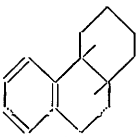
## 40. *Stereochemistry of* as-*Octahydrophenanthrene.*

By J. W. Cook, C. L. Hewett, and (Mrs.) A. M. Robinson.

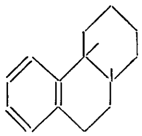
The two stereoisomeric *as*-octahydrophenanthrenes (I and II) have been prepared in a pure state, and their physical constants determined. The presence of both of them, and also of hydrindene-1-*spirocyclo*hexane (III), in the saturated hydrocarbon mixture formed by cyclisation of β-phenylethyl-$\Delta^1$-*cyclo*hexene, has been established by analysis of the ketone mixtures formed by oxidation with cold chromic acid. Separation of the three hydrocarbons could not be achieved by fractional distillation. A series of derivatives of *cis*-*as*-octahydrophenanthrene has been investigated, and two stereochemically pure perhydrophenanthrene derivatives [2-perhydrophenanthrol (XI) and 2 : 10-perhydrophenanthradiol (X)] of partly known configuration have been obtained. A by-product was perhydrophenanthrene (probably not stereochemically homogeneous), which was readily dehydrogenated to phenanthrene by selenium at 300°.

A simple method of synthesis of *as*-octahydrophenanthrene by cyclisation of β-phenylethyl-$\Delta^1$-*cyclo*hexene was worked out independently by Bogert (*Science*, 1933, **77**, 289; compare Perlman, Davidson, and Bogert, *J. Org. Chem.*, 1936, **1**, 288) and by Cook and Hewett (J., 1933, 1098). The substance so prepared gave phenanthrene on dehydrogenation and has been used in the synthesis of various compounds related to 1 : 2-benzanthracene (Cook and Haslewood, J., 1935, 767). Nevertheless, it soon became apparent that the tricyclic hydrocarbon did not necessarily consist entirely, or even mainly, of *as*-octahydrophenanthrene. A detailed study of an analogous cyclisation reaction (Cook and Hewett, J., 1934, 365), since supplemented by several investigations in this and other laboratories, showed that spirocyclic hydrocarbons may be formed in such reactions as well as purely hydroaromatic compounds, and that under certain conditions these spirocyclic hydrocarbons may undergo dehydrogenation with molecular rearrangement. Hence further examination of our " *as*-octahydrophenanthrene " seemed desirable. It was shown in a previous communication (Cook, Hewett, and Lawrence, J., 1936, 71) that at least two ketones are formed by oxidation of this hydrocarbon mixture; one of these was identical with a keto-octahydrophenanthrene synthesised by an independent method, and the other was regarded as derived from the spirocyclic hydrocarbon (III).

We have re-examined this oxidation and have been able to isolate in addition the oxime of the second stereoisomeric keto-octahydrophenanthrene which we had already synthesised. Thus, the two stereoisomeric *as*-octahydrophenanthrenes (I and II) and the spiran (III) are all formed in the cyclisation of β-phenylethyl-$\Delta^1$-*cyclo*hexene.



(I.)



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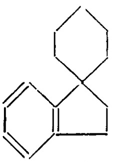
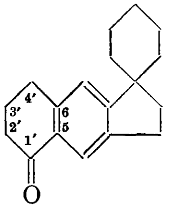


(III.)

van de Kamp and Mosettig (*J. Amer. Chem. Soc.*, 1936, **58**, 1063) prepared *as*-octahydrophenanthrene by direct dehydration of 1-β-phenylethyl*cyclo*hexanol with phosphoric oxide and claimed to have fractionated their product into two pure components differing in b. p. and refractive index; these they regarded as *cis*- and *trans*-isomerides (I and II). We have carried out a series of fractionations of the product obtained by this method, and also by our original method of cyclisation of the unsaturated hydrocarbon with aluminium chloride, and although there has been no difficulty in separating the hydrocarbon mixtures obtained by each procedure into fractions having refractive indexes corresponding with those given by van de Kamp and Mosettig, analysis of all the fractions by our oxidation technique has shown that none of the fractions was homogeneous; several contained all three hydrocarbons (I, II, and III). Moreover, the presence of the spirocyclic hydrocarbon (III) in the lower-boiling fractions has been shown independently by Perlman, Davidson, and Bogert (*loc. cit.*), who obtained by oxidation with permanganate a dicarboxylic acid of the anticipated structure (see also Perlman and Bogert, *J. Amer. Chem. Soc.*, 1937, **59**, 2534).

The proportions in which these three hydrocarbons are formed are doubtless influenced somewhat by minor variations in the experimental conditions. The spiran is clearly a lesser product in normal circumstances, a conclusion in keeping with the experiments of Bogert and of van de Kamp and Mosettig, and it is evident from our oxidation experiments that *cis*-*as*-octahydrophenanthrene (II) is very much more abundant in the mixture than the *trans*-isomeride. However, in one experiment on the condensation of the mixed hydrocarbons with succinic anhydride we isolated, not the keto-acid derived from octahydrophenanthrene (Cook and Haslewood, *loc. cit.*), but a mixture consisting chiefly of an *isomeride* evidently derived from the spiran (III). The new keto-acid was reduced to a *substituted butyric acid*, which was cyclised to a *ketone* (IV or V). Oxidation of this ketone with dilute nitric acid gave pyromellitic acid, a result consistent not only with the structure suggested, but also with that of a ketone stereoisomeric with the one originally obtained by Cook and Haslewood. The possibility of a stereoisomeride was excluded, however, by the composition of the *hydrocarbon* obtained by dehydrogenation of the product of interaction of the ketone with methylmagnesium iodide. This hydrocarbon gave analytical figures in agreement with $C_{19}H_{22}$ (VI or VII), whereas 5-methyl-1 : 2-benzanthracene ($C_{19}H_{14}$) should have resulted from a ketone derived from octahydrophenanthrene.



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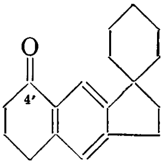

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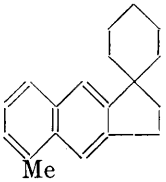

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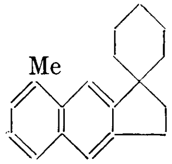
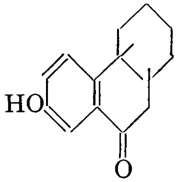


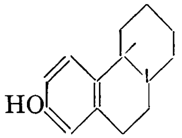
(VII.)

