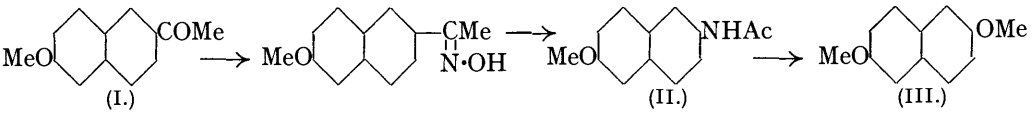
298. *Experiments on the Synthesis of Substances related to the Sterols. Part XXVII. The Synthesis of* x-*Noroestrone.*

By Sir Robert Robinson and H. N. Rydon.

The conversion of the readily accessible keto*cyclo*pentenophenanthrene compounds described in Part XXI (Robinson, J., 1938, 1390; cf. Koebner and Robinson, *ibid.*, p. 1994) into hydro-derivatives closely related to oestrone cannot conveniently be accomplished by direct hydrogenation. 4 : 7-Dimethoxy-3′-keto-1 : 2-*cyclo*pentenophenanthrene was converted into its *hydroxymethylene* derivative (VII) and then into the dibasic *acid* (IX). Hydrogenation of the related *dimethyl* ester (XI) afforded an *octahydrodemethoxy-acid* (XIV) which, on ketonisation, yielded x-*noroestrone methyl ether* (XV; R = Me); the latter has been converted into x-*noroestrone* (XV; R = H), characterised by its *acetyl* derivative. The physiological properties of the last two substances are being investigated.

The starting material for the synthesis was 6-methoxy-2-acetylnaphthalene (I); a modification of the method of preparation due to Haworth and Sheldrick (J., 1934, 864) which has given good results on a large scale is described in the experimental section. Haworth

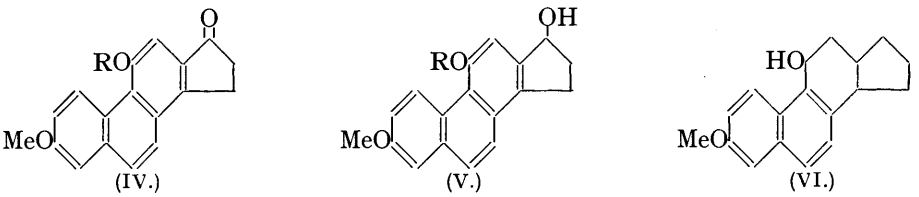
and Sheldrick (*loc. cit.*) converted this ketone into 6-methoxy-β-naphthoic acid, but in view of its importance for our purposes it was thought desirable to obtain further confirmation of its constitution. It was accordingly transformed into 2 : 6-dimethoxynaphthalene (III) by the following series of operations :



(I.) (II.) (III.)

In addition to identifying the end-product with an authentic specimen, the intermediary 2-*acetamido*-6-*methoxynaphthalene* (II) was shown to depress the m. p. of the 2 : 7-isomeride.

Our first experiments were concerned with the direct hydrogenation of compounds of type (IV). The dimethoxy-compound (IV; R = Me) and the methoxy-phenol (IV; R = H) were not suitable for this purpose, but some interesting results were obtained by the hydrogenation of the methoxy-acetate (IV; R = Ac) in the presence of Adams's catalyst in acetic acid at 70°. Three crystalline products were obtained; two of these, obtained in small amount by treating the hydrogenation product with solvents, proved to be the *dihydro-compound* (V; R = Ac) and the corresponding *phenol* (V; R = H). The third product was obtained from the hydrolysed hydrogenation product. It was isolated



(IV.) (V.) (VI.)

by direct precipitation with light petroleum and also as its p-*nitrobenzoate* and digitonide; analysis showed it to be a hydroxymethoxytetrahydro*cyclo*pentenophenanthrene. It was extremely resistant to oxidation, being recovered unchanged after treatment with chromic acid in acetic acid and from an attempted oxidation by Oppenauer's method. Since a 3'-hydroxyl should be readily oxidised to carbonyl, the substance is regarded as 4-*hydroxy*-7-*methoxy*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene* (VI). It is well known that carbonyl groups adjacent to an aromatic nucleus are completely reduced with the greatest of ease (cf. Vavon, *Compt. rend.*, 1912, **155**, 287; Zelinsky, Packendorff, and Leder-Packendorff, *Ber.*, 1933, **66**, 872; 1934, **67**, 300; Cook, Hewett, and A. M. Robinson, this vol., p. 168).

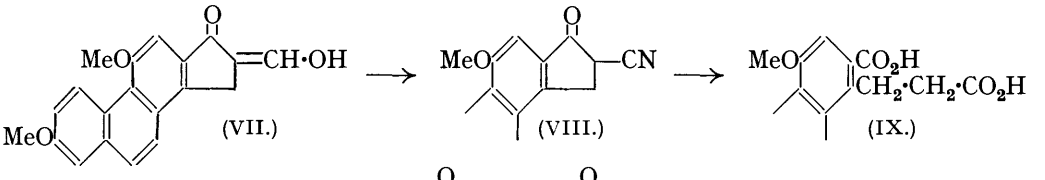
Distillation of the oily hydrolysed hydrogenation product gave two fractions of low oxygen content. Both of these were dehydrogenated by heating with palladised charcoal. The lower-boiling fraction gave a product, which was identified as 1 : 2-*cyclo*penteno-phenanthrene by mixed m. p. with an authentic specimen. This affords a valuable proof of the correctness of the structure put forward in Part XXI for compounds of type (IV) which contain a methoxyl group in position 7. The dehydrogenation product of the higher-boiling fraction was a mixture of *cyclo*pentenophenanthrene and a methoxy*cyclo*penteno-phenanthrene. It was not possible to obtain the latter absolutely pure, but strong evidence that it was the 7-methoxy-compound was obtained by mixed m. p. determinations of the methoxy-compound and its trinitrobenzene complex with authentic specimens. This may be regarded as experimental evidence for preferential de-oxygenation at the 4-position in the hydrogenation of 4 : 7-dihydroxyphenanthrene derivatives.

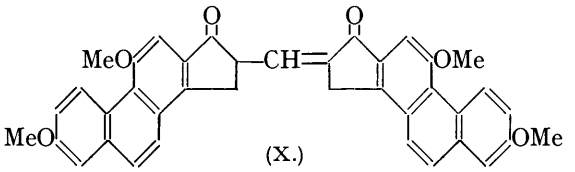
Owing to the unpromising results obtained in these direct hydrogenation experiments it became evident that, in order to obtain the desired 3'-keto-compounds, it would be necessary to open the five-membered ring before proceeding with the hydrogenation. Two methods seemed likely to lead to the desired result.

The dimethoxy-compound (IV; R = Me) was readily converted into the 2'-iso*nitroso*-derivative by the action of *iso*amyl nitrite in the presence of potassium *tert.*-butoxide.

