Synthesis of Polyoxygenated *trans*-Decalins as Potential Insect Antifeedants

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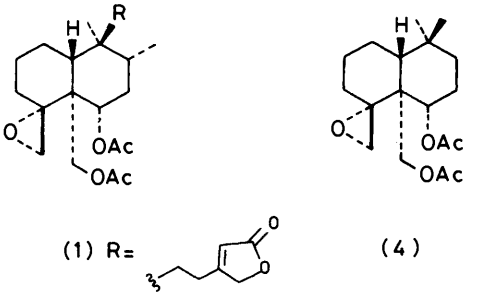
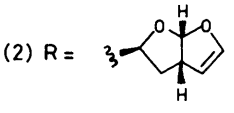
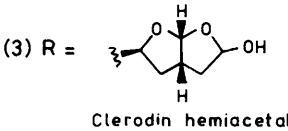
2α,Acetoxy-1α-acetoxymethyl-5,5-dimethyl-1α,6β,10Oα-bicyclo[4.4.0]decane-10-spiro-2'-oxiran (4) has been prepared from 4,4-dimethylcyclohex-2-enone as a model compound in order both to probe the biological activity of, and to develop a synthetic strategy to, a number of clerodane-related insect antifeedants. The *trans*-decalin (4) was shown to inhibit feeding of *Locusta migratoria* at a comparable level to that of the natural product clerodin hemiacetal. Three other related decalin analogues were also synthesised and shown to have negligible antifeedant properties.

ALTHOUGH a large number of natural products containing the diterpene clerodane skeleton are now known,[1] their synthesis, particularly of highly oxygenated derivatives, has attracted attention only recently.[2] Of the various biological activities associated with these molecules, the insect antifeedant properties shown by ajugarin I (1) and



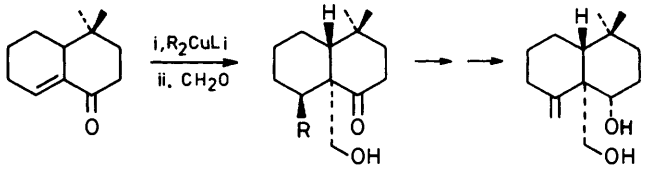




the clerodins (2) and (3) were of special interest to us.[3] Consequently, we have begun a synthetic programme designed both to probe the functionality responsible for biological activity and to develop a strategy which could be applied to the total synthesis of the natural products. Previously, we have described routes to various *cis*-fused clerodin analogues [4] and here we report in detail [5] a method for the stereospecific construction of a suitable model *trans*-fused decalin (4) [6] containing epoxy and diacetate groupings common to many diterpene antifeedants.

RESULTS AND DISCUSSION

The key features of the synthetic plan for the preparation of (4) involve firstly the conjugate addition of an appropriate cuprate to the enone (5) from the least hindered side followed by regio- and stereo-selective trapping of the resulting enolate from the opposite face by formaldehyde. This process achieves two goals, namely that of *trans*-ring formation and simultaneous introduction of the angular hydroxy-methylene substituent at its correct oxidation level. Secondly, if the cuprate is so chosen that the introduced functionality could be later transformed to an exocyclic methylene unit and subsequently to a diol such as (6), then by hydroxy-group-directed epoxidation one would obtain the requisite final epoxide geometry in (4) (Scheme 1).



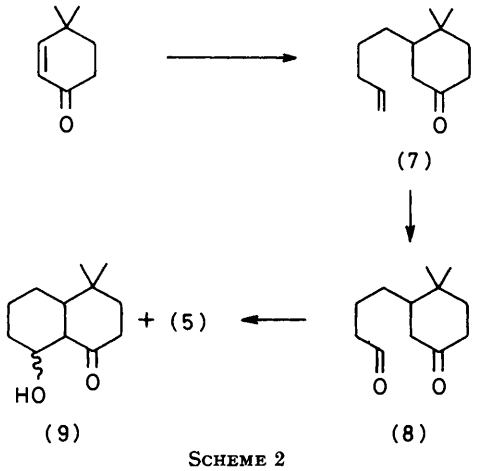
SCHEME 1

The preparation of (5) was straightforward following analogous literature procedures.[7] Hence CuBr·Me_2S catalysed conjugate addition of pent-4-enylmagnesium bromide to 4,4-dimethylcyclohex-2-enone gave (7) in essentially quantitative yield. Compound (7) was converted into the ketoaldehyde (8) by ozonolysis and reductive work-up with Zn–HOAc in 92% overall yield. Intramolecular aldol condensation of (8) using 0.25M-sodium hydroxide in aqueous methanol at room temperature gave (5) (46%) along with some of the keto-alcohol (9) (43%). Compound (9), however, could be readily dehydrated in benzene under Dean–Stark conditions to afford more (5) to give a combined yield of 73% (Scheme 2). Various attempts to improve this yield were not successful owing to the formation of unwanted intermolecular aldol products.

