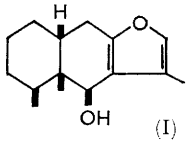
Studies on Sesquiterpenoids. Part XIII.[1] Components of the Root of *Ligularia Fischeri* Turcz.*

By Hiroshi Ishii, Takehiko Tozyo, and Hitoshi Minato

A new sesquiterpenic compound from the root of *Ligularia Fischeri* Turcz. has been named eremoligenol and identified as $\Delta^{1(10)}$eremophilen-11-ol. Petasalbine, furanoeremophilane, ligularone, and 6β-hydroxyeremophilenolide were also isolated.

We have previously reported[2] the isolation of ligularol (I, 1·2% yield †) from the root of *Ligularia Fischeri* Turcz.* ("Otakarako" in Japanese) and the characterisation of ligularol as furanoeremophilan-6β-ol (I), *i.e.*, petasalbine.[3] We now describe the isolation of four other sesquiterpenic components of eremophilane type. One of these is a new sesquiterpenoid, for which we propose the name eremoligenol and the structure $\Delta^{1(10)}$-eremophilen-11-ol (II, 0·44% yield †). The other three were identified with furanoeremophilane[4] (III, 0·04% yield †), ligularone[2] (IV, 0·05% yield †), and 6β-hydroxyeremophilenolide[3] (V, 0·01% yield †) by comparison with authentic specimens.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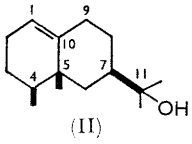
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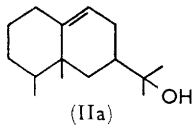
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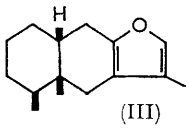
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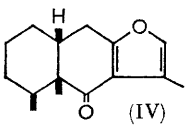
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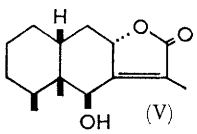
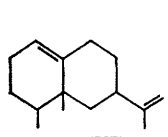

(V)

As described previously,[2] light petroleum extract of the root of the plant was fractionated by distillation into three portions (oil A, oil B, and distillation residue). Oil A was chromatographed on alumina and, from the first eluate, there was obtained a colourless oil, $C_{15}H_{22}O$, $[\alpha]_D$ −2·7°, which gave a positive Ehrlich test. Its infrared (i.r.) spectrum exhibited bands at 1650 and 1567 cm.$^{-1}$ due to a furan ring. Identity of the i.r. spectrum and optical activity of the oil with those of the known furanoeremophilane[4] establishes the structure (III) for the oil.

The second eluate gave a mixture of petasalbine and eremoligenol, which was acetylated and again chromatographed to separate eremoligenol from petasalbine acetate. Structure proof of the latter has already been reported.[2]

Eremoligenol (II) is a colourless oil, $C_{15}H_{26}O$, $[\alpha]_D$ −93·5°, the i.r. spectrum of which shows a band at 3400 cm.$^{-1}$ (hydroxyl group), a band at 1672 cm.$^{-1}$ (double bond), and bands at 1382 and 1372 cm.$^{-1}$ (*gem*-dimethyl group). The hydroxyl group in eremoligenol is tertiary, since it resisted acetylation and chromium trioxide oxidation.

The n.m.r. spectrum of eremoligenol has a singlet at τ 9·09 (3H) due to an angular methyl group, and a doublet at τ 9·13 (3H, J = 6 c./sec.) due to a secondary methyl group. A singlet at τ 8·88 (6H) is considered to belong to the *gem*-dimethyl group present in the form of a $-C(CH_3)_2OH$ grouping. A multiplet centred at τ 4·69 (1H) indicates the $>C{=}CH-$ grouping. Dehydration of eremoligenol with thionyl chloride in pyridine afforded an unsaturated hydrocarbon (VI), the i.r. spectrum of which revealed absorptions at 3090, 1647, and 885 cm.$^{-1}$ characteristic for a terminal methylene group, and was lacking in the doublet around 1380 cm.$^{-1}$ due to the *gem*-dimethyl group, showing that the methylene group in compound (VI) is a part of the isopropenyl grouping. These facts corroborate the presence of the $-C(CH_3)_2OH$ group in eremoligenol.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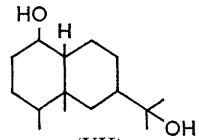
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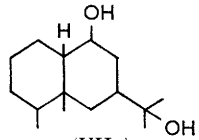
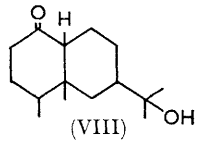

