906. *Sesquiterpenoids. Part II.*[1] *The Constitution and Stereochemistry of Drimenin, Isodrimenin, and Confertifolin.*

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The constitution and absolute stereochemistry of three isomeric sesquiterpenoid lactones, drimenin and isodrimenin, $C_{15}H_{22}O_2$, isolated from *Drimys winteri* Forst., and confertifolin, from *D. confertifolia* Phil., have been elucidated by relating them to drimenol. They are shown to arise from oxidation of the carbon atoms at positions 11 and 12 in drimane.

Continuing our investigation of the stem barks of South American *Drimys* species, we have isolated three new isomeric sesquiterpenoid lactones. Two of these, drimenin and confertifolin, have been described [2] in a preliminary communication. We now submit evidence for the constitution and stereochemistry of these compounds and the subsequently isolated isodrimenin.

Drimenin, $C_{15}H_{22}O_2$, was isolated from bark specimens of *Drimys winteri* Forst., which did not contain drimenol. Its infrared spectrum indicated the presence of a butanolide and one isolated, triply substituted ethylenic linkage ($\nu_{max.}$ 1780vs and 1670vw cm.$^{-1}$ in CCl_4; 808mw cm.$^{-1}$ in Nujol). Its lactonic nature is supported by reduction with lithium aluminium hydride to an unsaturated diol, $C_{15}H_{26}O_2$ (see p. 4691), whose ultraviolet and infrared spectra also revealed a triply substituted ethylenic linkage. Both the lactone and the diol gave a yellow colour with tetranitromethane.

Three factors suggested a bicyclofarnesol skeleton in drimenin: first, consideration of analytical data and the functional groups disclosed spectroscopically, lead to the conclusion that drimenin must be tricyclic; secondly, drimenin exhibited marked similarity to drimenol [1] in the CH deformation region of its infrared spectrum ($\nu_{max.}$ 1366 and 1389 cm.$^{-1}$

[1] The paper by Appel, Brooks, and Overton, *J.*, 1959, 3322, is regarded as Part I.
[2] Appel and Dohr, *Scientia (Chile)*, 1958, **25**, 137.

in CCl_4), indicative of a *gem*-dimethyl group attached to a six-membered ring; thirdly, drimenin occurs as a constituent of *D. winteri* in place of drimenol, thus lending biogenetic support to such a supposition. *Ab origine* and by analogy with iresin,[3] the γ-lactone of drimenin might be expected to arise from oxidation of the carbon atoms at positions 11 and 12 in drimane [1] and the double bond to be located at position 7,8 as in expression (IX). The evidence presented in the sequel shows this to be correct.