In a preliminary experiment to determine the stereochemical requirements involved in the conjugate addition of cuprates, (5) was treated with lithium dimethylcuprate to afford a single product which was isolated in 60% yield and shown, by detailed high-field (250 MHz) ^1H n.m.r. methods, to be the *trans*-decalin (10).

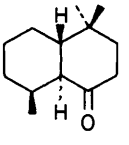
Similar reaction of (5) with vinylmagnesium bromide–

$CuBr{\cdot}Me_2S$ followed by quenching with a tetrahydrofuran (THF) or ether solution of monomeric formaldehyde gave the desired *trans*-fused product (11) in 63% yield. This product was contaminated with a small amount of what was thought to be the corresponding *cis*-isomer but which was not isolated at this stage since it was co-eluted on t.l.c. with (11); however, it was readily removed after the next stage.



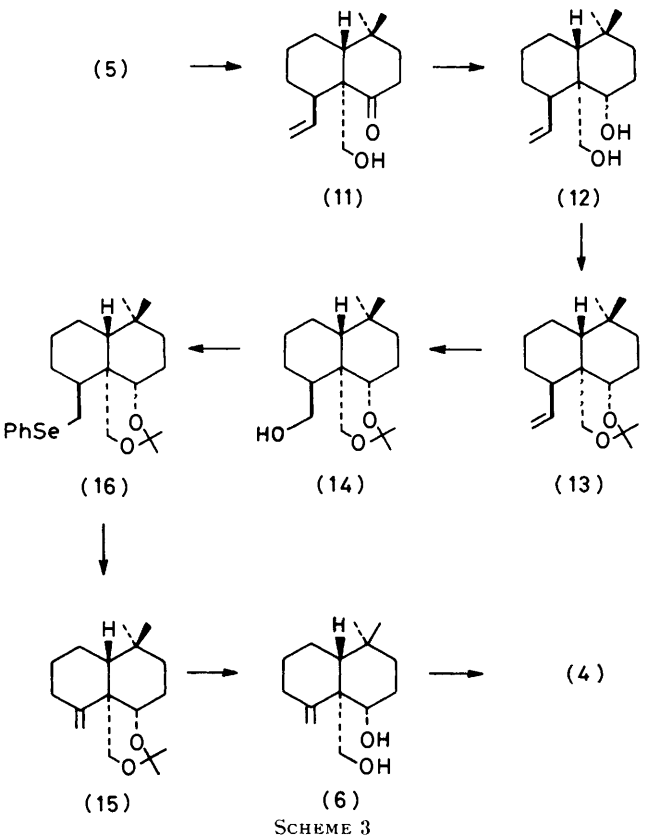
SCHEME 2

Direct stereospecific reduction of (11) using either lithium aluminium hydride or sodium borohydride was not possible. However, by first removing the reduction-directing properties of the primary hydroxy-group by reaction with diphenyl-t-butylsilyl chloride, followed by reduction with lithium aluminium hydride, (12) was formed as the only product after dilute acid work-up. The structure of (12) was fully consistent with its high-field n.m.r. spectral properties and was confirmed by an *X*-ray crystallographic structure determination of a later derivative (*vide infra*).



(10)

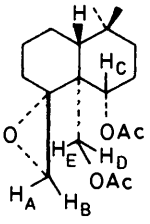
In order to elaborate further the vinyl substituent in (12), the primary and secondary hydroxy-groups were quantitatively protected by forming the acetonide (13) in the normal manner. Ozonolysis of (13) followed by reductive work-up with sodium borohydride gave the alcohol (14) in 86% overall yield (Scheme 3). By far the best method for effecting the dehydration of (14) to the *exo*-methylene derivative (15) involved prior conversion into the intermediate phenyl selenide (16) (89%) using *N*-phenylselenophthalimide-tri-n-butylphosphine according to the recently published method.[8] Subsequent oxidation to the selenoxide using ozone followed by *syn*-elimination in the presence of diethylamine in boiling CCl_4 gave (15) in 92% overall yield which was quantitatively deprotected to give the key diol (6) by treatment with trifluoroacetic acid in aqueous acetonitrile. Hydroxy-group-directed epoxidation of (6) took place as planned using $VO(acac)_2$–Bu^tOOH [9] in benzene at room temperature: diacetylation then completed the synthesis of the model *trans*-fused compound (4) in 52% overall yield from (6) (Scheme 3). Attempts to improve the epoxidation reaction using a variety of other methods have so far proved fruitless.



SCHEME 3

As it was not possible to prove the final orientation of the four relative chiral centres in (4) by *X*-ray crystallography, detailed high-field ^1H n.m.r. spectroscopic methods were employed. First, the most striking features of the ^1H n.m.r. spectrum of (4) were the very close similarities between equivalent resonances in, for example, ajugarin I,[10] both in terms of chemical shift and coupling constant (Scheme 4). Secondly, strong nuclear Overhauser effects were observed between the secondary acetate methine proton (H_C) and the proximal methine proton (H_B) on the epoxide ring and between the axial methyl group and one of the methylene protons (H_D) of the primary acetate unit. Additionally a small W-coupling ($<1/2$ Hz) was observed, which was removed upon decoupling, between H_C and H_E, again in accord with the assigned structure.

