Tetrahedron, 1961, Vol. 14, pp. 310 to 319. Pergamon Press Ltd. Printed in Northern Ireland

SYNTHESIS OF DITERPENES—IV[1]

METHYL (±)-DESISOPROPYLDEHYDROABIETATE

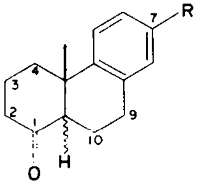
J. A. BARLTROP and A. C. DAY
Dyson Perrins Laboratory, Oxford University

(*Received* 25 *February* 1961)

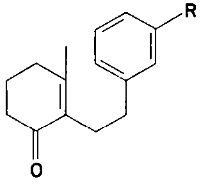
Abstract—The tricyclic ketone (I; R = H) has been synthesized by a new method, and converted into the bromo-ketone (XVII; R = Br). Favorskii rearrangement of the latter gave methyl (±)-desisopropyldehydroabietate (XX).

KETONES of the type I are synthetically readily available from phenethylcyclohexenones (II);[2,3,4] and their obvious potentialities for diterpene synthesis have stimulated work on the conversion of a carbonyl function into characteristic diterpenoid *gem*-groupings.[3,5] Applied to the tricyclic ketone (I; R = H), however, such investigations have led only to the *cis*-fused acids, (III)[6] and its C(1)-epimer.[7]

It is now well known that the introduction of angular groupings into fused systems increases the stability of a *cis*-compound relative to its *trans*-isomer.[8] Thus, although the ketone (IV) is approximately 80 per cent *trans* at equilibrium,[9] the ketone (I; R = Pr^i) from dehydroabietic acid is predominantly *cis* (ca. 60 per cent).[10] The



I



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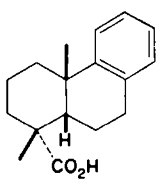

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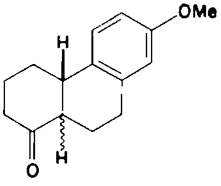
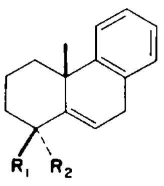


IV



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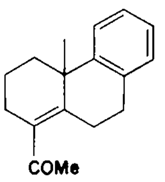

VI

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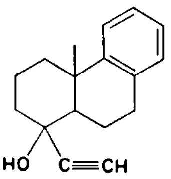
[1] Part III: D. B. Bigley, N. A. J. Rogers and J. A. Barltrop, *J. Chem. Soc.* 4613 (1960).
[2] G. Stork and A. Burgstahler, *J. Amer. Chem. Soc.* **73**, 3544 (1951).
[3] N. N. Saha, P. N. Bagchi and P. C. Dutta, *Chem. & Ind.* 1143 (1954).
[4] N. N. Saha, P. N. Bagchi and P. C. Dutta, *J. Amer. Chem. Soc.* 77, 3408 (1955).
[5] W. Parker and R. A. Raphael, *J. Chem. Soc.* 1723 (1955); U. R. Ghatak, N. N. Saha and P. C. Dutta, *Chem. & Ind.* 51 (1957); *J. Amer. Chem. Soc.* **79**, 4487 (1957).
[6] N. N. Saha, B. K. Ganguly and P. C. Dutta, *Chem. & Ind.* 412 (1956); *J. Amer. Chem. Soc.* **81**, 3670 (1959).
[7] U. R. Ghatak, D. K. Datta and S. C. Ray, *J. Amer. Chem. Soc.* **82**, 1728 (1960).
[8] *Inter al.* R. B. Turner, *J. Amer. Chem. Soc.* **74**, 2118 (1952); F. Sondheimer and D. Rosenthal, *Ibid.* **80**, 3995 (1958); H. E. Zimmerman and A. Mais, *Ibid.* **81**, 3644 (1959); E. Wenkert and J. W. Chamberlin, *Ibid.* **81**, 688 (1959).
[9] A. J. Birch, H. Smith and R. E. Thornton, *J. Chem. Soc.* 1339 (1957).
[10] D. Arigoni, J. Kalvoda, H. Heusser, O. Jeger and L. Ruzicka, *Helv. Chim. Acta* **38**, 1857 (1955).

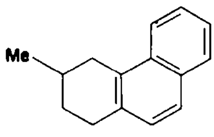
formation of *cis*-acids from the ketone (I; R = H) is therefore not surprising, for neither route[6,7] eliminates the ambiguity of configuration at C(11).

The aim of the present work was the conversion of the ketone (I; R = H) into a tricyclic acid, structurally and sterically analogous to the resin acids, by a route which should be free from this limitation. A suitable intermediate would be of the type V in which the presence of the angular methyl group would ensure formation of a *trans* ring-junction on hydrogenation.[11]

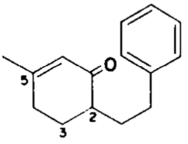
Having shown that methylation of acetylcyclohexene with methyl iodide and potassium t-butoxide gives 1-acetyl-1-methylcyclohex-2-ene, we considered it feasible to prepare the 1,1-disubstituted compound (V; R_1 = Ac, R_2 = Me) by alkylation of an unsaturated ketone (VI) which we expected to obtain *via* the ethynyl alcohol (VII) from the ketone (I; R = H). There was precedent[12] for assuming the stereostructure (V; R_1 = Ac, R_2 = Me) for the alkylation product.