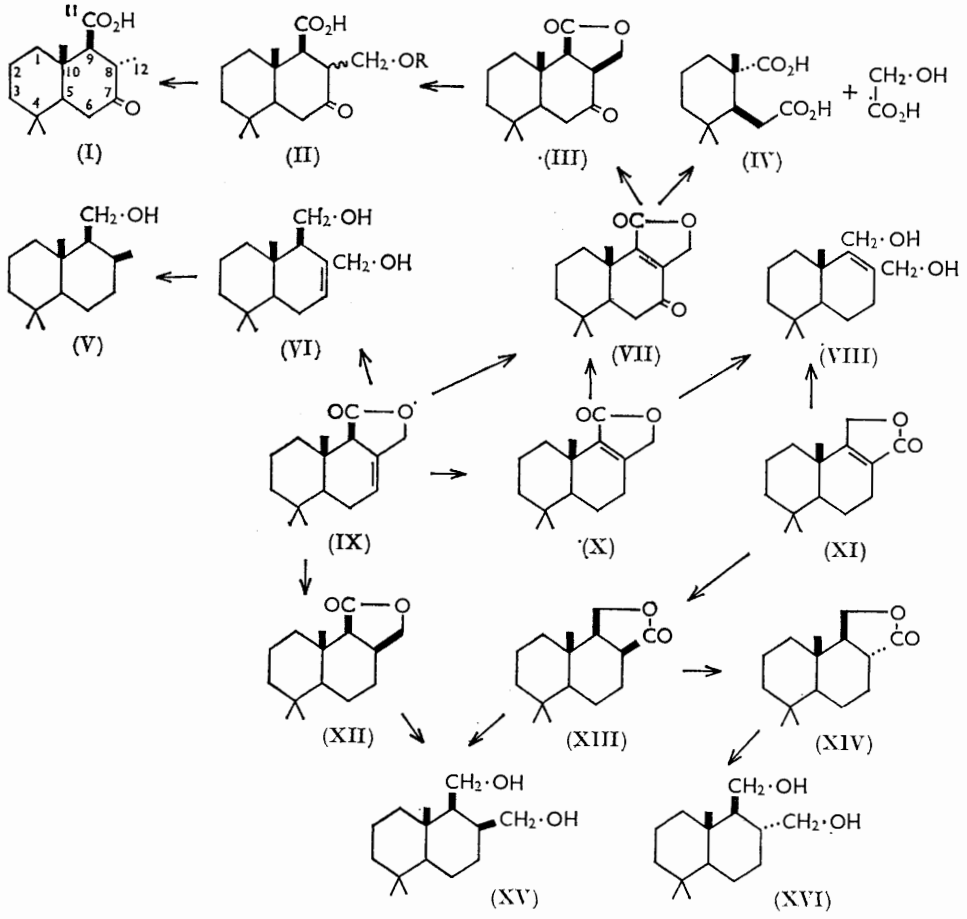
Treatment of drimenin with 10% ethanolic potassium hydroxide at 20° for 1 hr. afforded isodrimenin which is formulated as (X) on the basis of its infrared [$\nu_{max.}$ 1766vs (αβ-unsaturated butenolide) and 1671m cm.$^{-1}$ (conjugated C=C) in CCl_4; 783m cm.$^{-1}$ in Nujol; the significance of the last band which also appears in the spectra of the lactones (VII), (XI), and (XVIII) will be discussed elsewhere] and ultraviolet ($\lambda_{max.}$ 218 mμ; ε 10,000) spectra. Oxidation of either drimenin (IX) or isodrimenin (X) with Beckmann's mixture afforded oxoisodrimenin which we formulate as (VII) on the basis of its spectroscopic properties and subsequent transformations and by analogy with the corresponding acid [1] (XVII) obtained from drimenol. Thus it had infrared bands in carbon tetrachloride at 1774vs (αβ-unsaturated butenolide) and 1690vs cm.$^{-1}$ (αβ-unsaturated cyclohexenone) and in Nujol at 783m cm.$^{-1}$, and ultraviolet bands at 247 mμ (ε 10,600) in neutral ethanol and 259 mμ (rising to a maximum ε 5600 after $\frac{2}{3}$ hr.) in 0·01N-ethanolic potassium hydroxide. Reduction with zinc dust in refluxing acetic acid furnished the dihydro-oxo-lactone (III) showing infrared bands in carbon tetrachloride at 1781s (butanolide) and 1716ms cm.$^{-1}$ (cyclohexanone) (absence of band near 780 cm.$^{-1}$ in Nujol) and in the ultraviolet region $\lambda_{max.}$ 282 mμ (ε 30). The *cis*-fusion of the *stable* dihydro-oxo-lactone (III) obtained in the zinc reduction of lactone (VII) is shown by its ready dehydrogenation (see p. 4691) by selenium dioxide to the dienone lactone (XVIII). In contrast, the acid (XIX) is, even during working up, largely transformed into the 8α-methyl isomer. The difference in stabilities of the compounds (III) and (XIX) probably arises from the conformations of their 8β-substituents. In the acid (XIX) this is axial and results in 1,3,5-triaxial non-bonded interaction with the methyl groups at positions 4 and 10. In the lactone (III) the 8β-substituent is constrained, by virtue of its inclusion in the attached butanolide, in a quasi-equatorial conformation and thus the driving force for isomerisation to the 8α-lactone is diminished. When the lactone (III) was kept in 1% methanolic or ethanolic potassium hydroxide at 20° for 16 hr. in an attempt to bring about isomerisation at $C_{(8)}$, it was smoothly transformed into the corresponding alkoxy-acids (II; R = Me or Et respectively); these had infrared bands in chloroform at 3504w (OH of CO_2H monomer), 1740m (CO_2H monomer), and 1705s (superposed cyclohexanone and CO_2H dimer) cm.$^{-1}$ and are presumably formed by β-elimination of the lactone, followed by addition of alcohol to the resulting α-methylene ketone. The acids (II; R = Me or Et), when heated above their melting points, afforded a compound $(C_{15}H_{22}O_3)_n$, m. p. 258—260°, which on the basis of mass-spectroscopic molecular weight, yellow colour with tetranitromethane, infrared [3505w (OH of CO_2H monomer), 1740m (CO_2H monomer), and 1706m cm.$^{-1}$ (cyclohexanone; the expected [4] enol ether band is not resolved)] and ultraviolet [$\lambda_{max.}$ 205 mμ (ε 5400) (Hilger Uvispek)] spectra and recorded [4] precedent is formulated as the dimer (XX) (or equivalent).

Dehydro-oxoisodrimenin (XVIII) which is obtained either from the lactone (III) or directly from oxoisodrimenin (VII) with selenium dioxide has infrared absorption maxima at 1773vs (αβ-unsaturated butenolide), 1682s, and 1651vs cm.$^{-1}$ (cyclohexadienone) in carbon tetrachloride and at 783m cm.$^{-1}$ in Nujol, and resembles the analogous ester (XXIII) obtained from methyl cativate [5] [particularly in the appearance in its infrared spectrum of an intense third band near 1650 cm.$^{-1}$ compared with its precursor (VII); an ultraviolet maximum at 248 mμ (ε 14,800) supports this resemblance]. However, the

[3] Djerassi *et al.*, *J. Amer. Chem. Soc.*, 1954, **76**, 6410; 1957, **79**, 3528; *Tetrahedron*, 1959, **7**, 37.
[4] Romann, Frey, Stadler, and Eschenmoser, *Helv. Chim. Acta*, 1957, **40**, 1900.
[5] Halsall and Moyle, *J.*, 1960, 1324.

lactone (XVIII) no longer exhibits the bathochromic shift in basic solution observed with the compounds (VII) and (XVII). Observations on selected analogous compounds [6] indicate that this shift probably depends on the ability of the ketonic carbonyl group to enolise.

