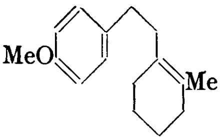
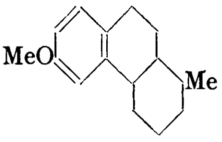
126. *Syntheses in the Phenanthrene Series. Part IX. 6-Methoxy-1-methylphenanthrene.*

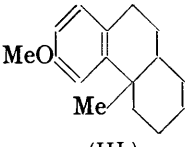
By Harold Plimmer, W. F. Short, and (in part) Peter Hill.

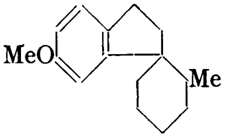
A synthesis of 6-*methoxy*-1-*methylphenanthrene* is described. The corresponding phenol is identical with the compound produced by the dehydrogenation of podocarpic acid.

In attempting the synthesis of 6-*methoxy*-1-*methylphenanthrene* we first prepared 1-β-p-*anisylethyl*-2-*methyl*cyclo*hexene* (I) by employing methods similar to those recorded in Part V. Ring closure of this compound could yield the octahydrophenanthrenes (II) and (III) or the spiran (IV) (compare Harper, Kon, and Ruzicka, J., 1934, 125; Cohen, Cook, Hewett, and Girard, *ibid.*, p. 654; Hill, Short, and Stromberg, J., 1937, 1619). Successive treatment with aluminium chloride and sulphur afforded a liquid which furnished a picrate of somewhat indefinite melting point. Decomposition of the picrate produced an oil which on demethylation afforded a phenol, m. p. 104—108°. The properties and analyses of these compounds indicated that the dehydrogenation product consisted mainly of 3-methoxyphenanthrene.

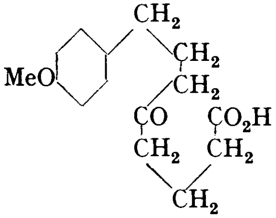

(I.)

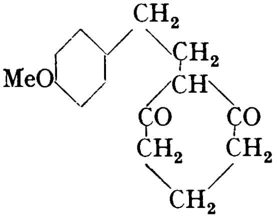

(II.)

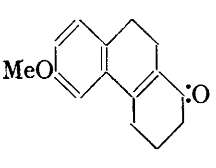

(III.)


(IV.)

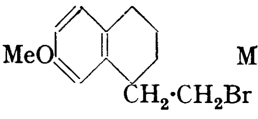
We then sought to obtain the desired phenanthrene by employing Robinson's hydrophenanthrene synthesis (J., 1935, 1288). γ-*p*-Anisylbutyryl chloride was condensed with ethyl sodio-α-acetylglutarate, and the product hydrolysed in stages to 5-*keto*-8-p-*anisyloctoic acid* (V). The yield was very small because the β-ketonic ester was mainly hydrolysed in the alternative direction. The *methyl* ester of (V) furnished β-p-*anisylethyl*cyclo*hexane*-2 : 6-*dione* (VI) when treated with sodium ethoxide in absolute ether, and dehydration with phosphoric oxide afforded 1-keto-6-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (VII), which was characterised as its 2 : 4-*dinitrophenylhydrazone* m. p. 230—232°. The overall yield of this ketone was so poor that an alternative synthesis was sought.

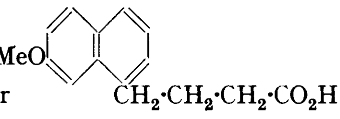

(V.)

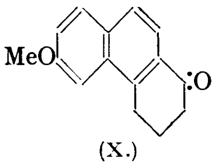

(VI.)

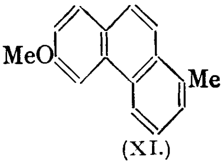

(VII.)

