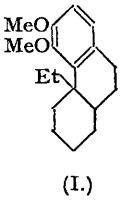
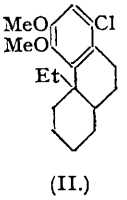
140. *Synthesis of Substances possibly obtainable as Degradation Products of Thebaine.*

By R. Ghosh and Sir Robert Robinson.

3 : 4-Dimethoxy-13-ethyl-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-octahydrophenanthrene (I) and its 1-*chloro*-derivative (II) could probably be obtained from thebaine (III) by a series of processes.



(I.)



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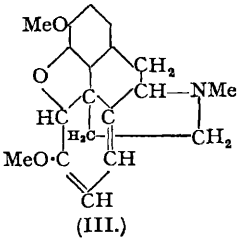
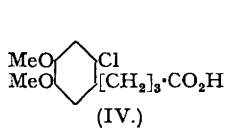


(III.)

Syntheses of both (I) and (II) in undetermined stereo-configuration are described. Ketonic intermediates have been characterised and may also be of interest in relation to the morphine–thebaine chemistry.

γ-3 : 4-DIMETHOXYPHENYLBUTYRIC acid (Haworth and Mavin, J., 1932, 1486) was chlorinated to *γ-2-chloro-4 : 5-dimethoxyphenylbutyric* acid (IV) with the object of directing the subsequent ring-closure into position 6. Difficulty was encountered in this cyclisation, and various methods, such as treatment of the acid with sulphuric acid, phosphoric anhydride in benzene, or phosphoryl oxychloride, proved to be unsatisfactory. Treatment of the acid chloride with aluminium chloride was also unsatisfactory. The yield of the ketone, *1-chloro-5-keto-3 : 4-dimethoxy-5 : 6 : 7 : 8-tetrahydronaphthalene* (V), was very unfavourable and the product was always accompanied by varying amounts of *1-chloro-5-keto-4-hydroxy-3-methoxy-5 : 6 : 7 : 8-tetrahydronaphthalene* (VI). Stannic chloride was then used to bring about the ring-closure of the acid chloride under various conditions and finally the ketone (V) was thus obtained in 80—90% yield, although accompanied by a trace of (VI), which could, however, be methylated to (V) by means of methyl sulphate and alkali. The next stage, a Grignard reaction with ethylmagnesium bromide and the ketone (V), was tried under various conditions and an 80—90% yield of the product was realised when one molecule of the ketone was treated with 4—5 molecules of ethylmagnesium bromide in ether. The product proved to be a mixture of 1-chloro-5-hydroxy-3 : 4-dimethoxy-5-ethyl-5 : 6 : 7 : 8-tetrahydronaphthalene and *1-chloro-3 : 4-dimethoxy-5-ethyl-7 : 8-dihydronaphthalene* (VII). The mixture was successfully dehydrated in good yield by distillation over phosphoric anhydride in a vacuum. Other methods, such as the use of the same reagent in boiling benzene or dehydration in presence of thionyl chloride and pyridine, formic acid, oxalic acid, and iodine, were tried, but none proved suitable. The dihydronaphthalene (VII) was then subjected to oxidation with (i) mercuric acetate, (ii) perbenzoic acid, (iii) hydrogen peroxide in acetic acid. In the first case a product was isolated, after the usual treatment with 10% sulphuric acid, which gave the same analysis as the desired β-tetralone derivative, but was devoid of ketonic properties and was probably the *oxide* (VIII). Treatment of (VII) with perbenzoic acid, followed by isomerisation of the resulting oxide to the ketone (IX), gave a very poor yield. Oxidation of (VII) with hydrogen peroxide in acetic acid gave more promising results, and the yield of the *ketone* (IX) so far attained is 33%. (IX) was then condensed with the methiodide of β-diethylaminoethyl methyl ketone in presence of sodamide, and the resulting product proved to be *1-chloro-7-keto-3 : 4-dimethoxy-13-ethyl-5 : 6 : 7 : 9 : 10 : 13-hexahydrophenanthrene* (X), having the properties of an αβ-unsaturated ketone and giving a scarlet-red *2 : 4-dinitrophenylhydrazone*. Reduction of (X) in presence of palladium–charcoal in alcohol gave *1-chloro-7-keto-3 : 4-dimethoxy-13-ethyl-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-octahydrophenanthrene* (XI), which was reduced to (II) by Clemmensen's method. As a result of the catalytic reduction, (XI) was accompanied by a small amount of *7-keto-3 : 4-dimethoxy-13-ethyl-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-octahydrophenanthrene* (XII), and consequently (II) by a small amount of (I).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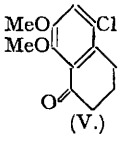
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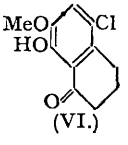
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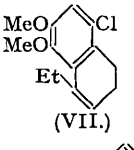
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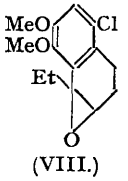
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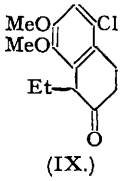
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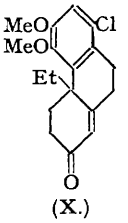
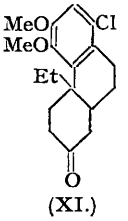
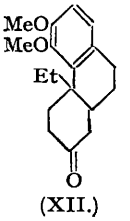
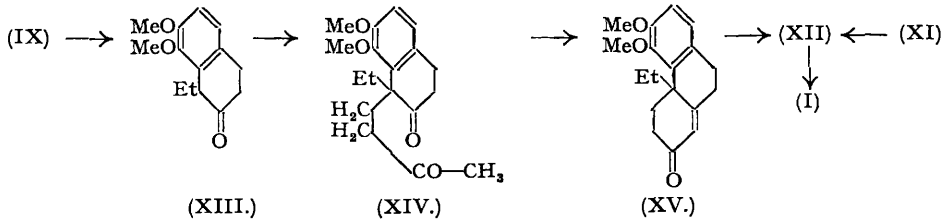

