448. *The Oxidation of 4-Methylthymol, Ferruginol, and Totarol.*

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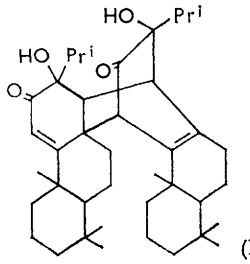
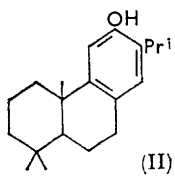
Periodate oxidation of 4-methylthymol yields the dimer of the corresponding *o*-hydroxycyclohexadienone, the pyrolytic decomposition of which gives propene and two pyrocatechols. One of the pyrocatechols is formed by migration of the isopropyl group, as is observed in the case of maytenone. Attempts to synthesise maytenone from ferruginol have been unsuccessful but among the oxidation products identified are derivatives of the corresponding *o*- and *p*-quinols and 7-oxoferruginol. Ferricyanide oxidation of totarol gives podototarin, 12,12-bitotarol, which has been isolated recently from natural sources.

Maytenone (I) has been isolated [1] from the outer root bark of *Maytenus dispermus*. It was presumed that it was formed biogenetically from the phenolic diterpene, ferruginol (II), by oxidation to the *o*-hydroxycyclohexadienone (III), which then underwent dimerisation of the Diels–Alder type involving the diene system of one molecule and the $\gamma\delta$-double

[1] Johnson, King, and Martin, *J.*, 1961, 4420.

bond of the unsaturated carbonyl system of the second molecule. Reactions of this type with simpler phenols, *e.g.*, 2,4- and 2,6-dimethyl- and 2,4,6-trimethylphenol, have been recorded.[2]


(I)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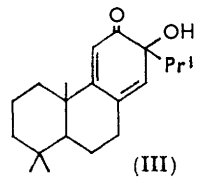
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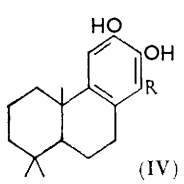
Of the reactions of maytenone, one of the most interesting is the pyrolytic decomposition which is apparently not acid-catalysed. The products are pure propene and a mixture of a C_{20} pyrocatechol derivative (IV; R = Pr^i) and a C_{17} pyrocatechol derivative (IV; R = H), both of which have been synthesised.[3,4] The formation of 6-hydroxytotarol (IV; R = Pr^i) involves a migration of the isopropyl group which is an unusual feature of a pyrolysis. In order to provide a simpler example of this type of rearrangement we have subjected 2-isopropyl-4,5-dimethylphenol[5] (4-methylthymol) to a similar series of reactions. Oxidation of 4-methylthymol with sodium periodate gave the colourless, crystalline dimer (V) of the corresponding *o*-hydroxycyclohexadienone, the infrared spectrum of which showed many resemblances to that of maytenone. The dimer decomposed just above its m. p. with evolution of an inflammable gas which was shown by vapour-phase chromatography to be mainly propene[6] but contaminated with traces (<1%) of methane, ethane, and possibly ethylene. The amount of gas evolved was only 0·21 mol. of propene by volume (cf. maytenone, 78%). The residue left after the pyrolysis was phenolic and gave a green ferric reaction. Benzoylation of the residue gave a single crystalline benzoate, $C_{25}H_{24}O_4$, corresponding to a pyrocatechol derivative $C_{11}H_{16}O_2$. However, examination of the crude pyrolysis product by paper chromatography showed that two pyrocatechol derivatives were present and direct comparison showed that they were 4,5-dimethyl- (VI; R = H) and 3-isopropyl-4,5-dimethyl-pyrocatechol (VI; R = Pr^i).

The dibenzoate of the latter pyrocatechol (VI; R = Pr^i) was synthesised for comparison from 2,3-dimethoxy-5,6-dimethylbenzoic acid[7] (CO_2H ⟶ CO_2Me ⟶ $CMe{=}CH_2$ ⟶ $CHMe_2$). The isopropylveratrole so obtained was demethylated with pyridine hydrochloride, and the phenol was converted into its dibenzoate which proved to be identical with that obtained from the pyrolysis product. Direct Friedel–Crafts isopropylation of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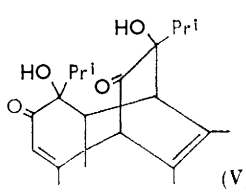
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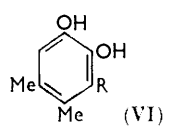
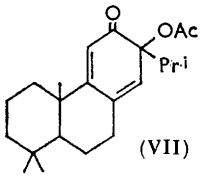

(VI)

4,5-dimethylveratrole was unsuccessful, probably for steric reasons. The pyrolysis of the dimer (V) thus proceeds in a manner qualitatively similar to the pyrolysis of maytenone.

