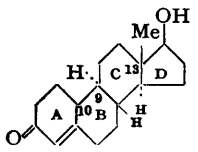
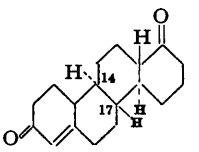
415. *Hydroaromatic Steroid Hormones. Part II.* Some Hydrochrysene Derivatives.*

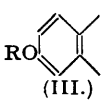
By Arthur J. Birch and Herchel Smith.

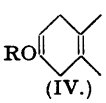
Some hydrochrysene derivatives substituted in the 3 : 10- or 4 : 10-positions by methoxyl, carbonyl, or hydroxyl, were prepared in an endeavour to obtain compounds with androgenic activity. Some stereochemical problems are discussed. Applications are described of the phosphoric anhydride–phosphoric acid reagent to some cyclisation reactions.

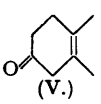
The 10-nortestosterone (I) prepared in Part I * has been shown to possess marked androgenic activity (Dodds, Lawson, and Simpson, personal communication), thus demonstrating that a steroid hormone of a type possessing high structure-specificity can retain much of its activity if the angular methyl group attached to $C_{(10)}$ is missing. The further suggestion made in Part I that activity may be retained in the absence of the methyl attached to $C_{(13)}$, if ring D is six-membered, is now to be tested. The synthesis of appropriate compounds starting from natural steroids would be difficult, and we are attempting to make by total synthesis the hydrochrysene derivative (II) in the racemic form, but with the correct alternating *trans*-configurations at the asymmetric centres. The present communication deals with some aspects of the formation of the correctly substituted ring system, and with some stereochemical problems.

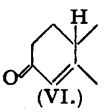
(I.) 

(II.) 

(III.) 

(IV.) 

(V.) 

(VI.) 

The αβ-unsaturated ketone system of ring A in (II) could conveniently be made as recorded in Part I (*loc. cit.*) by the reduction, with sodium and alcohol in liquid ammonia, of a phenol

* Part I, *J.*, 1950, 367.

ether (III) to the dihydro-derivative (IV), followed by hydrolysis with acid to the βγ-unsaturated ketone (V) and conversion of this into the more stable αβ-unsaturated ketone (VI) by the action of sodium ethoxide. The steric configuration of the hydrogen atom attached to the A–B ring-junction is therefore determined during the bond-migration. Whether this configuration is α or β is not known in the case of nortestosterone (I), and although the point is of no practical importance since (I) is physiologically active, the evidence so far available is of interest for its bearing on the general case.

The crystalline 10-nortestosterone (I) can be formed in 75—80% yield in the bond-migration reaction (Birch, unpublished) and is evidently the isomer of lower energy-level because the reaction occurs under conditions of reversible proton addition; the expectation is therefore that the $C_{(10)}$-H will be *trans* to the $C_{(9)}$-H, *i.e.*, will be β. This assumption is supported by the known facts about bond-migration in the steroid nucleus, where the hydrogen of a newly-formed asymmetric centre is usually found to be *trans* to the hydrogen atom or methyl group at the nearest ring-junction. Optical rotation data are inconclusive. The βγ-unsaturated precursor of nortestosterone has M_D +460° (in chloroform), compared with +205° for "α"-œstradiol; and 10-nortestosterone has M_D +184°, compared with +296° for testosterone itself. A change in configuration of the $C_{(10)}$-methyl group from β to α is usually accompanied by a marked increase in M_D, but the compounds so far examined have all been highly unsaturated in the vicinity of the asymmetric centre, and in any case the effect of replacing methyl by hydrogen is not known. The figures above are not inconsistent with the assumption of the β configuration at $C_{(10)}$ in the nortestosterone; the compound is being examined by *X*-ray methods.

One outstanding problem associated with the production of (II), with the hydrogen atoms at the ring-junctions in the correct alternating α- and β-configurations, is the orientation of the junction B–C, and it was hoped to find a stereospecific reaction which could be assumed with reasonable certainty in unknown cases to lead to the stable *trans*-configuration, as in the formation of the stable *trans*-ethylenes by the reduction of acetylenes with sodium in liquid ammonia. Reduction, by dissolving metals, of steroids containing a double bond terminating at a ring-junction is known to lead to the *trans*-isomer, but little evidence is available as to the reduction of a bond between two rings. Heer and Miescher (*Helv. Chim. Acta*, 1947, **30**, 777; cf. Shoppee, *Ann. Reports*, 1947, **44**, 200) reduced "α"-monodehydrodoisynolic acid by means of sodium and liquid ammonia, obtaining a poor yield of a mixture of the two possible 7-methyldoisynolic acids with a *trans*-C–D-ring-junction. To obtain further information about such reductions the preparation of (VIII) and its reaction with sodium have been carried out.