VII



VIII



IX

Condensation of the potassium derivative of 1-methoxy-5-methylcyclohexa-1,4-diene with phenethyl bromide in liquid ammonia and subsequent acid treatment (*cf.* refs. 13 and 14) gave an oil which analysed correctly for the desired cyclohexenone (II: R = H), and from which the 2,4-dinitrophenylhydrazone of this ketone could be obtained. However, the presence of an isomeric impurity (*vide infra*) was indicated by infra-red comparison with the authentic compound (II; R = H) obtained by the method of Saha *et al.*[3,4] Cyclization of the mixture with phosphoric acid gave an oily hydrocarbon C_{15}-H_{16} (9 per cent yield based on the phenethyl bromide) and the ketone (I; R = H; 13 per cent), identical in all respects with a sample prepared from the pure cyclohexenone (II; R = H). Although the yield of the tricyclic ketone was low, this method was preferred to the published procedures[2,3,4] because of its brevity.

The oily hydrocarbon, which gave a picrate (m.p. 104·5–105·5°), is formulated as 1,2,3,4-tetrahydro-3-methylphenanthrene (VIII) on the basis of its naphthalenic absorption spectrum and its dehydrogenation to 3-methylphenanthrene (m.p. 61–62°; picrate, m.p. 137–138°).[15] The hydrocarbon was presumably formed by cyclodehydration of a 5-methyl-2-phenethylcyclohexenone (as IX): the latter thus becomes a possible structure for the isomeric impurity in the crude cyclohexenone (II; R = H) as obtained by our method. Since comparable amounts of the two compounds, II

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[11] P. N. Rao and K. Raman, *Tetrahedron* **4**, 294 (1958) and refs therein cited.

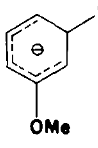
[12] G. Stork and J. W. Schulenberg, *J. Amer. Chem. Soc.* **78**, 250 (1956).

[13] A. J. Birch, *J. Chem. Soc.* 1551 (1950).

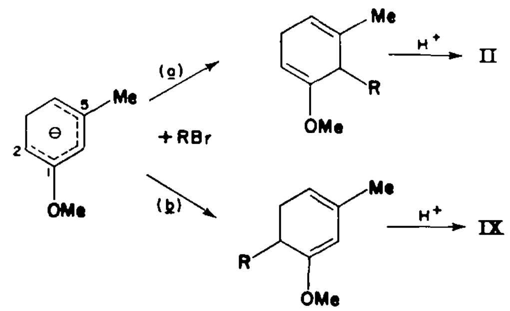
[14] A. J. Birch and H. Smith, *J. Chem. Soc.* 1887 (1951).

[15] The compound was originally supposed to be 1,2,3,4-tetrahydro-1-methylphenanthrene, which might have been formed by cyclodehydration of the unsaturated ketone (II; R = H); but it was clearly shown to be different from this compound and also from the 2- and 4-methyl isomers by the melting point data which have been recorded by W. E. Bachmann and his co-workers, *J. Amer. Chem. Soc.* **62**, 2219 (1940); *J. Org. Chem.* **12**, 876 (1947); **13**, 297 (1948); **15**, 1119 (1950); *cf.* S. M. Mukherji and N. K. Bhattacharyya, *Ibid.* **17**, 1202 (1952).

(R = H) and IX, were apparently produced in the alkylation of 1-methoxy-5-methylcyclohexa-1,4-diene, it is supposed that the dienate anion is susceptible to electrophilic attack at C(6) and C(2) at comparable rates (Paths *a* and *b* below). A possible alternative to Path *b* is the prototropic tautomerism[13] of the dienate anion to the anion (X), which should give rise by alkylation and subsequent hydrolysis to the Δ^2-isomer of IX. This explanation may be preferred, since it is normally the *central* carbon atom which suffers electrophilic attack in such mesomeric dienate systems.[13]

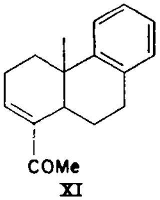


X

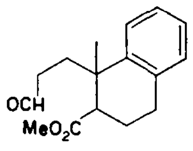


The ketone (I; R = H) is extremely unreactive; and treatment with lithium acetylide in liquid ammonia under very vigorous conditions[16] gave the ethynyl alcohol (VII) in only 40 per cent yield. Several other ethynylation techniques, which are described in the Experimental Section, were found to be even less satisfactory.