[2] (*a*) Adler, Weston, *et al.*, *Acta Chem. Scand.*, 1960, **14**, 1261, 1580; (*b*) Kende and McGregor, *J. Amer. Chem. Soc.*, 1961, **83**, 4197.
[3] Elmore and King, *J.*, 1961, 4425.
[4] Hill, Johnson, and King, *J.*, 1961, 4430.
[5] Clemmensen, *Ber.*, 1914, **47**, 51.
[6] Falshaw, Johnson, and King, *Proc. Chem. Soc.*, 1961, 265.
[7] Bruce and Sutcliffe, *J.*, 1956, 3824.

Quantitatively, however, the reactions differ in that the two pyrocatechols and propene are produced in roughly equimolecular proportions from maytenone whereas, in the case of the dimer (V), the aromatisation involving rearrangement occurs to a greater extent than the aromatisation involving elimination.[8] It is possible that maytenone may decompose by an overall concerted mechanism, whereas in the case of (V), the initial step is a reversed Diels–Alder reaction leading to the *o*-hydroxycyclohexadienone, which then rearranges to the pyrocatechols in the manner observed.

Attempts have been made to synthesise maytenone (I) from ferruginol (II) by direct oxidation of the type described above, but so far these have not been successful. Oxidation of ferruginol with sodium periodate in 80% acetic acid gave a gum which was purified by chromatography and yielded two crystalline products. The first of these was identified as the acetate (VII) [$\varepsilon_{max.}$ 2950 at 319 mμ; $\nu_{max.}$ 1670 cm.$^{-1}$ (conjugated C=O)]. The second oxidation product was 7-oxoferruginol (VIII), identified by direct comparison with an authentic specimen.[9] The formation of this compound is the first example of benzylic oxidation by periodate; a similar oxidation in aqueous ethanol also gave some of the 7-oxo-compound.



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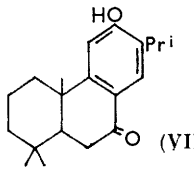

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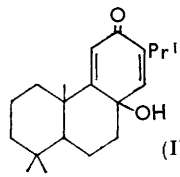


(IX)

Oxidation of ferruginol with periodate in the presence of dilute sulphuric acid gave another oxidation product, $C_{20}H_{30}O_2$, in very low yield. The spectral properties of this compound, $\varepsilon_{max.}$ 14,100 at 242 mμ; $\nu_{max.}$ 3610 (OH), 1660 (αβ-unsaturated C=O), and 1640 cm.$^{-1}$ (olefinic C=C), suggested that it had structure (IX). The action of lead tetra-acetate gave a low yield of the yellow acetate (VII), identical with the product obtained as above from a periodate oxidation. However, attempts to dimerise this substance have so far failed. Likewise, hydrolyses of the acetate under conditions which convert analogous simpler acetates into dimers, have not given maytenone. It is clear that steric effects of the tricyclic ferruginol system have a profound influence on the course of the dimerisation.

