH})_2$, $\text{BF}_3 \cdot \text{Et}_2\text{O}$, 95%; j) Raney Ni, 82%.

and 400 MHz) and ^{13}C NMR (22.5, 50, 67.5, 77.5 and 100 MHz) spectra were recorded on Varian T-60, Hitachi R-1500, JEOL FX-90Q and JNM λ -300, Bruker ACF-200, WH-270 and AMX-400 spectrometers. The chemical shifts (δ/ppm) and the coupling constants (J/Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for ^1H) or the central line (δ_{C} 77.1) of CDCl_3 (for ^{13}C). Low- and high-resolution mass measurements were carried out with a JEOL JMS-DX 303 GC-MS instrument using a direct-inlet mode. Relative intensities of the ions are given in parentheses. Elemental analyses were carried out using a Carlo Erba 1106 CHN analyser. Optical rotations were measured using a JASCO DIP-370 digital polarimeter; $[\alpha]_{\text{D}}$ values are given in units of $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$. Ozonolysis was carried out using a Penwalt Wallace and Tierman ozonator. Hydrogenation reactions were carried out using a balloon. All solvent evaporations were carried out using a Buchi rotary evaporator. Analytical TLC was performed on glass plates (7.5×2.5 and 7.5×5.0 cm) coated with Acme's silica gel G containing 13% calcium sulfate as binder, and various combinations of ethyl acetate and hexane were used as the developer. Acme's silica gel (100–200 mesh) was used for column chromatography. All small-scale dry reactions were carried out using standard syringe-septum techniques. Low-temperature reactions were conducted in a bath made of ethanol and liquid nitrogen.

(1*S*,5*S*)-5-Isopropenyl-2,3-dimethyl-cyclohex-2-en-1-ol (3-methylcaveol) **6**

To a magnetically stirred, cold (-70°C) solution of β -methylcarvone **8** (500 mg, 3.05 mmol) in dry diethyl ether (15 ml) was added LiAlH_4 (60 mg, 1.6 mmol). The reaction mixture was stirred at the same temperature for 2 h and allowed to attain RT over a period of 30 min. The reaction was quenched first with wet diethyl ether and then with dil. aq. HCl. It was then extracted with diethyl ether (3×10 ml) and the combined ethereal extract was washed successively with saturated aq. NaHCO_3 and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column, using CH_2Cl_2 as eluent, furnished the alcohol **6** (480 mg, 95%) as a low melting hygroscopic solid, which was recrystallised from hexanes, mp 56°C ; $[\alpha]_{\text{D}}^{25} +45.0$ (*c* 2, CHCl_3); ν_{max} (neat) 3340, 1640, 890 cm^{-1} ; δ_{H} (90 MHz; CDCl_3) 4.72 (2 H, s, $\text{C}=\text{CH}_2$), 4.15 (1 H, m, OCH), 1.82–2.40 (6 H, m), 1.74 (6 H, s) and 1.66 (3 H, s) (3 \times olefinic CH_3); δ_{C} (22.5 MHz; CDCl_3) 149.1 (s), 128.8 (s), 128.6 (s), 108.9 (t), 71.7 (d), 39.8 (d), 38.1 (t), 37.5 (t), 20.6 (q), 19.3 (q), 14.2 (q); m/z 166 (M^+ , 6%), 151 (18), 148 (25), 133 (25),

121 (80), 122 (100), 107 (70), 98 (55); HRMS m/z Calc. for $C_{11}H_{18}O$: M , 166.1358. Found: M^+ , 166.1352.

(1*S*,5*R*)-5-Isopropenyl-1,2-dimethylcyclohex-2-enylacetic acid 5

A solution of the allyl alcohol **6** (700 mg, 4.22 mmol), triethyl orthoacetate (3.8 ml, 21 mmol) and a catalytic amount (≈ 5 μ l) of propionic acid was placed in a sealed tube and heated to 160 °C for 5 days in an oil-bath. The reaction mixture was cooled, diluted with diethyl ether (25 ml), washed with 0.5 M aq. HCl followed by saturated aq. $NaHCO_3$ and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the ester **9** (800 mg, 80%) as an oil, $[\alpha]_D^{25} -20.0$ (c 2, $CHCl_3$); ν_{max} (neat) 1735, 1650, 885 cm^{-1} ; δ_H (90 MHz; $CDCl_3$) 5.41 (1 H, br s, C=CH), 4.72 (2 H, s, C=CH₂), 4.12 (2 H, q, J 7.2, OCH_2CH_3), 2.45 and 2.38 (2 H, AB q, J 14, $CH_2C=O$), 1.30–2.50 (5 H, m), 1.73 (3 H, s) and 1.66 (3 H, s) ($2 \times$ olefinic CH_3), 1.26 (3 H, t, J 7.2, OCH_2CH_3), 1.18 (3 H, s, *tert*- CH_3).

To a magnetically stirred solution of the ester **9** (500 mg, 2.1 mmol) in methanol (4 ml) was added 10% aq. NaOH (4 ml) and the reaction mixture was refluxed for 6 h. The solvent was evaporated under reduced pressure, and the residue was taken in water (10 ml) and washed with CH_2Cl_2 (2×5 ml). The aqueous phase was acidified with 3 M aq. HCl and extracted with CH_2Cl_2 (3×10 ml). The organic extract was then washed with water (10 ml) followed by brine and dried (Na_2SO_4). Evaporation of the solvent furnished the acid **5** (350 mg, 79%), which was recrystallised from a mixture of CH_2Cl_2 –hexane, mp 58 °C; $[\alpha]_D^{26} -30.0$ (c 2, $CHCl_3$); ν_{max} (neat) 3000, 1705, 1650, 890 cm^{-1} ; δ_H (90 MHz; $CDCl_3$) 5.42 (1 H, m, C=CH), 4.68 (2 H, s, C=CH₂), 2.42 (2 H, s, $CH_2C=O$), 1.30–2.50 (6 H, m), 1.72 (3 H, s) and 1.67 (3 H, s) ($2 \times$ olefinic CH_3), 1.17 (3 H, s, *tert*- CH_3). δ_C (22.5 MHz; $CDCl_3$) 178.4, 149.6, 137.9, 123.1, 108.7, 45.1, 40.4, 38.1, 37.7, 31.1, 26.0, 20.8, 18.5; m/z 208 (M^+ , 25%), 148 (96), 133 (92), 119 (30), 107 (100); HRMS m/z Calc. for $C_{13}H_{20}O_2$: M , 208.1463. Found: M^+ , 208.1454.

