Sesquiterpenoids. Part XIV.[†] The Constitution and Stereochemistry of Culmorin¹

By D. H. R. Barton * and N. H. Werstiuk, Imperial College, London S.W.7

The mould metabolite culmorin has been degraded in a stepwise manner to tetrahydroeucarvone and converted in a simple reaction sequence to enantiolongiborneol. These and related studies have shown that culmorin is 2,6,6,9-tetramethyltricyclo[5,4,0^{1,7},0^{2,9}]undecane-8,11-diol (Ia). The configurations assigned to the hydroxygroups are based on chemical evidence and confirmed by appropriate n.m.r. studies.

IN 1937 Ashley, Hobbs, and Raistrick² isolated the mould metabolite culmorin from a strain of Fusarium culmorum. This compound was shown to be a diol, C₁₅H₂₆O₂, and was characterised by the preparation of a diacetate and a di-p-bromobenzoate. We wish to report evidence that shows that culmorin is a saturated sesquiterpenoid diol of the constitution and stereochemistry, both relative and absolute, summarised in (Ia) (nomenclature cf. ref. 3).

The usual tests for unsaturation showed that culmorin was saturated and therefore must be tricyclic. In its n.m.r. spectrum culmorin showed sharp singlets at $\tau 9.07$ (3H), 9·11 (3H), 9·16 (3H), and 9·22 (3H) each indicative of a quaternary methyl group. A six-proton singlet at τ 8.63 was consistent with the presence of three methylene groups. A sextet at τ 5.71 (1H, $J \sim 9$, 5, and 4 c./sec.) and a doublet at τ 6.22 (1H, $J \sim 5$ c./sec.) were ascribed to the two CHOH groups (see further below). These signals are consistent with the partial formulae (II) and (III). Five peaks in the region of $\tau 8.3$ were shown by spin-decoupling to be three doublets centred at $\tau 8.16$ (1H), 8.28 (1H), and 8.37 (2H) with J = 4.5, 5, and 7 c./sec., respectively. These data are also consistent with the partial structures (II) and (III).

Chromic acid oxidation⁴ of culmorin gave a crystalline diketone (IVa), $C_{15}H_{22}O_2$, showing the presence of two secondary hydroxy-groups. The diketone had carbonyl maxima at 1740 and 1755 cm.⁻¹ in the infrared, most simply explained by the presence of two cyclopentanones. In its n.m.r. spectrum the diketone exhibited one-proton singlets at τ 7.23 and 8.15 as well as an AB quartet (2H) at τ 7.85 ($J \sim 18$ c./sec.). These data are consistent with a diketone obtained by oxidation of a diol containing part-structures (II) and (III). In addition, the original four quaternary methyl groups could be detected; in the following discussion it is to be understood that all culmorin derivatives give these, or equivalent, signals unless stated specifically to the contrary. Reduction of the culmorin diketone (IVa) with sodium and propanol gave culmorin and another diol (see further below) in the ratio of 3:2. The chromic acid oxidation of culmorin proceeds therefore without rearrangement of the carbon skeleton.

In the chemical work on the elucidation of the con-

† Part XIII, D. H. R. Barton and G. S. Gupta, J. Chem. Soc., 1962, 1961.

¹ D. H. R. Barton and N. H. Werstiuk, Chem. Comm., 1967, 30. ² J. N. Ashley, B. C. Hobbs, and H. Raistrick, *Biochem. J.*, stitution of limonin base-catalysed autoxidation of the ketonic function to the corresponding diosphenol played an important role.^{5 α} We applied the same technique to the culmorin diketone with equally gratifying results. In t-butanol solution containing potassium t-butoxide



the culmorin diketone absorbed oxygen to give a crystalline hydroxy-keto-acid (Va), C₁₄H₂₂O₄, in good yield. Methylation with diazomethane gave the methyl ester (Vb). The n.m.r. spectrum of this showed the methoxy-peak at τ 6.25 and two doublets at τ 7.70 (1H, $J \sim 1.5$ c./sec.) and 7.00 (1H, $J \sim 1.5$ c./sec.) consistent with two protons each situated α to a carbonyl group. ³ J. Meinwald and J. K. Crandall, J. Amer. Chem. Soc., 1966, 88, 1292.

^{1937,} **31**, 385.

⁴ H. C. Brown and C. P. Carg, J. Amer. Chem. Soc., 1961, 83, 2952.

⁵ (a) D. H. R. Barton, S. K. Pradhan, S. Sternhell, and J. F. Templeton, J. Chem. Soc., 1961, 255; (b) E. J. Bailey, D. H. R. Barton, J. Elks, and J. F. Templeton, J. Chem. Soc., 1962, 1578.

Spin-decoupling studies demonstrated that these two protons were mutually coupled. The low value of the coupling constant is nicely explained by the stereochemistry (dihedral angle of $H_A H_B$ about 90°) of formula (Vb). The spectrum of the ester (Vb) showed no peaks corresponding to $\supset CH \cdot O \cdot$ and therefore the alcohol function was taken to be tertiary. This was confirmed by its resistance to chromic acid oxidation.

The autoxidation of enolisable α -methylene ketones normally affords 5,6 a-diketones or the equivalent diophenols. The loss of a carbon atom as in the autoxidation of the culmorin diketone does have precedent,^{7,8} but only in systems where the β -carbon, with respect to the ketone function, is transformed into carbonyl. In these compounds the β -carbon becomes, after autoxidation of the α -position, a potential anion capable of reaction with oxygen. The mechanism in the case of the culmorin diketone is different; a possible explanation is the following. The anion of the diketone is assumed as usual to be oxidised to the hydroperoxide (VIa). Instead of fragmenting into α -diketone, a further oxidation may be supposed to furnish the bishydroperoxide (VIb). Rearrangement (VII) of the bishydroperoxide followed by attack by hydroxide ion and collapse of the intermediate [see (VIII)] would then afford the observed product in the observed stoicheiometry. Some alternative bond fission sequences based on (VII) can also, of course, be written.

This degradation of the culmorin diketone is also of interest because the closely related camphor,⁹ and the hydroxy-ketone from culmorin containing the 11-ketone function (see further below), are not oxidised under comparable experimental conditions. It is clear that the ketone at C-8 plays an important role in facilitating the reaction. This may influence the rate and degree of enolisation 10 by the kind of homoenolisation effect discussed by Nickon and his collaborators.^{11,12} In any event, it is clear that the autoxidation of the culmorin diketone, and of related ketones, deserves more extensive mechanistic investigation.