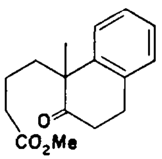
When treated with boiling formic acid, the ethynyl alcohol was converted in 50 per cent yield into an $\alpha\beta$-unsaturated ketone which had ν 1670 and 1355 cm^{-1} ($CH_3{\cdot}CO{\cdot}C{=}C$). This was shown to be an isomer (XI) of the required compound (VI) by its ultra-violet absorption maximum at 234 mμ (log ε 3·94) (*cf.* acetylcyclohexene[17] which has λ_{max} 232 mμ, log ε 4·10): one would predict λ_{max} 254 mμ for the ketone (VI). The possibility that the product actually had the structure VI, and that the conjugated carbonyl band was shifted by as much as 20 mμ by overlap with the aromatic K-band at 216 mμ (log ε 4·03) was intrinsically unlikely, and could be discounted because a subtraction curve of the ultra-violet spectrum of the saturated ketone (I; R = H) from that of our product had λ_{max} 235 mμ (log $\Delta\varepsilon$ 3·93). Finally, chemical proof of the position of the ethylenic bond was obtained by Castells and Meakins' degradative procedure.[18] Treatment with osmium tetroxide followed by lithium aluminium hydride gave a hydroxylated product which underwent fission with lead tetraacetate to give an aldehydo-acid. Both the aldehydo-acid and the corresponding methyl ester (XII),



XI



XII



XIII

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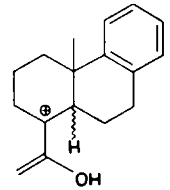
[16] *cf.* P. A. Robins and J. Walker, *J. Chem. Soc.* 3249 (1956).

[17] A. E. Gillam and E. S. Stern, *An Introduction to Electronic Absorption Spectroscopy* (2nd Ed) p. 278. Arnold, London (1957).

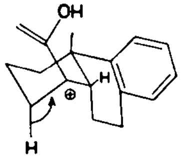
[18] J. Castells, Ph.D. Thesis, Manchester University (1955); J. Castells and G. D. Meakins, *Chem. & Ind.* 248 (1956).

ν 2857 (aldehydic CH) and 1739 cm^{-1} (aldehydic and ester C=O groups), gave positive Schiff tests. The isomeric ketone (VI) would have been converted into a *keto*-ester (XIII) by this sequence of reactions.

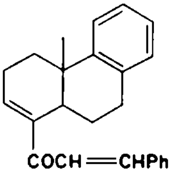
The formation from the ethynyl alcohol of the $\Delta^{1(2)}$-ketone (XI) rather than the isomer (VI) with the tetrasubstituted ethylenic bond has not been satisfactorily explained. It may imply that the angular hydrogen atom is unfavourably disposed for elimination from some cationic intermediate in the rearrangement, such as XIV,[19] i.e.



XIV



XIV A

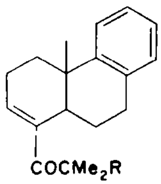


XV

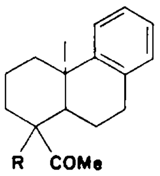
that the C(11)—H bond and the trigonal, positive centre of XIV are very nearly coplanar. This situation is possible only if the intermediate (XIV) is *cis*-fused and in the conformation XIV A. The axial hydrogen atom at C(2) would then be preferentially eliminated as a proton. The further implication would be that the AB-ring-fusion is *cis* in both the unsaturated ketone (XI) and its acetylenic precursor (VII).

In spite of the failure of the projected stereospecific synthesis at this stage, it was of interest to study the alkylation of the ketone (XI). With methyl iodide and either sodium t-amylate in benzene or potassium t-butoxide in t-butanol, no 1,1-disubstituted compound was obtained, the sole product being an $\alpha\beta$-unsaturated ketone (λ_{max} 229 mμ, ν 1674 cm^{-1}). Methylation had evidently occurred at the methyl group rather than C(1); for the infra-red band of the parent (XI) at 1355 cm^{-1} (CH_3 adjacent to C=O) had disappeared, and the compound did not react with benzaldehyde under conditions which converted XI into its benzylidene derivative (XV). These observations, together with the elementary analysis, indicate that the substance is either the t-butyl (XVI; R = Me) or the isopropyl (XVI; R = H) ketone.

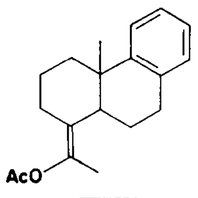
The Favorskii rearrangement has potential uses in diterpenoid synthesis as a method of introducing *gem*-groupings,[20,21] and the following reactions, which were also expected to establish the stereochemistry of the unsaturated ketone (XI), are illustrative.



XVI



XVII



XVIII

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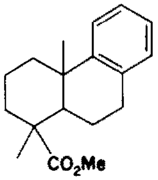
[19] M. S. Newman, *J. Amer. Chem. Soc.* **75**, 4740 (1953); *cf.* M. F. Ansell, J. W. Hancock and W. J. Hickinbottom, *J. Chem. Soc.* 911 (1956).

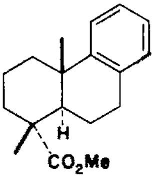
[20] Since the appearance of our preliminary communication, *Chem. & Ind.* 1450 (1959), G. Stork and I. J. Borowitz, *J. Amer. Chem. Soc.* **82**, 4307 (1960), have drawn further attention to applications of this type.

[21] For a steroidal example see N. L. Wendler, R. P. Graber and G. G. Hazen, *Tetrahedron* **3**, 144 (1958).