(1*R*,2*R*,4*R*,6*S*,9*S*)-4-Isopropenyl-1,6-dimethyltricyclo[4.3.0.0^{2,9}]nonan-8-one 4

A solution of the acid **5** (1.8 g, 8.65 mmol) and oxalyl dichloride (2 ml, 23 mmol) in dry benzene (2 ml) was magnetically stirred for 1 h at RT. Evaporation of benzene and excess of oxalyl dichloride under reduced pressure afforded the acid chloride, which was taken up in dry diethyl ether (10 ml) and added dropwise to a cold magnetically stirred ethereal solution of diazomethane (excess, prepared from 15 g of *N*-methyl-*N*-nitrosourea and 100 ml of 60% aq. KOH). The reaction mixture was stirred for 2 h at RT and the excess of diazomethane and diethyl ether were carefully evaporated on a water bath. Rapid purification by filtration of the product through a neutral alumina column, using CH_2Cl_2 as eluent, furnished the diazo ketone **10** (1.5 g, 75%) as yellow oil, ν_{max} (neat) 2100, 1635, 885 cm^{-1} ; δ_H (90 MHz; $CDCl_3$) 5.41 (1 H, br s, C=CH), 5.22 (1 H, s, CHN_2), 4.70 (2 H, s, C=CH₂), 2.36 (2 H, s, $CH_2C=O$), 1.50–2.30 (5 H, m), 1.72 (3 H, s) and 1.69 (3 H, s) ($2 \times$ olefinic CH_3), 1.14 (3 H, s, *tert*- CH_3).

To a magnetically stirred, refluxing (using two 100 W tungsten lamps) suspension of anhydrous copper(II) sulfate (6 g) in dry cyclohexane (125 ml) was added, dropwise, a solution of the diazo ketone **10** (1.5 g, 6.47 mmol) in cyclohexane (25 ml) over a period of 30 min. The reaction mixture was refluxed for 4 h, then cooled and the copper sulfate was filtered off using a sintered funnel. Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the cyclopropyl ketone **4** (998 mg, 76%) as oil, $[\alpha]_D^{24} +27.5$ (c 2, $CHCl_3$); ν_{max} (neat) 1710, 1640, 885 cm^{-1} ; δ_H (200 MHz; $CDCl_3$) 4.68 (2 H, s, C=CH₂), 2.38 (1 H, m), 2.19 and 1.97 (2 H, AB q, J 19.8, $CH_2C=O$), 1.50–2.25 (6 H,

m), 1.70 (3 H, s, olefinic CH_3), 1.23 (6 H, s, $2 \times$ *tert*- CH_3); δ_C (22.5 MHz; $CDCl_3$) 212.1 (s), 148.5 (s), 108.7 (t), 54.9 (t), 41.2 (d), 40.2 (d), 36.8 (t), 35.6 (s), 33.4 (s), 28.6 (q), 28.1 (d), 22.6 (t), 20.0 (q), 16.9 (q); m/z 204 (M^+ , 13%), 123 (40), 122 (40), 121 (85), 120 (40), 119 (40) 107 (85), 105 (45), 95 (55), 94 (56), 93 (100); HRMS m/z Calc. for $C_{14}H_{20}O$: M , 204.1514. Found: M^+ , 204.1535.

(1*S*,3*R*,6*R*)-3-Isopropenyl-1,6-dimethylbicyclo[4.3.0]nonan-8-one 11

To magnetically stirred, freshly distilled (over sodium) ammonia (50 ml) in a three-necked flask equipped with a Dewar condenser (cooled with ethanol and liquid nitrogen), was added a solution of the cyclopropyl ketone **4** (300 mg, 1.47 mmol) in dry THF (1.5 ml) followed by freshly cut lithium (41 mg, 5.88 mmol) in small pieces. The resulting blue coloured solution was stirred for 30 min and the reaction was quenched with solid NH_4Cl . After evaporation of ammonia, the residue was taken up in water (15 ml) and extracted with diethyl ether (3×25 ml). The combined extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the ketone **11** (230 mg, 76%) as a colourless oil, $[\alpha]_D^{24} -31.5$ (c 2, $CHCl_3$); ν_{max} (neat) 1735, 1640, 880 cm^{-1} ; δ_H (200 MHz; $CDCl_3$) 4.70 (1 H, s) and 4.67 (1 H, s) (C=CH₂), 2.65 and 1.80 (2 H, AB q, J 18.6, $CH_2C=O$), 2.35 and 2.00 (2 H, AB q, J 18.5, $CH_2C=O$), 1.20–2.25 (7 H, m), 1.71 (3 H, s, olefinic CH_3), 1.13 (3 H, s) and 1.00 (3 H, s) ($2 \times$ *tert*- CH_3); δ_C (22.5 MHz; $CDCl_3$) 218.3, 149.3, 108.4, 52.9, 50.5, 47.8, 41.7, 40.2, 39.6, 32.2, 26.6, 25.5, 20.8, 20.0; m/z 206 (M^+ , 55%), 191 (50), 163 (20), 149 (30), 123 (40), 110 (100), 107 (57), 95 (40), 93 (40); HRMS m/z Calc. for $C_{14}H_{22}O$: M , 206.1671. Found: M^+ , 206.1685.

(1*S*,3*R*,6*R*)-3-Isopropyl-1,6-dimethylbicyclo[4.3.0]nonan-8-one 3

To a magnetically stirred solution of the ketone **11** (390 mg, 1.89 mmol) in dry methanol (3 ml) was added 10% Pd/C (15 mg). The reaction mixture was stirred in an atmosphere of hydrogen, created by evacuative replacement of air using a balloon filled with hydrogen, for 6 h and the catalyst was filtered off. Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the saturated ketone **3** (385 mg, 98%) as a colourless oil, $[\alpha]_D^{23} -29.5$ (c 2, $CHCl_3$); ν_{max} (neat) 1740, 1460, 1405, 1385 cm^{-1} ; δ_H (200 MHz; $CDCl_3$) 2.61 and 1.77 (2 H, 2 d, J 18.7, $CH_2C=O$), 2.35 and 1.97 (2 H, 2 d, J 18.4, $CH_2C=O$), 1.00–1.60 (8 H, m), 1.08 (3 H, s) and 0.97 (3 H, s) ($2 \times$ *tert*- CH_3), 0.85 (6 H, d, J 6.6, CH_3CHCH_3); δ_C (22.5 MHz; $CDCl_3$) 219.0 (s), 53.3 (t), 48.2 (s), 48.0 (t), 40.4 (2 C, t and s), 39.3 (d), 32.5 (2 C, t and d), 25.7 (q), 24.8 (t), 20.3 (q), 19.7 (q), 19.5 (q); m/z 208 (M^+ , 53%), 193 (30), 165 (40), 151 (65), 137 (40), 123 (65), 110 (50), 109 (65), 107 (50), 95 (90), 81 (100); HRMS m/z Calc. for $C_{14}H_{24}O$: M , 208.1827. Found: M^+ , 208.1834.