(VIIa)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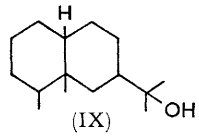
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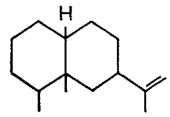
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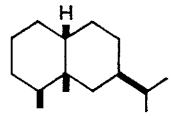

(XI)

The carbon skeleton of eremoligenol is established by the following reaction sequence: Hydroboration–oxidation of eremoligenol yielded a diol (VII), $C_{15}H_{28}O_2$, m. p. 149—151°, $[\alpha]_D$ +31·6°, which was oxidised with chromium trioxide in acetone[5] to give a ketol (VIII), $C_{15}H_{26}O_2$, m. p. 97°, $[\alpha]_D$ −76·2°. Huang-Minlon reduction of the ketol (VIII) provided an oily alcohol (IX), $C_{15}H_{28}O$, $[\alpha]_D$ +24·3°, which was dehydrated with thionyl chloride in pyridine to yield an unsaturated hydrocarbon (X). Catalytic hydrogenation of compound

* In ref. 2 we assigned an incorrect botanical name, *Liguralia siberica* Cass., for the plant. We are grateful to Professor T. Takahashi, University of Tokyo, for his correction of the name.

† Yields were calculated on the basis of the weight of dried root taken.

[1] Part XII, K. Takeda, H. Minato, and M. Ishikawa, *Tetrahedron*, in the press.

[2] H. Ishii, T. Tozyo, and H. Minato, *Tetrahedron*, 1965, **21**, 2605.

[3] L. Novotný, V. Herout, and F. Šorm, *Coll. Czech. Chem. Comm.*, 1964, **29**, 2189.

[4] M. Horák, O. Motl, J. Plíva, and F. Šorm, "Terpenspektren II," Akademie Verlag, Berlin, 1963.

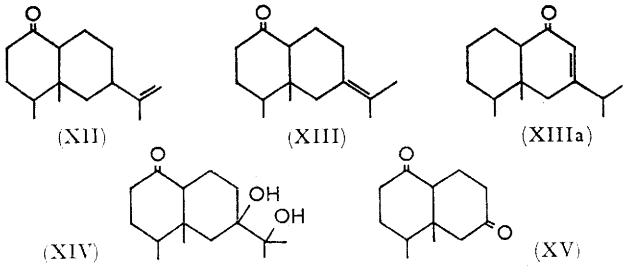
[5] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.

(X) followed by purification by means of gas chromatography produced the saturated liquid hydrocarbon (XI), $C_{15}H_{28}$, $[\alpha]_D$ +19·3°, the i.r. spectrum and optical activity of which were identical with those of 7β-eremophilane,[6] recently prepared by Šorm * from hydroxydihydroeremophilone of known absolute configuration.[7,8] There remains only the question of the position of the trisubstituted double bond.

The ultraviolet (u.v.) spectrum of the dehydrated product (VI) showed no absorption ascribable to a conjugated diene system, which indicate that the double bond in eremoligenol is not present at C-6(7) or C-7(8), but at C-1(10) or C-9(10). That is, alternative structures (II) and (IIa) follow for eremoligenol.

Since the diol (VII) was regenerated on reduction of the ketol (VIII) with lithium aluminium hydride, and since the ketol (VIII) was recovered unchanged on heating it in alkaline solution, it is clear that β-configuration of the hydrogen at C-10 has been retained in the course of transformations from the diol (VII) to 7β-eremophilane (XI). It is well known, on the other hand, that hydroboration involves *cis*-addition,[9] so that the new hydroxyl group introduced into the diol should be also β-oriented. Consequently the diol must be either eremophilan-1β,11-diol (VII) or eremophilan-9β,11-diol (VIIa).

It is unlikely that compounds (VII) and (VIIa) would exist in the non-steroid conformation,[10,11] since the bulky $-C(CH_3)_2OH$ group at C-7 would possess a 1,3-diaxial interrelation with the angular methyl group at C-5. In the preferred steroid conformation, the 1β-hydroxyl group in (VII) is axial whereas the 9β-hydroxyl group in (VIIa) is equatorial. In the n.m.r. spectrum, the angular methyl signal of the diol at τ 8·95 appears in a lower field than usual, and acetylation of the diol leads to upward shift of the signal (τ 9·04), indicating that there is a 1,3-diaxial relationship between the hydroxyl group and the angular methyl group in the diol.[12] This fact confirms the structure (VII) for the diol.