The dienone-lactone chromophore of dehydro-oxoisodrimenin can be accommodated

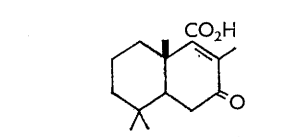


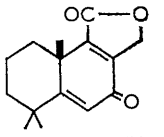
on the drimane template only as in (XVIII), which therefore defines the constitution (IX) of drimenin as drim-7-en-11,12-olide. This was supported by three experiments which also define its absolute stereochemistry.

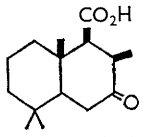
First, ozonolysis of oxoisodrimenin (VII) at −70° in ethyl acetate and decomposition of the ozonide with aqueous sodium hydrogen carbonate in presence of hydrogen peroxide furnished drimic acid (IV); glycollic acid could be isolated when the ozonide was decomposed with sodium hydrogen carbonate alone. Secondly, reduction of the methoxy-acid (II; R = Me) with zinc in acetic acid afforded the oxo-acid (I) obtained from drimenol.[1] Thirdly, reduction of drimenin with lithium aluminium hydride in ether afforded the diol (VI), which had an infrared band in Nujol at 834 cm.$^{-1}$ and ultraviolet absorption ($\varepsilon_{208\ m\mu}$ 2000; $\varepsilon_{212\ m\mu}$ 920; $\varepsilon_{220\ m\mu}$ 125) characteristic of a triply substituted ethylenic linkage. This on reduction with Adams catalyst in acetic acid consumed two mol. of hydrogen and furnished drimanol [1] (V) (characterised as the 3,5-dinitrobenzoate) in essentially quantitative yield.

[6] C. J. W. Brooks, unpublished observations; we gratefully acknowledge their disclosure before publication.

Reduction of drimenin over Adams catalyst in acetic acid or ethyl acetate resulted in formation of a 1 : 1 mixture of dihydrodrimenin (XII) [$\nu_{max.}$ in carbon tetrachloride 1780vs cm.$^{-1}$ (butanolide)] and isodrimenin (X), which was readily separable by chromatography. Drimenin was recovered unchanged after treatment with Adams catalyst alone in acetic acid. The migration during catalytic reduction of an ethylenic double bond, initially exocyclic to a butanolide, to a tetrasubstituted endocyclic location, has a parallel in the chemistry of ambrosin,[7] as has the stability of the resulting allylic lactone. A mechanism has been proposed[8] for a cognate migration which occurs during the reduction of


(XVII)


(XVIII)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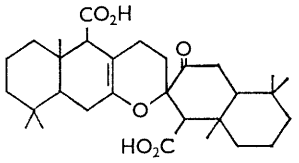
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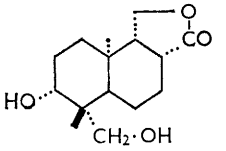
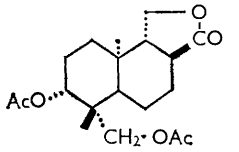
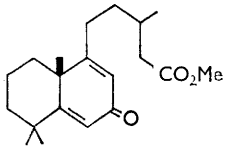
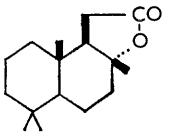
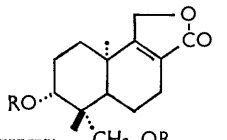
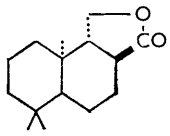

(XXI)


(XXII)


(XXIII)


(XXIV)


(XXV)


(XXVI)

protolichesterenic acid; here, as in drimenin, stabilisation resulting from double-bond conjugation with the carbonyl group may provide an additional driving force for the migration. Reduction of dihydrodrimenin (XII) with lithium aluminium hydride afforded the *cis*-diol (XV); its stereochemistry follows from identity with the (necessarily *cis*)-diol obtained from confertifolin (XI; see p. 4689) by the same reaction sequence, and from the known (see p. 4687) stereochemistry of drimenin at position 9. The stability to base of dihydrodrimenin (XII) under conditions which readily transform the isomeric lactone (XIII) and dihydroiresin (XXI) into the corresponding *trans*-lactones is readily rationalised by reference to molecular models; conversion into a *trans*-lactone by inversion at position 9 would force ring B into the boat conformation and is therefore not favoured. Similar conformational considerations[9] have led to a stereochemical assignment at $C_{(13)}$ in the lactone (XXIV) obtained from sclareol. Reduction of isodrimenin with lithium aluminium hydride afforded the unsaturated diol (VIII). Attempts to reduce isodrimenin catalytically even in presence of perchloric acid gave back only starting material.