(X.)


(XI.)


(XII.)

The product (II) proved to be a colourless viscous liquid, readily soluble in organic solvents. In the hope of obtaining the pure *cis*-modification, (X) was reduced in the presence of platinic oxide (cf. Ruzicka, Brüngger, Eichenberger, and Meyer, *Helv. Chim. Acta*, 1934, **17**, 1407), and the product further reduced by amalgamated zinc and hydrochloric acid. It was still an oil and could not be induced to crystallise.

The synthesis of (I) was achieved according to the following scheme :



(XIII.) (XIV.) (XV.)

Thus (IX) was dehalogenated to (XIII), and the latter condensed with the methiodide of 4-diethylaminobutan-2-one. The results of the condensation depended on the amount of sodamide used; in presence of a small

quantity of the reagent the product was mainly (XIV), while a large excess gave (XV), slightly contaminated with (XIV). Reduction of (XV) with hydrogen in the presence of platinic oxide, in alcohol, gave (XII), which was also obtained by dehalogenating (XI). Clemmensen reduction of (XII) gave (I) as a colourless, thick liquid, soluble in all organic solvents. Attempts to crystallise this substance have not yet been successful. It may be mentioned that dehalogenation of (II) to (I) could not be accomplished.

Further work on the preparation of crystalline derivatives of (I) is in progress and when oppportunity offers the conversion of thebaine into (I) will be attempted.

Experimental.

γ-3 : 4-*Dimethoxyphenylbutyric Acid*.—The method of Haworth and Mavin (*loc. cit.*) was slightly modified. Succinic anhydride (44 g.) and veratrole (64 g.) were added to a solution of aluminium chloride (120 g.) in nitrobenzene (400 c.c.), and the mass stirred mechanically with cooling in running water. After 24 hours it was decomposed with ice and hydrochloric acid, and steam-distilled. After removal of nitrobenzene and cooling, the solid was collected and dissolved in boiling sodium carbonate solution (charcoal). Acidification of the filtered solution gave veratroylpropionic acid, m. p. 159—161° (Haworth and Mavin, 160—161°). This was refluxed for 15 hours with amalgamated zinc (280 g.), and concentrated hydrochloric acid, replenished from time to time (1500 c.c. in all). The cooled mixture was extracted with chloroform, the extract washed with water, and the solvent removed. The residue was treated with aqueous sodium bicarbonate, and the solution washed with ether. It was then acidified, the acid isolated by means of chloroform, and distilled under 0·2 mm. The distillate solidified to a snow-white mass, and on crystallisation from chloroform–light petroleum (b. p. 60—80°) afforded colourless prisms, m. p. 58—59° (Haworth and Mavin, m. p. 57—59°) (yield, 70—80%).

