662. *Totarol. Part II.**†

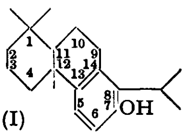
By W. F. Short and H. Wang.

(*With an Appendix on Absorption Spectra,* by J. D. S. Goulden.)

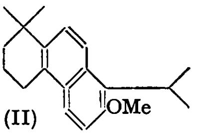
Further investigation of totarol, and particularly of the products of its partial dehydrogenation, indicate that this diterpene resinol is probably 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-7-hydroxy-1 : 1 : 12-trimethyl-8-*iso*propylphenanthrene (I). Its biogenesis is discussed in the light of its divergence from the " isoprene rule."

In Part I,* Short and Stromberg showed that totarol is a tricyclic resinol, $C_{20}H_{30}O$, and affords 7-hydroxy-1-methylphenanthrene and 1-methylphenanthrene on dehydrogenation. Catalytic reduction produced di- and tetra-hydro-compounds and, finally, a hydrocarbon, $C_{20}H_{36}$ (totarane), which was dehydrogenated to a hydrocarbon, $C_{18}H_{18}$, subsequently shown to be 1-methyl-8-*iso*propylphenanthrene (Short and Wang, *J.*, 1950, 991). Totarol afforded a hydrogen phthalate with phthalic anhydride at 140° but resisted dehydration and it was concluded that it contains a secondary alcoholic group. Subsequent oxidation experiments, under a variety of conditions, afforded a number of dimeric compounds but no ketone, and we have now found that totarol is a cryptophenol. The compound does not show a ferric chloride reaction in aqueous or alcoholic solution though it has a very slight but distinct solubility in 15% aqueous sodium hydroxide. The presence of a phenolic group is also indicated by the formation of substitution products, such as bromototarol, bromototaryl methyl ether, 2 : 4-dinitrophenylazototarol, m. p. 201—202°, and formyltotarol (2 : 4-dinitrophenylhydrazone, m. p. 230—231°), the last being obtained from totarol by the Gattermann hydrogen cyanide synthesis. Furthermore, aminototarol, m. p. 166—167°, obtained by the reduction of dinitrophenylazototarol with sodium dithionite, reacts with nitrous acid to give a diazonium salt which couples with β-naphthol in alkaline solution to give a red azo-dye. Spectroscopic data, reported in the Appendix by Dr. J. D. S. Goulden, are in full accord with the chemical evidence.

Ozonisation of totaryl acetate does not yield significant quantities of formaldehyde or acetone, indicating that the molecule does not contain either a terminal methylene group or an *iso*propylidene group, and this is consistent with the concentration of the three double bonds in an aromatic nucleus. The simplest interpretation of the degradation reactions is that totarol is 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-7-hydroxy-1 : 1 : 12-trimethyl-8-*iso*propylphenanthrene (I), and this sturcture is supported by the results obtained by the dehydrogenation of methyl totaryl ether. Vigorous dehydrogenation with selenium affords 7-methoxy-1-methylphenanthrene in high yield, but under milder conditions three other compounds are obtained and may be separated by chromatography on alumina. The proportions in which these compounds (*A*, *B*, and *C*) are produced vary with the experimental conditions, the maximum yields being *A* 31%, *B* 29%, and *C* 17%. *A* (9·5%) and *B* (32%) are also produced by the dehydrogenation of methyl totaryl ether with sulphur. Compound *A* is converted into compound *C* by vigorous dehydrogenation with sulphur, and compound *B* is similarly converted into 7-methoxy-1-methylphenanthrene. Compound *A*, m. p. 109·5—110°, has the formula $C_{20}H_{26}O$, and affords a trinitrobenzene complex, m. p. 151·5—152°; its composition and relation to compound *C* suggest that it is 1 : 2 : 3 : 4-tetrahydro-7-methoxy-1 : 1-dimethyl-8-*iso*propylphenanthrene (II). Compound *B*, $C_{17}H_{20}O$, m. p. 55·5—56°, is evidently produced by elimination of the *iso*propyl group from compound *A*; it affords a picrate, m. p. 105—106°, is demethylated by boiling pyridine hydrochloride to the corresponding phenol, m. p. 134—134·5°, and may be formulated as 1 : 2 : 3 : 4-tetrahydro-7-methoxy-1 : 1-dimethylphenanthrene (III). Evidence for the



(I)



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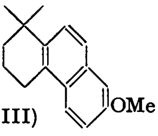

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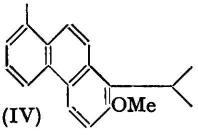

(IV)

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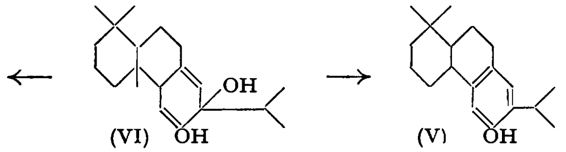
* Part I, *J.*, 1937, 516.

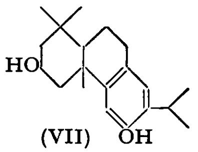
† This paper was presented in abstract at the International Congress of Pure and Applied Chemistry in New York, September, 1951.