When the model *trans*-decalin (4) was tested for insect antifeedant properties against *Locusta migratoria*, at 100 p.p.m. on GF/A discs containing 5% sucrose as a food source, a 70% inhibition of feeding was observed.



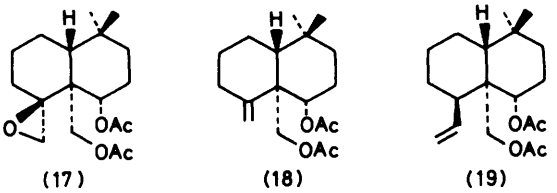
(4)

Compound (4)	Ajugarin I (1)
H_A 2.23 (d, *J* 4 Hz)	2.22 (d, *J* 4 Hz)
H_B 3.01 (dd, *J* 4 and 2 Hz)	2.99 (dd, *J* 4 and 2 Hz)
H_C 4.7 (dd, *J* 10 and 6 Hz)	4.7 (dd, *J* 11 add 5 Hz)
H_D 4.85 (d, *J* 11 Hz)	4.88 (d, *J* 12 Hz)
H_E 4.37 (d, *J* 12 Hz)	4.36 (d, *J* 12 Hz)

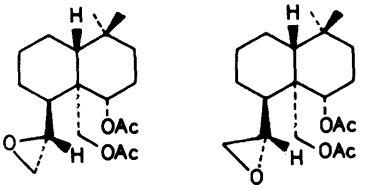
SCHEME 4 ^{1}H n.m.r. data

This activity was equivalent to that of natural clerodin hemiacetal (3) in a similar screen.*

In order to probe this activity in more detail, three other *trans*-epoxy-decalin diacetate analogues were prepared and their biological activities determined. One obvious candidate was the isomeric epoxide (17) which was obtained together with (4) by epoxidation of the diacetate (18) with *m*-chloroperbenzoic acid (*m*-CPBA);



(17) (18) (19)



(20) (21)

however, after separation from (4), (17) was shown to have negligible antifeedant activity even at 1 000 p.p.m.

Finally, acetylation of (12) gave the corresponding diacetate (19) which upon epoxidation with *m*-CPBA slowly gave two diastereoisomeric epoxides (20) and (21) in the ratio 1.3 : 1.0 in 84% combined yield. From their spectral properties, it was not possible to assign their structures fully, but an *X*-ray crystallographic determination † was performed on the major isomer. Once again, neither of these epoxides showed any significant antifeedant activity.

* We thank Dr. E. A. Bernays, Centre for Overseas Pest Research, London, for this and later biological results.

† We thank Dr. D. J. Williams, Imperial College, for this result.

From these results, therefore, it is clear that at least for *Locusta migratoria* the epoxy- and diacetate functional groups are required and that they must be precisely orientated in space in order to achieve good antifeedant activity.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. ^{1}H N.m.r. spectra were obtained for solutions in $CDCl_3$ (Me_4Si as internal standard). Thin-layer chromatography was carried out on silica gel (Merck GF_{254} Type 60), and column chromatography on silica gel (Merck Kieselgel 60/H). Light petroleum refers to the fraction b.p. 40—60 °C. Solutions were dried over magnesium sulphate and solvents by standard techniques. M.p.s are quoted for crystalline solid products; all others are colourless oils.

Preparation of 4,4-*Dimethyl*-3-*pent*-4-*enylcyclohexanone* (7).—To a stirred suspension of CuBr·SMe_2 (2.67 g, 13 mmol) in ether (20 ml) at −10 °C under argon, was added a solution of pent-4-enylmagnesium bromide (3.75 g, 25 mmol) in ether (30 ml). The resulting brown solution was stirred for 20 min at −10 °C and cooled to −40 °C, and 4,4-dimethylcyclohex-2-enone [11] (1.24 g, 10 mmol) added. The solution was stirred for 1 h at −40 °C, warmed slowly to 0 °C, and then worked-up with saturated NH_4Cl solution. The product was extracted into ether–light petroleum, washed with NH_4Cl solution, dried, and evaporated under reduced pressure, and the remaining oil subjected to column chromatography to yield 3-pent-4-enyl-4,4-dimethylcyclohexanone (7) (1.94 g, 100%); δ (6 MHz; $CDCl_3$), 0.93 (3 H, s), 0.98 (3 H, s), 0.6—2.4 (13 H, m), and 4.65—6.0 (3 H, m); $\nu_{max.}$ (film), 1 715, 1 1640, and 910 cm^{-1}; *m/z* 194.

