Synthesis of (±)-Cryptofauronol and Related Valerane Sesquiterpenes *via* Rearrangement of Bicyclo[5.3.0]decane Precursors

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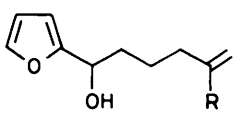
Alkenyl-substituted furfuryl alcohols have been converted into the corresponding alkenyl-substituted pyrylium species which undergo intramolecular cycloaddition to produce highly functionalised perhydroazulenes. These products, epoxybicyclo[5.3.0]decanones and the corresponding alcohols, can undergo acid-catalysed rearrangement reactions to give *cis*-fused bicyclo[4.4.0]decanes. The scope and limitations of these rearrangement reactions have been explored. The process has been adapted for use in the synthesis of the sesquiterpenes (±)-cryptofauronol, (±)-fauronyl acetate, (±)-valeranone, and (±)-valerane.

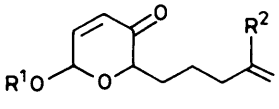
In recent papers we have described a simple route for the synthesis of 1,5-epoxyperhydroazulenes from substituted furans, and the rearrangement of such systems to *cis*-fused decalones.[1–4]

The 1,5-epoxyperhydroazulenes have been utilised in the synthesis of the guiane sesquiterpene (±)-bulnesene.[4] Herein we describe routes from the *cis*-fused decalones to naturally occurring sesquiterpenes of the valerane class, and some studies on the scope and stereochemistry associated with the perhydroazulene-to-decalone rearrangement.

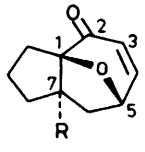
The 1,5-epoxybicyclo[5.3.0]decanones employed in these studies on the rearrangement process were prepared by using the previously reported intramolecular cycloaddition reaction between olefins and 3-oxidopyrylium.[1] Thus the substituted furan (**1**) was oxidised to give the pyranulose (**3**) which was acetylated and then transformed into the enone (**7**) by heating in acetonitrile with triethylamine (85% overall yield). A similar series of reactions, described below, was used to prepare the related enone (**8**) from the furan (**2**).



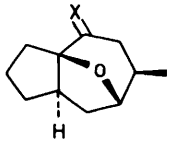
(**1**) R = H
(**2**) R = Me



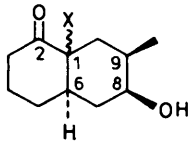
(**3**) $R^1 = R^2 = H$
(**4**) R^1 = Ac, R^2 = H
(**5**) R^1 = H, R^2 = Me
(**6**) R^1 = Ac, R^2 = Me



(**7**) R = H
(**8**) R = Me



(**9**) X = O
(**10**) X = OH, H
(**11**) X = H, OH
(**12**) X = H, Cl



(**13**) X = H
(**14**) X = H

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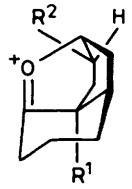
Reaction of the enone (**7**) with lithium dimethylcuprate afforded the conjugate adduct (**9**), the relative stereochemistry of which has been confirmed by *X*-ray crystallographic analysis.[2] Reduction of the ketone (**9**) with lithium aluminium hydride gave a 1:1.8 mixture of the epimeric alcohols (**10**) and (**11**) which were readily separated by chromatography on silica gel. The relative stereochemistry of these two alcohols followed from their ^{1}H n.m.r. spectra. Owing to the enhanced anisotropy of the bridge oxygen, proton 2-H in the α-alcohol (**11**),‡ resonating at δ 3.65, is deshielded relative to that in the *syn*-isomer (**10**), resonating at δ 3.50. A biological assay on the benzyl ethers of these two alcohols also supports this stereochemical assignment.[3]

Treatment of the alcohol (**11**) with thionyl chloride in hexamethylphosphoric triamide (HMPA) produced only the chloride (**12**), isolated in 68% yield. Similar treatment of the β-alcohol (**10**) did not give any of the corresponding chloride but, on aqueous work-up, afforded a keto alcohol, $\nu_{max.}$ 3 450 and 1 700 cm^{-1}, identified as the *cis*-fused decalone (**13**), isolated in 60% yield. Treatment of this *cis*-decalone with triethylamine catalysed its epimerisation to the corresponding *trans*-decalone (**14**). The rearrangement of the alcohol (**10**) to the decalone (**13**) must proceed *via* a 1,2 carbon-to-carbon bond shift, the resulting carbonium ion being stabilised by the ether oxygen, *cf.* structure (**15**). Models indicate that, for the alcohol (**10**), the



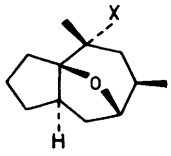
(**15**) R^1 = H, R^2 = Me
(**16**) R^1 = Me, R^2 = H

C–O bond of the alcohol group is antiperiplanar to the migrating C–C bond; in the α-alcohol (**11**) the corresponding bonds are not favourably orientated for rearrangement and thus substitution is observed.

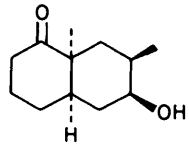
It was subsequently found that rearrangement of the β-alcohol (**10**) could also be promoted by Lewis acids such as titanium tetrachloride or tin tetrachloride, both producing the decalone (**13**) in yields around 60%.

‡ All cycloadducts are racemates; α-groups are assigned as those in which the substituent is on the opposite side of the carbon framework compared with the oxido bridge, β-substituents being on the same side.

Attention was next directed to the behaviour of the tertiary alcohol (**17**), obtained as the sole product by reaction of the ketone (**9**) with methylmagnesium iodide. Whereas treatment of the alcohol (**17**) with thionyl chloride in HMPA gave the corresponding chloride (**18**), as expected for an α-alcohol, exposure to either titanium tetrachloride or tin tetrachloride induced skeletal rearrangement to produce the *cis*-fused 2-decalone (**19**). Presumably, for the tertiary alcohol (**17**) formation of the carbonium ion is easier than for the corresponding secondary alcohol (**10**). In this case skeletal rearrangement to form the oxonium ion (**16**) is not concerted with loss of the hydroxy



(**17**) X = OH
(**18**) X = Cl



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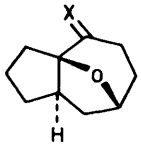
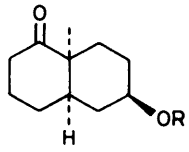


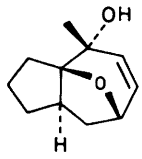
(**20**) X = O
(**21**) X = Me, OH
(**22**) X = Me, $OCOCF_3$



(**23**) R = H
(**24**) R = $COCF_3$

group. In studies on the tertiary alcohol (**21**), prepared from the ketone (**20**), the rearrangement was found to occur in *ca.* 30 min at room temperature with titanium tetrachloride or boron trifluoride–diethyl ether as catalyst (80% yield in each case). Treatment of the alcohol (**21**) with aqueous sulphuric acid in tetrahydrofuran (THF) or with trifluoroacetic acid (TFA) in chloroform did not induce rearrangement, but the derived trifluoroacetate (**22**) underwent slow rearrangement to give its isomer (**24**) when kept with an excess of TFA for several days. Basic hydrolysis of the ester (**24**) afforded the decalone (**23**) in good yield.

The rearrangement of the allylic tertiary alcohol (**25**) [obtained from the enone (**7**) by reaction with methyl-lithium] was next studied. Treatment of the alcohol with boron trifluoride–diethyl ether in dichloromethane gave an immediate deep red colour. Quenching with water quantitatively afforded the rearranged hydroxy ketones (**26**) and (**27**) in an 11:1 ratio. The stereochemistry of the major isomer was confirmed by hydrogenation of the mixture to give the alcohol (**23**). With titanium tetrachloride as the catalyst the alcohol (**25**) gave a mixture of the chloro ketones (**28**) and (**29**) in the ratio 3:1. Structural assignments for these products were obtained on the basis of extensive ^1H and ^{13}C n.m.r. studies. Thus, for the minor isomer (**29**) the 8α-proton is coupled strongly to both the protons at position 7 (*J* 8.9 and 13.2 Hz), indicating a pseudo-axial orientation, which can only be adopted for the 8β-chloro isomer. For the epimer (**28**) the 8β-proton couples with the protons at position 7 with smaller coupling constants (both about 4 Hz), indicating a pseudo-equatorial conformation as expected for the 8α-chloride. Presumably, during formation of the latter, the intermediate oxonium ion may cleave to give the



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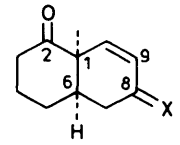
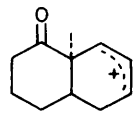


(**26**) X = OH, H
(**27**) X = H, OH
(**28**) X = H, Cl
(**29**) X = Cl, H

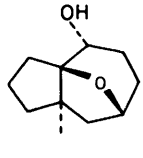


(**30**)

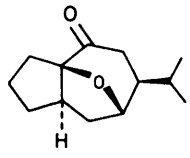
allylic carbonium ion (**30**), which is quenched by chloride anion present in solution. The absence of a good nucleophile in the boron trifluoride–diethyl ether-catalysed rearrangement ensures that the bridged oxonium ion intermediate persists until quenching with water gives mostly the hemiacetal and hence β-alcohol (**26**).