When the hydroxy-keto-acid (Va) was heated with acetic anhydride it gave the keto-lactone (IX). This had i.r. carbonyl absorptions at 1750 (cyclopentanone) and 1780 (γ -lactone) cm.⁻¹. Treatment of the lactone (IX) with alkali gave back the parent acid (Va) as shown by methylation with diazomethane to the ester (Vb).

Dehydration of the hydroxy-ester (Vb) with thionyl chloride and pyridine afforded two isomeric olefinic esters, $C_{15}H_{22}O_3$, which are formulated as (Xa) and (XIa). The n.m.r. spectrum of ester (Xa) showed a methoxygroup at τ 6.25 (3H), a one-proton multiplet at τ 6.98 and a three-proton doublet at $\tau 7.98 (J \sim 1 \text{ c./sec.})$. The last two signals represent the bridgehead proton and the vinylic methyl group splitting each other by long-range coupling.¹³ There was no signal for a vinyl proton. Spectral data showed that ester (Xa) was $\alpha\beta$ -unsaturated. Thus it gave carbonyl bands at 1715 (unsaturated ester) and 1745 (cyclopentanone) cm.⁻¹ and a conjugated double bond band at 1635 cm.⁻¹. Its u.v. spectrum (in light petroleum)showed maximal absorption at 225 and 305 (ϵ 8700 and 40) m μ , the former corresponding to an $\alpha\beta$ -unsaturated ester and the latter to the isolated cyclopentanone chromophore.

The n.m.r. spectrum of ester (XIa) showed methoxyabsorption at τ 6.36 and two one-proton doublets $(>C:CH_2)$ at $\tau 4.70 (J \sim 2 \text{ c./sec.})$ and $4.88 (J \sim 2 \text{ c./sec.})$. Since the corresponding acid (XIb) decarboxylated easily at 180° to give a liquid ketone (XII), it was suspected to be $\beta\gamma$ -unsaturated. Treatment of ester (XIa) with sodium methoxide caused a smooth isomerisation to the conjugated ester (Xa) and thus confirmed this suspicion. Since the starting hydroxy-ester (Va) was derived from a γ -hydroxy-acid (γ -lactone) it would be formally possible to obtain by its dehydration $\beta\gamma$ and, with proton shift, $\alpha\beta$ -unsaturated derivatives. However, the β_{γ} -unsaturation is methylenic (CCCH₂) see above) and *cannot* be derived from a tertiary alcohol without rearrangement of the carbon skeleton. In fact, the dehydration of (Vb) proceeds [(XIII); see arrows] to form a rearranged carbonium ion which loses a proton $(\operatorname{arrow} a)$ to give the ester (Xa) or an alternative proton $(\operatorname{arrow} b)$ to furnish the ester (XIa). The polymethylene bridge and the hydroxy-group of ester (Vb) are arranged in the correct anti-planar relationship for easy bondmigration.

The ester (Xa) was used for further degradation. Ozonolysis gave a stable ozonide ester, $C_{15}H_{22}O_6$, formulated as (XIV). Its n.m.r. spectrum showed a three-proton methoxy-signal at τ 6.15 and a threeproton singlet at $\tau 8.31$ corresponding to a methyl group attached to carbon bearing two oxygen functions and no hydogen. In addition, there was a one-proton singlet at τ 6.80 representing the proton on the carbon α to the ketone function now no longer split by long-range coupling. The mass spectrum of the ozonide (XIV) revealed, in addition to a molecular ion at m/e 298, peaks at M - 32 and M - 47 corresponding to the loss of O₂ and $O_2 + Me$. The ozonide (XIV) was cleaved by triphenylphosphine to a triketo-ester, $C_{15}H_{22}O_5$ (XV), which gave a molecular ion at m/e 282.

The formation of the above ozonide (XIV) effectively cleaves the second of the three rings of culmorin. We argued that at least one of the oxygenated functions of (XIV) might be placed β to the cyclopentanone function and that base treatment of (XIV) might lead to a

⁶ R. Hanna and G. Ourisson, Bull. Soc. chim. France, 1961,

^{1945.} ⁷ D. Lavie, E. Glotter, and Y. Shvo, *Tetrahedron*, 1963, **11**,

⁸ R. E. Corbett and H. Young, J. Chem. Soc. (C), 1966, 1556. 9 W. von E. Doering and R. M. Haines, J. Amer. Chem. Soc., 1954, 76, 482.

¹⁰ G. A. Russell, A. J. Moye, and K. Nagpal, J. Amer. Chem. Soc., 1962, 84, 4155. ¹¹ A. Nickon and J. L. Lambert, S.J., J. Amer. Chem. Soc.,

^{1966, 88, 1905.}

¹² A. Nickon, H. Kwasnik, J. Swartz, R. O. Williams, and

J. B. Di Giorgio, J. Amer. Chem. Soc., 1965, 87, 1615. ¹³ N. S. Bhacca and D. H. Williams, 'Applications of n.m.r. Spectroscopy to Organic Chemistry,' Holden-Day, San Francisco, 1964.

simplification of the structural problem. In the event hydrolysis of (XIV) in aqueous methanolic potassium hydroxide gave tetrahydroeucarvone (XVIa), identified by comparison with an authentic specimen and by the preparation of its 2,4-dinitrophenylhydrazone.¹⁴ An unstable β -keto-acid (XVIb) was also isolated. This gave tetrahydroeucarvone (XVIa) when heated at 160°



in a sealed tube. The i.r. spectrum of the ester (XVIc) of this acid showed carbonyl bands at 1700 and 1740 cm.⁻¹. Its n.m.r. spectrum contained a threeproton methoxy-singlet at τ 6.22 as well as other appropriate signals. There was no evidence for a methyl ketone group near $\tau 8.0.15$

Several intermediates can be written in the hydrolysis of the ester (XIV). Accepting that the corresponding acid is the first such intermediate, one can write two main degradation sequences (XVII) and (XVIII) (see arrows in both formulae). The first sequence would require the keto-acid (XVIb) as intermediate, which is in agreement with the experiment. The second demands the ketone (XVId) as intermediate. A nonconcerted fragmentation (with respect to the ketone function) would require the keto-acid (XVIe) as intermediate. In so far as no ketonic product was isolated (see above) we favour the view that the concerted fragmentation (XVII) is involved, rather than the other possibilities.

The formation of tetrahydroeucarvone (XVIa) from the above-described degradation sequence, coupled with the many spectroscopic observations, defines the constitution of all compounds up to and including (Xa) and (XIa). Since a rearrangement must be involved in the formation of the latter compounds, and since the chain ·[CH₂]₃CMe₂· defined by our experiments was reminiscent of the constitution of longifolene (XIX) 16-20 we attempted to construct a carbon skeleton based on longifolene. All preceeding formulae used in this paper reflect this hypothesis. The next phase of our investigation, then, was to confirm (or disprove) the supposed relationship to longifolene.