It had been intended to convert this compound into the corresponding dimethoxyphenanthrenecarboxylic acid by the modified Beckmann process used by Litvan and Robinson (J., 1938, 2000) in the case of *iso*nitroso-oestrone methyl ether. After reduction the five-membered ring could then have been resynthesised by the methods used by Litvan and Robinson (*loc. cit.*). In view, however, of the success of the shorter route, based on the transformations (VII) ⟶ (IX), this method was not pursued further.

The preparation of the *hydroxymethylene* derivative (VII) was complicated by the ease with which it passed into the condensation *product* (X) (cf. 2-formyl-1-hydrindone; Ruhemann and Levy, J., 1912, **101**, 2549). The latter was the sole product from the dimethoxy-compound (IV; R = Me) and *iso*amyl formate in the presence of potassium

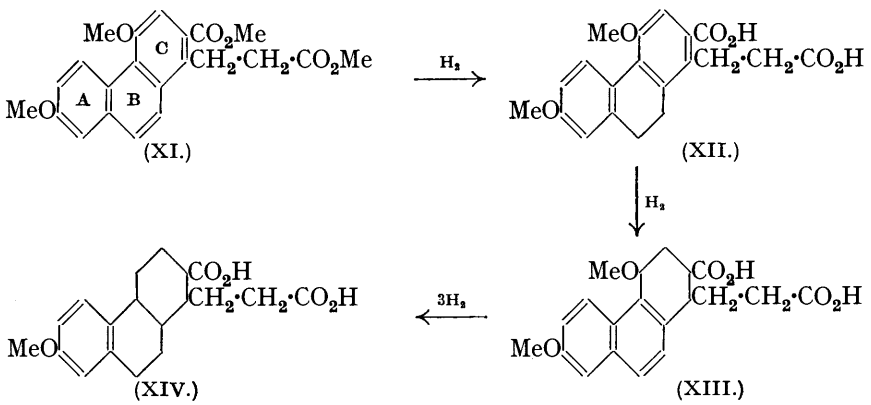




tert.-butoxide, and very little reaction occurred under the conditions used by Bardhan (J., 1936, 1851) in the case of oestrone methyl ether. Success was finally achieved by using ethyl formate in pyridine solution with alcoholic sodium ethoxide as catalyst.

The action of hydroxylamine hydrochloride on the hydroxymethylene derivative (VII) in alkaline solution (cf. Lapworth, J., 1900, **77**, 1058; Bardhan, *loc. cit.*) was unsatisfactory, and the cyano-ketone (VIII) was prepared, albeit in an impure condition, by treating the hydroxymethylene derivative with hydroxylamine hydrochloride in acetic acid (cf. cyanocamphor; Bishop, Claisen, and Sinclair, *Annalen*, 1894, **281**, 314). Prolonged hydrolysis with concentrated aqueous-alcoholic potassium hydroxide yielded 4 : 7-*dimethoxyphenanthrene*-1-β-*propionic*-2-*carboxylic acid* (IX) which was converted into its *dimethyl* ester (XI) and purified by means of an alumina column.

This ester was hydrogenated at 70° in acetic acid by using Adams's catalyst. Hydrolysis of the product, followed by fractional crystallisation, first from benzene and then from dilute acetic acid, yielded three saturated acids. These are tentatively regarded as 4 : 7-



dimethoxy-9 : 10-*dihydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XII), 4 : 7-*dimethoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XIII), and 7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XIV).

These constitutions are admittedly not yet proven; they are based on the following analogies:

(i) The simple picture of the hydrogenation of phenanthrene to the 9 : 10-dihydro-, the 1 : 2 : 3 : 4-tetrahydro-, and the 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-compounds, successively, afforded by the work of Schroeter (*Ber.*, 1924, **57**, 2025; Schroeter, Müller, and Huang, *ibid.*, 1929, **62**, 645) has been shown to be inadequate, as regards the octahydro-derivative, by Durland and Adkins (*J. Amer. Chem. Soc.*, 1938, **60**, 1501), who found that a change in the experimental conditions caused the formation of considerable amounts of the 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-compound.

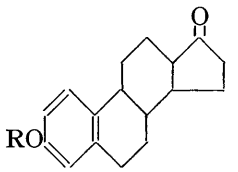
(ii) It has been shown by Schroeter (*Annalen*, 1922, **426**, 83; cf. Hückel, *ibid.*, 1927, **451**, 109) that α-naphthol undergoes de-oxygenation on catalytic hydrogenation more readily than does β-naphthol. Further, van Durzee and Adkins (*J. Amer. Chem. Soc.*, 1935, **57**, 147) have shown that benzyl ethers readily undergo fission to toluene and an alcohol on catalytic hydrogenation. For these reasons it is to be expected that the 4-methoxyl group would be preferentially eliminated in the hydrogenation of (XI) and (XIII). The same deduction may be made from the experimental evidence that it is a group in this position that is preferentially eliminated in the hydrogenation of the methoxy-acetate (IV; R = Ac).

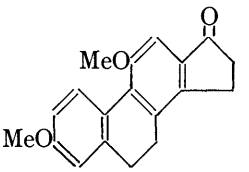
(iii) *m*-Hydroxybenzoic acid is readily hydrogenated to the hexahydro-compound under very mild conditions (Balaš and Kosik, *Casopis Ceskoslov. Lek.*, 1927, **7**, 136; Balaš and Šrol, *Coll. Czech. Chem. Comm.*, 1929, **1**, 658) and the hydroxyl group is then eliminated (Edson, *J. Soc. Chem. Ind.*, 1934, **53**, 138T). These results indicate a considerable increase of reactivity towards hydrogen in an aromatic nucleus carrying a carboxyl group, and a similar effect might be expected in ring C of the ester (XI). Consideration of Baeyer's classical work on the reduction of phthalic acid and other benzene derivatives leads to the same conclusion. Since the acid (XIV) can contain only one benzene nucleus and is the methyl ether of a phenol, there is only one alternative formula, and this is a highly improbable one, for it would necessitate the assumption that the nucleus bearing the carboxyl group remains unattacked, while all the other nuclei are preferentially reduced.

Since it has been shown that the hydrogenation of naphthalene in the presence of a platinum catalyst and in acetic acid solution yields exclusively *cis*-decalin (Willstätter and Seitz, *Ber.*, 1924, **57**, 683), it is probable that the reduced rings in the octahydro-demethoxy-acid (XIV) are fused in the *cis*-position. Application of the Auwers–Skita rule would also indicate a *cis*-configuration for the acidic side chains.

By pyrolysis of the lead salt in a vacuum the acid (XIV) was readily ketonised to x-*noroestrone methyl ether* (XV; R = Me). [The prefix "*x*" is used to indicate indeterminate stereochemical configuration (cf. Koebner and Robinson, J., 1938, 1994) but, on the basis

(XV.)