Reduction of the unsaturated ketone (XI) with sodium in liquid ammonia followed by reoxidation of some hydroxylic material gave the saturated ketone (XVII; R = H) in 82 per cent yield. The corresponding enol acetate (XVIII) was obtained by treatment with acetic anhydride and toluene-*p*-suiphonic acid, and converted into the bromo-ketone (XVII; R = Br) by reaction with hypobromous acid. The enol acetate and the bromo-ketone were not purified, since their infra-red spectra provided adequate confirmation of the structures assigned to them. The bromo-ketone underwent the Favorskii rearrangement when heated with methanolic sodium methoxide (*cf.* ref. 21) to give a mixture of methyl esters (ca. 45 per cent). By-products were the ketone (XVII; R = H) (ca. 10 per cent), which must have been present in the crude bromo-ketone, and some hydroxy-ketonic material. Rechromatography of the mixture of esters gave semi-solid fractions, from which a compound $C_{18}H_{24}O_2$, m.p. 114–115°, was isolated in very low yield by recrystallization from light petroleum.



XIX



XX

At this time, only three of the four possible racemic esters (XIX) had been described,[6,22] the unknown stereoisomer being methyl (±)-desisopropyldehydroabietate (XX). The melting point of our product showed that it was not identical with any of the known esters. In order to compare it with the known (±)-desisopropyldehydroabietic acid,[7] we hydrolysed the ester, but were unable to obtain a crystalline acid because of contamination of the material with oxidation products of the solvent (ethylene glycol). However, a minute sample of Ghatak's desisopropyldehydroabietic acid, m.p. 174–175°, was successfully converted into a methyl ester by the use of diazomethane. After sublimation, this had m.p. 115° undepressed by admixture with the Favorskii product.[23]

Since the *trans*-ester (XX) was obtained from the bromo-ketone only in very low yield (ca. 3 per cent) and since much uncrystallizable material was concomitantly produced, it is unjustifiable to conclude that the unsaturated ketone (XI) has a *trans* ring-junction. It need only have contained a very small proportion of the 11α-isomer, or even of the compound VI, the presence of which in trace quantity would not have been revealed by ultra-violet spectroscopy. In the latter case, sodium-ammonia reduction would presumably have given at least some 11α-material. The possible persistence of traces of isomeric impurity through several steps is understandable in view of the fact that, with the exception of the final product, all the compounds encountered in this work were oils.

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[22] Ref. 7 and refs therein cited.

[23] Methyl (±)-desisopropyldehydroabietate has very recently been synthesized by a different route by E. Wenkert and A. Tahara, *J. Amer. Chem. Soc.* **82**, 3229 (1960).

EXPERIMENTAL*

1-*Acetyl*-1-*methylcyclohex*-2-*ene*

A solution of 1-acetylcyclohexene (10 g) and potassium t-butoxide (from 9·6 g metal) in dry t-butanol (250 ml) was stirred and warmed gently under nitrogen for 15 min. With constant stirring and passage of nitrogen, the solution was treated dropwise with methyl iodide (70 g) at 0°, and then kept at room temp for 2½ hr. The precipitated potassium iodide was collected, and its aqueous solution extracted with ether. The dried ethereal extract was combined with the filtered reaction mixture and distilled to give 1-*acetyl*-1-*methylcyclohex*-2-*ene* (3·7 g), b.p. 58–67°/10 mm, n_D^{14} 1·4668. (Found: C, 77·8; H, 10·3. $C_9H_{14}O$ requires: C, 78·2; H, 10·2%). The *semicarbazone*, recrystallized twice from methanol, had m.p. 136°. (Found: C, 61·4; H, 8·7; N, 21·6. $C_{10}H_{17}ON_3$ requires: C, 61·5; H, 8·8; N, 21·5%).

3-*Methyl*-2-*phenethylcyclohex*-2-*enone* (II; R = H)

The ketone was obtained by Stork and Burgstahler's method[2] as a pale yellow oil, b.p. 118–120°/0·1 mm. (Found: C, 84·3; H, 8·5. Calc. for $C_{15}H_{18}O$: C, 84·1; H, 8·4%). Prepared by the method, of Saha *et al.*,[3,4] it had b.p. 110–117°/0·1 mm, n_D^{18} 1·5525. (Found: C, 84·4; H, 8·5%) and slowly solidified at room temp. The 2,4-dinitrophenylhydrazone had m.p. 172° (lit.,[4] 172°), the semicarbazone m.p. 183–184° (lit.,[2] 185°).

1,2,3,4,9,10,11,12-*Octahydro*-12-*methyl*-1-*oxophenanthrene* (I; R — H)

(A) Obtained from the preceding compound by treatment with phosphoric acid at 150–155° (ref. 4), the ketone had, after two distillations, b.p. 115–120°/0·7 mm, n_D^{18} 1·5643, λ_{max} 266, 273, inflexion at 290 mμ (log ε 2·69, 2·64, 1·74, respectively). (Found: C, 84·4; H, 8·7. Calc. for $C_{15}H_{18}O$: C, 84·1; H, 8·5%). The semicarbazone had m.p. 225–227° (lit.,[2] 227–228°).

