Synthetic Study on Several Eremophilane Sesquiterpenes using a Common Intermediate

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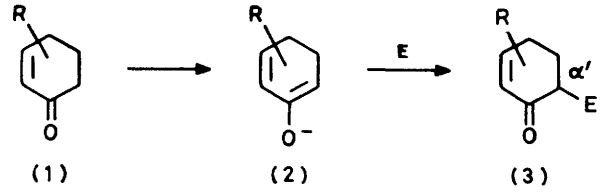
The syntheses of racemic ishwarane (6), dehydrofukinone (7), hydroxyeremophilone (8), 9,10-dehydrofuranoeremophilane (9), 10α-furanoeremophilone (10), and 9,10-dehydrofuranoeremophil-1-one (11) from a common intermediate, *cis*-4,4a,5,6,7,8-hexahydro-4a,5-dimethylnaphthalen-2(3*H*)-one (5), are described. For the synthesis of ishwarane (6) the key step is sequential Michael addition and displacement of the enolate of the isomeric octalone, *cis*-4a,5,6,7,8,8a-hexahydro-4a,5-dimethylnaphthalen-1(4*H*)-one (4), prepared from the octalone (5), with methyl α-bromoacrylate; for the syntheses of the other terpenes (7)—(11) the key step is the zinc chloride-assisted aldol condensation of the enolates of the octalone (5) and the suitably functionalised derivatives with acetone or acetonyl tetrahydropyranyl ether.

RECENTLY, there has been a surge of interest in the formation and reaction of the kinetic enolates of αβ-unsatured ketones for synthetic uses. For example, cyclohex-2-enones (1) generate, upon treatment with strong bases at low temperature, the kinetically controlled enolates (2), which undergo alkylation with alkyl halides,[1] aldol condensation with aldehydes and ketones,[2,3] and Michael addition with αβ-enolates [4] or a vinylphosphonium salt,[5] to afford the regioselectively α′-alkylated products (3). Among the examples, the



(1) (2) (3)

E = electrophile

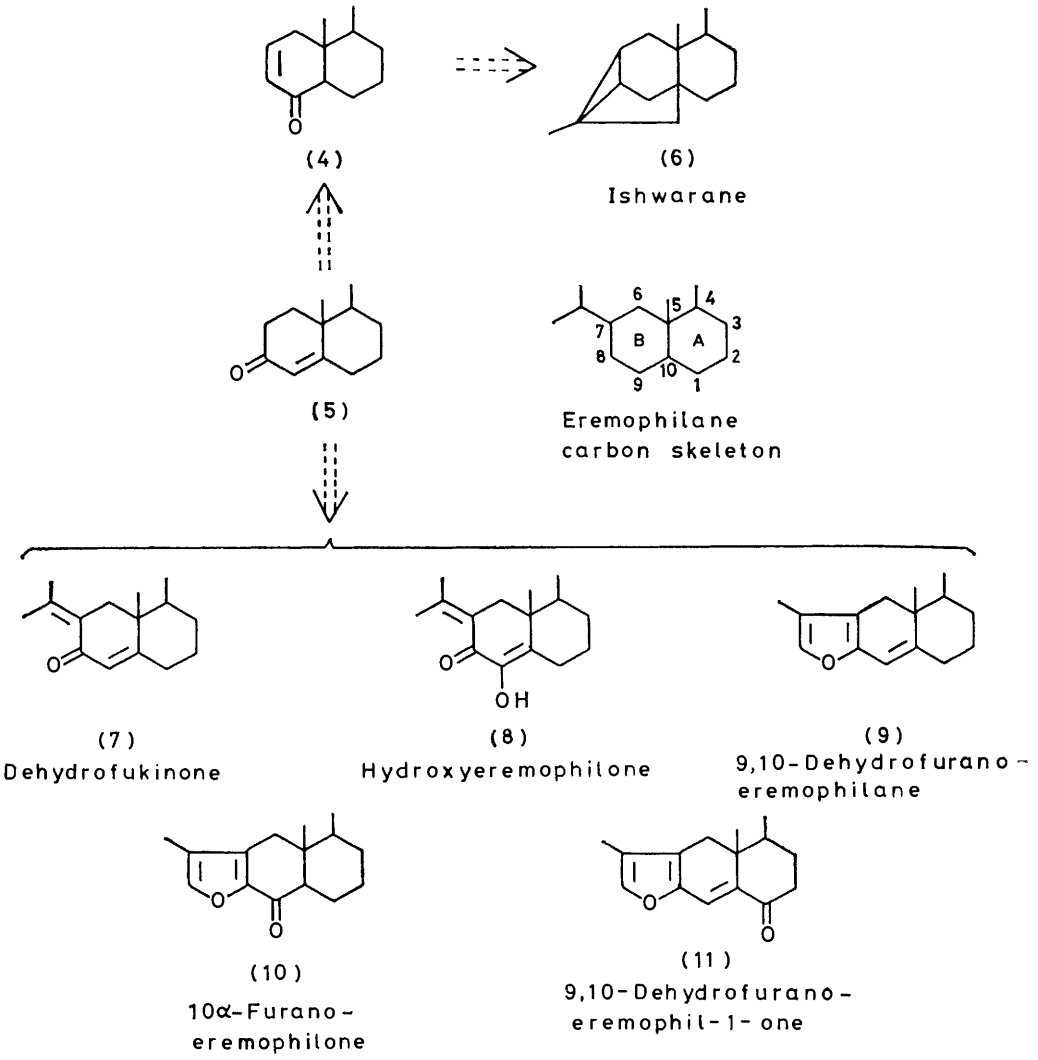
Michael reaction of dienolate anions (2) with methyl α-bromocrotonate, as previously communicated,[4c] is of particular interest. In this case, the initially formed Michael adduct subsequently underwent internal Michael attack to the enone moiety followed by an intramolecular displacement of the bromine atom by the enolate, giving rise to the tricyclo[3.2.1.0^{2,7}]octan-6-one system in one step (bicycloannelation), similar to the case of a vinylphosphonium salt [5] (see Scheme 2). We expected that if the kinetic enolate of the dimethyloctalone (4) was also generated and allowed to react with methyl α-bromoacrylate in the same manner, the carbon skeleton of ishwarane (6) would be produced in one step. We now describe, in addition to the synthesis of ishwarane (6), the syntheses of five eremophilane sesquiterpenes (7)—(11) [6] starting from the known dimethyloctalone (5),[7] which involve the aldol condensation of the kinetic enolates (Scheme 1).

RESULTS AND DISCUSSION

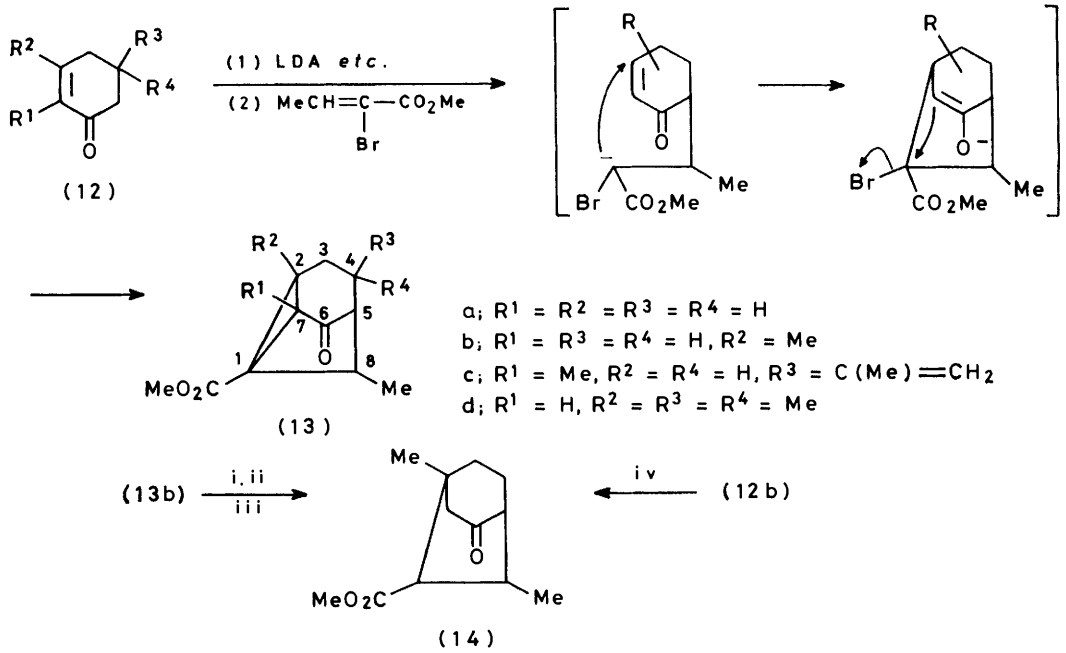
Model experiments for the bicycloannelation reaction of simple cyclohexenones with methyl α-bromocrotonate or methyl α-bromoacrylate in detail, and the application to the synthesis of ishwarane (6), are described first, followed by the syntheses of other eremophilanoids (7)—(11) including an approach to warburgiadione (55).

Model Experiments for Bicycloannelation of Cyclohex-2-en-1-ones and the Synthesis of (±)-*Ishwarane* (6).—The enolates of cyclohex-2-en-1-one (12a), 3-methylcyclohex-2-en-1-one (12b), (−)-carvone (12c), and isophorone (12d), generated by kinetically controlled treatment with lithium di-isopropylamide (LDA) or lithium cyclohexyl-isopropylamide [for (12d)], reacted with methyl α-bromocrotonate to afford the bromine-free bicycloannelated products (13a) (30%), (13b) (55%), (13c) (25%), and (13d) (20%), respectively (Scheme 2). Each of these products was seemingly a single compound, and the analytical and spectral data are in accord with the assigned tricyclo[3.2.1.0^{2,7}]octan-6-one structures (13). Reduction of compound (13b) with lithium in liquid ammonia, followed by oxidation with Jones reagent and esterification, afforded the bicyclic keto-ester (14) which was identified with the sample prepared by the reaction of 3-methylcyclohex-2-en-1-one (12b) with methyl crotonate. The conversion of compound (13b) into (14) could be accounted for by reductive cleavage of a cyclopropyl ketone function and unambiguously proves the structure of the products (13).

In order to clarify the stereochemistry of the reaction, the reactions of methyl α-bromoacrylate with 5,5-dimethylcyclohex-2-en-1-one (12; $R^1 = R^2 = H$, $R^3 = R^4 = Me$), 5-methylcyclohex-2-en-1-one (12; $R^1 = R^2 = R^3 = H$, $R^4 = Me$), and (−)-carvone (12c) were carried out and afforded the analogous tricyclic products (15a) (62%), (15b) (56%), and (15c) (35%), respectively (Scheme 3). From the normal n.m.r. spectrum, compound (15b) appeared to be a single stereoisomer, but, by the addition of a shift reagent [0.21 mol % of Eu(dpm)$_3$], the secondary methyl signal was clearly separated into two signals at δ 1.67 and 1.48 with an area ratio of *ca.* 4 : 1. Thus, compound (15b) was a *ca.* 4 : 1 mixture of the stereoisomers with respect to the secondary methyl group. Reduction of compound (15a) with sodium borohydride was found to proceed stereospecifically giving a single hydroxy-ester (16a). The reagent, hydride, would attack the C-6 carbonyl group from the less hindered C-1–C-8 side, and therefore,



SCHEME 1



SCHEME 2 Reagents: i, Li–liquid NH_3–Bu^tOH; ii, Jones reagent; iii, CH_2N_2; iv, LDA–HMPA–THF, then $MeCH{=}CHCO_2Me$

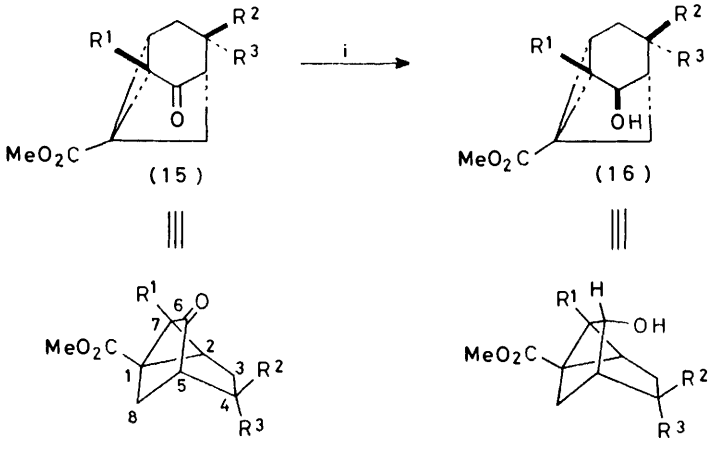
the hydroxy-group should be oriented in the C-3–C-4 side in compound (16a) as depicted. Indeed, this assignment is correct; in the Eu(dpm)$_3$-shifted n.m.r. spectrum the signal at δ 1.18 moved significantly downfield with a linear slope of 5.12 × 10^2 Hz/R_p, being assignable to the R^2-methyl group *cis* to the hydroxy-group, while the signal at δ 0.93 due to the R^3-methyl group moved more slowly (2.28 × 10^2 Hz/R_p) (Table 1). Similarly, compound (15b) was reduced to the hydroxy-ester (16b), in which the secondary methyl signal appeared as two doublets at δ 1.15 and 0.90 with the same area ratio of *ca.* 4 : 1 as the precursor (15b), indicating that the C-6 keto-group was also reduced stereospecifically to produce a hydroxy-group with the same orientation as in compound (16a). It was observed that, in the Eu(dpm)$_3$-shifted n.m.r. spectrum, the intense signal at δ 1.15 moved downfield rapidly, and the weak one at δ 0.90 slowly, with almost equal slopes, 5.12 and 2.46 × 10^2 Hz/R_p, for the R^2- and R^3-methyl groups in compound (16a), respectively. Hence, the major stereoisomer of compound (15b) has the *cis* configuration between the C-4 methyl and C-6 carbonyl groups on the C-1,2,3,4,5,8-carbocycle, as shown.

