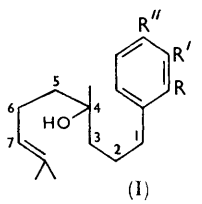
903. *Synthetic Studies in the Diterpene Series. Part IV.*[1] *Formation and Oxidation of Hydrophenalene Derivatives.**

By D. Nasipuri and (Miss) Gita Pyne.

The cyclodehydration of a few ω-arylalkanols (I and II; R = H or Pr^i, R′ = OMe, R″ = H) has been studied and the product identified in each case as the hexahydrophenalene derivative (V). Oxidation of these compounds by chromic acid did not give the expected aryl ketones (*e.g.*, VIII), but, instead, 4-hydroxycyclohexadienone derivatives (VII) as the major products. The structures of the products were ascertained by nuclear magnetic resonance and other spectral data.

The mechanism of the cyclisation is discussed.

Cyclodehydration of ω-arylalkanols to podocarpa-8,11,13-trienes [2] (IV) has recently been employed in our [3] and in other laboratories [4] for the synthesis of a few natural diterpenes. For instance, the alcohols (I and II; R = H, R′ = H or Pr^i, R″ = H or OMe) undergo double cyclisation to furnish a stereoisomeric mixture of the corresponding podocarpatriene derivatives (IV) almost exclusively or predominantly. Isomeric systems (III; R = H, R′ = OMe; and R = Pr^i, R′ = H) have also been cyclised, with similar results.[5] The reaction thus seems to be general. Evidence of an alternative ring-closure was, however, obtained with the alcohols (I and II; R = H, R′ = Me, R″ = OMe): oxidation of the product with chromic acid [6] afforded (±)-nimbiol methyl ether [7] and the corresponding *cis*-diketone only in traces, but mostly an unidentified monoketone (iso-nimbiol methyl ether), probably with a different ring-system.[1,4] The substituents in the benzene ring thus seems to affect the course of cyclisation.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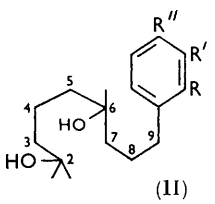
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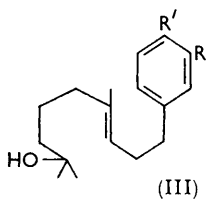
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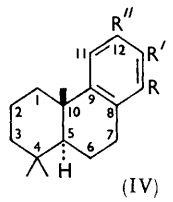
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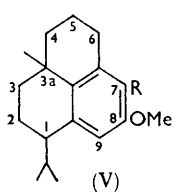
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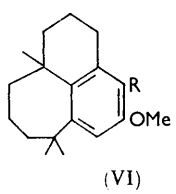
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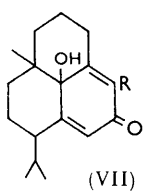
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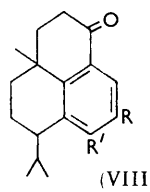

(VIII)

Next, the alcohols (I and II; R = R″ = H, R′ = OMe) were treated with polyphosphoric acid. The product was a liquid, and thus not (±)-13-methoxy-5α-podocarpa-8,11,13-triene [8] (IV; R = R″ = H, R′ = OMe), which has m. p. 86—88°. It contained

* A preliminary account of the work appeared in *Indian J. Chem.*, 1963, **1**, 227.

[1] Part III, Nasipuri and Roy, jun., *J. Indian Chem. Soc.*, 1963, **40**, 327.
[2] Nasipuri, *Chem. and Ind.*, 1957, 425.
[3] Nasipuri and Guha, *J.*, 1962, 4248.
[4] Delobelle and Fetizon, *Bull. Soc. chim. France*, 1961, 1632, 1900.
[5] Ansell and Gadsby, *J.*, 1959, 2994.
[6] Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211.
[7] Nasipuri and Roy, jun., *J. Sci. Ind. Res., India*, 1962, **21**, *B*, 50.
[8] Church, Ireland, and Marshall, *Tetrahedron Letters*, 1960, No. 17, 1.