1-Keto-7-methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene (Haworth and Sheldrick, J., 1934, 1951) was condensed with ethyl bromoacetate by the Reformatsky reaction to give ethyl 7-methoxy-3 : 4-dihydro-1-naphthylacetate, which on Bouveault–Blanc reduction afforded β-(7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)ethyl alcohol (3 : 5-*dinitrobenzoate*, m. p. 119·5—120°). The corresponding *bromide* (VIII) was condensed with ethyl sodiomalonate, and the product hydrolysed, decarboxylated, and dehydrogenated with sulphur to γ-(7-*methoxy*-1-*naphthyl*)*butyric acid* (IX). The cyclic ketone (X) [2 : 4-*dinitrophenylhydrazone*, m. p. 261—262° (decomp.)] was obtained from the acid by the action of phosphoric oxide, and successive treatment with methylmagnesium iodide and sulphur afforded 6-*methoxy*-1-*methylphenanthrene* (XI), m. p. 87—87·5° (*picrate*, m. p. 140°). The corresponding *phenanthrol*, m. p. 161°, is identical with the dehydrogenation product of the resin acid podocarpic acid (forthcoming publication).


(VIII.)


(IX.)


(X.)


(XI.)

EXPERIMENTAL.

β-p-*Anisylethyl Alcohol*.—The following modification of the method of Slotta and Heller *Ber.*, 1930, 63, 3029) gave a 50% yield of this alcohol. A solution of ethylene oxide (75·8 g.; 1·3 mols.) in dry benzene (200 c.c.) was added to an ice-cold Grignard solution prepared from magnesium (35 g.), *p*-bromoanisole (250 g.), and dry ether (1100 c.c.); dry toluene (440 c.c.) was then added and, after 60 hours, the mixture was distilled until the temperature reached 100°. The complex was decomposed in the usual way, and the product distilled. The alcohol had b. p. 145—147°/10 mm. and the fraction, b. p. 240—245°/10 mm., consisted of 4:4′-dimethoxydiphenyl, m.p.

171—173°. A 70% yield of β-p-*anisylethyl chloride*, b. p. 129·5—131°/10 mm., was obtained from the alcohol (93 g.), pyridine (75 c.c.), and thionyl chloride (54 c.c.) (Found : Cl, 20·7. $C_9H_{11}OCl$ requires Cl, 20·8%).

1-β-p-*Anisylethyl-2-methyl*cyclo*hexan-1-ol*.—The Grignard compound of the preceding chloride and 2-methyl*cyclo*hexanone afforded the tertiary *alcohol* as a viscous liquid, b. p. 173—175°/5 mm. (Found : C, 77·7; H, 9·8. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%), and dehydration with potassium hydrogen sulphate yielded 1-β-p-*anisylethyl-2-methyl*cyclo*hexene*, b. p. 156—156·5°/6 mm. (Found : C, 83·6; H, 9·4. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%). By the action of aluminium chloride on a solution of this compound in carbon disulphide, followed by dehydrogenation with sulphur at 180—240°, a viscous liquid was obtained. This gave an orange-red *picrate*, m. p. 114—116° after sintering at 95° (Found : C, 57·6; H, 3·6. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·5; H, 3·8%. $C_{15}H_{12}O,C_6H_3O_7N_3$ requires C, 57·7; H, 3·4%). Decomposition of the picrate with aqueous ammonia gave an oil, which on demethylation with hydrobromic–acetic acid afforded a *phenol*, m. p. 104—108° (Found : C, 86·2; H, 5·4. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%. $C_{14}H_{10}O$ requires C, 86·6; H, 5·15%). The m. p.'s recorded in the literature for 3-methoxyphenanthrene picrate and 3-hydroxyphenanthrene are 124—125° and 118—119° respectively.