(1*S*,3*R*,6*R*)-3-Isopropyl-1,6,8-trimethylbicyclo[4.3.0]nonan-8-ol 12

To a freshly prepared, magnetically stirred, ice-cold suspension of methylmagnesium iodide [prepared from magnesium (86 mg, 3.58 mmol) and methyl iodide (0.25 ml, 3.96 mmol)] in dry diethyl ether (5 ml) was added a solution of the ketone **3** (180 mg, 0.87 mmol) in dry diethyl ether (5 ml) over a period of 30 min. The reaction mixture was stirred at RT for 10 h and poured into an ice-cold solution of saturated aq. NH_4Cl . The ether layer was separated and the aqueous phase was extracted with diethyl ether (3×5 ml). The combined ether phases were washed with brine and dried (Na_2SO_4). Evaporation of the solvent, and purification of the residue on a silica gel column, using CH_2Cl_2 as eluent, furnished an $\approx 2:1$ epimeric mixture of

the *tert*-alcohol **12** (165 mg, 85%) as a colourless oil, ν_{\max} (neat) 3350 cm^{-1} ; δ_{H} (200 MHz; CDCl_3 , peaks due to major isomer) 1.00–2.50 (12 H, m), 1.41 (3 H, s, CH_3COH), 0.87 (3 H, s) and 0.85 (3 H, s) ($2 \times \text{tert-CH}_3$), 0.86 (6 H, d, J 6.6, CH_3CHCH_3); δ_{C} (50.0 MHz; $\text{CHCl}_3 + \text{CDCl}_3$, mixture of 2:1 diastereomers) 57.9, 56.9, 52.3, 51.4, 50.4, 43.8, 40.4, 39.8, 39.7, 39.5, 33.6, 33.4, 32.5, 26.1, 25.1, 24.1, 21.2, 20.9, 19.8, 19.4, 19.6; m/z 224 (M^+ , 2%), 206 (12), 191 (100), 181 (27), 163 (55), 151 (65), 123 (55), 121 (40), 109 (58), 107 (60), 95 (68); HRMS m/z Calc. for $\text{C}_{15}\text{H}_{28}\text{O}$: M , 224.2140. Found: M^+ , 224.2136.

(1S,3R,6R)-3-Isopropyl-1,6,8-trimethylbicyclo[4.3.0]non-7-ene and (1R,4R,6S)-4-isopropyl-1,6,8-trimethylbicyclo[4.3.0]non-7-ene 13

To a magnetically stirred solution of the epimeric mixture of the *tert*-alcohol **12** (200 mg, 0.89 mmol) in benzene (2 ml) was added PTSA (10 mg) and the reaction mixture was refluxed for 5 h, cooled, diluted with diethyl ether (15 ml) and washed successively with saturated aq. NaHCO_3 and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column, using hexane as eluent, furnished a 3:2 mixture of the alkenes **13** (180 mg, 98%) as a colourless oil, ν_{\max} (neat) 1450, 1380, 1365, 815 cm^{-1} ; δ_{H} (270 MHz; CDCl_3) 5.05 and 5.11 (1 H, s, olefinic H), 2.28 and 2.48 (1 H, AB q, J 15), 1.65 (3 H, s, olefinic CH_3), 1.00–1.80 (9 H, m), 0.98 and 0.91 (3 H, s) and 0.77 and 0.85 (3 H, s) ($2 \times \text{tert-CH}_3$), 0.82 (3 H, d, J 6.5) and 0.81 (3 H, d, J 6.5) (CH_3CHCH_3); δ_{C} (50.0 MHz; $\text{CHCl}_3 + \text{CDCl}_3$, a 3:2 mixture of olefin isomers) 135.8, 135.3, 51.7, 47.9, 47.3, 43.8, 42.2, 41.7, 39.7, 38.3, 34.4, 33.8, 32.5, 32.2, 29.5, 26.6, 25.9, 24.6, 20.2, 19.7, 19.5, 19.4, 19.3, 17.1, 16.9; m/z 206 (M^+ , 10%), 191 (18), 163 (10), 151 (10), 135 (12), 121 (20), 107 (20), 95 (20), 40 (100).

(1S,6R,9R)-9-Isopropyl-1,6-dimethylbicyclo[4.4.0]dec-4-en-3-one 16 and (1R,6S,8R)-8-Isopropyl-1,6-dimethylbicyclo[4.4.0]dec-4-en-3-one 17

Dry ozone in oxygen gas was passed through a cold (-70°C) suspension of the alkene **13** (262 mg, 1.27 mmol) and NaHCO_3 (10 mg) in 1:5 methanol– CH_2Cl_2 (5 ml) until the reaction mixture turned blue in colour. Excess of ozone was flushed off with oxygen. Triphenylphosphine (400 mg, 1.52 mmol) was added, and the reaction mixture was allowed to attain RT and was magnetically stirred for 4 h. Evaporation of the solvent and rapid purification of the product on a silica gel column, using ethyl acetate–hexane (1:20) as eluent, furnished a 2:1 mixture of the keto aldehydes **14** and **15** (249 mg, 83%) as an oil, ν_{\max} (neat) 1710 cm^{-1} ; δ_{H} (90 MHz; CDCl_3 , 2:1 mixture of **14** and **15**) 9.72 and 9.79 (1 H, s, CHO), 2.20–3.60 (2 H, m, $\text{CH}_2\text{C=O}$), 2.12 and 2.15 (3 H, s, $\text{CH}_3\text{C=O}$), 1.00–2.00 (8 H, m), 1.18 and 1.14 (3 H, s) and 1.15 and 0.98 (3 H, s) ($2 \times \text{tert-CH}_3$), 0.90 (3 H, d, J 6.7) and 0.88 (3 H, d, J 6.7) ($\text{CH}_3\text{CH-CH}_3$).