no ethylenic double bond and could therefore have structures (V or VI; R = H). With chromic acid it gave, not the expected aromatic ketone (VIII; R = OMe, R′ = H), but a non-aromatic product, $C_{17}H_{24}O_2$, that has structure (VII; R = H) on the basis of the following evidence: (*a*) It contains no methoxyl group (Zeisel) and gives a low-melting red dinitrophenylhydrazone. (*b*) It gives an infrared band at 3630 cm.$^{-1}$ (OH) and a doublet at 1663 and 1623 cm.$^{-1}$ (1,4-diene 3-ketone [9]). (*c*) Its ultraviolet absorption spectrum ($\lambda_{max.}$ 246 mμ, log ε 4·32 in EtOH) differed from that of a substituted *m*-methoxybenzoyl derivative, *e.g.*, 7-oxototaryl methyl ether ($\lambda_{max.}$ 219, 258, and 320 mμ) but was characteristic of a conjugated (or cross-conjugated) unsaturated ketone, *e.g.*, (VII). (*d*) The nuclear magnetic resonance spectrum showed a sharp singlet at 7·37 τ corresponding in area to one proton, due to OH, two overlapping doublets one centred at 9·07 τ and the other at 9·18 τ (*J* 10 c./sec.) due to isopropyl, and a sharp singlet at 9·27 τ due to one quaternary methyl group, the area of the last three bands corresponding to nine protons in all. It also showed a band at 4·06 τ corresponding in area to exactly two protons, indicating the presence of two α-protons on an αβ-unsaturated carbonyl system, as in 19-norprogesterone (4·13 τ) [10a] and piperitone (4·13 τ).[10b] A β-proton in such a system, on the other hand, would absorb much further downfield (cf. carvone, 3·25 τ).[10c] All other protons were lost in a shapeless maximum at ~8 τ. All these results conform to structure (VII; R = H).

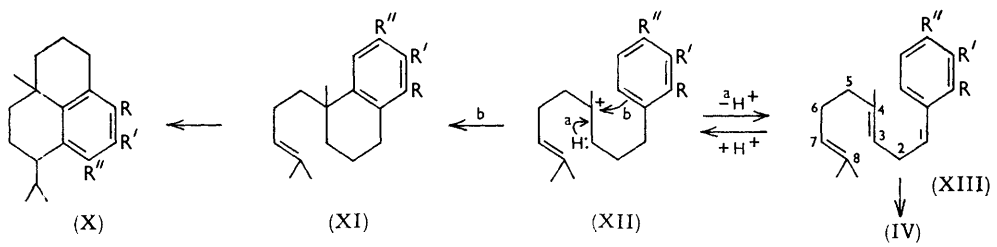
The original cyclised product had, therefore, the hydrophenalene structure (V; R = H) which was further corroborated by its nuclear magnetic resonance data (cf. Experimental section).

In line with these observations, 1-(2-isopropyl-3-methoxyphenyl)-4,8-dimethylnon-7-en-4-ol (I; R = Pr^i, R′ = OMe, R″ = H) and the corresponding diol (II) on cyclodehydration afforded, not the desired (±)-totaryl methyl ether [11] (IV; R = Pr^i, R′ = OMe, R″ = H), but the hydrophenalene derivative (V; R = Pr^i). The latter was oxidised by chromic acid to the ketone (VII; R = Pr^i), the structures of both the compounds being consonant with the nuclear magnetic resonance results and the ultraviolet and infrared absorption spectra.

3-(2-Isopropyl-3-methoxyphenyl)propan-1-ol (IX) required for the synthesis of the alcohol (I; R = Pr^i, R′ = OMe, R″ = H) was prepared from 2-isopropyl-3-methoxybenzonitrile by the following reactions:

$$RCN \longrightarrow R{\cdot}CHO \longrightarrow R{\cdot}CH{=}CH{\cdot}CO_2H \longrightarrow R{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH \quad (IX)$$

It thus seems established that alcohols (I and II; R′ = OMe) containing a *p*-methoxyphenyl group are cyclised to hydrophenalene systems, while those without this methoxy-substituent lead normally to podocarpa-8,11,13-triene derivatives. The first step in the reaction is formation of the carbonium ion (XII) which can competitively (a) undergo a β-proton elimination, giving the diene (XIII), or (b) succumb to nucleophilic attack by



