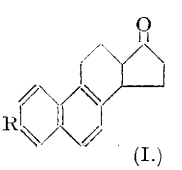
154. *The Synthesis of Substances related to the Sterols. Part XLIV.* dl-cis-*Equilenin.*

By A. J. Birch, (Mrs.) R. Jaeger, and Sir Robert Robinson.

cis-8-Methyl-α-hydrindanone (VII), 3′-keto-2-methyl-1 : 2 : 3 : 4-tetrahydro*cyclo*pentenophenanthrene (VIII, R = H), and *dl-iso*equilenin (VIII, R = OH) have been synthesised by application of the procedure of Birch and Robinson (J., 1944, 501) for angular methylation. All these compounds probably have the *cis*-configuration, and the method is therefore not directly applicable to the preparation of the natural *trans*-equilenin. Removal of the piperonylidene group from (II, R = OCH_3) by the method of Johnson (*J. Amer. Chem. Soc.*, **1943**, **65**, 1317) gave a chloro-*cis*-equilenin methyl ether (V). In view of the possible eventual therapeutic application of a substance so closely related to a hormone, it may be pointed out that *cis*-equilenin could be produced on a useful scale by the method now described. The only unsatisfactory stage is the cyclisation to a diketone (yield, 25%).

x-NOREQUILENIN (I, R = OH) was synthesised by Koebner and Robinson (J., 1938, 1994) who also methylated the piperonylidene derivative of its methyl ether to the derivative of an *x*-equilenin methyl ether (II, R = OCH_3), thought to have the *iso*-configuration. No method was then available for the removal of the piperonylidene group. Johnson (*loc. cit.*) later devised a method for the removal of the benzylidene group from benzylidene-9-methyl-α-decalone by chlorination at the double bond, followed by hydrolysis in several stages. When this process was applied to (II, R = OCH_3) it was found that a chlorine atom was introduced by substitution before addition to the double bond took place, and if chlorination was carried far enough to accomplish this, the product resulting from the initial stages of the hydrolysis was a *chloro-diketone*. Further hydrolysis of this with alkali gave a mixture of a *chloro-acid* and an x-*chloroequilenin methyl ether*. On the assumption, almost certainly correct, that the chlorine enters the 8-position these substances may be formulated as (III), (IV), and (V). Since oxidation of (II, R = OCH_3) by potassium permanganate in acetone solution gave the dicarboxylic acid (VI), which Bachmann, Cole, and Wilds (*J. Amer. Chem. Soc.*, 1940, **62**, 824) have converted into *iso*equilenin, this and the above compounds must belong to the *iso*-series, which is also probably the *cis*-series from results outlined below.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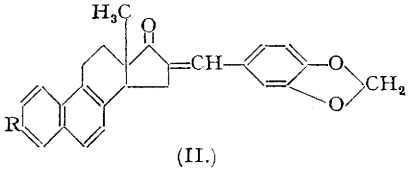
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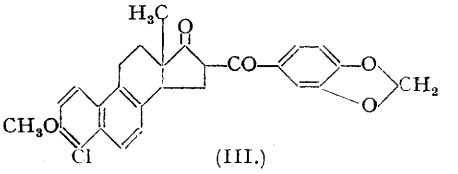
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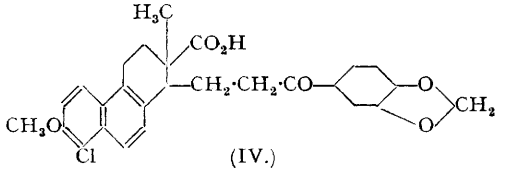
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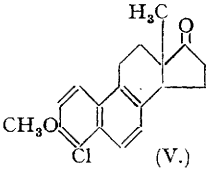
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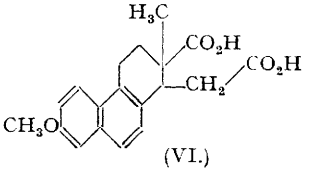
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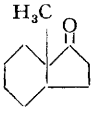
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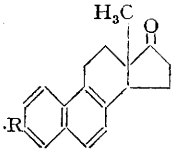

(VIII.)