The above examples illustrate that the rearrangement of the epoxyperhydroazulene alcohols is general for tertiary and β-secondary alcohols. In contrast all attempts to effect rearrangements of the α-secondary alcohols, such as compounds (**11**) and (**31**), failed, generally giving rise to complex mixtures in which none of the corresponding decalones could be detected.

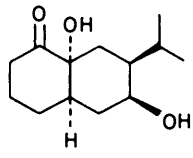
In an extension of the rearrangement process the behaviour of the precursor ketones was also examined. Thus treatment of the isopropyl-substituted ketone (**32**) with titanium tetrachloride in dichloromethane at room temperature for 16 h gave a moderate yield of the dihydroxy ketone (**33**). Likewise the 7-substituted ketone (**34**) gave the keto diol (**35**). Optimisation of the latter



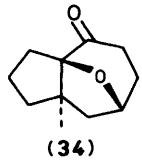
(**31**)



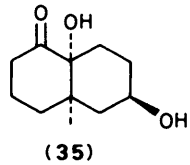
(**32**)



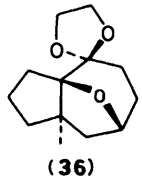
(**33**)



(**34**)



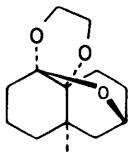
(**35**)



(**36**)

reaction showed that with acetonitrile as the solvent maximum conversion occurred in around 1 h at room temperature with 2—3 equiv. of titanium tetrachloride. Aqueous work-up at this stage typically gave a 1:1 mixture of starting material and product (**35**) with 95% total recovery. That an equilibrium was involved was confirmed by treatment of the product decalone (**35**) under the same reaction conditions, work-up giving the same 1:1 mixture of products (**34**) and (**35**).

In an attempt to carry out analogous rearrangement under milder conditions, the ethylene acetal (**36**) was first formed. On treatment with titanium tetrachloride this gave a mixture of products, the major one being a neutral, non-ketonic substance assigned as the rearranged acetal (**37**). Attempted formation of



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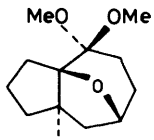

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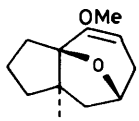

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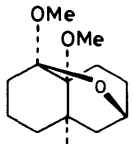

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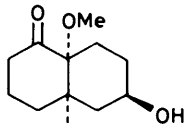

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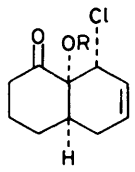


(42) R = H
(43) R = Ac

the dimethyl acetal (**38**) using trimethyl orthoformate and methanol in the presence of a catalytic amount of toluene-*p*-sulphonic acid (PTSA) gave a mixture of acetal (**38**), the rearranged acetal (**40**), and enol ether (**39**). Treatment of the pure acetal (**38**) with titanium tetrachloride or boron trifluoride–diethyl ether gave a complex mixture of products. However, warming in methanol with PTSA catalyst gave a 1:1 mixture of products (**38**) and (**40**). Acid-catalysed hydrolysis of compound (**40**) gave a good yield of the hydroxy(methoxy)-decalone (**41**).

Finally, rearrangement of the enone (**7**) with titanium tetrachloride in dichloromethane gave one major and at least two minor products. The major, crystalline product (56%) was assigned as the chloride (**42**). The *cis*-orientation of the hydroxy and chloro substituents was reflected in the stability of this compound to treatment with a variety of bases such as triethylamine or potassium t-butoxide. The alcohol group could be acetylated with acetic anhydride in pyridine with 4-dimethylaminopyridine (DMAP) as catalyst, to produce the ester (**43**). The regiochemistry of the chloride substitution followed from the shifts in ^{13}C n.m.r. resonances observed on this acetylation (Figure), as well as from the 400 MHz ^{1}H n.m.r. spectrum.

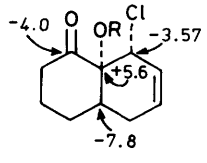
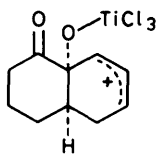


Figure. Shifts in ^{13}C resonances on changing R from H to Ac, *i.e.* (**42**) ⟶ (**43**)

Pyrolysis of the acetate (**43**) at 160 °C under nitrogen gave a good yield of α-tetralone, thus supporting the nature of the rearranged carbon skeleton present in the chloro alcohol. Presumably, in this series, chloride attack is directed at the site adjacent to the complexed allylic system, and may involve direct transfer from the complexed Lewis acid, *e.g.* (**44**) [*cf.* the product from allylic alcohol (**24**)].

The synthetic utility of the rearrangement of the epoxyperhydroazulenes into decalones has been demonstrated by application to the synthesis of certain members of the valerane class of sesquiterpenes. This family includes cryptofauronol (**47**),[5] fauronyl acetate (**48**),[5] and valeranone (**52**).[6] Although the former compounds have not previously been synthesised, two routes to valeranone (**52**) have been described.[7,8] The most important step in these syntheses is the stereoselective introduction of the second methyl group at the ring junction and neither of the previous routes uses direct methods to solve this problem.



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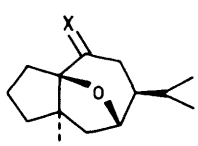
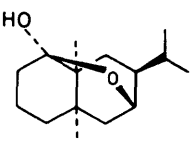


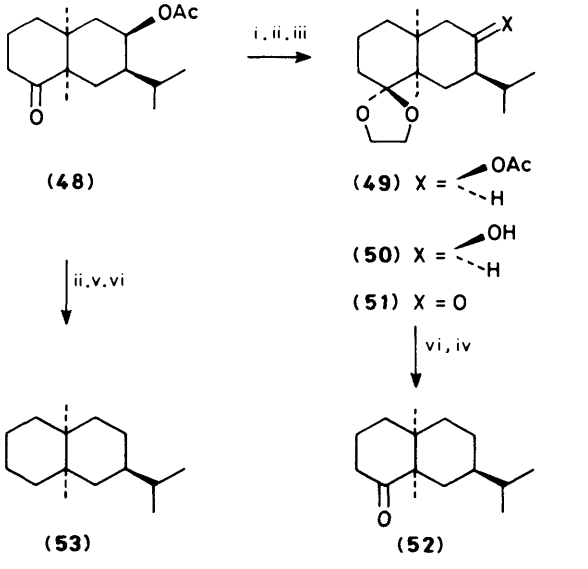
(45) X = O

(46) X = 



(47)

A retrosynthetic analysis of cryptofauronol based on the rearrangement reactions described above suggests the use of the enone (**8**), itself derived from the furan (**2**). The preparation of compound (**2**) was achieved by a Grignard reaction between 2-furaldehyde and 4-methylpent-4-enylmagnesium bromide. Selective oxidation of the furan ring of the alcohol (**2**) by standard reagents such as *m*-chloroperbenzoic acid[9] or bromine in methanol[10] was impeded by concurrent oxidation of the disubstituted terminal double bond. It is known that the relative epoxidation rates of olefins increase by more than an order of magnitude in changing from monosubstituted to disubstituted terminal double bonds.[11] In order to overcome this problem a more chemoselective oxidant was required and singlet oxygen was found to be suitable for this purpose. A solution of the alcohol (**2**) in methanol–dichloromethane containing Methylene Blue as a sensitiser was irradiated with visible light whilst a slow stream of oxygen was bubbled through the solution, while the temperature was kept below −40 °C. The intermediate methoxy hydroperoxide[12] was not isolated but immediately reduced with triphenylphosphine or dimethyl sulphide to afford the substituted pyranone (**5**) in high yield. This was then acetylated to give the pyranone acetate (**6**) which underwent smooth intramolecular cycloaddition when heated in refluxing acetonitrile and triethylamine, *via* the 3-oxidopyrylium zwitterion, to give the enone (**8**) in almost quantitative yield. Reaction of the cycloadduct (**8**) with isopropylmagnesium iodide in the presence of the dimethyl sulphide complex of copper(I) bromide, in order to catalyse conjugate addition, followed by reaction with methylmagnesium



Scheme. *Reagents:* i, $HOCH_2CH_2OH$, H^+; ii, KOH; iii, CrO_3, pyridine; iv, H_3O^+; v, $Na_2Cr_2O_7$, H^+; vi, N_2H_4, KOH

iodide afforded the perhydroazulenol (**46**), m.p. 102—103 °C, as a single isomer. The relative stereochemistry of the product (**46**) follows from its n.m.r. spectra and by comparison with previously described model systems, *e.g.* (**9**).[2] Treatment of the tertiary alcohol (**46**) with titanium tetrachloride in dichloromethane at 0 °C gave (±)-cryptofauronol (**47**), m.p. 107—109 °C, the overall yield from 2-furaldehyde being 42%. The synthetic material gave identical i.r., ^{1}H n.m.r., ^{13}C n.m.r., and mass spectra with those of a sample of the natural product. The spectroscopic data suggest that cryptofauronol exists mainly in the hemiacetal form, with only *ca.* 8% in the open form in deuteriochloroform; the i.r. spectrum shows only a weak absorption at 1 695 cm^{-1}.