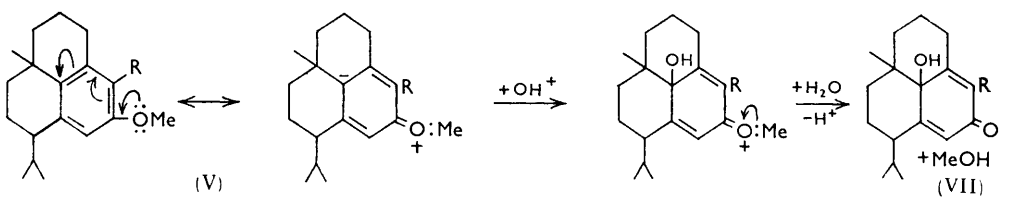
the aromatic ring, leading to the tetralin (XI). When the benzene ring is not activated by methoxyl the carbonium ion (XII) survives sufficiently to produce a fair quantity of the

[9] Fieser and Fieser, " Steroids," Reinhold Publ. Corp., New York, 1960, p. 170.
[10] Bhacca, Johnson, and Shoolery, " NMR Spectra Catalog," Varian Associates, 1962, spectrum nos. (*a*) 345, (*b*) 275, and (*c*) 271.
[11] Taylor, *J.*, 1961, 3319.

diene, which readily undergoes double cyclisation by a concerted or, more probably, by a non-concerted * process to afford the podocarpatrienes (IV) as almost the sole products. On the other hand, with the alcohols (I and II; R′ = OMe) where the electron-releasing effect of the methoxyl group is fully operative at the reaction site, and in the case of the alcohols (I and II; R = H, R′ = Me, R″ = OMe) where the nucleophilicity of the methoxyphenyl group is enhanced by methylhyperconjugation, reaction (b) becomes more important, and the tetralin (XI) is cyclised in the only possible way to give the hydrophenalene (X). This suggests structure (X; R = H, R′ = Me, R″ = OMe) for isodeoxonimbiol methyl ether and (VIII; R = Me, R′ = OMe) for isonimbiol methyl ether, which has recently been verified by synthesis.[13] The mechanism also explains the formation of (±)-ferruginol methyl ether [3] (IV; R = H, R′ = Pr^i, R″ = OMe) as a major product of cyclisation of the alcohols (I and II; R = H, R′ = Pr^i, R″ = OMe) where the replacement of methyl by isopropyl makes hyperconjugation almost negligible.

In accord with the above discussion, the alcohol (I; R = R″ = H; R′ = OMe) was first dehydrated with anhydrous copper sulphate and the resultant mixture of 3,7- and 4,7-dienes was cyclised by polyphosphoric acid. The product indeed afforded (±)-13-methoxy-5α-podocarpa-8,11,13-triene (IV; R = R″ = H, R′ = OMe), but only in very poor yield; the major fraction, a liquid, was identified as the hydrophenalene (V; R = H) by oxidation to the ketone (VII; R = H). Clearly, all the 4,7-diene and possibly much of the 3,7-diene (XIII) underwent protonation, affording finally the hydrophenalene through the carbonium ion (XII). When the alcohol (I; R = R″ = H, R′ = OMe) was cyclodehydrated, no trace of the 13-methoxypodocarpatriene (IV; R = R″ = H, R′ = OMe) could be found by chromatography, nor was there any indication of its presence in the nuclear magnetic resonance spectrum of the product.

The oxidation of the hydromethoxyphenalenes (V) to hydroxy-ketones (VII) requires comment. Recently a number of monoalkyl or monoaryl ethers of catechol and quinols, and a few polyalkylphenols, have been oxidised by Adler *et al.*[14] with sodium periodate to *o*- and *p*-quinones and in some cases to 4-hydroxycyclohexadienones. However, no similar oxidation of a methyl ether seems to have been reported. Apparently, the electrophilic species of the oxidising agent attacks the aromatic ring at the site of the greatest electron density, *i.e.*, *para* to the methoxyl group. The gross mechanism can be envisaged as follows:



On the other hand, isodeoxonimbiol methyl ether (X; R = H, R′ = Me, R″ = OMe) has been oxidised under similar conditions to isonimbiol methyl ether [13] (VIII; R′ = OMe, R = Me). It seems probable that the abnormal oxidation noted above is characteristic of the system (V) as a whole, since a model compound, 1,2,3,4-tetrahydro-6-methoxy-1,1-dimethylnaphthalene, underwent normal oxidation to 1,2,3,4-tetrahydro-6-methoxy-1,1-dimethyl-4-oxonaphthalene [15] in our hands, and a heterocyclic derivative of 13-methoxypodocarpatriene (IV; R = R″ = H, R′ = OMe) has recently been oxidised by Japanese

* A non-concerted mechanism is to be preferred, since a purely concerted cyclisation (cf. Stork and Burgstahler [12]) would lead to the *trans*(5α)-isomer exclusively.

[12] Stork and Burgstahler, *J. Amer. Chem. Soc.*, 1955, **77**, 5068.

[13] Nasipuri and Roy, jun., *Indian J. Chem.*, in the press.

[14] Adler *et al.*, *Acta Chem. Scand.*, 1959, **13**, 505; 1960, **14**, 512, 1261; 1962, **16**, 529; see also Goodwin and Witkop, *J. Amer. Chem. Soc.*, 1957, **79**, 179.

[15] Mukherjee, *J. Sci. Ind. Res., India*, 1960, **19**, *B*, 94.

workers [16] to the 7-oxo-derivative under identical conditions. Oxidations of analogous cases are being examined.

Experimental

M. p.s are corrected. Ultraviolet absorption spectra were recorded for ethanolic solutions on a Beckman spectrophotometer, unless otherwise stated. The nuclear magnetic resonance (n.m.r.) spectra were obtained on a 60 Mc. Varian (A-60) instrument, for deuteriochloroform solutions with tetramethylsilane as internal standard (δ 0·00). Light petroleum refers to the fraction of b. p. 40—60°.

3-m-*Methoxyphenylpropyl Chloride*.—Thionyl chloride (19·5 ml.) in dry chloroform (38 ml.) was added dropwise to a stirred solution of 3-*m*-methoxyphenylpropan-1-ol [17] (27·5 g.), chloroform (40 ml.), and dimethylaniline (31 g.) at 0°. The mixture was heated on the water-bath until evolution of hydrogen chloride ceased (1 hr.), cooled, and decomposed with cold dilute hydrochloric acid. The chloroform layer was separated, washed with dilute acid, water, sodium hydrogen carbonate solution, and again water, and dried ($CaCl_2$). The residue after evaporation of the solvent was distilled, to give 3-*m*-methoxyphenylpropyl chloride (27 g.), b. p. 146°/12 mm., n_D^{23} 1·5245.

1-m-*Methoxyphenyl*-4,8-*dimethylnon*-7-*en*-4-*ol* (I; R = R″ = H, R′ = OMe).—The Grignard reagent from 3-*m*-methoxyphenylpropyl chloride (22 g.), magnesium (3 g.), and ether (70 ml.) was treated with 6-methylhept-5-en-2-one (13 g.) in ether (30 ml.) and heated on the water-bath for 2 hr., then decomposed with cold dilute sulphuric acid and worked up in the usual way.[3] 1-m-*Methoxyphenyl*-4,8-*dimethylnon*-7-*en*-4-*ol* (I; R = R″ = H, R′ = OMe) was obtained (20 g.), having b. p. 170—175°/0·3 mm., n_D^{25} 1·5125 (Found: C, 78·0; H, 10·4. $C_{18}H_{28}O_2$ requires C, 78·3; H, 10·1%).

9-m-*Methoxyphenyl*-2,6-*dimethylnonane*-2,6-*diol* (II; R = R″ = H, R′ = OMe).—This was prepared from methyl 8-*m*-methoxyphenyl-5-oxo-octanoate [18] and an excess of methylmagnesium iodide as described in an analogous case [3] and was used directly for subsequent experiments.