The diketone (IVa) from culmorin was treated with boron trifluoride etherate²¹ and ethane-1,2-dithiol to give a single dithioketal (IVb). The n.m.r. spectrum of this derivative showed a four-proton multiplet at τ 6.80, one-proton singlets at τ 7.25 and 7.40, and an AB quartet (CH₂) centred at 7.68 ($J \sim 14$ c./sec.). If the dithioketal function had been formed from the 8-ketone the bridgehead proton at C-1 would not have been deshielded sufficiently to appear at τ 7.40.

The Raney nickel desulphurisation of the dithioketal (IVb) gave a liquid ketone, C₁₅H₂₄O (IVc). Reduction of this ketone with sodium and n-propanol afforded a crystalline alcohol, which was shown by direct comparison to be the enantiomer of the known longiborneol. It must, therefore, be represented in constitution and in absolute configuration as (Ib). The identification was confirmed by preparation of the acetate and 3,5-dinitrobenzoate.22

The configuration of the 8-hydroxy-group in culmorin was determined by the following method. Oxidation of culmorin with sufficient chromic acid to oxidise one hydroxy-group gave a mixture of two hydroxy-ketones, (XX), m. p. 120-121°, and (XXI), m. p. 107-108°. Sodium and n-propanol reduction of both compounds gave back culmorin (see further below) and excluded an oxidative rearrangement of the carbon skeleton. In our preliminary communication ¹ we noted that the hydroxyketone, m. p. 120-121°, did not autoxidise under the conditions that led to rapid reaction with the culmorin diketone. We therefore initially regarded this hydroxyketone as having the constitution (XXI) and not (XX). This must now be corrected on the basis of the following, more direct, evidence. Reduction of the hydroxyketone, m. p. 120-121°, by the Wolff-Kishner method gave the alcohol (Ib), further characterised as its acetate

¹⁴ J. R. B. Campbell, A. M. Islam, and R. A. Raphael, J.

Chem. Soc., 1956, 4096. ¹⁵ L. M. Jackman, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 1959.

¹⁶ P. Naffa and G. Ourisson, Chem. and Ind., 1953, 913.

¹⁷ P. Naffa and G. Ourisson, Bull. Soc. chim. France, 1954, 115.

¹⁸ P. Naffa and G. Ourisson, Bull. Soc. chim. France, 1954, 1410. ¹⁹ G. Ourisson, Bull. Soc. chim. France, 1955, 895. C. Ourisson, and A. Rassat, Bull.

²⁰ G. Jacob, G. Ourisson, and A. Rassat, Bull. Soc. chim. France, 1959, 1374.

²¹ L. F. Fieser and R. Stevenson, J. Amer. Chem. Soc., 1954, 76, 1728.

²² R. Nayak and Sukh Dev, Tetrahedron, 1960, 81, 42.

(Id). These experiments establish the configuration of the 8-hydroxy-group in culmorin. Because the constitutions assigned to the two ketones must be interchanged, the constitutions assigned previously ¹ to their lithium aluminium hydride reduction products (see further below) must also be interchanged.

The final problem to be solved was the configuration of the 11-hydroxy-group in culmorin. In the culmorin molecule (Ia) it is clear that the attack of reagents from the rear of the molecule is relatively unhindered, whereas attack from the top of the molecule past the doublebridge system must be very hindered. We argued,¹ therefore, that reduction of culmorin diketone (IVa) and the hydroxy-ketones (XX) and (XXI) by lithium aluminium hydride would afford three different diols, all of which would be different from culmorin *provided* that this had the configuration already implied in (Ia).



(XXV)

Reduction of (IVa), (XX), and (XXI) gave respectively diols (XXIIa), (XXIIIa), and (XXIVa). These are all different from each other and from culmorin. The diendo-configuration (Ia) of culmorin is, therefore, proved. The diol obtained along with culmorin (Ia) from the sodium and propanol reduction of the culmorin diketone was, in fact, the diol (XXIII).

Further support for the configurations of all four diols was gained from an n.m.r. study of the multiplicities of the 8- and 11-protons in the appropriate acetates. Culmorin readily furnished a diacetate (Ic) as already reported by Raistrick, and his collaborators.² In contrast diol (XXIIa) gave only a monoacetate (XXIIb) with acetic anhydride-pyridine at room temperature. The diol (XXIIIa) gave a diacetate (XXIIIb) under these conditions, but the diol (XXIVa) gave only a monoacetate (XXIVb). Clearly the *exo*-8-hydroxygroups in diols (XXIIa) and (XXIVa) are strongly hindered by the double-bridge system on the top side of the molecule as well as by the 2- and 9-methyl groups.

N.m.r. signals for the 11-proton of (a) diacetate (Ic), (b) monoacetate (XXIIb), (c) diacetate (XXIIIb), (d) monoacetate (XXIVb), and (e) hydroxy-ketone (XXI), and for the 8-proton of (f) diacetate (Ic) (g) monoacetate (XXIIb), (k) diacetate (XXIIb), (i) monoacetate (XXIVb), (j) acetate (Id), and (k) hydroxy-ketone (XX). Chemical shifts are given in the Table.

Extensive n.m.r. studies on norbornyl derivatives have shown that, in general, the following coupling constants [see (XXV)] can be assigned: $J_{AC} \sim 0$, $J_{CD} =$ $2\cdot4-6\cdot0$, and $J_{OE} = 5\cdot9-8\cdot4$ c./sec. when the substitutent at C-2 is *exo* and $J_{AB} = 3\cdot8-5\cdot6$, $J_{BD} = 7\cdot5 11\cdot5$, and $J_{BE} = 2\cdot2-5\cdot2$ c./sec. when the substituent is *endo*.²³

In some instances coupling $(J_{\rm BI}, J_{\rm BJ}, \text{ and } J_{\rm CF} = 1-2\cdot1$ c./sec.) through four sigma bonds has been observed.²⁴ N.m.r. data for relevant compounds are ²⁴ A. Rassat, C. W. Jefford, J. M. Lehn, and B. Waegell, *Tetrahedron Letters*, 1964, 233.

Org.

²³ P. Laszlo and P. von R. Schleyer, J. Amer. Chem. Soc., 1963, **85**, 2709; 1964, **86**, 1171; F. A. L. Anet, Canad. J. Chem., 1961, **39**, 784; R. Frazer, *ibid.*, 1962, **40**, 78; J. Meinwald and Y. C. Meinwald, J. Amer. Chem. Soc., 1963, **85**, 2514.