Ozonolysis of (7) *to give* 3-(3-*Formylpropyl*)-4,4-*dimethylcyclohexanone* (8).—A stream of dry ozone was passed through a solution of (7) (1.95 g, 10 mmol) in CH_2Cl_2 (50 ml) at −30 °C. When no starting material remained, the solution was added dropwise to a suspension of zinc powder (1 g) in 15% acetic acid (50 ml). After 30 min, the solids were filtered off and $NaHCO_3$ (solid) was added to the filtrate to neutralize the acetic acid. The organic phase was separated and the aqueous phase extracted with dichloromethane (3 × 20 ml). The combined organic extracts were dried and evaporated to give 3-(3-formylpropyl)-4,4-dimethylcyclohexanone (8) (1.79 g, 91%); δ (60 MHz; $CDCl_3$), 1.00 (3 H, s), 1.03 (3 H, s,) 0.7—2.50 (13 H, m), and 9.62 (1 H, t, *J* 3 Hz); $\nu_{max.}$ (film), 2 722, 2 720, 1 010, and 735 cm^{-1}; *m/z* 196.

Intramolecular Aldol Condensation of (8) *to give the Enone* (5) *and the Alcohols* (9).—To a solution of (8) (1.79 g, 9.13 mmol) in methanol (120 ml), was added 0.5M-NaOH solution (80 ml) at 0 °C. The solution was stirred for 10 h at room temperature, then poured into dilute HCl. After ether extraction, the organic extract was dried, evaporated, and subjected to column chromatography to yield 5,5-dimethylbicyclo[4.4.0]dec-1(10)-en-2-one (5) (0.75 g, 46%); δ (60 MHz; $CDCl_3$), 0.87 (3 H, s), 1.03 (3 H, s), 0.65—2.50 (11 H, m), and 6.75 (1 H, m); $\nu_{max.}$ (film) 1 690, 1 610, 1 608, and 1 615 cm^{-1}; *m/z* 178, 163, 150, 135, and 109; and 10-hydroxy-5,5-dimethylbicyclo[4.4.0]decan-2-one (9) (0.78 g, 45%); δ (60 MHz; $CDCl_3$), 0.97 (3 H, m), 1.06 (3 H, m), 0.7—2.55 (12 H, m), 3.5—3.7 (1 H, m) and 3.80 (1 H, br s, D_2O exch.); $\nu_{max.}$ (film) 3 540, 1 700, and 1 155 cm^{-1}.

Dehydration of (9) *to give the Enone* (5).—A solution of the alcohols (9) in benzene (40 ml) was heated under Dean–

Stark conditions for 15 min. After evaporation of solvent and column chromatography, the enone (5) was isolated in 62% yield, identical to the previously prepared material.

Preparation of 1α-*Hydroxymethyl*-5,5-*dimethyl*-10β-*vinyl*-1α,6β-*bicyclo*[4.4.0]*decan*-2-*one* (11).—A solution of vinylmagnesium bromide [prepared from vinyl bromide (0.79 ml, 11.0 mmol) in tetrahydrofuran (THF) (12 ml)] was added dropwise to a slurry of $CuBr{\cdot}Me_2S$ (1.1 g, 5.5 mmol) in ether (15 ml), under argon at −50 °C. After 30 min a solution of compound (5) (0.89 g, 5 mmol) in ether (10 ml) was added to the resulting green-brown suspension. After 20 min, an ethereal solution of formaldehyde was added, and the mixture was then allowed to warm slowly to room temperature. Usual work-up with NH_4Cl solution, followed by chromatography [ether–light petroleum (50 : 50)] gave 1α-*hydroxymethyl*-5,5-*dimethyl* 10β-*vinyl*-1α,6β-*bicyclo*[4.4.0]*decan*-2-*one* (11) (0.743 g, 63%); δ (250 MHz; $CDCl_3$), 5.87 (1 H, ddd, *J* 17.7, 9.9, and 8.8 Hz), 5.10 (1 H, m), 5.05 (1 H, m), 4.01 (1 H, dd, *J* 12.0 and 12.0 Hz), 3.74 (1 H, d, *J* 12.0 Hz), 3.19 (1 H, m), 2.70 (1 H, d, *J* 12.0 Hz, D_2O exch.), 2.35 (1 H, ddd, *J* 14.5, 14.5, and 4.0 Hz), 2.28 (1 H, ddd, *J* 14.5, 5.0, and 5.0 Hz), 1.93 (1 H, dd, *J* 12.5, and 3.0 Hz), 1.85—1.35 (8 H, m), 1.05 (3 H, s), and 0.88 (3 H, s); $\nu_{max.}$ (film) 3 450, 3 078, 1 698, 1 630, and 1 390 cm^{-1}; *m/z* 236 ($M^+ - H_2O$), 206, 205, 150, and 149 (Found: C, 76.2; H, 10.4. $C_{15}H_{24}O_2$ requires C, 76.2; H, 10.2%).