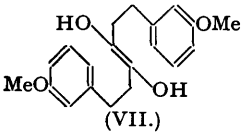
Methyl β-*m*-methoxyphenylpropionate and powdered sodium in toluene gave in good yield the acyloin (VII) (written for convenience in the enol-form) which underwent double cyclisation by the action of phosphoric anhydride in phosphoric acid to form 1 : 2 : 7 : 8-tetrahydro-4 : 10-dimethoxychrysene (VIII). The acyloin condensation appears to have been carried out only with aliphatic esters (*e.g.*, Hansley, *J. Amer. Chem. Soc.*, 1935, **57**, 2303), but the present example supports the assumption that it should be applicable to any esters which do not contain easily reducible groups. The formulation of (VIII) is supported by its close resemblance to the compound prepared by Salzer (*Z. physiol. Chem.*, 1942, **274**, 39), by the ready removal of four hydrogen atoms by sulphur, and by the reductions described below.

The action of sodium and butanol, or sodium and liquid ammonia, on (VIII) caused the addition of two hydrogen atoms to form a mixture of the two 1 : 2 : 7 : 8 : 14 : 17-hexahydro-4 : 10-dimethoxychrysenes-*a* and -*b* of Ramage and Robinson (*J.*, 1933, 607; Lewis, Ramage, and Robinson, *J.*, 1935, 1412) which were separated by chromatography on alumina. The isomer-*a*, m. p. 185°, was identified by direct comparison with an authentic specimen, kindly supplied by Dr. R. H. Jaeger. It very probably has the *trans*-C–D-ring-junction by analogy with the higher-melting hexahydrochrysene (Ramage and Robinson, *loc. cit.*), and may be formulated as (IX).* The results are disappointing in that there is little stereospecificity in the reduction, although the isomer-*a* is formed in somewhat greater amount than isomer-*b*.

It was found possible to reduce further the two hexahydrodimethoxychrysenes by the action of potassium and methanol in liquid ammonia, using a mixture of ether and dioxan to assist the process by keeping the substances in solution. Acid hydrolysis of the products gave rise to 1 : 2 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14 : 16 : 17-tetradecahydro-4 : 10-diketo-

* This, and other formulæ for (±)-compounds, imply also the presence of the enantiomer. For these formulæ and for the consequent nomenclature, the configuration at $C_{(14)}$ of the hydrochrysene skeleton has been arbitrarily taken as α, although of course an equal amount of $C_{(14)}$-β-compound is present in the (±)-compounds.

chrysene in stereoisomeric forms, *e.g.*, probably (X) * from the isomer-*a*. Each of the hexahydrodimethoxychrysenes-*a* and -*b* is capable of producing three (±)-tetradecahydrodiketochrysenes, but the product from the isomer-*a* appeared to be homogeneous and showed no evidence of separation on alumina. The product from isomer-*b* gave a series of fractions of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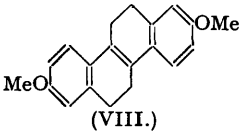
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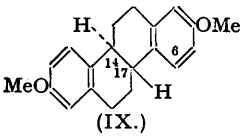
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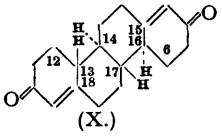
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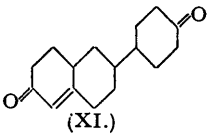
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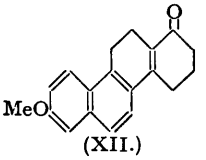
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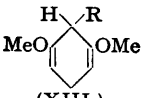
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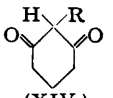
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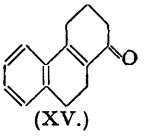
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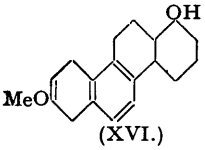
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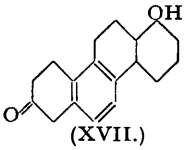
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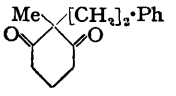
(XVIII.)