J. Chem. Soc. (C), 1968

listed in the Table. The coupling constants, $J_{app.}$, were obtained from n.m.r. spectra by simple first order analysis. A comparison of the coupling constants obtained experimentally $(J_{app.})$ with the J values that would be expected (averages of the values listed above) for the 8- and 11-protons in each of the compounds confirmed that the configurations assigned were correct.

Although a number of interesting structures based on sesquiterpenoid carbon skeletons have been recognised in recent years as products of microbiological metabolism,²⁵ culmorin is the first longifolene based product. Its biosynthesis certainly merits investigation, especially as its absolute configuration is the inverse of that found in longifolene, a product of plant metabolism.

EXPERIMENTAL

Melting points were taken on a Kofler hot-stage microscope. I.r. spectra were recorded on a Perkin-Elmer model 127 spectrophotometer equipped with sodium gave culmorin diketone (IVa) (4.0 g., 74%), m. p. 103—104°, $[\alpha]_{D} - 29^{\circ}$; ν_{max} (CHCl₃) 1755 and 1745 cm.⁻¹ (C=O); τ 7.29 (s, 1H), 8.15 (s, 1H), 7.85 (AB quartet, 2H. $J \sim 18$ c./sec.), 8.73 (s, 3H), 8.90 (s, 3H), 8.94 (s, 3H), and 8.97 (s, 3H) (Found: C, 76.9; H, 9.5. Calc. for $C_{15}H_{22}O_{2}$: C, 76.9; H, 9.45%).

Reduction of culmorin diketone (1.0 g.) with sodium in n-propanol in the usual manner gave a mixture (3:2) of culmorin and diol (XXIIIa) (800 mg., 81%).

Autoxidation of Culmorin Diketone.—Culmorin diketone (120 mg., 0.514 mmoles) in t-butanol (35 ml.) saturated with potassium t-butoxide was shaken under oxygen for 6 hr. The uptake of oxygen was 35 ml. (1 mol. = 12 ml.). The reaction mixture was poured into water (25 ml.), 6N-hydrochloric acid (5 ml.) was added, and the mixture was extracted with ether (25 ml.). The ethereal layer was washed with water (2×15 ml.) and dried. Evaporation of the solvent gave a solid which was decolourised twice with charcoal. Recrystallisation of the solid from cyclohexane-light petroleum gave the hydroxy-keto-acid (Va)

	$\overbrace{\tau \text{ Values}}^{11-H}$		11-H		8-H	
			Japp. a	J calc. b	Japp. c	Jcalc. d
Diacetate (Ic)	4.95 °	4 ·70	9, 5, 4	9.5, 7.5, 4.5	6, 1	5, 1.5
Monoacetate (XXIIb)	5.65 f	6.20	139	7.5, 5	9, 1.5	7.5, 1.5
Diacetate (XXIIIb)	5.40	4.80	9, 4	7.5, 5	7, 2	5, 1.5
Monoacetate (XXIVb)	5.05	6.10	10, 6, 4	9.5, 7.5, 4.5	9, 1.5	7, 1.5
Acetate (Id)		4.80			7, 2	5, 1.5
Hydroxy-ketone (XX)		5.95			5, 2	5, 1·5
Hydroxy-ketone (XXI)	5.45		10, 6, 4	9.5, 7.5, 4.5		

^a $J_{10,11}$, $J_{1,11}$, and $J_{10',11}$, observed experimentally. ^b Predicted J values for 11-H. See ref. 23. ^c $J_{7,8}$ and $J_{H_1}J_{H_8}$, observed experimentally. ^d Predicted J values for 8-H. See ref. 23. Peak positions indicate the centre of multiplets. ^f Triplet is explained by the theory of ABX systems if $J_{10,11} - J_{10',11} = 0$. See ref. 13. ^g The sum of $J_{10,11}$ and $J_{10',11}$.

chloride optics, a Perkin-Elmer model 257 grating spectrophotometer, and a Unicam model 200 spectrophotometer equipped with sodium chloride optics. U.v. spectra were recorded for purified light petroleum (b. p. 40-60°) solutions on a Unicam SP 800 spectrophotometer. N.m.r. spectra were taken in deuteriochloroform with tetramethylsilane as the internal standard on Varian A-60 and HA-100 spectrometers. Mass spectra were recorded at 70 ev on an AEI MS 9 spectrometer. Rotations were obtained for 1% chloroform solutions at room temperature. T.l.c. was carried out on silica gel GF chromatoplates eluted with light petroleum (b. p. 40-60°)-ether. To develop the spots, plates were sprayed with 6N-sulphuric acid and heated. Solutions were dried over anhydrous sodium or magnesium sulphate. Fuming sulphuric acid was used to purify the light petroleum (b. p. 40-60°) used for chromatography and recrystallisation.

Culmorin (Ia).—The culmorin, m. p. 178—179°, used in our studies was isolated by Ashley, Hobbs, and Raistrick; ² v_{max} . (CHCl₃) 3600 and 3450 cm.⁻¹ (OH); τ 5.68 (sextet, 1H), 6.14 (doublet with fine structure, 1H, $J \sim 5$ c./sec.), 7.24 (s, 2H), 8.16 (d, 1H, $J \sim 4.5$ c./sec.), 8.28 (d, 1H, $J \sim 5$ c./sec.), 8.37 (d, 2H, $J \sim 7$ c./sec.), 8.62 (s, 6H), 9.02 (s, 3H), 9.11 (s, 3H), 9.16 (s, 3H), and 9.22 (s, 3H). Spin-decoupling studies showed that the doublets at τ 8.16, 8.28, and 8.37 were the protons at C-1, C-7, and C-10, respectively.

Culmorin Dihetone (IVa).—Culmorin (5.0 g.; 2.10 mmoles) in preoxidised ether (200 ml.) was oxidised with chromic acid solution (30 ml.) by the Brown method.⁴ Recrystallisation of solids obtained from column chromatography of the crude product from light petroleum-ether

(110 mg., 83%), m. p. 162–164°; ν_{max} (CHCl₃) 3400–2400 (CO₂H), and 1740 and 1700 cm.⁻¹ (C=O); τ 6.98 (singlet with fine structure, 1H), 7.57 (s, 1H), 8.80 (s, 3H), 8.86 (s, 3H), and 8.91 (s, 3H) (Found: C, 66.1; H, 8.7. Calc. for C₁₄H₂₂O₄: C, 66.15; H, 8.65%).