(XII) (XIII) (XIIIa)

(XIV) (XV)

Furthermore the following experimental results exclude the structure (VIIa). (*a*) Dehydration of the ketol (VIII) with phosphorus oxychloride in pyridine gave a mixture of unsaturated ketones (XII and XIII). When the mixture was treated with acid or alkali, its u.v. spectrum did not show any absorption around 240 mμ characteristic for the Δ^7-9-one system (XIIIa). (*b*) The mixture of ketones (XII) and (XIII) was chromatographed after treatment with sulphuric acid to give the unsaturated ketone (XIII). The latter was oxidised with osmium tetroxide to furnish a dihydroxyketone (XIV), which was further oxidised with sodium periodate to yield a diketone (XV), $C_{12}H_{18}O_2$, m. p. 99—100°. The u.v. spectrum of compound (XV) does not exhibit any absorption due to β-diketone grouping, excluding the presence of the carbonyl group at C-9 in the ketol (VIII).

The establishment of the location at C-1 of the newly introduced hydroxyl group in the diol (VII) results in the proof of the structure $\Delta^{1(10)}$-eremophilen-11-ol (II) for eremoligenol.

Eremoligenol has been a hypothetical compound suggested by Zalkow *et al.*[13] to be a key intermediate having a migrated methyl group in a biogenetic pathway from β-eudesmol to eremophilone. Occurrence of the compound in this plant supports their suggestion.

Oil B was treated as described previously.[2] The first eluate from the chromatography of mother-liquor of petasalbine yielded a colourless crystalline substance, $C_{15}H_{20}O_2$, m. p. 65°, which was identical with ligularone (IV) [2] obtained from the aerial part of this plant. The second eluate afforded a mixture consisting of petasalbine (I) and eremoligenol (II). The mixture was divided into each component in the manner described for oil A.

The light petroleum-insoluble portion of the original ether extract [2] provided on alumina chromatography a compound (V) of molecular formula $C_{15}H_{22}O_3$ as colourless prisms, m. p. 208°, $[\alpha]_D$ +205·8°. This compound exhibits i.r. absorptions at 1750 and 1692 $cm.^{-1}$ typical of α,β-unsaturated γ-lactone, and the u.v. maximum at 218·5 mμ (ε 13,700) is comparable to such a chromophore. This lactone was also obtained when petasalbine (I) was oxidised with monoperphthalic acid,[14] although yield was very low. Physical constants of the lactone are in excellent agreement with those of 6β-hydroxyeremophilenolide.[3,15] From these facts, the structure (V) is assigned for the lactone.

EXPERIMENTAL

Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Rotations were taken in

* According to a private communication to Dr. K. Takeda, Director of this Laboratory, Professor F. Šorm has obtained a sample of 7β-eremophilane of $[\alpha]_D$ +16·8°. Comparison with our sample was carried out by Professor Šorm, to whom we express our deep gratitude.

[6] J. Hochmanová, L. Novotný, and V. Herout, *Coll. Czech. Chem. Comm.*, 1962, **27**, 1870.

[7] D. F. Grant and D. Rogers, *Chem. and Ind.*, 1956, 278.

[8] L. H. Zalkow, F. X. Markley, and C. Djerassi, *J. Amer. Chem. Soc.*, 1959, **81**, 2914.

[9] H. C. Brown, *Tetrahedron*, 1961, **12**, 117.

[10] C. Djerasssi, R. Mauli, and L. H. Zalkow, *J. Amer. Chem. Soc.*, 1959, **81**, 3424.

[11] L. H. Zalkow, A. M. Shaligram, Shih-En Hu, and C. Djerassi, *Tetrahedron*, 1966, **22**, 337.

[12] Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. and Pharm. Bull.* (*Japan*), 1962, **10**, 338.

[13] L. H. Zalkow, F. X. Markley, and C. Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 6354.

[14] K. Takeda, H. Minato, M. Ishikawa, and M. Miyawaki, *Tetrahedron*, 1964, **20**, 2655.