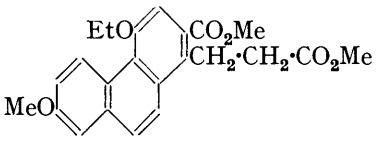
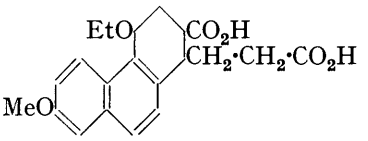
(XVI.)

of the above arguments, the substance probably has the *cis-cis*-configuration.] This methoxy-ketone was readily demethylated to a keto-phenol, x-*noroestrone* (XV; R = H), which, with acetic anhydride in pyridine, yielded x-*noroestrone acetate* (XV; R = Ac).

The dihydro-acid (XII) was readily ketonised in the same way, yielding 4 : 7-*dimethoxy*-9 : 10-*dihydro*-3′-*keto*-1 : 2-cyclo*pentenophenanthrene* (XVI), but the reaction failed with the tetrahydro-acid (XIII), probably owing to partial elimination of methyl alcohol during the pyrolysis.

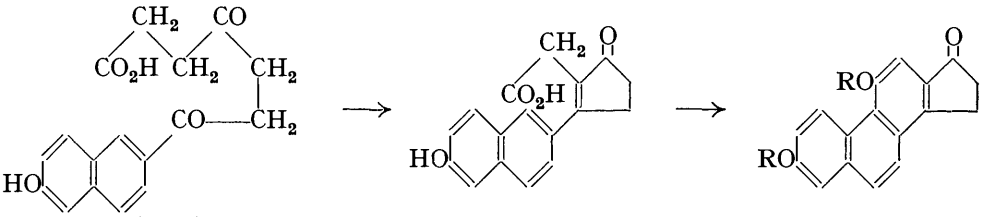
By the action of ethyl sulphate the methoxy-phenol (IV; R = H) was converted into the *methoxyethoxy*-compound (VI; R = Et). This was submitted to a series of reactions precisely similar to those described above for the dimethoxy-compound yielding, finally, *methyl* 7-*methoxy*-4-*ethoxyphenanthrene*-1-β-*propionate*-2-*carboxylate* (XVII). It was hoped that it would prove possible to isolate from the hydrogenation product of this ester the

octahydrodemethoxy-acid (XIV) and thus obtain conclusive proof of the structure of the

(XVII.)   (XVIII.)

latter. Unfortunately, the experimental difficulties of separation were much greater than in the dimethoxy-series and the only reduced acid isolated in a state approaching purity was *7-methoxy-4-ethoxy-1 : 2 : 3 : 4-tetrahydrophenanthrene-1-β-propionic-2-carboxylic acid* (XVIII). Careful search failed to reveal the presence of any of the desired acid (XIV) or of any other de-oxygenated material.

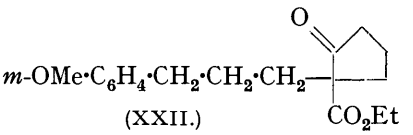
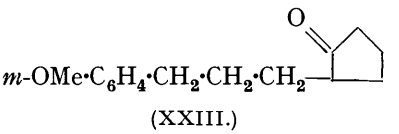
7-(β-6′-Methoxynaphthyl)-4 : 7-diketoheptoic acid was readily demethylated by refluxing with a mixture of acetic and hydrochloric acids. The resulting *7-(β-6′-hydroxynaphthyl)-4 : 7-diketoheptoic acid* (XIX) was cyclised by hot alkali to *3-(6′-hydroxy-β-naphthyl)-Δ²-cyclopentenone-2-acetic acid* (XX), which was, in turn, cyclised with acetic



(XIX.) (XX.) (XXI.)

anhydride to *4 : 7-diacetoxy-3′-keto-1 : 2-cyclopentenophenanthrene* (XXI; R = Ac). Experiments on the hydrogenation of this substance with Adams's catalyst in acetic acid gave no useful results. The diacetate was hydrolysed to the *diphenol* (XXI; R = H), which on methylation gave the dimethoxy-compound (IV; R = Me).

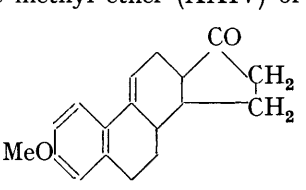
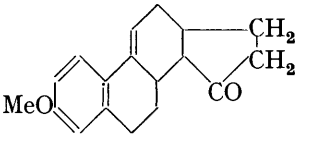
In connexion with another projected synthesis of *cyclo*pentenophenanthrene derivatives, *γ-m*-methoxyphenylpropyl iodide, the preparation of which from the chloride (Robinson and Schlittler, J., 1935, 1290) has been improved, was condensed with ethyl *cyclo*pentanone-

(XXII.) (XXIII.)

2-carboxylate and the resulting *keto-ester* (XXII) converted, by hydrolysis to the adipic acid followed by ketonisation, into 2-(γ-m-*methoxyphenylpropyl*)cyclo*pentanone* (XXIII).

Related to the subject matter of this communication is a very recent paper by Dane and Eder (*Annalen*, **1939**, **539**, 207), who have prepared an adduct from 6-methoxy-1-vinyl-3 : 4-dihydronaphthalene and *cyclo*pentenone. The ketone obtained might be dehydro-*x*-noroestrone methyl ether (XXIV) or the isomeride (XXV). If, as seems probable, the

(XXIV.)   (XXV.)

Diels reaction is initiated by the coupling of the more anionoid end of the diene system with a cationoid β-carbon atom of a catio-enoid system, then the choice between these alternatives can be made if we can locate the more reactive anionoid carbon atom in the methoxy-vinyldihydronaphthalene. The circumstances are somewhat complex in this cross-conjugated system and the most that can be said is that the more aliphatic site of the vinyl

group favours (XXV), whereas the combined effect of two unsaturated conjugated centres on the naphthalene double bond, as well as the influence of the methoxyl group and any steric factor, favours (XXIV).

Experimental.

6-Methoxy-2-acetylnaphthalene (I).—The following modification of Haworth and Sheldrick's method (*loc. cit.*) has yielded consistently good results.

Powdered aluminium chloride (200 g., Judex brand) is dissolved in nitrobenzene (1200 c.c.); 2-methoxynaphthalene (192 g.) is added followed by acetyl chloride (120 g.) introduced during 20 minutes with mechanical stirring and ice-cooling. After being kept in ice for 3 hours, and then at room temperature for 48 hours, the product is poured on to crushed ice (1000 g.), mixed with concentrated hydrochloric acid (400 c.c.) and water (400 c.c.), with good stirring. After being washed twice with water by decantation, the nitrobenzene is removed completely by steam-distillation. When cold the solid residue is broken up, collected, dried, and distilled. The fraction, b. p. 175—185°/0·8 mm., is poured, while molten, into methyl alcohol (300 c.c.). The almost pure ketone crystallises on cooling (yield about 120 g.).