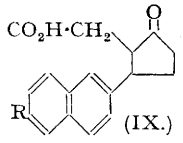
Recently, Birch and Robinson (*loc. cit.*) described the preparation of 9-methyl-α-decalone from α-decalone by blocking the methylene group adjacent to the carbonyl with a methylanilinomethylene group, methylation of the product, and hydrolysis. This process has now been carried out with *cis*-α-hydrindanone, which was prepared from 2-hydroxymethylene-α-decalone by oxidation with potassium permanganate in alkaline solution, and cyclisation of the resulting *trans-cyclo*hexane-1-propionic-2-carboxylic acid by heating with a trace of baryta to 300—320°. *cis*-8-Methyl-α-hydrindanone (VII) was obtained as the sole final product when the methylation was carried out with the sodium derivative in ether or boiling toluene, or with the potassium derivative in boiling butyl alcohol. The properties of the ketone and its derivatives agree with those observed by Johnson (*J. Amer. Chem. Soc.*, 1944, **66**, 216).

A similar methylation of (I, R = H) gave (VIII, R = H) in what is presumably the *cis*-form, which proved to be identical with the α-form, m. p. 100—101°, obtained by Bachmann and Wilds (*J. Amer. Chem. Soc.*, 1940, **62**, 2084). Its piperonylidene derivative is identical with that obtained by Koebner and Robinson (*loc. cit.*) by methylation of the piperonylidene derivative of (I, R = H).

The methylation of (I, R = OCH_3) was then examined in the hope of obtaining equilenin methyl ether. One step in the synthesis of this ketone by Koebner and Robinson (*loc. cit.*) is the ring closure of the acid (IX, R = OCH_3) to the diketone (X, R = OCH_3) which they accomplished by solution in phosphoric acid and addition of a large amount of phosphoric anhydride. Owing to the great evolution of heat the temperature is difficult to control, and inconsistent results were obtained. The process was modified, and under the conditions now prescribed it is possible to obtain reproducible yields in the neighbourhood of 25%. Other cyclising agents, including anhydrous hydrogen fluoride, gave none of the required product, although this reagent gave a small yield of the diketone (X, R = H) from the acid (IX, R = H). The phosphoric acid–phosphoric anhydride method may have wide application for small-scale cyclisations, since γ-phenylbutyric acid gave an 86% yield of α-tetralone and β-*m*-methoxyphenylpropionic acid gave a 61% yield of 5-methoxy-α-hydrindone.

The product of methylation of (I, R = OCH_3) was found to be identical with the *dl-iso*equilenin methyl ether, m. p. 125°, of Bachmann, Cole, and Wilds (*loc. cit.*). It seems almost certain from the results obtained with α-hydrindanone that this has the *cis*-configuration, and consequently that equilenin (and probably the other hormones and sterols) has the *trans*-configuration at the junction of rings C and D. No evidence of the formation of more than one stereoisomer was found in any of these methylations. Methylation of α-decalone

gave some of the *trans*-isomer (Birch and Robinson, *loc. cit.*), and it is therefore possible that the natural *trans*-series of hormones could be reached through chrysene derivatives such as (XI) (cf. also Johnson, *J. Amer. Chem. Soc.*, 1944, **66**, 215).*



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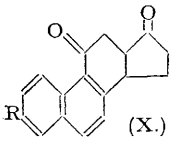

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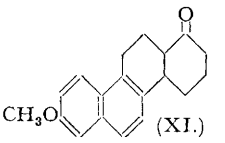

(XI.)

Experimental.

1-*Ketohydrindane* (cf. Windaus, Hückel, and Reverey, *Ber.*, 1923, **56**, 96).—2-Formyl-α-decalone (13 g.) was dissolved in ice-cold aqueous sodium hydroxide (200 c.c. of 3%), and powdered potassium permanganate (37 g.) slowly added with vigorous stirring, together with sufficient broken ice to maintain the temperature at about 0°. After 2 hours the precipitate was collected, well washed with warm water, and the combined solutions concentrated to about 70 c.c. under reduced pressure. Acidification gave pale brown crystals (9 g.) (colourless prisms from aqueous acetic acid; m. p. 143° after softening at about 138°) which were ground with baryta (0·8 g.) and slowly distilled from an air-bath at 300—320°. The distillate was washed with sodium carbonate solution, dried, and the ketone (4 g.) was obtained as a colourless oil, b. p. 218—220°; semicarbazone, m. p. 212—213°.