[15] L. Novotný and V. Herout, *Coll. Czech. Chem. Comm.*, 1955, **30**, 3579.

chloroform. Ultraviolet spectra were determined in 95% ethanol unless otherwise noted. N.m.r. spectra were recorded on a Varian A-60 spectrometer in deuteriochloroform.

Isolation of Petasalbine (I), *Eremoligenol* (II), *and Furanoeremophilane* (III).—Oil A[2] of b. p. 92—127°/1·5 mm. (6·6 g.) was chromatographed on 200 g. of neutral alumina (Merck, activity III). From the second eluate with light petroleum there was obtained a pale yellow oil (880 mg.) which showed a positive Ehrlich test. This oil was rechromatographed on neutral alumina to give pure furanoeremophilane (III) as a colourless oil, b. p. 85°/1 mm. (510 mg.), $[\alpha]_D^{24}$ −2·7° (±2°) (*c* 0·861), $\nu_{max.}$ (film) 1650 and 1567 cm.$^{-1}$. The n.m.r. spectrum showed absorptions centred at τ 9·10 (3H, singlet), 9·04 (3H, doublet, J = 7 c./sec.), 8·09 (3H, doublet, J = 1·1 c./sec.) and 2·92 (1H, quartet, J = 1·1 c./sec.) (Found: C, 82·4; H, 10·3. $C_{15}H_{22}O$ requires: C, 82·5; H, 10·15%).

Elution with light petroleum–ether (4 : 1) yielded a mixture (3·82 g.) of petasalbine (I) and eremoligenol (II). The mixture was acetylated with acetic anhydride (4 ml.) and pyridine (5 ml.) in the usual manner. The reaction product (4·18 g.) was chromatographed on 100 g. of acid alumina (Merck, activity IV). Elution with light petroleum afforded a crystalline substance (1·80 g.) which was recrystallised from light petroleum to furnish petasalbine acetate as colourless prisms, m. p. 83—84°. The i.r. spectrum of the acetate in carbon tetrachloride solution was identical with that of an authentic sample of m. p. 54—55°.[2] Subsequent elution with light petroleum–ether (1 : 1) gave a pale yellow oil (2·23 g.), which was distilled to produce *eremoligenol* (II) as a colourless oil, b. p. 120°/2 mm., $[\alpha]_D^{23}$ −93·5° (±3°) (*c* 0·675). The i.r. and n.m.r. absorptions are given above (Found: C, 81·05, H, 11·75. $C_{15}H_{26}O$ requires: C, 81·0; H, 11·8%).

Dehydration of Eremoligenol (II).—Thionyl chloride (0·3 ml.) was added to a cooled solution of compound (II) (500 mg.) in pyridine (2 ml.) and left for 1 hr. at room temperature. The mixture was poured into ice–water and the ether extract was washed with 2N-sulphuric acid and 2N-sodium carbonate, dried (Na_2SO_4), and evaporated, leaving a yellow oil (402 mg.). This was purified by chromatography on 25 g. of silica gel (Merck, Kieselgel 0·2—0·5 mm.) to yield an *unsaturated hydrocarbon* (VI) as a colourless oil, b. p. 79—81°/1 mm., $\nu_{max.}$ (film) 3090, 1647, and 885 cm.$^{-1}$. The u.v. spectrum showed no absorption in the region 215—250 mμ (Found: C, 88·25; H, 11·75. $C_{15}H_{26}$ requires: C, 88·15; H, 11·85%).

Hydroboration of Eremoligenol (II).—A solution of diborane (0·14 g.) in dry tetrahydrofuran (4 ml.) was added dropwise to a cooled solution of compound (II) (355 mg.) in dry tetrahydrofuran (5 ml.). The mixture was set aside under nitrogen overnight at room temperature. Excess of diborane was decomposed by adding small pieces of ice. To this solution, 3N-sodium hydroxide (3 ml.) was added, followed by 30% hydrogen peroxide (3 ml.). After 2 hr. at room temperature, the mixture was extracted with chloroform. The extract was washed, dried (Na_2SO_4), and evaporated to give a crystalline product (356 mg.), which was recrystallised from ether–light petroleum to afford a *diol* (VII) as colourless plates, m. p. 149—151°, $[\alpha]_D^{25.5}$ +31·6° (±3°) (*c* 0·608), $\nu_{max.}$ (in $CHCl_3$) 3610 and 3450 cm.$^{-1}$. The n.m.r. spectrum showed absorptions centred at τ 9·22 (3H, doublet, J = 6 c./sec.), 8·95 (3H, singlet), 8·85 (6H, singlet) and 6·23 (1H, multiplet) (Found: C, 74·9; H, 11·85. $C_{15}H_{28}O_2$ requires: C, 74·9; H, 11·75%).