The two stereoisomeric *as*-octahydrophenanthrenes (I and II) have been prepared in a pure state by Clemmensen reduction of their keto-derivatives synthesised from the phenyl*cyclo*hexylacetic acids (Cook, Hewett, and Lawrence, *loc. cit.*), and from a comparison of physical constants it may be concluded that the liquid hydrocarbon formed by reduction of the liquid ketone has the *cis*-configuration (II), and that the hydrocarbon, m. p. 24°, obtained by reduction of the crystalline ketone, m. p. 95°, has the *trans*-configuration (I). The figures which follow show that the differences in density and refractive index are of opposite sign to the differences of molecular refraction, in conformity with the relationships which hold in the decalin and the octalin series, but the density and refractive index differences between the octahydrophenanthrenes are smaller in magnitude than in the case of the simpler dicyclic compounds.

| | $d_{4°}^{20°}$. | $n_D^{20·7°}$. | $[R_L]_D$. |
|---|---|---|---|
| *cis*-*as*-Octahydrophenanthrene | 1·0110 | 1·5549 | 59·06 |
| *trans*-*as*-Octahydrophenanthrene | 1·0060 | 1·5528 | 59·20 |
| Difference | +0·0050 | +0·0021 | −0·14 |

Attempts have been made to secure chemical proof of configuration of the *cis*-compound, taking advantage of the comparatively ready availability of *cis*-hexahydrophenanthrone. This was nitrated, and the crystalline *nitro-ketone* reduced to the *amino-ketone*, which was converted into the *hydroxy-ketone* (VIII) by means of the diazo-reaction. Clemmensen reduction of (VIII) led to cis-7-as-*octahydrophenanthrol* (IX), the orientation of which was established by dehydrogenation to 2-phenanthrol. In spite of repeated attempts we have been unable to isolate *cis*-hexahydrohomophthalic acid from the products of oxidation of the hydroxy-ketone (VIII). This failure may have been due to the poor power of crystallisation of this acid when contaminated with adipic, glutaric, and oxalic acids, which were found among the oxidation products. An attempt to overcome this difficulty by making a similar study of the *trans*-hydroxy-ketone was precluded by the lack of a method of preparation of *trans*-hexahydrophenanthrone in satisfactory yield. The presence of the spiran (III) in the fractions of synthetic octahydrophenanthrene which are richest in the *trans*-hydrocarbon renders it impracticable to use this material as a source of the *trans*-ketone, and in the synthesis of the 2-phenyl*cyclo*hexylacetic acids by hydrogenation of 2-phenyl-$\Delta^1$-*cyclo*hexenylacetic acid the *cis*-acid is almost exclusively formed.* We have carried out hydrogenations of the sodium salt of the unsaturated acid in alkaline solution and of the ethyl ester in neutral solution without increasing the proportion of *trans*-compound formed, and the hydrogenation of 2-*phenyl*cyclo*hexylideneacetic acid*, formed by dehydration of the phenyl*cyclo*hexanolacetic acid with acetic anhydride (compare Wallach, *Annalen*, 1909, **365**, 261), has likewise failed to give the saturated *trans*-acid in useful amount.


(VIII.)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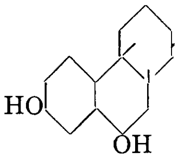
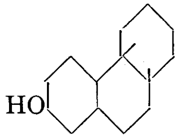

(X.)


(XI.)

When 7-hydroxy-9-keto-octahydrophenanthrene (VIII) was hydrogenated over a platinum catalyst, it gave a mixture of products, from which were isolated 7-hydroxyoctahydrophenanthrene (IX), a 2 : 10-*dihydroxyperhydrophenanthrene* (X), a 2-*hydroxyperhydrophenanthrene* (XI), and a liquid having the composition of perhydrophenanthrene, possibly a mixture of stereoisomerides. The orientation of (XI) was shown by the fact that the same carbinol was obtained by hydrogenation of 7-hydroxy-*as*-octahydrophenanthrene (IX). The relative simplicity of this mixture of hydrogenation products is of interest, for the reaction could give rise theoretically to eight carbinols (XI) and sixteen diols (X). It is to be observed that the two compounds (X and XI) represent stereochemically homogeneous simple derivatives of perhydrophenanthrene, in which the configuration is partly known.

Rather unexpectedly, the perhydrophenanthrene obtained in this hydrogenation was smoothly dehydrogenated to phenanthrene by selenium at 300—315°. Pinkney, Nesty, Wiley, and Marvel (*J. Amer. Chem. Soc.*, 1936, **58**, 986) were unable to effect dehydrogenation under these conditions of specimens of perhydrophenanthrene obtained by hydrogenation of phenanthrene and of a synthetic dodecahydrophenanthrene over Raney nickel at 250°. The most obvious explanation of this discrepancy lies in differences of configuration between our hydrocarbon and that of the American authors, the *cis*-structure which is known to be present at the fusion of 2 rings in our substance being probably more susceptible to dehydrogenation than the *trans*-structures which are likely to be formed by hydrogenation with nickel. More recently, Denisenko and Kotělnikova (*J. Gen. Chem.*, 1937, **7**, 2819) have reported that a perhydrophenanthrene obtained by hydrogenation of octahydrophenanthrene with noble metal catalysts was dehydrogenated to phenanthrene by platinised charcoal at 300°.

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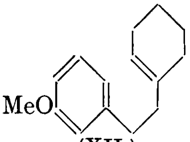
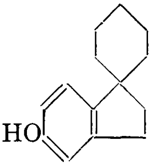
* Newman (*J. Amer. Chem. Soc.*, 1938, **60**, 2947) has obtained *cis*-hexahydrochrysene derivatives by an extension of the hydrophenanthrene synthesis of Cook, Hewett, and Lawrence (*loc. cit.*).

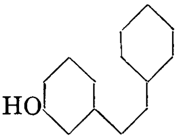
We have also examined the possibility of obtaining 7-hydroxy-*as*-octahydrophenanthrene (IX) (or its *trans*-isomeride) from the products of cyclisation of β-m-*methoxyphenylethyl*-$\Delta^1$-cyclo*hexene* (XII). In this case, however, the *spiro*-structure rather than the hydroaromatic structure was mainly formed, a good yield of the crystalline *phenol* (XIII) being isolated after demethylation.