γ-2-*Chloro*-4 : 5-*dimethoxyphenylbutyric Acid* (IV).—A solution of veratrylbutyric acid (75 g.) in glacial acetic acid (200 c.c.) was cooled to 10—15° and dry chlorine (from 27 g. of potassium permanganate), diluted with air, passed in with vigorous stirring. After 2 hours the mixture was slowly heated, and finally boiled for 5 minutes. It was then cooled and poured into ice-water, whereupon a mixture of the *chloro-acid* and unchanged material separated. This was triturated with cold ether, in which the chloro-acid was sparingly soluble, and the residue was twice crystallised from large volumes of ether (charcoal). Colourless, prismatic needles, m. p. 112°, were obtained (yield, 70%) (Found : C, 55·8; H, 5·7; equiv., 259. $C_{12}H_{15}O_4Cl$ requires C, 55·7; H, 5·8%; equiv., 258·5).

1-*Chloro*-4-*hydroxy*-5-*keto*-3-*methoxy*-5 : 6 : 7 : 8-*tetrahydronaphthalene* (VI).—Chlorodimethoxyphenylbutyric acid (6·0 g.) was mixed with sulphuric acid (8 c.c. of 80%) and warmed on the steam-bath for ½ hour. After addition to ice, an ether extract was washed with sodium bicarbonate solution, water, and dried. The yellowish product crystallised from methanol as pale yellow needles, m. p. 104—105° (yield, 2·0 g.) (Found : C, 57·5; H, 4·8. $C_{11}H_{11}O_2Cl$ requires C, 58·3; H, 4·9%). The *chloro-ketone* gives a greenish-yellow solution in dilute aqueous sodium hydroxide. The *oxime* (pyridine method) crystallised from methanol in colourless needles, m. p. 205—206° (Found : N, 6·0. $C_{11}H_{12}O_3NCl$ requires N, 5·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid as orange needles which decomposed above 286° (Found : N, 13·8. $C_{17}H_{15}O_6N_4Cl$ requires N, 13·8%).

1-*Chloro*-5-*keto*-3 : 4-*dimethoxy*-5 : 6 : 7 : 8-*tetrahydronaphthalene* (V).—(A) Chlorodimethoxyphenylbutyric acid (5 g.) was dissolved in benzene (60 c.c.), and phosphoric anhydride (20 g.) added in small portions during 3 hours. After cooling, the benzene was decanted, and the residue decomposed with ice and extracted with ether. The ethereal extract and the benzene solution were combined, washed with dilute aqueous sodium hydroxide and water, dried over potassium carbonate and the solvent removed. The residue was distilled from a bath at 134—140°/0·02 mm., and the distillate, which soon solidified, crystallised from alcohol as colourless needles, m. p. 77·5—78° (yield, 0·8 g.) (Found : C, 60·2; H, 5·4; Cl, 15·0. $C_{12}H_{13}O_3Cl$ requires C, 59·9; H, 5·4; Cl, 14·8%). On acidification of the above alkaline washings, and extraction with ether and removal of acidic materials with sodium bicarbonate solution, 1-chloro-4-hydroxy-5-keto-3-methoxy-5 : 6 : 7 : 8-tetrahydronaphthalene was obtained, m. p. 104—105° after crystallisation (0·3 g.).

The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid as red needles, m. p. 242—243° (Found : N, 13·5. $C_{18}H_{17}O_6N_4Cl$ requires N, 13·3%). The *semicarbazone* crystallised from alcohol in colourless, silky plates, m. p. 218° (Found : C, 52·5; H, 5·2; N, 13·9. $C_{13}H_{16}O_3N_3Cl$ requires C, 52·4; H, 5·4; N, 14·1%).

(B) *γ*-2-Chloro-4 : 5-dimethoxyphenylbutyric acid (10 g.) was boiled for 5 minutes with phosphoryl chloride (30 c.c.), then poured into ice-water, and the mixture extracted with ether and worked up as above. The alkali-insoluble ketone (0·5 g.) and the alkali-soluble ketone (1·6 g.) had the properties already described. Mixed m. p.'s with authentic samples were not depressed.