attachment of the *iso*propyl group to $C_{(8)}$ in totarol (I) rests on the cryptophenolic properties of the resinol and on the assumption that no alkyl migration occurs during its simultaneous reduction and dehydration to totarane, which affords 1-methyl-8-*iso*propylphenanthrene on dehydrogenation. This is a reasonable assumption, but in view of the fact that the structure assigned to totarol cannot be built up from isoprene units, further experimental justification was desired, and was obtained by examination of compound *C* which still retains the *iso*propyl group. This compound, $C_{19}H_{20}O$, m. p. 144·5—145°, affords a picrate, m. p. 188—189°, and is demethylated by boiling pyridine hydrochloride to a phenol, m. p. 139—140°, which does not couple with 2 : 4-dinitrobenzenediazonium sulphate. We find that 7-hydroxy-1-methylphenanthrene couples readily with diazonium salts, and the failure of the diazo-coupling reaction with the phenanthrol derived from totarol is consistent with the attachment of the *iso*propyl group at position 8 (rather than 6) and therefore with structure (IV) for compound *C*. It was expected that distillation of the phenol with zinc dust would yield 1-methyl-8-*iso*propylphenanthrene but the product obtained was 1-methylphenanthrene, and removal of the hydroxyl group under less energetic conditions was therefore attempted. Unfortunately, the *iso*propyl group is simultaneously eliminated when the phenol is heated at *ca.* 290° with ammonium chloride, sodium acetate, and acetic acid, the resulting acetamido-compound being identical with 7-acetamido-1-methylphenanthrene, m. p. 241—242°, obtained by heating 7-hydroxy-1-methylphenanthrene with the same reagents. We therefore turned our attention to the synthesis of compound *C* by introducing an *iso*propyl group at position 8 in 7-hydroxy-1-methylphenanthrene, the structure of which was established by synthesis (Short, Stromberg, and Wiles, *J.*, 1936, 319). Application of the Gattermann hydrogen cyanide synthesis to 7-methoxy-1-methylphenanthrene affords a methoxy-aldehyde, m. p. 184·5—185·5° (semicarbazone, m. p. 332—334°), demethylated by boiling pyridine hydrochloride to a hydroxy-aldehyde, m. p. 206—207°, which does not couple with dinitrobenzenediazonium sulphate and is therefore regarded as 8-formyl-7-hydroxy-1-methylphenanthrene. This aldehyde is also obtained from 7-hydroxy-1-methylphenanthrene by the Gattermann synthesis, and methylation gives the methoxy-aldehyde, m. p. 184·5—185·5°, which is oxidised by potassium permanganate to 7-methoxy-1-methylphenanthrene-8-carboxylic acid. It was expected that methyl 7-methoxy-1-methylphenanthrene-8-carboxylate, and methylmagnesium iodide would yield 7-methoxy-1-methyl-8-*iso*propenylphenanthrene which could be reduced to compound *C*, but the product of the Grignard reaction is a hydrocarbon, $C_{19}H_{20}$, m. p. 168·5—170°, which may be 1 : 7-dimethyl-8-*iso*propylphenanthrene. Haller and Schaffer (*J. Amer. Chem. Soc.*, 1939, **61**, 2175), Fuson and his collaborators (*J. Org. Chem.*, 1948, **13**, 496 and earlier papers), and Richtzenhain and Nippus (*Ber.*, 1949, **82**, 408 and earlier papers) have recorded the replacement of alkoxyl by alkyl groups by the action of Grignard reagents on sterically hindered aromatic cyanides and ketones. We are examining alternative methods for effecting the final stages of the synthesis of compound *C*.

(I)



(VI) (V)



(VII)

Totarol thus belongs to the group of natural diterpenoids, represented by podocarpic acid, hinokiol, and ferruginol, containing an aromatic nucleus, and it is interesting that three of these compounds occur in the flora of New Zealand. Totarol and podocarpic acid differ from all the diterpenoids whose constitutions have so far been elucidated by breaking the " isoprene rule " : the latter lacks the *iso*propyl group necessary to make up the final isoprene residue, and the aromatic nucleus of totarol is not divisible into isoprene units. It may well be that totarol is derived from a precursor which obeys the " isoprene rule," an *iso*propyl group subsequently migrating at the stage of the phytosynthetic process at which the aromatic system is produced. This step may resemble the santonin–desmotroposantonin rearrangement and the conversion of certain steroid dienones into aromatic compounds, both totarol (I) and ferruginol (V) being produced by dehydration of the hypothetical prototototarol (VI). The natural occurrence of a dihydroxy-compound, hinokiol, probably (VII), may be significant in this connexion.

The reaction of the aromatic nucleus in totarol, podocarpic acid, and ferruginol with 3 mols. of benzoyl hydroperoxide is probably associated with the presence of the hydroxyl group. Fernholtz (*Ber.*, 1951, **84**, 110) has recently shown that some aryl methyl ethers are oxidised by peracids to methyl 2-*o*-carboxyarylacrylates. Totarol consumes only 1·9 mols. of *o*-carboxybenzoyl hydroperoxide in ethereal solution, and totaryl acetate and bromototarol do not react with benzoyl hydroperoxide in chloroform solution.

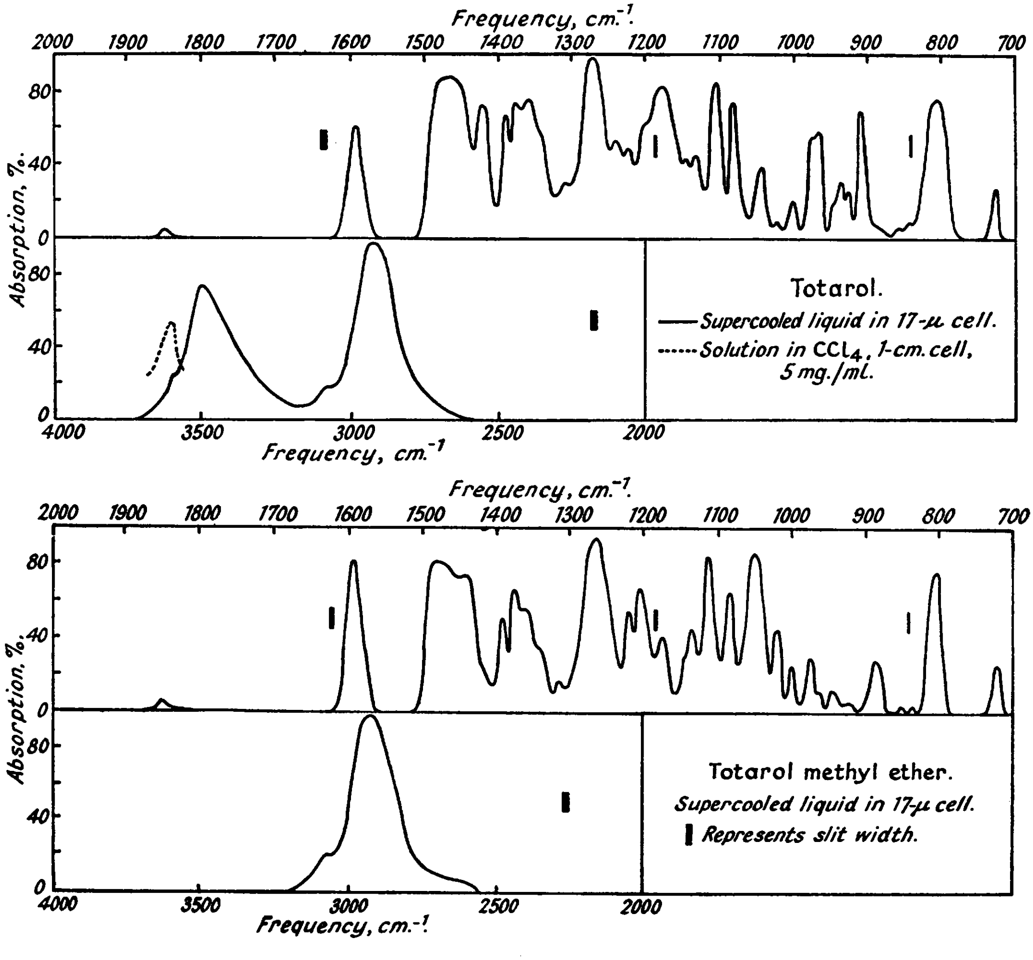
Synthetical work in relation to the suggested formula of totarol and its transformation products is in progress. The stereochemical problem is somewhat simpler than that involved in the synthesis of other diterpenoids, and the hydroaromatic rings probably have the *trans*-relationship.