Acetylation of (±)-cryptofauronol with acetic anhydride in the presence of sodium acetate afforded (±)-fauronyl acetate (**48**); hydrolysis of the latter substance gave back the starting material (±)-cryptofauronol.

Conversion of fauronyl acetate into (±)-valeranone (**52**)[5] and (±)-valerane (**53**)[13] was achieved using published procedures (Scheme). Both the valeranone and valerane had spectral data in agreement with those reported in the literature. This agreement serves to consolidate the earlier stereochemical assignments for the perhydroazulene adduct.

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H N.m.r. spectra were recorded on either a Perkin-Elmer R32 instrument (90 MHz), a Varian EM360 (60 MHz), a JEOL FX90Q FT Spectrometer, or a Bruker 400 MHz spectrometer using solutions in $CDCl_3$ with $SiMe_4$ as internal reference. ^{13}C Spectra were also recorded on the JEOL spectrometer. Mass spectra were recorded on a Kratos MS25 instrument with accurate mass measurement being carried out on an A.E.I.-Kratos MS 902/50 machine. I.r. spectra were recorded on either a Perkin-Elmer 297 or a 1420 spectrophotometer. Unless otherwise stated i.r. spectra were recorded as films for liquid samples and Nujol mulls for solids.

Only distinguishable peaks are listed for ^{1}H n.m.r. spectra (*i.e.* methylene envelope excluded); likewise only diagnostic absorbances in the i.r. are noted. ^{13}C Resonances are listed as singlet (s), doublet (d), triplet (t), or quartet (q) indicating splitting due to attached protons. The assignments were made on the basis of INEPT and DEPT experiments.

U.v. spectra were recorded on a Pye Unicam SP 800 spectrometer for solutions in ethanol.

T.l.c. was carried out on Kieselgel 60 GF_{254} (Merck) precoated 0.25 mm plates. Column chromatography was carried out on either Kieselgel 60 G (Merck) or MN-Kieselgel 60, 230—400 mesh (CAMLAB), columns being packed and developed under light pressure. Solvents for chromatography were generally dried and distilled before use. Solvent ratios are described as volume of solvents before mixing. Light petroleum refers to the fraction of boiling range 40—60 °C and ether refers to diethyl ether. Solutions of organic compounds isolated by extraction were dried over anhydrous magnesium sulphate. Removal of solvent refers to rotatory evaporation.

HMPA was purified by distillation from calcium hydride prior to use. The copper(I) bromide–dimethyl sulphide complex was prepared by the method of House.[14]

The preparation and properties of the alcohols (**10**) and (**11**), the furyl alcohol (**1**), the pyranone (**3**), the pyranyl acetate (**4**), cycloadduct (**7**), and methyl-substituted adduct (**9**) have been described previously.[3]

Grignard Reactions on 2-Furaldehyde.—5-Bromo-2-methylpent-1-ene (40.2 g, 0.25 mol) was added to magnesium (8 g) in THF (200 ml) at 50 °C, the reaction being initiated with 1,2-dibromoethane. The solution was stirred for a further 0.5 h at this temperature before being cooled at 10 °C and treated with 2-furaldehyde (24.2 g, 0.25 mol). The reaction mixture was decanted from excess of magnesium and quenched with aqueous ammonium chloride. The organic layer was separated and the aqueous phase was extracted with ether. The combined organic layers were dried, the solvent was removed, and the residue chromatographed (1% ethyl acetate in dichloromethane) to give 1-(2-*furyl*)-5-*methylhex*-5-*en*-1-*ol* (**2**) (41.1 g, 92%) as a pale yellow oil (Found: M^+, 180.115 06. $C_{11}H_{16}O_2$ requires M, 180.115 02); $\nu_{max.}$ 3 380 and 1 645 cm^{-1}; δ_H (90 MHz) 1.60 (3 H, s), 2.30 (1 H, br s, OH), 4.55 (1 H, m), 4.60 (1 H, br s), 6.32 (2 H, m), and 7.30 (1 H, m).

Likewise, 1-(2-furyl)hex-5-en-1-ol (**1**) was prepared as previously described.[3]

Oxidation of Furyl Alcohols.—The furyl alcohol (**2**) (42.52 g, 0.236 mol) was dissolved in a mixture of 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 cooling well (acetone–solid CO_2) and outer vacuum jacket, with four 2-ft, 40 W fluorescent tubes until t.l.c. showed complete disappearance of starting material (8 h). The solution was then decanted into dimethyl sulphide (34 ml, 2 equiv.), and the mixture was warmed to room temperature and left until the test for peroxides (starch–iodide paper) was negative (0.5 h). Removal of solvent at water-bath temp. (< 30 °C) and filtration through silica [300 g; ether–light petroleum (1:1) as eluant] gave 6-*hydroxy*-2-(4-*methylpent*-4-*enyl*)-2H-*pyran*-3(6H)-*one* (**5**) (38.2 g, 83%) as a white solid, m.p. 55 °C (major isomer, from hexane–ether) (Found: C, 67.3; H, 8.3. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%); $\nu_{max.}$ 3 400, 1 690, and 1 660 cm^{-1}; δ_H (90 MHz) 1.71 (3 H, br s, Me), 3.82 (1 H, br s, OH), 4.60 (1 H, m), 4.70 (2 H, br s), 5.70 (1 H, d, *J* 4 Hz), 6.15 (1 H, d, *J* 10 Hz), and 6.95 (1 H, dd, *J* 4 and 10 Hz).

Likewise, the furyl alcohol (**1**) gave the previously reported[3] 6-hydroxy-2-(pent-4-enyl)-2*H*-pyran-3(5*H*)-one (**3**) in 95% yield.

Acetylation of 6-Hydroxypyran-2(6H)-*ones* (**3**) *and* (**5**).—6-Hydroxy-2-(4-methylpent-4-enyl)-2*H*-pyran-3(6*H*)-one (**5**) (39.3 g, 0.20 mol) was dissolved in dichloromethane (300 ml) containing pyridine (22.6 ml, 1.4 equiv.), and acetyl chloride (17.1 ml, 1.2 equiv.) was added to the mechanically stirred solution while the temperature was kept below 0 °C by external cooling. The resulting precipitate was filtered off and the supernatant was washed with brine (2 × 100 ml, precooled to 0 °C) and dried, the solvent was removed, and the residue was filtered through silica (200 g) [ether–light petroleum (1:1) as eluant] to give 5,6-*dihydro*-6-(4-*methylpent*-4-*enyl*)-5-*oxo*-2H-*pyran*-2-*yl acetate* (**6**) (46.4 g, 97%). An analytical sample was prepared by distillation (Found: C, 65.3; H, 7.4%; M^+, 238.119 92. $C_{13}H_{18}O_4$ requires C, 65.5; H, 7.6%; M, 238.120 50); $\nu_{max.}$ 1 700 and 1 758 cm^{-1}; δ_H (90 MHz) 1.7 (3 H, s), 2.13 (3 H, s), 4.48 (1 H, m), 4.7 (2 H, br s), 6.19 (1 H, d, *J* 10 Hz), 6.5 (1 H, d, *J* 3.5 Hz), and 6.9 (1 H, dd, *J* 10 and 3.5 Hz).

Likewise, the previously reported[3] 5,6-dihydro-5-oxo-6-(pent-4-enyl)-2*H*-pyran-2-yl acetate (**4**) was prepared in 95% yield.

Formation of the Intramolecular Cycloadducts (**7**) *and* (**8**).—The acetate (**6**) (21.98 g, 0.924 mol) was dissolved in acetonitrile (600 ml) containing triethylamine (48 ml, 4 equiv.) and the solution was refluxed for 17 h (under nitrogen) before removal of the solvent under reduced pressure. The residue was distilled to give pure cycloadduct (14.07 g), b.p. 80—84 °C/1 mbar. The residue from distillation was chromatographed on silica [(1:2)

ether–light petroleum] and the relevant fractions were combined, the solvent was removed, and the residue was distilled to give more cycloadduct; the products were combined to give a total yield of 7α-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*dec*-3-*en*-2-*one* (**8**) of (15.5 g, 94%), pale yellow oil, freezing point ~ 5 °C (Found: C, 74.1; H, 7.8%; M^+, 178.099 65. $C_{11}H_{14}O_2$ requires C, 74.2; H, 7.9%; *M*, 178.099 373); $\nu_{max.}$ 1 696 cm^{-1}; δ_H (90 MHz) 1.0 (3 H, s), 4.97 (1 H, dd, *J* 4.3 and 6.8 Hz), 5.96 (1 H, d, *J* 10 Hz), and 7.17 (1 H, dd, *J* 10 and 4.3 Hz); δ_C (22.5 MHz) 196.65 (s, C-2), 152.45 (d, C-4), 126.44 (d, C-3), 100.17 (s, C-1), 75.03 (d, C-5), 50.33 (s, C-7), 43.72 (t), 43.18 (t), 36.70 (t, C-6), 29.53 (t), 25.08 (q, Me), and 24.22 p.p.m. (t); *m/z* 178 (M^+, 12.7%), 163 (0.9 $M - CH_3$), 150 (3.8), 135 (2.6), 123 (2.8), 122 (3.1), 121 (2.8), and 81 (100, pyrylium).