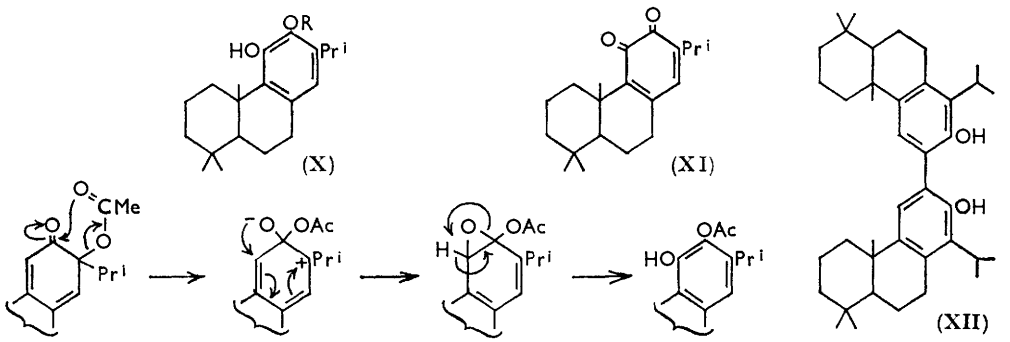
When the acetate (VII), which should form a diacetate of maytenone by Diels–Alder self-addition, was heated just above its melting point for 20 min., another product was obtained which proved to be the 12-monoacetate (X; R = Ac). The ultraviolet spectrum of this compound ($\varepsilon_{max.}$ 4900 at 271 mμ) suggested that the product was phenolic and this was supported by the green ferric reaction. A positive Gibbs test indicated a free phenolic *para*-position and thus a migration of oxygen to the 11-position had occurred (if we assume a more deep-seated skeletal rearrangement to be less likely). Infrared bands at 3600 and 1760 cm.$^{-1}$ were attributed to the phenolic group and the phenolic acetate-carbonyl, respectively. Alkaline hydrolysis of the acetate gave the pyrocatechol derivative (X; R = H) (identified as the dibenzoate), which yielded a deep red stable *o*-quinone (XI) on oxidation with silver oxide. The dibenzoate differed from 12-hydroxytotarol dibenzoate,[3] thus confirming that it was the oxygen and not the isopropyl group which had migrated. This type of rearrangement has been observed by Wessely[10] and its mechanism is probably as depicted.

Of the other oxidising agents tried with ferruginol, perchloryl fluoride[2b] in *NN*-dimethylformamide gave a product from which only 7-oxoferruginol could be isolated. No useful oxidation products were isolated from experiments with Caro's acid or from the

[8] Cf. Conradi and McLaren, *J. Amer. Chem. Soc.*, 1960, **82**, 4745.
[9] Bredenberg, *Acta Chem. Scand.*, 1957, **11**, 932.
[10] Zbiral, Wessely, and Lahrmann, *Monatsh.*, 1960, **92**, 331.

action of ceric ammonium sulphate on the product obtained from ferruginol, phosphorus oxychloride, and pyridine (cf. ref. 11).

Finally it is of interest that oxidation of totarol with alkaline potassium ferricyanide gave the bitotarol (XII) in 43% yield. This compound has recently been isolated [12] from



Podocarpus totara and was synthesised by Ullmann coupling of 12-bromototaryl methyl ether, followed by demethylation. It seems probable that our method of synthesis is related to the biogenetic route to podototarin, another bisditerpene formed by oxidation of the phenolic monomer.

Experimental

M. p. were determined on a Kofler block. Ultraviolet absorption spectra refer to ethanolic solutions and were measured either on the Unicam S.P. 700 or the Perkin-Elmer no. 197 spectrophotometer. Infrared spectra refer to carbon tetrachloride solutions except where otherwise stated. Light petroleum refers to the fraction of b. p. 60—80°.

3,5-*Dihydroxy*-3,5-*di-isopropyl*-8,9-*dimethyl*-1,4-(1,2-*dimethyletheno*)-Δ^7-*octalin*-2,6-*dione* (V).—2-Isopropyl-4,5-dimethylphenol (3·5 g., prepared from thymotinaldehyde [13] by Clemmensen reduction [5]) was dissolved in ethanol (200 c.c.) and added to a solution of sodium metaperiodate (9·15 g.) in water (600 c.c.). The mixture was stirred at room temperature for 24 hr., then extracted with chloroform (3 × 100 c.c.). The chloroform extract was washed and dried ($MgSO_4$), then evaporation gave an orange gum, chromatography of which on alumina and elution with ether–light petroleum gave a fraction which solidified. Crystallisation of this from light petroleum gave the *product* as colourless prisms (537 mg., 7·2%), m. p. 181—182° raised to 185—186° on sublimation at 130°/0·01 mm. [Found: C, 73·4; H, 8·95%; *M* (Rast), 173. $C_{22}H_{32}O_4$ requires C, 73·3; H, 8·95%; *M*, 360], $\lambda_{max.}$ 205 and 224 mμ (ε 8830 and 8310), $\nu_{max.}$ 3650, 3520 (OH), 1725 (saturated C=O), 1690 (αβ-unsaturated C=O), and 1640 cm.$^{-1}$ (C=C).