TABLE 1

Lanthanide-induced [Eu(dpm)$_3$] shifts of methyl signals

	Shift in Hz/R_p [a] (× 10^2)			
Compound	R^2-Me at C-4	R^3-Me at C-4	tertiary-Me at C-4	secondary-Me at C-5
(16a)	5.12	2.28		
(16b) Major	5.12			
Minor		2.46		
(26)			4.84	1.29

[a] R_p = Shift reagent (mol)/Substrate (mol).

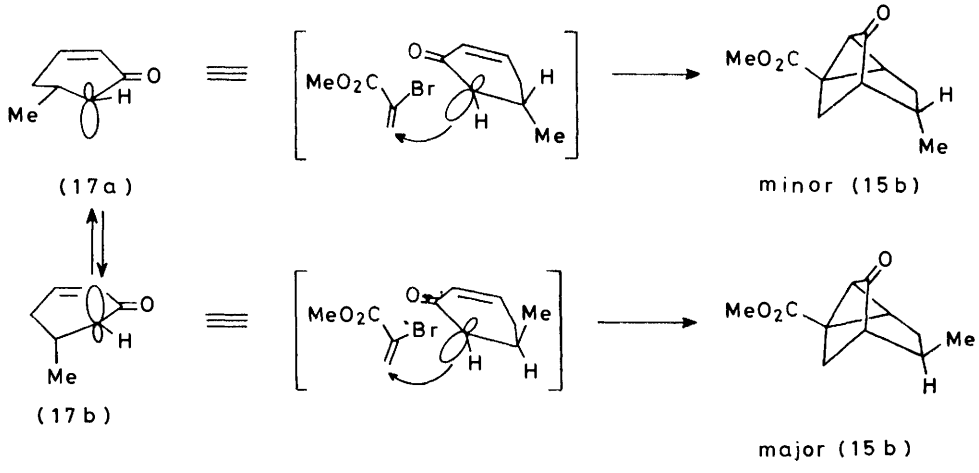


a; R^1 = H, R^2 = R^3 = Me

b; R^1 = R^3 = H, R^2 = Me major

R^1 = R^2 = H, R^3 = Me minor

c; R^1 = Me, R^2 = C(Me)=CH$_2$, R^3 = H

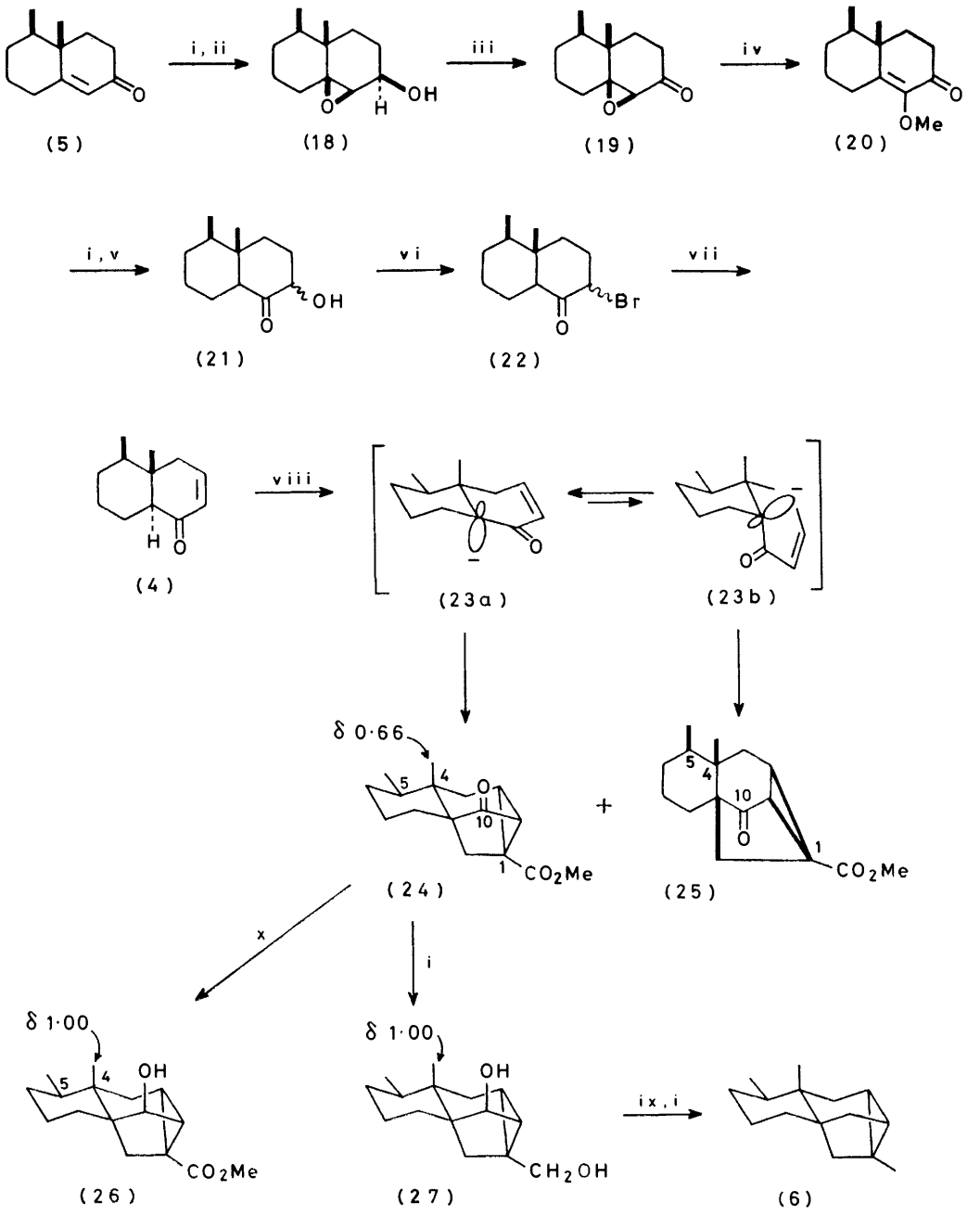


SCHEME 3 Reagents: i, $NaBH_4$–MeOH

The above findings provide some information on the

stereochemistry of the bicycloannelation reactions. The kinetically controlled enolate of 5-methylcyclohex-2-en-1-one should exist in equilibrium between the *cis*-(17a) and the *trans*-enolate (17b), with the latter sterically more favourable to react with methyl bromoacrylate, be assigned as indicated,[5] since the bulkiness of the isopropenyl group would favour markedly the reactivity of the *trans*-type enolate.

Analogously, in compound (13c), from the reaction of the crotonate, the configuration of the isopropenyl



SCHEME 4 Reagents: i, $LiAlH_4$–ether; ii, MCPBA–CH_2Cl_2; iii, Jones reagent; iv, NaOMe–MeOH, reflux; v, dil. HCl, 60—65 °C; vi, PBr_3–CCl_4; vii, LiBr–Li_2CO_3–DMF, reflux; viii, LDA–THF, −90 °C, then CH_2=C(Br)CO_2Me, −80 to −40 °C; ix, MsCl–Et_3N–CCl_4; x, $NaBH_4$–MeOH

leading to the major stereoisomer (Scheme 3). The *ca.* 4 : 1 ratio of the stereoisomers in compound (15b) would reflect roughly the reactivities of these two enolates. Compound (15c) was shown to be a single compound, and from the above argument, the stereochemistry may group would be same as that of compound (15c). In this and the other compounds (13), however, the configuration at C-8 remains unresolved.

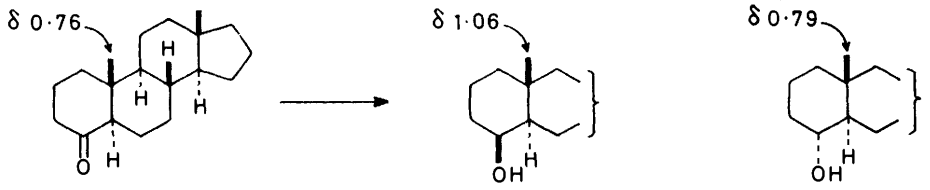
As is clear from the examples cited above, α-bromo-αβ-enolates are useful biannelating agents, and the pro-

cess is applicable to the synthesis of a complex ring system from monocyclic precursors in one step, although the yields of the products are not so high.

Ishwarane [8] is one of a number of sesquiterpenoid hydrocarbons isolated from *Aristolochia indica* Linn. and other tropical plant species, along with the related ketonic constituent, ishwarone,[9] and contains a unique tricyclo[3.2.1.$0^{2,7}$]octane system fused to an additional six-membered ring. Such is the structural interest in this compound that already three total syntheses have been reported,[10-12] in which construction of the tricyclo-octane system has been attained by the base-induced cyclisation of a γ-sulphonyloxy-ketone,[10] by the reductive cyclisation of a homoallylic sulphonate,[11] or by sequential carbene addition and insertion.[12] The bicycloannelation of the dimethyl-octalone (4) with methyl α-bromoacrylate, if successful, would provide an alternative approach to the synthesis of the carbon framework of ishwarane. Our synthetic course is outlined in Scheme 4.

Our first step was to prepare the key enone component (4), and the known *cis*-dimethyloctalone (5) [7] was chosen as the most suitable starting material. The octalone (5) was reduced by lithium aluminium hydride to give the allylic alcohol, which was transformed to the epoxy-alcohol (18) on treatment with *m*-chloroperbenzoic acid (MCPBA). Jones oxidation of compound (18) afforded the epoxy-decalone (19) in 86% yield. Direct epoxidation of the octalone (5) with hydrogen peroxide–sodium hydroxide was found to be fruitless. In the n.m.r. spectrum of the epoxy-alcohol (18), the signal of the proton attached to the carbon atom bearing the hydroxy-group was observed as a broad multiplet with a half-height width of 10 Hz, indicating that the proton was quasi-axial (*trans* to the dimethyl groups). Thus, the configuration of the epoxide ring in compounds (18) and (19) could be assigned to be *cis* to the hydroxy and methyl groups, as suggested by the well known stereochemistry of the epoxidation of cyclic allylic alcohols with peracids.[13] Reaction of compound (19) with two equivalents of sodium methoxide in refluxing methanol [14] produced in 56% yield the methoxy-octalone (20), which was treated with lithium aluminium hydride followed by hydrolysis to give the ketol (21). Direct dehydration of compound (21) to the desired octalone (4) was unsatisfactory and resulted in a complex mixture. Compound (21) was therefore converted into the bromoketone (22) [66% from (20)] by treatment with phosphorus tribromide; dehydrobromination then afforded the octalone (4) in 81% yield. The octalone (4) thus obtained was stable to base, indicating a *trans* configuration at the ring juncture.