slightly differing melting points on chromatography and is probably a mixture. The *trans*-hexahydrochrysene (IX) has a centre of symmetry, so in the single reduction product derived from it the same steric relationships should exist between the hydrogen atoms attached to $C_{(13)}$ and $C_{(14)}$ as between those attached to $C_{(16)}$ and $C_{(17)}$, *i.e.*, the product should be either the 13α : 14α : 16β : 17β or the 13β : 14α : 16α : 17β (X), probably the latter since this has the greater number of hydrogens *trans* to each other. Inspection of models supports the assumption that (X) should have the lower energy level. A decision in the nortestosterone case would be helpful here. The compound obtained was tested for androgenic activity, but possesses none (Dodds, Lawson, and Simpson, personal communication). This inactivity is disappointing in view of its resemblance to the compound (XI) of Wilds, Shunk, and Hoffman (*J. Amer. Chem. Soc.*, 1949, **71**, 3266) which is weakly androgenic.

Our first attempt to prepare (II) has been by reduction of (XII) with sodium and ethanol in ammonia in the hope of saturating the unsaturated ketone system and adding four hydrogen atoms to rings A and B in a manner analogous to the reduction of 2-methoxynaphthalene to 1 : 4 : 5 : 8-tetrahydro-2-methoxynaphthalene (Birch, Murray, and Smith, in the press). This process in fact led to the reduction of ring A but not of ring B. The resistance of the latter is not surprising because after reduction of ring A there are four saturated carbon atoms attached to ring B (cf. *Quart. Reviews*, 1950, **4**, 69), and αδ-reduction must take place in at least one occupied position.

The synthesis of (XII) which we have carried out takes advantage of some model reactions already briefly reported (Birch, *J.*, 1950, 1551). Potassamide in liquid ammonia reacts with (XIII; R = H) to give (XIII; R = K), which is converted by 2-phenylethyl bromide into (XIII; R = CH_2·CH_2Ph). This enol ether has now been hydrolysed by acid to (XIV; R = CH_2·CH_2Ph), which was converted (cf. Schlittler and Robinson, *J.*, 1935, 1288) into 1 : 2 : 3 : 4 : 9 : 10-hexahydro-4-ketophenanthrene (XV). The best reagent for the purpose was a solution of phosphoric anhydride in phosphoric acid. The compound (XV) has already been made by Johnson and Petersen (*J. Amer. Chem. Soc.*, 1946, **68**, 1928), but the present method is simpler and gives a product which can be crystallised immediately.

Extension of the process to 2-(6-methoxy-1-naphthyl)ethyl bromide gave rise to [XIII; R = 2-(6-methoxy-1-naphthyl)ethyl], the yield being 86% based on the bromide if a con-

* We are informed in a personal communication from Dr. R. H. Jaeger (Oxford) that she has also made this compound in a similar manner.

siderable excess of 1 : 5-dimethoxy*cyclo*hexa-1 : 4-diene (XIII; R = H) was used. The product was hydrolysed to (XIV) and this was cyclised as above to 1 : 2 : 3 : 4 : 5 : 6-hexahydro-3-keto-10-methoxychrysene (XII). The properties of this substance agree with those recorded by Robinson and Thompson (*J.*, 1939, 1739) who prepared it by a more difficult route. Robinson and Thompson were unable to hydrogenate the double bond of the unsaturated ketone system when using a palladium catalyst, and although we have found that the addition of alkali caused hydrogen to be absorbed the carbonyl group was preferentially hydrogenated. Reduction of (XII) with potassium and methanol in ammonia and chromatography of the product produced mostly gummy fractions, but small amounts of two crystalline substances were isolated; one obtained in larger amount appears to be a stereoisomer of 1 : 2 : 3 : 4 : 5 : 6 : 9 : 12 : 15 : 16-decahydro-3-hydroxy-10-methoxychrysene (XVI). Acid hydrolysis of the crude reduced product, obtained as above or by reduction with sodium and ethanol (Cornforth, Cornforth, and Robinson, *J.*, 1942, 689), produced a gum which showed all the reactions of a derivative of β-tetralone. It readily gave rise to a bisulphite compound, and produced with sodium methoxide in methanol in the presence of air a deep blue colour converted into red by acidification. After regeneration from the bisulphite compound part of the gummy material crystallised to yield one isomer of 1 : 2 : 3 : 4 : 5 : 6 : 9 : 10 : 11 : 12 : 16 : 17-dodecahydro-3-hydroxy-10-ketochrysene (XVII).

From these results it is evident that compounds in which rings A and B are aromatic are not feasible starting materials for compounds of type (II). Work is in progress with the object of making (II) from compounds containing a reduced B-ring.