This product (5 g.) was refluxed on the water-bath for 105 minutes with methyl alcohol (30 c.c.) and a concentrated aqueous solution of hydroxylamine hydrochloride (1·75 g.) and crystallised sodium acetate (3·4 g.). The *oxime* (5·2 g.; 97%) separated on cooling and addition of water; it crystallised from aqueous methyl alcohol in hexagonal plates, m. p. 169—170° (Found: N, 6·4. $C_{13}H_{13}O_2N$ requires N, 6·5%).

The oxime (1 g.) was suspended in dry ether (20 c.c.), gradually treated with phosphorus pentachloride (1 g.) with shaking, and kept at room temperature for 15 minutes; ether (10 c.c.) was added, and the mixture refluxed on the water-bath for 30 minutes. The ether was then evaporated, and the residue decomposed with ice-water; two crystallisations of the product from aqueous methyl alcohol yielded *6-acetamido-2-methoxynaphthalene* (II) as colourless needles, m. p. 162—163° (Found: N, 6·5. $C_{13}H_{13}O_2N$ requires N, 6·5%). The m. p. was depressed to 118—123° on admixture with an authentic specimen of 7-acetamido-2-methoxynaphthalene.

The crude acetamido-compound (2 g.) was refluxed for 50 minutes with concentrated hydrochloric acid (15 c.c.) and water (5 c.c.). The cooled solution was diluted, and made just alkaline with sodium hydroxide; the precipitated phenol was collected and crystallised from water (0·8 g.; m. p. 180—190°). This was dissolved in water (20 c.c.) and concentrated hydrochloric acid (4 c.c.) and diazotised (ice-cooling) by adding a concentrated aqueous solution of sodium nitrite (0·5 g.). The solution was poured into boiling water and boiled for a few minutes. The tarry precipitate was collected and extracted twice with boiling methyl alcohol (5 c.c.). Methyl sulphate (1 c.c.) was added to the cooled, filtered extract, followed by 10% sodium hydroxide solution (5 c.c.) added dropwise with shaking. Steam-distillation yielded 2 : 6-dimethoxynaphthalene (III) in leaflets which, after vacuum sublimation, had m. p. 145—148°, mixed m. p. with an authentic specimen, 146—149°.

4 : 7-Dimethoxy-3′-keto-1 : 2-cyclopentenophenanthrene.—3-(6′-Methoxy-β-naphthyl)-Δ^2-*cyclo*pentenone-2-acetic acid (Robinson, *loc. cit.*; Koebner and Robinson, *loc. cit.*) was converted into 4-acetoxy-7-methoxy-3′-keto-1 : 2-*cyclo*pentenophenanthrene (IV; R = Ac) by the following modification of the method previously described. A mixture of the remethylated *cyclo*pentenone acid (45 g.) and acetic anhydride (335 c.c.) was refluxed for 30 minutes. The dark mass remaining after 190 c.c. of solvent had been distilled was broken up under benzene, filtered off, washed with benzene, and dried in a vacuum desiccator. The product (37 g.; 74%) had m. p. 241—242° and was sufficiently pure for preparative purposes.

The corresponding phenol (6 g.), prepared in the usual way, was heated on a steam-bath for 5 hours with hydroxylamine hydrochloride (3 g.) and pyridine (50 c.c.). The *oxime*, which separated on cooling and dilution with water, crystallised from acetic acid–pyridine–water in needles, m. p. 268° (Found: N, 4·4. $C_{18}H_{15}O_3N,H_2O$ requires N, 4·5%).

It was found convenient to prepare the dimethoxy-compound (IV; R = Me) directly from the methoxy-acetate. 22 G. of the latter were refluxed on the water-bath for 1½ hours with sodium hydroxide (13 g.) in water (26 c.c.) and ethyl alcohol (320 c.c.). The mixture was then stirred mechanically and heated in a water-bath at 60° while methyl sulphate (20 c.c.) was added during 10 minutes. Stirring and heating were continued while three batches of 10% sodium hydroxide solution and 10 c.c. of methyl sulphate were added alternately during 25 minutes. The dimethoxy-compound, which separated on cooling and dilution, was collected, washed, and dried; it was sufficiently pure for preparative purposes (yield, 19·5 g. or 97%).

Hydrogenation of the Methoxy-acetate (IV; R = Ac).—(i) The methoxy-acetate (6·4 g.), suspended in acetic acid (130 c.c.), was stirred in hydrogen at 70° in the presence of Adams's catalyst (0·3 g.). 4 Mols. of hydrogen were taken up in 26 hours. After filtration from the catalyst and removal of the solvent under reduced pressure, the product was treated with methyl alcohol (40 c.c.). The solid which separated (1·5 g.) was crystallised, first from aqueous acetic acid and then from ethyl acetate. 0·2 G. of a new product, crystallising from ethyl acetate in prismatic needles, m. p. 139—140°, was obtained; analysis indicated that this should be 4 : 3′-*dihydroxy*-7-*methoxy*-1 : 2-cyclo*pentenophenanthrene* (V; R = H) (Found: C, 77·1; H, 5·7. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%).

In a similar experiment the hydrogenated product was triturated with light petroleum (b. p. 40—60°); a solid separated, and two crystallisations from methyl alcohol yielded 3′-*hydroxy*-4-*acetoxy*-7-*methoxy*-1 : 2-cyclo*pentenophenanthrene* (V; R = Ac) in feathery needles, m. p. 145° (Found: C, 75·0; H, 5·1. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%).

(ii) The methoxy-acetate (9·6 g.) was hydrogenated as described above; 5 mols. of hydrogen were taken up in 24 hours. After removal of the catalyst by filtration, and evaporation of the solvent under reduced pressure, the residue was refluxed on the steam-bath for 5 hours with potassium hydroxide (5 g.), water (5 c.c.) and methyl alcohol (50 c.c.). The product was added to water, extracted with ether, dried, and distilled, giving fractions (*a*) b. p. 175—195°/0·2 mm. and (*b*) b. p. 200—220°/0·3 mm., 1·7 g.

1 G. of (*b*) was dissolved in absolute alcohol (30 c.c.) and warmed with digitonin (1 g.) in 80% alcohol (50 c.c.). The digitonide that separated on keeping overnight was collected, and the filtrate treated with more digitonin. Several treatments gave, in all, 2·6 g. of digitonide. This was decomposed by solution in pyridine (40 c.c.); the digitonin was precipitated with ether (150 c.c.) and centrifuged. The ethereal solution was washed with water and dilute acid, dried, and evaporated. The residue (0·5 g.) was crystallised from light petroleum (b. p. 80—100°) and then had m. p. 140—141°; a mixed m. p. showed it to be the alcohol (VI).