Hydroxy-keto-ester (Vb).—The hydroxy-keto-acid (Va) (1·20 g., 4·47 mmoles) was treated with ethereal diazomethane in the usual manner. Recrystallisation of the product from cyclohexane-light petroleum gave the hydroxy-keto-ester (Vb) (1·1 g., 87%), m. p. 134—135°, $[\alpha]_{\rm D}$ +1°; $\nu_{\rm max}$ (CHCl₃) 3350 (OH), and 1740 and 1705 cm.⁻¹ (C=O); τ 5·20 (s, 1H), 6·25 (s, 3H), 7·00 (d, 1H, $J \sim 2$ c./sec.), 7·67 (d, 1H, $J \sim 2$ c./sec.), 8·82 (s, 6H), 8·91 (s, 3H), and 8·96 (s, 3H); mass spectrum: M^+ , m/e 268 (C₁₈H₂₄O₄).

Dehydration of Hydroxy-keto-ester (Vb).—The hydroxyketo-ester (Vb) (1.0 g., 3.73 mmoles) in pyridine (20 ml.) was treated with thionyl chloride (13 ml.) in pyridine (80 ml.). The reaction mixture was stirred at room temperature (25°) for 22 hr., poured into water (300 ml.), and extracted with ether (300 ml.). A viscous oil was obtained when this ethereal layer was washed with water (3 \times 200 ml.), dried, and evaporated, and the last traces of pyridine were removed *in vacuo*. Column chromatography of the oil, twice, over grade V alumina (eluted with light

²⁵ J. C. McMorris and M. Anchel, J. Amer. Chem. Soc., 1965, 87, 1594; K. Nakanishi, M. Ohashi, M. Tada, and Y. Yamada, *Tetrahedron*, 1965, 21, 1231; J. J. Dugan, P. de Mayo, M. Nisbet, and M. Anchel, J. Amer. Chem. Soc., 1965, 87, 2769; F. W. Comer, F. McCapra, I. H. Qureshi, J. Trotter, and A. I. Scott, *Chem. Comm.*, 1965, 310; J. A. Kempler, M. E. Wall, J. E. Mason, C. Basset, A. I. McPhail, and G. A. Sim, J. Amer. Chem. Soc., 1967, 89, 1261. petroleum-ether mixtures) gave the olefin ester (Xa) (260 mg., 27%), m. p. 45-47°, and the olefin ester (XIa) (250 mg., 27%), m. p. 62-63° (from light petroleum) $[\alpha]_{\rm D}$ +30°. Ester (Xa) had $\nu_{\rm max}$ (CS₂) 1745 and 1715 (C=O), and 1635 cm.⁻¹ (C=C); τ 6·25 (s, 3H), 6·98 (d, 1H, $J \sim 2$ c./sec.), 7.98 (d, 3H, $J \sim 1.5$ c./sec.), 8.88 (s, 3H), 8.92 (s, 3H), and 9.02 (s, 3H); $\lambda_{max.}$ (light petroleum) 225 and 300 m μ (ϵ 8700 and 40) (Found: C, 71.75; H, 8.85. Calc. for $C_{15}H_{22}O_3$: C, 71.95; H, 8.85%). Ester (XIa) had $\nu_{\text{max.}}$ (CS₂) 1740 and 1735 (C=O), 1655 (C=C), and 990 cm.⁻¹ (C=CH₂); τ 4.70 (d, 1H, $J \sim 2$ c./sec.), 6.36 (singlet which overlapped with another proton, 4H), 7.58 (d, 1H, J ~ 1.5 c./sec.), 8.76 (s, 3H), 8.84 (s, 3H), and 8.99 (s, 3H); $\lambda_{max.}$ (light petroleum) 300 m μ (ϵ 40) (Found: C, 71.95; H, 8.7%). The ester (XIa) (950 mg., 3.80 mmoles) was treated with sodium methoxide in methanol (100 ml., ca. 1 g. of sodium) at 25°. After 45 min. the mixture was poured into water (150 ml.) and extracted with ether $(2 \times 75 \text{ ml.})$. The combined ethereal layers were washed with water (2 imes 100 ml.) and dried. The solvent was evaporated to yield 850 mg. ester (Xa) (850 mg.), homogeneous by t.l.c.

Keto- γ -lactone (IX).—The hydroxy-keto-acid (Va) (900 mg., 3.54 mmoles) in acetic anhydride (1.5 ml.) was heated on a steam-bath for 3 hr. The reaction mixture was poured into water (10 ml.) and extracted with ether (15 ml.). The ethereal layer was washed with aqueous sodium hydrogen carbonate and water and dried. Removal of the solvent and recrystallisation of the residue from cyclohexane-light petroleum gave γ -lactone (IX) (470 mg., 57%), m. p. 136—137°, $[\alpha]_{\rm D}$ —24°; $\nu_{\rm max}$ (CHCl₃) 1780 and 1755 cm.⁻¹ (C=O); τ 7.10 (broad singlet, 1H), 7.90 (s, 1H), 8.70 (s, 3H), 8.75 (3, 3H) 8.83 (s, 3H), and 8.95 (s, 3H) (Found: C, 70.9; H, 8.4. Calc. for C₁₄H₂₀O₃: C, 71.15; H, 8.55%).

Hydrolysis of Keto- γ -lactone (IX).—The keto- γ -lactone (IX) (16 mg., 0.628 mmoles) in methanol-water (1:1) (5 ml.) containing one pellet of potassium hydroxide was heated on a steam-bath for 2 hr. and poured into water (10 ml.). Acidification with dilute hydrochloric acid and extraction with ether gave a viscous oil which was treated with an ethereal solution of diazomethane. The solid obtained after decolourisation with charcoal melted in two stages, 85—100 and 120—130°. Column chromatography over grade V alumina (elution with light petroleum-ether mixtures) yielded hydroxy-ester (Vb) (8 mg.).

Attempted Decarboxylation of Acid (Xb).—Hydrolysis of the ester (Xa) (11 mg., 0.043 mmoles) in 0.25M-aqueous methanolic potassium hydroxide (5 ml.) in the usual manner gave an acid (9 mg.), m. p. 88—92°; $\nu_{max.}$ (CHCl₃) 3300— 2200 (CO₂H), 1750 and 1695 (C=O), and 1630 cm.⁻¹ (C=C). This acid (5 mg.) was recovered when it was heated at 180—200° in a sealed tube for 25 min.