APPENDIX.

By J. D. S. GOULDEN.

Infra-red Absorption Spectrum.—The infra-red spectrum of totarol shows a strong band due to a hydroxyl stretching frequency at 3500 cm.$^{-1}$ which is raised to 3600 cm.$^{-1}$ on dissolution of the substance in carbon tetrachloride. This small frequency shift with dilution shows that the hydroxyl group is not hydrogen bonded in the liquid state. Phenols which take part in intermolecular hydrogen bonding are known to show a broad bonded-hydroxyl frequency at about 3300 cm.$^{-1}$ in the solid or liquid state. In dilute solution the intermolecular hydrogen bonds of such phenols are broken, so that the spectrum shows only the sharp frequency of the free hydroxyl group at about 3630 cm.$^{-1}$ Coggeshall (*J. Amer. Chem. Soc.*, 1947, **69**, 1620) has shown that the intermolecular hydrogen bonding of phenols can be prevented by steric factors. Chemical evidence shows the presence of an *iso*propyl group on the carbon atom *ortho* to the hydroxyl group. It is this *iso*propyl group which prevents the totarol molecules from aproaching each

FIG. 1.

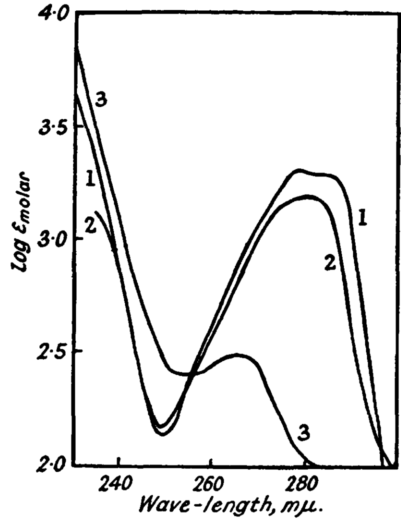


other close enough to form a strong hydrogen bond in the liquid state. In dilute carbon tetrachloride solution, the hydroxyl frequency is still about 30 cm.$^{-1}$ lower than the value usually observed, suggesting that the neighbouring *iso*propyl group still slightly affects the vibrations of the hydrogen atom in the hydroxyl group. Intermolecular forces are no doubt responsible for a lowering of about 130 cm.$^{-1}$ in the value of the hydroxyl stretching frequency shown in the solid state. A small shoulder on the side of the 3500 cm.$^{-1}$ band occurs at 3560 cm.$^{-1}$, showing that some of the totarol molecules in the liquid state are not subject to these forces.

The absence of a strong absorption band in the 1650—1850-cm.$^{-1}$ region of the spectrum shows that the totarol molecule cannot contain a keto-group. The very weak band shown at 1850 cm.$^{-1}$ may be due to an aromatic nucleus in the totarol molecule. Since both totarol and its methyl ether show this band at the same intensity, the totarol band could not be attributed to a small amount of the phenol existing as the keto-tautomer. The strong frequency at 1594 cm.$^{-1}$ is low for a carbonyl group and is again shown by both substances at equal intensity.

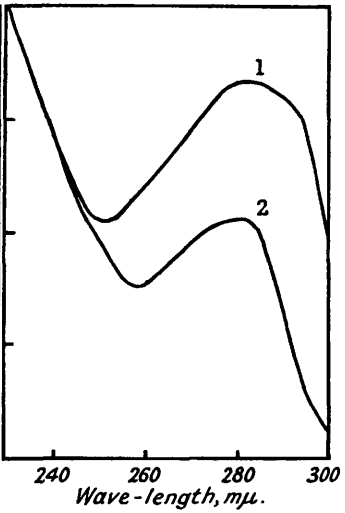
The hydroxyl bonding frequency of totarol shows as a broad band at 1173 cm.$^{-1}$. A skeletal frequency occurs at 1175 cm.$^{-1}$, as shown by the spectrum of the methyl ether, and this cannot be resolved from the strong hydroxyl bending frequency. The ether linkage of the methyl ether appears at 1052 cm.$^{-1}$ and cannot be resolved from the 1045-cm.$^{-1}$ skeletal frequency, as shown by the totarol spectrum. An ether-link frequency of 1052 cm.$^{-1}$ shows that the ether must be either aromatic or unsaturated, whilst the position of the hydroxyl bonding frequency of totarol indicates the presence of either a tertiary alcohol or a phenol. Evidence from other spectral bands shows that an aromatic nucleus is present and the ultra-violet absorption spectra show that the hydroxyl group is phenolic in nature.

FIG. 2.



1, *Totarol.*
2, *Methyl totarol ether.*
3, *Totaryl acetate.*

FIG. 3.



1, *Bromototarol.*
2, *Bromototarol methyl ether.*

A weak band at 3070 cm.$^{-1}$ can be resolved on the higher-frequency side of the C–H stretching frequencies at about 2900 cm.$^{-1}$. This weak band suggests the presence either of an aromatic nucleus or a $C{=}C$ group. The presence of a large number of C–H bonds in the molecule gives rise to a very intense freqency at 2900 cm.$^{-1}$ and makes the resolution of such a weak band difficult. Two strong bands of the aromatic nucleus are evident at 1593 and about 1490 cm.$^{-1}$. It is difficult to resolve the latter band from the intense C–H bending frequencies at 1460 cm.$^{-1}$. Further frequencies of the aromatic nucleus occur below 1300 cm.$^{-1}$, together with the skeletal frequencies of the molecule. Slight differences between the spectra of the two molecules are to be expected in this region of the spectrum. No unconjugated $C{=}C$ double bond frequency is observed at about 1650 cm.$^{-1}$.

The infra-red spectrum of totarol therefore confirms the presence of a phenolic group which is prevented from undergoing intermolecular hydrogen bonding by steric factors. No unconjugated C=C double bonds are present in the molecule, but the presence of methylene and other groups containing C–H bonds is indicated. This structural evidence is in full accord with the formula obtained from the chemical evidence.

Ultra-violet Absorption Spectra.—The presence of an aromatic nucleus in a molecule usually gives rise to three close absorption maxima in the 250—275-mμ. region. These bands are not always resolved into the separate components, and the molar extinction values are generally about 200. A phenolic ring, however, gives rise to a more intense maximum at a higher wavelength. Such behaviour is shown by totarol and its acetate, as shown by the absorption curves of Fig. 2. This behaviour is parallel to that of phenol and its derivatives (cf. Table) (Morton, " The Application of Absorption Spectra to the Study of Vitamins, Hormones, and Co-enzymes," Hilger, 1942, p. 25).