Fraction (*a*) was redistilled, giving 2 g., b. p. 178—182°/0·15 mm., $n_D^{17°}$ 1·5764 (Found: C, 86·9; H, 7·1%) (corresponding to $C_{29}H_{36}O$, but the material is probably a mixture). This was heated with 0·2 g. of 10% palladised charcoal at 280—300° for 40 minutes and then at 330—360° for an hour, hydrogen being evolved vigorously. After cooling, the solid residue was taken up in ether, filtered, the ether evaporated, and the residue crystallised from aqueous alcohol, yielding a mixture of *cyclo*pentenophenanthrene (80%) and a methoxy*cyclo*pentenophenanthrene (20%) (Found: C, 92·3; H, 6·5. Calc. for $C_{17}H_{14}$: C, 93·6; H, 6·4%. Calc. for $C_{18}H_{16}O$: C, 87·1; H, 6·4%). 100 Mg. were treated in alcohol with 0·2 mol. of 1 : 3 : 5-trinitrobenzene; an additive compound separated in orange needles, m. p. 144—148°. Recrystallisation from methyl alcohol yielded orange needles, m. p. 148—149°, not depressed on admixture with the authentic trinitrobenzene compound of 7-methoxy-1 : 2-*cyclo*pentenophenanthrene (m. p. 161°). A further 150 mg. of the mixture were converted into picrate; fractional crystallisation from alcohol gave much 1 : 2-*cyclo*pentenophenanthrene picrate and another picrate, m. p. 120—123° (50 mg.). This was decomposed with ammonia; the product crystallised from alcohol in shining leaflets, m. p. 123—126°, mixed m. p. with authentic 7-methoxy-1 : 2-*cyclo*pentenophenanthrene (m. p. 136—137°) 126—130°.

(iii) The methoxy-acetate (9·6 g.) was hydrogenated in the usual way, 6 mols. of hydrogen being absorbed in 48 hours; the product was isolated and hydrolysed as described above. Distillation afforded three fractions: (*a*) b. p. 160—170°/0·2 mm., 1·8 g. (Found: C, 88·8; H, 9·3%, corresponding to $C_{74}H_{93}O$); (*b*) b. p. 175—185°/0·2 mm., 1·9 g.; (*c*) b. p. 195—210°/0·2 mm., 2·1 g.

Fraction (*a*) was heated with 0·2 g. of 10% palladised charcoal for 50 minutes at 280—300° and then for 2 hours at 310—320°; evolution of hydrogen was vigorous. After cooling, the solid product was extracted (Soxhlet) with light petroleum (b. p. 60—80°). A little benzene was added to the extract, which was then run through a column of Brockmann alumina and eluted with 5 : 1 petroleum–benzene. The solid (1·3 g., m. p. 108—115°) was crystallised from light petroleum and from alcohol, and converted into the picrate, which formed long, stout, orange needles, m. p. 128—129°, from benzene. Regeneration gave a product which crystallised from alcohol in needles, m. p. 131—132°, mixed m. p. with authentic 1 : 2-*cyclo*pentenophenanthrene 132—134°.

Fraction (*c*), dissolved in dry ether (5 c.c.), was treated with light petroleum (b. p. 40—60°) (20 c.c.) and the solution kept in the refrigerator for some days. Rosettes of prisms separated and were collected (0·9 g., m. p. 128—134°). Recrystallisation, first from aqueous methyl alcohol and then from light petroleum (b. p. 80—100°) gave 4-*hydroxy*-7-*methoxy*-1 : 2 : 3 : 4-

tetrahydro-1 : 2-cyclo*pentenophenanthrene* (VI) as transparent prisms, m. p. 141—142° (Found : C, 80·8; H, 7·0; MeO, 12·0. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·45; 1MeO, 11·6%).

In another experiment the hydrolysed hydrogenated product (2 g.) was heated on a steam-bath with *p*-nitrobenzoyl chloride (2·6 g.) in pyridine (10 c.c.). The product was cooled, diluted and acidified. The sticky precipitate was triturated with light petroleum (b. p. 40—60°) and the resulting solid crystallised from alcohol. In this way the p-*nitrobenzoate* of the alcohol (VI) was obtained in prisms, m. p. 214—216° (Found : C, 71·75; H, 5·2; N, 3·7, 3·5. $C_{25}H_{23}O_5N$ requires C, 71·9; H, 5·5; N, 3·4%). Hydrolysis with boiling alcoholic potash yielded the alcohol (VI), m. p. and mixed m. p. 140—142°.

2′-iso*Nitroso*-4 : 7-*dimethoxy*-3′-*keto*-1 : 2-cyclo*pentenophenanthrene*.—2·9 G. of the dimethoxy-compound (IV; R = Me) were stirred for 1½ hours with a gently refluxing solution of potassium (0·4 g.) in dry *tert.*-butyl alcohol (100 c.c.). *iso*Amyl nitrite (1·2 g.) was then added and stirring was continued at room temperature overnight; the whole operation was carried out under nitrogen. The product was poured into 600 c.c. of water containing 5 c.c. of acetic acid. Crystallisation of the orange precipitate (3 g.) from nitrobenzene yielded the iso*nitroso*-compound in small prisms, m. p. 248—249° (decomp.) (Found : N, 4·3. $C_{19}H_{15}O_4N$ requires N, 4·4%). This substance gave a brilliant indigo-blue coloration in concentrated sulphuric acid solution.

4 : 7-*Dimethoxy*-2′-*formyl*-3′-*keto*-1 : 2-cyclo*pentenophenanthrene* (VII).—29 G. of the dimethoxy-compound (IV; R = Me) were dissolved in warm pyridine (300 c.c.) and treated successively with ethyl formate (45 c.c.) and sodium ethoxide from sodium (4·5 g.) and absolute alcohol (80 c.c.). A vigorous reaction set in and the contents of the flask set to a pasty mass. This was kept at room temperature for an hour, mixed with a little water, and filtered from tarry matter. Further dilution, followed by acidification with acetic acid, precipitated the formyl derivative as a yellow solid which was collected, washed, and dried on porous earthenware. The crude product (31 g.; 97%) was sufficiently pure for preparative purposes. This *formyl* derivative (VII) crystallised from ethyl acetate in pale yellow, prismatic needles, decomp. 195° (Found : C, 75·2; H, 5·6. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%). It is readily soluble in aqueous-alcoholic sodium hydroxide and gives a deep olive-green coloration with ferric chloride in alcoholic solution.