Pyrolysis of the Dimer (V).—(*a*) *Gaseous products.* The foregoing dimer (350 mg.) was pyrolysed at 10^{-4} mm. over a luminous Bunsen flame, and the gaseous product (31·25 c.c. at 130 mm.) was collected. Samples of the gas were mixed with nitrogen and chromatographed on a 20% solution of silver nitrate on a Celite column [14] at 23° with a flow rate of 1·4 l./hr. A major peak was observed (retention time, 19·4 min.) with 3 minor peaks (retention times, 13·4, 6·3, and 5·3 min.). Pure propene, obtained from maytenone by pyrolysis, had retention time of 19·9 min.

(*b*) *Liquid products.* (i) The dimer (53·2 mg.) was heated under nitrogen at 190°; there was a brisk evolution of gas which continued for 4 min. The resulting pale yellow liquid was cooled to −10° but it did not crystallise. Distillation from a bulb tube gave a colourless oil (31·6 mg.), b. p. 55—60° (bath-temp.)/0·01 mm., which was treated with benzoyl chloride (0·5 c.c.) and 10% aqueous sodium hydroxide (5 c.c.) to give the crude dibenzoate (70·3 mg.). Crystallisation from aqueous methanol gave colourless prisms, m. p. 148—149°, not depressed on admixture with 3-*isopropyl*-4,5-*dimethylcatechol dibenzoate* (see below) but depressed to

[11] Clark, Hutchinson, Kirby, and Todd, *J.*, 1961, 715.
[12] Cambie, Simpson, and Colebrook, *Chem. and Ind.*, 1962, 1757.
[13] Bell and Henry, *J.*, 1928, 2215.
[14] Bednas and Russell, *Canad. J. Chem.*, 1958, **36**, 1272.

120—125° on admixture with 4,5-dimethylcatechol dibenzoate, m. p. 108—110° [Found: C, 77·0; H, 5·95%; *M* (Rast), 394. $C_{25}H_{24}O_4$ requires C, 77·3; H, 6·2; *M*, 388]. The infrared spectrum was identical with that of 3-isopropyl-4,5-dimethylpyrocatechol dibenzoate.

(ii) The pyrolysis products were chromatographed on Whatman No. 1 paper with the upper layer of benzene–acetic acid–water (4 : 5 : 1) as the developing solvent. The chromatogram gave two spots, R_F 0·77 and 0·85, after treatment with diazotised *p*-nitroaniline, corresponding to 4,5-dimethyl- and 3-isopropyl-4,5-dimethyl-pyrocatechol, respectively, and identical in position with the spots obtained from standard compounds.

Methyl 2,3-Dimethoxy-5,6-dimethylbenzoate.—4,5-Dimethylveratrole [7] (30·4 g.) in dry ether (100 c.c.) was added during 1 hr., at 0° and in an atmosphere of nitrogen, to a solution of n-butyl-lithium [prepared [15] from lithium (8·6 g.) and butyl bromide (68·5 g.) in ether (250 c.c.)]. The solution was stirred at 0° for 1 hr. and at room temperature for a further 16 hr., then poured on solid carbon dioxide (*ca.* 400 g.). The mixture was allowed to warm to room temperature, then decomposed by addition of an excess of 10% aqueous hydrochloric acid. The ethereal layer was separated and washed with 10% aqueous sodium hydroxide (3 × 50 c.c.) and then water and dried. Evaporation gave unchanged 4,5-dimethylveratrole, m. p. and mixed m. p. 43° (1·5 g., 4·9%). The alkaline extract was acidified and the oil re-extracted into ether. The acidic product was extracted into aqueous sodium hydrogen carbonate solution and acidification of this extract with concentrated hydrochloric acid, followed by extraction into ether, gave the acid. The ethereal extract was washed and dried and after removal of the solvent the residual gum was dissolved in light petroleum (50 c.c.; b. p. 100—120°) and moisture removed in a Dean and Stark separator. On cooling of the light petroleum solution, the acid crystallised as colourless needles, m. p. 118—119° (lit.,[7] 120°) (8·5 g.; 22%). The corresponding *methyl ester* was prepared by the action of diazomethane and formed colourless stout rods, m. p. 69—70° (Found: C, 64·5; H, 7·3. $C_{12}H_{16}O_4$ requires C, 64·3; H, 7·2%).