Likewise, the previously reported[3] 1β,5β-epoxy-1β,7α-bicyclo[5.3.0]dec-3-en-2-one (**7**) was prepared in 95% yield.

Conjugate Isopropylation of Cycloadducts (**7**) and (**8**).—A solution of isopropylmagnesium iodide [prepared from 2-iodo-2-methylpropane (5.73 g, 33.7 mmol) and magnesium (0.81 g, 33.7 mmol)] in ether (35 ml) was added to a stirred suspension of copper(I) bromide–dimethyl sulphide complex (1.8 g, 8.7 mmol) in ether (25 ml) at 25 °C. The resulting brown suspension was stirred for 0.5 h at −10 °C before addition of a solution of the intramolecular cycloadduct (**8**) (1.0 g, 5.6 mol) in ether (10 ml), at −40 °C. The solution was stirred for 1 h at this temperature, warmed to 0 °C, quenched with saturated aqueous ammonium chloride, and extracted with ether (3 × 150 ml). The combined extracts were washed with water, dried, and the solvent was removed under reduced pressure. Chromatography on silica gel [100 g; ether–light petroleum (1:3) as eluant] gave 4β-*isopropyl*-7α-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]-*decan*-2-*one* (**45**) (1.07 g, 86%) as an oil (Found: C, 75.9; H, 9.9%; M^+, 222.162 36. $C_{14}H_{22}O_2$ requires C, 75.7; H, 9.9%; *M*, 222.161 97); $\nu_{max.}$ 1 720 cm^{-1}; δ_H (400 MHz) 0.92 (3 H, d, *J* 7 Hz, *Me*CH), 0.94 (3 H, d, *J* 7 Hz, *Me*CH), 1.13 (3 H, s, 7-Me), 1.48—2.45 (12 H, m, CH and CH_2), and 4.40 (1 H, ddd, *J* 1.25, 1.5, and 7 Hz, 5-H).

Likewise, cycloadduct (**7**) gave 4β-*isopropyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decan*-2-*one* (**32**) in 85% yield (Found: C, 74.9; H, 9.7. $C_{13}H_{20}O_2$ requires C, 74.9; H, 9.7); $\nu_{max.}$ 1 720 cm^{-1}; δ_H (90 MHz) 0.89 (6 H, two overlapping d, *J* 6.5 Hz) and 4.42 (1 H, dd, *J* 2 and 7.7 Hz).

Hydrogenation of Cycloadducts (**7**) *and* (**8**).—Cycloadduct (**8**) (14.05 g, 79 mmol) and 5% palladium–charcoal (1.5 g) were stirred in ethanol (300 ml) under hydrogen at room temperature and pressure until the theoretical volume of hydrogen had been absorbed (4.5 h). The solution was filtered through Celite then chromatographed on silica [ether–light petroleum (1:1)] to give 7α-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decan*-2-*one* (**34**) (13.44 g, 95%) as an oil (Found: C, 73.3; H, 9.1%; M^+, 180.115 14. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.9%; *M*, 180.115 02); $\nu_{max.}$ 1 171 cm^{-1}; δ_H (90 MHz) 1.0 (3 H, s), 1.6—2.5 (12 H, m), and 4.6 (1 H, br t, *J* 6 Hz); *m/z* 180 (M^+, 15.6%) 152 (21.1), 137 (5.9), 124 (4.7), 123 (5.1), 111 (7.1), 108 (52.8), and 98 (52.9).

Likewise, cycloadduct (**7**) was hydrogenated to give 1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decan*-2-*one* (**20**) (Found: C, 72.3; H, 8.5. $C_{10}H_{14}O_2$ requires C, 72.3; H, 8.5%); $\nu_{max.}$ 1 722 cm^{-1}; δ_H (90 MHz) 4.7 (1 H, br t, *J* 6 Hz).

Methylation of the Ketones (**9**), (**20**), *and* (**45**).—A solution of the ketone (**45**) (1.0 g, 4.5 mmol) in ether (20 ml) was added to a stirred solution of methylmagnesium iodide [prepared from iodomethane (1.28 g, 9 mmol) and magnesium (0.22 g, 9 mmol)] in ether (50 ml) at 0 °C. The reaction mixture was stirred for 0.5 h at room temperature before work-up with dil. hydrochloric acid and extraction with ether. The crude product was chromatographed on silica gel [75 g; ether–light petroleum (1:2) as eluant] to afford 4β-*isopropyl*-2β,7α-*dimethyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decan*-2α-*ol* (**46**) (0.915 g, 85%) m.p. 102—103 °C (from hexane) (Found: C, 75.5; H, 10.9%; M^+, 238.192 85. $C_{15}H_{26}O_2$ requires C, 75.6; H, 10.9%; *M*, 238.193 27); $\nu_{max.}$ 3 420 cm^{-1}; δ_H (90 MHz) 0.90 (6 H, d, *J* 7 Hz), 1.38 (3 H, s), 1.40 (3 H, s), 1.82 (1 H, br s, OH), and 4.55 (1 H, m, *J* 1.25, 1.5, and 7.5 Hz); *m/z* 238 (M^+, 15%), 180 (7), 163 (6), 125 (37), and 98 (100).

Likewise, ketone (**9**)[3] gave 2β,4β-*dimethyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decan*-2α-*ol* (**17**) in 83% yield, m.p. 55 °C (from hexane) (Found: C, 73.5; H, 10.2. $C_{12}H_{20}O_2$ requires C, 73.5; H, 10.2%); $\nu_{max.}$ 3 450 cm^{-1}; δ_H (90 MHz) 1.15 (3 H, d, *J* 7 Hz, 4-Me), 1.40 (3 H, s, 2-Me), and 4.15 (1 H, m, 5-H).

Likewise, ketone (**20**) gave 2β-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decan*-2α-*ol* (**21**) in 97% yield, m.p. 70—70.5 °C (from hexane) (Found: C, 72.5; H, 9.9. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.9%); $\nu_{max.}$($CHCl_3$) 3 610 cm^{-1}; δ_H (60 MHz) 1.36 (3 H, s, Me) and 4.44 (1 H, br d, *J* 6 Hz).

Chlorination of the Alcohols (**11**) *and* (**17**).—Thionyl chloride (0.3 g, 2.5 mmol) was added dropwise to a solution of the α-alcohol (**11**)[3] (0.20 g, 1.1 mmol) in HMPA (2.5 ml) and the solution was stirred for 16 h at room temperature before being poured into water (10 ml), and extraction with ether (3 × 20 ml). The combined extracts were washed with water, dried, and the solvent was removed. Chromatography of the residue on silica gel [20 g; ether–light petroleum (1:5) as eluant] gave 2α-*chloro*-4β-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decane* (**12**) (0.15 g, 68%) as a pale yellow oil (Found: M^+, 200.096 92. $C_{11}H_{17}ClO$ requires *M*, 200.096 79); $\nu_{max.}$ 2 960 cm^{-1}; δ_H (90 MHz), 1.10 (3 H, d, *J* 7 Hz, Me), 3.90 (1 H, m, 2-H), and 4.30 (1 H, m, *J* 1.5, 2, and 8 Hz, 5-H).

Likewise, alcohol (**17**) gave 2α-*chloro*-2β,4β-*dimethyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*decane* (**18**) (76%) as a pale yellow oil (Found: M^+, 214.111 69. $C_{12}H_{19}ClO$ requires *M*, 214.112 44); $\nu_{max.}$ 2 940, 1 450, 1 375, and 710 cm^{-1}; δ_H (90 MHz) 1.05 (3 H, d, *J* 7 Hz, 4-Me), 1.65 (3 H, s, 2-Me), and 4.20 (1 H, m, 5-H).

Lewis Acid–catalysed Rearrangement of the Secondary Alcohol (**10**).—Tin tetrachloride (0.05 g) was added dropwise to a stirred solution of the β-alcohol (**10**)[3] (0.20 g, 1.1 mmol) in dichloromethane (2 ml) at 0 °C. The reaction mixture was stirred at room temperature for 16 h before being quenched with water, and extraction with ether. The combined extracts were dried, the solvent was removed, and the residue was chromatographed on silica gel [51 g; ether–light petroleum (1:1) as eluant] to afford 8β-*hydroxy*-9β-*methyl*-1α,6α-*bicyclo*[4.4.0]-*decan*-2-*one* (**13**) (0.12 g, 60%), m.p. 85 °C (Found: C, 72.4; H, 9.8%; M^+, 182.130 68. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.9%; *M*, 182.130 67); $\nu_{max.}$ 3 450 and 1 700 cm^{-1}; δ_H (90 MHz) 0.95 (3 H, d, *J* 7 Hz, Me), 2.12 (1 H, br s, OH), and 3.85 (1 H, m, *J* 1.5, 2.5, and 4.5 Hz, 8-H).