Isodrimenin, isolated from a specimen of *D. winteri* Forst., is probably not an artefact, since drimenin is substantially unchanged when subjected to the conditions used in the isolation procedure.

The constitution and stereochemistry of confertifolin, $C_{15}H_{22}O_2$, previously[2] isolated from *D. confertifolia* Phil. and subsequently in much better yield from *D. winteri* Forst., follow simply from the following considerations. Confertifolin does not give a colour with tetranitromethane; it has infrared bands in carbon tetrachloride at 1769vs (αβ-unsaturated butenolide) and 1677vw cm.$^{-1}$ (conjugated C=C) and in Nujol at 783mw cm.$^{-1}$. In the

[7] Šorm, Suchy, and Herout, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1548.
[8] Van Tamelen, Osborne, and Bach, *J. Amer. Chem. Soc.*, 1955, **77**, 4625.
[9] Klyne, *J.*, 1953, 3072.

ultraviolet region it has $\lambda_{max.}$ 217 mμ (ε 11,750). These spectroscopic properties very closely resemble those of isodrimenin (X) and isoiresin (XXV; R = H), suggesting for confertifolin the constitution (XI) of drim-8-en-12,11-olide, either directly or enantiomerically related to isoiresin. The validity of the second alternative was confirmed as follows. First, reduction of confertifolin with lithium aluminium hydride in ether afforded the unsaturated diol (VIII) previously obtained from isodrimenin (X). Secondly, unlike isodrimenin (X), but like isoiresin (XXV; R = H), confertifolin was smoothly hydrogenated by Adams catalyst in acetic acid and afforded the lactone (XIII) [$\nu_{max.}$ in CCl_4 1784vs cm.$^{-1}$ (butanolide)]. Lithium aluminium hydride converted this into the saturated diol (XV) previously obtained from drimenin. The difference in behaviour during catalytic reduction of the isomeric lactones (X) and (XI) appears to us to merit comment. This can be rationalised if reduction is supposed to proceed *via* the Δ^7-isomer (or equivalent); with the lactones (XI) and (XXV; R = H) conjugation with the lactonic carbonyl group is retained in the intermediate whereas this would not be the case with isodrimenin (X). Significantly, the lactones (XI) and (XXV; R = Ac) [10] are not hydrogenated in ethyl acetate. As expected, the *cis*-lactone (XIII) was readily converted into the *trans*-lactone (XIV) [$\nu_{max.}$ in CCl_4 1792vs cm.$^{-1}$ (butanolide)] with methanolic potassium hydroxide at 20°. The constraint imposed on a parallel change with the isomeric lactone (XII) does not operate here. The physical constants of the *trans*-lactone (XIV) do not accord well with those recorded [11] for the enantiomeric lactone (XXVI) obtained from iresin, which unfortunately was not available for comparison. However, there is satisfactory correspondence between the molecular-rotation changes associated with the transformations isoiresin diacetate (XXV; R = Ac) ⟶ isodihydroiresin diacetate (XXII) ($\Delta[M]_D$ + 245°) and confertifolin (XI) ⟶ isodihydroconfertifolin (XIV) ($\Delta[M]_D$ − 216°). Reduction with lithium aluminium hydride of the lactone (XIV) led to the new *trans*-diol (XVI).

Catalytic hydrogenation of both drimenin and confertifolin is thus seen to take place from the more accessible α-face of the molecule, as occurs predominantly with drimenol.[1]

The behaviour, on oxidation, of drimenin, isodrimenin, and confertifolin merits comment. Drimenin and isodrimenin are transformed into oxoisodrimenin at similar rates by either Beckmann's mixture or chromium trioxide in 95% acetic acid [contrast the difference in reactivity [12] of methyl 19-oxo-olean-12- and -13(18)-enolate acetate]. Confertifolin does not yield the corresponding oxo-lactone with these reagents and is recovered largely unchanged.

Drimenin, isodrimenin, and confertifolin represent three additional members of the small class of bicyclofarnesol derivatives having the same absolute stereochemistry as drimenol and notably also lacking an oxygen function at position **3**.[13] The occurrence in the same plant of two isomeric lactones resulting from transposition of the oxygen functions attached to the same carbon atoms is a novel phenomenon in terpenoid chemistry.

Experimental

M. p.s were determined on the Kofler block. Infrared solution and KCl disc spectra were kindly recorded by Mrs. F. Lawrie with a Unicam S.P. 100 double-beam infrared spectrometer and are accurate to ±1 cm.$^{-1}$; Nujol spectra were taken with a Perkin–Elmer 13 spectrometer, ultraviolet spectra with a Unicam S.P. 500 spectrometer for solutions in ethanol unless stated to the contrary. Microanalyses are by Mr. J. M. L. Cameron and his staff. Extractions of plant material were kindly carried out by Sr. J. Olivares. Chromatographic alumina was prepared and standardised by Brockmann's procedure.[14] The light petroleum used was of b. p. 60—80° unless stated to the contrary.