To a solution of a mixture of the keto aldehydes **14** and **15** (250 mg, 1.05 mmol) in dry THF (2 ml) was added 1 M KOH in methanol (1.05 ml, 1.05 mmol) and the reaction mixture was stirred at RT for 12 h. The solvent was evaporated under reduced pressure, and the residue was taken up in water (3 ml) and extracted with diethyl ether (3×5 ml). The combined extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:20) as eluent, furnished a 2:1 mixture of the enones **16** and **17** (115 mg, 50% from alkene **13**) as an oil, ν_{\max} (neat) 1670 cm^{-1} ; δ_{H} (200 MHz; CDCl_3 , a 2:1 mixture of **16** and **17**) 6.53 and 6.48 (1 H, d, J 10.0, CH=CHC=O), 5.91 and 5.86 (1 H, d, J 10.0, CH=CHC=O), 2.58 and 2.02 (AB q, J 16.9) and 2.88 and 1.81 (AB q, J 16.3) (2 H, $\text{CH}_2\text{C=O}$), 0.95–1.70 (8 H, m), 1.10 and 0.89 (3 H, s) and 1.05 (3 H, s) ($2 \times \text{tert-CH}_3$), 0.87 (3 H, d, J 6.4) and 0.80 (3 H, d, J 6.4) ($2 \times \text{CH}_3\text{CHCH}_3$); δ_{C} (67.5 MHz; CDCl_3) 200.9, 200.0, 160.3, 158.9, 127.6, 125.7, 49.3, 48.8, 47.3, 46.5, 41.0,

39.9, 39.4, 38.8, 38.5, 38.1, 36.3, 35.8, 34.9, 32.6, 26.8, 25.0, 24.0, 23.3, 22.9, 22.1, 21.2, 19.8, 19.6; m/z 220 (M^+ , 3%), 191 (100), 135 (25), 122 (35), 121 (55), 109 (40), 108 (55), 107 (50), 93 (30); HRMS m/z Calc. for $\text{C}_{15}\text{H}_{24}\text{O}$: M , 220.1827. Found: M^+ , 220.1836.

(1R,3R,6S)-3-Isopropyl-1,6-dimethylbicyclo[4.4.0]decane [(+)-valerane] 2

To a magnetically stirred solution of a mixture of the enones **16** and **17** (50 mg, 0.23 mmol) and boron trifluoride–diethyl ether (0.1 ml, 0.68 mmol) in 0.5 ml of dry THF was added sodium cyanoborohydride (43 mg, 0.68 mmol) and the mixture was refluxed for 10 min. The reaction mixture was cooled, quenched with saturated aq. NaHCO_3 , and extracted with diethyl ether (3×5 ml). The solvent was carefully evaporated and the product was purified on a silica gel column with hexane as eluent to furnish a mixture of the alkenes **18** (42 mg, 89%) as an oil, ν_{\max} (neat) 1460, 1365, 1020 cm^{-1} ; δ_{H} (400 MHz; CDCl_3) 5.48–5.60 (1 H, m), 5.20–5.32 (1 H, m), 0.85–2.20 (12 H, m), 0.80–0.90 (12 H, m, $4 \times \text{CH}_3$).

Hydrogenation of a mixture of the alkenes **18** (20 mg, 0.09 mmol) in dry methanol (0.3 ml), using 10% Pd/C (5 mg) as catalyst for 10 h, as described for compound **3**, and careful purification of the product on a silica gel column, using hexane as eluent, furnished valerane **2** (17 mg, 84%) as a colourless oil.^{4i,5j} $[\alpha]_{\text{D}}^{25} + 88.0$ (c 0.5, CHCl_3), $+60.0$ (c 0.3, CH_3OH) [lit.,⁴ⁱ $+76.0$ (c 5, CHCl_3)]; ν_{\max} (neat) 1470, 1450, 1390, 1370 cm^{-1} ; δ_{H} (400 MHz; CDCl_3) 0.98–2.00 (16 H, m), 0.86 (3 H, s, *tert-CH*₃), 0.86 (6 H, d, J 6.54, CH_3CHCH_3), 0.84 (3 H, s, *tert-CH*₃); δ_{C} (100 MHz; CDCl_3) 39.5 (CH), 37.31 (CH_2), 37.28 (CH_2), 37.0 (CH_2), 35.5 (C), 34.9 (C), 33.16 (CH), 33.12 (CH_2), 25.1 (CH_2), 24.8 (CH_3), 23.7 (CH_3), 22.5 (CH_2), 21.9 (CH_2), 20.1 (CH_3), 19.8 (CH_3).

(–)-2-[(1S,5R)-5-Isopropenyl-1,2-dimethylcyclohex-2-enyl]-ethanol 22

To a cold (-70°C), magnetically stirred solution of the ester **9** (3.8 g, 16.1 mmol) in dry diethyl ether (60 ml) was added LiAlH_4 (1.1 g, 28.9 mmol). The reaction mixture was slowly warmed to RT, stirred for 2 h and worked up as described for **6**. Purification of the product over a silica gel column, using ethyl acetate–hexane (1:5 to 1:2.5) as eluent, furnished the alcohol **22** (2.8 g, 90%), $[\alpha]_{\text{D}}^{25} - 19.1$ (c 4.5, CHCl_3); ν_{\max} (neat) 3420, 1635, 880 cm^{-1} ; δ_{H} (90 MHz; CDCl_3) 5.30–5.50 (1 H, m, C=CH), 4.72 (2 H, s, C=CH_2), 3.50–3.80 (2 H, m, CH_2OH), 1.45–2.40 (7 H, m), 1.75 (3 H, s) and 1.68 (3 H, s) ($2 \times$ olefinic CH_3), 1.47 (1 H, s, OH), 1.09 (3 H, s, *tert-CH*₃); δ_{C} (22.5 MHz; CDCl_3) 149.2 (s), 138.4 (s), 122.5 (d), 108.2 (t), 58.5 (t), 42.7 (t), 40.3 (t), 37.4 (d), 37.1 (s), 31.0 (t), 26.4 (q), 20.5 (q), 18.1 (q); m/z 194 (M^+ , 14%), 149 (50), 133 (26), 121 (64), 107 (100), 93 (82); HRMS m/z for $\text{C}_{13}\text{H}_{22}\text{O}$: M , 194.1671. Found: M^+ , 194.1672.