Compounds related to (XII), but containing an angular methyl group in the equivalent of the steroid $C_{(13)}$-position (cf. I) would be of interest. Attempts were accordingly made to prepare (XVIII) by the action of 2-phenylethyl bromide on the potassium salt of (XIII; R = Me) and by the action of methyl iodide on the salt of (XIII; R = $CH_2 \cdot CH_2Ph$), but neither succeeded. The reason for the failure of the alkylation probably lies in the non-formation of the potassium salt owing to the reduced acidity of (XIII; R = alkyl) compared with that of (XIII; R = H); this assumption is supported by the fact that there is little change in the colour of the pale yellow potassamide solution on the addition of the substance, in contrast to the deep red-brown obtained with the unalkylated derivative.

Solutions of phosphoric anhydride in phosphoric acid are often valuable cyclising reagents. They have already been proposed as general reagents for the cyclisation of γ-arylbutyric acids and some arylpropionic acids to the tetralone or hydrindone, *e.g.*, β-*m*-methoxyphenylpropionic acid gave 5-methoxyindanone, γ-phenylbutyric acid gave 1 : 2 : 3 : 4-tetrahydro-1-ketonaphthalene, and a more complicated analogue of the latter could be cyclised in no other way (Birch, Jaeger, and Robinson, *J.*, 1945, 582). The formation of six-membered rings occurs rapidly and in very good yields (85—95%) under appropriate conditions; that of five-membered rings is more difficult and good yields are obtained only when activating groups such as methoxyl are present. The present and other work shows that cyclodehydration of aryl ketones to give compounds with six-membered rings occurs readily and the products are very clean. The reaction mixture can be worked up simply by dilution with water and extraction or filtration. The time required is short (5—60 minutes) and the conditions can be varied by altering the time, concentration, and particularly the temperature to suit each case. In the event of non-reaction the starting-material is recovered. In all cases tried so far it is superior to sulphuric acid, phosphoric anhydride in benzene or toluene, and in some cases to hydrogen fluoride. Recently, Snyder and Werber (*J. Amer. Chem. Soc.*, 1950, **72**, 2962, 2965) have described some similar cyclisations using " polyphosphoric " acid; presumably this reagent is of the same nature as that reported above.

Experimental.

The alumina used is designated as follows: Type A, Spence H. Type B, British Aluminium Co. " burntisland " alumina, activated at 360° for 3 hours. Type C, the same as type B, but submitted to preliminary acid washing. M. p.s are uncorrected.

1 : 2 : 7 : 8-*Tetrahydro*-4 : 10-*dimethoxychrysene* (VIII).—Sodium (2·43 g., 4 atoms) was melted under toluene (80 c.c.) in a nitrogen atmosphere. The solvent was refluxed in an oil-bath at 115° and methyl β-*m*-methoxyphenylpropionate (10 g.) in toluene (15 c.c.) added during 30 minutes with vigorous stirring. After a further 30 minutes, methanol (2 c.c.) was added to decompose any remaining sodium, the mixture cooled to 80°, and water (30 c.c.) added. The toluene layer was separated, washed with water, and dried, and the solvent removed under reduced pressure in a stream of nitrogen. The viscous residue (8·1 g.) could not be crystallised; it reduced Fehling's solution and gave rise by the standard method to 1 : 6-*di*-m-*methoxyphenylhexane*-3 : 4-*dione osazone* as yellow needles which, crystallised

from acetic acid, had m. p. 138—138·5° (Found: C, 75·85; H, 6·0; N, 11·2. $C_{32}H_{34}O_2N_4$ requires C, 75·9; H, 6·7; N, 11·1%).

A mixture of orthophosphoric acid (9 c.c.) and phosphoric anhydride (6 g.) at 60° was added to the acyloin (0·8 g.), the solution becoming purple-brown. After 20 minutes at 70° water (100 c.c.) was added, the organic material taken up in ethyl acetate, washed with sodium hydroxide solution (10%), and dried, and the solvent removed. The crystalline residue (0·7 g.) was recrystallised from ethyl acetate to give 1 : 2 : 7 : 8-tetrahydro-4 : 10-dimethoxychrysene (0·52 g.), m. p. 172—173° (Found: C, 81·9; H, 6·8. Calc. for $C_{20}H_{20}O_2$: C, 82·2; H, 6·85%). Salzer (*loc. cit.*) gives m. p. 164°. The *trinitrobenzene* complex separated from ethanol in dark purple needles, m. p. 172—173° (decomp.; rapid heating) [Found: C, 54·0; H, 3·7; N, 11·9. $C_{20}H_{20}O_2,2(C_6H_3O_6N_3)$ requires C, 53·5; H, 3·6; N, 11·7%]. A picrate was formed as almost black prisms, but could not be recrystallised without decomposition, and decomposed at about 130°.