Extraction of ***Drimenin, Isodrimenin and Confertifolin.***—The dried powdered bark was in

[10] Crabbe, Burstein, and Djerassi, *Bull. Soc. chim. belges*, 1958, **67**, 632.
[11] Djerassi, Donvan, Burstein, and Mauli, *J. Amer. Chem. Soc.*, 1958, **80**, 1972.
[12] Barton, Holness, Overton, and Rosenfelder, *J.*, 1952, 3751.
[13] Djerassi, Cais, and Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 2386.
[14] Brockmann, *Ber.*, 1941, **74**, 73.

each case exhaustively extracted with light petroleum (b. p. 70—80°) in a Soxhlet apparatus. Removal of solvent, distillation *in vacuo* of the residue, and working up of the appropriate fractions then afforded the lactones as follows.

Drimenin (IX). From *Drimys winteri* Forst. (Loncoche). Obtained by washing of the fraction of b. p. 160—185°/8 mm. with a little cold methanol, drimenin (2% by weight of the extract) crystallised from methanol and sublimed at 110°/0·1 mm., then having m. p. 133°, $[\alpha]_D$ −42° (*c* 0·76 in C_6H_6) (Found: C, 77·2; H, 9·5%. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·45%).

Confertifolin (XI). From *Drimys winteri* Forst. (Valdivia). The fractions of b. p. 250—300°/8—5 mm. afforded, on dilution with light petroleum and refrigeration, crude confertifolin (3·8% by weight of the extract). Recrystallised from light petroleum this had m. p. 152°, $[\alpha]_D$ +72° (*c* 2·00 in $CHCl_3$), +93° (*c* 2·10 in C_6H_6) (Found: C, 76·75; H, 9·65%).

Isodrimenin (X). From *Drimys winteri* Forst. (Loncoche). Obtained from the fraction of b. p. 195—210°/3 mm. in 0·56% yield based on the extract. Crystallised from n-hexane and sublimed at 100°/0·1 mm., it had m. p. 131—132°, $[\alpha]_D$ +87° (*c* 2·02 in $CHCl_3$), +78° (*c* 0·80 in C_6H_6) (Found: C, 76·55; H, 9·5%).

Isomerisation of Drimenin.—Drimenin (40 mg.) was dissolved and kept in 10% ethanolic potassium hydroxide (2 ml.) at 20° for 1 hr. Acidification, dilution, and extraction into ether afforded isodrimenin (X) (36 mg.) which, crystallised (rods) from n-hexane and sublimed at 115°/0·1 mm., had m. p. 129—131°, $[\alpha]_D$ +79° (*c* 1·03 in C_6H_6); it was identical in m. p., mixed m. p. and infrared spectrum with isodrimenin isolated from *D. winteri* Forst. (see above) and by hydrogenation of drimenin (see below).

Oxidation of Drimenin and Isodrimenin with Beckmann's Mixture.—(*A*) Drimenin (200 mg.) in " AnalaR " acetic acid (8 ml.) and Beckmann's mixture (2 ml.) was kept at 20° for 24 hr. Dilution, extraction into ether, washing of the ether extract successively with saturated aqueous sodium hydrogen carbonate and water, and chromatography over alumina (activity III; 6 g.) in benzene, afforded oxoisodrimenin (VII) (120 mg.), plates (from n-hexane), m. p. 112—113°, $[\alpha]_D$ +52° (*c* 1·89 in C_6H_6). (*B*) Isodrimenin (200 mg.), oxidised in the same manner, afforded oxoisodrimenin (160 mg.), identical in m. p., mixed m. p., and infrared spectrum with material obtained as in (A).

Relative Rates of Oxidation of Drimenin, Isodrimenin, and Confertifolin with (a) *Beckmann's Mixture and* (b) *Chromium Trioxide in* 95% *Acetic Acid.*—The compound (100 mg.) in (*a*) acetic acid (4 ml.) and Beckmann's mixture (1 ml.) or (*b*) acetic acid (2 ml.) containing chromium trioxide (43 mg., 1·5O) was kept at 20° for 16 hr. The total neutral product obtained in the usual way was examined in the ultraviolet region. Drimenin: (*a*) the neutral product (80 mg.) had $\lambda_{max.}$ 247 mμ (ε 5600); (*b*) 93 mg. $\lambda_{max.}$ 247 mμ (ε 4200). Isodrimenin: (*a*) 95 mg., $\lambda_{max.}$ 219 (ε 7000), 247 mμ (ε 5500); (*b*) 95 mg., $\lambda_{max.}$ 219 (ε 7400), 247 mμ (ε 5000). Confertifolin; (*a*) 78 mg., $\lambda_{max.}$ 217 mμ (ε 9500).