(1S,5R)-(5-Isopropenyl-1,2-dimethylcyclohex-2-enyl)acetaldehyde 21

To a magnetically stirred suspension of PCC (750 mg, 3.5 mmol) and silica gel (750 mg) in CH_2Cl_2 (2 ml) was added a solution of the alcohol **22** (370 mg, 1.90 mmol) in CH_2Cl_2 in one portion. The reaction mixture was stirred at RT for 2 h, filtered through a silica gel column, and the column was eluted with more CH_2Cl_2 . The solvent was evaporated to furnish the aldehyde **21** (350 mg, 95%) as oil, $[\alpha]_{\text{D}}^{21} - 31.8$ (c 0.88, CHCl_3); ν_{\max} (neat) 2740, 1715, 1645, 885 cm^{-1} ; δ_{H} (300 MHz; CDCl_3) 9.67 (1 H, dd, J 3.7 and 2.4, CH=O), 5.50 (1H, br s), 4.73 (1 H, s) and 4.70 (1 H, s) (C=CH_2), 2.52 (1 H, dd, J 15.6 and 4.2) and 2.26 (1 H, dd, J 15.3 and 3.7) ($\text{CH}_2\text{C=O}$), 2.10–1.50 (5 H, m), 1.73 (3 H, s) and 1.70 (3H, s) ($2 \times$ olefinic CH_3), 1.08 (3 H, *tert-CH*₃); δ_{C} (75 MHz; CDCl_3 , DEPT) 203.8 (CH), 149.3 (C), 137.0 (C), 124.3 (CH), 108.9 (CH_2), 53.0 (CH_2), 41.7 (CH_2), 37.7 (C),

37.4 (CH), 31.2 (CH₂), 26.6 (CH₃), 20.8 (CH₃), 18.6 (CH₃); *m/z*: 192 (M⁺, 4%), 149 (20), 148 (18), 133 (30), 121 (30), 107 (100), 93 (30).

3-[(1*R*,5*R*)-5-Isopropenyl-1,2-dimethylcyclohex-2-enyl]propionic acid **19**

To a magnetically stirred solution of methoxymethyl(triphenyl)phosphonium chloride (2.8 g, 8.18 mmol) in dry THF (2 ml) at RT was added potassium *tert*-amylate (1 g, 8.18 mmol) in THF (2 ml) and the resulting red-coloured solution was stirred at RT for 5 min. To the methoxymethylene(triphenyl)phosphorane thus formed was added a solution of the aldehyde **21** (350 mg, 1.82 mmol) in THF (1 ml) and the mixture was stirred for 30 min. The reaction mixture was then diluted with diethyl ether (10 ml), washed with brine and dried (Na₂SO₄). Evaporation of the solvent furnished the enol ether **23**, which was taken up in acetone (3 ml) and treated with freshly prepared Jones reagent (1.6 M; 3 ml, 4.8 mmol). The reaction mixture was stirred at RT for 1 h. Excess of reagent was consumed by adding a few drops of propan-2-ol and the mixture was then extracted with diethyl ether. The extract was washed with brine and dried (Na₂SO₄). Evaporation of the solvent furnished the acid **19** (243 mg, 60% from aldehyde **21**).

A solution of the acid **19** (50 mg, 0.22 mmol) in diethyl ether was added to a cold, magnetically stirred, ethereal solution of diazomethane (excess, prepared from 0.5 g of *N*-methyl-*N*-nitrosourea and 5 ml of 60% aq. KOH). The reaction mixture was stirred for 2 h at RT and the excess of diazomethane and diethyl ether were carefully evaporated on a water-bath. Filtration on a silica gel column furnished the ester **19a** (42 mg, 88%) as a colorless oil, [α]_D²² -20.1 (*c* 1.0, CHCl₃); ν_{\max} (neat) 1735, 1635, 1170, 885 cm⁻¹; δ_{H} (300 MHz; CDCl₃ + CCl₄) 5.43 (1 H, d, *J* 5.4), 4.69 (1 H, s) and 4.67 (1 H, s) (C=CH₂), 3.65 (3 H, s, OCH₃), 2.40–1.30 (9 H, series of m), 1.72 (3 H, s, olefinic CH₃), 1.60 (3 H, d, *J* 1.2, olefinic CH₃), 1.08 (3 H, s, *tert*-CH₃); δ_{C} (75 MHz; CDCl₃ + CCl₄) 174.4 (C), 149.6 (C), 138.2 (C), 124.0 (CH), 108.9 (CH₂), 51.5 (CH₃), 39.9 (CH₂), 38.3 (C), 37.8 (CH), 35.2 (CH₂), 31.5 (CH₂), 29.4 (CH₂), 26.7 (CH₃), 21.0 (CH₃), 18.4 (CH₃); *m/z* 237 (M + 1, 4%), 205 (10), 149 (20), 121 (20), 121 (20), 107 (60), 49 (100).

(1*R*,2*S*,6*R*,8*R*,10*R*)-8-Isopropenyl-1,6-tricyclo[4.4.0.0^{2,10}]decan-3-one **20**

A solution of the acid **19** (300 mg, 1.35 mmol) and oxalyl dichloride (0.5 ml, 5.75 mmol) in dry benzene (1 ml) was magnetically stirred for 2 h at RT. Evaporation of both benzene and oxalyl dichloride under reduced pressure afforded the acid chloride, which was taken up in dry diethyl ether (1 ml) and added dropwise to a cold, magnetically stirred, ethereal solution of diazomethane (excess, prepared from 1.5 g of *N*-methyl-*N*-nitrosourea and 15 ml of 60% aq. KOH). The reaction mixture was stirred for 2 h at RT and the excess of diazomethane and diethyl ether were carefully evaporated on a water-bath. Rapid purification by filtration of the product through a neutral alumina column, using CH₂Cl₂ as eluent, furnished the diazo ketone **24** as yellow oil.