(B) A solution of 1-methoxy-5-methylcyclohexa-1,4-diene[24] (100 g) and potassium amide (from 44 g metal) in liquid ammonia (2·5 l.) was stirred for 20 min, and then treated dropwise over 2 hr with phenethyl bromide (100 g) in dry ether (200 ml). The mixture was stirred for 2 hr, then treated with ammonium chloride (100 g), followed by water (2·5 l.). Isolation with ether gave an oil which was heated under reflux with 2 N sulphuric acid (200 ml) for 2 hr. The product was extracted with ether, washed with 10% sodium carbonate solution and then with water, dried and distilled. The fraction of b.p. 102–112°/0·05 mm gave, on redistillation, an oil (54 g), b.p. 124–130°/0·3 mm, n_D^{17} 1·5512. (Found: C, 83·8; H, 8·3%). There were significant differences between the infra-red spectrum of this product and that of 3-methyl-2-phenethylcyclohex-2-enone (II; R = H). However, when treated with Brady's reagent, the product gave the 2,4-dinitrophenylhydrazone (m.p. and mixed m.p. 172°) of the latter ketone.

The oil (53 g) was treated with phosphoric acid under the conditions used in (A) above, and then twice distilled at 0·05 mm to give an oil (31 g), n_D^{18} 1·5860. Its infra-red spectrum showed all the bands which were present in the spectrum of authentic octahydro-12-methyl-1-oxophenanthrene, and several additional bands due to impurities. Chromatography of a portion (960 mg) on alumina (60 g) and elution with light petroleum (350 ml) gave fraction 1 (360 mg) which was non-ketonic. Elution with 1:1 light petroleum–benzene (200 ml) gave the tricyclic ketone (I; R = H; 480 mg), the infra-red spectrum of which was identical with that of the authentic ketone. The semicarbazone prepared from this specimen had m.p. 225–227°. Further elution with the same solvent (150 ml) gave an unidentified saturated ketone (60 mg), which was unaffected by treatment with ethanolic sodium ethoxide.

Fraction 1 (2·03 g), from a similar chromatogram, was rechromatographed on alumina (100 g). Elution with light petroleum (b.p. 40–60°; 200 ml) gave, after distillation, 1,2,3,4,-*tetrahydro*-3-*methylphenanthrene* (VIII; 1·64 g) as an oil, b.p. 155° (bath)/13 mm, n_D^{19} 1·6110, ν 815, 792, 767, 745 cm^{-1}, λ_{max} 229, 274·5, 280, 291, 307·5, 314, 321·5 mμ (log ε 4·99, 3·74, 3·77, 3·67, 3·03, 2·82, 2·96, respectively). (Found: C, 91·9; H, 8·1. $C_{15}H_{16}$ requires: C, 91·8; H, 8·2%). The *picrate*, orange-yellow needles from ethanol, had m.p. 104·5–105·5°. (Found: C, 59·1; H, 4·3; N, 9·5. $C_{21}H_{19}O_7N_3$

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* Ultra-violet spectra were measured for ethanol solutions, infra-red spectra for liquid films. Melting points were taken 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°.

[24] A. J. Birch, *J. Chem. Soc.* 593 (1946).

requires: C, 59·3; H, 4·5; N, 9·9%). Further elution with light petroleum (100 ml) gave an intermediate fraction (198 mg) and then (with 300 ml solvent) *3-methyl-2-phenethylanisole* (198 mg), b.p. 153° (bath)/13 mm, n_D^{18} 1·5636, ν 1255 (s), 1034 (m), 803 (m), 772 (m), 696 (s) cm^{-1}, λ_{max} 275, 280 mμ (log ε 3·41, 3·40 respectively). (Found: C, 84·7; H, 7·9. $C_{16}H_{18}O$ requires: C, 84·9; H, 8·0%).

The tricyclic ketone (I; R = H) obtained by this method (B) was not in general purified chromatographically, since its contaminants were easily removed during the purification of the ethynylation product (VII).

Dehydrogenation of the tetrahydromethylphenanthrene (VIII)

The above hydrocarbon (1 g) was heated under nitrogen with 5% palladized charcoal at 300° for 1 hr. Chromatography on alumina (50 g) and elution with light petroleum (b.p. 40–60°; 100 ml) gave a mixed fraction (126 mg) containing much starting material; further elution with this solvent (150 ml) gave 3-methylphenanthrene (736 mg), which, after three recrystallizations from ethanol, had m.p. 57·5–60° (lit.,[25] 62–63°), λ_{max} 252, 276·5, 284, 295·5, 317·5, 324·5, 332, 340, 347·5 mμ (log ε 4·91, 4·19, 4·06, 4·17, 2·57, 2·52, 2·75, 2·54, 2·81, respectively). The picrate, orange yellow needles from ethanol, had m.p. 137–138° (lit.,[25] 137–138°). (Found: C, 60·2; H, 3·6; N, 10·2. Calc. for $C_{21}H_{15}O_7N_3$: C, 59·9; H, 3·6; N, 10·0%). The picrate was dissolved in benzene and adsorbed on an alumina column. Benzene eluted 3-methylphenanthrene, which was obtained as needles, m.p. 61–62°, after two recrystallizations from ethanol.