1-*Keto*-2-*hydroxymethylenehydrindane*.—A mixture of the above ketone (4 g.), ethyl formate (5 g.), powdered sodium (1·3 g.), and dry ether (45 c.c.) was kept for 12 hours with occasional shaking. The product was decomposed with ice and water, the aqueous solution acidified with acetic acid, and the oil collected with ether and distilled. The *ketone* formed a pleasant smelling, colourless oil, b. p. 126—128°/12 mm. (3·2 g.) (Found: C, 71·5; H, 8·4. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%).

1-*Keto*-2-*methylanilinomethylenehydrindane*.—The formyl derivative (3·2 g.) and methylaniline (4 g.) in toluene (15 c.c.) were heated together on the steam-bath for an hour, the solvent evaporated under diminished pressure, and the residue crystallised from ethyl acetate–light petroleum (b. p. 40—60°), forming colourless, flat prisms (3·7 g.), m. p. 98° (Found: C, 79·6; H, 8·0. $C_{17}H_{21}ON$ requires C, 80·0; H, 8·2%).

Methylation.—(I) The above compound (1·5 g.) was treated with sodamide (from 0·15 g. of sodium and a trace of ferric nitrate in liquid ammonia) in boiling toluene (15 c.c.) during an hour. Methyl iodide (2 g.) was then added to the boiling solution, and refluxing continued for 15 minutes. The pale yellow resinous product was hydrolysed by refluxing for 2 hours with a mixture of water (20 c.c.), alcohol (15 c.c.), and concentrated sulphuric acid (4 c.c.), the product was extracted with ether, and then boiled for 2 hours with 5% sodium hydroxide solution (30 c.c.). A pale yellow oil with a camphoraceous odour was isolated by extraction with ether and converted directly into the semicarbazone. This was obtained as colourless, flat prisms (0·3 g.), m. p. 223—224° (Found: C, 63·1; H, 9·0. Calc. for $C_{11}H_{19}ON_3$: C, 63·1; H, 9·1%).

(II) A similar experiment, ether (25 c.c.) being substituted for the toluene, gave as final product the same semicarbazone (0·48 g.) (yield 40%). This on treatment with 2 : 4-dinitrophenylhydrazine sulphate in aqueous alcohol gave the 2 : 4-dinitrophenylhydrazone, which crystallised from ethyl acetate–alcohol as pale orange prisms, m. p. 140—141° (lit., 140—141°).

The semicarbazone was mixed with 10% hydrochloric acid and steam-distilled, the *cis*-8-methyl-α-hydrindanone being obtained as a colourless, camphor-like substance, m. p. 32—34°; oxime, m. p. 88—89°; 2 : 4-dinitrophenylhydrazone, m. p. 140—141°; *p*-nitrophenylhydrazone, m. p. 178—179°. Johnson (*J. Amer. Chem. Soc.*, 1944, **66**, 216) gives the following m. p.'s, respectively: 35·4—36°, 87—88°, 140·5—141°, and semicarbazone, m. p. 224·5—225·5°.

(III) A mixture of the methylanilinomethylene derivative (2·0 g.), a solution of potassium (2·0 g.) in *tert.*-butyl alcohol (35 c.c.), and methyl iodide (15 g.) was refluxed for an hour, most of the solvent removed under reduced pressure, and the residue diluted with water and extracted with ether. Hydrolysis as in (I) above, and treatment with semicarbazide acetate, gave a semicarbazone (0·7 g.), m. p. 215—220°. Several crystallisations from dioxan–alcohol gave the pure *cis*-derivative (0·6 g.), m. p. 224—225°.