To a magnetically stirred suspension of copper powder (450 mg, 7.1 mmol) and anhydrous copper(II) sulfate (75 mg, 0.33 mmol) in dry cyclohexane (25 ml) was added, dropwise, a solution of the diazo ketone **24** (300 mg) in cyclohexane (2 ml) and the reaction mixture was refluxed for 2 h. It was then cooled, and filtered through a sintered funnel. Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the cyclopropyl ketone **20** (150 mg, 51% from acid **19**) as oil, [α]_D²³ +105 (*c* 1.8, CHCl₃); ν_{\max} (neat) 1690, 1635, 885 cm⁻¹; δ_{H} (300 MHz; CDCl₃ + CCl₄) 4.67 (1 H, s) and 4.61 (1 H, s) (C=CH₂), 2.35–1.80 (4 H, m), 1.67 (3 H, s, olefinic CH₃), 1.60–0.90 (7 H, series of m), 1.24 (3 H, s) and 1.11 (3 H, s) (2 × *tert*-CH₃); δ_{C} (75

MHz; CDCl₃ + CCl₄) 210.7 (C), 148.7 (C), 109.4 (CH₂), 39.9 (CH₂), 39.7 (CH), 38.4 (CH₂), 37.3 (CH₂), 33.4 (CH), 31.1 (C), 29.9 (CH), 29.6 (CH₃), 26.3 (CH₂), 24.6 (C), 24.2 (CH₃), 21.0 (CH₃); *m/z* 219 (M + 1, 12%), 203 (11), 161 (20), 147 (25), 133 (30), 121 (50), 119 (40), 109 (55), 106 (50), 107 (80), 105 (50), 93 (100); HRMS *m/z* Calc. for C₁₅H₂₂O: *M*, 218.1670. Found: M⁺, 218.1649.

(1*R*,6*R*,8*R*)-8-Isopropenyl-1,6-dimethylbicyclo[4.4.0]decan-3-one **25**

To magnetically stirred, freshly distilled (over sodium) ammonia (30 ml) in a three-necked flask equipped with a Dewar condenser, was added a solution of the cyclopropyl ketone **20** (140 mg, 0.64 mmol) in dry THF (1 ml) followed by freshly cut lithium (30 mg, 4.3 mmol), in small pieces. The resulting blue-coloured solution was stirred for 15 min and the reaction was quenched with solid NH₄Cl. After evaporation of the ammonia, the residue was taken up in water (5 ml) and extracted with diethyl ether (3 × 5 ml). The combined extract was washed with brine and dried (Na₂SO₄). Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the ketone **25** (77 mg, 55%) as a colourless oil, [α]_D²³ +47.5 (*c* 1.6, CHCl₃); ν_{\max} (neat) 1705, 1635, 885 cm⁻¹; δ_{H} (300 MHz; CDCl₃ + CCl₄) 4.71 (2 H, s, C=CH₂), 2.87 (1 H, d, *J* 14.1), 2.49 (1 H, d t, *J* 14.6 and 6.9), 2.35–2.10 (2 H, m), 2.05–1.85 (2 H, m), 1.75–1.10 (7 H, m), 1.75 (3 H, s, olefinic CH₃), 1.02 (3 H, s) and 0.86 (3 H, s) (2 × *tert*-CH₃); δ_{C} (75 MHz; CDCl₃ + CCl₄) 212.1 (C), 149.7 (C), 108.9 (CH₂), 49.1 (CH₂), 40.7 (C), 40.1 (CH), 38.4 (CH₂), 37.9 (CH₂), 37.7 (CH₂), 36.2 (CH₂), 35.7 (C), 27.0 (CH₂), 24.0 (CH₃), 23.5 (CH₃), 21.3 (CH₃); *m/z* 220 (M⁺, 10%), 149 (15), 123 (20), 109 (20), 107 (35), 95 (45), 41 (100); HRMS *m/z* Calc. for C₁₅H₂₄O: *M*, 220.1827. Found: M⁺, 220.1823.

(1*R*,6*R*,8*R*)-8-Isopropyl-1,6-dimethylbicyclo[4.4.0]decan-3-one **26**

To a magnetically stirred solution of the ketone **25** (50 mg, 0.22 mmol) in dry ethanol (1 ml) was added 10% Pt/C (10 mg). The reaction mixture was stirred in an atmosphere of hydrogen, created by evacuative replacement of air using a balloon filled with hydrogen, for 12 h and the catalyst was filtered off. Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished valeran-3-one **26** (49 mg, 98%) as a colourless oil, [α]_D²³ +28.1 (*c* 1.6, CHCl₃); ν_{\max} (neat) 1700 cm⁻¹; δ_{H} (300 MHz; CDCl₃ + CCl₄) 2.83 (1 H, d, *J* 14), 2.46 (1 H, d t, *J* 14.3 and 6.9), 2.18 (1 H, m d, *J* 14.7), 1.92 (1 H, d t, *J* 14 and 5.1), 1.72 (1 H, t, *J* 12.4), 1.64 (1 H, dd, *J* 14 and 2.5), 1.70–1.30 (8 H, m), 0.97 (3 H, s) and 0.84 (3 H, s) (2 × *tert*-CH₃), 0.90 (6 H, d, *J* 6.2, 2 × *sec*-CH₃); δ_{C} (75 MHz; CDCl₃ + CCl₄) 212.5 (C), 49.1 (CH₂), 40.7 (C), 39.1 (CH), 38.0 (CH₂), 37.9 (CH₂), 36.9 (CH₂), 36.3 (CH₂), 35.5 (C), 33.2 (CH), 25.4 (CH₂), 24.0 (CH₃), 23.6 (CH₃), 20.2 (CH₃), 19.9 (CH₃); *m/z* 222 (M⁺, 8%), 151 (40), 149 (30), 123 (40), 121 (35), 111 (40), 109 (60), 107 (40), 97 (50), 95 (90).

