**134.** *Synthesis of Diterpenes. Part II.* An Intermediate for the Synthesis of Diterpenoid Acids.*

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Cyclisation with phosphoric oxide (but not with polyphosphoric acid) of the tertiary alcohol (II) gives the *cis*- and *trans*-octahydrophenanthrene-carboxylic esters (VI; $R = CO_2Et$) and (V; $E = Et$) respectively. The latter is converted into the tricyclic $(\pm)$-keto-ester (I; $R = CO_2Me$), identical with a degradative product of agathenedicarboxylic acid.

WORK on the synthesis of the diterpenoid resin acids has so far concerned those which contain an aromatic ring,[1] and has culminated in the total syntheses of podocarpic acid by King, King, and Topliss [2] and of dehydroabietic acid by Stork and Schulenberg.[3] Difficulties would be expected to be greater with non-aromatic resin acids, *e.g.*, abietic and agathenedicarboxylic acids, where the number of asymmetric centres is greater.

A possible approach to such acids is offered by the tricyclic keto-esters (I; $R = CO_2Me$) and (VIII) which were obtained by degradation of agathenedicarboxylic acid [4] and *neo*-abietic acid [5] respectively; and a route analogous to that to the ketone [6] (I; $R = Me$) has now led to one of these intermediates (I; $R = CO_2Me$).

Condensing ethyl 1 : 3-dimethyl-2-oxo*cyclo*hexanecarboxylate with the Grignard reagent from *m*-methoxyphenylacetylene in tetrahydrofuran gave a 57% yield of ethyl 2-hydroxy-2-*m*-methoxyphenylethynyl-1 : 3-dimethyl*cyclo*hexanecarboxylate, the triple bond of which was almost quantitatively reduced over palladized charcoal to give the 2-*m*-methoxyphenethyl-alcohol (II).

Cyclization of this compound was first tried with polyphosphoric acid (cf. refs. 2 and 6), but loss of the elements of ethanol and carbon monoxide occurred, giving a material whose analyses indicated a hexahydro-7-methoxy-1 : 12-dimethylphenanthrene but which was probably a mixture of double-bond isomers. On hydrogenation it absorbed less than 0·5 mol. of hydrogen, suggesting that the isomer (III) with a tetrasubstituted double bond predominated. The unsaturated ester (IV) also lost ethanol and carbon monoxide when
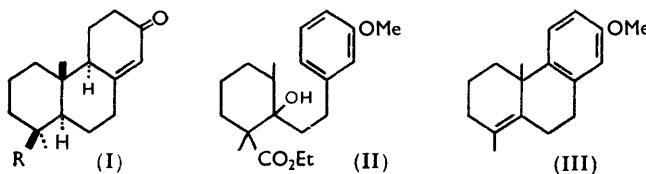


cyclized under these conditions. However, treatment of the hydroxy-ester (II) with phosphoric oxide at 140—145° (cf. ref. 7) gave a mixture from which two stereoisomeric, tricyclic esters, A (V; $R = Et$) (25%) and B (VI; $R = CO_2Et$) (21%), were isolated by chromatography. Each ester was shown to be stereochemically homogeneous by the infrared spectra of fractions collected during chromatography. Minor products were the unsaturated ester (IV) (2%) and the mixture of hexahydro-7-methoxy-1 : 12-dimethylphenanthrenes (14%). The unsaturated ester (IV) gave a similar mixture when treated with phosphoric oxide.

* Part I, *J.*, 1958, 2566.

[1] Haworth and Barker, *J.*, 1939, 1299; Bhattacharyya, *J. Indian Chem. Soc.*, 1945, **22**, 165; Haworth and Moore, *J.*, 1946, 633; Parham, Wheeler, and Dodson, *J. Amer. Chem. Soc.*, 1955, **77**, 1166; Saha, Ganguly, and Dutta, *Chem. and Ind.*, 1956, 412.

[2] King, King, and Topliss, *ibid.*, p. 113.

[3] Stork and Schulenberg, *J. Amer. Chem. Soc.*, 1956, **78**, 250.

[4] Ruzicka, Bernold, and Tallichet, *Helv. Chim. Acta*, 1941, **24**, 223.

[5] Harris and Sanderson, *J. Amer. Chem. Soc.*, 1948, **70**, 339.

[6] Barltrop and Rogers, *Chem. and Ind.*, 1957, 20; *J.*, 1958, 2566.

[7] King, King, and Topliss, *Chem. and Ind.*, 1954, 108; *J.*, 1957, 573.