(C) Chlorodimethoxyphenylbutyric acid (5 g.) was dissolved in benzene (35 c.c.) at 50°, and powdered phosphorus pentachloride (6 g.) gradually added. The acid chloride was formed with evolution of hydrogen chloride and the mixture was kept at 40—50° for 2 hours. After cooling to 0°, stannic chloride (6 c.c.) was added with shaking and the temperature maintained for 36 hours. The mixture was then poured into concentrated hydrochloric acid (30 c.c.), ether (30 c.c.) and ice, with stirring. The layers were separated, and the aqueous solution extracted with 6 portions of ether (150 c.c.). The combined extracts were then washed with hydrochloric acid, sodium hydroxide solution, and water and dried. The residue after removal of the solvent was purified as already described. M. p. and mixed m. p. with an authentic sample of 1-chloro-5-keto-3 : 4-dimethoxy-5 : 6 : 7 : 8-tetrahydronaphthalene were 77·5—78° (yield 85—90%).

From the alkali washings the partly demethylated ketone was obtained in the usual way; m. p. and mixed m. p. with an authentic sample, 104—105°. Only a very small quantity of this phenolic substance was isolated.

(D) The above phenolic ketone (VI) (5 g.) was dissolved in methanol (70 c.c.), and methyl sulphate (12 c.c.) and methanolic potassium hydroxide (15 g. in 80 c.c.) gradually added with refluxing on the steam-bath. After 4 hours, most of the methanol was distilled, and the residue was cooled and extracted with chloroform. The chloroform extract was washed with water, dried, and evaporated. The residue was distilled under reduced pressure and crystallised as mentioned above; m. p. 78°, alone or mixed with an authentic sample.

1-*Chloro*-3 : 4-*dimethoxy*-5-*ethyl*-7 : 8-*dihydronaphthalene* (VII).—A solution of chlorodimethoxytetralone (6·0 g.) in ether (190 c.c.) was slowly added to one of ethylmagnesium bromide (from 3 g. of magnesium, 10 c.c. of ethyl bromide, and 50 c.c. of ether), and the mixture kept for 48 hours at the room temperature. It was then refluxed for 2 hours, cooled and decomposed with ice and hydrochloric acid, and the ethereal layer separated. The aqueous solution was further extracted with ether, and the combined extracts were washed with water, dilute alkali, water, and dried. The solvent was removed and the residue distilled at 0·1—0·2 mm. The distillate (6·0 g.), which contained some carbinol, was dissolved in ether (20 c.c.), and the solution treated with phosphoric anhydride (6·0 g.). Ether was then removed and the residue slowly distilled at $<0·1$ mm.

In redistillation the *chloro-compound* was collected at 110° (bath temp.)/0·02 mm. as a colourless, sweet-smelling liquid (yield, 5·0—5·5 g.) (Found : C, 67·1; H, 6·6. $C_{14}H_{17}O_2Cl$ requires C, 66·5; H, 6·7%).

Oxidation of 1-*Chloro*-3 : 4-*dimethoxy*-5-*ethyl*-7 : 8-*dihydronaphthalene with Mercuric Acetate*.—Chlorodimethoxy-

ethyldihydronaphthalene (2·5 g.) was added to a solution of mercuric acetate (6·4 g.) in acetic acid (80 c.c.) and water (20 c.c.), and the mixture heated on the steam-bath. Very soon mercurous acetate began to separate in shining plates. Heating was continued for 1 hour, the mixture was then cooled and filtered, and the residue washed with acetic acid. The filtrate and washings were combined and the solvent removed under reduced pressure. The residue was refluxed with dilute sulphuric acid (50 c.c., 15%) for 3 hours, cooled and extracted with ether in the usual way. After removal of ether, the residue was distilled and a fraction (0·8 g.), b. p. 125—140° (bath temp.)/0·02 mm., was collected. This was treated with alcohol (15·0 c.c.), Girard reagent T (1·0 g.) and acetic acid (2·2 g.), refluxed for 2 hours, then cooled and poured into a cold solution of sodium carbonate (1·7 g.) in water (50 c.c.). The mixture was extracted with ether and the non-ketonic part so separated. The aqueous solution was acidified with hydrochloric acid and warmed for 2 hours in the steam-bath, cooled and extracted with ether; on removal of ether a very small residue was obtained and was not further investigated. The non-ketonic material (? VIII) was distilled and collected as a pale yellow viscous oil, b. p. 135° (bath temp.)/0·02 mm. (Found: C, 62·8; H, 6·3. $C_{14}H_{17}O_3Cl$ requires C, 62·6; H, 6·3%).