(XII.)



(XIII.)



(XIV.)

The methyl ether of (XIII) was resistant to the dehydrogenating action of platinum at 300°, in conformity with the structure assigned. The phenols present in the mother-liquors from which (XIII) had been isolated were remethylated and dehydrogenated, and gave 2-methoxyphenanthrene, indicating that the octahydrophenanthrene derivative was also formed in the cyclisation of (XII).

In view of the relationships between the molecular dimensions of ergosterol and calciferol (compare Bernal and Crowfoot, *Chem. and Ind.*, 1935, **54**, 701) it seemed of interest to make a comparison of molecular dimensions by *X*-ray crystallographic methods of the perhydrophenanthrol (XI) and the corresponding dicyclic compound (XIV), although the absence of double bonds renders the structures of these two carbinols only partially analogous to those of ergosterol and calciferol. A crystalline *carbinol* of structure (XIV) was isolated from the products of hydrogenation with platinum of β-(*m*-hydroxyphenyl)ethyl*cyclo*hexane, which was prepared from (XII) by palladium-hydrogenation, followed by demethylation. It was also thought that the crystal structures of (IX) and (XIII) would be worthy of attention, as possibly affording corroboration of the constitutions assigned to them. Neither of these objectives was realised, as the complexity of structure of the unit cells of all four compounds made it impossible to draw any significant conclusions from the *X*-ray diffraction measurements. These experiments were carried out by Dr. John Iball, who gives the following data for the compounds in question :

β-3′-*Hydroxy*cyclo*hexylethyl*cyclo*hexane* (XIV). The crystals are very small, imperfect plates elongated in the direction of the *b*-axis. The crystals appear to be triclinic with the following cell dimensions, $a = 42{\cdot}8$ A., $b = 5{\cdot}49$ A., $d(001) = 22{\cdot}70$ A., $\gamma = 90°$. The optic sign is (+) and the optic axial angle is large ; the intersection of the optic axial plane in (100) makes an angle of approximately 20° with $b$ ; the acute bisectrix $\gamma$ is approximately 30° from the perpendicular to (001).

2-*Perhydrophenanthrol* (XI). This substance crystallises from hexane in thin monoclinic needles slightly tabular on (001). The unit cell dimensions are as follows ; the *b*-axis is parallel to the length of the needle :

$a = 20{\cdot}08$ A., $b = 8{\cdot}69$ A., $c = 28{\cdot}25$ A., $\beta = 100{\cdot}3°$. 12 mols. ($C_{14}H_{24}O$) per unit cell.

The halvings observed on moving-film photographs taken about each of the above axes are ($hkl$) when ($h + k + l$) is odd, ($h0l$) when $h$ or $l$ is odd, and ($0k0$) when $k$ is odd. The space group is therefore either $C^6_{2h}$ — $I2/a$ or $C^4_s$ — $Ia$.

cis-7-*Octahydrophenanthrol* (IX) crystallises from hexane in clusters of needles. The needles are orthorhombic and are slightly tabular on (001). The unit cell dimensions are as follows, the *b*-axis is parallel to the length of the needle :

$a = 21{\cdot}58$ A., $b = 6{\cdot}38$ A., $c = 25{\cdot}86$ A. 12 mols. ($C_{14}H_{18}O$) per unit cell.

The observed halvings are ($h00$) when $h$ is odd, ($0k0$) when $k$ is odd, and ($00l$) when $l$ is odd. The space group is therefore $D^4_2$ — $P2_12_12_1$. The optic sign is (+), $\beta = a$ and $\gamma = c$.

5-*Hydroxyhydrindene*-1-spirocyclo*hexane* (XIII). Crystallisation from amyl acetate gives rather thin, poorly developed needles. These are monoclinic, flattened on (001) and elongated along $b$. The unit cell dimensions are as follows :

$a = 33{\cdot}50$ A., $b = 6{\cdot}47$ A., $c = 39{\cdot}37$ A., $\beta = 106{\cdot}5°$. 24 mols. ($C_{14}H_{18}O$) per unit cell.

The observed halvings are (*h*0*l*) when *h* or *l* is odd and (0*k*0) when *k* is odd. The space group is therefore $C_{2h}^5$ — $P2_1/a$ or $P2_1/c$.

## EXPERIMENTAL.

*Pure* as-*Octahydrophenanthrenes.*—cis-*Isomeride.* The liquid hexahydrophenanthrone (Cook, Hewett, and Lawrence, *loc. cit.*) (10 g.) was boiled under reflux for 7 hours with concentrated hydrochloric acid (20 c.c.), water (40 c.c.), and amalgamated zinc (30 g.), additional portions of hydrochloric acid (5 c.c.) being added after each hour. The hydrocarbon was distilled in steam, extracted with ether, dried with calcium chloride, and distilled in a vacuum over sodium. cis-as-*Octahydrophenanthrene* (II) formed a colourless liquid, b. p. 88—90°/0·1—0·15 mm., $d_{4^\circ}^{13^\circ}$ 1·0164, $d_{4^\circ}^{25^\circ}$ 1·0072, $n_{\mathrm{D}}^{12\cdot2^\circ}$ 1·5586, $n_{\mathrm{D}}^{20\cdot7^\circ}$ 1·5549 (Found : C, 90·6; H, 9·8. $C_{14}H_{18}$ requires C, 90·3; H, 9·7%).

trans-*Isomeride.* The crystalline ketone, m. p. 95° (Cook, Hewett, and Lawrence, *loc. cit.*) (1·75 g.), was similarly reduced, and the product distilled at 0·05—0·1 mm. from a boiling-water bath. The amount of hydrocarbon (0·45 g.) was insufficient for a b. p. determination. trans-as-*Octahydrophenanthrene* (I) readily crystallised at room temperature to a mass of colourless needles, m. p. 23—24° (Found : C, 90·55; H, 9·8%). The supercooled liquid hydrocarbon had $d_{4^\circ}^{20^\circ}$ 1·006, $n_{\mathrm{D}}^{20\cdot7^\circ}$ 1·5528.