Esters A and B, and methyl $O$-methylpodocarpate, which are all esters of tricyclic, tertiary acids, were shown by infrared spectroscopy to lose the ethoxycarbonyl group when treated with polyphosphoric acid. In view of these results, the success of King *et al.*[2] in cyclising the hydroxy-ester (VII) with polyphosphoric acid to a mixture of diastereoisomeric, tricyclic esters (including ethyl $O$-methylpodocarpate) in 88·5% yield is surprising. In the polyphosphoric acid reactions carried out in the present investigation, loss of ethanol and carbon monoxide is presumably preceded by generation of $R\cdot CO^+$ from the protonated ester group:[8] the retention of the ethoxycarbonyl group in the phosphoric oxide cyclization can then be understood in terms of steric factors which make interaction between this group and the Lewis acid difficult.

Hydrolysis of the esters A (V; R = Et) and B (VI; R = $CO_2Et$) was very difficult; but comparative experiments showed that ester A contains an ester group appreciably more hindered than that of ester B. Thus, when heated with a 30% solution of potassium hydroxide in slightly aqueous ethylene glycol at 150° for 5 hr., esters A and B gave 35 and 87% yields, respectively, of the corresponding acids. Both acids gave methyl esters when treated with diazomethane.



(IV)                    (V)                    (VI)
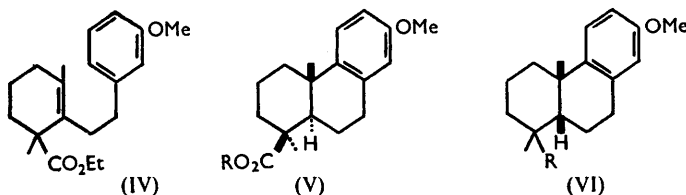
Reduction of the aromatic ring of esters A and B with lithium, ethanol, and liquid ammonia required very vigorous conditions. Wilds and Nelson's technique [9] reduced the esters to the corresponding primary alcohols (cf. ref. 10), leaving the aromatic ring unchanged: the acids (V; R = H) and (VI; R = $CO_2H$) were unaffected, and the alcohol (VI; R = $CH_2\cdot OH$) and its tetrahydropyranyl ether showed only traces of further reduction when treated with lithium under these conditions. However, by use of " lithium-bronze " and a greater proportion of ethanol,[11] followed by fission of the resulting enol ether with ethanolic hydrochloric acid, ester A was converted into 16-hydroxypodocarp-8-en-7-one (I; R = $CH_2\cdot OH$) in 57% yield. [The nomenclature of compounds derived from ester A is based [12] on the hydrocarbon podocarpane (IX).] Oxidation of this hydroxy-ketone with a 2% solution of chromium trioxide in acetic acid gave 7-oxo-podocarp-8-en-16-oic acid (I; R = $CO_2H$). The keto-acid was also obtained by reduction of acid A with " lithium-bronze," followed by treatment with ethanolic hydrochloric acid, but the yield was very poor.

Methyl ($\pm$)-7-oxopodocarp-8-en-16-oate (I; R = $CO_2Me$), m. p. 98—99°, was obtained by treatment of the keto-acid with diazomethane. Its infrared absorption spectrum, determined in carbon disulphide solution, was identical with that of the pure dextro-rotatory keto-ester, which had been obtained [4] from agathenedicarboxylic acid. The synthetic and the dextrorotatory keto-ester showed identical conjugated-carbonyl absorptions in the ultraviolet region ($\lambda_{max.}$ 241 m$\mu$, log $\varepsilon$ 4·25).

Similarly, reduction of ester B by " lithium-bronze," followed by treatment with acid, gave a hydroxy-ketone (X; R = $CH_2\cdot OH$) which was converted by chromic acid into a keto-acid. Esterification with diazomethane gave a keto-ester (X; R = $CO_2Me$), m. p.

[8] Elliott and Hammick, *J.*, 1951, 3402.
[9] Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5360, 5366.
[10] Chablay, *Compt. rend.*, 1913, **156**, 1020; *Ann. Chim.*, 1917, **8**, 213; Kharasch, Sternfeld, and Mayo, *J. Org. Chem.*, 1940, **5**, 362.
[11] Cf. Johnson *et al.*, *J. Amer. Chem. Soc.*, 1956, **78**, 6331, 6339, 6354.
[12] Klyne, *J.*, 1953, 3072.

106—107°. That the synthetic keto-ester was not identical with the tricyclic keto-ester (VIII) derived [5] from *neo*abietic acid was shown by comparison of their infrared spectra.