2,3,3a,4,5,6-*Hexahydro*-7-*isopropyl*-8-*methoxy*-3a-*methyl*-1H-*phenalene* (V; R = H).—(*a*) The alcohol (I; R = R″ = H, R′ = OMe) (5 g.) was heated with polyphosphoric acid [from phosphorus pentoxide (62 g.), and 89% phosphoric acid (40 ml.)] at 80—90° for 1 hr. The mixture was decomposed with ice and extracted with ether. Evaporation of the solvent and distillation of the residue afforded the *hydrophenalene* (V; R = H) (3 g.), b. p. 150—155°/0·2 mm., n_D^{36} 1·5420 (Found: C, 83·5; H, 10·2; OMe, 12·5. $C_{18}H_{26}O$ requires C, 83·7; H, 10·1; OMe, 12·0%), $\lambda_{max.}$ 281 mμ (log ε 3·37). The n.m.r. data (with relative areas, splitting patterns, and assignments in parentheses) were as follows: τ 3·44 and 3·56 (2, singlets, aromatic hydrogens), τ 6·29 (3, sharp singlet, methoxyl group), τ 8·91, 9·08, 9·12, 9·24, and 9·34 (9, two doublets and one singlet, isopropyl and a quaternary methyl group); other principal peaks at τ 7·22, 7·31, and 8·46.

(*b*) 9-*m*-Methoxyphenyl-2,6-dimethylnonane-2,6-diol (II; R = R″ = H, R′ = OMe) was likewise cyclised with polyphosphoric acid and the identity of the product with the preceding hydrophenalene derivative was established by oxidation (see below).

Oxidation of 2,3,3a,4,5,6-*Hexahydro*-1-*isopropyl*-8-*methoxy*-3a-*methyl*-1H-*phenalene* (V; R = H).—The above hydrophenalene derivative (V; R = H) (2 g.) in acetic acid (25 ml.) was mixed with a solution of chromic acid (2·5 g.) in 80% acetic acid (35 ml.) in the cold. After 24 hr. at room temperature, the mixture was diluted with water, the organic matter taken up in ether, and the ethereal extract washed with dilute sodium hydroxide solution, dried, and evaporated. The residue, on being kept at 0° in contact with light petroleum, afforded crystals (1·2 g., 60%) which were chromatographed over neutral alumina and crystallised from benzene–light petroleum to give 1,2,3,3a,4,5,6,9b-*octahydro*-9b-*hydroxy*-3a-*methylphenalen*-8-*one* (VII; R = H) as needles, m. p. 158° (Found: C, 78·7; H, 9·3%; OMe, 0; *M*, 258. $C_{17}H_{24}O_2$ requires C, 78·5; H, 9·2%; *M*, 260). It gave a *dinitrophenylhydrazone* forming red needles, m. p. 124° (from benzene–methanol) (Found: C, 62·8; H, 6·3; N, 12·6. $C_{23}H_{28}N_4O_5$ requires C, 62·7; H, 6·4; N, 12·7%).

[16] Iwai, Ogiso, and Shimizu, *Chem. and Ind.*, 1962, 1288.
[17] Nasipuri, Roy, and Rakshit, *J. Indian Chem. Soc.*, 1960, **37**, 369.
[18] Nasipuri and Chaudhuri, *J.*, 1958, 2579.

2-*Isopropyl*-3-*methoxyphenethyl Alcohol*.—This was prepared from 2-isopropyl-3-methoxybenzonitrile [19] essentially by the method described before.[18] The yield of amide was, however, improved to 90% by recovering the unchanged nitrile after hydrolysis with alkaline hydrogen peroxide and submitting it to a second treatment. Hydrolysis of the nitrile with polyphosphoric acid [20] at 110—120° for several hours furnished the amide in poorer yield. 2-Isopropyl-3-methoxyphenethyl alcohol was now obtained in prisms, m. p. 67·5—68° (from light petroleum) (Found: C, 74·1; H, 9·4. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·3%). The corresponding bromide, prepared from the alcohol by the action of phosphorus tribromide,[18] was also obtained in prisms, m. p. 48—49° (from light petroleum) (Found: C, 56·1; H, 6·9. Calc. for $C_{12}H_{17}BrO$: C, 56·0; H, 6·6%).

9-(2-*Isopropyl*-3-*methoxyphenyl*)-2,6-*dimethylnonane*-2,6-*diol* (II; R = Pr^i, R′ = OMe, R″ = H).—Methyl 8-(2-isopropyl-3-methoxyphenyl)-5-oxo-octanoate [18] was treated with an excess of methylmagnesium iodide in the same way as before and the product worked up to furnish the diol which was cyclised directly after the removal of the lower-boiling fractions at the oil-pump.