Attempted condensations of the dimethoxy-compound with ethyl or *iso*amyl formate in benzene, ether, or dioxan with powdered sodium and in ether with sodium ethoxide were fruitless, but a more interesting result was obtained in the following experiment. 2·9 G. of the dimethoxy-compound were stirred under nitrogen for 2 hours on the water-bath and then for 2 hours at room temperature with a solution of potassium (0·4 g.) in dry *tert.*-butyl alcohol (100 c.c.). *iso*Amyl formate (2·6 c.c., 2 mols.) was added, and the mixture stirred overnight under nitrogen. The product was poured into water and the orange precipitate filtered off, washed, and dried; 2·9 g., m. p. 275—285°. This condensation *product* (X) crystallised from nitrobenzene in orange needles, m. p. 301—302° (Found : C, 78·8; H, 4·6. $C_{39}H_{30}O_6$ requires C, 78·8; H, 5·05%). It gave a purple coloration with concentrated sulphuric acid and a plum-coloured solution with a marked bright red fluorescence in hot acetic acid containing a little hydrochloric acid. This reaction is probably due to the formation of a pyrylium salt.

4 : 7-*Dimethoxyphenanthrene*-1-β-*propionic*-2-*carboxylic acid* (IX).—24 G. of the crude formyl derivative (VII) were suspended in acetic acid (1200 c.c.) and stirred at 70° while powdered hydroxylamine hydrochloride (5·7 g.) was added, and then for a further 15 minutes. The mixture was diluted with water, and the crude cyano-ketone (VIII) collected, washed, and dried on porous earthenware. The product (23 g.) gave a brilliant violet colour with alcoholic alkali; it could not be purified for analysis.

This crude cyano-ketone (26 g.) was refluxed for 3 days on the steam-bath with potassium hydroxide (50 g.), water (50 c.c.), and alcohol (50 c.c.), ammonia being copiously evolved. A further 50 g. of potassium hydroxide in 50 c.c. of water were then added and refluxing was continued for 7 days more, after which ammonia was no longer evolved. The product was diluted with water, cooled, and the insoluble neutral material centrifuged off, washed, and dried. Crystallisation from nitrobenzene gave the condensation product (X) in orange needles, m. p. and mixed m. p. 302°. The centrifuged liquor was acidified, and the precipitate collected, washed, and dried on porous earthenware; yield, 20 g. (crude). The new *acid* (IX) crystallised from nitrobenzene in clusters of prisms, m. p. 285° (decomp.) (Found : C, 67·4; H, 5·3. $C_{20}H_{18}O_6$ requires C, 67·8; H, 5·1%).

Methyl 4 : 7-*Dimethoxyphenanthrene*-1-β-*propionate*-2-*carboxylate* (XI).—(i) A mixture of the recrystallised acid (IX) (0·7 g.), methyl alcohol (20 c.c.), and sulphuric acid (1 c.c.) was refluxed

on the steam-bath for 12 hours. The cooled solution was diluted and the precipitate collected. The *methyl* ester (XI) crystallised from dilute methyl alcohol in colourless laths, m. p. 115° (Found: C, 69·0; H, 5·7. $C_{22}H_{22}O_6$ requires C, 69·1; H, 5·8%).

(ii) The following procedure was best for preparative purposes: A mixture of crude precipitated acid (20 g.), methyl alcohol (400 c.c.), and sulphuric acid (20 c.c.) was refluxed for 12 hours and the product was poured into water and extracted with benzene. The dark brown benzene extract was dried, evaporated to 250 c.c., percolated through a column of Brockmann alumina, and eluted with 100 c.c. of benzene. The orange percolate was diluted with 70 c.c. of light petroleum (b. p. 60—80°) and once more passed through a column. Elution with 150 c.c. of 5 : 1 benzene–light petroleum gave a pale yellow percolate with a purple fluorescence. This was evaporated under reduced pressure, yielding 6·9 g. (21% calc. on the formyl derivative) of ester, m. p. 108—110°, which was sufficiently pure for hydrogenation.

Hydrogenation of the Ester (XI).—The ester, dissolved in 25 volumes of acetic acid, was stirred at 70° under hydrogen in the presence of Adams's catalyst (10% by weight). Absorption of hydrogen usually ceased when 1 mol. had been taken up; the catalyst then flocculated and it was necessary to add a further amount of catalyst, whereupon hydrogen absorption proceeded smoothly once more; after a total of 5 mols. of hydrogen had been absorbed, uptake usually ceased and the catalyst again flocculated. The reduction occupied 12—48 hours according to the activity of the catalyst.

The solution was cooled, filtered, and evaporated under reduced pressure. The residue was refluxed for 4 hours with an equal weight of potassium hydroxide dissolved in its own weight of water and 10 vols. of methyl alcohol. The cooled product was diluted with water, and a small amount of neutral material extracted with ether; the alkaline solution was then acidified and extracted with ether.

The gum obtained on evaporation of the dried extract was fractionally crystallised from benzene, yielding three crystalline acids, together with gummy material which has not yet been fully investigated:

(i) About 10% of a very sparingly soluble acid, m. p. 195—198°. Recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave 4 : 7-*dimethoxy*-9 : 10-*dihydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XII) in small, shining rods, m. p. 208—209° [Found: C, 67·7, 67·6; H, 6·1, 6·0; MeO, 17·4. $C_{18}H_{14}O_4(OCH_3)_2$ requires C, 67·4; H, 5·6; MeO, 17·4%].

(ii) A more soluble acid, m. p. 135—145°. Several further crystallisations from benzene yielded 4 : 7-*dimethoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XIII) in small rhombs, m. p. 138—140° (Found: C, 67·1, 66·9; H, 6·4, 6·5. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·15%).

(iii) The principal product (*ca.* 50%), m. p. 115—118°. Repeated recrystallisations from benzene yielded small amounts of the above acids and a substance crystallising in small, well-formed, prisms, m. p. 118—120°. This appeared to be a very stable molecular compound [Found in three different preparations: C, 67·5, 67·35, 67·2; H, 6·8, 6·8, 7·0%; equiv. (by titration), 173·5] and was successfully broken up by several crystallisations from dilute acetic acid. In this way 7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XIV) was obtained in small spherical clusters of acicular prisms, m. p. 233° (Found: C, 68·3; H, 7·3. $C_{19}H_{24}O_5$ requires C, 68·7; H, 7·2%). This acid forms about 25% of the hydrogenation product.

x-*Noroestrone Methyl Ether* (XV; R = Me).—352 Mg. of the octahydro-demethoxy-acid (XIV) were dissolved in aqueous alcohol and neutralised (phenolphthalein) with sodium hydroxide solution. The diluted solution was treated with an aqueous solution of 600 mg. of lead acetate. After being warmed on the steam-bath for some time, the precipitated lead salt was filtered off from the cooled solution, washed and dried, first in the steam oven and then in a vacuum desiccator over phosphoric oxide.