Reduction of Oxoisodrimenin with Zinc and Acetic Acid.—Oxoisodrimenin (70 mg.) was refluxed with zinc dust (1·5 g.) in glacial acetic acid (20 ml.) for 3 hr. Removal of zinc and solvent left a residue (60 mg.) of *dihydro-oxoisodrimenin* (III), which, thrice crystallised from benzene–n-hexane (needles), had m. p. 124—126°, $[\alpha]_D$ −115° (*c* 1·0 in C_6H_6), $\lambda_{max.}$ 282 mμ (ε 29) (Found: C, 71·8; H, 8·8. $C_{15}H_{22}O_3$ requires C, 71·95; H, 8·85%).

12-*Ethoxy*-7-*oxodriman*-11-*oic Acid* (II; R = Et).—Dihydro-oxoisodrimenin (56 mg.), dissolved in 1% ethanolic potassium hydroxide (6 ml.), was kept at 20° for 16 hr. The acidic product (59 mg.), obtained in the usual way, afforded needles (50 mg.) of 12-*ethoxy*-7-*oxo-driman*-11-*oic acid* from acetone–light petroleum; these had m. p. 175—179° and resolidified at 230—245° (see below). Sublimed at 130°/10^{-3} mm. and recrystallised from the same solvents, this acid had m. p. 182—184°, $[\alpha]_D$ +21° (*c* 1·17 in $CHCl_3$) (Found: C, 68·9; H, 9·5. $C_{17}H_{28}O_4$ requires C, 68·9; H, 9·5%).

The corresponding *methoxy-acid* (II; R = Me) obtained in the same way with methanolic alkali had (from the same solvent) m. p. 170—171°, $[\alpha]_D$ +12° (*c* 1·17 in $CHCl_3$) (Found: C, 68·2; H, 9·4. $C_{16}H_{26}O_4$ requires C, 68·05; H, 9·3%).

7-*Oxo*-8α-*driman*-11-*oic Acid* (I).—The methoxy-acid (II; R = Me) (7 mg.) in " AnalaR " acetic acid (2 ml.) was refluxed with zinc dust (35 mg.) for 3 hr. Removal of zinc and solvent afforded 7-*oxo*-8α-*driman*-11-*oic acid* (6 mg.), prisms (from ether–hexane), m. p. 200—202° alone and mixed with the acid obtained by reduction of 7-oxodrim-8-en-11-oic acid, and of identical infrared spectrum.

Dimer (?XX).—(*a*) The above ethoxy-acid (31 mg.), heated in nitrogen at 200° until gas

evolution ceased (2—3 min.), solidified on cooling to afford the *dimer*. Crystallised from acetone–benzene (needles) (12 mg.), this had m. p. 258—260°; a second crop (10 mg.) had m. p. 254—258°. The dimer had a mass-spectroscopic molecular weight 506 ± 10 (calc., 500) (kindly determined by Dr. R. I. Reed and his colleagues on a Metropolitan-Vickers Ltd. M.S. 2 Mass-spectrometer) (Found: C, 71·45; H, 8·4. $C_{15}H_{22}O_3$ requires C, 71·95; H, 8·85%). (*b*) Pyrolysis of the methoxy-acid afforded the dimer, m. p. alone and mixed 255—260°, and identical in infrared spectrum with that obtained as in (*a*).

Oxidation of Dihydro-oxoisodrimenin and Oxoisodrimenin with Selenium Dioxide.—(i) Dihydro-oxoisodrimenin (15 mg.) and selenium dioxide (100 mg.) were refluxed in glacial acetic acid (3 ml.) for 2 hr. Removal of solids and solvent and filtration of the residue in benzene through alumina (activity V; 1 g.) afforded a yellow oil (12 mg.). Crystallisation from hexane furnished dehydro-oxoisodrimenin (XVIII) as rods, m. p. 98—100°, contaminated with red selenium.

(ii) Oxoisodrimenin (25 mg.) was oxidised with selenium dioxide (100 mg.) as in (i). The crude product in benzene (10 ml.) was shaken with precipitated silver for 4 hr., and the benzene solution filtered through silver and alumina (activity III; 1 g.). The residue obtained on removal of solvent from the eluate was dissolved in benzene–hexane (1 : 5) and chromatographed over alumina (activity III; 1 g.), affording selenium-free *dehydro-oxoisodrimenin* (XVIII) (18 mg.) which crystallised spontaneously. Recrystallised from hexane this had m. p. 100—102° and was identical in mixed m. p. and infrared spectrum with material obtained as in (i). The product had $[\alpha]_D$ +21° (*c* 1·95 in C_6H_6) and $\lambda_{max.}$ 248 mμ (ε 15,800) in EtOH and 0·001N-ethanolic KOH (Found: C, 73·45; H, 7·25. $C_{15}H_{18}O_3$ requires C, 73·15; H, 7·35%).