Preparation of the Diphenyl-t-butylsilyl Derivative of Compound (11).—A solution of (11) (80 mg, 0.31 mmol), diphenyl-t-butylsilyl chloride (0.33 ml, 0.37 mmol), and imidazole (46 mg, 0.62 mmol) in dry dimethylformamide (DMF) (1 ml) was stirred overnight at room temperature. The mixture was poured into ether (50 ml) and washed with water (3 × 10 ml), followed by brine (10 ml). After drying and removal of the solvent *in vacuo*, the residue was chromatographed [ether–light petroleum (10 : 90)] to give 5,5-dimethyl-1α-(diphenyl-t-butylsilyloxymethyl)-10β-vinyl-1α,6β-bicyclo[4.4.0]decan-2-one (0.145 g, 98%), δ (250 MHz, $CDCl_3$), 7.65 (4 H, m), 7.40 (6 H, m), 5.85 (1 H, ddd, *J* 16.7, 10.8, and 5.8 Hz), 5.12 (1 H, ddd, *J* 16.7, 2.6, and 2.6 Hz), 5.11 (1 H, ddd, *J* 10.8, 2.6 and 2.6 Hz), 4.02 (1 H, d, *J* 6.8 Hz), 3.95 (1 H, d, *J* 6.8 Hz), 3.28 (1 H, m), 2.27 (1 H, ddd, *J* 15.7, 11.25, and 4.6 Hz), 2.10 (1 H, ddd, *J* 15.7, 8.3, and 4.6 Hz), 1.73 (1 H, dd, *J* 12.1 and 3.2 Hz), 1.67—1.45 (6 H, m), 1.40—1.25 (2 H, m), 1.05 (9 H, s), 0.93 (3 H, s), and 0.76 (3 H, s); $\nu_{max.}$ (film) 3 065, 3 040, 2 855, 1 700, 1 585, and 700 cm^{-1}; *m/z* 474 (M^+), 459, 416, 387, 337, and 267.

Preparation of 1α-*Hydroxymethyl*-5,5-*dimethyl*-10β-*vinyl*-1α,6β-*bicyclo*[4.4.0]*decan*-2α-*ol* (12).—Lithium aluminium hydride (18 mg, 0.47 mmol) was added, in portions, to a stirred solution of the silyl protected keto-alcohol prepared in the preceding experiment (0.22 g, 0.47 mmol) in dry ether (10 ml) at room temperature. The mixture was stirred for 1 h, quenched with water, shaken with dilute sulphuric acid, and extracted into CH_2Cl_2 (4 × 25 ml). After removal of the solvent *in vacuo*, the residue was chromatographed (90 : 10 [ether–light petroleum (90 : 10)] to give 1α-*hydroxymethyl*-5,5-*dimethyl*-10β-*vinyl*-1α,6β-*bicyclo*[4.4.0]-*decan*-2α-*ol* (12) (86 mg, 77%); δ (250 MHz, $CDCl_3$) 6.24 (1 H, ddd, *J* 16.7, 10.0, and 10.0 Hz), 5.23 (1 H, dd, *J* 16.7 and 1.6 Hz), 5.13 (1 H, dd, 10.0 *J* and 1.6 Hz), 4.30 (1 H, d, *J* 11.3 Hz), 3.86 (1 H, dd, *J* 11.3 and 10.8 Hz), 3.67 (1 H, ddd, *J* 11.6, 3.3, and 1.7 Hz), 3.18 (1 H, m), 3.07 (1 H, d, *J* 10.8 Hz, D_2O exch.), 2.04 (1 H, d, *J* 3.3 Hz, D_2O exch.), 1.95—1.80 (2 H, m), 1.70—1.20 (9 H, m), 0.88 (3 H, m), and 0.78 (3 H, m); $\nu_{max.}$ (film) 3 350, 3 075, 1 660, and 910 cm^{-1}; *m/z* 238 (M^+), 220, and 189 (Found: C, 75.8; H, 11.3. $C_{15}H_{26}O_2$ requires C, 75.8; H, 11.0%).

Preparation of the OO-*Isopropylidene Derivative* (13) *of the Diol* (12).—A solution of (12) (70 mg, 0.29 mmol), 2,2-dimethoxypropane (45 mg, 0.5 mmol), and toluene-*p*-sulphonic acid (5 mg) in benzene (25 ml) was heated to reflux in a Dean–Stark apparatus for 2 h. After cooling, the solution was diluted with ether (50 ml) and washed with saturated aqueous sodium hydrogen carbonate (2 × 50 ml) followed by brine (5 ml). The organic layer was dried and filtered, and the solvent removed *in vacuo* to give the crude acetonide. Chromatography [ether–light petroleum (5 : 95)] gave the *isopropylidene derivative* (13) (81 mg, 99%); δ (60 MHz, $CDCl_3$) 6.3—5.6 (1 H, m), 5.25—4.80 (2 H, m), 4.20—3.50 (3 H, m), 2.95 (1 H, m), 2.30—1.00 (17 H, m), and 0.85 (6 H, m); $\nu_{max.}$ (film) 3 078, 1 632, 1 460, and 915 cm^{-1}; *m/z* 263 ($M^+ - CH_3$) and 203 (Found: C, 77.75; H, 11.0. $C_{18}H_{30}O_2$ requires C, 77.65; H, 10.9%).