*Analysis of Tricyclic Hydrocarbons from* 1-β-*Phenylethyl*cyclo*hexanol.*—(a) The product from the action of aluminium chloride on β-phenylethyl-Δ¹-*cyclo*hexene in carbon disulphide (18 hours at room temperature) (compare Cook and Hewett, J., 1933, 1098) was freed from traces of unsaturated compounds by washing with 80% sulphuric acid and the purified hydrocarbons (165 g.) were slowly fractionated through a column at 0·3 mm. The b. p.'s of the fractions (*ca.* 100—110°) are not recorded, as the values were much influenced by rate of distillation, temperature of bath, etc., and it was found more satisfactory to use the refractive indices as a guide to the fractionation. In the first distillation the following fractions were collected : I, $n_{\mathrm{D}}^{21\cdot2^\circ}$ 1·5448; 31 g. II, $n_{\mathrm{D}}^{21\cdot2^\circ}$ 1·5442; 32·5 g. III, $n_{\mathrm{D}}^{21\cdot2^\circ}$ 1·5512; 41 g. IV, $n_{\mathrm{D}}^{21^\circ}$ 1·5527; 32·7 g. V, $n_{\mathrm{D}}^{21^\circ}$ 1·5529; 15·3 g. Each of these fractions was redistilled, sub-fractions of similar refractive index combined and redistilled, and the process repeated several times. In this way were obtained, among others, the following fractions : (A) $n_{\mathrm{D}}^{19\cdot7^\circ}$ 1·5466; 16 g. (B) $n_{\mathrm{D}}^{19\cdot3^\circ}$ 1·5508; 34 g. (C) $n_{\mathrm{D}}^{19\cdot3^\circ}$ 1·5528; 31 g. (D) $n_{\mathrm{D}}^{19\cdot3^\circ}$ 1·5534, $n_{\mathrm{D}}^{15\cdot2^\circ}$ 1·5544; 56 g. These values may be compared with those cited by van de Kamp and Mosettig (*loc. cit.*) for their lower-boiling ($n_{\mathrm{D}}^{15^\circ}$ 1·5460) and higher-boiling fractions ($n_{\mathrm{D}}^{10\cdot6^\circ}$ 1·5592) as well as those given above for the pure octahydrophenanthrenes.

The following procedure was employed in the analysis of the fractions : A solution of chromic acid (8 parts) in 80% acetic acid (16 parts) was added slowly to an ice-cold mixture of the hydrocarbon fraction (7 parts) in glacial acetic acid (70 parts). The solution was kept for 4 days at room temperature, poured into water, and extracted with ether. The extract was washed with water and dilute sodium carbonate solution, dried, and distilled. The ketonic fraction had b. p. *ca.* 135°/0·2 mm. (2—2·5 parts), and this was heated on the water-bath for 4 hours with hydroxylamine hydrochloride in anhydrous pyridine. The resulting mixture of oximes was fractionally crystallised from aqueous alcohol and methyl alcohol.

Fraction I was redistilled and the lower-boiling portion ($n_{\mathrm{D}}^{19^\circ}$ 1·5298; 5·5 g.) was oxidised. The oxime, m. p. 176—177°, of *trans-as*-hexahydrophenanthrone was isolated in the pure state, identification being completed by hydrolysis to the pure crystalline ketone with boiling aqueous-alcoholic sulphuric acid. From fraction (D) were isolated the oximes of all three ketones (corresponding with both octahydrophenanthrenes, I and II, and the spiran, III). In all oxidation experiments the oxime of *cis*-hexahydrophenanthrone was abundantly formed, but on account of its much lower m. p. (124°) this was difficult to obtain pure. The oximes of the *trans*-ketone (m. p. 176°) and the spirocyclic ketone (m. p. 187°) had similar solubilities, and from the m. p.'s of the oxime fractions it was clear that they were always present together. Whether the one or the other was eventually obtained pure was largely determined by the proportions in which they were present in the mixture.

(b) 1-β-Phenylethyl*cyclo*hexanol was dehydrated with phosphoric oxide (compare van de Kamp and Mosettig, *loc. cit.*). The saturated hydrocarbon mixture was distilled at 3 mm. into four fractions : I, $n_{\mathrm{D}}^{15\cdot2^\circ}$ 1·5505; II, $n_{\mathrm{D}}^{15\cdot2^\circ}$ 1·5505; III, $n_{\mathrm{D}}^{15\cdot2^\circ}$ 1·5526; IV, $n_{\mathrm{D}}^{15\cdot2^\circ}$ 1·5550. After oxidation, the oximes of the *trans*-ketone and the spirocyclic ketone were isolated from fractions I and II, and the oximes of the *cis*-ketone and the spirocyclic ketone were isolated from fraction IV.

Condensation of fraction IV (20 g.) with succinic anhydride by means of aluminium chloride in nitrobenzene solution gave a mixture of keto-acids (6·6 g.), m. p. 136—138°, from which the keto-acid, m. p. 160°, derived from the spiran (III), was isolated through the semicarbazone of its methyl ester (see below).

*Keto-acid arising from Condensation of the Spirocyclic Hydrocarbon* (III) *with Succinic Anhydride.*—Many batches of the hydrocarbon mixture obtained by cyclisation of β-phenylethyl-$\Delta^1$-*cyclo*hexene with aluminium chloride have been condensed with succinic anhydride to give β-6-*as*-octahydrophenanthroylpropionic acid, m. p. 140° (Cook and Haslewood, *loc. cit.*). One batch, however, was evidently unusually rich in the spiran (III), for, when it (250 g.) was condensed with succinic anhydride, it gave an acid (70 g.) of the expected m. p. (139—141°), but subsequent examination showed that it was a mixture containing a considerable proportion of a new keto-acid. The new acid was more resistant to Clemmensen reduction than octahydrophenanthroylpropionic acid, and was isolated from the mixture after Clemmensen reduction by repeated crystallisation from benzene and then alcohol, β-(5 or 6)-cyclo*hexane*-1-spiro*hydrindoylpropionic acid* being obtained in small colourless prisms, m. p. 162—163° (Found : C, 75·3; H, 7·7. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·75%). This keto-acid did not depress the m. p. of octahydrophenanthroylpropionic acid, m. p. 140°, and could not be separated from it by fractional crystallisation. Its sodium salt was sparingly soluble in water.