Ozonolysis of Oxoisodrimenin.—(i) Oxoisodrimenin (100 mg.) in ethyl acetate (10 ml.) was treated with ozonised oxygen at −70° until the absorption peak at 247 mμ had disappeared (2¾ hr.). The solution was allowed to warm to 20°, saturated aqueous sodium hydrogen carbonate (5 ml.) was added, and the ethyl acetate removed by distillation *in vacuo*. 30% Hydrogen peroxide (2 ml.) was then added and the solution kept at 20° for 10 hr. Acidification, saturation with ammonium sulphate, and extraction with ether afforded a clear oil (90 mg.) which was adsorbed from benzene on chromatographic silica gel (B.D.H.; 6 g.). Elution with 4 : 1 benzene–ether furnished the only semicrystalline fractions (41 mg.), which on sublimation at 140°/0·1 mm. gave drimic acid [1] (IV), m. p. alone and mixed with material prepared from nordrimenone,[1] 165—167°, and of essentially identical infrared spectrum.

(ii) Oxoisodrimenin (150 mg.) was ozonised for 3¾ hr. as in (i), and the ozonide was decomposed without hydrogen peroxide. Saturation with ammonium sulphate of the aqueous solution and hand-extraction with ether afforded a colourless oil (155 mg.) which was not further investigated. Continuous extraction with ether for 36 hr. furnished a crystalline acid (17 mg.) which, recrystallised from ether–benzene, had m. p. 76—77°, alone and mixed with glycollic acid, and of correct infrared spectrum.

Reduction of Drimenin with Lithium Aluminium Hydride.—Drimenin (100 mg.) in ether (5 ml.) was added dropwise to lithium aluminium hydride (200 mg.) in ether (10 ml.), and the suspension was stirred for 4 hr. The product obtained in the usual way was a clear oil (87 mg.), showing only residual carbonyl absorption in the infrared spectrum. Adsorption on alumina (activity V; 3 g.) from benzene–hexane (1 : 1) and elution with benzene afforded drim-7-ene-11,12-diol (VI) (53 mg.), rods (from hexane), m. p. 73·5—74·5°, $[\alpha]_D$ −7° (*c* 1·38 in C_6H_6), giving a yellow colour with tetranitromethane (Found: C, 75·6; H, 11·25. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%).

Hydrogenation of the Diol.—The above diol (25 mg.) in glacial acetic acid (5 ml.) was hydrogenated with Adams catalyst (23 mg.) at 20°/1 atm.; 2·2 mol. hydrogen were absorbed in 30 min. The crystalline product (26 mg.), twice crystallised from hexane, had m. p. 109—110° alone and mixed with drimanol [1] (V) (identical infrared spectrum) and $[\alpha]_D$ +18° (*c* 0·39 in C_6H_6). The derived 3,5-dinitrobenzoate had m. p. 138—139° alone and mixed with drimanyl 3,5-dinitrobenzoate.

Hydrogenation of Drimenin.—Drimenin (600 mg.) in ethyl acetate (120 ml.) was hydrogenated with Adams catalyst (270 mg.) at 20°/1 atm.; 1·18 mol. hydrogen were absorbed in 40 min. The crude product was adsorbed on alumina (activity III; 18 g.) from light petroleum. Elution with 1 : 9 benzene–light petroleum afforded *dihydrodrimenin* (XII) (347 mg.), rods (from hexane), m. p. 71—73°, $[\alpha]_D$ −79° (*c* 1·14 in C_6H_6) (Found: C, 76·4; H, 10·2. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·25%). Elution with benzene–light petroleum (1 : 4 to 1 : 0) afforded isodrimenin (X) (207 mg.), rods (from benzene–hexane), m. p. 131—132°, $[\alpha]_D$ +79° (*c* 1·03 in C_6H_6).

Drimenin was recovered after treatment with acetic acid at 70° or with Adams catalyst and acetic acid at 20°.

When drimenin in acetic acid was hydrogenated in presence of 10N-hydrochloric acid or perchloric acid the hydrogen uptake was 1—1·1 mol. and there was no acidic product.

Dihydrodrimenin was recovered after 24 hr. in 5% methanolic potassium hydroxide.

Isodrimenin (20 mg.) in acetic acid (5 ml.) and perchloric acid (1 drop) did not consume hydrogen during 72 hr. and was recovered.

Reduction of Dihydrodrimenin and Isodrimenin with Lithium Aluminium Hydride.—8β,9β-*Drimane*-11,12-*diol* (XV). Dihydrodrimenin (100 mg.) was reduced with excess of lithium aluminium hydride in refluxing ether (10 ml.) for 1·5 hr. The *diol* (XV) (93 mg.) obtained in the usual way, crystallised from chloroform in rods, m. p. 151—152°, $[\alpha]_D$ +27° (*c* 0·98 in $CHCl_3$) (Found: C, 75·15; H, 11·9. $C_{15}H_{28}O_2$ requires C, 74·95; H, 11·8%).