Decarboxylation of Acid (X1b).—Hydrolysis of ester (X1a) (48 mg., 0·14 mmoles) as described gave an acid (5 mg., 35%), m. p. 117—125° (from cyclohexane); v_{max} . (CHCl₃) 3300—2200 (CO₂H), 1738 and 1705 (C=O), and 1635 cm.⁻¹ (C=C). This acid (15 mg.) was heated at 160° in a sealed tube for 25 min. Column chromatography of the product over silica gel (eluted with 10% ether-cyclohexane) yielded ketone (XII) (7 mg., 58%), v_{max} . (CHCl₃) 1738 (C=O), 1650 (C=C), and 850 cm.⁻¹ (\geq C=C \leq H); mass spectrum: M^+ , m/e 192 (C₁₃H₂₀O).

Ozonolysis of Olefin Ester (Xa).—The olefin ester (Xa) (880 mg., 3.5 mmoles) in dry ethyl acetate (150 ml.) was ozonised at -20 to -30° . After 3 hr. the olefin was L

consumed (t.1.c.). The solvent was taken off in the cold in vacuo and the viscous oil that remained was chromatographed over grade V alumina (elution with cyclohexaneether). The solid obtained from the chromatography was decolourised with charcoal and gave the ozonide ester (XIV) (380 mg., 37%), homogeneous by t.1.c. A portion, which was recrystallised several times (with difficulty) from light petroleum-cyclohexane, melted at 107—108°. [α]_D +30°; ν_{max} (CHCl₃) 1760, 1745, 1718 (C=O), and 1100 cm.⁻¹ (C=O); τ 6·12 (s, 3H), 6·80 (s, 1H), 8·30 (s, 3H), 8·80 (s, 3H), 8·90 (s, 3H), and 8·95 (s, 3H); mass spectrum: M^+ , m/e 248 (C₁₅H₂₂O₆) and peaks at M — 32 and M — 48 (Found: C, 60·75; H, 7·4. Calc. for C₁₅H₂₂O₆: C, 60·4; H, 7·45%).

Cleavage of Ozonide Ester (XIV) with Triphenylphosphine. —The crude ozonide ester (XIV), prepared from olefin ester (Xa) (95 mg.), in chloroform (5 ml.) was treated with triphenylphosphine (80 mg.) under reflux for 25 min. The chloroform was evaporated. Column chromatography of the residue that remained over silica gel (elution with etherlight petroleum mixtures) gave a viscous oil (40 mg.), purified by t.l.c.; ν_{max} (CHCl₃) 1730, 1710sh, and 1695sh cm.⁻¹ (C=O); τ 5·29 (s, 1H), 6·17 (s, 3H), 7·78 (s, 3H), 8·78 (s, 3H), and 8·92 (s, 3H); mass spectrum: M^+ , m/e 282 (C₁₅H₂₂O₅).

Subsequent t.l.c. of the purified product showed tailing and thus indicated that the compound decomposed readily.

Hydrolysis of Ozonide Ester (XIV).—The ozonide ester (380 mg., 1·27 mmoles) in 0·25M-aqueous methanolic potassium hydroxide (70 ml.) was heated for 2 hr. on a steam-bath. The mixture was poured into water (70 ml.) and extracted with ether (2 × 50 ml.). The combined ethereal layers were washed with water and dried and the solvent was distilled off through a beaded column (1 ft.) to yield an oil (100 mg.), $v_{max.}$ (CHCl₃) 1695 (C=O) and 1380—1370 cm.⁻¹ (CMe₂); mass spectrum: M^+ , m/e 154 (C₁₀H₁₈O).

Methanol (1 ml.) and Brady's reagent (3 ml.) were added to the oil and the mixture was heated for 2 min. on a steambath. Several drops of 2N-sulphuric acid were added and the solution was placed in a cold room. The tetrahydroeucarvone 2,4-dinitrophenylhydrazone (200 mg.), m. p. 110—120°, which was collected showed one spot on t.l.c. The derivative was dissolved in absolute ethanol (10 ml.) and heated at reflux for 24 hr. Five recrystallisations from cyclohexane-ether gave the 2,4-dinitrophenylhydrazone (15 mg.), m. p. and mixed m. p. 133—135°; ν_{max} . (CHCl₃) 3320 (NH) and 1640 cm.⁻¹ (C=N) (Found: C, 57·35; H, 6·8. Calc. for C₁₆H₂₂O₄N₄: C, 57·45; H, 6·65%).

The aqueous alkaline layer from the initial extraction was acidified with dilute hydrochloric acid and extracted with ether (3 \times 50 ml.). The combined ethereal layers were washed with water and dried and the solvent was evaporated. The residue was decolourised with charcoal and recrystallised from cyclohexane-light petroleum-ether to yield the acid (XVIb) (90 mg., 35%), m. p. 117–125°, v_{max} (CHCl₃) 3300–2500 (CO₂H), and 1740 and 1695 cm.⁻¹ (C=O).

When the acid was heated at 168° in a sealed tube for 20 min., tetrahydroeucarvone (10 mg.) was obtained.

The acid (20 mg.), with ethereal diazomethane, gave a liquid ester which was purified by t.l.c., $\nu_{max.}$ (CHCl₃) 1740 and 1700 cm.⁻¹ (C=O); τ 6·34 (singlet which overlapped with another proton, 4H), 7·40 (broad multiplet, 1H), 8·45 (broad multiplet, 6H), and 8·80 and 8·92 (singlets, total of *ca*. 9H); mass spectrum: M^+ , m/e 212 (C₁₂H₂₀O₃).

Culmorin Diketone Dithioketal (IVb).—Culmorin diketone (4.5 g., 18.9 mmoles) in boron trifluoride etherate (30 ml.) and ethanedithiol (3 ml.) was allowed to stand at room temperature for 15 hr. and was then diluted with ether (20 ml.) and poured into water (20 ml.). The ethereal layer was washed with water (2 \times 20 ml.), dilute sodium hydroxide (20 ml.), dilute hydrochloric acid (25 ml.), and water (20 ml.), and dried. Evaporation of the solvent gave a solid which was recrystallised from absolute ethanol to vield the dithioketal (IVb) (4.9 g., 83%), m. p. $75-76^\circ$, $[\alpha]_{D}$ 104°, $\nu_{max.}$ (CHCl₃) 1735 (C=O) and 1380–1370 cm.⁻¹ (CMe₂); ~ 6.80 (multiplet, 4H), 7.26 (s, 1H), 7.40 (s, 1H), 7.68 (AB quartet, 2H, $J \sim 14$ c./sec.), 8.72 (unsymmetrical doublet, 6H), 8.95 (s, 3H), and 9.10 (s, 3H) (Found: C, 65.5; H, 8·45; S, 20·8. Calc. for C₁₇H₂₆OS₂: C, 65·8; H, 8·45; S, 20.65%).