In another experiment in which the mixed keto-acids were reduced with hydrochloric acid and amalgamated zinc (7 hours' boiling) a small amount of acid sparingly soluble in ether was isolated. The sparingly soluble sodium salt of this was crystallised and the free acid was then crystallised from benzene, forming soft colourless needles, m. p. 140—141°. This appeared to be a molecular *compound* of keto-acid and a butyric acid formed by reduction of the keto-acid or its isomeride (Found : C, 77·3; H, 8·2. $C_{18}H_{22}O_3,C_{18}H_{24}O_2$ requires C, 77·4; H, 8·2%). Alternatively, this product may be an oxide formed by dehydration of a pinacol reduction product of the keto-acid ($C_{36}H_{44}O_5$ requires C, 77·7; H, 7·8%).

In order to separate the *cyclo*hexane*spiro*hydrindoylpropionic acid from the crude mixture, without previous reduction, this was first purified by crystallisation of the sodium salt, and the liberated acid (m. p. 143—147°) was esterified with diazomethane. The syrupy methyl ester was treated with semicarbazide in aqueous alcoholic solution, and the *semicarbazone* of the methyl ester was recrystallised from methyl alcohol, forming colourless prismatic needles, m. p. 185—186° (Found : C, 67·2; H, 7·5. $C_{20}H_{27}O_3N_3$ requires C, 67·2; H, 7·6%). Hydrolysis first with sulphuric acid, alcohol, and water, and then with alcoholic sodium hydroxide, gave the pure *cyclo*hexane*spiro*hydrindoylpropionic acid, m. p. 162°.

The *semicarbazone* of the methyl ester of β-6-*as*-octahydrophenanthroylpropionic acid formed stout colourless crystals (from alcohol), m. p. 175·5—176·5°, depressed about 6—7° by the corresponding spirocyclic semicarbazone (Found : C, 67·0; H, 7·5%).

γ-(5 or 6)-cyclo*Hexane*-1-spiro*hydrindylbutyric acid* was obtained when the semicarbazone (1 g.), m. p. 207°, of the keto-acid was heated for 18 hours with alcoholic sodium ethoxide (1 g. of sodium in 15 c.c. of alcohol). The *butyric acid* was distilled at 0·05 mm. from an air-bath at 160°, and crystallised from hexane, forming colourless needles, m. p. 105—107° (Found : C, 79·5; H, 9·0. $C_{18}H_{24}O_2$ requires C, 79·3; H, 8·9%). The same acid was also isolated from the more soluble products of the Clemmensen reduction of the original mixture of keto-acids.

1′-(or 4′)*Keto*-1′ : 2′ : 3′ : 4′-*tetrahydro*-5 : 6-*benzhydrindene*-1-spirocyclo*hexane* (IV or V). The aforesaid butyric acid (1 g.) was dehydrated by heating at 100° for ¾ hour with sulphuric acid (5 c.c.; 4 vols. of conc. acid, 1 vol. of water). The tetracyclic *ketone* (IV or V) was sublimed at 120°/0·001 mm. and recrystallised from methyl alcohol, forming colourless needles, m. p. 109—110° (Found : C, 84·7; H, 8·7. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%).

This ketone (0·4 g.) was oxidised by heating at 170—180° for 6 hours with dilute nitric acid (2·5 c.c. of conc. acid, 7·5 c.c. of water), and the water-soluble acids so formed were esterified by heating their silver salts with methyl iodide in benzene solution. The resulting tetramethyl pyromellitate had m. p. 140—141°, alone or mixed with an authentic sample.

1′-(or 4′)*Methyl*-5 : 6-*benzhydrindene*-1-spirocyclo*hexane* (VI or VII). The tetracyclic ketone (IV or V) (0·6 g.) was added to an ice-cold solution of methylmagnesium iodide, the whole kept in the ice-bath for ½ hour, and then boiled for 1½ hours. The resinous product, isolated in the normal manner, was dehydrogenated by heating with platinum-black (0·1 g.) at 295—300° for an hour. The resulting *hydrocarbon* (VI or VII) crystallised from alcohol in colourless plates, m. p. 109—110° (Found : C, 91·0; H, 9·05. $C_{19}H_{22}$ requires C, 91·1; H, 8·9%).

*Derivatives of* cis-as-*Octahydrophenanthrene.*—cis-7-*Nitro*-9-*keto*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene.* Powdered potassium nitrate (17·5 g.) was slowly added to a mechanically stirred solution of the liquid ketone (30 g.) (obtained by dehydration of 2-phenyl*cyclo*hexylacetic acid, m. p. 168—170°; Cook, Hewett, and Lawrence, *loc. cit.*) in concentrated sulphuric acid (150 c.c.). During addition of the nitrate the solution was cooled in a bath of ice and salt, and was then kept in an ice-bath for an hour, and poured on ice. The *nitro-ketone* was collected and recrystallised from aqueous acetone (yield, 26 g.). A sample, recrystallised from alcohol, formed colourless plates, m. p. 151·5—152° (Found: C, 68·8; H, 6·1. $C_{14}H_{15}O_3N$ requires C, 68·5; H, 5·7%).

cis-7-*Amino-9-keto-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene.* A solution of the nitro-ketone (14 g.) in acetone (250 c.c.) was shaken with hydrogen and palladium-black (1 g.) until absorption ceased. The acetone was removed on the water-bath, and the residue recrystallised from benzene–*cyclo*hexane. The *amino-ketone* (33·4 g. from 41·5 g. of nitro-compound) formed yellow needles or colourless plates, m. p. 118·5—119° (Found: C, 78·0; H, 8·4. $C_{14}H_{17}ON$ requires C, 78·0; H, 8·0%). Its *acetyl* derivative formed colourless leaflets (from alcohol), m. p. 178—179° (Found: C, 74·6; H, 7·5. $C_{16}H_{19}O_2N$ requires C, 74·7; H, 7·45%).