1-*Ethynyl*-1,2,3,4,9,10,11,12-*octahydro*-1-*hydroxy*-12-*methylphenanthrene* (VII)

(A) Lithium (4·2 g) was dissolved in liquid ammonia (500 ml) through which a rapid stream of dry, acetone-free acetylene was being passed, and the solution was placed in a cooled steel bomb (capacity ca. 1 l.) together with the crude tricyclic ketone (I; R = H; 8·5 g) in dry tetrahydrofuran (200 ml). The mixture was saturated with acetylene at −60° (ca 1 hr); then the bomb was sealed and shaken at room temp for 46 hr. After being cooled to −60°, the bomb was opened and its contents were treated with brine and ether. The oily product (6·9 g), which was isolated with ether, was chromatographed on deactivated alumina (500 g). Elution with 9:1 light petroleum–benzene (1·5 l.) gave non-ketonic material (2·85 g) (the impurities in the starting material); further elution with the same solvent mixture (2 l.) gave the pure ketone (I; R = H; 0·58 g), and then (with 0·5 l. solvent) a mixed fraction (0·09 g). Elution with 1:1 light petroleum–benzene (3·5 l.) gave the *ethynyl alcohol* (VII; 1·90 g) as a viscous oil, ν 3521 and 3430 (OH), and 3295 cm^{-1} ($\equiv$CH). (Found: C, 84·6; H, 8·5. $C_{17}H_{20}O$ requires: C, 85·0; H, 8·4%).

(B) Solutions of (i) the crude tricyclic ketone (12·3 g) in dry ether (200 ml), and (ii) potassium (50 g) in dry t-amyl alcohol (800 ml) and dry ether (250 ml) were simultaneously added dropwise over 1¼ hr to dry ether (200 ml) cooled to −5° to 0°, saturated with dry, acetone-free acetylene and vigorously stirred. Passage of acetylene was continued during the addition and for a further 24 hr, during which time the solution was vigorously stirred at room temp. After the addition of brine (500 ml), the mixture was acidified with conc hydrochloric acid and extracted with ether. Evaporation of the dried organic solution gave a dark oil which was dissolved in 95% ethanol (200 ml) and treated with a 5% solution of silver nitrate in 95% ethanol (50 ml). The precipitated silver derivative, m.p. 118–122°, was washed with ethanol and ether. The filtrate and washings were poured into brine, and the oil, which was collected with ether, was treated with silver nitrate solution as before. The silver derivative (3·1 g) was heated under reflux with sodium cyanide (15 g), water (150 ml) and ethanol (10 ml) for 2½ hr. Extraction with ether gave the crude ethynyl alcohol (1·25 g), shown by its infra-red spectrum to be free from starting material.

Less vigorous ethynylating conditions (excesses of lithium acetylide in liquid ammonia or in mixtures of liquid ammonia and ether; ethynylmagnesium bromide in tetrahydrofuran) were without effect on the ketone. In an experiment using lithium acetylide in boiling ether, the silver derivative of the ethynyl alcohol was isolated in very low yield. Extensive decomposition occurred with lithium acetylide in boiling dioxan and no product could be obtained. These reactions were followed by infrared spectroscopy, and by the testing of samples with a 5% solution of silver nitrate in 95% ethanol.

[25] R. D. Haworth, *J. Chem. Soc.* 1132 (1932).

1-*Acetyl*-3,4,9,10,11,12-*hexahydro*-12-*methylphenanthrene* (XI)

The ethynyl alcohol (VII; 1·71 g) was heated under reflux with 90% formic acid (50 ml) and ethanol (5 ml) for 2½ hr. The reaction mixture was poured into 10% sodium bicarbonate solution and extracted with ether. The ethereal solution was washed with bicarbonate solution, dried and evaporated. Chromatography of the viscous residue (1·66 g) on deactivated alumina (300 g) and elution with light petroleum (700 ml) gave an oil (60 mg), ν 3290 (≡CH) and 2110 cm^{-1} (C≡C); further elution (with 700 ml) gave mixed fractions (440 mg), and then (with 1400 ml) the *unsaturated ketone* (XI; 637 mg) as a viscous oil, b.p. 108–111° (bath)/0·04 mm, n_D^{17} 1·5740, λ_{max} 216, 234 mμ (log ε 4·03, 3·94 respectively). (Found: C, 85·1; H, 8·3. $C_{17}H_{20}O$ requires: C, 85·0; H, 8·4%). The orange-yellow 2,4-*dinitrophenylhydrazone*, recrystallized twice from ethanol–ethyl acetate, had m.p. 209–213°. (Found: C, 65·2; H, 5·9. $C_{23}H_{24}O_4N_4$ requires: C, 65·7; H, 5·8%). Rechromatography of the mixed fractions (440 mg) gave an unidentified oil (74 mg), ν 1717 cm^{-1}, and the acetylhexahydromethylphenanthrene (250 mg).

The ketone was obtained in 8% yield when phosphoric oxide in benzene was used to effect the rearrangement.

Oxidative degradation of the unsaturated ketone (XI)

A solution of the ketone (XI; 23 mg) and osmium tetroxide (ca. 35 mg) in dry ether (3 ml) and dry pyridine (0·1 ml) was boiled for 1 hr, and then left overnight at room temp. The reagents were removed at 100° *in vacuo*, and the residue was heated under reflux with pure tetrahydrofuran (5 ml) and lithium aluminium hydride (ca. 200 mg) for ½ hr. The excess of lithium aluminium hydride was decomposed with ethyl acetate, and water was added. The viscous product (24 mg), which was isolated with chloroform, had ν 3390 (OH) and 1709 cm^{-1} (w) (satd ketone).