(1*R*,6*R*,8*R*)-3,3-Ethylenedithio-8-isopropyl-1,6-dimethylbicyclo[4.4.0]decane **27**

To an ice-cold, magnetically stirred solution of the ketone **26** (30 mg, 0.13 mmol) and ethane-1,2-dithiol (0.7 ml, 8.3 mmol) in benzene (1 ml) was added a catalytic amount of boron trifluoride–diethyl ether. The reaction mixture was stirred at RT for 1 h, diluted with diethylether (5 ml), washed successively with 5% aq. NaOH and brine, and dried (Na₂SO₄). Evaporation of the solvent and purification of the product on a silica gel column, using ethyl acetate–hexane (1:40) as eluent, furnished the thioether **27** (38 mg, 95%) as colourless oil, [α]_D²⁴ 50.0 (*c* 1.0, CHCl₃); ν_{\max} (neat) 1450, 1430, 1380, 1365, 1270 cm⁻¹; δ_{H} (300 MHz; CDCl₃ + CCl₄) 3.40–3.20 (4 H, m, SCH₂CH₂S), 2.60 (1 H, d, *J* 14.3), 2.12 (1 H, d t, *J* 14.4 and 3.5), 1.95–1.80 (2 H,

m), 1.60–1.00 (10 H, m), 1.03 (3 H, s) and 0.87 (3H, s) ($2 \times$ *tert*-CH₃), 0.86 [6 H, d, J 5.7, CH(CH₃)₂]; δ_C (75 MHz; CDCl₃ + CCl₄) 68.1 (C), 46.4 (CH₂), 39.8 (CH₂), 39.7 (CH₂), 39.3 (CH), 37.5 (CH₂), 37.1 (CH₂), 36.9 (2 C, C and CH₂), 36.3 (CH₂), 34.8 (C), 33.0 (CH), 25.7 (CH₃), 25.4 (CH₂), 24.3 (CH₃), 20.2 (CH₃), 19.9 (CH₃); m/z 298 (M⁺, 25%), 283 (24), 152 (25), 131 (25), 109 (50), 47 (100); HRMS m/z Calc. for M, C₁₇H₃₀S₂: 298.1788. Found: M⁺, 298.1788.

(1*R*,3*R*,6*S*)-3-Isopropyl-1,6-dimethylbicyclo[4.4.0]decane [(+)-valerane] 2

A magnetically stirred solution of the thioketal **27** (40 mg, 0.13 mmol) and Raney nickel (30 mg) in dry ethanol (3 ml) was refluxed for 8 h. The reaction mixture was cooled and filtered through a silica gel column. Evaporation of the solvent furnished valerane **2** (23 mg, 82%) as colourless oil, $[\alpha]_D^{26} +72$ (c 1, CHCl₃) [lit.,⁴ⁱ +76 (c 5, CHCl₃)], which was identified by comparison of the ¹H and ¹³C NMR spectra with those of the sample prepared above.

Acknowledgements

We thank the Council of Scientific and Industrial Research, New Delhi for financial support and for the award of a research fellowship to C. D., and the University Grants Commission for the award of a research fellowship to R. V. We are grateful to Dr M. Vairamani, I.I.C.T., Hyderabad for providing HRMS for some of the compounds.