As expected, the kinetically controlled enolate of the octalone (4) reacted with methyl α-bromoacrylate yielding the bicycloannelated product. It was found, however, that the reaction was not stereoselective and proceeded in low yield, giving rise to the stereoisomers (24) and (25) in 20 and 12% yields, respectively. Analytical and spectral properties of both isomers were entirely consistent with the assigned tetracyclic keto-ester structures. It is apparent that compounds (24) and (25) arose from two stereoisomeric enolates, a *trans*-decalin-type enolate (23a) and a *cis*-one (23b), respectively. In such a rigid bicyclic system, the *trans*-enolate (23a) is probably more stable than the inverted *cis*-one (23b) and will thus predominate and give the major product (24), possessing the ishwarane stereochemistry as indicated. This assignment was substantiated by comparison of the chemical-shift values of the tertiary methyl signals for the keto-ester (24) and the hydroxy-ester (26). Reduction of the major keto-ester (24) with sodium borohydride afforded the single hydroxy-ester (26). The tertiary methyl signal was shifted downfield



(28) (29) (30)

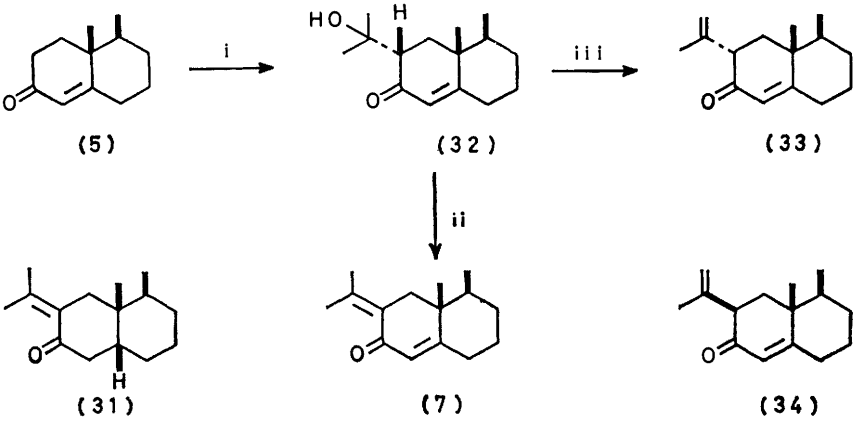
(0.34 p.p.m.) upon conversion of the keto-group (24) into the hydroxy-group (26). The shift is approximately the same (0.30 p.p.m.) as that observed upon conversion of androstan-4-one (28) into androstan-4β-ol (29).[15] Furthermore, in the Eu(dpm)$_3$-shifted spectrum of compound (26), the tertiary methyl signal moved significantly downfield with a linear slope of 4.84×10^2 Hz/R_p, similar to the case of compounds (16) discussed earlier (Table 1). These facts clearly establish a *cis*-diaxial relationship between the tertiary methyl and hydroxy-groups in the hydroxy-ester (26) and thus the stereochemistry of the keto-ester (24).

Reduction of compound (24) with lithium aluminium hydride also proceeded stereoselectively to give a single diol (27), in which the configuration of the secondary hydroxy-group was similarly assigned as *cis* to the tertiary methyl group by observation of the methyl n.m.r. signal at δ 1.00. The diol (27) was mesylated and the resulting unstable dimesylate, without purification, was reduced with lithium aluminium hydride to (±)-ishwarane (6). The synthetic material, isolated by preparative g.l.c., was identical with a sample of natural ishwarane (comparison of infrared, n.m.r., and mass spectra, and g.l.c. behaviour).

Synthesis of Other Sesquiterpenoids.—The successful generation and reaction of the kinetically controlled enolate of the octalone (4) was extended to other

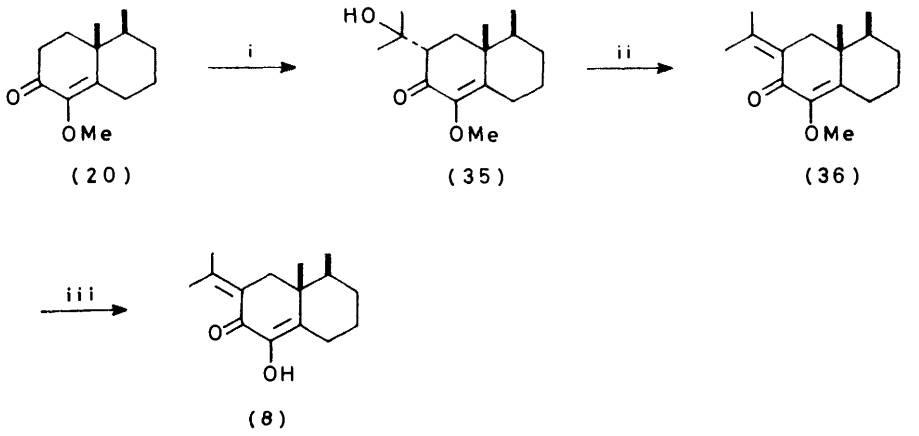
octalones, not only the parent compound (5) but also the derivatives (20) and (41), in order to synthesise other sesquiterpenoids *via* the kinetic enolates. This section describes the syntheses of five eremophilane sesquiterpenes

(±)-*Dehydrofukinone* (7).—Dehydrofukinone was first prepared by dehydrogenation of a natural sesquiterpenoid, fukinone (31) (from *Petasites japonicus* Maxim.),[16] and was recently found in *Cacalia hastata* L. subsp. *orientalis* Kimura.[17] Its synthesis has already been achieved by Ohashi by isoxazole annelation.[18] Reaction of the enolate of the octalone (5), generated by treatment with LDA, with acetone in the presence of zinc chloride [19] gave the single aldol product (32) in 94% yield. Absence of zinc chloride resulted in considerably decreased yields. Treatment of the adduct (32) in refluxing benzene with a catalytic amount of toluene-*p*-sulphonic acid afforded dehydrofukinone (7) (81%), identical with an authentic sample (Scheme 5).* When the dehydration was conducted by treatment with thionyl chloride–pyridine at 0 °C, a mixture of dehydrofukinone (7) and the isopropenyl derivative (33) was produced. However it was found that compound (33) was not identical with alloeremophilone (34),[21] and is thus the stereoisomer, in respect of the isopropenyl group, with the newly introduced substituent in the aldol product (32) occupying a quasi-equatorial configuration as depicted.[22]



SCHEME 5 Reagents: i, LDA–$ZnCl_2$–THF, −50 to −36 °C, then acetone, −36—0 °C; ii, *p*-TsOH–benzene, reflux; iii, $SOCl_2$–pyridine, 0 °C

(±)-*Hydroxyeremophilone* (8).—Hydroxyeremophilone is one of a trio of bicyclic sesquiterpene ketones isolated from *Eremophila mitchelli* as the first example of eremophilane sesquiterpenoids; [23] the synthesis of the natural (+)-compound has already been accomplished by Pinder and Torrence.[24] As described above, the methoxyoctalone (20) was subjected to aldol condensation with acetone followed by dehydration of the resulting adduct (35) to give an 83% yield of hydroxyeremophilone methyl ether (36). Treatment of the methyl ether (36) with boron tribromide led to hydroxyeremophilone (8) in 90% yield. The u.v. and i.r. spectra of both synthetic materials (8) and (36) were identical with those of authentic samples.

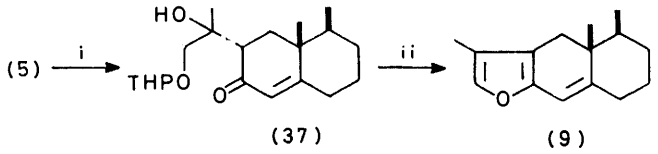


SCHEME 6 Reagents: i, LDA–$ZnCl_2$–THF, −55 to −40 °C, then acetone, −40—0 °C; ii, *p*-TsOH–benzene, reflux; iii, BBr_3–CH_2Cl_2, −100 to −20 °C

(±)-9,10-*Dehydrofuranoeremophilane* (9).—9,10-Dehydrofuranoeremophilane is one of the furanoeremophilanoid constituents isolated from *Senecio teretifolius* DC.[25]

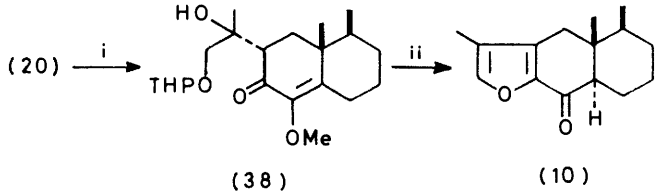
* Very recently, Torii *et al.* have also synthesised dehydrofukinone, using the same method as ourselves (ref. 20).

In order to construct the fused 3-methylfuran ring, acetonyl tetrahydropyranyl ether was used instead of acetone for the aldol condensation. The reaction of the kinetically controlled enolate of the octalone (5) with acetonyl tetrahydropyranyl ether under identical conditions proceeded well, as expected, to give the adduct



SCHEME 7 Reagents: i, LDA–$ZnCl_2$–THF, −100 to −85 °C, then acetonyl tetrahydropyranyl ether, −85 to −40 °C; ii, *p*-TsOH–H_2O–THF, 60 °C

(37) in 86% yield. Treatment of compound (37) with toluene-*p*-sulphonic acid in refluxing aqueous tetrahydrofuran furnished directly a 60% yield of fairly unstable 9,10-dehydrofuranoeremophilane (9) (Scheme 7). The spectral data (u.v., i.r., n.m.r., and mass) of the synthetic material taken immediately after the isolation were in accord with the reported values.*

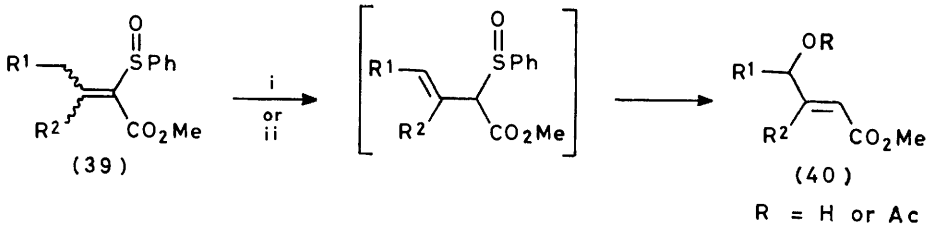


SCHEME 8 Reagents: i, LDA–$ZnCl_2$–THF, −100 to −85 °C, then acetonyl tetrahydropyranyl ether, −65 to −38 °C; ii, *p*-TsOH–H_2O–THF, 60 °C

(±)-10α-*Furanoeremophilone* (10).—In similar fashion, the reaction of the methoxyoctalone (20) with acetonyl tetrahydropyranyl ether gave in 65% yield the adduct (38), which was transformed quantitatively by treatment with acid to 10α-furanoeremophilone (10) (Scheme 8), one of the sesquiterpenoids isolated from *Petasites hybridus* (L.) rhizomes [27] and also from *Senecio teretifolius* DC.[25,28]

(±)-9,10-*Dehydrofuranoeremophil*-1-*one* (11) *and Synthetic Approach to* (±)-*Warburgiadione* (55).—9,10-Dehydrofuranoeremophil-1-one and warburgiadione were next chosen as targets for synthesis; these terpenes possess an additional functional group(s) on ring A. Previously,[29] we reported a regiospecific conversion of α-phenylsulphinylacrylates (39) into (*E*)-γ-hydroxyacrylates (40) through a base-catalysed sequential prototropic shift and allylic sulphoxide–sulphenate rearrangement (Scheme 9). This process appeared to be applicable to introduce a hydroxy-group onto ring A (C-1 position of the eremophilane system), and our initial efforts were directed towards the preparation of the phenylsulphinyl-octalone (42). The synthesis of the precursory phenylthio-octalone (41) was accomplished easily and in high yield by the reaction of the epoxyoctalone (19) with thiophenol.[14] Oxidation of compound (41) with *m*-chloroperbenzoic acid gave quantitatively the desired phenylsulphinyloctalone (42) (Scheme 10). Compound (42), as expected, underwent smoothly, on treatment with pyridine–acetic anhydride, rearrangement to afford a 1 : 1 mixture of stereoisomers of the acetoxyoctalones (43) and (44), which were hydrolysed to the corresponding hydroxyoctalones (45) and (46) in 50% yield. The hydroxyoctalones (45) and (46) were directly and more efficiently obtained by reaction of compound (42) with aqueous pyridine (73% yield) or diethylamine–aqueous tetrahydrofuran (83% yield). Assignment of the configuration of the hydroxy-group in each isomer, being α-equatorial in (45) or β-axial in (46) as depicted in Scheme 10, follows from comparison of the half-height width of the 1-H signal in the n.m.r. spectra, 17 Hz (axial) in (45) and 5 Hz (equatorial) in (46). It was found, however, that even the tetrahydropyranyl ethers of the hydroxyoctalones (45) and (46) were extremely sensitive to base and, therefore, could not be subjected to the next stage of synthesis, the aldol condensation.