A solution of the hydroxylated material and lead tetra-acetate (100 mg) in acetic acid (4 ml) was set aside at room temp for 12 hr, then evaporated at 100°/0·05 mm. After the addition of water, the product (29 mg) was isolated with ether. The infra-red spectrum indicated the presence of CO_2H and CHO. A portion (10 mg), dissolved in pure dioxan (0·5 ml), gave a positive Schiff test.

The remainder (19 mg) in dry ether (1·5 ml) was esterified with ethereal diazomethane, then chromatographed on deactivated alumina (3 g). Elution with ether (15 ml) gave the ester (XII) as a viscous oil (12 mg): ν 2857 (aldehydic CH) and 1739 cm^{-1} (aldehydic and ester C=O groups): Schiff test positive.

Simultaneously with the Schiff tests carried out in this experiment, blank tests were done on the dioxan used as solvent: these gave only very faint pink colorations after standing for several minutes.

Condensation of the ketone (XI) *with benzaldehyde*

The ketone (XI; 190 mg) was heated under reflux in ethanol (2 ml) with benzaldehyde (0·08 ml) and potassium hydroxide (25 mg) for ½ hr. The dark solution was diluted with water, acidified with dil hydrochloric acid and extracted with ether. The ethereal solution was washed with saturated sodium bisulphite solution and then with water, dried and evaporated. Chromatography of the residue on deactivated alumina (25 g) and elution of the yellow band with 4:1 light petroleum–benzene (135 ml) gave 1-*cinnamoyl*-3,4,9,10,11,12-*hexahydro*-12-*methylphenanthrene* (XV; 112 mg) as a yellow glass which, after drying at 80° *in vacuo*, had λ_{max} 227, 297 mμ (log ε 4·03, 4·20 respectively). (Found: C, 87·7; H, 7·4. $C_{24}H_{24}O$ requires: C, 87·8; H, 7·4%).

Methylation of the unsaturated ketone (XI)

A mixture of the ketone (XI; 320 mg), methyl iodide (8 ml) and 16 ml of a 0·8 M solution of sodium t-amylate in benzene was set aside under nitrogen at room temp for 1½ hr. After dilution with water and acidification, the product was isolated with ether and chromatographed on deactivated alumina (20 g). Elution with 9:1 light petroleum–benzene (80 ml) gave an *αβ-unsaturated ketone* (140 mg) which, after distillation, was obtained as a pale yellow oil, b.p. 115° (bath)/0·05 mm, λ_{max} 229 mμ ($E_{1cm}^{1\%}$ 209), ν 1674 cm^{-1}. (Found: C, 85·2; H, 9·1. $C_{19}H_{24}O$ requires: C, 85·0; H, 9·0. $C_{20}H_{26}O$ requires: C, 85·1; H, 9·3%). Attempts to prepare a 2,4-dinitrophenylhydrazone were unsuccessful.

Similar results were obtained by the use of potassium t-butoxide in t-butanol as basic reagent.

The ketone was unaffected (almost quantitative recovery) by treatment with benzaldehyde and ethanolic potassium hydroxide under the conditions used for the preparation of the benzylidene derivative (XV).

1-Acetyl-1,2,3,4,9,10,11,12-octahydro-12-methylphenanthrene (XVII; R = H)

Sodium (110 mg, 3 g atoms) was added with swirling to a solution of the unsaturated ketone (XI; 368 mg) in dry ether (10 ml) and liquid ammonia (25 ml). After 15 min, the solution was treated with sufficient ammonium chloride to destroy the blue colour. After the addition of water, extraction with ether gave an oil (368 mg), ν 3448 (OH) and 1700 cm^{-1} (satd ketone), which was dissolved in acetic acid (2 ml) and treated with 5·2 ml of a 2% solution of chromium trioxide in acetic acid. After 1 hr at room temp, the product (340 mg) was isolated by dilution with water and extraction with ether, and chromatographed on alumina (30 g). Elution with 1:1 light petroleum–benzene (400 ml) gave the *saturated ketone* (XVII; R = H; 305 mg) as an oil. A portion distilled for analysis had b.p. 107° (bath)/0·15 mm. (Found: C, 84·3; H, 9·2. $C_{17}H_{22}O$ requires: C, 83·9; H, 9·2%).

The enol acetate (XVIII) (*cf.* ref. 26)

A solution of the ketone (XVII; R=H; 240 mg) and toluene-*p*-sulphonic acid (600 mg) in redistilled acetic anhydride (20 ml) was slowly distilled. After 1 hr, fresh acetic anhydride (10 ml) was added to replace that which had been distilled out of the mixture. Similar replacements with fresh acetic anhydride were made at intervals over a further 1½ hr. At the end of this period, the anhydride was removed by distillation, finally at 100°/12 mm. The residue was dissolved in ether, and the solution was washed with ice-cold 5% sodium hydroxide solution and then with water, dried and evaporated to give the enol acetate (290 mg) as a dark brown oil, ν 1750 and 1208 cm^{-1} (enol acetate): no infra-red bands due to ketone or $\rangle C{=}CH_2$.