Acetylation of the Diol (VII).—The diol (VII) (23 mg.) was acetylated with acetic anhydride (0·4 ml.) and pyridine (0·5 ml.) overnight at room temperature. The mixture was treated in the usual manner to give a pale yellow oil (28 mg.) which was purified by chromatography, giving an *acetate* as a colourless oil, $\nu_{max.}$ (film) 3480, 1752, and 1252 cm.$^{-1}$. The n.m.r. spectrum showed absorptions centred at τ 9·20 (3H, doublet, J = 6 c./sec.), 9·04 (3H, singlet), 8·86 (6H, singlet), 7·98 (3H, singlet) and 5·23 (1H, multiplet).

Oxidation of the Diol (VII) *with Chromium Trioxide*.—Jones reagent[5] (0·5 ml.) was added dropwise to a cooled solution of compound (VII) (360 mg.) in acetone (4 ml.). After a period of 5 min., water was added and the mixture was extracted with chloroform. The extract was washed, dried (Na_2SO_4), and evaporated to yield an oil (362 mg.), which was chromatographed on 12 g. of neutral alumina (Merck, activity III). Elution with light petroleum–ether (4 : 1) afforded a crystalline product (343 mg.) which was recrystallised from ether–light petroleum to give a *ketol* (VIII) as colourless prisms (214 mg.), m. p. 97°, $[\alpha]_D^{24}$ −76·2° (±2°) (*c* 1·021); $\nu_{max.}$ (in $CHCl_3$) 3625, 3470, and 1695 cm.$^{-1}$; o.r.d. $[\alpha]_{700}$ −56°, $[\alpha]_{317}$ (trough) −2178°, $[\alpha]_{273}$ (peak) +2014°, $[\alpha]_{250}$ +1371° (*c* 1·021 in $CHCl_3$; t = 25°). The n.m.r. spectrum showed absorptions centred at τ 9·21 (3H, singlet), 9·12 (3H, doublet, J = 6·5 c./sec.) and 8·83 (6H, singlet) (Found: C, 75·8; H, 11·2. $C_{15}H_{26}O_2$ requires: C, 75·6; H, 11·0%).

Treatment of the Ketol (VIII) *with Potassium Hydroxide*.—The ketol (VIII) (30 mg.) was dissolved in 5% methanolic potassium hydroxide solution (2 ml.) and heated under reflux for 1 hr. Water was added to the mixture, which was extracted with ether. The extract was washed, dried (Na_2SO_4), and evaporated, leaving a colourless oil (27 mg.), which was crystallised from ether–light petroleum to recover the starting material (VIII) as colourless prisms, m. p. 97°.

Reduction of the Ketol (VIII) *with Lithium Aluminium Hydride*.—A solution of the ketol (VIII) (98 mg.) in dry ether (10 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (30 mg.) in dry ether (10 ml.) and stirred for a further 30 min. at room temperature. The mixture was decomposed by addition of ice–water and extracted with ether. The extract gave, after removal of the solvent, a crystalline residue (97 mg.), which was purified by chromatography to yield the diol (VII) as colourless plates, m. p. 149—151° (from ether–light petroleum, 63 mg.). This was identical with the hydroboration product of (II) (mixed m. p. and i.r. spectrum).

Huang-Minlon Reduction of the Ketol (VIII).—A mixture of the ketol (VIII) (407 mg.), hydrazine hydrate (80%, 5·4 ml.), triethylene glycol (15 ml.), and potassium hydroxide (1·8 g.) was heated at 125—130° (internal temperature) for 1 hr., the temperature was gradually raised, and heating continued at 195—205° for 2 hr. Water was added to the mixture, which was extracted with ether; the extract was washed, dried (Na_2SO_4), and evaporated, leaving a pale yellow oil (330 mg.). This oil was purified by chromatography to give an *alcohol* (IX) as a colourless oil (315 mg.), b. p. 125°/3 mm. (bath temperature), $[\alpha]_D^{24.5}$ +24·3° (±2°) (*c* 0·859), $\nu_{max.}$ (film) 3400 cm.$^{-1}$. The n.m.r. spectrum showed absorptions centred at τ 9·25 (3H, doublet, J = 6·5 c./sec.), 9·13 (3H, singlet) and 8·84 (6H, singlet) (Found: C, 80·0; H, 12·35. $C_{15}H_{28}O$ requires: C, 80·3; H, 12·6%).