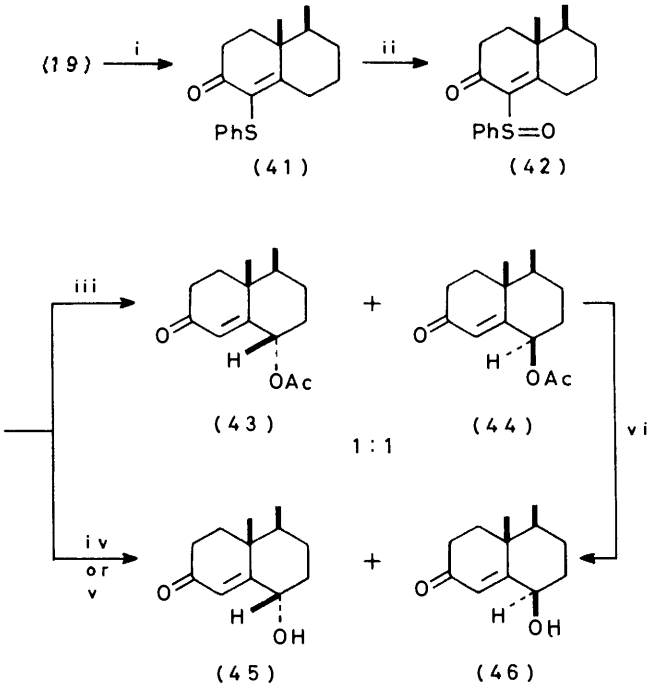
We therefore adopted aldol condensation of the phenylthio-octalone (41) before the rearrangement–hydroxylation. Aldol condensation of compound (41) with acetonyl tetrahydropyranyl ether proceeded cleanly to afford the adduct (47) in 62% yield (Scheme 11). Oxidation of the adduct (47) with *m*-chloroperbenzoic acid followed by treatment with diethylamine in aqueous tetrahydrofuran produced a mixture of the hydroxy-octalones (48), which, without separation, was oxidised by Collins reagent to give the keto-octalone (49) [52% yield from compound (47)]. Hydrolysis and ring-closure of compound (49) as described above led to an 85% yield of 9,10-dehydrofuranoeremophil-1-one (11), one of the sesquiterpenes isolated from *Senecio teretifolius* DC.[25] The spectral properties of the synthetic material were identical with the reported values.



SCHEME 9 Reagents: i, pyridine–H_2O; ii, pyridine–Ac_2O

* Yamakawa and Satoh have also recently synthesized this compound.[26]

Warburgiadione has been isolated from *Warburgia ugandensis* Sprague,[30] and the synthesis has been achieved by Yamakawa and his co-workers.[31] Our approaches to the synthesis of (±)-warburgiadione



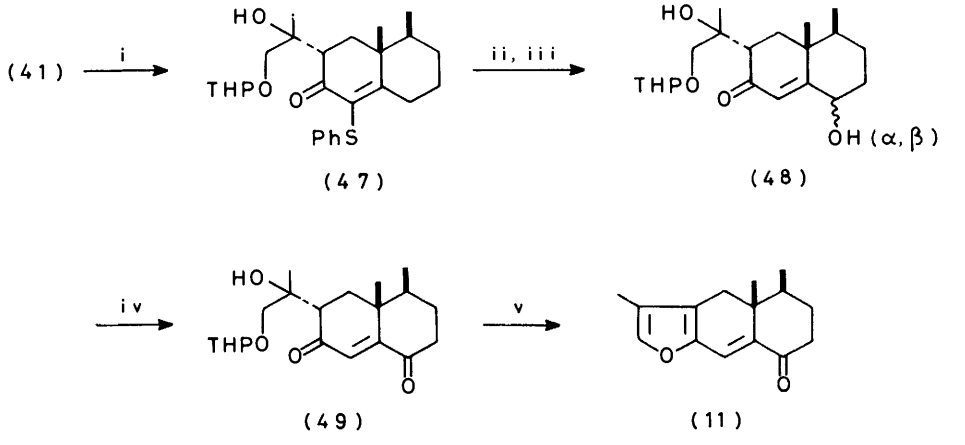
SCHEME 10 Reagents: i, PhSH–15%NaOH–EtOH, room temp.; ii, MCPBA–CH_2Cl_2; iii, pyridine–Ac_2O, room temp.; iv, pyridine–H_2O, 90 °C; v, Et_2NH–H_2O–THF, room temp.; vi, K_2CO_3–MeOH

(55) are shown in Scheme 12. Similar sequential reactions (aldol condensation with acetone, dehydration, oxidation, and rearrangement) of the phenylthio-octalone (41) *via* compound (50) gave the isopropylidene-hydroxy-octalones (51) and (52) (1—5 : 1) in 42% overall yield. The configuration of the hydroxy-group in each isomer was assigned as in the case of compounds (45) and (46). It was noteworthy that the axial hydroxy-isomer (52) was much less reactive towards the tosylation reagent than the equatorial hydroxy-isomer (51) and, in fact, it was completely unreactive under conditions (Scheme 12) which were conducive to essentially complete reaction of the isomer (51). The tosyloxyoctalone (53) thus obtained afforded, in 88% yield, the isopropylidene-dienone, 3-deoxowarburgiadione (54), on treatment with lithium bromide in hot dimethylformamide. At present, however, all attempts to introduce an oxygen-function at C-3, leading to warburgiadione (55), under a wide variety of conditions, have been unsuccessful.

EXPERIMENTAL

Liquids were normally purified by evaporative short-path distillation; oil-bath temperatures are recorded. I.r. spectra were obtained for solutions in carbon tetrachloride (unless otherwise indicated) with a Hitachi EPI-G2 spectrophotometer. U.v. spectra were run for solutions in ethanol (unless otherwise indicated) on a Hitachi EPS-3T or JASCO UVIDEC-505 spectrophotometer. ^1H N.m.r. spectra [for solutions in carbon tetrachloride (unless otherwise indicated)] and ^{13}C n.m.r. spectra [for solutions in deuteriochloroform] were recorded with a JEOL C-60HL or PMX-60 instrument (for ^1H spectra) and a JEOL JNM-MH-100 or MFT-100 instrument (for ^{13}C spectra), with tetramethylsilane as internal standard. Mass spectra were obtained on a Shimadzu LKB-9000 spectrometer. Microanalyses were carried out in the microanalytical laboratory of this Institute.

Methyl 8-Methyl-6-oxotricyclo[3.2.1.$0^{2,7}$]*octane-1-carboxylate* (13a).—To a solution of lithium di-isopropylamide (2.4 mmol) in anhydrous tetrahydrofuran (THF) (2 ml) and hexane (1.6 ml) was added dropwise a solution of cyclohex-2-en-1-one (195 mg, 2 mmol) in THF (2 ml) and then a solution of hexamethylphosphoric triamide (HMPT) (430 mg, 2.4 mmol) in the same solvent (2 ml) at −30 °C under nitrogen, and the solution was stirred at −30 to −19 °C for 1 h. A solution of methyl α-bromocrotonate (429 mg, 2.4 mmol) in THF (3 ml) was added, and the resulting mixture was stirred at −19 °C to room temperature for 1 h



SCHEME 11 Reagents: i, LDA–$ZnCl_2$–THF, −80 to −75 °C, then acetonyl tetrahydropyranyl ether, −75 to −40 °C; ii, MCPBA–CH_2Cl_2; iii, Et_2NH–H_2O–THF, room temp.; iv, Collins reagent–CH_2Cl_2; v, *p*-TsOH–H_2O–THF, 60 °C

and then at room temperature for 1 h. The progress of the reaction was monitored by t.l.c. on silica gel [eluant hexane–ethyl acetate (5 : 1)]. Saturated aqueous ammonium chloride was added, and the product was extracted

with ether. The combined extracts were washed with water and brine, dried, and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *tricyclic keto-ester* (13a) (110 mg, 28%); negative Beilstein test; b.p. 75 °C at 1 mmHg; $\nu_{max.}$ ($CHCl_3$) 1 730 and 1 165 cm^{-1}; δ 1.25 (3 H, d, *J* 6.0 Hz, Me at C-8), 1.50—3.00 (8 H, m), and 3.63 (3 H, s, CO_2Me) (Found: C, 67.7; H, 7.0%; M^+, 194. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.3%; *M*, 194).

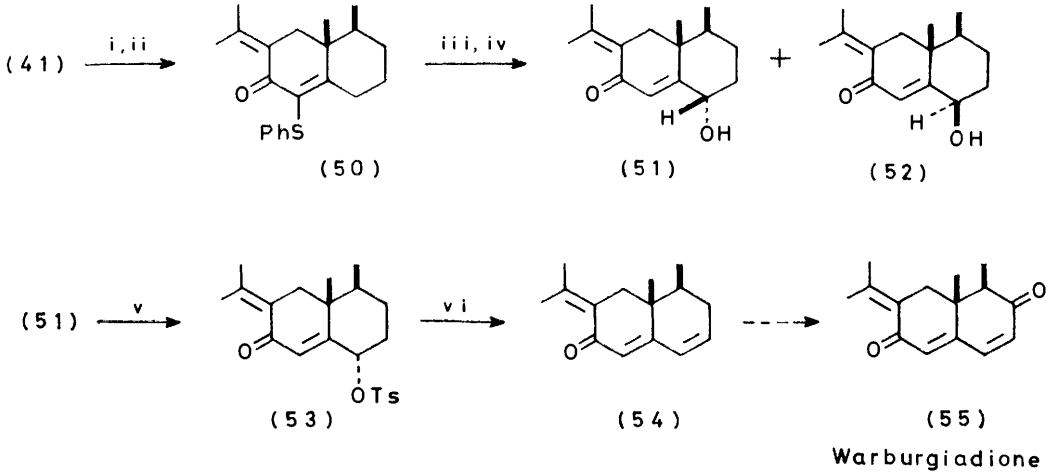
Methyl 2,8-*Dimethyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]*octane*-1-*carboxylate* (13b).—The reaction of 3-methylcyclohex-2-en-1-one (226 mg, 2 mmol) was carried out as in the preceding experiment. Preparative t.l.c. [eluant light petroleum–diethyl ether (3 : 1)] gave the *tricyclic keto-ester* (13b) (235 mg, 55%); negative Beilstein test; b.p. 100 °C at 3 mmHg; $\nu_{max.}$ ($CHCl_3$) 1 735, 1 720, 1 710, 1 430, 1 280, and 1 260 cm^{-1}; δ 1.30 (3 H, s, 2-Me), 1.32 (3 H, d, *J* 7.0 Hz, 8-Me), 1.71—2.33 (7 H, m), and 3.67 (3 H, s, CO_2Me); δ_C 13.84 (q, 8-Me), 20.19 (q, 2-Me), 23.35 (t, C-4), 24.07 (t, C-3), 33.49 (d, C-8), 40.98 (s, C-2), 44.77 (s, C-1), 44.94 (d, C-7), 46.92 (d, C-5), 51.75 (q, CO_2Me), 170.75 (s, CO_2Me), and 211.98 (s, C-6) (Found: C, 69.0; H, 7.9%; M^+, 208. $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7%; *M*, 208).

Methyl 4-*Isopropenyl*-7,8-*dimethyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]-*octane*-1-*carboxylate* (13c).—The reaction of (−)-carvone (301 mg, 2 mmol) was carried out as described above. Preparative t.l.c. [eluant hexane–ethyl acetate (3 : 1)] gave the *tricyclic keto-ester* (13c) (114 mg, 23%); negative Beilstein test; b.p. 110 °C at 3 mmHg; $\nu_{max.}$ 1 725, 1 645, 1 245, and 980 cm^{-1}; δ 1.13 (3 H, s, 7-Me), 1.21 (3 H, d, *J* 7.0 Hz, 8-Me), 1.63 [3 H, s, $-C(Me)=CH_2$], 1.76—3.00 (6 H, m), 3.67 (3 H, s, CO_2Me), and 4.68 [2 H, br, $-C(Me)=CH_2$]; δ_C 9.02 (q, 8-Me), 13.93 [q, $-C(Me)=CH_2$], 21.82 (t, C-3), 21.82 (q, 7-Me), 31.96 (d, C-8), 36.93 (d, C-2), 40.51 (d, C-4), 43.24 (s, C-7), 44.69 (s, C-1), 49.25 (d, C-5), 51.92 (q, CO_2Me), 111.13 [t, $-C(Me)=CH_2$], 146.31 [s, $-C(Me)=CH_2$], 170.16 (s, CO_2Me), and 210.44 (s, C-6) (Found: C, 72.7; H, 8.0%; M^+, 248. $C_{15}H_{20}O_3$ requires C, 72.6; H, 8.1%; *M*, 248).

Methyl 2,4,4,8-*Tetramethyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]*octane*-1-*carboxylate* (13d).—To a solution of lithium cyclohexyl-isopropylamide (1.3 mmol) in anhydrous THF (1.5 ml) and hexane (0.8 ml) was added dropwise a solution of isophorone (138 mg, 1 mmol) in THF (1.5 ml) at −30 °C under nitrogen, and the mixture was stirred at −30 °C for 1 h. Then a solution of methyl α-bromocrotonate (216 mg, 1.2 mmol) in THF (2 ml) was added to the above solution at −21 °C, and the reaction mixture was stirred at that temperature for 2 h. More bromocrotonate (90 mg) was added, and the mixture was further stirred at room temperature for 2 h. Work-up as above and preparative t.l.c. of the crude product on silica gel [eluant light petroleum–diethyl ether (2 : 1)] gave the *tricyclic keto-ester* (13d) (46 mg, 20%); negative Beilstein test; $\nu_{max.}$ 1 725, 1 250, and 1 145 cm^{-1}; δ 0.83 (3 H, s, 2-Me), 1.11—1.31 (6 H, br, 4-*gem*-Me_2), 1.46 (3 H, d, *J* 7.8 Hz, 8-Me), 1.55—2.91 (5 H, m), and 3.65 (3 H, s, CO_2Me) (Found: M^+, 236. $C_{14}H_{20}O_3$ requires *M*, 236).