This lead salt was carefully pyrolysed, over a free flame, in a Pyrex tube at 0·25 mm. A yellow oil distilled over and crystallised at once (180 mg.; 63%). Recrystallisation from aqueous acetone gave 7-*methoxy*-3′-*keto*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-1 : 2-cyclo*pentenophenanthrene* (XV; R = Me) in small prismatic needles, m. p. 142—143° [Found: C, 79·5, 79·6; H, 7·9, 7·9; MeO, 10·6. $C_{17}H_{19}O(OCH_3)$ requires C, 80·0; H, 8·15; MeO, 11·5%]. With concentrated sulphuric acid this material gave a yellow colour passing to orange on warming; no fluorescence was developed. Equilenin under these conditions gives an intensely green fluorescent solution and so does *x*-norequilenin (Koebner and Robinson, *loc. cit.*). A specimen of natural oestrone in our possession also exhibited the reaction but this was probably due to contamination by equilenin or equilin, the complete removal of which is difficult. The oestrone

methyl ether obtained by Litvan and Robinson (J., 1938, 1997) by cyclisation of Bardhan's acid by way of the lead salt gave no fluorescence in sulphuric acid solution.

x-*Noroestrone* (XV; R = H).—530 Mg. of crude noroestrone methyl ether were heated in an oil-bath with 25 c.c. of acetic acid and 25 c.c. of hydriodic acid (*d* 1·7), 140° being reached in 10 minutes and maintained for 15 minutes. The product was cooled, poured into water, decolorised with sulphur dioxide, basified with sodium hydroxide, and filtered from tarry matter. The clear filtrate was acidified, whereupon a phenol separated in pale yellow flocks and was collected, washed, and dried in a vacuum desiccator (135 mg.; 27%). This material contained a small amount of iodine which was not removed by recrystallisation and led to low carbon values on analysis. It was accordingly redissolved in dilute sodium hydroxide, boiled for a few minutes with a pinch of zinc dust, filtered, and reprecipitated with acid. Crystallisation from dilute alcohol then yielded 7-*hydroxy*-3′-*keto*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-1 : 2-cyclo*penteno*-*phenanthrene* (XV; R = H) in beautiful, colourless, rectangular plates, m. p. 222° (Found : C, 79·5; H, 7·85. $C_{17}H_{20}O_2$ requires C, 79·7; H, 7·8%). This substance gave a positive reaction with Brady's reagent and a clear yellow colour with concentrated sulphuric acid, unaltered on gently warming or on keeping; it became brown when strongly heated.

100 Mg. of noroestrone were heated on a steam-bath for 2 hours with dry pyridine (1 c.c.) and acetic anhydride (0·4 c.c.). The cooled solution was diluted with water and a gum was precipitated which crystallised on scratching. The *acetate* (XV; R = Ac) crystallised from dilute alcohol in needles, m. p. 145—146° (Found : C, 76·2; H, 7·3. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·9%).

4 : 7-*Dimethoxy*-3′-*keto*-9 : 10-*dihydro*-1 : 2-cyclo*pentenophenanthrene* (XVI).—100 Mg. of the dihydro-acid (XII) were converted into the lead salt in the usual way and this was pyrolysed in a Pyrex tube at 0·2 mm. The product was a brown glass; crystallisation from dilute acetone yielded the *ketone* (XVI) in laths, m. p. 143° (Found : C, 77·55; H, 6·2. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·1%). The m. p. was depressed to 105—112° on admixture with *x*-noroestrone methyl ether. The substance gave a bright yellow colour with concentrated sulphuric acid, a brilliant green fluorescence developing on warming. The 2 : 4-*dinitrophenylhydrazone* crystallised from dilute acetic acid in deep red prisms, m. p. 242—243° (Found : N, 11·6. $C_{25}H_{22}O_6N_4$ requires N, 11·8%).

Methyl 7-*Methoxy*-4-*ethoxyphenanthrene*-1-β-*propionate*-2-*carboxylate* (XVII).—10 G. of the methoxy-phenol (IV; R = H) were dissolved in ethyl alcohol (200 c.c.) and sodium hydroxide solution (50 c.c. of 10%). The solution was stirred mechanically and heated in a water-bath at 60° while 5 c.c. of ethyl sulphate were added during 5 minutes. Stirring and heating were continued while 4 similar batches of 10% sodium hydroxide solution and ethyl sulphate were added alternately during 30 minutes. After being stirred for a further 10 minutes, the product was diluted and cooled, and the precipitated methoxy-ethoxy-compound collected, washed, and dried at 100° (11 g.; 100%). 7-*Methoxy*-4-*ethoxy*-3′-*keto*-1 : 2-cyclo*pentenophenanthrene* (IV; R = Et) crystallised from ethyl alcohol in small needles, m. p. 194° (Found : C, 78·2; H, 5·7. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%).

5 G. of this compound were refluxed for an hour on the steam-bath with pyridine (25 c.c.), ethyl formate (7·5 c.c.), and sodium ethoxide [from sodium (0·75 g.) and absolute alcohol (15 c.c.)]. The pasty product was mixed with water and filtered. Acidification of the filtrate precipitated the formyl derivative as a yellow solid, which was collected, washed, and dried at 100° (5·9 g.). 5·7 G. of this crude product were dissolved in 600 c.c. of acetic acid at 75°; powdered hydroxylamine hydrochloride (1·25 g.) was added, and the mixture stirred at 70° for 1½ hours. The cyano-ketone was collected after dilution, washed, and dried (4·5 g.); the substance gave a purple colour with alcoholic alkali but could not be purified for analysis.

The above material was refluxed on the steam-bath for 3 days with potassium hydroxide (9 g.), water (9 c.c.), and ethyl alcohol (9 c.c.). At the end of this time a further 9 g. of potassium hydroxide in 9 c.c. of water were added and refluxing was continued for 7 days, the evolution of ammonia then having ceased. After dilution, the neutral matter was separated by centrifugation, the liquor was acidified, and the precipitate collected, washed, and dried at 100° (3·2 g.). 7-*Methoxy*-4-*ethoxyphenanthrene*-1-β-*propionic*-2-*carboxylic acid* crystallised from nitrobenzene in thin needles, m. p. 268—269° (Found : C, 68·3; H, 5·3. $C_{21}H_{20}O_6$ requires C, 68·5; H, 5·4%).

0·75 G. of the recrystallised acid was refluxed on the steam-bath for 6 hours with concentrated sulphuric acid (2 c.c.) and methyl alcohol (30 c.c.). The crystalline solid precipitated on dilution was collected, washed, and recrystallised from methyl alcohol; *methyl* 7-*methoxy*-4-*ethoxyphenanthrene*-1-β-*propionate*-2-*carboxylate* (XVII) formed colourless needles, m. p. 118°

(Found: C, 69·6; H, 6·0. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·1%). It was found better, for preparative purposes, to use the crude acid; 3·2 g. of this were refluxed for 6 hours on the water-bath with sulphuric acid (8 c.c.) and methyl alcohol (120 c.c.). The hot solution was filtered from some tar and diluted with water; the sticky precipitate was collected, dried, dissolved in benzene (200 c.c.) containing 10 c.c. of light petroleum (b. p. 60—80°), and percolated through a column of Brockmann alumina. After elution with 50 c.c. of benzene containing 2 c.c. of light petroleum, the percolate was evaporated, yielding 1·75 g. (26% calc. on the formyl derivative) of ester, m. p. 110—113°, which was pure enough for hydrogenation.