*5-Keto-8-*p-*anisyloctoic Acid* (V).—β-4-Methoxybenzoylpropionic acid, prepared in 95% yield by the method of Fieser and Hershberg (*J. Amer. Chem. Soc.*, 1936, **58**, 2315), was reduced to γ-*p*-anisylbutyric acid as described by Haworth and Sheldrick (J., 1934, 1951). The average yield was 62% and it was usually unnecessary to purify the acid by esterification : a much lower yield was obtained by Martin's method (*J. Amer. Chem. Soc.*, 1936, **58**, 1438). The acid (70 g.) was converted into γ-*p*-anisylbutyryl chloride, which was carefully freed from thionyl chloride and dissolved in anhydrous ether (190 c.c.). The solution was slowly added below 15° to ethyl sodio-α-acetylglutarate (from 77·3 c.c. of the ester and 8·4 g. of powdered sodium) in dry ether (640 c.c.). After 59 hours at room temperature and 1 hour at the b. p. the mixture was added to ice-water and extracted with ether. The ethereal solution was washed with aqueous sodium carbonate (recovered *p*-anisylbutyric acid, 1·0 g.), dried, and evaporated. The residual liquid (134 g.) was shaken with 2·5% aqueous potassium hydroxide (3216 c.c.) for 17 hours, the strength of the alkali was then raised to 4%, and shaking continued for 4 hours. A small amount of undissolved ester was extracted with ether, and the aqueous solution acidified and extracted with ether. Evaporation of the ether left a brown oil, which was warmed on the steam-bath until evolution of carbon dioxide ceased and then heated with 2N-sodium hydroxide (432 c.c.) for 2 hours. The acids were liberated, extracted with ether, and esterified with a slight excess of diazomethane, and the esters fractionated. The following fractions were collected : (1) b. p. up to 160°/0·7 mm., mainly methyl γ-*p*-anisylbutyrate, and (2) b. p. 160—215°/0·7 mm. Fraction (2) solidified to a paste on cooling and, after removal of the solid, was redistilled, cooled, and filtered. These operations were repeated as long as solid fractions could be obtained. *Methyl 5-keto-8-*p-*anisyloctoate* separated from light petroleum (b. p. 40—60°) in white plates, m. p. 52° (Found : C, 69·2; H, 7·8. $C_{16}H_{22}O_4$ requires C, 69·1; H, 7·9%). The corresponding *acid* crystallised from light petroleum (b. p. 60—80°) in microscopic plates, m. p. 68° (Found : C, 68·1; H, 7·35. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%). The yield, calculated on the γ-*p*-anisylbutyric acid employed, was 8·5%.

β-p-*Anisylethyl*cyclo*hexane-2 : 6-dione* (VI).—Coarsely powdered sodium ethoxide (12 g.) was added to a solution of the preceding ester (6 g.) in dry ether (60 c.c.); the mixture was kept for 25 hours with occasional shaking and refluxed for ½ hour. Ice-water was then added, and neutral impurities removed from the alkaline solution by extraction with ether. The *dione*, liberated with cold dilute sulphuric acid, was collected in chloroform and recrystallised from light petroleum (b. p. 60—80°); it then had m. p. 167—169° (Found : C, 73·1; H, 7·3. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). Yield, 47%.

1-Keto-6-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (VII).—Phosphoric oxide (25 g.) was added in portions with stirring during 1½ hours to a boiling solution of the above dione (2·5 g.) in moist benzene (310 c.c.). The mixture was cooled, shaken with ice, made strongly alkaline, and extracted with ether. Acidification of the alkaline layer gave 0·2 g. of recovered dione. The benzene–ether solution was washed with water, dried, and evaporated in a vacuum. The residue (0·25 g.), which partly solidified, was characterised by its 2 : *4-dinitrophenylhydrazone*. The red solid was purified by washing with alcohol, but could not be recrystallised; m. p. 230—232° (decomp.) (Found : C, 62·0; H, 5·05. $C_{21}H_{20}O_5N_4$ requires C, 61·8; H, 4·9%).

1-Keto-7-methoxy-1 : 2 : 3 : 4-tetrahydronaphthalene.—This ketone was obtained in 51% yield by the action of aluminium chloride on γ-*p*-anisylbutyryl chloride in tetrachloroethane solution

(Haworth and Sheldrick, *loc. cit.*). A good yield (up to 61%) of the ketone was obtained by adding phosphoric oxide (9 mols.) to a boiling solution of the acid in dry benzene, refluxing for 3 hours with mechanical stirring, and working up the product as described in previous parts of this series.