Methyl 1,3-*Dimethyl*-5-*oxobicyclo*[2.2.2]*octane*-2-*carboxylate* (14).—(a) *From* 3-*methylcyclohex*-2-*en*-1-*one*. To a solution of lithium di-isopropylamide (2.3 mmol) in anhydrous THF (2 ml) and hexane (1.8 ml) was added dropwise a solution of 3-methylcyclohex-2-en-1-one (194 mg, 1.76 mmol) in THF (2 ml) and then a solution of HMPT (379 mg, 2.1 mmol) in the same solvent (2 ml) at −60 °C under nitrogen. After being stirred at −60 °C for 1 h, a solution of methyl crotonate (454 mg, 4.54 mmol) in THF (2 ml) was added, and the reaction mixture was stirred at −60 °C to room temperature for 3 h, and at room temperature for a further 30 min. The reaction was quenched by addition of dilute hydrochloric acid, and the product was extracted with dichloromethane. The combined extracts were washed with water and brine, and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant light petroleum–diethyl ether (1 : 1)] gave the *bicyclic keto-ester* (14) (350 mg, 95%); b.p. 105—115 °C at 3 mmHg; $\nu_{max.}$ 1 730 and 1 165 cm^{-1}; δ 0.90 (3 H, s, tertiary Me), 1.09 (3 H, d, *J* 6.5 Hz, secondary Me), 1.33—2.60 (9 H, m), and 3.65 (3 H, s, CO_2Me) (Found: C, 68.8; H, 8.7%; M^+, 210. $C_{12}H_{18}O_3$ requires C, 68.5; H, 8.6%. *M*, 210).

(*b*) *From the tricyclic keto-ester* (13b). A solution of compound (13b) (263 mg, 1.26 mmol) in ethanol (5 ml), followed by a small amount of t-butyl alcohol, was added dropwise to freshly distilled liquid ammonia under nitrogen and cooling with a methanol–solid CO_2-bath. Lithium metal (at first 68 mg, 7.7 mol. equiv. then an additional 25



SCHEME 12 Reagents: i, LDA–$ZnCl_2$–THF, −70—0 °C, then acetone −53—0 °C; ii, *p*-TsOH–benzene, reflux; iii, MCPBA–CH_2Cl_2; iv, Et_2NH–H_2O–THF, room temp.; v, TsCl–pyridine, −50 °C to room temp.; vi, LiBr–DMF, 60 °C

mg) was then added portionwise to the above solution. After 30 min, saturated aqueous ammonium chloride (2 ml) was added, and the mixture was allowed to stand at room temperature and then at 30—40 °C until almost all the ammonia had evaporated off. Dilute hydrochloric acid was added, and the resulting mixture extracted with ether. Evaporation of the extracts left an oily residue (166 mg); $\nu_{max.}$ 3 620 and 1 715 cm^{-1}. To a solution of the residue in acetone (5 ml) was added dropwise Jones reagent [32] at room temperature until the orange colour persisted. Usual work-up (dilution with water, extraction with ether, and evaporation) gave the product (114 mg), which was treated with an excess of ethereal diazomethane in the usual manner. After evaporation of the solvent, preparative t.l.c. of the residue on silica gel [eluant light petroleum–diethyl ether (1 : 1)] gave the *bicyclic keto-ester* (14) (41 mg, 15% overall).

Methyl 4,4-*Dimethyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]*octane*-1-*carboxylate* (15a).—To a solution of lithium di-isopropylamide (5.8 mmol) in anhydrous THF (4 ml) and hexane (4 ml) was added dropwise a solution of 5,5-dimethylcyclohex-2-en-1-one (642 mg, 5.2 mmol) in THF (7 ml) at −80 °C under nitrogen, and the mixture was stirred at −80 to *ca.* −70 °C for 30 min. A solution of methyl α-bromoacrylate (875 mg, 5.3 mmol) in THF (5 ml) was added, and the resulting mixture stirred at −70 to −10 °C for 3 h. Saturated aqueous ammonium chloride was added and the product was extracted with ether. The combined extracts were washed with water and brine, dried, and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *tricyclic keto-ester* (15a) (663 mg, 62%), along with the recovered enone (64 mg, 10%); negative Beilstein test; b.p. 75—85 °C at 0.4 mmHg; $\nu_{max.}$ 1 740 and 1 245 cm^{-1}; δ($CDCl_3$) 0.90 (3 H, s, R^3-Me), 1.03 (3 H, s, R^2-Me), 1.50—2.50 (7 H, m), and 3.65 (3 H, s, CO_2Me); δ_C 23.47 (t, C-8), 29.24 and 29.36 each q, Me_2 at C-4), 30.82 (d, C-7), 31.91 (t, C-3), 33.85 (s, C-4), 35.67 (d, C-2), 37.55 (s, C-1), 51.93 (q, $CO_2\mathit{Me}$), 53.32 (d, C-5), 171.51 (s, $\mathit{C}O_2Me$), and 208.76 (s, C-6) (Found: C, 69.4; H, 7.7. $C_{12}H_{16}O_3$ requires C, 69.2; H, 7.7%).

Methyl 4-*Methyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]*octane*-1-*carboxylate* (15b).—The reaction of 5-methylcyclohex-2-en-1-one (582 mg, 5.3 mmol) was carried out as described in the preceding experiment. Preparative t.l.c. [eluant hexane–ethyl acetate (3 : 1)] gave the *tricyclic keto-ester* (15b) (574 mg, 56%), along with the recovered enone (146 mg, 25%); negative Beilstein test; $\nu_{max.}$ 1 735 and 1 210 cm^{-1}; δ($CDCl_3$) 0.92 [3 H, d, *J* 6.0 Hz, 4-Me; δ 1.68 and 1.48 [(area ratio *ca.* 4 : 1, each d) by addition of 0.21 mol % of Eu(dpm)$_3$], 1.50—2.70 (8 H, m), and 3.67 (3 H, s, CO_2Me); δ_C 21.65 (q, 4-Me), 25.42 and 28.57 (each t, C-3 and C-8), 33.06 (d, C-4), 35.00 (s, C-1), 36.28 (d, C-7), 37.79 (d, C-2), 48.59 (d, C-5), 52.05 (q, $CO_2\mathit{Me}$), 171.75 (s, $\mathit{C}O_2Me$), and 209.61 (s, C-6) (Found: M^+, 194. $C_{11}H_{14}O_3$ requires *M*, 194).

Methyl 4-*Isopropenyl*-7-*methyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]-*octane*-1-*carboxylate* (15c).—The reaction of (−)-carvone (311 mg, 2.07 mmol) was carried out as described above and gave the *tricyclic keto-ester* (15c) (156 mg, 36%); negative Beilstein test; $\nu_{max.}$ 1 730, 1 645, and 895 cm^{-1}; δ 1.21 (3 H, s, 7-Me), 1.67 [3 H, s, C(Me)=CH_2], 1.20—2.80 (7 H, m), 3.71 (3 H, s, CO_2Me), and 4.77 [2 H, br s, C(Me)=$\mathit{C}H_2$] (Found: M^+, 234. $C_{14}H_{18}O_3$ requires *M*, 234).

Methyl 6-*Hydroxy*-4,4-*dimethyltricyclo*[3.2.1.$0^{2,7}$]*octane*-1-*carboxylate* (16a).—To a solution of the keto-ester (15a) (54 mg, 0.26 mmol) in methanol (3 ml) was added sodium borohydride (10 mg, 0.27 mmol) at −62 °C. After stirring at −62 to −32 °C for 40 min, the reaction mixture was worked up in the usual manner to give the *tricyclic hydroxy-ester* (16a) (56 mg, quantitative); $\nu_{max.}$ 3 600, 3 450, 1 725, 1 260, and 1 140 cm^{-1}; δ($CDCl_3$) 0.93 (3 H, s, R^3-Me), 1.18 (3 H, s, R^2-Me), 1.13—2.20 (7 H, m), 2.17 (1 H, B part of AB q, *J* 11.0 Hz, 8-H), 2.60 (1 H, br s, OH), 3.60 (3 H, s, CO_2Me), and 4.42 (1 H, t, *J* 4.0 Hz, 6-H). The Eu(dpm)$_3$ shifts are shown in Table 2.

TABLE 2

Eu(dpm)$_3$ Methyl shifts for compound (16a)

Weight of Eu(dpm)$_3$ added to 63 mg of (16a) (mg)	Shift (Hz)	
	R^2-Me	R^3-Me
0.0	71	55
5.0	72	56
10.5	84	61
15.5	99	67
22.0	114	73

Methyl 6-*Hydroxy*-4-*methyltricyclo*[3.2.1.$0^{2,7}$]*octane*-1-*carboxylate* (16b).—To a solution of the keto-ester (15b) (81 mg, 0.42 mmol) in methanol (3 ml) was added sodium borohydride (15 mg, 0.41 mmol) at −60 °C. After stirring at −60 to −55 °C for 30 min, the reaction mixture was worked up in the usual manner to give the *tricyclic hydroxy-ester* (16b) (83 mg, quantitative); $\nu_{max.}$ 3 600, 3 500, 1 725, 1 435, 1 270, 1 200, and 1 180 cm^{-1}; δ($CDCl_3$, 100 MHz) 0.90 (weak d, *J* 6.0 Hz) and 1.15 (intense, d, *J* 6.0 Hz) (1 : 4, total 3 H, 4-Me), 1.50—2.50 (8 H, m), 2.95 (1 H, br, OH), 3.66 (3 H, s, CO_2Me), and 4.50 [1 H, m, 6-H, separated into two peaks at δ 4.40 and 4.49 (ratio *ca.* 1 : 4) upon irradiation at δ 1.85].

TABLE 3

Eu(dpm)$_3$ Methyl shifts for compound (16b)

Weight of Eu(dpm)$_3$ added to 75 mg of (16b) (mg)	Shift (Hz)	
	Intense Me	Weak Me
0.0	67	54
6.0	68	53
12.5	78	59
23.0	97	71
26.5	109	76

1,8a-*Epoxy*-3,4,4a,5,6,7,8,8a-*octahydro*-4a,5-*dimethylnaphthalen*-2(1H)-*one* (19).—Reduction of the octalone (5) [7] with lithium aluminium hydride was carried out in the ordinary manner to give quantitatively 2,3,4,4a,5,6,7,8-*octahydro*-4a,5-*dimethyl*-2-*naphthol*.

To a solution of the naphthol (2.26 g, 12 mmol) in dichloromethane (20 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (2.77 g, 16 mmol) in dichloromethane (45 ml) at 0 °C. After being stirred at room temperature for 40 min, the reaction mixture was washed with aqueous sodium hydrogencarbonate, water, and brine. Evaporation of the solvent left almost pure 1,8a-epoxyperhydro-4a,5-dimethyl-2-naphthol (18) (2.74 g); $\nu_{max.}$ 3 570, 3 400, 1 420, and 1 090 cm^{-1}; δ 0.83 (3 H, br d, 5-Me), 0.93 (3 H, s, 4a-Me), 3.00 (1 H, exchangeable by D_2O), 3.06 (1 H, d, *J* 4.0 Hz, 1-H), and 3.93 (1 H, m, $W_{1/2}$ 10 Hz, 2-H).

Jones oxidation of the naphthol (18) in the usual manner gave the *epoxy-decalone* (19) (1.70 g, 68%), b.p. 70—80 °C

at 0.15 mmHg; $\nu_{max.}$ 1 710 cm^{-1}; δ 0.90 (3 H, br d, 5-Me), 1.06 (3 H, s, 4a-Me), and 2.86 (1 H, s, 1-H) (Found: C, 74.0; H, 9.6. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%).

4,4a,5,6,7,8-*Hexahydro*-1-*methoxy*-4a,5-*dimethylnaphthalen*-2(3H)-*one* (20).—To a solution of sodium methoxide (171 mg, 3.17 mmol) in anhydrous methanol (1 ml) was added dropwise a solution of the epoxy-decalone (19) (350 mg, 1.8 mmol) in anhydrous methanol (5 ml), and the mixture was heated under reflux for 20 h under nitrogen. After cooling to room temperature, the mixture was diluted with water and extracted with ether. The combined extracts were washed with water until neutral (litmus) and then with brine. Removal of the solvent, followed by preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *methoxy-octalone* (20) (208 mg, 56%); b.p. 70—80 °C at 2.5 mmHg; $\nu_{max.}$ 1 680 and 1 610 cm^{-1}; $\lambda_{max.}$ 255 nm (ε 11 250); δ 0.92 (3 H, br d, 5-Me), 1.10 (3 H, s, 4a-Me), and 3.50 (3 H, s, OMe) (Found: C, 74.8; H, 9.3. $C_{13}H_{20}O_2$ requires C, 75.0; H, 9.7%).