Evaporation of the ethereal layer from the sodium hydrogen carbonate extraction gave 4,5-dimethylguaiacol (2·4 g., 7·8%), m. p. 67° (lit.,[7] 68·5°).

3-Isopropenyl-4,5-dimethylveratrole.—The foregoing ester (7 g., 1 mol.) in dry benzene (100 c.c.) was added to a stirred solution of methylmagnesium iodide (*ca.* 5 mol.) in benzene (300 c.c.). The solution was heated under reflux for 24 hr., then the complex was decomposed with saturated aqueous ammonium chloride (500 c.c.). The benzene layer was separated, washed with water, 10% sodium hydroxide solution (2 × 50 c.c.) (extract A, see below), and water (50 c.c.). The benzene layer was dried ($MgSO_4$), and the solvent removed to give a pale yellow oil which was heated under reflux with 20% sulphuric acid (40 c.c.) for 4 hr. and then cooled. The product was extracted with ether (3 × 20 c.c.), and the ethereal extract washed with aqueous sodium hydrogen carbonate and dried ($MgSO_4$). After evaporation of the solvent, the residual oil was chromatographed on alumina (70 g.) to give two fractions: (i) eluted with light petroleum and then distilled from a bulb-tube, to give *3-isopropenyl-4,5-dimethylveratrole* (1·2 g., 18%), b. p. 64—66° (bath-temp.)/0·04 mm. (Found: C, 76·0; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%), $\lambda_{max.}$ 286 mμ (ε 2180), $\nu_{max.}$ (liquid film) 1640 and 895 cm.$^{-1}$ (C=CH_2). Fraction (ii) was eluted with light petroleum–benzene (1 : 1) and then distilled, to give *2,3-dimethoxy-5,6-dimethylacetophenone* (1·7 g., 27%), b. p. 72—74°/0·02 mm. (Found: C, 68·8; H, 7·6. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%), $\lambda_{max.}$ 219 and 289 mμ (ε 13,300 and 2440), $\nu_{max.}$ (liquid film) 1690s cm.$^{-1}$ (aromatic C=O).

Solution A (above) was acidified and yielded a mixture of demethylated ketone and demethylated styrene. The product was re-methylated with dimethyl sulphate and aqueous sodium hydroxide; chromatography and distillation as above gave further quantities of the styrene (400 mg.) and the acetophenone (320 mg.).

3-Isopropyl-4,5-dimethylpyrocatechol Dibenzoate.—3-Isopropenyl-4,5-dimethylveratrole (600 mg.) in glacial acetic acid (20 c.c.) was hydrogenated in presence of Adams platinum catalyst (250 mg.) at room temperature. After uptake of 1 mol. (1 hr.) the catalyst was separated and the solvent evaporated, leaving a colourless oil, which was heated with pyridine hydrochloride (3 g.) at 180° during 4 hr. Water (20 c.c.) was added to the cooled product, and the solution extracted with ether (3 × 10 c.c.). The ethereal extract was washed with 10% hydrochloric acid (10 c.c.) and then extracted with aqueous sodium hydroxide (20 c.c.; 1 × 10 c.c., 1 × 5 c.c.). The alkaline extracts were shaken with benzoyl chloride (2·5 c.c.) at room temperature for 30 min., then the aqueous solution was decanted from the yellow gum which had separated.

[15] Gilman, Beel, Brannen, Bullock, Dunn, and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 1499.

Trituration of the gum with methanol gave the dibenzoate as a solid which was crystallised from methanol as prisms (210 mg.), m. p. 148—149° (cf. above) (Found: C, 77·6; H, 5·8. Calc. for $C_{25}H_{24}O_4$: C, 77·3; H, 6·2%).