1-*Chloro*-6-*keto*-3 : 4-*dimethoxy*-5-*ethyl*-5 : 6 : 7 : 8-*tetrahydronaphthalene* (IX).—(A) Chlorodimethoxyethyldihydronaphthalene (5·3 g.) was dissolved in acetic acid (40 c.c.) and perhydrol (4 c.c. of 30%) added. The clear solution was kept at room temperature for 4 days, and then most of the acetic acid was removed under reduced pressure and the residue refluxed with dilute sulphuric acid (14 c.c., *d* 1·84, in 100 c.c. of water) for 7 hours. It was then cooled, extracted with ether, the ethereal extract washed with water and sodium bicarbonate solution, and dried. The residue, after removal of ether, was distilled and a fraction, collected at 120—150° (bath temp.)/0·01 mm., was dissolved in alcohol and treated with a saturated aqueous solution of semicarbazide hydrochloride (2 g.) and sodium acetate (5·0 g.). Just enough alcohol was then added to give a clear solution. It was then warmed for 5 minutes and left at room temperature for 12 hours. The crystalline precipitate was collected, washed with alcohol, water, alcohol, and crystallised from a large volume of alcohol; colourless needles, m. p. 219—220° (yield, 33%) (Found: C, 55·0; H, 6·2; N, 12·5. $C_{15}H_{20}O_3N_3Cl$ requires C, 55·3; H, 6·1; N, 12·9%). The *semicarbazone* (0·4 g.) was refluxed with dilute sulphuric acid (5·6 c.c., *d* 1·84, in 30 c.c. of water) for 1½ hours, cooled and extracted with ether. The residue after removal of solvent distilled as a colourless oil, b. p. 136—140° (bath temp.)/0·01 mm., which soon solidified (yield, 0·32 g.). This was crystallised from ether–light petroleum (b. p. 40—60°) and colourless prisms, m. p. 66·5—67°, were obtained (Found: C, 62·9; H, 6·4; Cl, 13·4. $C_{14}H_{17}O_3Cl$ requires C, 62·6; H, 6·3; Cl, 13·2%). The *ketone* does not give the iodoform test.

The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol as orange, microscopic needles, m. p. 140° (Found: C, 54·2; H, 4·7; Cl, 12·7. $C_{20}H_{21}O_6N_4Cl$ requires C, 53·6; H, 4·7; Cl, 12·5%).

(B) Chlorodimethoxyethyldihydronaphthalene (2·6 g.) in chloroform (10 c.c.) was treated with perbenzoic acid (1·5 g. in 28 c.c. of chloroform) and the solution kept at 0° for 5 days. More chloroform was then added, and after being washed several times with 10% sodium hydroxide solution, the chloroform layer was dried. After removal of solvent, the residue was distilled and a colourless viscous liquid (2·4 g.), b. p. 130—150° (bath temp.)/0·01 mm., was obtained. This was dissolved in light petroleum (b. p. 60—80°, 50 c.c.), and dry hydrogen chloride passed in for 1½ hours. Ice-cold water was then added and the mixture extracted several times with ether, the ether–petroleum extract washed with water, sodium bicarbonate solution, and dried. After removal of the solvent, the residue was distilled under reduced pressure, and the distillate treated with semicarbazide hydrochloride and sodium acetate as in the previous experiment. A precipitate (0·098 g.) was obtained, which crystallised from alcohol in colourless needles, m. p. 219—220°, alone or mixed with an authentic sample.