	$\lambda_{max.}$ (mμ.)	log $\varepsilon_{max.}$ (molar)		$\lambda_{max.}$ (mμ)	log $\varepsilon_{max.}$ (molar)
Totarol	280—285	3·29	Phenol	273	3·38
,, methyl ether	281	3·185	Anisole	271	3·35
,, acetate	266	2·48	Phenyl acetate ...	261	2·36

These results show that the hydroxyl group of totarol is phenolic. If totarol contained a hydroxyl group attached to a non-aromatic ring containing double bonds, the above substitution effects would not have shown and $\varepsilon_{max.}$ (molar) would most probably have been greater.

The similarity of the curves shown in Fig. 3 to those of totarol and its methyl ether confirm that bromination was a substitution reaction. Addition to double bonds would have caused the spectra to show more marked changes from those of the unbrominated compounds.

Addition of a few drops of concentrated hydrochloric acid or a few drops of concentrated sodium hydroxide solution to an alcoholic solution of totarol did not change the absorption spectrum. This is consistent with the chemical evidence which showed that totarol would only dissolve with difficulty even in concentrated sodium hydroxide solutions. A change in spectrum with pH was therefore not expected.

The infra-red absorption spectra were examined with a single-beam Grubb Parsons S3 spectrometer employing a rock-salt prisms. A Hilger–Schwarz thermocouple was used as a detector, with a chopped radiation beam. The cells were sealed with Araldite resin and their thicknesses measured by the interferometric method. They were heated in an oven to just above the melting points of the totarol and methyl ether and the compounds were allowed to run into the cells as liquids. If the filled cells were cooled slowly to room temperature, the liquids remained supercooled for several days and their spectra could easily be obtained.

The ultra-violet spectra were examined in 1-cm. quartz cells with ethyl alcohol as solvent. Totarol was examined with a Unicam S.P.500 spectrophotometer employing a constant slit width of 2 mμ. The remainder of the spectra were examined with a Beckman spectrophotometer and the author thanks Dr. W. F. Elvidge and Mr. L. Brealey of the Standards Division of Boots Pure Drug Co. Ltd. for supplying these data.

EXPERIMENTAL.

Totarol.—The resinol was extracted from the wood of *Podocarpus totara* and was purified as previously described (*loc. cit.*). A Zerewitinoff determination showed the presence of one atom of active hydrogen per molecule (Found, 0·98 atom) but there was no coloration with ferric chloride either in aqueous or in alcoholic solution. When a xylene solution of totarol was extracted with 15% aqueous sodium hydroxide and the filtered alkaline solution was acidified, a distinct flocculent precipitate was obtained, and the phenolic nature of the resinol was confirmed by coupling reactions with diazonium salts (below).

Totaryl Benzoate.—Benzoyl chloride (1 c.c., 1 mol.) was added to a solution of totarol (2·4 g.) in pyridine (10 c.c.) and, after the solution had been kept overnight, the product was precipitated with water, washed, and crystallised from alcohol, giving white plates (2·32 g., 71%) of *totaryl benzoate*, m. p. 144·5—145° (Found: C, 83·2; H, 8·5. $C_{27}H_{34}O_2$ requires C, 83·1; H, 8·7%).

Oxidation of Totarol and its Derivatives with Peracids.—Weighed quantities of each of the compounds were mixed with an excess of a standard solution of the peracid and kept at room temperature until oxidation was complete. A portion of the solution was removed from time to time and the peracid content determined with potassium iodide and sodium thiosulphate, a solution of the reagent being simultaneously assayed so that allowance could be made for spontaneous decomposition of the peracid. The previous results (*loc. cit.*) obtained with totarol and a 5% solution of benzoyl hydroperoxide in chloroform were confirmed, but different results were obtained with a 2% ethereal solution of *o*-carboxybenzoyl hydroperoxide.

	5% Benzoyl hydroperoxide in chloroform		2% *o*-Carboxybenzoyl hydroperoxide in ether	
	Atoms of oxygen absorbed	Hours	Atoms of oxygen absorbed	Hours
Totarol	3·2	48	1·9	96
Totaryl acetate	0	168	—	—
Bromototarol	0	192	0·2	96

Ozonisation of Totaryl Acetate.—(1) An ice-cold solution of totaryl acetate (0·2086 g.) in purified chloroform (10 c.c.) was ozonised for 7 hours in a stream of 5·8% ozone (about 9·4 l. per hour). The ozonisation vessel was followed by a wash-bottle containing water (10 c.c.) to collect volatile products, and the resulting solution and additional water (25 c.c.) were added to the residue obtained after removal of the chloroform from the ozonised solution at room temperature. The mixture was heated under reflux on the steam-bath for an hour and then distilled into ice-water (5 c.c.) until only 5 c.c. remained undistilled. M-Sodium acetate (25 c.c.), N-hydrochloric acid (25 c.c.), and saturated aqueous dimedone (50 c.c.) were added to the distillate, and the formaldehyde–dimedone compound (0·0033 g.), m. p. and mixed m. p. 184—186°, was collected after 12 hours. This yield is equivalent to 0·02 mol. of formaldehyde per mol. of totaryl acetate and, since Clemo and Macdonald (*J.*, 1935, 1295) have shown that compounds containing a doubly bound methylene group afford at least 0·2 mol. of formaldehyde under the conditions of the experiment, it is concluded that totaryl acetate does not contain this group.

(2) Totaryl acetate (0·02—0·06 g.) in purified acetic acid (12 c.c.) was ozonised for 4½ hours with 7·8% ozone (8·7 l. per hour), volatile products being collected in water (6 c.c.). The product was decomposed and the acetone, determined as described by Kuhn and Roth (*Ber.*, 1932, **65**, 1291), was equivalent to 0·30 and 0·28 *iso*propylidene group per molecule of totaryl acetate. Ozonisation of citral (0·05 g.) under the same conditions afforded acetone equivalent to 0·83 *iso*propylidene groups. Kuhn and Roth (*loc. cit.*) found that substances which contain an *iso*propylidene group afford 0·6—1·0 mol. of acetone, whereas several compounds not containing this group give 0—0·3 mol.