Oxidations of Ferruginol.—7-*Acetoxy*-1,2,3,4,4a,6,7,9,10,10a-*decahydro*-7-*isopropyl*-1,1,4a-*trimethyl*-6-*oxophenanthrene* (VII). Ferruginol (3·2 g.) was intimately mixed with lead tetra-acetate (6·6 g.), and glacial acetic acid (10 c.c.) was added. When the mixture was stirred it became viscous, the temperature rose to 60°, and a deep red colour quickly developed. After 30 min. water (100 c.c.) was added and the precipitated red gum extracted in ether. The extract was washed free from acid with dilute aqueous sodium carbonate, dried ($MgSO_4$), and evaporated. The residue was chromatographed in light petroleum on alumina. Elution with light petroleum–benzene (1 : 1) gave a fraction which after concentration yielded the *acetate* (VII) (130 mg., 3·3%). Crystallisation from light petroleum gave pale yellow needles, m. p. 162—164° (Found: C, 77·1; H, 9·2. $C_{22}H_{32}O_3$ requires C, 76·7; H, 9·4%), $\lambda_{max.}$ 319 mμ (ε 295), $\nu_{max.}$ 1740 (acetate C=O) and 1670 (conjugated ketonic C=O) cm.$^{-1}$.

11-*Hydroxyferruginol* 12-*Monoacetate* (3-*Acetoxy*-4b,5,6,7,8,8a,9,10-*octahydro*-2-*isopropyl*-4b,8,8-*trimethyl*-4-*phenanthrol*) (X; R = Ac) *and* 11,12-*Dibenzoate.*—The acetate (VII) was heated at 170° in an atmosphere of nitrogen. The melt quickly became yellow and after 20 min. the product was cooled and dissolved in light petroleum (10 c.c.). 11-*Hydroxyferruginol* 12-*monoacetate* separated at −10° as colourless needles (130 mg.), m. p. 175—180°, raised to 182—184° on crystallisation from light petroleum (Found: C, 76·9; H, 9·15. $C_{22}H_{32}O_3$ requires C, 76·7; H, 9·4%), $\lambda_{max.}$ 271 mμ (ε 4900), $\nu_{max.}$ 3600 (OH) and 1760 (acetate C=O) cm.$^{-1}$, giving a green ferric reaction and a deep blue colour with Gibbs's reagent.

The monoacetate (140 mg.) was dissolved in methanol (4 c.c.), and a solution of sodium hydroxide (250 mg.) in water (5 c.c.) added. The mixture was heated under reflux in an atmosphere of nitrogen on the steam-bath for 1 hr. The solvent was then removed *in vacuo*. To the residue dissolved in 10% aqueous sodium hydroxide (10 c.c.), benzoyl chloride (1·5 c.c.) was added. The mixture was shaken for 1 hr. and the precipitated *dibenzoate* separated. After crystallisation from ethanol, this (115 mg.) was obtained as colourless prisms, m. p. 204—205°, depressed to 180—190° on admixture with 12-hydroxytotarol dibenzoate [3] (Found: C, 80·2; H, 7·3. $C_{34}H_{38}O_4$ requires C, 80·0; H, 7·5%). The ester gave strong benzoate bands at 1750 and 1250 cm.$^{-1}$ but had no hydroxyl absorption.

11,12-*Ferruginoquinone* (4b,5,6,7,8,8a,9,10-*Octahydro*-2-*isopropyl*-4b,8,8-*trimethyl*-3,4-*phenanthraquinone*) (XI).—11-Hydroxyferruginol 12-monoacetate (100 mg.) was hydrolysed as described in the previous experiment. The residue left after evaporation of the solvent was acidified with dilute hydrochloric acid, and the crude diol extracted into ether (20 c.c.). The ethereal extract was washed free from acid, and a mixture of anhydrous magnesium sulphate (1 g.) and silver oxide (1 g.) was added. The whole was shaken at room temperature for 10 hr., then the solids were separated and the ethereal solution was concentrated (to *ca.* 10 c.c.). The *quinone* separated as dark red needles, which recrystallised from ether giving the quinone, m. p. 166—168° (Found: C, 80·2; H, 9·2: $C_{20}H_{28}O_2$ requires C, 79·95; H, 9·4%), $\lambda_{max.}$ 243 and 355 mμ (ε 24,000 and 13,200, respectively).

7-*Oxoferruginol* (1,2,3,4,4a,9,10,10a-*Octahydro*-6-*hydroxy*-7-*isopropyl*-1,1,4a-*trimethyl*-9-*oxophenanthrene*) (VIII).—In a model experiment it was shown that aliquot parts of a solution of ferruginol (1·056 g.) in 80% acetic acid (250 c.c.), when oxidised with aqueous 0·0775N-sodium metaperiodate in the dark at room temperature, required *ca.* 20 hr. for the consumption of 1 mol. of reagent.