(VII)          (VIII)          (IX)
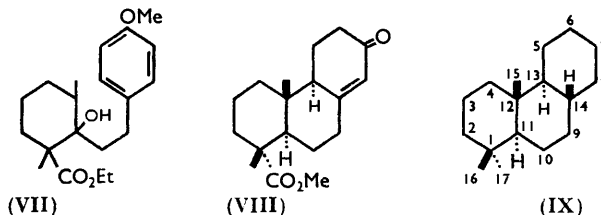
Ester B and the compounds related to it are considered to have a *cis*-AB-ring junction; the possibility that they are spirans, *e.g.*, (XI), is excluded because oxidation of ester B with a 20% solution of chromium trioxide in acetic acid [13] gave a compound which had the infrared absorption characteristic of an α-tetralone (carbonyl band at 1686 cm.$^{-1}$). A spiran structure (XI) for ester B would lead on oxidation to an indan-1-one which would show carbonyl absorption at a higher frequency [14] (1715—1706 cm.$^{-1}$). The oxidation product is therefore formulated as (XII), the stereochemistry at position 1 (phenanthrene numbering) being as yet undefined. The formation of an appreciable amount of acidic material in the chromic acid oxidation of the ester is in accord with Wenkert and Jackson's observations [13] on the oxidative behaviour of 1 : 1-disubstituted *cis*-AB-hydrophenanthrenes related to the diterpene acids.



(X)          (XI)          (XII)
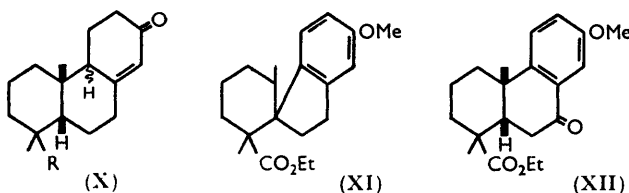
The stereochemistry at position 13 in the hydroxy-ketone (X; R = CH$_2$·OH) and in the related keto-acid and ester (X; R = CO$_2$H, and CO$_2$Me) is uncertain: models fail to reveal any decisive difference between the 13α-H and 13β-H isomers.

A preliminary account of this work has been published.[15]

## EXPERIMENTAL

Ultraviolet spectra were measured for ethanol solutions; infrared spectra were determined for liquid films unless otherwise stated. M. p.s were determined on a Kofler block. For chromatography, Peter Spence's " Grade H " alumina was used; deactivated alumina contained 5% of 10% aqueous acetic acid. Unless otherwise stated, " light petroleum " refers to the fraction of b. p. 60—80°.

*m*-Methoxyphenylacetylene, prepared from *m*-methoxyacetophenone,[16] or much more conveniently [17] from *m*-methoxycinnamic acid, had b. p. 86—88°/12—13 mm., $n_D^{16}$ 1·5581 (lit.,[16] b. p. 85°/13 mm., $n_D^{25}$ 1·5560).

Ethyl 1 : 3-dimethyl-2-oxo*cyclo*hexanecarboxylate, prepared by Haworth and Barker's method,[1] had b. p. 117°/16 mm., $n_D^{18}$ 1·4498 (lit.,[18] $n_D^{20}$ 1·4491).

*Ethyl 2-Hydroxy-2-m-methoxyphenylethynyl-1 : 3-dimethylcyclohexanecarboxylate.*—To a boiling solution of the Grignard reagent prepared from magnesium (7·7 g.) and ethyl bromide (37 g.)

[13] Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211.

[14] Gutsche, *ibid.*, 1951, **73**, 786.

[15] Barltrop and Day, *Chem. and Ind.*, 1958, 439.

[16] Johnson, Banerjee, Schneider, Gutsche, Shelberg, and Chinn, *J. Amer. Chem. Soc.*, 1952, **74**, 2843.

[17] Barltrop, Bigley, and Rogers, unpublished work.

[18] Parham, Wheeler, Dodson, and Fenton, *J. Amer. Chem. Soc.*, 1954, **76**, 5380.

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in dry ether (100 c.c.) and pure tetrahydrofuran (200 c.c.) under nitrogen, *m*-methoxyphenyl-acetylene (42 g.) in tetrahydrofuran (80 c.c.) was added during $\frac{1}{2}$ hr. with stirring. Boiling was continued for 1 hr., and then ethyl 1 : 3-dimethyl-2-oxo*cyclo*hexanecarboxylate (70 g.) in tetrahydrofuran (100 c.c.) was added dropwise during 40 min. The solution was heated under reflux for 1 hr., then treated cautiously with saturated aqueous ammonium chloride (400 c.c.). Isolation with ether followed by distillation gave the *ethynyl-alcohol* (60 g.), b. p. 158—159°/0·05 mm., $n_D^{20}$ 1·5415 (Found: C, 72·4; H, 8·1. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%), ν 3510 s, 2220 w, and 1730 s cm.$^{-1}$, $\lambda_{max.}$ 243, 253, 289, 297 mμ (log ε 4·20, 4·22, 3·49, 3·50, respectively). Yields were lower when the reaction was carried out in ether without nitrogen.