Degradation of 3′-*Keto*-7-*methoxy*-4′-*piperonylidene*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene* (II; R = OMe).—(A) *Oxidation*. The methylated piperonylidene derivative (Koebner and Robinson, J., 1938, 1994) (160 mg.) in pure acetone (15 c.c.) was stirred and cooled in ice, and finely powdered potassium permanganate (250 mg.) added in portions. When all the permanganate had disappeared the acetone was evaporated, and the residue thrice extracted with boiling water (10 c.c.). Acidification gave a crystalline solid, which crystallised in colourless prisms from acetone–ethyl acetate, m. p. 229—231° (Found: C, 68·9; H, 6·0. Calc. for $C_{19}H_{20}O_5$: C, 69·4; H, 6·1%). Bachmann, Cole, and Wilds (*loc. cit.*) give m. p. 231—232° for the expected acid (VI).

(B) *Chlorination and hydrolysis* (cf. Johnson, *J. Amer. Chem. Soc.*, 1943, **65**, 1317). (I) The piperonylidene compound (800 mg.) was dissolved in pure dioxan (15 c.c.), and 1·75 c.c. of an 8% solution of chlorine in carbon tetrachloride added slowly with ice-cooling. Evaporation of the solvent at room temperature under reduced pressure left a yellow resin, which was treated with sodium ethoxide and acid as below. The *product* was a yellow solid which gave no colour with ferric chloride, and was unaffected by refluxing with aqueous-alcoholic potash. It was purified by passage of its alcohol–ethyl acetate solution through a column of alumina, and crystallisation from dioxan–alcohol, and then formed a pale yellow crystalline powder, m. p. 203—204° (Found: C, 71·2; H, 5·5; Cl, 7·4. $C_{27}H_{23}O_4Cl$ requires C, 72·5; H, 5·2; Cl, 7·6%). This substance is evidently a *mono-chloro*-derivative of (II).

(II) Chlorine in carbon tetrachloride (3 c.c. of 8% solution) was added to the piperonylidene compound (900 mg.) in dioxan (15 c.c.) cooled in ice, and the solvent removed at room temperature under reduced pressure. The gummy residue was taken up in a little benzene, a solution of sodium (0·2 g.) in alcohol (10 c.c.) added, and the mixture heated on the steam-bath for an hour. The solvent was then removed, and the residue refluxed for ½ hr. with 15% hydrochloric acid (20 c.c.). The product was taken up in benzene, and refluxed for an hour with 2% aqueous sodium hydroxide (100 c.c.). A pale yellow sodium salt separated, and was collected. Neither the benzene nor the aqueous layer contained

* Professor W. S. Johnson and his collaborator, Mr. H. Posvic, have kindly informed us that, under the conditions described in Part XXXV (J., 1941, 467), no condensation occurred between *cyclo*pentanone and ethyl orthoformate and that the only product was *cyclo*pentylidene*cyclo*pentanone. This finding is in agreement with the only analysis quoted (% N in a semicarbazone) and with the properties of the supposed ethoxymethylene*cyclo*pentanone (cf. Kon and Nutland; J., 1926, 3011). In view of the exiguous evidence and the inapplicable catalyst we had intended to expunge the record of this experiment but the matter was unfortunately forgotten.—L. E. K., R. R.

the expected products, and treatment of the solid sodium salt with dilute acid gave a solid which crystallised from ethyl acetate as colourless prisms, m. p. 178° (Found : C, 70·1; H, 5·0; Cl, 7·55. $C_{27}H_{23}O_5Cl$ requires C, 70·0; H, 5·0; Cl, 7·7%). As stated on p. 583, this *chloro-diketone* is probably (III). It gave a cherry-red colour with alcoholic ferric chloride. Hydrolysis of this substance (35 mg.) was finally accomplished by refluxing for 2½ hours with a solution of potassium hydroxide (3 g.) in water (12 c.c.) and alcohol (12 c.c.). Dilution with water (50 c.c.) and extraction with a large volume of ether gave a brownish solid which was boiled with alcohol (5 c.c.) (charcoal); on concentration to a small bulk, the solution deposited colourless prisms, m. p. 178—180°. Sublimation at 0·1 mm. and crystallisation from alcohol gave colourless, well-formed prisms, m. p. 183—184° (Found : C, 71·9; H, 6·0. $C_{19}H_{19}O_2Cl$ requires C, 72·5; H, 6·0%). This *chloro*-cis-*equilenin methyl ether* (V) gave an orange, very sparingly soluble 2 : 4-*dinitrophenylhydrazone*, m. p. 290° (Found : C, 59·9; H, 4·8. $C_{25}H_{23}O_5N_4Cl$ requires C, 60·7; H, 4·9%). Acidification of the alkaline solution from the hydrolysis gave an *acid* (IV), which crystallised from acetic acid as colourless prisms, m. p. 212° (Found : C, 67·5; H, 5·3. $C_{27}H_{25}O_6Cl$ requires C, 67·4; H, 5·2%).