2-*Isopropyl*-3-*methoxybenzaldehyde*.—A suspension of lithium aluminium hydride (4 g.) in dry ether (100 ml.) was cooled in a freezing mixture, while ethanol (16 ml.) was gradually introduced with stirring.[21] After a few minutes, 2-isopropyl-3-methoxybenzonitrile (17 g.) was added rapidly and the mixture stirred vigorously for 1 hr. The product was decomposed by the successive addition of methanol (15 ml.) and dilute sulphuric acid and then extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue afforded 2-isopropyl-3-methoxybenzaldehyde (13·5 g., 80%), b. p. 125°/7 mm. (Found: C, 74·4; H, 8·2. Calc. for $C_{11}H_{14}O_2$: C, 74·2; H, 7·9%). It was contaminated with a little nitrile but was sufficiently pure for subsequent experiments. It gave a *dinitrophenylhydrazone*, orange needles (from benzene–methanol), m. p. 215° (Found: C, 56·9; H, 5·3; N, 15·5. $C_{17}H_{18}N_4O_5$ requires C, 57·0; H, 5·0; N, 15·6%).

2-*Isopropyl*-3-*methoxycinnamic Acid*.—The foregoing aldehyde (10 g.), malonic acid (15 g.), pyridine (20 ml.), and a few drops of piperidine were heated at 80° for 1 hr., then at 100° for 2 hr., and finally at the b. p. for 30 min. The product was poured into cold dilute hydrochloric acid. The *cinnamic acid* was collected, washed with water, and crystallised from aqueous methanol in needles (8 g.), m. p. 149° (Found: C, 70·9; H, 7·1%; Equiv., 218. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%; Equiv., 220). The corresponding β-*arylpropionic acid* was obtained by shaking a solution of the cinnamic acid (15 g.) in 2N-potassium carbonate (60 ml.) under hydrogen in presence of 10% palladium–charcoal (0·2 g.) for 8 hr. and crystallised from aqueous methanol in needles, m. p. 103—104° (Found: C, 70·2; H, 8·2. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%). The *methyl ester* had b. p. 160—161°/7 mm. (Found: C, 71·0; H, 8·3. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%).

3-(2-*Isopropyl*-3-*methoxyphenyl*)*propan*-1-*ol* (IX).—The preceding ester (15 g.) in dry ether (50 ml.) was gradually added to a suspension of lithium aluminium hydride (3·5 g.) in ether (100 ml.), then stirred and gently refluxed for 2 hr. The *alcohol* was worked up in the usual way and had b. p. 160°/7 mm. (12·3 g.) (Found: C, 74·6; H, 9·3. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·6%). It formed a 3,5-*dinitrobenzoate*, yellow plates (from methanol), m. p. 83° (Found: N, 7·2. $C_{20}H_{22}N_2O_7$ requires N, 7·0%). 3-(2-*Isopropyl*-3-*methoxyphenyl*)*propyl chloride* (12 g.), b. p. 145°/4 mm., n_D^{36} 1·5135, was prepared from the alcohol (13 g.) by the action of thionyl chloride (6·5 ml.) in presence of dimethylaniline (10·3 g.) and chloroform (25 ml.).

1-(2-*Isopropyl*-3-*methoxyphenyl*)-4,8-*dimethylnon*-7-*en*-4-*ol* (I; R = Pr^i, R′ = OMe, R″ = H).—The Grignard reagent from the above chloride (10 g.) and 6-methylhept-5-en-2-one (7 g.), on condensation in the usual way, gave the unsaturated *alcohol* (I; R = Pr^i, R′ = OMe, R″ = H) (10 g.) after removal of a lower-boiling fraction at 140°/0·2 mm.