*Ethyl 2-Hydroxy-2-m-methoxyphenethyl-1* : *3-dimethyl*cyclohexanecarboxylate (II).—The above ethynyl-alcohol (20 g.) in ethyl acetate (120 c.c.) with 10% palladized charcoal (1 g.) absorbed 2 mols. of hydrogen. The product (19·7 g.), on distillation, gave the *phenethylcyclohexanol*, b. p. 157—160°(bath)/0·05 mm. (Found: C, 71·7; H, 9·1. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%), ν 3550 m, and 1725 s cm.$^{-1}$, $\lambda_{max.}$ 217, 273, 279·5 mμ (log ε 3·88, 3·31, 3·29, respectively).

*Cyclization of the Hydroxy-ester* (II).—*(A)* (cf. ref. 7). The preceding compound (10 g.) and phosphoric oxide (23 g.) were heated together at 12 mm., the temperature being raised to 145° during $\frac{1}{2}$ hr. and kept at 140—145° for 1 hr. Ice was added to the cooled mixture, which was then made alkaline with 2N-sodium hydroxide. The product, a brown oil (7 g.), was isolated with ether. The combined products from several such experiments were distilled to give a yellow, viscous oil with a blue fluorescence, b. p. 100—180°/0·15 mm. Chromatography of the oil (10 g.) on alumina (1·5 kg.) and elution with 9 : 1 light petroleum–benzene (8·25 l.) gave a yellow oil (1·69 g.), shown by its infrared absorption spectrum to contain no ethoxycarbonyl group, and to be similar to the product of cyclization of the hydroxy-ester (II) with poly-phosphoric acid (below). Elution with 1 : 1 light petroleum–benzene (2·25 l.) gave semisolid material (fraction 1) (5·11 g.); further elution with the same solvent (3 l.) and then benzene (1·5 l.) gave an oil (fraction 2) (2·78 g.). Chromatography of fraction 1 on alumina (1·5 kg.) and elution with 3 : 1 light petroleum–benzene (1·5 l.) gave ester C (0·15 g.). Elution with 1 : 1 light petroleum–benzene (0·75 l.) gave semisolid material (fraction 3) (0·93 g.); the same solvent (3 l.) eluted ester A (3·02 g.), m. p. 69—72°, and then (1·5 l.) semisolid material (fraction 4) (0·36 g.). Successive elution with this solvent (1·5 l.) and benzene (2·25 l.) gave ester B (0·43 g.) as an oil. Chromatography of fraction 3 on alumina (300 g.) in a similar manner gave ester C (0·17 g.), a mixture of esters A and C (0·28 g.), and ester A (0·41 g.). Fractions 2 and 4 were combined and chromatographed on alumina (1 kg.). Elution with 1 : 1 light petroleum–benzene (1·5 l.), then 1 : 2 light petroleum–benzene (0·75 l.) gave a mixture of esters A and B (fraction 5) (1·03 g.): the last solvent mixture (5·25 l.) eluted ester B (2·07 g.). Chromatography of fraction 5 gave ester A (0·30 g.), a mixture of A and B (0·05 g.), and ester B (0·63 g.).

Ester A (3·73 g.) was identified as *ethyl 1 : 2 : 3 : 4 : 9 : 10 : 11α : 12-octahydro-7-methoxy-1α : 12β-dimethylphenanthrene-1β-carboxylate* (V; R = Et), m. p. 73—74° [from light petroleum (b. p. 40—60°)] (Found: C, 76·1; H, 8·7. $C_{20}H_{28}O_3$ requires C, 75·9; H, 8·9%), $\lambda_{max.}$ 219·5, 277, 285 mμ (log ε 3·96, 3·30, 3·31, respectively). Ester B (3·13 g.) was identified as *ethyl 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-octahydro-7-methoxy-1ξ : 12β-dimethylphenanthrene-1ξ-carboxylate* (VI; R = CO₂Et), b. p. 146—150°/0·25 mm. (Found: C, 76·1; H, 9·3%), $\lambda_{max.}$ 219·5, 277·5, 284·5 mμ (log ε 3·89, 3·27, 3·26, respectively). Ester C, identified as ethyl 2-*m*-methoxy-phenethyl-1 : 3-dimethyl*cyclo*hex-2-enecarboxylate (IV), had b. p. 152—155° (bath)/0·3 mm. (Found: C, 75·5; H, 8·8. Calc. for $C_{20}H_{28}O_3$: C, 75·9; H, 8·9%), ν 1728 s, 1134 m, 1080 m, 776 m, 741 m cm.$^{-1}$, $\lambda_{max.}$ 273, 279·5 mμ (log ε 3·09, 3·12, respectively) (cf. Haworth and Moore [1]).