cis-7-*Hydroxy-9-keto-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene* (VIII). An ice-cold solution of the amino-ketone (15 g.) in N-sulphuric acid (150 c.c.) was diazotised with sodium nitrite solution (5 g. in 50 c.c. of water). Excess of nitrous acid was destroyed with urea (0·5 g.) and the diazonium salt was added to boiling N-sulphuric acid (2·5 l.). Boiling was continued for 5 minutes, and the solution cooled and extracted with ether. The ethereal extract, filtered from insoluble colouring matter, was shaken with dilute sodium hydroxide solution, and the alkaline solution was acidified and re-extracted with ether. The extract was dried with sodium sulphate, the ether removed, and the residual brown gum dissolved in benzene, treated with *cyclo*hexane, and boiled with charcoal. The filtered solution was set aside in the refrigerator for 2 days, and the brown crystalline solid (9 g.) collected. This was sublimed at 140—150°/0·001 mm., recrystallised from benzene–*cyclo*hexane (yield, 7·5 g.) and then, for analysis, from benzene. cis-7-*Hydroxy-9-hexahydrophenanthrone* (VIII) formed a colourless crystalline powder, m. p. 141—142° (Found: C, 78·0; H, 7·4. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·5%). This hydroxy-ketone gave no oestrous response when injected in 10 mg. doses into ovariectomised mice. Its semicarbazone formed colourless crystals (from methyl alcohol), m. p. 233—234°. In another experiment the crude hydroxy-ketone was extracted with sodium carbonate, and 11·9 g. of material of m. p. 141° were obtained from 16·5 g. of amino-ketone.

Many fruitless attempts were made to obtain proof of configuration of the foregoing hydroxy-ketone by oxidation to hexahydrohomophthalic acid, both geometrical isomerides of which are known (Windaus, Hückel, and Reverey, *Ber.*, 1923, **56**, 91; compare Chuang and Tien, *Ber.*, 1936, **69**, 25). The following is a description of one such experiment: A solution of potassium permanganate (15 g.) in water (300 c.c.) was added during ½ hour to a mechanically stirred ice-cooled solution of *cis*-7-hydroxy-9-hexahydrophenanthrone (2·1 g.) in dilute aqueous potassium hydroxide (1 g. in 75 c.c.). The whole was heated on the water-bath, acidified with sulphuric acid, and treated with more permanganate (7 g.). The solution was warmed until the permanganate colour was destroyed, filtered, and concentrated under reduced pressure. It was then extracted five times with ether, the extract dried over sodium sulphate, and the ether removed. The residual gum gave a solid when triturated with benzene, and this, after two recrystallisations from water, had m. p. 150°, not depressed by adipic acid. The identification was completed by comparison of the *p*-bromophenacyl ester with an authentic specimen prepared from adipic acid (Kelly and Kleff, *J. Amer. Chem. Soc.*, 1932, **54**, 4444). The slowly crystallising gum obtained from the benzene liquors was similarly treated with *p*-bromophenacyl bromide and gave an ester which crystallised from alcohol in colourless leaflets, m. p. 124—125°. Analysis showed that this consisted mainly of *p*-bromophenacyl glutarate, which had m. p. 134·5—135·5°, and a mixed m. p. determination showed no depression (Found: C, 48·3, 48·5; H, 3·6, 3·6; Br, 30·2, 30·0. Calc. for $C_{21}H_{18}O_6Br_2$: C, 47·9; H, 3·45; Br, 30·4%). In another oxidation experiment in which the treatment with acid permanganate was omitted oxalic acid was isolated. Yet another oxidation was carried out entirely in the cold in alkaline solution, and the acidic products were esterified, and the esters distilled. One fraction gave after hydrolysis a water-soluble acid, m. p. 218—220°, which appeared to be *trans*-hexahydrophthalic acid. This does not invalidate the *cis*-configuration assigned to the series of octahydrophenanthrene derivatives in question, as the *trans*-acid may well have been formed by alkaline hydrolysis of the *cis*-ester (compare Hückel and Goth, *Ber.*, 1925, **58**, 449).

In connexion with this work a specimen of the *p*-bromophenacyl ester of *trans*-hexahydrohomophthalic acid * was prepared and had m. p. 178—179° (from acetone). The *p*-bromo-

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* We are indebted to Professor R. P. Linstead for the gift of a specimen of this acid.

phenacyl ester of *cis*-hexahydrohomophthalic acid could not be obtained crystalline, but its p-*phenylphenacyl* ester formed a colourless crystalline powder, m. p. 146—147° (Found : C, 77·1; H, 6·1. $C_{37}H_{34}O_6$ requires C, 77·3; H, 6·0%).

cis-7-*Hydroxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene* (IX). The hydroxy-ketone (VIII) (10 g.) was boiled under reflux for 7½ hours with concentrated hydrochloric acid (20 c.c.), water (40 c.c.), toluene (20 c.c.), and amalgamated zinc (30 g.), additional hydrochloric acid (5 c.c.) being added after each hour. The product was extracted with ether and distilled, giving 6 g. of distillate, b. p. 190°/2·5 mm. cis-7-*Hydroxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene* (IX) crystallised from ligroin in colourless needles, m. p. 94—95° (Found : C, 83·2; H, 8·9. $C_{14}H_{18}O$ requires C, 83·1; H, 9·0%). Its *benzoate* formed small colourless needles (from alcohol), m. p. 100—101° (Found : C, 82·2; H, 7·3. $C_{21}H_{22}O_2$ requires C, 82·3; H, 7·25%), and its 3 : 5-*dinitrobenzoate* formed soft, almost colourless needles (from ethyl acetate), m. p. 165·5—166·5° (Found : C, 63·6; H, 5·1. $C_{21}H_{20}O_6N_2$ requires C, 63·6; H, 5·1%).

The octahydrophenanthrol (IX) was rapidly dehydrogenated by heating with platinum-black at 235—240°. After an hour at this temperature the acidic product was extracted with dilute alkali and recrystallised from aqueous methyl alcohol. The crystals, m. p. 162°, gave a benzoate, m. p. 136°, and there was insufficient material for further purification (2-phenanthrol has m. p. 168°, and its benzoate, 139—140°).