1-*Chloro*-7-*keto*-3 : 4-*dimethoxy*-13-*ethyl*-5 : 6 : 7 : 9 : 10 : 13-*hexahydrophenanthrene* (X).—The above ethylated ketone (0·84 g.) was dissolved in dry ether (15·0 c.c.), and finely powdered sodamide (0·3 g.) added under nitrogen. Dry ether was added from time to time to maintain the original volume. After 6 hours an alcoholic solution (10 c.c.) of the methiodide of 4-diethylaminobutan-2-one (from 0·6 g. of the base) was added, and the whole kept at the room temperature for 12 hours in an atmosphere of nitrogen. It was then refluxed for 1½ hours, cooled, and poured into an ice-cold, dilute hydrochloric acid, the mixture extracted with ether, and the extracts washed with water, dilute aqueous sodium hydroxide and water. After drying over anhydrous sodium sulphate, the solvent was removed, and the residue distilled. A fraction, b. p. 180—200° (bath temp.)/0·02 mm., was collected and redistilled. The product was obtained as a pale yellow glass, b. p. 175—180° (bath temp.)/0·005 mm. (Found: C, 67·6; H, 6·5%). The *chloro-ketone* crystallised from methanol in colourless prisms, m. p. 149—149·5° (Found: C, 67·1; H, 6·6; Cl, 11·1. $C_{18}H_{21}O_3Cl$ requires C, 67·4; H, 6·6; Cl, 11·4%). The 2 : 4-*dinitrophenylhydrazone* was obtained as scarlet-red plates, m. p. 206—207°, after crystallisation from alcohol (Found: C, 57·5; H, 4·8. $C_{24}H_{25}O_6N_4Cl$ requires C, 57·5; H, 5·0%).

1-*Chloro*-7-*keto*-3 : 4-*dimethoxy*-13-*ethyl*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-*octahydrophenanthrene* (XI).—(A) The above ketone (X) (0·296 g.) in alcohol (30 c.c.) was hydrogenated in the presence of palladised charcoal; 20·4 c.c. of hydrogen were absorbed (calc., 20 c.c.). The concentrate from the filtered solution was refluxed for 8 hours with amalgamated zinc (10·0 g.) and concentrated hydrochloric acid, the latter being added in small quantities (total, 50·0 c.c.). The product was isolated by means of ether and was a colourless, viscous oil, b. p. 152—155° (bath temp.)/0·16 mm. (Found: C, 70·4; H, 8·0; Cl, 11·8. $C_{18}H_{25}O_3Cl$ requires C, 70·0; H, 8·1; Cl, 11·5%). It is insoluble in water but soluble in organic solvents. It does not decolourise permanganate solution. Attempts to crystallise it have not been successful.

(B) The ketone (0·25 g.) was dissolved in alcohol (30 c.c.) and reduced with hydrogen in the presence of platinic oxide (Adams's catalyst). The reduction was over in 1½ hours, the theoretical volume of hydrogen being absorbed. The filtrate, on concentration and cooling, afforded crystals, m. p. 95—100°, and on recrystallisation from alcohol 1-*chloro*-7-*keto*-3 : 4-*dimethoxy*-13-*ethyl*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-*octahydrophenanthrene* (XI) was obtained as colourless cubes, m. p. 99—100° (Found: C, 67·01; H, 6·97. $C_{18}H_{23}O_3Cl$ requires C, 66·97; H, 7·13%).

This reduced ketone (XI) (0·073 g.) was refluxed for 5 hours with amalgamated zinc (10 g.) and hydrochloric acid, the acid being added in small quantities (total, 70 c.c.), and worked up as before. The product distilled as a colourless viscous oil at 140—143° (bath temp.)/0·06 mm. (Found: C, 70·3; H, 8·1; Cl, 12·1. $C_{18}H_{25}O_3Cl$ requires C, 70·0; H, 8·1; Cl, 11·5%).

7-*Keto*-3 : 4-*dimethoxy*-13-*ethyl*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-*octahydrophenanthrene* (XII).—The ketone (XI; m. p. 99—100°; 0·3 g.) in alcohol (50 c.c.) was mixed with palladised calcium carbonate (cf. Busch and Stöve, *Ber.*, 1916, **49**, 1063) (1·5 g.) and alcoholic potassium hydroxide (0·4 g. in 5 c.c.) and shaken in an atmosphere of hydrogen. After 3 hours the solution was filtered from the catalyst, acetic acid (5 c.c.) added, and the solvent removed under reduced pressure. The product was isolated by means of ether and distilled at 155—160° (bath temp.)/0·02 mm. The ketone in the distillate was converted into its *semicarbazone*, which crystallised from alcohol in colourless, microscopic prisms, m. p. 198·5° (Found: C, 65·8; H, 7·6; N, 12·2. $C_{19}H_{27}O_3N_3$ requires C, 66·1; H, 7·8; N, 12·2%). The *ketone* regenerated from this derivative by means of boiling dilute sulphuric acid (10%) was collected at 158° (bath temp.)/0·03 mm. as a colourless viscous oil (Found: C, 75·5; H, 8·9. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·3%).