Desulphurisation of Culmorin Diketone Dithioketal (IVb). —The dithioketal (IVb) (1.5 g., 4.85 mmoles) in absolute ethanol was heated to reflux and Raney nickel (W-4) in ethanol was added in portions until desulphurisation was complete as shown by t.l.c. The catalyst was filtered off and the ethanol removed through a beaded column (1 ft.). After the last traces of ethanol were removed *in vacuo*, the oil which remained was decolourised with charcoal to yield longicamphor (IVc) (950 mg., 90%), 98% pure t.l.c., $v_{max.}$ (CHCl₃) 1738 cm.⁻¹ (C=O); mass spectrum: M^+ , m/e 220 (C₁₅H₂₄O).

Sodium in n-Propanol Reduction of Longicamphor (IVc).— To longicamphor (820 mg., 98% pure), obtained from the desulphurisation of (IVb), in dry n-propanol (50 ml.) was added sodium (1 g.) in small portions followed by more sodium (300 mg.) in one portion. The reaction mixture was heated at reflux for 2 hr. and worked up in the usual manner. Column chromatography of the product over grade V alumina (elution with light petroleum–ether mixtures) gave a solid which was recrystallised from light petroleum to yield (—)-longiborneol (480 mg., 58%), m. p. 110—111°, $[\alpha]_{\rm p}$ —16°; $\nu_{\rm max}$ (Nujol) 3400 (OH) and 1040 cm.⁻¹ (C–O); τ 6·25 (quartet, 1H, $J \sim$ 6·1 cps.), 8·57 (s, 6H), 9·07 (s, 6H), and 9·17 (unsymmetrical doublet, 6H).

The 3,5-dinitrobenzoate, prepared in the usual manner and recrystallised from cyclohexane-ether, melted at 156— 157° (lit.,²² 156—157°). The acetate, prepared with acetic anhyride in pyridine, crystallised when cooled with dry ice, and melted at 44—47° (lit.,¹⁶ 46—47°), $[\alpha]_D - 18^\circ$; $\tau 4.79$ (quartet, 1H, $J \sim 6$, 1.5 c./sec.), 7.96 (s, 3H), 9.07 (s, 3H), 9.16 (s, 3H), and 9.22 (s, 3H).

Hydroxy-ketones (XX) and (XXI).-Culmorin (3 g., 1.26 mmoles) in preoxidised ether (150 ml.) was oxidised with one equivalent of chromic acid as described. The reaction mixture, worked up in the usual manner, gave a solid which was chromatographed over grade V alumina (elution with ether-light petroleum mixtures) to yield culmorin diketone (70 mg.), culmorin (200 mg.), and a mixture of the hydroxyketones (XX) and (XXI). Four recrystallisations of the mixture from cyclohexane-light petroleum gave hydroxyketone (XX) (850 mg.), m. p. 120-121°. The motherliquor from the second recrystallisation was recrystallised from cyclohexane and gave a mixture of crystalline forms which were separated manually. The form in smallest proportion was recrystallised from cyclohexane-petroleum ether and gave hydroxy-ketone (XXI) (16 mg.), m. p. 106-108°. When the mother-liquors were combined and evaporated, 1.0 g. of the hydroxy-ketone mixture was obtained. The hydroxy-ketones were also separated by

J. Chem. Soc. (C), 1968

repeated chromatography over grade V alumina. (XX) had $[\alpha]_D - 18^{\circ}$, v_{max} . (Nujol) 3400 (OH), 1730 (C=O), and 1035 cm.⁻¹ (C=O); $\tau 5.90$ (quartet, 1H, $J \sim 5$ and 2 c./sec.), 8.52 (s, 6H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 8.75 (d, 1H, $J \sim 5$ c./sec.), 8.97 (s, 3H), 9.00 (s, 3H), and 9.08 (s, 3H) (Found: C, 75.95; H, 10.25. C₁₅H₂₄O₂ requires C, 76.2; H, 10.25%). (XXI) had v_{max} . (Nujol) 3400 (OH), 1720 (C=O), and 1045 cm.⁻¹ (C=O); $\tau 5.45$ (quintet, 1H, $J \sim 10$, 6, and 4 c./sec.), 7.45 (s, 1H), 7.80 (multiplet, 2H), 7.95 (s, 1H), 8.65 (broad absorption from which a singlet protruded, 9H), 9.00 (s, 3H), 9.04 (s, 3H), and 9.11 (s, 3H) (Found: C, 76.05; H, 10.0%).

Reduction of hydroxy-ketones (XX) (90 mg.) and (XXI) (20 mg.) with sodium in n-propanol in the usual manner gave 13 and 12 mg. of culmorin, respectively.

Wolff-Kishner Reductions of Hydroxy-ketones (XX) and (XXI).--(a) Hydroxy-ketone (XX). To (XX) (120 mg., 0.51 mmoles) in absolute ethanol (6 ml.) was added 65%hydrazine hydrate (2 ml.). Nitrogen was bubbled through the solution and the excess of ethanol and hydrazine was distilled off over a period of 1.5 hr. When ca. 2-3 ml. of the solution remained diethylene glycol (6 ml.) was added and the distillation was continued until a temperature of 150-180° was reached. Potassium in diethylene glycol was added and the solution was heated to 200°. The solid which collected in the condenser was washed out periodically with ether. After 1.5 hr., the reaction mixture was poured into water and acidified with dilute hydrochloric acid. Extraction with ether $(2 \times 20 \text{ ml.})$ gave a product which was combined with the solid which collected in the condenser and chromatographed over grade V alumina (elution with light petroleum-ether mixtures). After column chromatography recrystallisation of the product from light petroleum gave (-)-longiborneol (Ib) (63 mg., 56%), m. p. 109—110°, $[\alpha]_{\rm D} = 17^{\circ}$.

(b) Hydroxy-hetone (XXI). Hydroxy-ketone (XXI) (130 mg., 0.55 mmoles) in absolute ethanol (6 ml.) was treated with 65% hydrazine hydrate (2 ml.) as above. The solid which was obtained from the usual work up was recrystallised from light petroleum to yield 95 mg. (78%) of the starting material (XXI), m. p. 108—109°, $[\alpha]_p -10°$, identified by its i.r. spectrum. The 3,5-dinitrobenzoate, prepared in the usual manner, melted at 132—133° (Found: C, 61·1; H, 6·2; N, 6·3. Calc. for C₂₂H₂₆N₂O₇: C, 61·4; H, 6·1; N, 6·5%).