Preparation of the Hydroxymethyl Compound (14).—The vinyl compound (13) (81 mg, 0.29 mmol) was dissolved in methanol (2 ml) and cooled to 0 °C. Ozone was bubbled through the stirred solution until starting material was consumed as indicated by t.l.c. [ether–light petroleum (10 : 90)]. Sodium borohydride was then added in small portions (5 mg) until t.l.c. indicated that reduction was complete. Water (0.25 ml) was added and after the removal of the solvent *in vacuo* the residue was extracted into ether (3 × 10 ml). The combined extracts were dried and filtered and the solvent removed *in vacuo*. The crude product was chromatographed [ether–light petroleum (40 : 60)] to give the *hydroxymethyl compound* (14) (70 mg, 86%); δ (250 MHz, $CDCl_3$) 4.20 (1 H, d, *J* 11.5 Hz), 3.90 (dd, *J* 11.0 and 6.25 Hz), 3.85 (1 H, dd, *J* 10.0 and 6.0 Hz), 3.83 (1 H, d, *J* 11.5 Hz), 3.62 (1 H, dd, *J* 11.0 and 5.0 Hz), 2.65 (1 H, m), 2.25 (1 H, dddd, *J* 12.5, 11.0, 11.0, and 3.0 Hz), 2.15 (1 H, br s, D_2O exch.), 1.80—1.50 (6 H, m), 1.47 (3 H, s), 1.40 (3 H, s), 1.30—1.05 (4 H, m), and 0.87 (6 H, m); $\nu_{max.}$ (film) 3 470, 1 460, 1 380, 1 370, and 1 230 cm^{-1}; *m/z* 282 (M^+), 267, 224, and 207 (Found: C, 72.1; H, 10.7. $C_{17}H_{30}O_3$ requires C, 72.3; H, 10.7%).

Preparation of the Phenyl Selenide (16).—A solution of (13) (70 mg, 0.25 mmol), *N*-phenylselenophthalimide (0.15 g, 0.5 mmol), and tri-n-butylphosphine (0.125 ml, 0.5 mmol) in dry THF (3 ml) was stirred at room temperature for 2 h. The solvent was removed *in vacuo* and the residue was chromatographed [light petroleum → ether–light petroleum (5 : 95)] to give the *phenyl selenide* (16) (93 mg, 89%); δ (250 MHz, $CDCl_3$) 7.55 (2 H, m), 7.25 (3 H, m), 4.06 (1 H, d, *J* 11.8 Hz), 3.82 (1 H, d, *J* 11.8 Hz), 3.80 (dd, *J* 8.5 and 4.2 Hz), 3.15 (1 H, ddd, *J* 11.8, 3.4, and 1.7 Hz), 2.93 (1 H, dd, *J* 11.8 and 11.8 Hz), 2.60 (1 H, m), 2.15—1.88 (2 H, m), 1.80—1.20 (9 H, m), 1.39 (3 H, m), 1.17 (3 H, m), 0.87 (3 H, m), and 0.86 (3 H, m); $\nu_{max.}$ (film) 3 075, 3 055, 2 876, 1 580, 908, and 690 cm^{-1}; *m/z* 422 (M^+) 407, 364, 265, and 207 (Found: C, 65.7; H, 8.2. $C_{23}H_{34}O_2Se$ requires C, 65.5; H, 8.1%).

Preparation of the Methylene Derivative (15).—A solution of the selenide (16) (93 mg, 0.22 mmol) in CH_2Cl_2 (2 ml) was cooled to −78 °C. Ozone was bubbled through the stirred solution until it showed a persistent blue colouration and t.l.c. [ether–light petroleum (5 : 95)] showed the absence of starting material. Nitrogen was then passed through the solution until it was once more colourless and, after dilution with CCl_4 (15 ml), diethylamine (10 drops) was added and

the mixture was heated to reflux. After 30 min, the solution was cooled, the solvent removed *in vacuo*, and the residue chromatographed [ether–light petroleum (5 : 95)] to give the *methylene derivative* (15) (53 mg, 92%); δ (250 MHz, $CDCl_3$), 5.06 (1 H, br s), 4.90 (1 H, br s), 4.24 (1 H, d, *J* 11.5 Hz), 4.03 (1 H, dd, *J* 11.5 and 4.7 Hz), 3.94 (1 H, dd, *J* 11.5 and 1.0 Hz), 3.40—3.18 (3 H, m), 2.95—2.75 (2 H, m), 1.65—1.60 (1 H, m), 1.55—1.45 (1 H, m), 1.47 (3 H, s), 1.45—1.15 (3 H, m), 1.32 (3 H, s), 1.04 (1 H, m), 0.93 (s, 3 H), and 0.86 (s, 3 H); $\nu_{max.}$ 3 090, 1 639, 1 375, 1 365, and 1 240 cm^{-1}; *m/z* 264 (M^+) 249, 189, and 176 (Found: C, 77.75; H, 11.0. $C_{17}H_{28}O_2$ requires C, 77.65; H, 11.0%).