References

- B. M. Fraga, *Nat. Prod. Rep.*, 1985, **2**, 147; B. M. Fraga, *Nat. Prod. Rep.*, 1986, **3**, 273; B. M. Fraga, *Nat. Prod. Rep.*, 1987, **4**, 473; B. M. Fraga, *Nat. Prod. Rep.*, 1988, **5**, 497; B. M. Fraga, *Nat. Prod. Rep.*, 1990, **7**, 61; B. M. Fraga, *Nat. Prod. Rep.*, 1992, **9**, 217, 557; B. M. Fraga, *Nat. Prod. Rep.*, 1993, **10**, 397; B. M. Fraga, *Nat. Prod. Rep.*, 1994, **11**, 533; B. M. Fraga, *Nat. Prod. Rep.*, 1995, **12**, 303; B. M. Fraga, *Nat. Prod. Rep.*, 1996, **13**, 307; B. M. Fraga, *Nat. Prod. Rep.*, 1997, **14**, 145; B. M. Fraga, *Nat. Prod. Rep.*, 1998, **15**, 73; B. M. Fraga, *Nat. Prod. Rep.*, 1999, **16**, 21, 711.
- (a) C. H. Heathcock, *The Total Synthesis of Natural Products*, ed. J. Apsimon, Wiley, New York, 1973, vol. 2; (b) C. H. Heathcock, S. L. Graham, M. C. Pirrung, F. Plavac and C. T. White, *The Total Synthesis of Natural Products*, ed. J. Apsimon, Wiley, New York, 1983, vol. 5.
- (a) von A. Stoll, E. Seebeck and D. Stauffacher, *Helv. Chim. Acta*, 1957, **40**, 1205; (b) T. R. Govindachari, S. Rajadurai and B. R. Pai, *Chem. Ber.*, 1958, **91**, 908; (c) J. Krepinsky, V. Herout and F. Sorm, *Tetrahedron Lett.*, 1960, issue 3, 9; (d) J. Krepinsky, V. Herout and F. Sorm, *Chem. Listy*, 1958, **52**, 1784; J. Krepinsky, V. Herout and F. Sorm, *Collect. Czech. Chem. Commun.*, 1959, **24**, 1884; (e) H. Hikino, Y. Hikino, H. Kato, Y. Takeshita and T. Takemoto, *Yakugaku Zasshi*, 1963, **83**, 219; *Chem. Abstract*, **59**, 3087d; (f) H. Hikino, Y. Hikino, Y. Takeshita, Y. Isurugi and T. Takemoto, *Yakugaku Zasshi*, 1963, **83**, 555; *Chem. Abstract*, **59**, 4971a; (g) H. Hikino, Y. Hikino, Y. Takeshita, H. Kato and T. Takemoto, *Yakugaku Zasshi*, 1965, **85**, 179; *Chem. Abstract*, **62**, 12969f; (h) Y. R. Naves, *Helv. Chim. Acta*, 1963, **46**, 2139; (i) C. S. Narayanan, K. S. Kulkarni, A. S. Vaidya, S. Kanthamani, G. Lakshmi Kumari, B. V. Bapat, S. K. Paknikar, S. N. Kulkarni, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron*, 1964, **20**, 963; (j) H. Hikino, Y. Takeshita, Y. Hikino and T. Takemoto, *Chem. Pharm. Bull.*, 1965, **13**, 631; H. Hikino, Y. Takeshita, Y. Hikino and T. Takemoto, *Chem. Pharm. Bull.*, 1966, **14**, 735; (k) H. Hikino, Y. Hikino and T. Takemoto, *Chem. Pharm. Bull.*, 1963, **11**, 1210.
- (a) D. K. Banerjee, *J. Indian Chem. Soc.*, 1972, **49**, 1; (b) T. R. Govindachari, B. R. Pai, K. K. Purushothaman and S. Rajadurai, *Tetrahedron Lett.*, 1959, issue 15, 5; (c) J. Krepinsky, M. Romanuk, V. Herout and F. Sorm, *Tetrahedron Lett.*, 1960, issue 7, 9; (d) T. R. Govindachari, B. R. Pai, K. K. Purushothaman and S. Rajadurai, *Chem. Ind. (London)*, 1960, 1059; T. R. Govindachari, B. R. Pai, K. K. Purushothaman and S. Rajadurai, *Tetrahedron*, 1961, **12**, 105; (e) C. Djerassi, T. R. Govindachari, B. R. Pai and K. K. Purushothaman, *Tetrahedron Lett.*, 1961, 226; (f) J. Krepinsky, M. Romanuk, V. Herout and F. Sorm, *Tetrahedron Lett.*, 1962, 169; J. Krepinsky, M. Romanuk, V. Herout and F. Sorm, *Collect. Czech. Chem. Commun.*, 1962, **27**, 2638; (g) W. Klyne, *Tetrahedron*, 1961, **13**, 29; (h) H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro and T. Takemoto, *Chem. Pharm. Bull.*, 1963, **11**, 1207; (i) H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro and T. Takemoto, *Chem. Pharm. Bull.*, 1965, **13**, 1408.
- (a) J. A. Marshall, W. I. Fanta and G. L. Bundy, *Tetrahedron Lett.*, 1965, 4807; J. A. Marshall, G. L. Bundy and W. I. Fanta, *J. Org. Chem.*, 1968, **33**, 3913; (b) E. Wenkert and D. A. Berges, *J. Am. Chem. Soc.*, 1967, **89**, 2507; E. Wenkert, D. A. Berges and N. F. Golob, *J. Am. Chem. Soc.*, 1978, **100**, 1263; (c) D. J. Dawson and R. E. Ireland, *Tetrahedron Lett.*, 1968, 1899; (d) T. R. Govindachari, N. Viswanathan, B. R. Pai, P. S. Santhanam and M. Srinivasan, *Indian J. Chem.*, 1968, **6**, 475; (e) P. N. Rao, *J. Org. Chem.*, 1971, **36**, 2426; (f) D. K. Banerjee and V. B. Angadi, *Indian J. Chem.*, 1973, **11**, 511; (g) G. H. Posner, C. E. Whitten, J. J. Sterling and D. J. Brunelle, *Tetrahedron Lett.*, 1974, 2591; G. H. Posner, J. J. Sterling, C. E. Whitten, C. M. Lentz and D. J. Brunelle, *J. Am. Chem. Soc.*, 1975, **97**, 107; (h) S. M. Baldwin and R. E. Gawley, *Tetrahedron Lett.*, 1975, 3969; (i) P. G. Sammes and L. J. Street, *J. Chem. Soc., Chem. Commun.*, 1983, 666; P. G. Sammes, L. J. Street and R. J. Whitby, *J. Chem. Soc., Perkin Trans. 1*, 1986, 281; (j) P. J. Garratt, M. Pielke and J. R. Porter, *Tetrahedron Lett.*, 1987, **28**, 589; (k) G. D. Vite and T. A. Spencer, *J. Org. Chem.*, 1988, **53**, 2560; (l) T. Shono, N. Kise, T. Fujimoto, N. Tominaga and H. Morita, *J. Org. Chem.*, 1992, **57**, 7175; (m) H. Takeshita, Y.-S. Ciu, N. Kato and A. Mori, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 2694; (n) G. Datwani and G. V. Bhide, *Indian J. Chem., Sect. B*, 1993, **32**, 716; (o) A. Srikrishna and R. Viswanjani, *Indian J. Chem., Sect. B*, 1996, **35**, 521; (p) A. Srikrishna and C. Dinesh, *Indian J. Chem., Sect. B*, 2000, **39**, 323; (q) J. G. Jun and B. P. Mundy, *Bull. Korean Chem. Soc.*, 1987, **8**, 489.
- T. L. Ho, *Enantioselective Synthesis. Natural Products from Chiral Terpenes*, Wiley, Chichester, 1992.
- Part of our work has appeared as a preliminary communication: see A. Srikrishna and R. Viswanjani, *Tetrahedron Lett.*, 1996, **37**, 2863.
- A. Srikrishna and P. Hemamalini, *Indian J. Chem., Sect. B*, 1990, **29B**, 152.
- Y.-D. Wu, K. N. Houk, J. Florez and B. M. Trost, *J. Org. Chem.*, 1991, **56**, 3656.
- L. Garver, P. van Eikeren and J. E. Byrd, *J. Org. Chem.*, 1976, **41**, 2773.
- W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T.-T. Li, D. J. Faulkner and M. R. Petersen, *J. Am. Chem. Soc.*, 1970, **92**, 741; W. S. Johnson, T. J. Brocksom, P. Loew, D. H. Rich, L. Werthemann, R. A. Arnold, T.-T. Li and D. J. Faulkner, *J. Am. Chem. Soc.*, 1970, **92**, 4463.
- G. Stork and J. Ficini, *J. Am. Chem. Soc.*, 1961, **83**, 4678; S. D. Burke and P. A. Grieco, *Org. React.*, 1979, **26**, 361; L. N. Mander, *Synlett*, 1991, 134; A. Padwa and K. E. Krumpke, *Tetrahedron*, 1992, **48**, 5385.
- T. Norin, *Acta Chem. Scand.*, 1963, **17**, 738; W. G. Dauben and E. J. Deviny, *J. Org. Chem.*, 1966, **31**, 3794; W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, 1970, **35**, 374; W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, 1970, **35**, 2361; T. Norin, *Acta Chem. Scand.*, 1965, **19**, 1289.
- A. Srikrishna, J. A. Sattigeri, R. Viswanjani and C. V. Yelamaggad, *Synlett*, 1995, 93; A. Srikrishna, R. Viswanjani, J. A. Sattigeri and C. V. Yelamaggad, *Tetrahedron Lett.*, 1995, **36**, 2347.
- Part 45, A. Srikrishna and S. J. Gharpure, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3191; Part 44, A. Srikrishna and D. Vijaykumar, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2583.