3,4,4a,5,6,7,8,8a-*Octahydro*-2-*hydroxy*-4a,5-*dimethylnaphthalen*-1(2H)-*one* (21).—To a solution of the methoxy-octalone (20) (403 mg, 1.94 mmol) in anhydrous ether (20 ml) was added portionwise lithium aluminium hydride (39 mg, 1.05 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 15 min. Usual work-up gave 2,3,4,4a,5,6,7,8-octahydro-1-methoxy-4a,5-dimethyl-2-naphthol (395 mg); $\nu_{max.}$ 3 550, 1 120, and 1 060 cm^{-1}; δ 0.87 (3 H, br d, 5-Me), 0.95 (3 H, s, 4a-Me), 3.50 (3 H, s, OMe), and 4.20 (1 H, br m, $W_{1/2}$ 16 Hz, 2-H).

To a solution of the above methoxy-naphthol (395 mg) in aqueous dioxan (70%, 10 ml) was added concentrated hydrochloric acid (6 drops), and the resulting solution was heated at 60—65 °C for 4 h. The hydroxy-decalone (21) (378 mg, 99%), $\nu_{max.}$ 3 450, 1 710, 1 380, 1 140, and 1 060 cm^{-1}, δ 0.90 (6 H, m, 4a- and 5-Me) and 3.70 [2 H, br, 2-H and OH, changed to 1 H ($W_{1/2}$ 25 Hz) by addition of D_2O], was obtained on addition of water followed by extraction with ether.

4a,5,6,7,8,8a-*Hexahydro*-4a,5-*dimethylnaphthalen*-1(4H)-*one* (4).—To a solution of the hydroxy-decalone (21) (378 mg) in carbon tetrachloride (6 ml) was added dropwise a solution of phosphorus tribromide (540 mg, 2 mmol) in carbon tetrachloride (4 ml) at room temperature, and the reaction mixture was stirred at room temperature for 4 h. After addition of water, the water layer was extracted with ether. The combined organic layers were washed with water and brine. Evaporation left 2-bromo-3,4,-4a,5,-6,7,8,8a-octahydro-4a,5-dimethylnaphthalen-1(2*H*)-one (22) (416 mg, 66%); $\nu_{max.}$ 1 710, 1 450, and 1 350 cm^{-1}; δ 0.67. (3 H, s, 4a-Me), 0.85 (3 H, br d, *J* 4.0 Hz, 5-Me), and 4.23 (1 H, br, $W_{1/2}$ 7 Hz, 2-H).

A solution of the bromo-decalone (22) (416 mg, 1.55 mmol), lithium bromide monohydrate (669 mg, 6.37 mmol), and lithium carbonate (476 mg, 6.43 mmol) in DMF (10 ml) was heated under reflux for 8 h. After cooling to room temperature, water was added and the product extracted with ether. The combined extracts were washed with water and brine, and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *octalone* (4) (170 mg, 81%); $\nu_{max.}$ 1 680, 1 460, 1 440, 1 385, and 1 225 cm^{-1}; $\lambda_{max.}$ 228 nm (log ε 3.91); δ 0.75 (3 H, s, 4a-Me), 0.85 (3 H, d, *J* 6.0 Hz, 5-Me), 5.85 (1 H, dt, *J* 11.0 and 2.0 Hz, 2-H), and 6.68 (1 H, ddd, *J* 11.0, 6.0, and 3.0 Hz, 3-H) (Found: M^+, 178. $C_{12}H_{18}O$ requires *M*, 178). The sample, which was recovered after treatment with potassium carbonate in methanol overnight, revealed exactly the same spectral and chromatographic behaviour as those of the starting material.

Methyl 4,5-*Dimethyl*-10-*oxotetracyclo*[7.2.1.$0^{2,11}$.$0^{4,9}$]*dodecane*-1-*carboxylates* (24) *and* (25).—To a solution of lithium di-isopropylamide (1.13 mmol) in anhydrous THF (1.5 ml) and hexane (0.75 ml) was added a solution of the octalone (4) (150 mg, 0.84 mmol) in THF (2 ml) at −90 °C under nitrogen. After the mixture had been stirred at −90 to −80 °C for 30 min, a solution of methyl α-bromoacrylate (321 mg, 1.95 mmol) in THF (1 ml) was added, and the mixture stirred at −80 to −40 °C for 3 h. Work-up as described earlier and careful preparative t.l.c. of the product on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *tetracyclic keto-esters* (24) (43 mg, 20%) and (25) (25 mg, 12%), along with the recovered octalone (4) (56 mg, 37%). The major keto-ester (24) had $\nu_{max.}$ 1 730, 1 435, and 1 235 cm^{-1}; δ 0.66 (3 H, s, 4-Me), 0.80 (3 H, d, *J* 6.0 Hz, 5-Me), 1.00—2.63 (13 H, m), and 3.67 (3 H, s, CO_2Me) (Found: M^+, 262. $C_{16}H_{22}O_3$ requires *M*, 262); and the minor one (25) had $\nu_{max.}$ 1 730, 1 440, and 1 240 cm^{-1}; δ 0.77 (3 H, d, *J* 6.0 Hz, 5-Me), 1.00 (3 H, s, 4-Me), 1.16—2.80 (13 H, m), and 3.67 (3 H, s, CO_2Me); [*m/e* 262 (M^+)].

Methyl 10-*Hydroxy*-4,5-*dimethyltetracyclo*[7.2.1.$0^{2,11}$.$0^{4,9}$]-*dodecane*-1-*carboxylate* (26).—To a solution of the major keto-ester (24) (816 mg, 3.11 mmol) in methanol (10 ml) was added portionwise sodium borohydride (58 mg, 1.57 mmol) with stirring and ice-cooling. The mixture was stirred at that temperature for 1 h and then poured into water and the product extracted with ether. The combined extracts were washed with water and brine, and dried. Evaporation of the ether left the chromatographically homogeneous *hydroxy-ester* (26) (824 mg, quantitative); $\nu_{max.}$ 3 600, 3 450, 1 725, and 1 245 cm^{-1}; δ 0.70 (3 H, d, *J* 6.0 Hz, 5-Me), 1.00 (3 H, s, 4-Me), 0.80—2.20 (12 H, m), 2.30 (1 H, B part of AB q, *J* 12.0 Hz, 12-H), 3.06 (1 H, br s, OH), 3.67 (3 H, s, CO_2Me), and 3.83 (1 H, d, *J* 3.0 Hz, 10-H); δ([$^2H_6$]DMSO) 0.87 (3 H, d, *J* 6.0 Hz) and 1.00 (3 H, s) (Found: M^+, 264. $C_{16}H_{24}O_3$ requires *M*, 264).

TABLE 4

$Eu(dpm)_3$ Methyl shifts for compound (26)

Weight of $Eu(dpm)_3$ added to 62 mg of (26) (mg)	Shift (Hz) tertiary-Me
0.0	63
5.0	68
10.5	83
17.0	102
24.5	127

1-*Hydroxymethyl*-4,5-*dimethyltetracyclo*[7.2.1.$0^{2,11}$.$0^{4,9}$]-*dodecan*-10-*ol* (27).—To a solution of the major keto-ester (24) (85 mg, 0.32 mmol) in anhydrous ether (5 ml) was added portionwise lithium aluminium hydride (24 mg, 0.65 mmol) with cooling in an ice-bath. After addition of the reagent, the reaction mixture was heated under reflux for 1.5 h. More lithium aluminium hydride (13 mg) was added, and the refluxing was continued for 1 h. Usual work-up gave the crystalline *diol* (27) (78 mg, quantitative); m.p. 135.0—136.5 °C (from hexane–diethyl ether); $\nu_{max.}$ ($CHCl_3$) 3 600, 3 400, 1 380, 1 050, 1 030, and 1 010 cm^{-1}; δ([$^2H_6$]-DMSO) 0.67 (3 H, d, *J* 6.0 Hz, 5-Me), 1.00 (3 H, s, 4-Me), 0.93—2.30 (13 H, m), 3.33 (2 H, s, CH_2OH), 3.63 (1 H, d, *J* 3.0 Hz, 10-H), and 4.23 (2 H, br s, 2 OH) (Found: M^+, 236. $C_{15}H_{24}O_2$ requires *M*, 236).

(±)-*Ishwarane* (1,4,5-*Trimethyltetracyclo*[7.2.1.$0^{2,11}$ $0^{4,9}$]-

dodecane) (6).—A solution of methanesulphonyl chloride (168 mg, 1.47 mmol) in carbon tetrachloride (1 ml) was added to a solution of the diol (27) (76 mg, 0.32 mmol) and triethylamine (0.5 ml) in carbon tetrachloride (1 ml) at ice-bath temperature, and the mixture was stirred at that temperature for 3 h and then at room temperature for 1 h. The mixture was poured into ice–water and extracted with ether. The combined extracts were washed with water and brine, and dried. Evaporation of the solvent under reduced pressure left the bis(methanesulphonate) (118 mg, 93%). This compound was fairly unstable; we were unable to purify it even by t.l.c.

The crude bis(methanesulphonate) was dissolved in anhydrous ether (5 ml). Lithium aluminium hydride (35 mg, 0.95 mmol) was added portionwise to this solution at 0 °C. The mixture was stirred at room temperature for 30 min and at reflux temperature for 30 min. After usual work-up, the ethereal solution was concentrated by distillation through a Vigreux column. The concentrate was chromatographed on silica gel (preparative t.l.c.; eluant hexane), and the adsorbed product was thoroughly extracted with pentane. Careful evaporation of the pentane through a Vigreux column left (±)-ishwarane (6) (28 mg, 43%). The pure sample was collected by preparative g.l.c. and had a retention time of 6.3 min on a 5% SE-30 column on Chromosorb-W (2 m, 150 °C, He pressure 1.0 kg cm^{-2}); $\nu_{max.}$ 1 445, 1 380, 1 370, and 1 300 cm^{-1}; δ 0.51 (1 H, m, cyclopropane H), 0.73 (3 H, d, *J* 6.0 Hz, 5-Me), 0.78 (3 H, s, 4-Me), and 1.12 (3 H, s, 1-Me); *m/e* 204 (M^+; 76%) and 118 (100%). The spectra were identical with those of a natural sample.

(±)-*Dehydrofukinone* [4,4a,5,6,7,8-*Hexahydro*-3-*isopropylidene*-4a,5-*dimethylnaphthalen*-2(3H)-*one*] (7).—To a solution of lithium di-isopropylamide (1.79 mmol) in anhydrous THF (2 ml) and hexane (1.2 ml) was added dropwise a solution of the octalone (5) (278 mg, 1.56 mmol) at −50 °C under nitrogen, and the resulting solution was stirred at −50 to −36 °C for 30 min. A solution of zinc chloride (280 mg, 2.05 mmol) in THF (2 ml) was added and after stirring at −36 °C for 5 min, a solution of acetone (125 mg, 2.16 mmol) in THF (1 ml) was added, and the mixture stirred at −36 °C for 5 min and then at 0 °C for 2 h. Aqueous ammonium chloride was added, and the product extracted with ether. The combined extracts were washed with water and brine, and the ether removed. Preparative t.l.c. of the residual oil (411 mg) on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave 4,4a,5,6,7,8-hexahydro-3-(1-hydroxy-1-methylethyl)-4a,5-dimethylnaphthalen-2(3*H*)-one (32) (345 mg, 94%); $\nu_{max.}$ 3 450, 1 660, 1 620, and 1 240 cm^{-1}; δ 0.96 (3 H, br d, 5-Me), 1.13 (9 H, br s, 4a-Me and $^{-}CMe_2OH$), 4.36 (1 H, br, exchangeable by D_2O), and 5.60 (1 H, m, 1-H).

A solution of the naphthalenone (32) (240 mg) in anhydrous benzene (20 ml) containing a catalytic amount of fused toluene-*p*-sulphonic acid was heated under reflux for 2.5 h using a Dean–Stark water-separator. The reaction mixture was poured into a cold solution of sodium hydrogencarbonate, and the organic layer was washed with water and brine, and evaporated to dryness. Preparative t.l.c. of the residue (249 mg) on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave, in addition to the retro-aldol product (5) (29 mg, 16%), (±)-dehydrofukinone (7) (180 mg, 81%), b.p. 69—74 °C at 0.2 mmHg; $\nu_{max.}$ 1 660 and 1 623 cm^{-1}; $\lambda_{max.}$ 249 (ε 12 310) and 276 nm (7 650); δ 0.96 (6 H, br s, 4a- and 5-Me), 1.83 and 2.03 (both 3 H, br s, $C{=}CMe_2$), and 5.61 (1 H, br s, 1-H) (Found: M^+, 218. $C_{15}H_{22}O$ requires *M*, 218), identical (i.r. spectrum) with an authentic sample.