Bromototarol.—A solution of bromine (1 g.) in acetic acid (10 c.c.) was added in small portions with shaking to totarol (1 g.) in dry ether (10 c.c.). A positive starch–iodide test was obtained after the addition of 1·2 mols. of bromine, and the solvents were then removed below 50° and the solid was recrystallised from methanol, giving prisms of *bromototarol* (1·02 g.), m. p. 89—89·5° (Found : C, 65·9; H, 7·9; Br, 22·0, 22·8. $C_{20}H_{29}OBr$ requires C, 65·75; H, 7·95; Br, 21·9%). The cryptophenol was not extracted from xylene solution by 15% aqueous sodium hydroxide. Bromototarol did not react with perbenzoic acid in 190 hours at room temperature but consumed 0·23 mol. of permonophthalic acid during 140 hours in ether–chloroform. Methyl totaryl ether (1 g.) in ether (10 c.c.) absorbed 1 mol. of bromine from 10% bromine–acetic acid and when the solid obtained by removing the solvents below 50° was crystallised from methanol containing a little chloroform successive crops of crystals, m. p. 128—129° (0·76 g.) and m. p. 121—124° (0·13 g.), were obtained. Repeated crystallisation from ethanol–chloroform gave long needles of *bromototaryl methyl ether*, m. p. 128·5—129° (Found : C, 66·45, 66·4; H, 8·4, 7·9; Br, 21·9. $C_{21}H_{31}OBr$ requires C, 66·5; H, 8·2; Br, 21·1%).

Aminototarol.—2 : 4-Dinitroaniline (25 g.) was dissolved in a hot mixture of acetic acid (150 c.c.) and concentrated sulphuric acid (15 c.c.), the solution was cooled rapidly, and amyl nitrite was added in small portions to the supension of finely divided sulphate until a clear solution was obtained. The diazonium sulphate was precipitated with ether (3 vols.) and purified by repeated precipitations with ether from acetic acid solution. A cold solution of the diazonium salt in acetic acid (150 c.c.) was slowly added to a solution of totarol (35 g.) in acetic acid (200 c.c.), and the red solid, collected after an hour, had m. p. 201—202° (decomp.) (12·7 g., 22%). Repeated crystallisation from alcohol did not alter the m. p. and 2 : 4-*dinitrophenylazototarol* was obtained in red plates which had m. p. 201—202° (decomp.) when rapidly heated or m. p. 196° (decomp.) when slowly heated (Found ; C, 65·1; H, 6·8; N, 11·7. $C_{26}H_{32}O_5N_4$ requires C, 65·0; H, 6·7; N, 11·7%). Addition of water to the acetic acid mother-liquors precipitated a red solid, m. p. 61—71°, which became oily on attempted crystallisation and which was shown by chromatography to be a mixture of three or four compounds.

A solution of sodium dithionite (44 g.) in water (295 c.c.) was rapidly added to a boiling solution of 2 : 4-dinitrophenylazototarol (4·4 g.) in alcohol (365 c.c.), most of the alcohol was removed from the clear yellow solution by distillation, and the solid, precipitated from the residue by water, was repeatedly crystallised from alcohol, giving white plates, m. p. 160—162° (2·45 g., 89%). Recrystallisation from light petroleum afforded *aminototarol* in prisms, m. p. 166—167° with darkening at 160° (Found : N, 4·7. $C_{20}H_{31}ON$ requires N, 4·65%), which gave a hydrochloride, m. p. 204—208° (decomp.). Benzoyl chloride (1 c.c.) was added to a solution of the hydrochloride (1 g.) in pyridine (10 c.c.), and next morning water was added to precipitate an oil which rapidly solidified. Crystallisation from methanol gave white prisms of the *dibenzoyl* derivative, m. p. 142—143° (Found : C, 80·0; H, 7·8; N, 3·3, 3·3. $C_{32}H_{39}O_3N$ requires C, 80·2; H, 7·7; N, 2·75%). Aminototarol was readily diazotised in concentrated sulphuric acid–acetic acid, and the diazo-solution afforded a bright red precipitate with alkaline β-naphthol.

Formyltotarol.—Dry hydrogen chloride was passed for an hour into an ice-cold stirred mixture of totarol (5 g.), hydrogen cyanide (5·1 c.c., 7·5 mols.), powdered aluminium chloride (4·4 g., 1·9 mols.), and dry benzene (50 c.c.). The mixture was heated at 45° for 4 hours in a stream of hydrogen chloride, then poured on ice, and finally heated on the steam-bath for 3 hours. The benzene layer was separated, added to a benzene extract of the aqueous solution, washed, dried, and evaporated, giving a pale transparent glass. This was dissolved in light petroleum and adsorbed on Grade III alumina (160 g.). The single yellow band was eluted with light petroleum and afforded the hydroxy-aldehyde as a brownish glass (3·95 g., 72%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in red prisms, m. p. 230—231° (decomp.) (Found : N, 11·4. $C_{27}H_{34}O_5N_4$ requires N, 11·3%).

Dehydrogenation of Methyl Totaryl Ether.—(A) *With selenium.* Four compounds, *A*, *B*, *C* (see below), and 7-methoxy-1-methylphenanthrene are produced by the dehydrogenation of methyl totaryl ether with selenium (2 parts). The composition of the product is determined by the duration and temperature of the dehydrogenation and to some extent by the scale of the operation, as illustrated by the examples recorded in the annexed Table.

The dehydrogenations were carried out by heating a mixture of methyl totaryl ether and powdered selenium (2 parts) in a flask deeply immersed in an electrically heated air-bath, the external temperature, indicated by a thermometer with its bulb level with the bottom of the flask, remaining constant to within 5°. The product was extracted with hot acetone, the solution then being boiled with charcoal and evaporated to dryness. The residue was dissolved in benzene or light petroleum (b. p. 60—80°), and the constituents were separated by chromatography on a column of activated, " alkaline " alumina having an activity of II on the Brockmann scale (Brockmann and Schodder, *Ber.*, 1941, **74**, 73). A few typical experiments are described to illustrate the method of separation.

Expt. no.	Methyl totaryl ether, g.	Dehydrogenation,		Recovered methyl ether, %	Dehydrogenation products (%)			
		temp.	time (hr.)		*A*	*B*	*C*	7-Methoxy-1-methyl-phenanthrene
(1)	4	300—305°	35	—	—	—	—	82
(2)	2	300—305	24	—	—	—	6	60
(3)	2	285—290	12	—	—	—	17	37
(4)	2	275—280	24	—	19	25	1	—
(5)	2	275—280	12	9	31	17	10	—
(6)	10	275—280	30	—	27	29	—	—
(7)	10	275—280	24	8	17	23	—	—
(8)	10	275—280	24	14	24	21	—	—
(9)	10	270—275	24	26	17	10	—	—
10)	10	275—280	12	84	9·5	2	—	—

(1) The residue (2·85 g.) from the acetone solution was dissolved in benzene (50 c.c.), adsorbed on a column of Grade II alumina (200 g.), and eluted with light petroleum (b. p. 60—80°) and benzene, the separation being followed by means of the fluorescent bands visible in ultra-violet light. A band with a violet fluorescence was eluted by light petroleum (600 c.c.), and the solution afforded an oily solid (0·29 g.). The next 150 c.c. of light petroleum removed an intermediate fraction giving a solid, m. p. 103—115° (0·12 g.). Elution with benzene (450 c.c.) removed a band with a blue fluorescence, and the solution afforded a solid, m. p. 121—125° (2·44 g., 82·5%), raised to 132—133° by crystallisation from alcohol. The m. p. was undepressed on admixture of this solid with 7-methoxy-1-methylphenanthrene (Short, Stromberg, and Wiles, *J.*, 1936, 321). The *picrate* was somewhat unstable but crystallised from alcoholic picric acid in orange needles, m. p. 140—141° (Found: C, 58·5; H, 3·7; N, 9·3. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·6; H, 3·8; N, 9·3%). The methyl ether did not yield a stable styphnate.