Lithium Aluminium Hydride Reductions.—(a) Culmorin diketone. Culmorin diketone (900 mg., 3.85 mmoles) in ether was reduced with lithium aluminium hydride in the usual manner. Work up gave a product which was shown by t.l.c. to be a mixture of culmorin (5%), diol (XXIIa) (80%), diol (XXIIa) (5%), and diol (XXIVa) (10%). Recrystallisation of the solid from cyclohexane-ether-light petroleum gave diol (XXIIa) (600 mg., 65%), m. p. 140— 141°, $[\alpha]_{\rm p}$ —28° (Found: C, 75.55; H, 11.15. Calc. for C₁₅H₂₆O₂: C, 75.6; H, 11.0%).

(b) Hydroxy-ketone (XX). The reduction of (XX) (470 mg., 1-99 mmoles) in the usual manner gave a solid which was shown to be a mixture of culmorin (10%) and diol (XXIIIa) (90%). Recrystallisation of the product from benzene-light petroleum gave diol (XXIIIa) (300 mg., 64%), m. p. 160-161°, $[\alpha]_p$ +6° (Found: C, 75.4; H, 11.15%). The m. p. of 160-161° recorded for diol (XXIIIa) represents the temperature at which sintering begins, although the melting is not complete until 170-175° at which point sublimation is very rapid. Samples

of diol (XXIIIa), which was shown to be pure by t.l.c., exhibited this behaviour even after two sublimations.

(c) Hydroxy-ketone (XXI). The reduction of (XXI) (120 mg., 0.51 mmoles) in the usual manner gave a solid which was a mixture of culmorin (5%), diol (XXIIIa) (10%), and diol (XXIVa) (85%) as shown by t.l.c. Recrystallisation of the solid from light petroleum-ether gave diol (XXIVa) (90 mg., 74%), m. p. 116-118°, $[\alpha]_{\rm p} - 25^{\circ}$ (Found: C, 75.5; H, 10.85%).

Preparation of Acetates.—(a) From diol (XXIIa). Diol (XXIIa) (100 mg., 0.42 mmoles) in acetic anhydridepyridine (1:2) (2 ml.) was allowed to stand at room temperature for 24 hr. The reaction mixture was poured into water (8 ml.) and extracted with ether (2 × 10 ml.). The combined ethereal layers were washed with dilute hydrochloric acid and water and dried. Removal of the solvent gave a solid which, recrystallised from light petroleum–ether, afforded the monoacetate (XXIIb) (100 mg., 85%), m. p. 123—124°; ν_{max} , (CCl₃) 3640, 3520 (OH), 1738 (C=O), and 1240 cm.⁻¹ (C–O); τ 5.55 (t, 1H, sum of $J \sim 13$ c./sec.), 8.00 (s, 3H), 7.86 (s, 3H), and 9.00 (s, 9H) (Found: C, 72.65; H, 10.3. C₁₇H₂₈O₃ requires C, 72.8; H, 10.05%).

A reaction mixture, as above, was heated at reflux for 18 hr., but only the monoacetate (XXIIb) was isolated.

(b) From diol (XXIIIa). Diol (XXIIIa) (600 mg., 10·42 mmoles) was acetylated in acetic anhydride-pyridine at room temperature as described. Recrystallisation of the product from light petroleum-ether gave the diacetate (XXIIIb) (100 mg., 85%), m. p. 83–84°; ν_{max} (CCl₄) 1740 (C=O) and 1240 cm.⁻¹ (C-O); τ 4·80 (quartet, 1H, $J \sim 7$ and 2 c/sec.), 5·35 (quartet, 1H, $J \sim 9$ and 3·5 c./sec.), 7·98 (s, 3H), 8·00 (s, 3H), 8·97 (s, 3H), 9·05 (s, 3H), 9·15 (s, 3H), and 9·22 (s, 3H) (Found: C, 70·65; H, 9·2. C₁₉H₃₀O₄ requires C, 70·7; H, 9·4%).

(c) From diol (XXIVa). Diol (XXIVa) (85 mg., 0.36 mmoles) was acetylated with acetic anhydride-pyridine at room temperature as described. Recrystallisation of the product from light petroleum gave the monoacetate (XXIVb)

(85 mg., 85%), m. p. 153–154°, ν_{max} (CCl₄) 3640 and 3520 (OH), 1740 (C=O) and 1245 cm.⁻¹ (C=O), n.m.r. spectrum: τ , 5·05 (quartet, 1H, $J \sim 10$, 6, 4 cps.), 6·10 (quartet, 1H, $J \sim 9$, 3 cps.), 7·96 (s, 3H), 8·82 (s, 3H) and 9·08 (unsymmetrical doublet, 9H) (Found: C, 72·6; H, 10·15%).

(d) From Culmorin. The diacetate of culmorin prepared previously,² melted at 92–93°, v_{max} (CHCl₃) 1730 cm.⁻¹ (C=O); τ 4·70 (doublet with fine structure, 1H, $J \sim 6$ and 1 c./sec.), 4·95 (octet, 1H, $J \sim 9$, 5, and 4 c./sec.), 7·75 (d, 1H, $J \sim 5$ c./sec.), 7·91 (s, 6H), 8·25 (m, 3H), 8·52 (s, 6H), 9·07 (s, 3H), 9·13 (s, 6H), and 9·22 (s, 3H).

Attempted Autoxidation of Hydroxy-ketone (XX).—Hydroxy-ketone (XX) (50 mg., 0.21 mmoles) in ca. 1M-potassium t-butoxide-t-butanol (25 ml.) was shaken under oxygen for 24 hr. at room temperature. Approximately 5 ml. of oxygen were taken up. The reaction mixture was poured into water (50 ml.) and extracted with ether (3×25 ml.). The combined ethereal layers were extracted with dilute sodium hydrogen carbonate, washed with water (25 ml.), and dried, and the solvent was evaported to yield unchanged hydroxy-ketone (XX) (23 mg.).

The aqueous sodium hydrogen carbonate layer was worked up and gave a viscous oil which exhibited a broad band at 3400-2500 cm.⁻¹ (CO₂H) in the i.r. spectrum. Treatment of the oil with an ethereal solution of diazomethane gave a viscous oil which contained at least 6 components as was determined by t.l.c. No further work was done on the oil.

We thank Professor H. Raistrick, F.R.S., for the culmorin used in this work and Professor R. A. Raphael, F.R.S., for the authentic specimen of tetrahydroeucarvone. Professor G. Ourisson kindly provided us with authentic longifolene and (+)-longiborneol. We thank the S.R.C. and the Wellcome Trust for financial assistance. One of us (N. H. W.) acknowledges the award of a N.R.C. (Canada) Postdoctoral Fellowship.

[7/792 Received, June 28th, 1967]