*(B)* (cf. ref. 2). The hydroxy-ester (II) (0·55 g.) was stirred under nitrogen with a solution of phosphoric oxide (30 g.) in 88—90% orthophosphoric acid (25 c.c.) at 80—85° for 45 min. Some effervescence was observed during the first few minutes. The mixture was poured into ice and water, and the oil was collected with ether. The ethereal solution was washed with brine, 2N-sodium hydroxide, and water, dried, and evaporated to give a brown, viscous oil (0·33 g.), shown by its infrared spectrum to contain no ethoxycarbonyl group. Acidification of the alkaline washings gave a negligible quantity of acid. The oil (0·57 g.) obtained in a similar experiment was chromatographed on alumina (50 g.). Elution with 1 : 1 light petroleum–benzene (250 c.c.) and distillation gave a mixture of hexahydro-7-methoxy-1 : 12-dimethyl-phenanthrenes (0·23 g.), b. p. 140°(bath)/0·05 mm. (Found: C, 84·1, 84·9; H, 9·1, 9·4. Calc. for $C_{17}H_{22}O$: C, 84·3; H, 9·2%), ν 1240 s, 1030 ms, 848 m, 810 m cm.$^{-1}$, $\lambda_{max.}$ 227, 261 mμ (log ε 4·33, 3·80, respectively).

This mixture did not absorb hydrogen in the presence of Adams catalyst. In ethyl acetate over 5% palladized charcoal it absorbed 0·4 mol. of hydrogen: in ethanol containing a trace of perchloric acid and with 10% palladized charcoal it absorbed 0·3 mol. of hydrogen.

Similar results were obtained when the cyclization was performed with polyphosphoric acid at 100° and at 120°.

*Cyclization of Ethyl* 2-m-*Methoxyphenethyl*-1 : 3-*dimethylcyclohex-2-enecarboxylate* (IV).—
(*A*). The reaction between the ester (43 mg.) and phosphoric oxide (300 mg.), carried out under the conditions used for the cyclization (*A*) of the hydroxy-ester (II), gave a crude product (31 mg.) shown by comparison of infrared spectra to be similar in composition to the crude product of the latter reaction.

(*B*). The ester (30 mg.) was treated with polyphosphoric acid under the conditions used for the cyclization (*B*) of the hydroxy-ester (II). The crude product (21 mg.) was shown by its infrared spectrum to contain no ethoxycarbonyl group and to be identical with the product obtained from the hydroxy-ester.

*Action of Polyphosphoric Acid on Esters of Tricyclic, Tertiary Acids.*—The distilled mixture of esters A and B from the cyclization (*A*) of the hydroxy-ester (II), treated at 80—85° or at 100° with polyphosphoric acid as in the cyclization (*B*) of the preceding paragraph, gave a crude product containing no ethoxycarbonyl group and spectroscopically identical with the product obtained from the two cyclizations (*B*).

Methyl *O*-methylpodocarpate likewise gave a product containing no methoxycarbonyl group under these conditions.

*Hydrolysis of Esters A and B.*—(i) Ester B (574 mg.) was heated under reflux for 5 hr. with a solution of potassium hydroxide (5 g.) in ethylene glycol (15 c.c.) and water (5 c.c.) which had previously been boiled until the temperature of the liquid reached 150°. Dilution with water, followed by the usual acid–alkali treatment, gave unhydrolysed ester (28 mg.) and crystalline 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro*-7-*methoxy*-1ξ : 12-*dimethylphenanthrene*-1ξ-*carboxylic acid* (VI; R = CO₂H) (456 mg.), which was sufficiently pure for further reactions. Recrystallized twice from methanol, it had m. p. 192—193·5° (Found: C, 74·8; H, 8·4. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·4%). The *methyl ester*, obtained by treatment of the acid with diazomethane, had b. p. 138—140° (bath)/0·15 mm. (Found: C, 75·7; H, 8·3. $C_{19}H_{26}O_3$ requires C, 75·5; H, 8·7%).

Hydrolysis of ester A by this procedure gave a 35% yield of the crude, resinous acid. When the reaction time was extended to 12 hr., the yield was increased to 74%. On treatment with diazomethane, the acid gave the *methyl ester*, which, after filtration through alumina, crystallized from light petroleum as needles, m. p. 107·5—108·5° (Found: C, 75·5; H, 8·7%).

(*B*) (cf. ref. 19). The ester (*ca.* 70 mg.) was heated at 150° for 4 hr. in a sealed tube with 2 c.c. of a solution of potassium hydroxide (5 g.) in ethanol (15 c.c.) and water (5 c.c.). The acid and unchanged ester were isolated in the usual way. The yield of acid from ester A was 24%, from ester B 59%.