(2) The dehydrogenation product (1·27 g.) was dissolved in benzene and adsorbed on Grade II alumina (125 g.). On elution with light petroleum the first 450 c.c. of effluent contained only 0·02 g. of solid; the next 450 c.c. gave compound *C* (0·1 g.), isolated as picrate, m. p. 178—179° (see below). Subsequent elution with 75 c.c. of benzene gave a mixture (0·21 g.), and further elution with the same solvent (400 c.c.) afforded crude 7-methoxy-1-methylphenanthrene (0·89 g.), m. p. 124—128°, raised to 131—132° by one crystallisation from alcohol.

(5) The product was dissolved in light petroleum, adsorbed on Grade II alumina (125 g.), and eluted successively with light petroleum and benzene. The first portion of light petroleum (150 c.c.) produced a non-fluorescent solution containing a solid, m. p. 61—68° (0·18 g.), probably impure methyl totaryl ether. Light petroleum (145 c.c.) then removed a grey-black band and the solution afforded a solid, m. p. 91—98° (0·87 g., 46·5%), which gave compound *A*, m. p. 108—109·5° (0·58 g., 31%) after one crystallisation from alcohol. A dark violet fluorescent band was removed by light petroleum (230 c.c.), and evaporation of the solvent left an oily solid which afforded compound *B*, m. p. 53—55° (0·27 g., 17%), on crystallisation from alcohol. Benzene (300 c.c.) removed a band with a light violet fluorescence and evaporation of the solvent gave a solid (0·24 g., 13·5%) which gave compound *C*, m. p. 144—145° (0·18 g., 10%), on crystallisation from alcohol.

(7) The dehydrogenation products were adsorbed on a column of Grade II alumina (600 g.), black and dark violet bands being visible in ultra-violet light, and these were developed and eluted with light petroleum (b. p. 60—80°). The first effluent from the column was a non-fluorescent solution (400 c.c.) containing a mixture of solids (0·43 g.), and the lower part of the black band was removed from the column by the next 100 c.c. of solvent, the solution containing a solid (3·92 g.) which had m. p. 65—75° after crystallisation from ethanol. The rest of the black band, eluted with 240 c.c. of light petroleum, afforded a solid (3·55 g.; m. p. 103—108°) which gave compound *A*, m. p. 108—109° (1·62 g.), on crystallisation from ethanol. The dark violet band was removed in 650 c.c. of light petroleum, giving a solid (2·68 g.) which afforded compound *B*, m. p. 53—55° (1·63 g.), on crystallisation from methanol. The solid, m. p. 65—75°, obtained from the lower part of the black band and those recovered from the mother-liquors obtained in the crystallisation of compounds *A* and *B* were adsorbed on Grade I alumina (200 g.), and the column was percolated with light petroleum. The first effluent was a non-fluorescent solution (200 c.c.) containing a solid, m. p. 70—80° (1·08 g.), which afforded methyl totaryl ether, m. p. 92—93° (0·78 g.), on crystallisation from ethanol. A faint violet band was removed from the column by the next 250 c.c. of solvent and afforded a solid, m. p. 60—65° (2·07 g.), unaltered by one crystallisation from ethanol, which was evidently a mixture. The next 200 c.c. of effluent did not contain a solid, and a violet band, removed by 250 c.c. of solvent, afforded a solid m. p. 40—47° (0·56 g.), which gave compound *B*, m. p. 54·5—55·5° (0·18 g.), on crystallisation from methanol.

(B) *With sulphur.* Dehydrogenation of methyl totaryl ether with sulphur (4 atoms) at 220—260° afforded compound *C* as the main product, accompanied in some experiments by smaller quantities of compound *A*. In a typical experiment, methyl totaryl ether (5 g.) and sulphur (2·14 g.) were heated for 5 hours, the temperature being slowly raised from 220° to 260°. The mixture was then distilled, and the distillate dissolved in light petroleum and adsorbed on a column of Grade II alumina (300 g.). Elution with light petroleum (400 c.c.) removed a colourless band and afforded an oily solid (0·62 g.) which gave compound *A*, m. p. 105—106° (0·45 g., 9·5%), after two crystallisations from ethanol. A blue-violet band was removed by the next 150 c.c. of solvent, and the solution contained a solid, m. p.

87—115° (0·37 g.), which gave only a small quantity of solid, m. p. 130—134°, on crystallisation from ethanol. A violet band finally passed out of the column, and the solution (335 c.c.) contained a solid, m. p. 140—145° (1·14 g.), which afforded compound *C*, m. p. 147—148°, (0·91 g., 21%) on crystallisation from ethanol. Other dehydrogenations are summarised in the annexed Table.

Methyl totaryl ether, g.	Hours at 220—260°	Yields of dehydrogenation products (%)		Methyl totaryl ether, g.	Hours at 220—260°	Yields of dehydrogenation products (%)	
		A	*C*			*A*	*C*
5	5	9·5	21	20	8	—	23
10	8	4·0	28	20	8	—	25
10	10	—	32	15	8	—	31·5

1 : 2 : 3 : 4-*Tetrahydro*-7-*methoxy*-1 : 1-*dimethyl*-8-iso*propylphenanthrene* (*Compound* A).—This *compound* separated from methanol in rods, m. p. 109·5—110° (Found : C, 85·25; 85·0; H, 9·3, 9·4. $C_{20}H_{26}O$ requires C, 85·1; H, 9·2%). The picrate was unstable but the *trinitrobenzene complex* crystallised from alcohol in red needles, m. p. 151·5—152° (Found : N, 8·7. $C_{20}H_{26}O,C_6H_3O_6N_3$ requires N, 8·5%). Dehydrogenation with sulphur converted compound *A* into compound *C* (see below).