The tetrahydrochrysene (297 mg.) was heated with sulphur (72 mg., followed after 1 hour by 30 mg.) at 180—230° during 2 hours. The product was extracted with boiling toluene (3 × 200 c.c.) and filtered through "Hyflo Supercel," and the solvent removed under reduced pressure to leave a crystalline residue. This crystallised from toluene to give 4 : 10-*dimethoxychrysene* (280 mg.), m. p. 273—275° (Found: C, 83·3; H, 5·85. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%).

1 : 2 : 7 : 8 : 14 : 17-*Hexahydro*-4 : 10-*dimethoxychrysene*-a *and* -b (IX).—(i) Sodium (11·6 g.), in small pieces, was slowly added to a boiling solution of 1 : 2 : 7 : 8-tetrahydro-4 : 10-dimethoxychrysene (1·685 g.) in *n*-butanol (350 c.c.) and followed after 1 hour by more sodium (5·6 g.). After complete dissolution of the sodium (2 hours) the mixture was cooled and water (100 c.c.) added. The organic material was taken up in ethyl acetate (700 c.c.), which was washed with water and concentrated to 500 c.c. From this solution there separated crystalline material *A* (0·91 g.), m. p. 168—171° (Found: C, 81·6; H, 7·3. Calc. for $C_{20}H_{22}O_2$: C, 81·6; H, 7·5%). On concentration of the mother-liquor, a substance *B* (201 mg.), m. p. 160—165°, was obtained; evaporation to dryness then left a gum. Substance *A*, in benzene (250 c.c.)–light petroleum (b. p. 60—80°; 250 c.c.), was passed through a column of alumina, type B (250 g.). The column was developed with the solvent mixture (1250 c.c.) and then eluted by adding increasing proportions of benzene until finally pure benzene was used. The eluate was divided arbitrarily into fractions (50 c.c.) which were evaporated under reduced pressure. The earlier fractions contained mostly 1 : 2 : 7 : 8 : 14 : 17-hexahydro-4 : 10-dimethoxychrysene-*b* (277 mg.), m. p. 145—147°, the middle fractions were a mixture, and finally the isomer-*a* (350 mg.), m. p. 185°, was obtained.

(ii) 1 : 2 : 7 : 8-Tetrahydro-4 : 10-dimethoxychrysene (500 mg.) in dioxan (15 c.c.)–ether (50 c.c.) was added to sodium (1 g.) in ammonia (130 c.c.). After 3 minutes, ammonium chloride (3 g.) discharged the colour, water (100 c.c.) was added, and the organic product extracted with 1 : 1 ether–ethyl acetate (3 × 50 c.c.). The product *C* (194 mg.), crystallised from glacial acetic acid, had m. p. 153—157°. The mother-liquor yielded further material *D*, m. p. 130—135° (66 mg.). The product *C* gave with trinitrobenzene a yellow complex, m. p. 172—174°, but the product *D* gave a trinitrobenzene complex which was purple and therefore contained unreduced material. Product *C* was chromatographed as above on alumina, type B (100 g.), to give 1 : 2 : 7 : 8 : 14 : 17-hexahydro-4 : 10-dimethoxychrysene-*b* (30 mg.), m. p. 146—147°, and the isomer-*a* (65 mg.), m. p. 185°, undepressed by an authentic specimen (m. p. 183—184°) prepared by Ramage and Robinson's method (*loc. cit.*) (Found: C, 82·0; H, 7·2. Calc. for $C_{20}H_{22}O_2$: C, 81·6; H, 7·5%). The *trinitrobenzene* complex of isomer-*a* crystallised as yellow prisms (from ethanol), m. p. 187—188° (decomp.) [Found: C, 53·8; H, 4·2; N, 11·3. $C_{20}H_{22}O_2,2(C_6H_3O_6N_3)$ requires C, 53·3; H, 3·9; N, 11·7%].