β-(7-*Methoxy*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthyl*)*ethyl Alcohol*.—A mixture of the cyclic ketone (1 mol.), zinc needles (1 atom), bromoacetic ester (1 mol.), dry benzene (5 c.c. per c.c. of ester), and a crystal of iodine was warmed at 60° until reaction set in and was then allowed to stand till the action ceased. After refluxing for ½ hour, the mixture was worked up in the known manner, and a benzene solution of the product refluxed for ½ hour with a little phosphoric oxide. The average yield of ester, b. p. 155—170°/0·8 mm., mostly at 165—167°/0·8 mm., was 67%. The ester (1 mol.) was dissolved in absolute alcohol (15 mols.) and reduced with sodium (7 atoms). A small amount of 7-*methoxy*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthylacetic acid*, obtained from the alkaline layer, crystallised from aqueous methyl alcohol in white rectangular plates, m. p. 88—89° (Found : C, 70·9; H, 7·3. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The average yield of the alcohol, b. p. *ca.* 165°/0·4 mm., was 53% and the substance was characterised by its 3 : 5-*dinitrobenzoate*, which crystallised from ligroin in yellow needles, m. p. 119·5—120° (Found : C, 59·7; H, 5·1. $C_{20}H_{20}O_7N_2$ requires C, 60·0; H, 5·0%). A mixture of phosphorus tribromide (4 c.c.) and chloroform (24 c.c.) was slowly added to a mechanically stirred ice-cold solution of the alcohol (23·3 g.) in chloroform (58 c.c.), and the β-(7-*methoxy*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthyl*)*ethyl bromide*, b. p. 155—160°/0·4 mm., isolated in the usual way (Found : Br, 29·1. $C_{13}H_{17}OBr$ requires Br, 29·7%). Average yield, 64·5%.

γ-7-*Methoxy*-1-*naphthylbutyric Acid* (IX).—A solution of the preceding bromide (1 mol.) in dry toluene (1 c.c. per g.) was slowly added at room temperature to ethyl potassiomalonate (from the metal, 1·7 atoms; ethyl malonate, 2 mols.; toluene, 13·0 c.c. per g. of metal), and the mixture heated at 120—130° for 68 hours and worked up in the usual way. The ethyl β-(7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)ethylmalonate was obtained in 82% yield as a viscous liquid, b. p. 220—230°/0·6 mm.; reduction in the amount of malonic ester resulted in a greatly diminished yield. Hydrolysis of the ester afforded the acid as a viscous liquid, which was decarboxylated at 120—200°. The resulting γ-(7-methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)butyric acid (yield, 79%) would not crystallise and was therefore heated at 215—230° for 5 hours with ¼ of its weight of sulphur. The residual black mass was repeatedly extracted with warm dilute aqueous sodium hydroxide; the solution was filtered, extracted with ether, and acidified. The acid was collected and purified by solution in dilute aqueous sodium carbonate and recrystallisation from methyl alcohol. γ-7-*Methoxy*-1-*naphthylbutyric acid* crystallised in long rods, m. p. 105—106° (Found: C, 73·5; H, 6·5. $C_{15}H_{16}O_3$ requires C, 73·8; H, 6·6%). Yield, 34%.

1-*Keto*-6-*methoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene* (X).—Ring closure was effected by addition of phosphoric oxide (20 g.) to a solution of the butyric acid (3 g.) in boiling benzene (45 c.c.) as previously described and the cyclic ketone was isolated in 83% yield as a glassy mass. The 2 : 4-*dinitrophenylhydrazone* crystallised from boiling benzene in bright red, stout needles, m. p. 261—262° after sintering at 256° (Found : C, 61·9; H, 4·6. $C_{21}H_{18}O_5N_4$ requires C, 62·1; H, 4·4%).

6-*Methoxy*-1-*methylphenanthrene* (XI).—An ethereal solution of the cyclic ketone (1 mol.) was added to an ice-cold solution of methylmagnesium iodide (3 mols.), and the mixture refluxed for 6 hours and worked up in the known manner. The crude condensation product (yield, 80%) was treated at 180—250° for 5 hours with sulphur (1 atom) and distilled in a vacuum. The viscous brown distillate was warmed with excess of alcoholic picric acid, and the crude picrate pressed on porous tile and decomposed with warm aqueous ammonia. The oily globules solidified on cooling and were washed with water until free from ammonium picrate. Successive crystallisation from methyl alcohol (charcoal) and light petroleum (b. p. 40—60°) gave cream-coloured clustered needles of 6-*methoxy*-1-*methylphenanthrene*, m. p. 87—87·5° (Found : C, 86·6; H, 6·4. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *picrate* consisted of vermilion needles, m. p. 140—141·5° (Found : C, 58·4; H, 3·8. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·5; H, 3·8%). Demethylation of the methyl ether with hydrobromic–acetic acid afforded 6-*hydroxy*-1-*methylphenanthrene*, which crystallised from chloroform in white plates, m. p. 161° (Found : C, 86·4; H, 6·0. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%).

We are grateful to the Chemical Society for a grant.

The College of Technology, Manchester. [*Received, March 24th,* 1938.]