1 : 2 : 3 : 4-*Tetrahydro*-7-*methoxy*-1 : 1-*dimethylphenanthrene* (*Compound* B).—*Compound* B was purified by crystallisation from methanol and separated in matted needles, m. p. 55·5—56° (Found : C, 85·3; H, 8·3. $C_{17}H_{20}O$ requires C, 85·0; H, 8·3%). The *picrate* crystallised from alcohol in red needles, m. p. 105—106° when heated slowly or 94° when heated rapidly (Found : C, 59·2, 59·3; H, 5·05, 4·6; N, 9·0, 8·9. $C_{17}H_{20}O,C_6H_3O_7N_3$ requires C, 58·8; H, 4·9; N, 8·95%). The methyl ether and boiling hydrobromic–acetic acid afforded a black solid, m. p. 42—48°, but normal demethylation occurred when the ether (1·5 g.) and pyridine hydrochloride (4·5 g.) were stirred and boiled in an atmosphere of nitrogen for 2 hours. The resulting *phenol* (0·7 g., 50%) crystallised from benzene–light petroleum in small needles, m. p. 134—134·5° (Found : C, 85·0; H, 7·9. $C_{16}H_{18}O$ requires C, 85·0; H, 7·9%). The methyl ether (2 g.) was dehydrogenated by heating it with sulphur (0·56 g.) at 220—260° for 5 hours. The distillate (0·98 g.) afforded a solid, m. p. 123—125° (0·42 g., 23%), on crystallisation from alcohol, and further crystallisation raised the m. p. to 129—130°, undepressed on admixture with 7-methoxy-1-methylphenanthrene. The picrate melted at 141—142°, either alone or after admixture with authentic 7-methoxy-1-methylphenanthrene picrate.

7-*Methoxy*-1-*methyl*-8-iso*propylphenanthrene* (*Compound* C).—This compound was obtained by the dehydrogenation of methyl totaryl ether (above) or of compound *A*. A mixture of compound *A* (3·95 g.) and sulphur (0·9 g., 2 atoms) was heated to 220° and the temperature was slowly raised to 260° during 5 hours. The product was distilled at 2 mm. and the distillate (2·3 g.) was dissolved in light petroleum (b. p. 60—80°) and adsorbed on Grade II alumina (200 g.). The column was extracted with light petroleum (b. p. 60—80°), the effluent being collected in fractions. The first effluent (160 c.c.) was non-fluorescent and contained 0·17 g. of solid. Two subsequent fractions (125 and 250 c.c.) had a blue fluorescence and afforded solids, m. p. 98—125° (1·36 g.) and m. p. 125—134° (0·35 g.) respectively. Recrystallisation from ethanol gave white plates (1·21 g., 33%) of *compound* C, m. p. 144·5 –145° (Found : C, 86·4, 86·7; H, 7·4, 7·9. $C_{19}H_{20}O$ requires C, 86·4; H, 7·6%). The *picrate* crystallised from alcohol containing picric acid in orange-red needles, m. p. 186—187° (Found : C, 60·9; H, 4·7; N, 8·7; $C_6H_3O_7N_3$, 45·9. $C_{19}H_{20}O,C_6H_3O_7N_3$ requires C, 60·9; H, 4·7; N, 8·5; $C_6H_3O_7N_3$, 46·5%). The *trinitrobenzene complex* consisted of orange needles, m. p. 208—209° (Found : C, 62·9; H, 4·8; N, 8·7. $C_{19}H_{20}O,C_6H_3O_6N_3$ requires C, 62·9; H, 4·8; N, 8·8%). Poor yields were obtained when the methyl ether was demethylated with boiling hydrobromic–acetic acid or with methylmagnesium iodide (1·4 mols.) in boiling tetrahydronaphthalene. The methyl ether (4·4 g.) and pyridine hydrochloride (12 g.) were boiled and stirred in an atmosphere of nitrogen for 2 hours and the product was repeatedly extracted with boiling dilute sodium hydroxide solution containing a little sodium sulphite. The solid, m. p. 131—134° (3·48 g., 84%), obtained by acidifying the filtered solution was crystallised from light petroleum (b. p. 60—80°) and gave prisms of the *phenol*, m. p. 139—140° (Found : C, 86·6; H, 6·9. $C_{18}H_{18}O$ requires C, 86·4; H, 7·2%). This phenol dissolved readily in hot 2N-sodium hydroxide; it did not couple with 2 : 4-dinitrobenzenediazonium sulphate in alkaline solution, whereas 7-hydroxy-1-methylphenanthrene gave a dark red precipitate of azo-dye under the same conditions. When a mixture of the phenol (0·5 g.) and zinc dust (10 g.) was heated and the vapour passed through a column of heated zinc dust (50 g.) a white sublimate (0·28 g.) was produced. This was purified by adsorption on a column of Grade II alumina (65 g.), elution with light petroleum (b. p. 60—80°) removing a blue violet fluorescent band and affording a white solid, m. p. 112—115° (0·19 g., 49%), which crystallised from alcohol in plates, m. p. 119·5—120° (Found : C, 93·05; H, 6·6. Calc. for $C_{15}H_{12}$: C, 93·75; H, 6·25%). This compound did not depress the m. p. of 1-methylphenanthrene and its identity was confirmed by a comparison of specimens of the picrates and styphnates. No further material was obtained by extracting the alumina column with other solvents.

7-*Hydroxy*-1-*methylphenanthrene*.—(1) Dehydrogenation of totarol (15 g.) with selenium (30 g.) as previously described (*loc. cit.*, p. 519) afforded 7-hydroxy-1-methylphenanthrene, m. p. 190—191° in 53% yield. (2) A 43% yield of the phenanthrol was obtained when 7-methoxy-1-methylphenanthrene (1 g.), 48% hydrobromic acid (100 c.c.), and acetic acid (100 c.c.) were boiled for 5 hours. (3) The methyl ether (2 g.) and pyridine hydrochloride (6 g.) were stirred vigorously at the b. p. for 2 hour in an atmosphere of nitrogen. The liquid was then cooled, the resulting solid was triturated with water, and the residue extracted with dilute aqueous sodium hydroxide (2 × 300 c.c.). Acidification of the filtered solution gave 7-hydroxy-1-methylphenanthrene, m. p. 190—191° (1·13 g., 60%).

This phenol coupled readily with benzenediazonium chloride and 2 : 4-dinitrobenzenediazonium sulphate.