Treatment of the *cis*-2-decalone (**13**) with triethylamine (1 equiv.) afforded its epimer, 8β-*hydroxy*-9β-*methyl*-1β-6α-*bicyclo*[4.4.0]*decan*-2-*one* (**14**) as a more polar component, m.p. 92 °C (from hexane–ethyl acetate) (Found: M^+, 182.130 67. $C_{11}H_{18}O_2$ requires *M*, 182.130 67); $\nu_{max.}$ 3 450 and 1 700 cm^{-1}; δ_H (90 MHz) 0.90 (3 H, d, *J* 6.5 Hz, Me), 2.2 (1 H, br s, OH), and 3.80 (1 H, m, 8-H).

Rearrangement of the Tertiary Alcohols (**17**), (**21**), *and* (**46**).—(a) *Rearrangement of alcohol* (**46**). Titanium tetrachloride (0.1 g) was added dropwise to a stirred solution of the teritary alcohol (**46**) (0.20 g, 0.84 mmol) in dichloromethane (2 ml) at 0 °C. The reaction mixture was stirred for 2 h at room temperature, hydrolysed with water, and extracted with ether. Chromatography of the residue (obtained on evaporation of the extract)

through silica gel [20 g; ether–light petroleum (1:2) as eluant] afforded (±)-cryptofauronol (**47**) (0.17 g, 83%), m.p. 108—109 °C (from light petroleum) (Found: C, 75.6; H, 10.9. Calc. for $C_{15}H_{26}O_2$: C, 75.6; H, 10.9%); $\nu_{max.}$ 3 410 and 1 695w cm^{-1}; δ_H (400 MHz) 0.90 (3 H, m, 6-Me), 0.92 (3 H, d, *J* 7 Hz, *Me*CH), 0.93 (3 H, d, *J* 7 Hz, *Me*CH), 0.96 (3 H, s, 1-Me), 1.00—2.00 (12 H, m, CH and CH_2), 1.56 (1 H, br s, OH), and 4.08 (1 H, br d, *J* 5.5 Hz, 8-H); δ_C (22.5 MHz; $CDCl_3$) (lactol form; 92%) 15.7 (q), 19.0 (t), 20.8 (q), 21.1 (q), 27.5 (q), 28.8 (t), 30.9 (d), 34.0 (t), 34.3 (t), 35.3 (t), 38.0 (s), 41.7 (s), 45.8 (d), 68.4 (d, C-8), and 99.5 p.p.m. (s, C-2); (ketol alcohol form; 8%) 16.8 (q), 20.5 (t), 20.8 (q), 21.8 (t), 24.8 (q), 28.4 (q), 32.7 (t), 34.3 (t), 34.0 (t), 37.4 (s), 38.6 (d), 43.2 (d), 43.8 (s), 67.6 (d, C-8), and 209.1 p.p.m. (s, C-2); *m/z* 238 (M^+, 23%) 195 (50), 155 (42), 137 (20), 125 (22), 110 (74), 95 (100), 81 (42), 69 (54), 55 (62), and 43 (31).

(b) *Rearrangement of alcohol* (**17**). Tin tetrachloride (0.5 g) was added to a stirred solution of tertiary alcohol (**17**) (0.25 g, 1.27 mmol) in dichloromethane (2 ml). The reaction mixture was stirred at room temperature for 16 h, quenched with water, and extracted with ether. The residue from evaporation of the ether was chromatographed on silica gel [20 g; ether–light petroleum (1:1) as eluant] to afford 8β-*hydroxy*-1α,9β-*dimethyl*-1α,6α-*bicyclo*[4.4.0]*decan*-2-*one* (**19**) (0.16 g, 65%), m.p. 46 °C (from ether–light petroleum) (Found: C, 73.4; H, 10.3. $C_{12}H_{20}O_2$ requires C, 73.5; H, 10.2%); $\nu_{max.}$ 3 400 and 1 700 cm^{-1}; δ_H (90 MHz) 0.90 (3 H, d, *J* 6 Hz, 9-Me), 1.15 (3 H, s, 1-Me), 2.40 (1 H, br s, OH), and 3.91 (1 H, m, 8-H).

(c) *Rearrangement of alcohol* (**21**). Boron trifluoride–ether complex (0.2 ml) was added dropwise to a solution of tertiary alcohol (**21**) (0.26 g, 1.43 mmol) in dichloromethane (6 ml) at 0 °C. After being stirred at room temperature for 1 h the reaction mixture was quenched with water and extracted successively with dichloromethane and ether. The combined extracts were dried, the solvents were removed, and the residue was chromatographed on silica gel [ether–light petroleum (1:1) as eluant] to give 8β-*hydroxy*-1α-*methyl*-1α,6α-*bicyclo*[4.4.0]-*decan*-2-*one* (**23**) m.p. 73—74.5 °C (Found: C, 72.3; H, 9.9. $C_{11}H_{18}O_2$ requires C, 72.50; H, 9.9%); $\nu_{max.}$($CHCl_3$) 3 610 and 1 700 cm^{-1}; δ_H (90 MHz) 1.21 (3 H, s), 3.15 (1 H, br s, OH), and 3.60 (1 H, tt, *J* 11 and 4.5 Hz); *m/z* 182 (M^+, 4.2%), 164 (60.5) 149 (21.2) 146 (11.5), and 121 (100).

Treatment of alcohol (**21**) with titanium tetrachloride in the manner described above also gave the ketone (**23**) in 86% yield.

(d) *Rearrangement of the trifluoroacetate* (**22**). The tertiary alcohol (**21**) (82 mg, 0.45 mmol) was dissolved in deuteriochloroform (0.4 ml) and trifluoroacetic anhydride (TFAA) (95 mg, 1 equiv.) was added. After 16 h, formation of the trifluoroacetate was complete as indicated by n.m.r. spectroscopy. Removal of solvent gave crude 2β-methyl-1β,5β-epoxy-1β,7α-bicyclo[5.3.0]decan-2α-yl trifluoroacetate (**22**) (118 mg, 94%). In a separate experiment this product was purified by chromatography (dichloromethane as eluant) and distillation to give the pure *trifluoroacetate* (Found: C, 55.9; H, 6.2; F, 20.7. $C_{13}H_{17}F_3O_3$ requires C, 56.1; H, 6.2; F, 20.5%); $\nu_{max.}$ 1 780 cm^{-1}; δ_H (90 MHz) 1.77 (3 H, s) and 4.5 (1 H, vbr s).

The trifluoroacetate (**22**) (118 mg, 0.42 mmol) was dissolved in deuteriochloroform (0.4 ml) and TFA (0.2 ml) was added. After 7 days at room temperature, ^1H n.m.r. spectroscopy showed complete conversion into the rearranged compound (**24**). Removal of solvent and chromatography of the residue on silica gel [ether–light petroleum (1:3) as eluant] gave pure 6α-*methyl*-7-*oxo*-1α,6α-*bicyclo*[4.4.0]*decan*-3β-*yl trifluoroacetate* (**24**) as an oil (78 mg, 62% from the initial alcohol) (Found: C, 56.3; H, 6.1; F, 20.6. $C_{13}H_{17}F_3O_3$ requires C, 56.1; H, 6.1; F, 20.5%); $\nu_{max.}$ 1 781 and 1 710 cm^{-1}; δ_H (90 MHz) 1.24 (3 H, s, Me) and 4.90 (1 H, tt, *J* 10.7 and 4.8 Hz); *m/z* 278 (M^+, 1.4%), 234 (1.4), 165 (23.8), 164 (79.2), 149 (22.9), 164 (23.7), and 121 (100). The structure of compound (**24**) was confirmed by its identity with the compound obtained by treatment of alcohol (**23**) with TFAA. Trifluoroacetate (**24**) could be hydrolysed quantitatively to the alcohol (**23**) with aqueous sodium hydrogen carbonate.

2β-*Methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*dec*-3-*en*-2α-*ol* (**25**).—To a solution of cycloadduct (**7**) (0.35 g, 2.1 mmol) at −30 °C in ether was added methyl-lithium (1.9 ml of a 1.5M solution in ether). After having warmed to 0 °C the reaction mixture was quenched with water and extracted with ether. Chromatography on silica [ether–light petroleum (1:1) as eluant] gave the *title compound* (**25**) (0.27 g, 71%) as white crystals, m.p. 99—100 °C (from hexane) (Found: C, 73.6; H, 9.1%; M^+, 180.114 91. $C_{11}H_{16}O_2$ requires C, 73.3; H, 9.0%; *M*, 180.115 02); $\nu_{max.}$($CHCl_3$) 3 660w, 3 600s, 3 440brs, and 1 600w cm^{-1}; δ_H (90 MHz) 1.29 (3 H, s), 2.13 (1 H, dd, *J* 9 and 12 Hz), 2.77 (1 H, br q, *J* 8 Hz, OH), 4.40 (1 H, dd, *J* 4 and 5 Hz), 5.37 (1 H, d, *J* 9 Hz), and 5.75 (1 H, dd, *J* 9 and 4 Hz); *m/z* 180 (M^+, 17.5%), 165 ($M - CH_3$, 1.7), 162 ($M - H_2O$, 5.7), 147 (5.3), 123 (10.9), 119 (17.5), and 97 (100).