When the liquid methyl ether of the octahydrophenanthrol (IX), prepared by methylation with methyl *p*-toluenesulphonate and aqueous alkali at 100°, was heated with platinum-black at 300°, it was dehydrogenated to 7-*methoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*, m. p. 60—61° (from aqueous alcohol) (Found : C, 85·1; H, 6·65. $C_{15}H_{16}O$ requires C, 84·9; H, 7·6%), the *picrate* of which formed slender, light red needles, m. p. 125·5—126·5° (Found : C, 57·5; H, 4·3. $C_{15}H_{16}O,C_6H_3O_7N_3$ requires C, 57·1; H, 4·3%). The incompleteness of the dehydrogenation was doubtless due to catalyst poisoning, for the tetrahydro-compound was rapidly dehydrogenated to 2-methoxyphenanthrene, m. p. 98° (picrate, m. p. 124—125°), by selenium at 300°. The identification of these last-named compounds was completed by comparison with specimens prepared from β-*m*-methoxyphenylethyl-$\Delta^1$-*cyclo*hexene (below).

9-*Hydroxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*.—When 2-phenyl-$\Delta^1$-*cyclo*hexenylacetic acid (Cook, Hewett, and Lawrence, *loc. cit.*) was dehydrated with cold concentrated sulphuric acid, it gave, in rather poor yield, a viscous liquid phenol, the 3 : 5-*dinitrobenzoate* of which formed lemon-yellow leaflets (from benzene), m. p. 220° (Found : C, 64·4; H, 4·15. $C_{21}H_{16}O_6N_2$ requires C, 64·3; H, 4·1%).

2-*Phenyl*cyclo*hexylideneacetic Acid*.—A solution of 2-phenyl*cyclo*hexanolacetic acid (Cook, Hewett, and Lawrence, *loc. cit.*) (8 g.) in acetic anhydride (20 c.c.) was boiled for 2 hours, cooled, poured into water, and kept overnight. The oil was extracted with ether, and the extract shaken with dilute sodium carbonate solution. Acidification of the alkaline solution gave 2-*phenyl*cyclo*hexylideneacetic acid*, which, after recrystallisation from ligroin and then benzene, formed colourless prisms, m. p. 168—169° (Found : C, 77·9; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·5%).

*Perhydrophenanthrene Derivatives*.—(a) *Hydrogenation of* cis-7-*hydroxy*-9-*keto*-as-*octahydrophenanthrene* (VIII). A solution of the hydroxy-ketone (4·7 g.) in acetic acid (75 c.c.) was shaken with hydrogen and Adams's platinum catalyst (0·5 g.). In 30 hours, 2·2 l. of hydrogen were absorbed. The acetic acid was removed under reduced pressure, and the residue treated with light petroleum. The solid in suspension (0·8 g.) was collected and recrystallised from alcohol, forming colourless elongated plates, m. p. 239—240°. This was 2 : 10-*dihydroxyperhydrophenanthrene* (X) (Found : C, 74·5; H, 10·7; *M*, 228, 243. $C_{14}H_{24}O_2$ requires C, 74·9; H, 10·8%; *M*, 224); a crystalline benzoate could not be obtained, nor was a crystalline diketone formed by oxidation with chromic acid in cold acetic acid. The material from the light petroleum mother-liquors from which this diol had been separated was distilled into two main fractions. The lower fraction (1 g.) consisted of perhydrophenanthrene, and after redistillation had b. p. 133—135°/13—14 mm., and $n_D^{10·2°}$ 1·5152 (Found : C, 87·4; H, 12·7. Calc. for $C_{14}H_{24}$ : C, 87·4; H, 12·6%). The higher fraction (1·7 g.), b. p. 120°/0·1 mm., formed a thick colourless gum, which was treated with 3 : 5-dinitrobenzoyl chloride (2·5 g.) in pyridine (7·5 c.c.) at 100° for 15 minutes. The resulting mixture of 3 : 5-dinitrobenzoates was fractionally crystallised from *cyclo*hexane into the 3 : 5-dinitrobenzoate, m. p. 166°, of octahydro-7-phenanthrol (IX), the less soluble component, and the 3 : 5-*dinitrobenzoate* of 2-hydroxyperhydrophenanthrene (XI), which crystallised from alcohol in colourless needles, m. p. 167—168° (Found : C, 63·1; H, 6·6. $C_{21}H_{26}O_6N_2$ requires C, 62·7; H, 6·5%). 2-*Hydroxyperhydrophenanthrene* (XI), obtained from this dinitrobenzoate by hydrolysis with aqueous alcoholic potash, crystallised from ligroin in colourless silky needles, m. p. 108—109° (Found : C, 80·5; H, 11·6. $C_{14}H_{24}O$ requires C, 81·0; H, 11·6%).

Oxidation of the last-named carbinol with chromic acid in cold acetic acid (24 hours) gave a liquid ketone which formed a *semicarbazone*, a colourless microcrystalline powder, m. p. 179—180° (from alcohol) (Found : C, 68·3; H, 9·6. $C_{15}H_{25}ON_3$ requires C, 68·4; H, 9·6%), together with a *dicarboxylic acid*, m. p. 170° (from benzene and then aqueous alcohol) (Found : C, 66·1; H, 8·8. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·7%).

In another hydrogenation experiment the crude distilled carbinol fraction was oxidised with chromic acid, and the neutral product treated with semicarbazide. There was isolated by crystallisation from dioxan a *semicarbazone* isomeric with that mentioned in the preceding paragraph. The new semicarbazone formed a colourless microcrystalline powder, m. p. 209—210° (Found : C, 68·3; H, 9·7. $C_{15}H_{25}ON_3$ requires C, 68·4; H, 9·6%).

(b) *Hydrogenation of* cis-7-*hydroxy*-as-*octahydrophenanthrene* (IX). This phenol (4·5 g.) was hydrogenated in acetic acid with Adams's platinum catalyst, and the product fractionally distilled into perhydrophenanthrene (1·2 g.) and a carbinol mixture (2·5 g.), b. p. 123°/0·1 mm., which was dissolved in light petroleum, and the solution kept overnight in the refrigerator. The resulting crystals were recrystallised from hexane and gave 0·9 g. of the perhydro-2-phenanthrol, m. p. 108—109°, described under (a). Treatment of the material from the mother-liquors with 3 : 5-dinitrobenzoyl chloride in pyridine gave a mixture of dinitrobenzoates from which the only homogeneous substance isolated was the dinitrobenzoate of unreduced octahydrophenanthrol.