7-*Amino*-1-*methylphenanthrene*.—(1) A mixture of 7-hydroxy-1-methylphenanthrene (2·08 g.), anhydrous sodium acetate (3·61 g.), ammonium chloride (2·57 g.), and acetic acid (4 c.c.) was heated at 285—295° for 16 hours. The product was extracted with hot dilute sodium hydroxide solution (2 × 400 c.c.) to remove a little unchanged phenol, and the residue was crystallised from alcohol, giving the crude amide, m. p. 233—235° (0·92 g., 37%). Further crystallisation from alcohol (charcoal) gave 7-*acetamido*-1-*methylphenanthrene* as white prisms, m. p. 241—242° (Found : C, 82·1; H, 6·2; N, 5·7. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·0; N, 5·6%). The corresponding amine was obtained in 70% yield by boiling the acetyl derivative (0·6 g.), hydrochloric acid (4 c.c.), water (2 c.c.), and alcohol (20 c.c.) for 5 hours. The hydrochloride was collected, warmed with dilute aqueous ammonia, and the *amine* crystallised from light petroleum (b. p. 60—80°) in clustered needles, m. p. 103—104° (Found : N, 6·4. $C_{15}H_{13}N$ requires N, 6·7%). (2) 7-Hydroxy-1-methyl-8-*iso*propylphenanthrene (2·5 g.; m. p. 139—140°), anhydrous sodium acetate (3·61 g.), ammonium chloride (2·57 g.), and acetic acid (4 c.c.) heated at 285—295° for 20 hours gave some unchanged phenanthrol (0·14 g., 6%), m. p. 134—137°, and 7-acetamido-1-methylphenanthrene (1·06 g., 43%), m. p. and mixed m. p. 241—242°. The phenanthrol (60%) was recovered when the mixture was heated at 225—235° for 18 hours.

8-*Formyl*-7-*methoxy*-1-*methylphenanthrene*.—(1) Hydrogen chloride was passed for an hour into a stirred, ice-cold mixture of 7-methoxy-1-methylphenanthrene (1·08 g.), hydrogen cyanide (1·4 c.c., 7·3 mols.), aluminium chloride (1·2 g., 1·8 mols.), and dry benzene (20 c.c.). After being heated at 45° for 2 hours, the mixture was diluted with ether, added to water, and distilled to remove ether, and the residue boiled for 3 hours. The product was collected in benzene, the solution being washed, dried, concentrated, and adsorbed on a column of Grade I alumina (100 g.). Elution with dry benzene afforded a single product, m. p. 183—184° (0·75 g., 61·5%), and crystallisation from alcohol gave 8-*formyl*-7 *methoxy*-1-*methylphenanthrene* as pale yellow plates, m. p. 184·5—185·5° (Found : C, 81·6; H, 5·4. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%). The *semicarbazone* had m. p. 332—334° (decomp.) (Found : N, 13·8. $C_{18}H_{17}O_2N_3$ requires N, 13·7%).

The methoxy-aldehyde (0·1 g.) was demethylated by boiling it for 20 minutes with pyridine hydrochloride (1 g.) in an atmosphere of nitrogen, and the resulting hydroxy-aldehyde crystallised from alcohol in yellow plates, m. p. 203—205°, which did not depress the m. p. of the aldehyde, m. p. 206—207°, prepared directly from 7-hydroxy-1-methylphenanthrene (see below).

(2) 7-Hydroxy-1-methylphenanthrene was converted into the hydroxy-aldehyde in 42—48% yield by using the method described above for the preparation of its methyl ether, except that the crude aldehyde was isolated directly from the benzene solution and purified by crystallisation from benzene and alcohol. 8-*Formyl*-7-*hydroxy*-1-*methylphenanthrene* crystallised from alcohol in pale yellow plates, m. p. 206—207° (Found : C, 81·7; H, 4·8. $C_{16}H_{12}O_2$ requires C, 81·4; H, 5·1%). The 2 : 4-*dinitrophenylhydrazone* crystallised from nitrobenzene–light petroleum in brick red needles, m. p. 327° (decomp.) (Found : N, 13·6. $C_{22}H_{16}O_5N_4$ requires N, 13·5%). The aldehyde did not couple with 2 : 4-dinitrobenzenediazonium sulphate. The hydroxy-aldehyde (1 g.), methyl iodide (3 c.c.), potassium carbonate (0·6 g.), and acetone (30 c.c.) afforded the methyl ether, m. p. 184·5—185·5° (83%), when boiled for 12 hours.

7-*Methoxy*-1-*methylphenanthrene*-8-*carboxylic Acid*.—A solution of the corresponding aldehyde (0·5 g.) in acetone (40 c.c.) was stirred at 50° during the slow addition of an aqueous solution (30 c.c.) of potassium permanganate (1 g., equiv. to 4·75 atoms of oxygen). Heating was continued for 1½ hours, and the acid was isolated by saturating the mixture with sulphur dioxide at 0° and removing the acetone by distillation. The crude product (0·41 g., 77%) had m. p. 287—290° (decomp.), and 7-*methoxy*-1-*methylphenanthrene*-8-*carboxylic acid* crystallised from acetone in white plates, m. p. 299—300° (decomp.) (Found : C, 76·8; H, 5·0. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·25%). The acid is sparingly soluble in hot aqueous sodium hydroxide. The acid (1·2 g.), powdered silver oxide (7·5 g.), methyl iodide (5 c.c.), and benzene (200 c.c.) were boiled for 15 hours and filtered hot to remove silver salts. The solid which separated from the filtrate had m. p. 189—191° (1·1 g., 87%); crystallisation from light petroleum gave colourless needles of *methyl* 7-*methoxy*-1-*methylphenanthrene*-8-*carboxylate*, m. p. 191—192° (Found : C, 77·2; H, 5·6. $C_{18}H_{16}O_3$ requires C, 77·2; H, 5·7%).

Methyl 7-*methoxy*-1-*methylphenanthrene*-8-*carboxylate and Methylmagnesium Iodide*.—A solution of the ester (1 g.) in dry benzene (40 c.c.) was slowly added at 0° to a stirred solution of methylmagnesium iodide (3 mols.), prepared from magnesium (0·26 g.), methyl iodide (0·9 c.c.), and ether (10 c.c.), and the mixture was boiled for 3 hours. The complex was decomposed with ice-cold dilute hydrochloric acid, and the product, isolated by extraction with benzene, was distilled at 2 mm. pressure from powdered potassium hydrogen sulphate (0·4 g.). The distillate, m. p. 146—155° (0·86 g.), was crystallised successively from alcohol and benzene–light petroleum, giving a *hydrocarbon* which separated in clusters of plates, m. p. 168·5—170° (Found : C, 91·6; H, 8·2. $C_{19}H_{20}$ requires C, 91·7; H, 8·1%). This compound gave a faint colour with tetranitromethane in chloroform and was recovered unchanged on attempted reduction under atmospheric conditions in alcoholic solution in presence of samples of palladium–strontium carbonate or platinum oxide catalysts capable of effecting rapid reduction of *iso*eugenyl benzoate to the dihydro-compound. The hydrocarbon afforded a *trinitrobenzene complex*, m. p. 177—179° (Found : N, 8·8. $C_{19}H_{20},C_6H_3O_6N_3$ requires N, 9·1%), and its properties indicate that it is probably 1 : 7-dimethyl-8-*iso*propylphenanthrene.

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