3 : 4-*Dimethoxy*-13-*ethyl*-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-*octahydrophenanthrene* (I).—The above ketone (XII) (0·35 g.) was refluxed with amalgamated zinc (10·0 g.) and hydrochloric acid (56 c.c.) for 5 hours, and the product isolated by extraction with ether in the usual way. After removal of solvent, the residue was distilled as a colourless viscous oil,

at 110—112° (bath temp.)/0·09 mm. (Found: C, 79·3; H, 9·2. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·5%). I: does not decolourise permanganate solution.

6-*Keto*-3 : 4-*dimethoxy*-5-*ethyl*-5 : 6 : 7 : 8-*tetrahydronaphthalene* (XIII).—The chloro-ketone (IX) (0·27 g.) was dissolved in alcohol (50 c.c.), palladised strontium carbonate (1·5 g.) and alcoholic potassium hydroxide (5 c.c. of 10%) added, and the mixture shaken with hydrogen. After 2½ hours, it was acidified with acetic acid (4 c.c.), filtered, and the filtrate evaporated to dryness. The residue was treated with water and extracted with ether in the usual was. After removal of solvent the residue was distilled, and a colourless liquid, b. p. 114° (bath temp.)/0·03 mm., was collected (yield, 0·18 g.) (Found: C, 72·2; H, 7·9. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). The *semicarbazone* crystallised from alcohol in needles, m. p. 183—184° (Found: C, 61·8; H, 7·3; N, 13·9. $C_{15}H_{21}O_3N_3$ requires C, 61·9; H, 7·2; N, 13·4%).

6-*Keto*-3 : 4-*dimethoxy*-5-*ethyl*-5-*γ*-*ketobutyl*-5 : 6 : 7 : 8-*tetrahydronaphthalene* (XIV).—The ketone (XIII) (0·9 g.) was dissolved in dry ether (15 c.c.), finely powdered sodamide (0·3 g.) added, and nitrogen passed in slowly at room temperature for 6 hours, the volume being maintained by addition of dry ether from time to time. The methiodide of 4-diethylaminobutan-2-one (from 2·0 g. of the base) was dissolved in alcohol (20 c.c.) and added to the above mixture cooled in ice. After 1½ hours the contents were refluxed for 2 hours. They were then cooled, poured into ice and hydrochloric acid and extracted with ether, and the product isolated in the usual way. A colourless, viscous oil was collected at 148—150° (bath temp.)/0·02 mm. (Found: C, 71·0, 71·0; H, 7·8, 8·2. $C_{18}H_{24}O_4$ requires C, 71·1; H, 7·9%).

7-*Keto*-3 : 4-*dimethoxy*-13-*ethyl*-5 : 6 : 7 : 9 : 10 : 13-*hexahydrophenanthrene* (XV).—The ketone (XIII) (1·0 g.) was dissolved in ether (30 c.c.), finely powdered sodamide (3·5 g.) added, and nitrogen passed in continuously during the reaction. After 5 hours the methiodide of 4-diethylaminobutan-2-one (from 3·0 g. of the base) in alcohol (20 c.c.) was added, and the mixture left overnight in an atmosphere of nitrogen. It was then refluxed for 1½ hours, cooled, poured into ice and hydrochloric acid, and the product isolated with ether. It distilled at 140—150° (bath temp.)/0·02 mm. and crystallised from ether–light petroleum (b. p. 40—60°) in colourless cubes, m. p. 112° (Found: C, 75·0; H, 7·6. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in scarlet-red plates, m. p. 179—180° (Found: N, 11·8. $C_{24}H_{26}O_6N_4$ requires N, 12·0%). 7-Keto-3 : 4-dimethoxy-13-ethyl-5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-octahydrophenanthrene was obtained by reduction of this ketone (0·18 g.) in alcohol (10·0 c.c.) in the presence of platinic oxide. After 1 mol. of hydrogen had been absorbed, the solution was filtered, concentrated, and treated with semicarbazide hydrochloride and sodium acetate in the usual way. The precipitate was collected, washed with water and crystallised from alcohol; m. p. 198—199° alone or mixed with an authentic sample.

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