Ferruginol (5·3 g.) was dissolved in 80% acetic acid (150 c.c.), and a solution of sodium metaperiodate (9 g.) in 80% acetic acid was added. The mixture was kept at room temperature for 24 hr., then water (400 c.c.) was added, and the solution extracted with chloroform (3 × 100 c.c.). The chloroform extract was washed with water and dilute aqueous sodium hydrogen carbonate and dried ($MgSO_4$). After removal of the solvent, the dark red residue was dissolved in light petroleum and chromatographed on alumina, two main crystalline fractions being obtained: (i) eluted with light petroleum–benzene (1 : 1), yielded the acetate (VII) (115 mg.), m. p. and mixed m. p. 162—164°, $\lambda_{max.}$ 320 mμ (ε 290); (ii) eluted with ether, gave 7-oxoferruginol [9] (80 mg.), m. p. and mixed m. p. 288—290° (Found: C, 79·8; H, 8·95. Calc. for $C_{20}H_{28}O_2$: C, 79·95; H, 9·4%), $\lambda_{max.}$ 234 and 286 mμ (ε 15,500 and 13,200).

7-Oxoferruginol was also isolated from several metaperiodate oxidations of ferruginol in aqueous ethanol.

1,2,3,4,4a,6,8a,9,10,10a-*Decahydro*-8a-*hydroxy*-7-*isopropyl*-1,1,4a-*trimethyl*-6-*oxophenanthrene* (IX).—A solution of ferruginol (5 g.) in ethanol (320 c.c.) was added in one portion to a stirred solution of sodium metaperiodate (5 g.) in water (370 c.c.) containing concentrated sulphuric acid (10 c.c.). A deep red colour rapidly developed and, after being stirred for 14 hr., the solution was diluted with water (1·5 l.) and extracted with ether (1 × 200 c.c.; 2 × 100 c.c.). The combined ethereal extracts were washed with water, aqueous sodium hydrogen carbonate, and water again, and dried ($MgSO_4$). After removal of the solvent, the residue was chromatographed in benzene–light petroleum (1 : 1) on alumina (25 × 2·5 cm.). No significant product was obtained from the benzene–light petroleum or pure benzene eluates, but elution with ether (750 c.c.) gave a solution which on concentration yielded the *product* (IX) (49·8 mg., 1%), m. p. 170—173° raised to 172—173° on crystallisation from methanol; it formed colourless plates (Found: C, 79·2; H, 9·85. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%), $\lambda_{max.}$ 242 mμ (ε 14,000), $\nu_{max.}$ 3610 (OH), 1660 (conjugated C=O), and 1640 (C=C) cm.$^{-1}$.

Podototarin.—A solution of totarol (5·2 g.) in benzene (100 ml.) was added to a solution of potassium hydroxide (5 g.) in water (100 ml.) in an atmosphere of nitrogen. Potassium ferricyanide (10 g.) in water (300 c.c.) was added dropwise to the stirred alkaline totarol dispersion, after which the stirred mixture was kept at room temperature for 1 hr. and then heated on the steam-bath for 15 min. The solution was then neutralised with 5N-hydrochloric acid, and the benzene layer separated, washed with water, and dried ($MgSO_4$). After removal of the solvent, the residual orange gum was triturated with methanol (30 ml.) and yielded a colourless solid (3 g.) which was twice crystallised from ethanol to give colourless prisms of podototarin (containing one mol. of ethanol) (2·2 g.), m. p. 220—223° (lit.,[12] 225—226°) (Found: C, 81·5, 81·3; H, 10·7, 10·7. Calc. for $C_{40}H_{58}O_2,C_2H_5{\cdot}OH$: C, 81·75; H, 10·45%), $\lambda_{max.}$ 219, 254, and 290 mμ (ε 45,700, 14,800, and 8320, respectively). The diacetate formed prisms, m. p. 236—238° (lit.,[12] 237—238°), from ethanol (Found: C, 80·3, H, 9·5. Calc. for $C_{44}H_{62}O_4$: C, 80·65; H, 9·55%), and had $\nu_{max.}$ 1730s cm.$^{-1}$ (ester C=O).

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