The diol (22 mg.) and toluene-*p*-sulphonyl chloride (27 mg.) were kept in dry pyridine (7 ml.) for 16 hr. The product (22 mg.) obtained in the usual way was adsorbed on alumina (1·5 g.; activity III) from 1 : 1 benzene–hexane. Elution with the same solvent afforded 11,12-epoxy-8β,9β-drimane (10 mg.). Sublimed at 25°/0·1 mm., this had m. p. 38—38·5°, $\lambda_{max.}$ (in Nujol) 1069 $cm.^{-1}$ (cyclic ether) (no OH or CO band) (Found: C, 81·35; H, 11·5. $C_{15}H_{26}O$ requires C, 81·0; H, 11·8%). Elution with benzene furnished 8β,9β-*drimane*-11,12-*diol ditoluene*-p-*sulphonate* (8 mg.), needles (from ether–hexane), m. p. 143—145°, $\lambda_{max.}$ 225 mμ (ε 24,000) (Found: C, 63·3; H, 7·15. $C_{29}H_{40}O_6S_2$ requires C, 63·5; H, 7·35%).

Drim-8-*ene*-11,12-*diol* (VIII).—Isodrimenin (30 mg.) was reduced with excess of lithium aluminium hydride in ether (7 ml.) for 2 hr. Working up in the usual way afforded *drim*-8-*ene*-11,12-*diol* (VIII) (27 mg.), plates (from benzene), m. p. 123—124°, $[\alpha]_D$ +118° (*c* 1·03 in C_6H_6), giving a yellow colour with tetranitromethane, $\varepsilon_{205\ m\mu}$ 10,150, $\varepsilon_{210\ m\mu}$ 5900, $\varepsilon_{215\ m\mu}$ 2650, $\varepsilon_{220\ m\mu}$ 850 (Found: C, 75·9; H, 10·9. $C_{15}H_{26}O_2$ requires C, 75·6; H, 11·0%).

Confertifolin and Congeners (With Mr. R. P. M. Bond).—*Reduction of confertifolin with lithium aluminium hydride.* Confertifolin (343 mg.) was refluxed with lithium aluminium hydride (700 mg.) in ether (30 ml.) for 2 hr. Working up in the usual way afforded drim-8-ene-11,12-diol (VIII) (214 mg.). Twice crystallised from benzene this had m. p. 121—123° alone and mixed with material obtained from isodrimenin (identical infrared spectrum; KCl disc), $[\alpha]_D$ +119° (*c* 1·78 in C_6H_6).

Dihydroconfertifolin (XIII). Confertifolin (23 mg.) in acetic acid (5 ml.) was hydrogenated with Adams catalyst (22 mg.) at 20°/1 atm.; 1·18 mol. hydrogen were absorbed in 4 hr. Removal of catalyst and solvent furnished dihydroconfertifolin (XIII) (21 mg.), needles (from light petroleum), m. p. 134—135°, $[\alpha]_D$ ±0° (*c* 4·28 in $CHCl_3$) (Found: C, 76·4; H, 10·0. $C_{15}H_{24}O_2$ requires C, 76·25; H, 10·15%). When confertifolin was shaken with hydrogen and Adams catalyst in ethyl acetate there was no hydrogen uptake, and confertifolin was recovered.

Isodihydroconfertifolin (XIV). Dihydroconfertifolin (31 mg.) was kept in 5% methanolic potassium hydroxide for 48 hr. Dilution with aqueous hydrochloric acid and extraction into chloroform afforded *isodihydroconfertifolin* (XIV) (28 mg.), plates (from hexane), m. p. 121—123°, $[\alpha]_D$ −9° (*c* 1·1 in $CHCl_3$) (Found: C, 76·3; H, 9·9%).

Reduction of dihydroconfertifolin and isodihydroconfertifolin with lithium aluminium hydride. (i) 8β,9β-Drimane-11,12-diol (XV). Dihydroconfertifolin (63 mg.) in tetrahydrofuran (15 ml.) was refluxed with excess of lithium aluminium hydride for 2 hr. Working up in the usual way gave 8β,9β-drimane-11,12-diol (XV) (42 mg.) which, crystallised from hexane and sublimed at 120°/0·1 mm., had m. p. 151—153° alone or mixed with the diol obtained from drimenin (see above) (identical infrared spectrum; KCl disc), $[\alpha]_D$ +24° (*c* 1·04 in $CHCl_3$).

(ii) 8α,9β-Drimane-11,12-diol (XVI.) Isodihydroconfertifolin (23 mg.) was reduced as in (i), and the product (18 mg.) chromatographed over alumina (750 mg.; activity V). Elution with benzene afforded 8α,9β-*drimane*-11,12-*diol* (XVI) (14 mg.), prisms (from hexane), m. p. 102—103°, $[\alpha]_D$ +26° (*c* 3·1 in $CHCl_3$) (Found: C, 74·75; H, 11·5. $C_{15}H_{26}O_2$ requires C, 74·95; H, 11·75%).

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