1 : 2 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13(?) : 14α : 16(?) : 17β-*Tetradecahydro*-4 : 10-*diketochrysene*.—The above isomer-*a* (300 mg.) in pure dioxan (40 c.c.), pure ether (160 c.c.), and absolute ethanol (16 c.c.) was added to ammonia (800 c.c.), and followed by potassium (8 g.) in small pieces. Water (200 c.c.) was then added and most of the ammonia evaporated, finally under reduced pressure. The product was taken up in ethyl acetate (200 c.c.), and after evaporation of the solvent the partly crystalline solid was heated under nitrogen on the steam-bath with 2N-sulphuric acid (10 c.c.) for 30 minutes. The organic material was taken up in ethyl acetate, which was washed and dried, and the solvent was removed. The residue in benzene (20 c.c.) was chromatographed on alumina, type *C* (50 g.), the chromatogram being developed with benzene and eluted with benzene containing an increasing proportion of ethyl acetate. The eluate was divided arbitrarily into fractions (50 c.c.) which were tested with Brady's reagent. The earlier fractions contained traces of ketonic material, but separation was not complete, only the later fractions giving a pure crystalline ketonic product consisting of 1 : 2 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14 : 16 : 17-*tetradecahydro*-4 : 10-*diketochrysene*, m. p. 210—228° (in air), 233—235° (in a vacuum) (Found: C, 79·9; H, 8·1. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·1%). Rechromatography of the first fractions gave more of the same material (13 mg.). The light absorption at $\lambda_{max.}$ 2400—2420 ($\varepsilon_{max.}$ 35,000), 3070—3100 A. ($\varepsilon_{max.}$ 178), is in accordance with the postulated structure, and may be compared with that of 10-nortestosterone containing only one chromophore (Part I, *loc. cit.*), $\lambda_{max.}$ 2400—2415 ($\varepsilon_{max.}$ 17,000), 3075 A. ($\varepsilon_{max.}$ 92·5).

1 : 2 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13(?) : 14α : 16(?) : 17α-*Tetradecahydro*-4 : 10-*diketochrysene*.—The above isomer-*b* (274 mg.; m. p. 145—147°), reduced as above and chromatographed on alumina, type B (50 g.), gave first a non-ketonic gum (82 mg.) followed by crystalline material (25 mg.), m. p. 229—232° (in a vacuum; preliminary softening) (Found: C, 80·25; H, 8·3. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·1%), $\lambda_{max.}$ 2430—2435 A. (ε_{max} 29,500). Another product (10 mg.), possibly a stereoisomer, m. p. 209—211° (in a vacuum), was obtained from the later fractions of the chromatogram (Found: C, 79·65; H, 8·2%), $\lambda_{max.}$ 2425—2435 A. ($\varepsilon_{max.}$ 29,500).

Reduction of 1 : 2 : 7 : 8-*Tetrahydro*-4 : 10-*dimethoxychrysene*.—Reduction of the substance (200 mg.) with potassium and ethanol in ammonia, as above, followed by acid hydrolysis and chromatography

on alumina, type B (50 g.), gave in the earlier fractions a mixture of the hexahydrodimethoxychrysenes-*a* and -*b* (93 mg.) and in the later fractions 1 : 2 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13(?) : 14*a* : 16(?) : 17*β*-tetradecahydro-4 : 10-dimethoxychrysene (25 mg.), m. p. 232—235° (vac.). The mother-liquor gave a small amount of substance (4 mg.), m. p. 209—212° undepressed by the material above (m. p. 209—211°).

2-2′-*Phenylethyl*cyclo*hexane*-1 : 3-*dione*.—1 : 5-Dimethoxy*cyclo*hexa-1 : 4-diene (Birch, *J.*, 1947, 102) (7·0 g.) and potassamide (from the metal, 2 g.) in ammonia (100 c.c.) were left for 10 minutes, and 2-phenylethyl bromide was slowly added with stirring until the red colour was discharged. Water (100 c.c.) was added, and the product taken up in ether and distilled, giving 1 : 3-*dimethoxy*-2-2′-*phenylethyl*cyclo*hexa*-3 : 6-*diene* (5·9 g.), b. p. 163—164°/2 mm. or 152—154°/1 mm. (Found : C, 79·2; H, 8·2. $C_{16}H_{20}O_2$ requires C, 78·7; H, 8·3%). This substance (1 g.) was heated on the steam-bath for 20 minutes with 2N-sulphuric acid (4 c.c.) and extracted with ether (3 × 10 c.c.), and the ethereal solution shaken with small portions of sodium hydroxide solution (10%) until acidification gave no further precipitate. The crystalline solid so obtained was removed by filtration and crystallised from 1 : 1 (vol.) ethyl acetate–light petroleum (b. p. 60—80°), to form colourless prisms of 2-2′-phenylethyl*cyclo*hexane-1 : 3-dione (0·72 g.), m. p. 147—148° (Found : C, 78·3; H, 7·7. Calc. for $C_{14}H_{16}O_2$: C, 77·8; H, 7·4%).