Rearrangement of Tertiary Allylic Alcohol (**25**).—(a) *Preparation of* 8-*hydroxy*-1α-*methyl*-1α,6α-*bicyclo*[4.4.0]*dec*-9-*en*-2-*ones* (**26**) *and* (**27**). The tertiary allylic alcohol (**25**) (93 mg) was dissolved in dichloromethane (6 ml) and boron trifluoride–ether complex (0.1 ml) was added at room temperature. After 10 min the reaction was quenched with water and the products were extracted into ether. The extract was evaporated and the residue eluted through silica with ether–light petroleum gave the *title material* as a pale yellow oil (89.4 mg, 96%), b.p. 92 °C/0.5Torr (Found: C, 73.3; H, 8.9%; M^+, 180.115 023. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.9%; *M*, 180.115 023); $\nu_{max.}$ 3 400brs and 1 704s cm^{-1}; *m/z* 180 (M^+, 17.3%), 162 (3.2), 147 (6.6), 118 (18.9), and 93 (100). ^{13}C and ^1H N.m.r. spectroscopy showed this to be an 11:1 mixture of isomers (only major isomer resonances are listed): δ_H (400 MHz) 1.274 (3 H, s), 1.40 (1 H, dt, *J* 9.38 and 12.65 Hz), 1.59 (1 H, dm, *J* 14 Hz), 1.78—1.89 (3 H, m), 1.96 (1 H, dm, *J* 13 Hz), 2.05—2.27 (3 H, m), 2.55 (1 H, ddd, *J* 14.6, 12.3, and 7.2 Hz), 5.65 (1 H, dd, *J* 10.1 and 1.67 Hz), and 5.74 (1 H, dt, *J* 10.1 and 1.66 Hz); δ_C (22.5 MHz; $CDCl_3$) 22.75 (t), 25.19 (q), 27.30 (t), 36.03 (t), 38.30 (t), 41.77 (s), 50.54 (s), 67.61 (d), 130.99 (d), 133.59 (d), and 215.13 p.p.m. (s). The major isomer was assigned as the 8β-alcohol (**26**).

(b) *Preparation of* 8-*chloro*-1α-*methyl*-1α,6α-*bicyclo*[4.4.0]-*dec*-9-*en*-2-*ones* (**28**) *and* (**29**). Tertiary allylic alcohol (**25**) (90 mg, 0.5 mmol) was dissolved in dichloromethane (2 ml), and titanium tetrachloride (0.1 ml) was added at room temperature. After 5 min the reaction was quenched with water. Usual work-up gave a 3:1 mixture of the *title chlorides*, m.p. range 45—65 °C (Found: C, 66.6; H, 7.7; Cl, 17.6%; M^+, 198.081 08 and 200.0784. $C_{11}H_{15}ClO$ requires C, 66.5; H, 7.6; Cl, 17.8%; *M*, 198.081 14 and 200.078 24); $\nu_{max.}$($CHCl_3$) 1 700 cm^{-1}; δ_H (400 MHz) (major isomer) 1.39 (3 H, s, Me), 1.62 (1 H, ddq, *J* 14, 1.5, and 3.5 Hz), 1.8—2.0 (3 H, m, includes 5-H at δ 1.87), 2.02 (1 H, ddd, *J* 14.5, 11.8, and 4.5 Hz, 5-H), 2.34 (1 H, m), 2.2—2.3 (2 H, m), 2.60 (1 H, ddd, *J* 14.5, 12.5, and 6.5 Hz), 4.66 (1 H, br q, *J* 4.5 Hz), 5.78 (1 H, dt, *J* 10 and 0.8 Hz, 2-H), 5.91 (1 H, ddd, *J* 10, 4.5, and 1.2 Hz, 3-H); irradiation at δ 4.66 removes couplings of 4.5 Hz from 3-H, 0.8 Hz from 2-H, and 4.5 Hz from 5-H, and changes the multiplet in the region of δ 1.9. Decoupling experiments showed that this isomer is most likely the 8α-chloride (**28**). δ_H (Minor isomer; only visible resonances listed) 1.30 (3 H, s, Me), 1.71 (1 H, ddq, *J* 14, 1.5, and 4 Hz), 2.075 (1 H, dddd, *J* 13, 6, 2.5 and 1.2 Hz), 2.30 (1 H, ddt, *J* 15, 4.5, and 1.8 Hz), 2.56 (1 H, ddd, *J* 15, 10.5, and 8.5 Hz), 4.585 (1 H, ddt, *J* 9, 7.5, and 2 Hz), 5.75 (1 H, ddd, *J* 10, 2, and 0.8 Hz), and 5.82 (1 H, ddd, *J* 10, 2, and 1.2 Hz); decoupling experiments showed that this isomer is most likely the 8β-chloride (**29**); *m/z* 200 (M^+, 5.6%), 198 (M^+,

15.9), 185 (0.7), 183 (2.7), 163 (6.4), 162 (6.9), 152 (3.0), 145 (63.5), 119 (27.9), 118 (68.6), 105 (38.3), and 93 (100).

Rearrangement of the Ketones (**32**) and (**34**).—(a) 1α,8β-*Dihydroxy*-6α-*methyl*-1α,6α-*bicyclo*[4.4.0]*decan*-2-*one* (**35**). Ketone (**34**) (4.056 g, 22.5 mmol) was dissolved in acetonitrile (40 ml), and titanium tetrachloride (7 ml) was added during 5 min, the solution being allowed to get warm, to give a deep red colour. After 2 h the reaction mixture was quenched with water (30 ml) and thoroughly extracted with ether. The combined ether extracts were dried, the solvent was removed, and the residue was chromatographed [silica; ether–light petroleum (1:1)] to give recovered ketone (1.844 g, 45.5%) and *title compound* (**35**) (2.239 g, 50.2%, 92% based on consumed starting material), m.p. 126.5—128 °C (from dichloromethane) (Found: C, 66.8; H, 9.2%; M^+, 198.125 68. $C_{11}H_{10}O_2$ requires C, 66.7; H, 9.1%; M, 198.125 59); $\nu_{max.}$($CHCl_3$) 3 450 and 1 700 cm^{-1}; δ_H (90 MHz) 0.82 (3 H, s), 3.8 (1 H, br s, exchanged by D_2O shake, OH), and 4.14 (1 H, m); δ_C (22.5 MHz; CD_3OD) 21.508 (t), 21.725 (q, C-11), 27.847 (t), 29.473 (t), 35.269 (t), 36.894 (t), 41.607 (t), 41.715 (s, C-6), 49.896 (d, C-4), 66.202 (s, C-1), and 214.045 p.p.m. (s, C-10); *m/z* 198 (M^+, 21.3%), 181 (M − OH, 11.5), 180 (M − H_2O, 4.9), 170 (16.7), 164 (9.4), 162 (13.8), 152 (21.6), and 128 (100).

(b) 1α,8β-*Dihydroxy*-9β-*isopropyl*-1α,6α-*bicyclo*[4.4.0]*decan*-2-*one* (**33**). Ketone (**32**) (86 mg, 0.38 mmol) was dissolved in dry dichloromethane (2 ml), and titanium tetrachloride (0.1 ml) was added at room temperature. After 16 h the reaction was quenched with water and the products were extracted into ether. Chromatography gave, as the major product, *title keto diol* (**33**) (45 mg, 48%) (Found: C, 69.9; H, 9.9%; M^+, 226.156 75. $C_{13}H_{22}O_3$ requires C, 69.0; H, 9.8% M, 226.156 89); $\nu_{max.}$ 3 680w, 3 610, 3 480br, and 1 702s cm^{-1}; δ_H (90 MHz) 0.91 (3 H, d, *J* 4.3 Hz), 0.98 (3 H, d, *J* 3.6 Hz), 3.96 (1 H, s, OH), and 4.2 (1 H, br s); *m/z* 226 (M^+, 32.6%), 208 (10.8), 182 (15.4), 156 (18.7), and 151 (47).