Dehydration of the Alcohol (IX). Phosphorus oxychloride (1 ml.) was added dropwise to a cooled solution of

compound (IX) (265 mg.) in pyridine (5 ml.) and the mixture was left to stand overnight at room temperature. The solution was poured into ice–water and extracted with ether. The extract was washed with 2N-sulphuric acid and 2N-sodium carbonate, dried (Na_2SO_4), and evaporated to afford an *unsaturated hydrocarbon* (X) as a pale yellow oil (217 mg.), $\nu_{max.}$ (film) 3100, 1645 and 880 cm.$^{-1}$.

7β-*Eremophilane* (XI).—A mixture of 10% palladium–charcoal (30 mg.) and compound (X) (217 mg.) in ethanol (30 ml.) was reduced catalytically at room temperature. When 29·2 ml. (1·15 mole) of hydrogen had been absorbed, uptake of hydrogen stopped. Removal of the catalyst and solvent gave an oil (185 mg.), which was purified by gas chromatography. The preparative gas chromatography was run on a 10 ft. × ⅜ in. o.d. column consisting of Carbowax 20 M (25% on Chromosorb W, 45—60 mesh) at 180° with a flow of rate of 150 ml./min. of helium using an Aerograph Autoprep model A-700 instrument. The fraction which showed a peak at retention time 23·5 min. yielded 7β-eremophilane (XI) as a colourless oil, b. p. 80°/2 mm. (bath temperature), $[\alpha]_D^{24}$ +19·3° (±2°) (*c* 1·023) (Found: C, 86·35; H, 13·4. $C_{15}H_{28}$ requires: C, 86·45; H, 13·55%).

Dehydration of the Ketol (VIII).—Phosphorus oxychloride (0·5 ml.) was added dropwise to a cooled solution of compound (VIII) (299 mg.) in pyridine (3 ml.), and the mixture was left overnight at room temperature. The solution was poured into ice–water and extracted with chloroform. The extract was washed with 2N-sulphuric acid and 2N-sodium carbonate, dried (Na_2SO_4), and evaporated to give a mixture of compounds (XII) and (XIII) as a yellow oil (263 mg.), $\nu_{max.}$ (film) 3090, 1650 and 885 (C=CH_2), and 1708 cm.$^{-1}$ (C=O). The oil was unchanged (i.r. spectrum) after heating under reflux in a nitrogen atmosphere for 1 hr. with 5% methanolic potassium hydroxide solution (10 ml.).

The resulting oil (255 mg.) was heated under reflux for 1 hr. with 5% methanolic sulphuric acid solution (10 ml.). The solution was treated in the usual manner to produce a yellow oil (250 mg.), $\nu_{max.}$ (film) 1708 cm.$^{-1}$. The u.v. spectrum showed no absorption in the region 215—250 mμ. This oil (250 mg.) was chromatographed on neutral alumina (Merck, activity III). Elution with light petroleum afforded an *unsaturated ketone* (XIII) as a colourless oil (94 mg.), $\nu_{max.}$ (film) 1710 cm.$^{-1}$.

Oxidation of the Unsaturated Ketone (XIII) *with Osmium Tetroxide*.—A solution of osmium tetroxide (120 mg.) in dry benzene (2 ml.) was added to a solution of the ketone (XIII) (94 mg.) in dry benzene (5 ml.) and dry pyridine (0·5 ml.) in an ice-bath, and the mixture was left at room temperature for 6 days. Benzene was evaporated and the residue was dissolved in ethanol (10 ml.). The solution was added to a solution of sodium sulphite (1 g.) in water (10 ml.) and the mixture was heated under reflux for 2 hr. The brown precipitate was removed by filtration and the filtrate was extracted with chloroform. The extract was washed, dried (Na_2SO_4), and evaporated to give a pale yellow oil (109 mg.). This oil was chromatographed on 3 g. of neutral alumina (Merck, activity IV). Elution with light petroleum–ether (1 : 1) furnished a *dihydroxy-ketone* (XIV) as a colourless viscous oil (66 mg.), $\nu_{max.}$ (film) 3400—3600 (broad) and 1700 cm.$^{-1}$.