Preparation of 1α-*Hydroxymethyl*-5,5-*dimethyl*-10-*methylene*-1α,6β-*bicyclo*[4.4.0]*decan*-2α-*ol* (6).—A solution of compound (15) (40 mg, 0.18 mmol) in acetonitrile (2 ml), water (0.25 ml) and trifluoroacetic acid (1 drop) was kept for 30 min and sodium hydrogen carbonate (0.5 g) was added, followed by ether (5 ml) and magnesium sulphate (1 g). After filtration and re-extraction of the residue (ether; 2 × 5 ml), the combined ethereal extracts were concentrated *in vacuo* to give 1α-*hydroxymethyl*-5,5-*dimethyl*-10-*methylene*-1α,6β-*bicyclo*[4.4.0]*decan*-2α-*ol* (6) (33 mg, 99%); δ (250 MHz, $CDCl_3$) 5.10 (1 H, br s), 4.95 (1 H, br s), 4.15 (1 H, dd, *J* 8.3 and 2.0 Hz), 3.99 (1 H, ddd, *J* 7.3, 4.2, and 2.6 Hz), 3.92 (1 H, dd, *J* 8.3 and 6.25 Hz), 3.79 (1 H, *d*, *J* 2.6 Hz, D_2O exch.), 3.33 (1 H, dd, *J* 6.25 and 2.0 Hz, D_2O exch.), 2.40—2.18 (2 H, m), 2.0—1.60 (4 H, m), 1.50—1.20 (4 H, m), 1.10 (1 H, m), 0.83 (3 H, s), and 0.77 (3 H, s); $\nu_{max.}$ (film) 3 345, 3 090, and 1 639 cm^{-1}; *m/z* 224 (M^+) 206, 176, and 120 (Found: C, 74.7; H, 10.8. $C_{14}H_{24}O_2$ requires C, 74.95; H, 10.8%).

2α-*Acetoxy*-1α-*acetoxymethyl*-5,5-*dimethyl*-1α,6β,10Oα-*Preparation of bicyclo*[4.4.0]*decane*-10-*spiro*-2′-*oxiran* (4).—To a stirred solution of (6) (30 mg, 0.13 mmol) and $VO(acac)_2$ (Hacac = pentane-2,4-dione) (10 mg) in benzene (2 ml) was added 8% t-butyl hydroperoxide in benzene (0.5 ml, 0.39 mmol). After 4 h, the solvent was removed *in vacuo* and pyridine (0.1 ml), acetic anhydride (0.05 ml), and 4-(dimethylamino)pyridine (5 mg) were added. After 10 h, excess of reagents were removed *in vacuo* and the residue chromatographed [light petroleum ⟶ ether–light petroleum (50 : 50)] to give 2α-*acetoxy*-1α-*acetoxymethyl*-5,5-*dimethyl*-1α,6β,10Oα-*bicyclo*[4.4.0]*decane*-10-*spiro*-2′-*oxiran* (4) (23 mg, 53%), m.p. 105.5—106 °C (from ether–light petroleum); δ (250 MHz; $CDCl_3$) 4.88 (1 H, d, *J* 12.3 Hz), 4.70 (1 H, dd, *J* 11.4 and 4.75 Hz), 4.36 (1 H, d, *J* 12.3 Hz), 2.99 (1 H, dd, *J* 4.0 and 2.4 Hz), 2.22 (1 H, d, 4.0 Hz), 2.12 (1 H, m), 2.11 (3 H, s), 1.96 (3 H, s), 1.80—1.25 (9 H, m), 1.04 (1 H, m), 0.90 (3 H, s), and 0.84 (3 H, s); $\nu_{max.}$ ($CHCl_3$) 2 780, 2 760, 1 730, 1 725, 1 365, 1 260, and 1 038 cm^{-1}; *m/z* 295 (M^+ — CHO), 282, 251, 221, 204, 191, and 174.6 (M^*, 209—191) (Found: C, 66.9; H, 8.75. $C_{18}H_{28}O_5$ requires C, 66.6; H, 8.75%).