2,3,3a,4,5,6-*Hexahydro*-1,7-*di*-*isopropyl*-8-*methoxy*-3a-*methyl*-1H-*phenalene* (V; R = Pr^i).—The preceding unsaturated alcohol (5 g.) was cyclised with polyphosphoric acid [from phosphorus pentoxide (93 g.) and 89% phosphoric acid (60 ml.)] at 80—90° for 45 min. The product was worked up as usual and distilled, to give an oil (3·2 g.), b. p. 160°/0·3 mm. This was absorbed on alumina and eluted with light petroleum. The middle fraction (2·6 g.) solidified

[19] Richtzenhain and Nippus, *Ber.*, 1944, **77**, 566; Fuson, Gaertner, and Chadwick, *J. Org. Chem.*, 1948, **13**, 489.
[20] Snyder and Elston, *J. Amer. Chem. Soc.*, 1954, **76**, 3039.
[21] Brown, Shoaf, and Garg, *Tetrahedron Letters*, 1959, No. 3, 9.

and crystallised from ether–methanol to give the *hydrophenalene* (V; R = Pr^i) in plates, m. p. 84° (Found: C, 84·2; H, 10·6. $C_{21}H_{32}O$ requires C, 84·0; H, 10·7%), $\lambda_{max.}$ 288 mμ (log ε 3·32). The n.m.r. data (with relative areas, splitting patterns, and assignments in parentheses) were: τ 3·45 (1, singlet, aromatic hydrogen), τ 6·26 (3, sharp singlet, methoxyl group), τ 8·64 and 8·76 (6, a doublet, isopropyl group attached to benzene ring), τ 8·91, 9·05, 9·18, and 9·3 (9, one isopropyl and one quaternary methyl group), other protons appearing at τ 6·72 (irregular multiplet) and ~8·5. Cyclodehydration of the *diol* (II; R = Pr^i, R′ = OMe, R″ = H) afforded the same hydrophenalene derivative but in poorer yield.

Oxidation.—This hydrophenalene (600 mg.) in acetic acid (20 ml.) was kept with a solution of chromic acid (1·0 g.) in 80% acetic acid (14 ml.) for 24 hr. at room temperature, then diluted with water and extracted with ether. The residue on evaporation of the solvent solidified and crystallised from benzene–light petroleum to give 1,2,3,3a,4,5,6,9b-*octahydro*-9b-*hydroxy*-1,7-*di*-*isopropyl*-3a-*methylphenalen*-8-*one* (VII; R = Pr^i) as needles (350 mg.), m. p. 168° (Found: C, 79·2; H, 10·2. $C_{20}H_{30}O_2$ requires C, 79·4; H, 9·9%), $\lambda_{max.}$ 250 mμ (log ε 4·2), $\nu_{max.}$ (Nujol) 3425 (OH) and 1662 and 1620 cm.$^{-1}$ (C:C·CO·C:C), τ 4·03 (1, sharp singlet, one α-proton on an αβ-unsaturated carbonyl system), τ 7·95 (1, sharp singlet, OH), τ 8·73 and 8·85 (6, a doublet, isopropyl at unsaturated carbon), τ 8·99, 9·07, 9·16, and 9·27 (9, one isopropyl and a quaternary methyl group), τ 6·75 (1, multiplet, hydrogen at α-isopropyl group), other peaks at τ 7·27 and ~8. The ketone formed a *dinitrophenylhydrazone*, red needles (from methanol), m. p. 145—146° (Found: C, 64·5; H, 7·2; N, 11·5. $C_{26}H_{34}N_4O_5$ requires C, 64·7; H, 7·1; N, 11·8%).

Dehydration of 1-m-*Methoxyphenyl*-4,8-*dimethylnon*-7-*en*-4-*ol* (I; R = R″ = H, R′ = OMe).—1-m-*Methoxyphenyl*-4,8-*dimethylnon*-7-*en*-4-*ol* (13·4 g.) was heated with anhydrous copper sulphate (5 g.) at 150° for 2 hr. The cooled mixture was diluted with water and the organic matter taken up in ether. Evaporation of ether and distillation of the residue afforded a mixture of olefins (10 g.), b. p. 135—140°/0·2 mm. (Found: C, 83·1; H, 10·4. Calc. for $C_{18}H_{26}O$: C, 83·7; H, 10·1%).