Dehydrogenation of redistilled perhydrophenanthrene (1 g.) with selenium (2·75 g.) at 300—315° for 27 hours, and treatment of the product with picric acid, gave phenanthrene picrate (1·3 g. = 60% yield), m. p. 143—144° (lit., 145°), from which pure phenanthrene, m. p. 99—100°, was obtained.

β-m-*Methoxyphenylethyl*cyclo*hexanol and its Products.*—β-m-*Methoxyphenylethyl*cyclo*hexanol.* β-*m*-Methoxyphenylethyl alcohol, obtained as outlined by Hewett (J., 1936, 51), was converted into its chloride by treatment with thionyl chloride in dimethylaniline (compare Darzens, *Compt. rend.*, 1911, **152**, 1316). *cyclo*Hexanone (37 g.), diluted with dry ether (60 c.c.), was added to an ice-cooled Grignard solution prepared from β-*m*-methoxyphenylethyl chloride (60 g.), magnesium turnings (9 g.), and anhydrous ether (300 c.c.). The whole was kept at room temperature overnight and decomposed with ammonium chloride solution, and the tertiary carbinol isolated by distillation. It formed a colourless viscous liquid (58 g.), b. p. 160—165°/0·5 mm. β-*m*-Methoxyphenylethyl*cyclo*hexanol gave a 3 : 5-*dinitrobenzoate*, m. p. 93·5—94·5° (Found : C, 61·7; H, 5·9. $C_{22}H_{24}O_7N_2$ requires C, 61·7; H, 5·65%).

β-m-*Methoxyphenylethyl*-$\Delta^1$-cyclo*hexene* (XII). The tertiary carbinol (40 g.) was dehydrated by heating for 1½ hours at 160° with potassium hydrogen sulphate (40 g.). The product (b. p. 185°/22 mm.; 33·5 g.) consisted essentially of the unsaturated *compound* (XII) (Found : C, 81·85; H, 9·4. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). A little (8 g.) was redistilled in a vacuum over zinc chloride and then hydrogenated with palladium-black in alcoholic solution. The resulting β-m-*methoxyphenylethyl*cyclo*hexane* had b. p. 120—125°/0·5 mm. and $n_D^{18·8°}$ 1·5217 (Found : C, 81·9; H, 10·2. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%).

β-3′-*Hydroxy*cyclo*hexylethyl*cyclo*hexane* (XIV). β-*m*-Methoxyphenylethyl*cyclo*hexane (7·2 g.) was demethylated by boiling for 3 hours with hydrobromic acid (48%; 20 c.c.) in glacial acetic acid (50 c.c.). The distilled product (b. p. 145—147°/0·8 mm.; 5·1 g.) was hydrogenated in acetic acid solution with Adams's platinum catalyst. The hydrogenated material was fractionated into a mobile liquid, b. p. 98—102°/0·8 mm. (2·2 g.), and a viscous liquid, b. p. 132—133°/0·8 mm. (2·2 g.). The higher fraction was essentially the desired carbinol (Found : C, 80·7; H, 12·6%), and was treated with 3 : 5-dinitrobenzoyl chloride in pyridine at 100° (15 minutes). The resulting mixture of dinitrobenzoates was fractionally crystallised from alcohol, the only pure component isolated being a 3 : 5-*dinitrobenzoate* which formed colourless leaflets, m. p. 105·5—106·5° (Found : C, 62·6; H, 7·1. $C_{21}H_{28}O_6N_2$ requires C, 62·4; H, 7·0%). This, on hydrolysis with aqueous alcoholic potash, gave β-3′-*hydroxy*cyclo*hexylethyl*cyclo*hexane*, which separated from aqueous methyl alcohol in colourless crystals, m. p. 57—58° (Found : C, 79·8; H, 12·3. $C_{14}H_{26}O$ requires C, 79·9; H, 12·5%).

*Cyclisation of* β-m-*methoxyphenylethyl*-$\Delta^1$-cyclo*hexene* (XII). An ice-cold solution of the unsaturated compound (45 g.) in carbon disulphide (450 c.c.) was treated with powdered anhydrous aluminium chloride (45 g.), the mixture kept at 0° for 7 hours and decomposed with ice and hydrochloric acid, and the product distilled (b. p. 185—190°/22 mm.; 34 g.). Dehydrogenation of a specimen of this with selenium at 300° for 24 hours gave a mixture of products from which 2-methoxyphenanthrene was isolated in small yield. The remainder of the cyclised material (32 g.) was demethylated by 7 hours' boiling with concentrated hydrobromic acid (48%; 160 c.c.) in acetic acid (400 c.c.). The product (29 g.), b. p. 140—150°/0·6 mm., crystallised readily and was recrystallised from ligroin, giving 20 g. of material, m. p. 80—85°. This phenol was purified through its *benzoate*, which crystallised from alcohol in colourless fibrous needles, m. p. 103·5—104·5° (Found: C, 82·3; H, 7·5. $C_{21}H_{22}O_2$ requires C, 82·3; H, 7·25%). Hydrolysis of this benzoate gave 11·5 g. of 5-*hydroxyhydrindene*-1-spirocyclo*hexane* (XIII), which crystallised from ligroin in colourless needles, m. p. 96—97° (Found: C, 83·1; H, 9·0. $C_{14}H_{18}O$ requires C, 83·1; H, 9·0%). Its 3 : 5-*dinitrobenzoate* formed almost colourless, slender needles, m. p. 146—147° (Found: C, 63·65; H, 5·2. $C_{21}H_{20}O_6N_2$ requires C, 63·6; H, 5·1%). The material from the original ligroin liquors from which the crude spirocyclic phenol had been isolated was converted into 3 : 5-dinitrobenzoates; these consisted mainly of the dinitrobenzoate of (XIII), which was the only component which could be isolated.

5-*Methoxyhydrindene*-1-spirocyclo*hexane*. The pure crystalline phenol (XIII) was treated with an ethereal solution of diazomethane and kept overnight in the refrigerator. The resulting *methyl ether* formed a colourless viscous liquid, b. p. 120°/0·15 mm. (Found: C, 83·0; H, 9·4. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%). This did not undergo dehydrogenation when heated with platinum-black at 300°, and the pure phenol (XIII) was subsequently recovered by demethylation with hydrobromic acid in acetic acid.

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