16-*Hydroxypodocarp*-8-*en*-7-*one* (I; R = CH₂·OH) (cf. ref. 11).—To a stirred solution of ester A (V; R = Et) (2·5 g.) in dry dioxan (50 c.c.), dry ethanol (250 c.c.), and liquid ammonia (*ca.* 500 c.c.) were added lithium (27·5 g.) in thin strips, dry ethanol (300 c.c.), and further portions (each *ca.* 50 c.c.) of liquid ammonia at such a rate as to maintain the lithium-rich phase which formed bronze-red globules on the surface. After the addition, which required *ca.* 45 min., stirring was continued until the bronze layer disappeared (*ca.* 10 min.). Brine (1 l.) and ether were then added, followed by sufficient water to dissolve the inorganic material. The product, isolated with ether, was a resin (2·1 g.) [ν (in CS₂) 3623 w, 1698 m, 1653 w, 1224 s, 1020 s, 784 m cm.⁻²]. Acidification of the aqueous phase followed by extraction with ether gave no acid. The solid was heated at 70° for 1 hr. with ethanol (50 c.c.) and 5 c.c. of a solution of concentrated hydrochloric acid (5 c.c.) in water (2·5 c.c.) and ethanol (2·5 c.c.). After dilution with water and extraction with ether, the combined organic solutions were washed with brine, dried, and evaporated to give a pale fawn, solid (1·8 g.). The material (3 g.) obtained from this and a similar experiment gave, on recrystallization from ethyl acetate, 16-*hydroxypodocarp*-8-*en*-7-*one* (2·1 g.), as laths, m. p. 187—191°. Recrystallized again for analysis it had m. p. 190—191° (Found: C, 77·8; H, 10·2. $C_{17}H_{26}O_2$ requires C, 77·8; H, 10·0%), ν (in Nujol) 3390 s, 1650 s, 1613 m; (in CS₂) 3610 w, 1678 s cm.⁻¹, $\lambda_{max.}$ 241 mμ (log ε 4·23). When recrystallized from methanol, the compound retained solvent tenaciously and was

¹⁹ Sherwood and Short, *J.*, 1938, 1010.

not obtained analytically pure. The deep red 2 : 4-*dinitrophenylhydrazone*, recrystallized twice from chloroform–methanol, had m. p. 219—220° (Found: C, 60·4; H, 6·8; N, 11·4. $C_{23}H_{30}O_5N_4,CH_3\cdot OH$ requires C, 60·7; H, 7·2; N, 11·8%).

The mother-liquors from the recrystallization of the hydroxy-ketone were evaporated, and the residue was chromatographed on deactivated alumina (100 g.). Elution with benzene (500 c.c.) gave non-ketonic material (0·64 g.); 9 : 1 benzene–ether (300 c.c.) eluted a solid βγ-unsaturated ketone (0·15 g.), ν 1709 cm.⁻¹ (non-conjugated C=O). Elution with the same solvent (100 c.c.) and then 1 : 1 benzene–ether (100 c.c.) gave, after recrystallization from ethyl acetate, 16-hydroxypodocarp-8-en-7-one (100 mg.).

The βγ-unsaturated ketone eluted from the column was isomerized to the hydroxy-ketone (I; R = $CH_2\cdot OH$) on treatment with ethanolic hydrochloric acid under the conditions described above for the conversion of the crude reduction product into the hydroxy-ketone.

The aromatic ring of ester A could not be reduced by milder methods; the results were similar to those obtained in the reduction of the methyl ester (VI; R = $CO_2Me$).

*7-Oxopodocarp-8-en-16-oic Acid* (I; R = $CO_2H$).—(*A*). The preceding hydroxy-ketone (2·17 g.) in glacial acetic acid (50 c.c.) was treated portionwise at room temperature with a 2% solution of chromium trioxide in acetic acid (74 c.c.) and then set aside for 2 hr. The acetic acid was removed *in vacuo*, and water and ether were added to the residue. The layers were separated, and the aqueous layer was extracted with ether. The combined ethereal solutions were washed with water, 2N-sodium carbonate, and water again, then dried and evaporated to give a yellow solid (0·52 g.). Acidification of the carbonate washings, and extraction with ether, afforded 7-*oxopodocarp*-8-*en*-16-*oic acid* (1·12 g.). Reoxidation of the neutral material with chromium trioxide solution gave more of the crude keto-acid (0·21 g.). After recrystallization from ethanol, the keto-acid (1·04 g.) had m. p. 209—211°. Recrystallized again for analysis, it had m. p. 211—211·5° (Found: C, 73·8; H, 9·0. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·8%), ν (in Nujol) 1724 ($CO_2H$), 1640 (αβ-unsaturated ketone), 1621 cm.⁻¹ (C=C); (in $CHCl_3$) 1695, 1667 cm.⁻¹; $\lambda_{max.}$ 241 mμ (log ε 4·25).

(*B*). The acid (V; R = H) (190 mg.) was treated with lithium, ethanol, and liquid ammonia followed by ethanolic hydrochloric acid, as described for the reduction of ester A. The usual acid–alkali treatment gave neutral material (32 mg.), the spectrum of which [ν 1695 cm.⁻¹ (weak shoulder at 1739 cm.⁻¹)] did not resemble that of the hydroxy-ketone (I; R = $CH_2\cdot OH$). The resinous acid (110 mg.) gave, after decolorization with charcoal and two recrystallizations from ethanol, the keto-acid (I; R = $CO_2H$) (12 mg.), m. p. 209—211°, which was identified by infrared comparison and mixed m. p.