(±)-13-*Methoxy*-5α-*podocarpa*-8,11,13-*triene* (IV; R = R″ = H, R′ = OMe).—(*a*) The above mixture (5 g.) was cyclised with polyphosphoric acid under above conditions and the product (3·5 g.), b. p. 140°/0·2 mm., was chromatographed on activated alumina. (±)-13-Methoxy-5α-podocarpa-8,11,13-triene (150 mg.), m. p. 86—88° (Found: C, 83·5; H, 10·3. Calc. for $C_{18}H_{26}O$: C, 83·7; H, 10·1%), was obtained in the last few fractions. It did not depress the m. p. of a specimen prepared by method (*b*) of Church *et al.*[8] The earlier liquid fractions of the chromatogram on chromic acid oxidation yielded the ketone (VII; R = H), m. p. 158°.

(*b*) *m*-Methoxybenzaldehyde (6 g.), isopropyl methyl ketone (3·6 g.), ethanol (16 ml.), and 5% aqueous sodium hydroxide (8 ml.) were shaken for 10 hr. at room temperature. The product was worked up in the usual way and distilled, to give isopropyl 3-methoxystyryl ketone (5·6 g.), b. p 140°/4 mm. The *dinitrophenylhydrazone* crystallised from benzene–methanol in red nodules, m. p. 185—190° (Found: N, 14·4. $C_{19}H_{20}N_4O_5$ requires N, 14·6%).

The ketone (6·5 g.) in dry benzene (15 ml.) was added to the methiodide of 1-diethylaminopentan-3-one [22] (7 g.), followed by a solution of potassium (3 g.) in absolute ethanol (50 ml.). The mixture was refluxed for 4 hr. and then worked up in the usual way, to yield 3-3′-methoxystyryl-2,4,4-trimethylcyclohex-2-en-1-one (5 g.), b. p. 170—190°/0·4 mm., as a gum, $\lambda_{max.}$ 302 mμ (log ε 4·15). The chocolate *dinitrophenylhydrazone* (from ethyl acetate) had m. p. 155—156° (Found: N, 12·1. $C_{24}H_{26}N_4O_5$ requires N, 12·4%). The ketone (4 g.) in ethanol (25 ml.) was reduced by hydrogen in presence of 10% palladium–charcoal (500 mg.). 3-*m*-Methoxyphenethyl-2,4,4-trimethylcyclohexan-1-one (4 g.), b. p. 160°/1 mm., thus obtained, was directly reduced by lithium aluminium hydride (2 g.), and the product cyclised by polyphosphoric acid [from phosphorus pentoxide (62 g.) and 89% phosphoric acid 40 ml.)] to yield the podocarpatriene derivative (IV; R = R″ = H, R′ = OMe) as a stereoisomeric mixture. On chromatography, the *trans*-isomer (5α) was obtained with m. p. 86—88° (from ether–methanol).

1,2,3,4-*Tetrahydro*-6-*methoxy*-1,1-*dimethylnaphthalene.*—Methyl γ-*m*-methoxyphenylbutyrate (10 g.) was treated with ethereal methylmagnesium iodide [from magnesium (5 g.), methyl iodide (15 ml.), and ether (200 ml.)]. 5-*m*-Methoxyphenyl-2-methylpentan-2-ol, thus obtained, was cyclised by a mixture of phosphorus pentoxide (15 g.) and 89% phosphoric acid

[22] Aktar and Weedon, *J.*, 1959, 4058.

(75 ml.) at 170° for 3 hr. The product was worked up, to give 1,2,3,4-*tetrahydro*-6-*methoxy*-1,1-*dimethylnaphthalene* (6·5 g.), b. p. 113—115°/12 mm. (Found: C, 81·8; H, 9·5. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%), n_D^{33} 1·5285.

1,2,3,4-*Tetrahydro*-6-*methoxy*-1,1-*dimethyl*-4-*oxonaphthalene*.—The foregoing tetralin derivative (2 g.) was oxidised with chromic acid (2·5 g.) in 80% acetic acid in the usual way. The product, a mixture of the unchanged starting material and ketone, was converted directly into the dinitrophenylhydrazone. The latter crystallised from ethyl acetate in red needles, m. p. and mixed m. p.[15] 238° (Found: C, 58·9; H, 5·5; N, 15·2. Calc. for $C_{19}H_{20}N_4O_5$: C, 59·4; H, 5·2; N, 14·9%).

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