Ethylene Acetal (**26**).—The ketone (**34**) (580 mg) was dissolved in ethylene glycol (10 ml) with trimethyl orthoformate (1 ml) and PTSA (20 mg), and the mixture was heated at 85 °C for 2 h under conditions where liberated methanol was distilled off. The reaction mixture was then diluted with water and extracted with ether, the combined extracts being washed successively with aqueous sodium carbonate and brine. Chromatography gave the *acetal* (**26**) (654 mg, 91%) as white crystals, m.p. 51—52 °C (from hexane) (Found: C, 69.5; H, 8.9%; M^+, 224.141 45. $C_{13}H_{20}O_3$ requires C, 69.6; H, 8.9%; M, 224.141 20); δ_H (90 MHz) 1.20 (3 H, s), 3.93 (4 H, m), and 4.38 (1 H, br d); *m/z* 224 (M^+, 3.5%), 127 (45.8), 99 (41.0), and 86 (100).

Rearrangment of Ethylene Acetal (**36**).—Acetal (**36**) (200 mg) was dissolved in dichloromethane (8 ml), and titanium tetrachloride (0.2 ml, 2 equiv.) was added. The reaction mixture was immediately quenched with water and extracted with ether. The crude product was chromatographed through silica with ether–light petroleum as eluant to give the *rearranged acetal* (**37**) (101 mg, 50%) (Found: M^+, 224.141 54. $C_{13}H_{20}O_3$ requires M, 224.141 45); δ_H (90 MHz) 1.05 (3 H, s), 2.4—2.9 (2 H, m), 3.4—3.6 (1 H, m), 3.7 (1 H, m), and 3.85—4.2 (3 H, m); δ_C (22.5 MHz), 14.46 (t), 18.58 (t), 23.84 (q, C-11), 27.14 (t), 27.90 (t), 34.24 (t), 36.12 (s, C-6) 42.09 (t), 58.83 (t, C-12/13), 62.46 (t, C-13/12), 67.28 (d, C-4), 72.92 (s, C-1), and 98.60 p.p.m. (s, C-10); *m/z* 224 (M^+, 34.40%), 180 (4.6), 127 (12.1), 115 (14.1), 110 (100), and 95 (58.5).

Formation and Rearrangement of the Dimethyl Acetal (**38**).—Ketone (**34**) (2.18 g, 0.12 mol) was dissolved in methanol (10 ml) and trimethyl orthoformate (12 ml) and PTSA (50 mg) were then added. The mixture was refluxed for 3 h before being quenched with potassium carbonate. Removal of volatiles and chromatography [ether–light petroleum (1:10 → 1:2)] gave the products (**40**) (723.3 mg, 26%) as a solid foam, (**39**) (683.5 mg, 29%) as an oil, and (**38**) (951 mg, 35%) as an oil. These showed the following properties.

1α,2α-*Dimethoxy*-7α-*methyl*-2β,8β-*epoxy*-1α,6α-*bicyclo*-[4.4.0]*decane* (**40**) (Found: M^+, 226.157 03. $C_{13}H_{22}O_3$ requires M, 226.156 89); $\nu_{max.}$ nothing above 1 500 cm^{-1}; δ_H (90 MHz) 1.0 (3 H, s), 3.26 (3 H, s), 3.34 (3 H, s), and 3.85 (1 H, m); *m/z* 226 (M^+, 68.7%), 195 (14.4), 194 (52.4), 185 (23.5), 151 (100), and 139 (88.4).

2-*Methoxy*-7α-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]*dec*-2-*ene* (**39**) (Found: C, 74.2; H, 9.2%; M^+, 194.130 89. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%; M, 194.130 67); $\nu_{max.}$ 1 654 cm^{-1} (enol ether); δ_H (90 MHz) 0.98 (3 H, s), 2.7 and 2.23 (2 H, AB quartet, *J* 13 Hz, with fine splitting which is removed on irradiation at δ 4.45), 3.48 (3 H, s), and 4.45 (2 H, m); *m/z* 194 (M^+, 45.1%), 179 (3.8), and 151 (100).

2,2-*Dimethoxy*-7α-*methyl*-1β,5β-*epoxy*-1β,7α-*bicyclo*[5.3.0]-*decane* (**38**) (Found: C, 69.0; H, 9.8%; M^+, 226.156 66. $C_{13}H_{22}O_3$ requires C, 69.0; H, 9.7%; M, 226.156 88); δ_H (90 MHz) 1.18 (3 H, s), 3.25 (3 H, s), 3.30 (3 H, s), and 4.4 (1 H, br d, *J* 8 Hz); *m/z* 226 (M^+, 3.7%), 195 (M − CH_3O, 24.5) 194 (M − CH_3OH, 12.5), 151 (21.9), 135 (17.3), 129 (63.9), 101 (52.0), and 88 (100).

8β-*Hydroxy*-1α-*methoxy*-6α-*methyl*-1α,6α-*bicyclo*[4.4.0]-*decan*-2-*one* (**41**).—The rearranged product (**40**) (640 mg) was dissolved in THF (15 ml), and dil. sulphuric acid (3 ml) was added. After 24 h the reaction mixture was neutralised with aqueous sodium carbonate and extracted with several portions of ether. The crude product obtained on work-up was chromatographed [silica; ether–light petroleum (1:1) as eluant] to give the *title compound* (**41**) (553 mg, 92%) as white crystals m.p. 100—101 °C (ether) (Found: C, 67.9; H, 9.6%; M^+, 212.141 53. $C_{12}H_{20}O_3$ requires C, 67.9; H, 9.4%; M, 212.141 24); $\nu_{max.}$($CHCl_3$) 3 600 and 1 711 cm^{-1}; δ_H (90 MHz) 1.08 (3 H, s), 1.40 (1 H, br s, OH), 3.06 (3 H, s, OMe), and 3.93 (1 H, m); δ_C (22.5 MHz) 21.24 (t), 22.43 (t), 22.64 (q), 32.29 (t), 34.78 (t), 38.08 (t), 42.42 (t), 42.91 (t), 50.71 (q), 66.42 (d), 82.89 (s), and 212.15 p.p.m. (s); *m/z* 212 (M^+, 27.6%), 194 (13.0), 152 (18.1), 151 (29.2), and 142 (96.7).

Rearrangement and Chlorination of Enone (**7**).—Titanium tetrachloride (0.3 ml) was added to a solution of cycloadduct (**7**) (0.25 g) in dichloromethane (5 ml) and the mixture was stirred at room temperature for 16 h. After the mixture had been quenched with water the products were extracted into ether, the extract was dried, the solvent was removed, and the residue was chromatographed on silica [ether–light petroleum (1:2)] to give 8α-*chloro*-1α-*hydroxy*-1α,6α-*bicyclo*[4.4.0]*dec*-8-*en*-2-*one* (**42**) (0.17 g, 56%), m.p. 90—92 °C (from ether–hexane) (Found: C, 60.1; H, 6.6; Cl, 17.1%; M^+, 200.060 17 and 202.056 97. $C_{10}H_{13}ClO_2$ requires C, 59.9; H, 6.5; Cl, 17.7%; M, 200.060 40 and 202.057 45); $\nu_{max.}$ 3 490 and 1 715 cm^{-1}; δ_H (400 MHz; C_6H_6) 0.9—1.1 (3 H, m), 1.3 (2 H, m), 1.70 (1 H, br ddd, *J* 11, 5.5, and 5.5 Hz, 1.86 (1 H, ddd, *J*, 14.5, 13.5, and 7 Hz), 2.15 (1 H, dddd, *J* 14.5, 4.5, 2.5 and 1.5 Hz), 2.41 (1 H, dddt, *J* 18.5, 6, 3.8, and 2.5 Hz), 4.3 (1 H, br s, OH), 4.49 (1 H, dddd, *J* 3.8, 2.5, 2.0, and 1.8 Hz, 2-H), 5.45 (1 H, dddt, *J* 10, 5, 1, and 2.5 Hz, 4-H), and 5.51 (1 H, ddt, *J* 10, 3, and 2 Hz, 3-H); δ_C (22.5 MHz; $CDCl_3$) 25.57 (t), 27.14 (t), 28.50 (t), 36.89 (t), 44.15 (d), 58.45 (d), 78.12 (s), 124.69 (d), and 209.28 p.p.m. (s); *m/z* 202 (M^+, 4.3%), 200 (M^+, 10.5), 184 (12.1), 182 (37.8), 165 (6.1), 164 (9.6), 154 (13.8), 147 (57.3), and 84 (100).