1 : 2 : 3 : 4 : 9 : 10-*Hexahydro*-1-*ketophenanthrene*.—The above diketone (1 g.) was added as a fine powder to a stirred mixture of orthophosphoric acid (3 c.c.) and phosphoric anhydride (4 g.) at 120°. The temperature was raised to 160° and kept there for 45 minutes, the mixture was cooled, water (100 c.c.) was added, the product extracted with ether (4 × 50 c.c.), and the extract dried and evaporated. The oil (0·87 g.) so obtained crystallised on the addition of a little light petroleum (b. p. 40—60°), to give 1 : 2 : 3 : 4 : 9 : 10-hexahydro-1-ketophenanthrene as prisms, m. p. 48—49° (Found : C, 85·3; H, 7·1. Calc. for $C_{14}H_{14}O$: C, 84·8; H, 7·1%). Johnson and Petersen (*loc. cit.*) give m. p. 49—49·5° for material purified through the semicarbazone. The 2 : 4-*dinitrophenylhydrazone* formed dark purple needles (from toluene), m. p. 262—263° (Found : C, 63·8; H, 4·6; N, 14·4. $C_{20}H_{18}O_4N_4$ requires C, 63·5; H, 4·8; N, 14·8%). In agreement with Johnson and Petersen the oxime had m. p. 141—142° and the semicarbazone, m. p. 250—251°.

1 : 2 : 3 : 4 : 5 : 6-*Hexahydro*-3-*keto*-10-*methoxychrysene*.—1 : 5-Dimethoxy*cyclo*hexa-1 : 4-diene (44·5 g.) was stirred into potassamide (from the metal, 3·6 g.) dissolved in liquid ammonia (500 c.c.). After 8 minutes a solution of 1-2′-bromoethyl-6-methoxynaphthalene (14·5 g.) in ether (100 c.c.) was added with stirring during 10 minutes. Water (400 c.c.) was then added, the product extracted with 1 : 1 ether–ethyl acetate (100 c.c.; 3 × 50 c.c.), and the extract washed, dried, and evaporated under reduced pressure in a stream of nitrogen. The oil was hydrolysed under nitrogen with 2N-sulphuric acid (30 c.c.) for 25 minutes on the steam-bath. A solution of the product in ethyl acetate was shaken with portions (10 c.c.) of sodium hydroxide solution (10%) until acidification gave no further precipitate. The crude product separated on acidification as an oil which rapidly solidified. It was removed by filtration, washed with water followed by a little ethanol, and crystallised from ethyl acetate (2 vols.)–light petroleum (b. p. 40—60°; 1 vol.) to give 1-[2-(1 : 3-diketo*cyclo*hexyl)ethyl]-6-methoxynaphthalene (12·5 g.) as colourless needles, m. p. 172—174° (Found : C, 76·6; H, 6·9. Calc. for $C_{19}H_{20}O_3$: C, 77·0; H, 6·8%). Concentration of the mother-liquor yielded a further amount (1·55 g.) of the product (total yield, 86% based on the bromide). Robinson and Thompson (*loc. cit.*) give m. p. 170—172° and Chuang, Tien, and Huang (*Ber.*, 1937, **70**, 858) give m. p. 168—170°.

The above product (2·2 g.) was finely powdered and to it was added a mixture of orthophosphoric acid (9 c.c.) and phosphoric anhydride (9 g.) at 100°. The dark red solution was kept at 95—100° for 15 minutes and then poured into water (50 c.c.). The organic material was taken up in ethyl acetate, (400 c.c.), the solution washed with dilute aqueous sodium hydroxide, and dried, and the solvent removed under reduced pressure. The solid residue was crystallised from ethanol to give 1 : 2 : 3 : 4 : 5 : 6-hexahydro-3-keto-10-methoxychrysene (1·53 g.) as slightly yellow plates, m. p. 177—178° (Found : C, 82·0; H, 6·75. Calc. for $C_{19}H_{18}O_2$: C, 82·0; H, 6·5%). The 2 : 4-dinitrophenylhydrazone crystallised as reddish-purple prisms from ethyl acetate, m. p. 284°.