Hydrogenation. A solution of this ester (2·2 g.) in acetic acid (75 c.c.) was stirred under hydrogen at 70° in the presence of Adams's catalyst. Uptake of 5 mols. of hydrogen required 36 hours and the use of 0·6 g. of catalyst added in 4 portions; the completion of the reaction was not marked by any break in the absorption of hydrogen. After working up and hydrolysis in the usual way, the gummy acid was treated with benzene. The precipitated solid (1·15 g.; m. p. 140—150°) was fractionally crystallised from benzene and from dilute acetic acid, but the only definite substance isolated was 7-*methoxy*-4-*ethoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*-1-β-*propionic*-2-*carboxylic acid* (XVIII), which crystallised from dilute acetic acid in beautiful needles, m. p. 160° (Found: C, 68·6; H, 6·6. $C_{21}H_{24}O_6$ requires C, 67·8; H, 6·5%).

7-(β-6′-*Hydroxynaphthyl*)-4 : 7-*diketoheptoic acid* (XIX).—10 G. of 7-(β-6′-methoxynaphthyl)-4 : 7-diketoheptoic acid were refluxed for 3 hours with acetic acid (50 c.c.) and concentrated hydrochloric acid (50 c.c.). The product was boiled with charcoal, filtered, and diluted; on cooling, the crude *acid* (XIX) crystallised and was collected, washed, and dried (8 g.; 84%). It crystallised from aqueous alcohol in leaflets, m. p. 171—172° (Found: C, 68·2; H, 5·8. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·3%).

3-(6′-*Hydroxy*-β-*naphthyl*)-Δ^2-cyclo*pentenone*-2-*acetic acid* (XX).—25·5 G. of the crude hydroxydiketo-acid (XIX) were heated in a boiling water-bath for an hour with potassium hydroxide (50 g.) and water (2500 c.c.). Acidification precipitated the crude *cyclo*pentenone acid, which was collected, washed, and dried (24 g.; 100%). This *acid* crystallised from dilute methyl alcohol in yellowish prisms, m. p. 221—222° (Found: C, 72·0; H, 5·1. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%).

4 : 7-*Dihydroxy*-3′-*keto*-1 : 2-cyclo*pentenophenanthrene*.—24 G. of precipitated *cyclo*pentenone acid (XX) were refluxed for 30 minutes with acetic anhydride (170 c.c.). After distillation of 140 c.c., the residue was cooled, treated with benzene, broken up, filtered, washed with benzene, and dried (19 g.; 64%).

4 : 7-*Diacetoxy*-3′-*keto*-1 : 2-cyclo*pentenophenanthrene* (XXI; R = Ac) crystallised from dilute acetic acid in small needles, m. p. 196—197° (Found: C, 72·2; H, 4·8. $C_{21}H_{16}O_5$ requires C, 72·4; H, 4·6%). 1 G. of this material was refluxed on the steam-bath for 2 hours with sodium hydroxide (1 g.) in water (1 c.c.) and ethyl alcohol (2 c.c.). The 4 : 7-*dihydroxy*-compound was precipitated by pouring into water (100 c.c.) containing acetic acid (5 c.c.); it was collected, washed, and crystallised from aqueous pyridine, forming shining, prismatic needles, m. p. 338° (decomp.) (Found: C, 77·0; H, 4·6. $C_{17}H_{12}O_3$ requires C, 77·25; H, 4·55%).

γ-m-*Methoxyphenylpropyl Iodide*.—A solution of the corresponding chloride (135 g.) and sodium iodide (150 g.) in acetone (1050 c.c.) was refluxed for 4 hours. The precipitated sodium chloride was separated, and the filtrate refluxed for a further 3 hours. After once more removing the sodium chloride, a further 60 g. of sodium iodide were added and refluxing was continued, with filtration after 4 hours and, finally, after 8½ hours. On working up as usual, 184 g. (91%) of iodide were obtained, b. p. 155—160°/11 mm., $n_D^{20°}$ 1·5773.

2-(γ-m-*Methoxyphenylpropyl*)cyclo*pentanone*.—184 G. of the above iodide were refluxed on the steam-bath for 22 hours with the mixture obtained by refluxing ethyl *cyclo*pentanone-2-carboxylate (104 g.) overnight with powdered potassium (26 g.) and benzene (650 c.c.). On working up in the usual way, 115 g. (57%) of *ethyl* 2-(γ-m-*methoxyphenylpropyl*)cyclo*pentanone*-2-*carboxylate* (XXII) were obtained as a colourless oil, b. p. 187—190°/0·5 mm., $n_D^{19°}$ 1·5167 (Found: C, 71·4; H, 7·8. $C_{18}H_{24}O_4$ requires C, 71·1; H, 7·9%). The *semicarbazone* crystallised from aqueous methyl alcohol in small, transparent prisms firmly holding solvent of crystallisation (Found: N, 9·4. $C_{19}H_{27}O_4N_3,2CH_3{\cdot}OH$ requires N, 9·9%).

115 G. of the above keto-ester were refluxed on the steam-bath with potassium hydroxide (230 g.) in water (460 c.c.) and ethyl alcohol (460 c.c.) for 12 hours. The alcohol was then removed under reduced pressure, and neutral material extracted with ether. The residual solution was acidified, extracted with ether, and the extract dried and evaporated. The residue was treated with acetic anhydride (150 c.c.) and slowly distilled, first at atmospheric and then under reduced pressure; decomposition set in at 260—270°/100 mm. and was completed by distillation over a

free flame. The distillate was taken up in ether, added to the neutral material extracted from the hydrolysis product, washed with water and aqueous sodium carbonate, and the solution dried and distilled, yielding 56 g. (64%) of 2-(γ-m-*methoxyphenylpropyl*)cyclo*pentanone* (XXIII) as a pale yellow oil, b. p. 173—177°/0·8 mm., $n_D^{18°}$ 1·5280 (Found : C, 77·3; H, 8·6. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·6%). The *semicarbazone* crystallised from dilute alcohol in small, glistening prisms, m. p. 180°, containing firmly-held solvent of crystallisation (Found : N, 12·5. $C_{16}H_{23}O_2N_3,C_2H_5{\cdot}OH$ requires N, 12·5%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol containing a little water in burrs of orange needles, m. p. 103—104° (Found : N, 13·4. $C_{21}H_{24}O_5N_4$ requires N, 13·6%).

We are grateful to the Royal Society for a grant and to the Royal Commissioners for the Exhibition of 1851 for a Senior Studentship awarded to one of us (H. N. R.).

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, July 24th,* 1939.]