Oxidation of the Dihydroxy-ketone (XIV) *with Sodium Periodate*.—To a solution of compound (XIV) (66 mg.) in methanol (2 ml.) was added a solution of sodium periodate (80 mg.) in water (2 ml.), and the mixture was left at room temperature for 3 days. Water was added to the mixture, which was extracted with ether. The ether extract was washed, dried (Na_2SO_4), and evaporated to afford a colourless oil (47 mg.). This oil was purified by chromatography to give a *diketone* (XV) as colourless needles (32 mg.), m. p. 99—100° (from ether–light petroleum), $\nu_{max.}$ (Nujol) 1695—1715 cm.$^{-1}$ (broad). The u.v. spectrum of the diketone in methanol (2·115 mg. in 5 ml.) showed a maximum at 288 mμ (ε 50), which was unchanged when 1 drop of 0·1N-sodium hydroxide was added to the solution (Found: C, 74·3; H, 9·65. $C_{12}H_{18}O_2$ requires: C, 74·2; H, 9·35%).

Isolation of Ligularone (IV).—Oil B[2] of b. p. 127—139°/1·5 mm. (6·14 g.) was dissolved in light petroleum (10 ml.) and left in a refrigerator overnight to yield petasalbine (I) as colourless prisms, m. p. 80—81° (1·24 g.). The mother-liquor (4·9 g.) was chromatographed on 150 g. of neutral alumina (Merck, activity III). From the tail eluate with light petroleum there was obtained a crystalline substance (343 mg.), which was recrystallised from light petroleum to furnish ligularone (IV) as colourless plates, m. p. 64—65°. This was identical with an authentic sample [2] (mixed m. p. and comparison of i.r. spectra).

Elution with light petroleum–ether (9 : 1) yielded a pale yellow oil (3·98 g.) which was crystallised from light petroleum to give petasalbine (I) as colourless plates, m. p. 80—81° (1·82 g.). The mother-liquor (2·15 g.) was divided in the same manner as described for oil A (*vide supra*) into petasalbine acetate (1·06 g.) and eremoligenol (II) (0·98 g.).

Isolation of 6β-*Hydroxyeremphilenolide* (V).—The neutral portion [2] (128 g.) of the ether extract (150 g.) of the dried root was extracted with light petroleum (1 l.) to give a reddish brown extract (114 g.) and a dark brown residue (13 g.) The residue (5·6 g.) was chromatographed on 60 g. of neutral alumina (Merck, activity III). Elution with ether yielded a brown viscous oil (1·09 g.), which was crystallised from ether to give an α,β-unsaturated lactone (V) as colourless prisms (148 mg.), m. p. 208°, $[\alpha]_D^{24}$ +205·8° (±2°) [15] (*c* 1·021), $\lambda_{max.}$ 218·5 mμ (ε 13,700); $\nu_{max.}$ (in $CHCl_3$) 3604, 3455, 1750, and 1692 cm.$^{-1}$. The n.m.r. spectrum showed absorptions centred at τ 9·23 (3H, methyl signal split in nonresolved pattern by neighbouring CH group), 8·90 (3H, singlet), 8·19 (3H, doublet, J = 1·7 c./sec.), 7·46 (1H, doublet, J = 3 c./sec.; removable by exchange with D_2O), 5·35 (1H, doublet, J = 3 c./sec.; convertible to singlet by exchange with D_2O) and 4·93 (1H, multiplet) (Found: C, 72·05; H, 8·9. $C_{15}H_{22}O_3$ requires: C, 71·95; H, 8·85%).

Oxidation of Petasalbine (I) *with Monoperphthalic Acid*.—A solution of monoperphthalic acid (1·7 g.) in ether (20 ml.) was added to a solution of petasalbine (I) (1·99 g.) in chloroform (50 ml.) in an ice-bath, and the mixture was left overnight at 0°. The solution was washed with 2N-potassium iodide and 2N-sodium thiosulphate, dried (Na_2SO_4), and evaporated, leaving a yellow oil (2·25 g.). This oil was chromatographed on 60 g. of neutral alumina (Merck, activity III). From the tail eluate with light petroleum–ether (1 : 1), there was obtained a crystalline substance (200 mg.), which was recrystallised from ether to give 6β-hydroxyeremophilenolide (V) as colourless prisms, m. p. 208°. This was identical with the naturally occurring lactone (mixed m. p. and comparison of i.r. spectra).

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