*Methyl* (±)-7-*Oxopodocarp-8-en-16-oate* (I; R = $CO_2Me$).—The preceding keto-acid (92 mg.) in dioxan (5 c.c.) was treated with an excess of ethereal diazomethane. After dilution with ether, the solution was washed with 2N-sodium carbonate and water, dried, and evaporated. The residue, which slowly crystallized, gave on recrystallization from light petroleum (b. p. 40—60°) *methyl* (±)-7-*oxopodocarp-8-en-16-oate* (45 mg.), m. p. 97—99°. Partial evaporation of the mother-liquors from the recrystallization gave a further crop (7 mg.). Chromatography of the uncrystallizable residue from the second recrystallization on deactivated alumina (2 g.), and elution with benzene (12 c.c.), gave the crystalline keto-ester (6 mg.). After a second recrystallization, the compound had m. p. 98—99° (Found: C, 74·3; H, 8·9. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%), $\lambda_{max.}$ 241 mμ (log ε 4·25). The *semicarbazone*, platelets from methanol, had m. p. 221·5° (Found: C, 65·8; H, 8·5; N, 12·1. $C_{19}H_{29}O_3N_3$ requires C, 65·7; H, 8·4; N, 12·1%).

The authentic (+)-keto-ester from agathenedicarboxylic acid,[4] recrystallized from light petroleum, had m. p. 119—120°, $\lambda_{max.}$ 241 mμ (log ε 4·25) [lit.,[4] m. p. 117°, $\lambda_{max.}$ 242 mμ (log ε 4·26)]. The infrared spectra (in $CS_2$) of this compound and the synthetic (±)-keto-ester were identical. The mixed m. p. lay between the m. p.s of the (+)- and the (±)-compound.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*Dodecahydro*-1ξ-*hydroxymethyl* - 1ξ : 12β -*dimethyl-phenanthren-7-one* (X; R = $CH_2\cdot OH$).—Ester B (0·61 g.) was treated with lithium, ethanol, and liquid ammonia as described for the reduction of ester A. The resinous dihydro-compound (0·53 g.) had infrared bands at 3361 s, 1701 ms, 1667 ms, 1214 s, 1031 s, and 785 ms cm.⁻¹. Treatment with ethanolic hydrochloric acid gave a resin (0·48 g.). On crystallization from ether it gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*dodecahydro*-1ξ-*hydroxymethyl*-1ξ : 12β-*dimethylphenanthren-7-one* (110 mg.), m. p. 154—158°, which separated from acetone in plates, m. p. 158—160° (Found: C, 78·0; H, 9·8. $C_{17}H_{26}O_2$ requires C, 77·8; H, 10·0%),

ν (in Nujol) 3400 s, 1658 s, 1618 m cm.⁻¹, λ_max. 244 mμ (log ε 4·25). Chromatography of the residues from the crystallization on deactivated alumina (50 g.) and elution with 9 : 1 benzene–ether (200 c.c.) gave non-ketonic material (59 mg.). Further elution with the same solvent (150 c.c.) gave a resin (73 mg.) having infrared bands at 3413 s, 1724 s cm.⁻¹. Elution with 4 : 1 benzene–ether (150 c.c.) and recrystallization from ether gave more of the hydroxy-ketone (24 mg.).

*Lithium Reduction under Milder Conditions* (*cf. ref.* 9).—A solution of the methyl ester (VI; R = CO₂Me) (218 mg.) and lithium (130 mg., *ca.* 25 g.-atoms/mole) in dry ether (34 c.c.) and liquid ammonia (85 c.c.) was stirred vigorously for 15 min. Dry ethanol (1 c.c.) was then added during 15 min. When the blue colour had disappeared, water was added, and the mixture was extracted with ether. The ethereal solution was washed with water, dried, and evaporated to a pale yellow oil (140 mg.). The infrared absorption spectrum showed that no reduction of the aromatic ring had occurred; in confirmation of this, no ketonic material could be detected after treatment of the compound with ethanolic hydrochloric acid. Distillation of the crude product gave 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro*-1ξ-*hydroxymethyl*-7-*methoxy*-1ξ : 12β-*dimethylphenanthrene* (VI; R = CH₂·OH), b. p. 140—143°(bath)/0·1 mm. (Found: C, 78·2; H, 9·2. C₁₈H₂₆O₂ requires C, 78·8; H, 9·6%), ν 3356 s, 1241 s, 1036 s, 867 m, 844 m, 813 m cm.⁻¹.