Attempts to prepare the compound using acetic anhydride and perchloric acid in carbon tetrachloride solution[27] failed.

1-Acetyl-1-bromo-1,2,3,4,9,10,11,12-octahydro-12-methylphenanthrene (XVII; R = Br) (*cf.* ref. 28)

Solutions of (i) the crude enol acetate (XVIII; 332 mg) in dry t-butanol (10 ml), and (ii) N-bromosuccinimide (220 mg, 1·05 mol) in t-butanol (20 ml) and N sulphuric acid (11 ml) were mixed and set aside in the dark for 3 hr at room temp. The solution was treated with saturated sodium bisulphite solution, diluted greatly with water and extracted with ether. The ethereal solution was washed with 5% sodium hydroxide solution and then with water, dried and evaporated to give the crude bromo-ketone (XVII; R = Br; 300 mg) as a dark brown oil, ν 1700 and 1351 cm^{-1} (methyl ketone): positive Beilstein test (Br).

Favorskii rearrangement of the bromo-ketone (XVII; R = Br)

The bromo-ketone (300 mg) was heated under reflux for 6 hr with a solution of sodium methoxide (from 1 g sodium metal) in dry methanol (30 ml). After removal of most of the methanol by distillation, water and ether were added, and the organic material was separated into neutral (195 mg) and acidic (49 mg) fractions by the usual acid-alkali treatment. The acidic material was esterified with diazomethane to give a second neutral fraction. The combined neutral products (238 mg), which gave a faint Beilstein test, were chromatographed on deactivated alumina (50 g). Light petroleum (350 ml) eluted oils (98 mg), ν 1727 and 1245 cm^{-1} (carboxylic ester); 19:1 light petroleum–benzene (100 ml) gave a mixed fraction (10 mg) which was combined with the earlier fractions for rechromatography. Further elution with the same solvent mixture (150 ml) gave the ketone (XVII; R = H; 29 mg). Stronger solvents eluted oily material (33 mg) which was shown by its infra-red spectrum to contain OH and C=O.

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[26] C. W. Marshall, T. H. Kritchevsky, S. Liebermann and T. F. Gallagher, *J. Amer. Chem. Soc.* **70**, 1837 (1948).

[27] D. H. R. Barton, R. M. Evans, J. C. Hamlet, P. G. Jones and T. Walker, *J. Chem. Soc.* 747 (1954).

[28] H. V. Anderson, E. R. Garrett, F. H. Lincoln, A. H. Nathan and J. A. Hogg, *J. Amer. Chem. Soc.* **76**, 743 (1954); B. J. Magerlein, D. A. Lyttle and R. H. Levin, *J. Org. Chem.* **20**, 1709 (1955).

The ester-containing fractions (108 mg) from the previous chromatogram were rechromatographed on "Grade H" alumina (10 g). Elution with 4:1 light petroleum-benzene (170 ml) gave an oil (52 mg) which solidified slowly; then 1:2 light petroleum-benzene (30 ml) eluted more acetyloctahydromethylphenanthrene (5 mg). The semisolid product gave plates (9 mg), m.p. 113–115°, after two recrystallizations from light petroleum (b.p. 40–60°). After filtration in light petroleum solution through charcoal and a third recrystallization from the same solvent, *methyl* (±)-*desisopropyldehydroabietate* (XX; 6·3 mg) was obtained as plates, m.p. 114–115°. (Found: C, 79·1; H, 8·7. $C_{18}H_{24}O_2$ requires: C, 79·4; H, 8·9%). The m.p. was undepressed by admixture with an authentic sample of the ester (m.p. 115°) prepared from (±)-desisopropyldehydroabietic acid (*vide infra*).

Correlation of the ester (XX) *with Ghatak's* (±)-*desisopropyldehydroabietic acid*[7]

(A) The ester (4·0 mg) was heated under reflux for 5 hr with 5 ml of a solution of potassium hydroxide (5 g) in water (3 ml) and ethylene glycol (15 ml), which had previously been boiled until the temp of the liquid reached 150°. Dilution with water, addition of ether, and the usual acid-alkali treatment gave neutral (6·1 mg) and acidic (9·3 mg) fractions. Both fractions must have been contaminated with glycol oxidation products, as crystalline material could be isolated from neither.

(B) Ghatak's (±)-desisopropyldehydroabietic acid (0·25 mg), m.p. 174–175°, in pure tetrahydrofuran (0·1 ml) was esterified with an excess of ethereal diazomethane. Removal of the solvents and reagent *in vacuo* at room temp gave an oil which solidified when scratched (m.p. 100–105°, traces to 115°). Recrystallization of the minute amount of the ester so obtained was impossible, but after sublimation at 93°/0·05 mm, it melted sharply at 115°. The m.p. was undepressed by admixture with methyl (±)-desisopropyldehydroabietate (m.p. 114–115°) prepared by the Favorskii rearrangement.

Acknowledgements—We are grateful to Drs. P. C. Dutta and U. R. Ghatak for a sample of (±)-desisopropyldehydroabietic acid. One of us (A. C. D.) thanks the Department of Scientific and Industrial Research for a Maintenance Allowance, and the Principal and Fellows of Brasenose College, Oxford, for the award of a Senior Hulme Scholarship.