2α-*Chloro*-10-*oxo*-1α,6α-*bicyclo*[4.4.0]dec-3-*en*-1α-*yl Acetate* (**43**).—The alcohol (**42**) (91 mg) was dissolved in a mixture of

acetic anhydride (1 ml) and pyridine (0.5 ml), and DMAP (10 mg) was added. After the mixture had been stirred overnight at room temperature, volatiles were removed (40 °C; 1 Torr) and the residue was chromatographed on silica (1% ethyl acetate in dichloromethane as eluant). This gave the *title acetate* (**43**) (100 mg, 91%) as white crystals, m.p. 118.5—120 °C (from ether) (Found: C, 59.2; H, 6.1; Cl, 14.5. $C_{12}H_{15}ClO_3$ requires C, 59.4; H, 6.2; Cl, 14.6%); $\nu_{max.}$(CHCl$_3$) 1 745s, with shoulder at 1 730 cm^{-1}; $\lambda_{max.}$(EtOH) 202.7 nm (ε 5 040); δ_H (400 MHz), 1.48 (1 H, m), 1.9—2.0 (2 H, m), 2.05—2.20 (2 H, m, 7-H$_2$), 2.19 (3 H, s, Me), 2.25—2.38 (2 H, m), 2.62 (1 H, dt, *J* 7.6 and 12.7 Hz), 2.82 (1 H, m), 5.27 (1 H, br d, *J* 5.1 Hz, 10-H), 5.74 (1 H, ddd, *J* 9.8, 4.7, and 2.8 Hz, 8-H), and 5.90 (1 H, dddd, *J* 9.8, 5.1, 2.6, and 1.6 Hz, 9-H); δ_C (22.5 MHz) 20.75 (q), 23.9 (t), 24.32 (t), 26.55 (t), 36.41 (d), 38.36 (t), 54.88 (d), 83.70 (s), 126.33 (d), 127.47 (d), 170.11 (s), and 205.27 p.p.m. (s).

(±)-*Fauronyl Acetate* (**48**).—Sodium acetate (0.2 g) was added to a solution of (±)-cryptofauronol (**47**) (0.1 g, 0.42 mmol) in acetic anhydride (2 ml) and the suspension was stirred under reflux for 4 h. The solvent was evaporated under reduced pressure and the residue was chromatographed through silica gel [10 g; ether–light petroleum (1:3)] to afford (±)-fauronyl acetate (**48**) (0.094 g, 82%), m.p. 80.82 °C (from light petroleum).

(±)-*Fauronyl Acetate Ethylene Acetal* (**49**).—Fauronyl acetate (**48**) (0.1 g, 0.36 mmol), ethylene glycol (5 ml), and PTSA (0.02 g) were heated in benzene (25 ml) in a Dean–Stark apparatus for 18 h before addition of ether. The extract was washed with water and dried, and the solvent was removed under reduced pressure. The residue was chromatographed through silica gel (10 g), with ether–light petroleum as eluant, to give the *title acetal* (**49**) (0.07 g, 60%) as platelets, m.p. 102—104 °C; $\nu_{max.}$ 2 960, 2 880, 1 725, 1 239, 1 195, and 1 075 cm^{-1}; δ_H 0.85 (3 H, d, *J* 7 Hz, *Me*CH), 0.88 (3 H, s, Me), 0.91 (3 H, d, *J* 7 Hz), 0.95 (3 H, s, Me), 2.30 (3 H, s, OAc), 1.15—2.40 (12 H, m), 3.80—4.10 (4 H, m acetal CH$_2$), and 5.05 (1 H, q, *J* 4 Hz); *m/z* 324 (*M*$^+$, 5%), 265 (27), 113 (15), 99 (100), 86 (64), 69 (13), 55 (28), and 43 (77) (Found: *M*$^+$, 324.230 01. $C_{19}H_{32}O_4$ requires *M*, 324.230 05).

(±)-*Fauronol Ethylene Acetal* (**50**).—A solution of the acetate (**49**) (70 mg, 0.2 mmol) in 1M- ethanolic KOH (2 ml) was heated to reflux for 4 h before work-up under standard conditions to afford the *title alcohol* (**50**) (50 mg, 82%), m.p. 70 °C (from ether–hexane); $\nu_{max.}$ 3 600, 3 400, 2 960, 1 195, and 1 082 cm^{-1}; δ_H (90 MHz), 0.85 (3 H, s, Me), 0.88 (3 H, d, *J* 6.5 Hz, *Me*CH), 0.92 (3 H, s, Me), 0.96 (3 H, d, *J* 6.5 Hz, *Me*CH), 1.00—2.80 (13 H, m), 3.95 (4 H, m, acetal CH$_2$), and 4.12 (1 H, m) (Found: *M*$^+$, 282.219 47. $C_{17}H_{30}O_3$ requires *M*, 282.219 48).

Oxidation of the Acetal (**50**).—A solution of acetal (50 mg, 0.18 mmol) in pyridine (1.5 ml) was added to a solution of chromium trioxide (0.2 g) in pyridine (1.5 ml) and the mixture was stirred at room temperature for 7 h. After addition of ether and extraction with water the organic phase was dried, the solvent was distilled off, and the residue was chromatographed through silica, with ether–light petroleum as eluant, to give the corresponding ketone (**51**) (0.04 g, 80%) as a pale yellow liquid, $\nu_{max.}$(CHCl$_3$) 2 950, 2 880, 1 712, 1 195, and 1 080 cm^{-1}; δ_H (60 MHz) 0.83 (3 H, s, Me), 0.85 (3 H, d, *J* 6.5 Hz, Me), 0.90 (3 H, s, Me), 1.10 (3 H, d, *J* 6.5 Hz, Me) 1.00—2.35 (10 H, m), 2.15 (2 H, ABq, *J* 14 Hz, CH$_2$), and 3.95 (4 H, m, OCH$_2$CH$_2$O); *m/z* 280 (*M*$^+$, 7%), 265 (6), 237 (5), 181 (9), 113 (22), 99 (100), 86 (8), 69 (12), 55 (21), and 43 (17) (Found: *M*$^+$, 280.204 30. $C_{17}H_{28}O_3$ requires *M*, 280.203 83).

(±)-*Valeranone* (**52**).—The ketone (**51**) (0.04 g) was heated with hydrazine hydrate (0.3 ml) to reflux for 4 h. Triethylene glycol (1.5 mol) was added and the mixture was heated to 170 °C for 0.5 h to remove volatile fractions. Potassium hydroxide (0.04 g) was added and the mixture was heated at 195 °C for 2 h. The reaction mixture was allowed to cool to room temperature, water (5 ml) was added, the organic product was extracted with ether, and the crude product was subjected to column chromatography through silica gel (5 g), with ether–light petroleum (1:5) as eluant. The major fraction (25 mg, 66%), which showed $\nu_{max.}$(CHCl$_3$) 2 960, 2 800, 1 198, and 1 078 cm^{-1}, was immediately heated in refluxing aqueous ethanolic HCl [1 ml of a solution prepared from conc. HCl (0.5 ml), water (0.5 ml), and ethanol (3.5 ml)] for 1 h. The solution was cooled and poured into ether (10 ml); the organic phase was washed with water and dried, and solvent was removed under reduced pressure. Chromatography of the residue through silica gel (5 g), with ether–light petroleum (1:5) as solvent, gave the title ketone (**52**) (15 mg, 90%) as an oil, $\nu_{max.}$(CHCl$_3$) 2 960, 2 880, and 1 700 cm^{-1}; δ_H 0.80 (3 H, s, Me), 0.86 (6 H, d, *J* 7 Hz, *Me*$_2$CH), 1.05 (3 H, s, Me), and 1.15—2.90 (14 H, m); *m/z* 222 (*M*$^+$, 34%), 151 (14), 125 (15), 109 (39), 98 (100), 81 (49), 69 (62), 35 (64), and 43 (50) (Found: *M*$^+$, 222.198 27. Calc for $C_{15}H_{26}O$: *M*, 222.198 36).

(±)-*Valerane* (**53**).—A solution of sodium dichromate (0.06 g) in a mixture of conc. H_2SO_4 (0.076 g) and water (1 ml) was added to a solution of (±)-cryptofuranol (**47**) (50 mg) in ether (3 ml) and the mixture was stirred at room temperature for 5 h. The mixture was extracted with ether, the extract was dried and evaporated, and the residue was chromatographed through silica gel (10 g) with ether–light petroleum (1:1) as solvent to give (±)-valerane-2,8-dione (48 mg, 97%), m.p. 51—53 °C. This material was dissolved in ethanol and the solution was treated with hydrazine hydrate (0.1 ml) at reflux for 1 h. Potassium hydroxide (0.2 g) and triethylene glycol (0.75 ml) were added and this solution was heated to 190 ± 5 °C for 4 h, while the volatile fraction was removed by distillation. The mixture was cooled, poured into water (5 ml), and extracted with ether. The extract was dried, the solvent was removed by careful evaporation, and the residue was chromatographed through silica gel (5 g), with light petroleum as eluant, to afford (±)-valerane[15] (**53**) (40 mg, 93%) as a mobile oil, $\nu_{max.}$(CHCl$_3$) 2 940, 2 880, 1 530, 1 400, and 1 382 cm^{-1}; δ_H 0.85 (3 H, s, Me), 0.87 (6 H, d, *J* 5 Hz, *Me*$_2$CH), 0.88 (3 H, s, Me), and 0.90—2.20 (16 Hz, m); *m/z* 208 (*M*$^+$, 15%), 193 (66), 164 (25), 137 (26), 123 (23), 109 (78), 95 (74), 83 (92), 69 (100), 55 (83), and 43 (39) (Found: *M*$^+$, 208.219 05. Calc. for $C_{15}H_{28}$: *M*, 208.219 09).

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