3′-*Keto*-4′-*formyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene*.—3′-Keto-1 : 2 : 3 : 4-tetrahydro*cyclo*pentenophenanthrene (3 g.), ethyl formate (3·5 c.c.), and powdered sodium (0·8 g.) in benzene (30 c.c.) were shaken for an hour and left for 12 hours. The mixture was then decomposed with ice and dilute acetic acid, the benzene layer removed and shaken with ice-cold 3% aqueous potassium hydroxide until no more acidic material was extracted. Acidification with acetic acid gave the *formyl* compound as a cream-coloured solid (3 g.), which crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as cream-coloured plates (2·4 g.), m. p. 134° (Found : C, 81·2; H, 6·3. $C_{18}H_{16}O_2$ requires C, 81·0; H, 6·35%). It gave a purple-brown coloration with alcoholic ferric chloride.

3′-*Keto*-4′-*methylanilinomethylene*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene*.—A mixture of the above formyl compound (2·3 g.), methylaniline (1 g.), and toluene (20 c.c.) was heated on the steam-bath for 4 hours, the water formed being removed occasionally by distilling a little solvent. Addition of light petroleum (b. p. 80—100°) (15 c.c.) to the hot solution and cooling gave pale yellow prisms (2·5 g.), m. p. 164°. These were dissolved in benzene (60 c.c.) and added to sodamide, formed by catalytic decomposition by a trace of ferric nitrate of sodium (0·25 g.) in liquid ammonia (15 c.c.) followed by removal of the solvent. After 80 mins.' heating on the steam-bath in a stream of hydrogen, ammonia ceased to be evolved, and a mixture of methyl iodide (2 g.) and benzene (5 c.c.) was added. After a further 45 minutes' heating the mixture was cooled, shaken with dilute acetic acid, dried, and most of the solvent removed under reduced pressure. A little methyl alcohol was added to the residue, and crystallisation then occurred. The solid *product* (A) formed pale yellow prisms (0·6 g.) from methyl alcohol, m. p. 149—150° (Found : C, 84·7; H, 6·9. $C_{26}H_{25}ON$ requires C, 85·0; H, 6·8%). The mother-liquor contained a pale yellow gum (2 g.) (B).

3′-*Keto*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene* (VIII; R = H).—Compound (A), above, was refluxed with 10% hydrochloric acid (35 c.c.) for 1½ hours, the product collected with ether, and refluxed for a further hour with 5% aqueous sodium hydroxide. The product was taken up in ethyl acetate, passed through alumina, sublimed at 0·1 mm., and finally crystallised from methyl alcohol; colourless prisms, m. p. 100—101° (Found : C, 85·7; H, 7·2. Calc. for $C_{18}H_{18}O$: C, 86·4; H, 7·2%). The gum (B) was submitted to the same process, and gave some of the same compound, together with a little lower-melting material. The pure product depressed the m. p. of the starting ketone. It gave a piperonylidene derivative as pale yellow plates from ethyl acetate–alcohol, m. p. 158—159°, alone or mixed with a specimen, m. p. 157—158°, prepared by Koebner and Robinson.