Reduction of the methyl ester, the above alcohol, or of its tetrahydropyranyl ether under more forcing conditions gave essentially the same results, only traces of ketone being detected by infrared absorption after treatment of the reduction product with ethanolic hydrochloric acid. When this procedure was applied to acid B (VI; R = CO₂H), the acid was recovered in high yield, even after treatment with 200-g.-atoms of lithium. Other solvents (tetrahydrofuran and 1 : 2'-dimethoxyethane) were used in some experiments, with the same results.

*Oxidation of the Alcohol* (VI; R = CH₂·OH).—The alcohol (51 mg.) in acetone (3 c.c.) was treated with aqueous 8N-chromic acid (0·1 c.c.). After 5 min., water and ether were added. The usual acid–alkali treatment gave neutral material (27 mg.) which had m. p. 98—100° after recrystallization from ethanol and ν (in CS₂) 2680 w and 1727 s, shoulder at 2860 cm.⁻¹ (aldehyde). The acidic material (8 mg.), after recrystallization from methanol, had m. p. 183—186°, but was shown by comparison of infrared spectra to be the acid (VI; R = CO₂H) (m. p. 192—193·4°). The neutral aldehydic oxidation product (7·6 mg.) was converted into the same acid (3·7 mg.) by oxidation with an excess of 8N-chromic acid. After recrystallization from aqueous methanol this had m. p. 187—191°, and was shown to be identical with an authentic sample by mixed m. p., and by infrared comparison.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*Dodecahydro*-1ξ : 12β-*dimethyl*-7-*oxophenanthrene*-1ξ-*carboxylic Acid* (X; R = CO₂H).—The hydroxy-ketone (X; R = CH₂·OH) (108 mg.), oxidized with 2% chromium trioxide solution under the conditions described for the oxidation of the isomeric hydroxyketone (I; R = CH₂·OH), gave the *keto-acid* (65 mg.). Recrystallized twice from ether, the compound formed elongated plates, m. p. 172—173·5° (Found: C, 73·4; H, 8·7. C₁₇H₂₄O₃ requires C, 73·9; H, 8·8%), ν (in Nujol) 1733 s and 1681 s cm.⁻¹, λ_max. 242 mμ (log ε 4·24).

*Methyl* 1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*Dodecahydro*-1ξ : 12β-*dimethyl*-7-*oxophenanthrene*-1ξ-*carboxylate* (X; R = CO₂Me).—The above crude keto-acid (45 mg.) in dioxan (3 c.c.) was esterified by an excess of ethereal diazomethane. The oil (42 mg.) was chromatographed on deactivated alumina (5 g.). Elution with benzene (40 c.c.) gave the *keto-ester* (25 mg.) which crystallized when scratched (m. p. 96—104°). It crystallized from light petroleum as needles, m. p. 106—107° (Found: C, 74·4; H, 9·0. C₁₈H₂₆O₃ requires C, 74·4; H, 9·0%), λ_max. 243 mμ (log ε 4·21). The *semicarbazone*, recrystallized twice from methanol, had m. p. 208° (Found: C, 65·7; H, 8·3. C₁₉H₂₉O₃N₃ requires C, 65·7; H, 8·4%).

The infrared spectra (in CS₂) of this compound and of the (+)-keto-ester (VIII) from *neo*-abietic acid,⁵ which had m. p. 128—130° (lit., 127—128°), showed considerable differences. The mixed m. p. was considerably lower than the m. p. of either compound.

*Chromic Acid Oxidation of Ester B* (VI; R = CO₂Et) (*cf. ref.*13).—To a solution of ester B (470 mg.) in glacial acetic acid (5 c.c.) were added 2·2 c.c. of a solution of chromium trioxide (2 g.) in 80% acetic acid (10 c.c.). After 18 hr. at room temperature, the solution was diluted with brine and extracted with chloroform. The organic solution was washed with 5% sodium hydroxide solution and water, dried, and evaporated to give a viscous, brown oil (320 mg.). Chromatography on alumina (30 g.) and elution with benzene (200 c.c.) gave starting material

(84 mg.); 3 : 1 benzene–ether (200 c.c.) eluted *ethyl* 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro-7-methoxy*-1ξ : 12β-*dimethyl-9-oxophenanthrene*-1ξ-*carboxylate* (XII) (52 mg.), b. p. 140—145° (bath)/0·05 mm. (Found: C, 72·6; H, 8·1. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%), ν 1725 s, 1686 s, 1245 s, 1034 ms, 873 w, 826 w cm.$^{-1}$, $\lambda_{max.}$ 223, 258, 325 mμ (log ε 4·34, 4·00, 3·45 respectively). Acidification of the alkali washings of the chloroform extracts gave a brown oil (50 mg.), which had a rather broad infrared band at 1725 cm.$^{-1}$ (cf. ref. 13).