Preparation of 2α-*Acetoxy*-1α-*acetoxymethyl*-5,5-*dimethyl*-1α,6β,10Oα-*bicyclo*[4.4.0]*decane*-10-*spiro*-2′-*oxiran* (17).—To a solution of (6) (76.2 mg, 0.34 mmol) in pyridine (2 ml) were added 4-(dimethylamino)pyridine (10 mg) and acetic anhydride (0.2 ml). The mixture was stirred for 20 min and then excess of reagents and pyridine were removed under reduced pressure. The nonvolatile residue was dissolved in CH_2Cl_2 (5 ml), and Na_2HPO_4 (0.1 g) was added followed by *m*-chloroperbenzoic acid (0.1 g, 0.58 mmol). The solution was stirred overnight, washed with saturated $NaHCO_3$ solution, dried and evaporated, and the residue chromatographed to give the two diastereoisomeric epoxides (4), (42 mg, 38%) identical to previous samples (by t.l.c., ^1H n.m.r.) and (17) (51 mg, 47%), m.p. 125—127 °C; δ (250 MHz, $CDCl_3$), 0.82 (3 H, s), 0.90 (3 H, s), 1.95 (3 H, s), 2.04 (3 H, s), 2.54 (1 H, d, *J* 4.0 Hz), 2.72 (1 H, d, *J* 4.0 Hz), 4.29 (1 H, d, *J* 11.5 Hz), 4.60 (1 H, dd, *J* 10.8 and 4.7 Hz), 4.87 (1 H, d, *J* 11.5 Hz), and 1.08—2.10 (11 H, m); $\nu_{max.}$ ($CHCl_3$), 3 070, 1 735, 1 245, and 1 030 cm^{-1}; *m/z* 295 (M^+ — CHO), 281, 251, 221, and 191 (Found: M^+ — $COCH_3$ 281.1749; calc., 281.1743).

Preparation of the Epoxides (20) *and* (21).—To a solution of (12) (0.323 g, 1.4 mmol) in pyridine (5 ml) was added 4-(dimethylamino)pyridine and acetic anhydride (0.5 ml). The mixture was stirred for 20 min, solvents were removed and replaced with dichloromethane (5 ml), and then Na_2HPO_4 (0.35 g) and *m*-chloroperbenzoic acid (0.34 g, 0.2 mmol) were added. The mixture was stirred for 3 days, and work-up followed by chromatography gave the epoxide (20) (0.215 g, 48%), m.p. 142—143 °C; δ (250 MHz; $CDCl_3$), 0.83 (3 H, s), 0.92 (3 H, s), 1.98 (3 H, s), 2.03 (3 H, s), 2.28 (1 H, dd, *J* 5.3 and 2.5 Hz), 2.85 (1 H, dd, *J* 5.3 and 3.8 Hz), 3.19 (1 H, ddd, *J* 9.7, 3.8, and 2.5 Hz), 4.16 (1 H, d, *J* 12.5 Hz), 4.80 (1 H, dd, *J* 9.7 and 6.0 Hz), 4.94 (1 H, d, *J* 12.5 Hz), and 0.82—2.08 (12 H, m); $\nu_{max.}$ ($CDCl_3$) 1 735, 1 245, 1 030, and 900 cm^{-1}; *m/z* 339 ($M^+ + 1$), 279 (M^+ — HOAc), 218, 206, and 204 (Found: C, 67.1; H, 8.83. Calc. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.4%); the epoxide (21) m.p. 136—138 °C (0.059 g, 13%); δ (250 MHz; $CDCl_3$), 0.85 (3 H, s), 0.90 (3 H, s), 1.95 (3 H, s), 2.04 (3 H, s), 1.26—2.05 (12 H, m), 2.39 (1 H, dd, *J* 5 and 2.5 Hz), 2.77 (1 H, dd, *J* 5 and 3.8 Hz), 3.22 (1 H, ddd, *J* 8.8, 3.8, and 2.5 Hz), 4.15 (1 H, d, *J* 12.5 Hz), 4.85 (1 H, dd, *J* 11.3 and 3.8 Hz), and 4.98 (1 H, d, *J* 12.5 Hz); $\nu_{max.}$ ($CHCl_3$) 1 735, 1 245, 1 030, and 900 cm^{-1}; and the vinyl diacetate (19), m.p. 80—82 °C (0.114 g, 26%); δ (250 MHz; $CDCl_3$), 0.82 (3 H, s), 0.87 (3 H, s), 1.18—1.83 (11 H, m), 1.96 (3 H, s), 2.10 (3 H, s), 2.85 (1 H, d of m, *J* 10.2 Hz), 4.21 (1 H, d, *J* 12.5 Hz), 4.54 (1 H, dd, *J* 11.0 and 5.6 Hz), 4.92 (1 H, d, *J* 12.5 Hz), 4.96 (1 H, ddd, *J* 16.5 and 2.5 Hz), 5.08 (1 H, dd, *J* 10.2 and 2.5 Hz), and 6.17 (1 H, ddd *J* 16.5, 10.2, and 10.2 Hz); $\nu_{max.}$ (film) 1 735, 1 640, and 1 240 cm^{-1}; *m/z* 322 (M^+), 262 (M^+ — HOAc), 220, 202, and 187.

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