Ethyl 3-β-6′-*Methoxynaphthyl*-Δ²-cyclo*penten*-1-*one*-2-*acetate*.—3-β-6′-Methoxynaphthyl-Δ²-*cyclo*penten-1-one-2-acetic acid (30 g.; cf. Koebner and Robinson, *loc. cit.*) was refluxed with 5% alcoholic hydrogen chloride (300 c.c.) for 2 hours. The *ester* separated on cooling after dilution with a small volume of water. It was purified for the subsequent hydrogenation by passing a solution of the crude product in ethyl acetate through a column of charcoal. After removal of the solvent the residue crystallised from alcohol in slightly yellow needles (30 g.), m. p. 114—115° (Found : C, 73·9; H, 6·3. $C_{20}H_{20}O_4$ requires C, 74·0; H, 6·2%).

3-β-6′-*Methoxynaphthyl*cyclo*pentan*-1-*one*-2-*acetic Acid* (IX; R = OMe).—The unsaturated ester (5 g.), suspended in pure ethyl acetate (75 c.c.), was hydrogenated at the room temperature in the presence of palladised strontium carbonate (2 g. of 1·5%), hydrogen being absorbed at the rate of 60 c.c. per hour. The reduced ester was hydrolysed as described by Koebner and Robinson (*loc. cit.*).

3′ : 4-*Diketo*-7-*methoxy*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene* (X; R = OMe).—The following conditions are the result of many comparative experiments and should be closely observed. The above acid (3 g.) was stirred by means of a thermometer into a mixture of phosphoric anhydride (10 g.) and syrupy phosphoric acid (10 c.c.; *d* 1·75) at 120°. The mixture was maintained at 120—125° (bath at 145°) for 2—3 minutes with vigorous stirring, cooled quickly to about 60°, and decomposed with water (100—150 c.c.). The ketone was extracted with ether (total 300 c.c.), the ethereal extract washed with dilute aqueous sodium hydroxide and with water, and dried. After removal of the solvent the residue was taken up in ethyl acetate and passed through a short column of charcoal. The ketone (average yield, 25%) crystallised from methyl alcohol as colourless prisms, m. p. 133°.

3′-*Keto*-7-*methoxy*-4-*methylanilinomethylene*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene*.—A mixture of 3′-keto-7-methoxy-1 : 2 : 3 : 4-tetrahydro-1 : 2-*cyclo*pentenophenanthrene (3 g.; Koebner and Robinson, *loc. cit.*), ethyl formate (4·2 g.), powdered sodium (1·3 g.), and dry thiophen-free benzene (50 c.c.) was stirred for 7 hours at room temperature under nitrogen. After decomposition with a little ice and water, the sparingly soluble sodium salt was collected, washed with benzene, and moistened with alcohol. Treatment with acetic acid (10 c.c.) and water (90 c.c.) liberated 3′-keto-7-methoxy-4′-formyl-1 : 2 : 3 : 4-tetrahydro-1 : 2-*cyclo*pentenophenanthrene as a cream-coloured solid (yield, 3·1 g. or 95%). A small sample crystallised from aqueous acetone as colourless transparent plates, m. p. 145—146° (decomp.), which gave a purplish-blue coloration with alcoholic ferric chloride.

A mixture of the crude formyl derivative (3 g.), toluene (50 c.c.), and freshly distilled methylaniline (1·5 g.) was heated on the steam-bath for 1½ hours. After removal of water and solvents under diminished pressure, the yellow solid residue was crystallised from toluene; yellow needles (2·9 g.), m. p. 206° (Found : C, 80·9; H, 6·5; N, 3·9. $C_{26}H_{25}O_2N$ requires C, 81·4; H, 6·5; N, 3·7%).

3′-*Keto*-7-*methoxy*-4′-*methylanilinomethylene*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene*.—A solution of the foregoing compound (2 g.) in hot benzene (50 c.c.) was added to sodamide, freshly prepared from sodium (0·3 g.) and liquid ammonia and suspended in toluene (20 c.c.). The mixture was refluxed in an atmosphere of nitrogen until the evolution of ammonia ceased (about 1 hour). Methyl iodide (6 g.), dissolved in benzene (10 c.c.), was added to the hot reaction mixture, followed after 15 minutes by a further amount of methyl iodide (1 g.), refluxing being continued for 2 hours. When cold, very dilute acetic acid was added; the benzene layer was separated, washed, dried, and concentrated under reduced pressure. Light petroleum (b. p. 60—80°) was added until the solution became cloudy and the whole was passed through a column of activated alumina. Repeated washing of the column with benzene–light petroleum and eventually with benzene alone separated the methylated product from unchanged starting material, which was the more strongly adsorbed and could be recovered (0·6 g.) by elution with ethyl acetate. The course of the chromatographic separation was easily followed in ultra-violet light. After removal of the solvents, the methylated material crystallised from alcohol as lemon-yellow, triclinic prisms (1 g.), m. p. 165°. The *substance* is dimorphic, and was also