1 : 2 : 3 : 4 : 5 : 6 : 9 : 10 : 11 : 12 : 15 : 16-*Dodecahydro*-3-*hydroxy*-10-*ketochrysene*.—(i) (Cf. Cornforth, Cornforth, and Robinson, *loc. cit.*) Hexahydroketomethoxychrysene (500 mg.) in ethanol (70 c.c.) was heated to boiling and sodium (3 g.) added slowly in small pieces. After the metal had dissolved, water (40 c.c.) and concentrated hydrochloric acid (40 c.c.) were added and the mixture was heated on the steam-bath for 15 minutes with agitation. Water (100 c.c.) was then added and the product extracted with 1 : 1 ether–ethyl acetate. The gummy substance obtained by evaporation of the solvents was taken up in ethyl acetate (3 c.c.), shaken with saturated sodium hydrogen sulphite solution for 2·5 hours and then left for 36 hours. The solid product was centrifuged, washed with ether, filtered, suspended in water (25 c.c.), and decomposed with N-sodium carbonate (50 c.c.). The product (110 mg.) was a gum which dissolved in *iso*propanol (1 c.c.), and on being left overnight deposited crystals (25 mg.) of 1 : 2 : 3 : 4 : 5 : 6 : 9 : 10 : 11 : 12 : 15 : 16-*dodecahydro*-3-*hydroxy*-1-*ketochrysene*, m. p. 145—147° (Found : C, 80·15; H, 8·4. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·15%). It gave a yellow precipitate with Brady's reagent and a deep blue colour with sodium methoxide in methanol.

(ii) The hexahydroketomethoxychrysene (1·00 g.) in dioxan (12 c.c.)–ether (100 c.c.)–methanol (16 c.c.) was added to ammonia (500 c.c.) to give a clear yellow solution. Potassium (8·5 g.) was added in small pieces with stirring, followed by water (500 c.c.) when the colour had disappeared. The gummy product was taken up in ethyl acetate, hydrolysed with 2N-sulphuric acid, and converted into the bisulphite compound as above. The gum (250 mg.) obtained from this deposited the dodecahydro-hydroxyketochrysene (61 mg.) when dissolved in *iso*propanol.

1 : 2 : 3 : 4 : 5 : 6 : 9 : 12 : 15 : 16-*Decahydro*-3-*hydroxy*-10-*methoxychrysene*.—1 : 2 : 3 : 4 : 5 : 6-Hexahydro-3-keto-10-methoxychrysene (800 mg.) was reduced with potassium and methanol in ammonia

as recorded in (ii) above. The product was taken up in ethyl acetate (5 c.c.)–light petroleum (b. p. 60—80°; 5 c.c.) and absorbed on a column of alumina, type B (100 g.). The chromatogram was developed with the solvent mixture (250 c.c.), then with an increasing proportion of ethyl acetate, and finally with pure ethyl acetate. The eluate was arbitrarily divided into fractions (50 c.c.) each of which was evaporated to dryness to give a series of gums, all of which gave a yellow precipitate with Brady's reagent but no tetralone blue reaction with methanolic sodium methoxide. After treatment with acid, a test portion of each did give a tetralone blue and it is evident that they all contain a tetralone enol ether grouping. Addition of ethyl acetate to the fractions caused some of them to crystallise to form, in the order of elution: (*A*) (21 mg.), m. p. 152—155° (Found: C, 79·7; H, 9·2%), $\lambda_{max.}$ 2740—2750 A.; (*B*) (10 mg.), m.p. 118—113° (Found: C, 79·9; H, 8·9%); and (*C*) (89 mg.) m. p. 155—158° which appears to be 1 : 2 : 3 : 4 : 5 : 6 : 9 : 12 : 15 : 16-*decahydro*-3-*hydroxy*-10-*methoxychrysene* (Found: C, 80·0; H, 8·9. $C_{19}H_{24}O_2$ requires C, 80·3; H, 8·5%).

Attempted Methylation of 1 : 3-*Dimethoxy*-2-2′-*phenylethyl*cyclo*hexa*-3 : 6-*diene*.—The dimethoxyphenylethyl*cyclo*hexadiene (4·8 g.) was treated with potassamide (from the metal, 1·68 g.) in liquid ammonia, followed by an equivalent amount of methyl iodide. The product, worked up as in the original preparation of the substance, was hydrolysed with 2N-sulphuric acid to give mainly the alkali-soluble *cyclo*hexanedione corresponding to unchanged starting material. The small amount of neutral product gave no ketonic material after treatment with the phosphoric oxide–phosphoric acid reagent. Similarly 1 : 3-dimethoxy-2-methyl*cyclo*hexa-3 : 6-diene, obtained by the reduction of 2-methylresorcinol dimethyl ether, was treated by the same procedure with potassamide and 2-phenylethyl bromide, giving almost entirely methyl*cyclo*hexanedione corresponding to unchanged starting material.

Absorption spectra are by Dr. R. N. Haszeldine.

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