To a solution of compound (32) (95 mg, 0.4 mmol) in pyridine (1.5 ml) was added dropwise thionyl chloride (0.025 ml) using a microsyringe at 0 °C. After being stirred at 0 °C for 35 min, the mixture was poured into ice–water and extracted with ether. The combined extracts were washed with water and brine. Evaporation followed by preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave a 3 : 1 mixture of the *stereoisomer* (33) of alloeremophilone and dehydrofukinone (7) (total 55 mg, 63%). A pure sample of compound (33) was collected by preparative g.l.c. on a 20% Carbowax 20M on Chromosorb-W column (2 m) at 220 °C (He pressure 1.5 kg cm^{-2}) and had $\nu_{max.}$ 1 675, 1 620, 1 190, and 890 cm^{-1}; δ 0.95 (3 H, br d, 5-Me), 1.17 (3 H, s, 4a-Me), 1.70 [3 H, br s, $^{-}C(Me){=}CH_2$], 3.01 (1 H, dd, *J* 12.0 and 6.5 Hz, 4-H), 4.73 and 4.86 [both 1 H, m, $^{-}C(Me){=}CH_2$], and 5.63 (1 H, br s, 1-H)(Found: M^+, 218. $C_{15}H_{22}O$ requires *M*, 218). The i.r. spectrum was not identical with that of alloeremophilone (34).

(±)-*Hydroxyeremophilone Methyl Ether* [4,4a,5,6,7,8-*Hexahydro*-3-*isopropylidene*-1-*methoxy*-4a,5-*dimethylnaphthalen*-2(3H)-*one*] (36).—To a solution of lithium di-isopropylamide (0.9 mmol) in anhydrous THF (1 ml) and hexane (0.55 ml) was added dropwise a solution of the methoxyoctalone (20) (130 mg, 0.63 mmol) in THF (2 ml) at −55 °C under nitrogen, and the resulting solution was stirred at −55 to −40 °C for 30 min. A solution of zinc chloride (137 mg, 1 mmol) in THF (1.5 ml) was then added and the mixture stirred at −40 °C for 5 min. A solution of acetone (215 mg, 3.7 mmol) in THF (1 ml) was added, and the reaction mixture stirred at −40 °C for 10 min and then at 0 °C for 30 min. Aqueous ammonium chloride was added, and the product extracted with ether. The combined extracts were washed with water and brine, and evaporated to dryness. Chromatography of the residue [preparative t.l.c. on silica gel; eluant hexane–ethyl acetate (5 : 1)] gave 4,4a,5,6,7,8-hexahydro-3-(1-hydroxy-1-methylethyl)-1-methoxy-4a,5-dimethylnaphthalen-2(3*H*)-one (35) (142 mg, 86%); $\nu_{max.}$ 3 480, 1 660, and 1 610 cm^{-1}; δ 0.93 (3 H, br d, 5-Me), 1.11 (6 H, s, $^{-}CMe_2OH$), 1.16 (3 H, s, 4a-Me), 3.55 (3 H, s, OMe), and 4.33 (1 H, br, exchangeable by D_2O).

A solution of the adduct (35) (110 mg) in anhydrous benzene (10 ml) containing a catalytic amount of fused toluene-*p*-sulphonic acid was heated under reflux for 30 min using a Dean–Stark water-separator. After cooling to room temperature, the reaction mixture was diluted with ether, washed with water and brine, and evaporated to dryness. Preparative t.l.c. of the residue (103 mg) on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *methyl ether* (36) (97 mg, 96%); b.p. 100—105 °C at 0.4 mmHg; $\nu_{max.}$ 1 662 and 1 615 cm^{-1}; $\lambda_{max.}$ (MeOH) 266 (log ε 3.99) and 288 nm (3.96) [lit.,[23] 265 (log ε 3.95) and 285 nm (log ε 3.93)]; δ 0.95 (6 H, br s, 4a- and 5-Me), 1.83 and 2.06 (both 3 H, br s, $C{=}CMe_2$), and 3.60 (3 H, s, OMe) (Found: C, 77.1; H, 9.7. $C_{16}H_{24}O_2$ requires C, 77.4; H, 9.7%). The i.r. spectrum was identical with that of the methyl ether of natural hydroxyeremophilone.

(±)-*Hydroxyeremophilone* [4,4a,5,6,7,8-*Hexahydro*-1-*hydroxy*-3-*isopropylidene*-4a,5-*dimethylnaphthalen*-2(3H)-*one*] (8).—To a solution of the methyl ether (36) (50 mg, 0.2 mmol) in dichloromethane (1 ml) was added boron tribromide (*ca.* 0.02 ml) at −100 °C, and the mixture was stirred at −100 to −20 °C for 2 h. After addition of water, the

resulting mixture was diluted with ether and washed with aqueous sodium hydrogencarbonate, water, and brine. Removal of the solvent, followed by preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave (±)-hydroxyeremophilone (8) (43 mg, 90%); positive ferric chloride test; m.p. 57—65 °C (sublimed at 80 °C and 0.5 mmHg) (lit.,[23] 64.5—65 °C); $\nu_{max.}$ 3 380, 1 660, 1 640, 1 615, 1 380, 1 290, and 1 020 cm^{-1}; $\lambda_{max.}$ 310 nm (log ε 3.81) [lit.,[23] 309 nm (log ε 4.01)]; δ 0.93 (6 H, br s, 4a- and 5-Me), 1.90 and 2.15 (both 3 H, br s, C=CMe_2), and 6.40 (1 H, s, exchangeable by D_2O). The i.r. spectrum was identical with that of natural hydroxyeremophilone.

(±)-9,10-*Dehydrofuranoeremophilane* (4,4a,5,6,7,8-*Hexahydro*-3,4a,5-*trimethylnaphtho*[2,3-*b*]*furan*) (9).—Acetonyl tetrahydropyranyl ether was prepared by the following manner. A solution of hydroxyacetone [510 mg, the commercially available solution (50% v/v) in methanol was dried over molecular sieves], 3,4-dihydro-2*H*-pyran (1.15 g), and a catalytic amount of fused toluene-*p*-sulphonic acid in ether (5 ml) was stirred at room temperature for 2 days. Several drops of diethylamine were added, and the resulting mixture was passed through a short column of neutral alumina with the aid of ether. The eluate was fractionally distilled through a Vigreux column and the fraction boiling at 120—140 °C collected to yield acetonyl tetrahydropyranyl ether (596 mg).

To a solution of lithium di-isopropylamide (0.63 mmol) in anhydrous THF (1 ml) and hexane (0.46 ml) was added a solution of the octalone (5) (78 mg, 0.44 mmol) in THF (2 ml) at −100 °C under nitrogen, and the resulting solution was stirred at −100 to −85 °C for 30 min. A solution of zinc chloride (135 mg, 1 mmol) in THF (1.5 ml) and then a solution of acetonyl tetrahydropyranyl ether (233 mg, 0.9 mmol) in THF (1 ml) were added, and the stirring continued at −85 to −40 °C for 2 h. The reaction mixture was worked up as described for the reaction with acetone, and preparative t.l.c. of the crude product on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave 4,4a,5,6,7,8-hexahydro-3-[1-hydroxy-1-(tetrahydropyranyloxymethyl)ethyl]-4a,5-dimethylnaphthalen-2(3*H*)-one (37) (127 mg, 86%); $\nu_{max.}$ 3 450, 1 655, 1 620, 1 130, and 1 120 cm^{-1}; δ 0.93 (3 H, br d, 5-Me), 1.10 [6 H, s, 4a-Me at C-4a and $-C(Me)(OH)-(CH_2OTHP)$], 2.80—4.00 (4 H, m), 4.51 (2 H, br), and 5.57 (1 H, br s, 1-H).

A solution of the naphthalenone (37) (84 mg) in THF–water (3 ml; 2 : 1) containing a catalytic amount of toluene-*p*-sulphonic acid was heated at 60—65 °C for 15 min. The reaction mixture was poured into aqueous sodium hydrogencarbonate and the product extracted with ether. The ether was distilled off *in vacuo* at room temperature, and the residue was immediately chromatographed on silica gel [preparative t.l.c.; eluant hexane–ethyl acetate (5 : 1)] to give (±)-9,10-dehydrofuranoeremophilane (9) (40 mg, 74%). This compound was fairly unstable, decomposing partially during the n.m.r. measurement and completely on standing even at −20 °C overnight. The spectral properties taken immediately after the isolation were: $\nu_{max.}$ 2 800, 1 460, 1 100, and 720 cm^{-1}; $\lambda_{max.}$ 291 nm (ε 5 900); δ 0.92 (3 H, s, 5-Me), 0.93 (3 H, d, 4-Me), 1.90 (3 H, br s, furan-Me), 5.87 (1 H, br s, $W_{1/2}$ 3 Hz, 9-H), and 6.87 (1 H, br s, $W_{1/2}$ 3 Hz, furan-H) (Found: M^+, 216. $C_{15}H_{20}O$ requires *M*, 216). The spectral properties were identical with the reported values.[25]

(±)-10α-*Furanoeremophilone* {4a,5,6,7,8,8a-*Hexahydro*-3,4a,5-*trimethylfurano*[2,3-b]*naphthalen*-9(4H)-*one*} (10).—The reaction of the methoxy-octalone (20) (126 mg, 0.6 mmol) with acetonyl tetrahydropyranyl ether, and the subsequent hydrolysis and ring-closure of the resulting tetrahydropyranyl ether (38) were carried out in the same manner as described in the preceding experiments to yield (±)-10α-furanoeremophilone (10) (92 mg, 65%); m.p. 109—110 °C (from hexane) (lit.,[28] 109—111 °C); $\nu_{max.}$ (KBr) 3 100, 1 660, and 1 410 cm^{-1}; $\lambda_{max.}$ 279 nm (log ε 4.05); δ($CDCl_3$) 0.80 (3 H, s, 5-Me), 0.93 (3 H, d, *J* 6.0 Hz, 4-Me), 2.00 (3 H, s, furan-Me), 2.45 and 2.72 (1 H, each, AB q, *J* 16.0 Hz, 6-methylene), and 7.33 (1 H, br s, furan-H) (Found: M^+, 232. $C_{15}H_{20}O_2$ requires *M*, 232) identical (i.r. and n.m.r. spectra) with an authentic sample.

4,4a,5,6,7,8-*Hexahydro*-4a,5-*dimethyl*-1-*phenylthionaphthalen*-2(3H)-*one* (41) *and the Corresponding Sulphinyl Derivative* (42).—To a solution of the epoxy-octalone (19) (709 mg, 3.65 mmol) in ethanol (5 ml) and aqueous sodium hydroxide (15%; 0.2 ml) was added thiophenol (546 mg, 4.96 mmol) at room temperature. After stirring at room temperature overnight, the reaction mixture was poured into dilute hydrochloric acid and extracted with ether. The extracts were combined and washed with water and brine. Evaporation of the ether, followed by preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *phenylthio-octalone* (41) (986 mg, 94%); b.p. 175—185 °C at 0.2 mmHg; $\nu_{max.}$ 1 690, 1 480, 1 440, 1 020, and 690 cm^{-1}; $\lambda_{max.}$ 202 (log ε 4.41) and 248 nm (log ε 4.21); δ 0.90 (3 H, m, 5-Me), 1.16 (3 H, s, 4a-Me), and 7.00—7.40 (5 H, m) (Found: C, 75.7; H, 7.8. $C_{18}H_{22}OS$ requires C, 75.5; H, 7.7%).

To a solution of the phenylthio-octalone (41) (216 mg, 0.76 mmol) in dichloromethane (4 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (80%; 169 mg, 0.79 mmol) in dichloromethane (5 ml) at −60 °C. After stirring at room temperature for 20 min, the reaction mixture was washed with aqueous sodium hydrogencarbonate, water, and brine. Evaporation of the solvent, followed by preperative t.l.c. of the residue on silica gel [eluant hexane–ethel acetate (1 : 1)] gave the phenylsulphinyl-octalone (42) (168 mg, 74%); δ 0.93 (3 H, br d, 5-Me), 1.06 and 1.20 (total 3 H, each s, 4a-Me), and *ca.* 7.5 (5 H, m), which was used without further purification.