obtained as colourless, fluffy needles, m. p. 152°, which were convertible into the higher-melting form (Found : C, 81·3; H, 6·8; N, 3·8. $C_{27}H_{27}O_2N$ requires C, 81·6; H, 6·8; N, 3·5%). The product, m. p. 152°, was also obtained in very poor yield by the potassium *tert.*-butoxide–methyl iodide method.

3′-*Keto*-7-*methoxy*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene* (dl-iso*Equilenin Methyl Ether*).—The methylated methylanilinomethylene derivative (850 mg.) was refluxed for 3 hours with a mixture of concentrated sulphuric acid (2 c.c.), water (6 c.c.), and alcohol (13 c.c.). The solution was diluted with water, the product isolated by means of ethyl acetate and, after removal of the solvent, boiled for 3 hours with 10% aqueous-alcoholic potassium hydroxide (40 c.c.; 1 : 1) under nitrogen. The reaction mixture was diluted with water, and the material extracted with ether, washed, and dried. The pink crystalline residue was dissolved in benzene–light petroleum (b. p. 60—80°) and passed through a column of alumina, which was finally well washed with benzene. After removal of the solvent, the colourless oil (350 mg.) crystallised in contact with alcohol as colourless prisms (330 mg.), m. p. 125—126° (Found : C, 81·5; H, 7·2. Calc. for $C_{19}H_{20}O_2$: C, 81·4; H, 7·2%). Bachmann, Cole, and Wilds (*loc. cit.*) give m. p. 127—127·5°.

3′-*Keto*-7-*hydroxy*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydro*-1 : 2-cyclo*pentenophenanthrene* (dl-iso*Equilenin*).—A mixture of *dl-iso*equilenin methyl ether (90 mg.), acetic acid (3 c.c.), and hydrobromic acid (3 c.c., *d* 1·7) was refluxed under nitrogen for 2 hours. The cold solution was diluted with water, shaken with ether, and the phenolic material dissolved in aqueous potassium hydroxide (3%). Acidification of the alkaline solution precipitated *dl-iso*equilenin, which was collected in ether and crystallised from acetic acid and a little water. It formed faintly coloured prisms, m. p. 222—223° (Found : C, 81·0; H, 7·1. Calc. for $C_{18}H_{18}O_2$: C, 81·2; H, 6·8%) (B., C., and W., *loc. cit.*, give m. p. 223—224°).

Cyclisation of γ-Phenylbutyric Acid and β-m-*Methoxyphenylpropionic Acid.*—Phosphoric anhydride (8 g.) and syrupy phosphoric acid (6 c.c.) were mixed and stirred with a thermometer until the temperature fell to 145°. Phenylbutyric acid (2 g.) was then stirred in, and stirring continued for 3 minutes. The α-tetralone formed was isolated in the usual way and converted into the semicarbazone; colourless needles (2·15 g.) from dioxan–alcobol, m. p. 218—220°. Kipping and Hill (J., 1899, **75**, 148) give m. p. 217°. *β-m*-Methoxyphenylpropionic acid (2 g.) was treated similarly and the crude product was extracted repeatedly with boiling light petroleum (b. p. 60—80°) until only a little tar was left; the combined solutions were concentrated to a small bulk, cleared by addition of a little ethyl acetate, and on cooling, gave the ketone as very pale yellow needles (1·1 g.), m. p. 105—108°, raised to 108—109° by several recrystallisations. The crude product may contain a little of the isomeric 4-methoxy-α-hydrindone, since Ingold and Piggott (J., 1923, **123**, 1469) give m. p. 110° for the pure 5-methoxy-α-hydrindone.

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