4,4a,5,6,7,8-*Hexahydro*-8-*hydroxy*-4a,5-*dimethylnaphthalen*-2(3H)-*ones* (45) *and* (46).—(a) *With diethylamine–water–tetrahydrofuran.* A solution of the phenylsulphinyl-octalone (42) (75 mg) and diethylamine (0.5 ml) in aqueous THF (2 ml; 50% v/v) was stirred at room temperature for 42 h. The reaction mixture was diluted with water and extracted with ether. The combined extracts were washed with dilute hydrochloric acid, water, and brine, and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (1 : 1)] gave the *hydroxy-octalones* (45) (20 mg, 42%) and (46) (21 mg, 44%). The isomer (45) had $\nu_{max.}$ 3 400, 1 680, and 1 660 cm^{-1}; δ 0.95 (3 H, br d, 5-Me), 1.10 (3 H, s, 4a-Me), 3.67 (1 H, br s, exchangeable by D_2O), 4.20 (1 H, br, $W_{1/2}$ 17 Hz, 8-H), and 6.07 (1 H, br s, $W_{1/2}$ 4 Hz, 1-H) (Found: M^+, 194. $C_{12}H_{18}O_2$ requires *M*, 194). The isomer (46) had m.p. 63—64.5 °C (from hexane–diethyl ether); $\nu_{max.}$ 3 600, 3 400, 1 675, and 1 650 cm^{-1}; δ 0.95 (3 H, br d, *J* 6.0 Hz, 5-Me), 1.10 (3 H, s, 4a-Me), 3.58 (1 H, br, exchangeable by D_2O), 4.28 (1 H, br s, $W_{1/2}$ 5 Hz, 8-H), and 5.55 (1 H, s, 1-H); *m/e* 194 (M^+).

(b) *With pyridine–water.* A solution of the phenylsulphinyl-octalone (42) (109 mg) in aqueous pyridine (2 ml;

50% v/v) was heated at 90 °C for 2 h. Work-up as before afforded the hydroxy-octalones (45) (24 mg, 34%) and (46) (27 mg, 39%).

(*c*) *With pyridine–acetic anhydride.* A solution of the phenylsulphinyl-octalone (42) (93 mg) in pyridine–acetic anhydride (3 ml; 1 : 2 v/v) was stirred at room temperature for 48 h. The mixture was poured into water and extracted with ether. The extracts were combined and washed successively with dilute sulphuric acid, aqueous sodium hydrogencarbonate, water, and brine. After removal of the solvent, the residue was chromatographed on silica gel [preparative t.l.c.; eluant hexane–ethyl acetate (1 : 1)] to give a mixture of 8-acetoxy-4,4a,5,6,7,8-hexahydro-4a,5-dimethylnaphthalen-2(3*H*)-ones (43) and (44); δ 0.93 (br d), 1.20 (s), 1.96 (s), 2.11 (s), 5.35 (br s), and 5.83 (s), which contained a considerable amount of inseparable impurities (total 100 mg, over 100%).

The crude mixture was dissolved in dilute methanol (60%; 5 ml) containing potassium carbonate (200 mg), and the resulting solution was stirred at room temperature for 3 h. Work-up as before (dilution with water, extraction with ether, and preparative t.l.c. on silica gel) gave the hydroxy-octalones (45) (14 mg, 23%) and (46) (30 mg, 50%).

(±)-9,10-*Dehydrofuranoeremophil*-1-*one* {4a,5,6,7-*Tetrahydro*-3,4a,5-*trimethylfurano*[2,3-b]*naphthalen*-8(4H)-*one*} (11).—To a solution of lithium di-isopropylamide (1.39 mmol) in anhydrous THF–hexane (2 ml; 1 : 1 v/v) was added dropwise a solution of the phenylthio-octalone (41) (292 mg, 1.02 mmol) in THF (3 ml) at −80 °C under nitrogen, and the resulting mixture was stirred at −80 to −75 °C for 40 min. A solution of zinc chloride (156 mg, 1.15 mmol) in THF (1 ml) and then a solution of acetonyl tetrahydropyranyl ether (254 mg, 1.61 mmol) in THF (1 ml) were added at −75 °C. After being stirred at −75 to −40 °C for 2 h, aqueous ammonium chloride was added at that temperature, and the product was extracted with ether. The combined extracts were washed with water and brine, and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (1 : 1)] gave, along with the recovered starting material (41) (100 mg, 34%), the tetrahydropyranyl ether (47) (283 mg, 62%). Oxidation of this compound (47) (98 mg) with *m*-chloroperbenzoic acid was carried out as usual to give the corresponding phenylsulphinyl-naphthalenone (123 mg). A solution of this compound and diethylamine (0.5 ml) in aqueous THF (60%, 3 ml) was stirred at room temperature overnight. Work-up as described for compounds (45) and (46) afforded the diol (48) as a mixture of isomers (105 mg).

To a slurry of Collins reagent [33] (641 mg, 2.84 mmol) in dichloromethane (8 ml) was added dropwise a solution of compound (48) (105 mg, 0.3 mmol) in dichloromethane (4 ml). After stirring at room temperature for 10 min, the reaction mixture was passed through a short column of silica gel with the aid of ether. Removal of the solvent, followed by preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (1 : 1)] gave the ene-dione (49) [40 mg, 52% from compound (47)]; $\nu_{max.}$ 3 400, 1 710, 1 700, 1 680, 1 660, and 1 020 cm^{-1}. A solution of the ene-dione (49) (40 mg) and toluene-*p*-sulphonic acid (trace) in aqueous THF (60%; 3 ml) was heated at 60 °C for 4 h. Work-up as described earlier and purification by preparative t.l.c. on silica gel [eluant hexane–ethyl acetate (1 : 1)] gave (±)-9,10-dehydrofuranoeremophil-1-one (11) (22 mg, 85%); $\nu_{max.}$ 1 670, 1 565, 1 520, 1 355, and 1 200 cm^{-1}; δ($CDCl_3$) 0.98 (3 H, s, 5-Me), 1.08 (3 H, d, *J* 6.0 Hz, 4-Me), 1.97 (3 H, br s, furan-Me), and 7.23 (2 H, br s, furan-H and 9-H) (Found: M^+, 230. $C_{15}H_{18}O_2$ requires *M*, 230). The spectral data were consistent with the reported values.[25] Compound (11) was so unstable as to decompose at −20 °C within 2 days.

4,4a,5,6,7,8-*Hexahydro*-3-*isopropylidene*-4a,5-*dimethyl*-1-*phenylthionaphthalen*-2(3H)-*one* (50).—Aldol condensation of the phenylthio-octalone (41) (422 mg) with acetone at −70 to 0 °C, with work-up as described earlier yielded, along with recovered octalone (41) (102 mg, 24%), 4,4a,5,6,7,8-*hexahydro*-3-(1-*hydroxy*-1-*methylethyl*)-4a,5-*dimethyl*-1-*phenylthionaphthalen*-2(3H)-*one* (342 mg, 67%), m.p. 126—127 °C (from hexane); $\nu_{max.}$ 3 500, 1 670, and 1 185 cm^{-1}; δ 0.92 (3 H, br d, 5-Me), 1.13 [6 H, br s, $-C(Me_2)OH$], 1.20 (3 H, s, 4a-Me), 4.23 (1 H, br, exchangeable by D_2O), and 7.08 (5 H, s) (Found: C, 73.4; H, 8.3. $C_{21}H_{28}O_2S$ requires C, 73.2; H, 8.2%).

A solution of the above compound (95 mg) and fused toluene-*p*-sulphonic acid (trace) in anhydrous benzene (10 ml) was heated under reflux for 1 h using a Dean–Stark head. The reaction mixture was diluted with ether and washed with water and brine. After removal of the solvent, preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (5 : 1)] gave the *isopropylidenephenylthio-octalone* (50) (73 mg, 81%); b.p. 135—140 °C at 0.15 mmHg; $\nu_{max.}$ 1 670, 1 630, 1 475, 1 435, 1 290, and 1 195 cm^{-1}; $\lambda_{max.}$ 202 (log ε 4.37), 248 (4.27), and 276 nm (3.86, sh); δ 0.97 (3 H, br d, 5-Me), 1.01 (3 H, s, 4a-Me), 1.80 and 1.92 (3 H each, br s, $C{=}CMe_2$), 2.83 (1 H, B part of AB q, *J* 13.0 Hz, 4-H), and 7.01 (5 H, br s) (Found: C, 77.5; H, 8.3. $C_{21}H_{26}OS$ requires C, 77.3; H, 8.3%).

4,4a,5,6,7,8-*Hexahydro*-8-*hydroxy*-3-*isopropylidene*-4a,5-*dimethylnaphthalen*-2(3H)-*ones* (51) *and* (52).—Oxidation of the isopropylidene-phenylthio-octalone (50) by *m*-chloroperbenzoic acid in the usual manner gave quantitatively the corresponding isopropylidene-phenylsulphinyl-octalone.

A solution of this compound (242 mg, 0.7 mmol) and diethylamine (1 ml) in aqueous THF (80%; 5 ml) was stirred at room temperature overnight. The mixture was poured into dilute hydrochloric acid, and the product extracted with ether. The combined extracts were washed with water and brine and evaporated to dryness. Preparative t.l.c. of the residue on silica gel [eluant hexane–ethyl acetate (1 : 1)] gave the *hydroxy-isopropylidene-octalones* (51) (120 mg, 73%) and (52) (23 mg, 14%). The isomer (51) had $\nu_{max.}$ 3 400, 1 660, 1 620, 1 300, and 1 070 cm^{-1}; δ 0.93 (6 H, br s, 4a- and 5-Me), 1.80 and 2.00 (each 3 H, br s, $C{=}CMe_2$), 4.03 (1 H, br, $W_{1/2}$ 14 Hz, 8-H), 4.36 (1 H, br, exchangeable by D_2O), and 5.97 (1 H, br s, $W_{1/2}$ 4 Hz, 1-H) (Found: M^+, 234. $C_{15}H_{22}O_2$ requires *M*, 234). The isomer (52) had $\nu_{max.}$ 3 400, 1 660, 1 620, 1 610, 1 300, and 1 040 cm^{-1}; δ 0.98 (3 H, br d, 5-Me), 1.01 (3 H, s, 4a-Me), 1.85 and 2.03 (each 3 H, s, $C{=}CMe_2$), 3.32 (1 H, br, exchangeable by D_2O), 4.25 (1 H, br s, $W_{1/2}$ 5 Hz, 8-H), and 5.70 (1 H, s, 1-H); *m/e* 234 (M^+).

4,4a,5,6-*Tetrahydro*-3-*isopropylidene*-4a,5-*dimethylnaphthalen*-2(3H)-*one* (3-*Deoxowarburgiadione*) (54).—A solution of the hydroxy-isopropylidene-octalone (51) (46 mg, 0.2 mmol) and toluene-*p*-sulphonyl chloride (70 mg, 0.37 mmol) in pyridine–dichloromethane (1 : 1 v/v; 1 ml) was stirred at −50 °C to room temperature overnight. The oily toluene-*p*-sulphonate (53) (53 mg, 70%), $\nu_{max.}$ 1 670, 1 630, 1 380, 1 190, and 1 180 cm^{-1}, δ 0.93 (6 H, br s, 4a- and 5-Me), 1.78 and 1.98 (each 3 H, br s, $C{=}CMe_2$), 2.41 (3 H,

br s), 2.76 (1 H, d, J 13.0 Hz, 4-H), 4.90 (1 H, br, $W_{1/2}$ 17 Hz, 8-H), 5.72 (1 H, d, J 2.0 Hz, 1-H), and 7.30 and 7.78 (2 H each, AB q, J 8.0 Hz), was obtained on removal of the solvent followed by preparative t.l.c. on silica gel [eluant hexane–ethyl acetate (1 : 1)].

To a solution of the toluenesulphonate (53) (47 mg, 0.12 mmol) in DMF (0.5 ml) was added fused lithium bromide (28 mg, 0.32 mmol), and the reaction mixture was heated at 60 °C for 2.5 h under nitrogen. Usual work-up (addition of water, extraction with ether) and preparative t.l.c. [silica gel; eluant hexane–ethyl acetate (5 : 1)] gave the *trienone* (54) (23 mg, 88%); $\nu_{max.}$ 1 665, 1 620, 1 200, and 895 cm^{-1}; $\lambda_{max.}$ 203 (log ε 3.98), 270 (4.12), and 300 nm (3.98, sh); δ 0.93 (3 H, s, 4a-Me), 1.00 (3 H, d, J 6.0 Hz, 5-Me), 1.90 and 2.13 (each 3 H, br s, C=CMe_2), 2.90 (1 H, d, J 14.0 Hz, 4-H), 5.60 (1 H, s, 1-H), and 6.01 (2 H, br, $W_{1/2}$ 3 Hz, 7- and 8-H) (Found: M^+, 216. $C_{15}H_{20}O$ requires M, 216).

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Note added in proof. Very recently Bohlmann and Knoll have isolated both compounds (51) and (52) from *Senecio suaveolens* (*Annalen*, 1979, 470).

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