173. *Synthetic Uses of* as-*Octahydrophenanthrene. Part I.*

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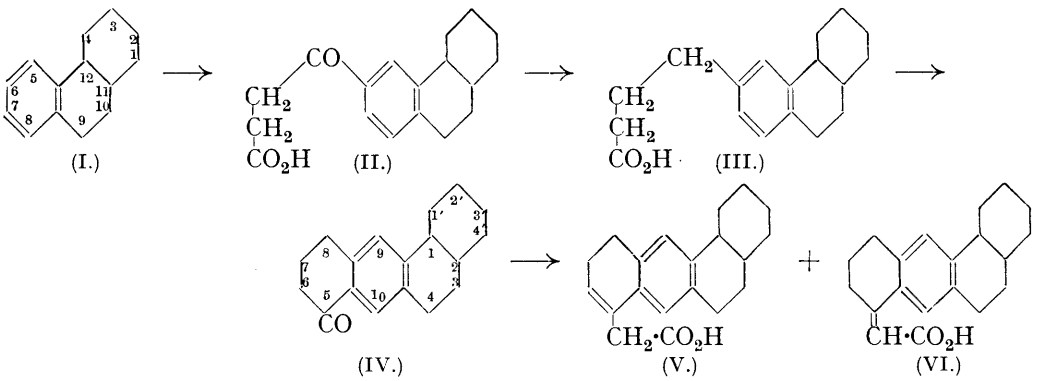
as-Octahydrophenanthrene is readily available in quantity by the method of Cook and Hewett (J., 1933, 1098) and furnishes a convenient starting point for the synthesis of more complex hydroaromatic compounds, some of which are now described.

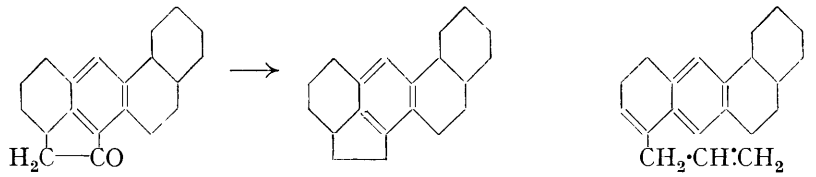
By analogy with tetralin it was anticipated that Friedel–Crafts reactions with acyl chlorides would lead to substitution at position 6 or 7 of the octahydrophenanthrene ring system (I). Reaction with succinic anhydride and aluminium chloride in nitrobenzene led to a crystalline keto-acid as the only product which could be isolated, and this was shown to have structure (II) by oxidation to 6-as-*octahydrophenanthroic acid*, followed by dehydrogenation to 3-phenanthroic acid. The position of substitution in the Friedel–Crafts reaction thus corresponds to that in phenanthrene itself, which gives mainly the 3-compounds with acyl chlorides (Mosettig and van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704; Haworth and Mavin, J., 1933, 1012; Cook and Haslewood, J., 1934, 428).

β-6-as-*Octahydrophenanthroylpropionic acid* (II) * was reduced by Clemmensen's method to γ-6-as-*octahydrophenanthrylbutyric acid* (III), which was smoothly cyclised by 88% sulphuric acid to 5-*ketododecahydro*-1 : 2-*benzanthracene* (IV). This passed, on Clemmensen reduction, into the corresponding *dodecahydro*-1 : 2-*benzanthracene*, isomeric with that already described (Cook and Hewett, J., 1934, 375).



(I.) (II.) (III.) (IV.) (V.) (VI.)

The tetracyclic ketone (IV) had a much higher solubility than the 5-keto-5 : 6 : 7 : 8-tetrahydro-1 : 2-benzanthracene of Haworth and Mavin (*loc. cit.*), and probably on this account the dodecahydro-ketone readily condensed with ethyl bromoacetate under suitable conditions, whereas the tetrahydro-ketone did not. This Reformatsky reaction with (IV) led to a mixture of unsaturated *acids* (V and VI), one of which was isolated in the pure state. This, or the mixture of the two, could be hydrogenated with palladium-black to the crystalline *dodecahydro*-1 : 2-*benzanthrylacetic acid*, which was cyclised by sulphuric acid to *ketododecahydrocholanthrene* (VII). This pentacyclic ketone was reduced by amalgamated zinc and hydrochloric acid to *dodecahydrocholanthrene* (VIII), which was dehydrogenated by platinum-black at 300° to cholanthrene, identical with that obtained by two other methods (this vol., pp. 667, 770).



(VII.) (VIII.) (IX.)

* To avoid the use of unnecessarily cumbersome series of figures, the positions of hydroaromatic hydrogen atoms are not denoted in the names of compounds. The systems of numbering which are intended to be used are given in formulæ (I) and (IV).

In an attempt to obtain the dodecahydro-1 : 2-benzanthryl-5-acetic acid in better yield, the tetracyclic ketone (IV) was condensed with allylmagnesium bromide, and the crude carbinol dehydrated. The resulting hydrocarbon (probably IX), formed in good yield, was treated with sodium and boiling amyl alcohol, by which means it was hoped to reduce the nuclear double bond, with subsequent oxidation to the desired acid. This project could not be realised, as the hydrocarbon (IX) was unaffected by sodium and amyl alcohol (compare Haslewood and Roe, this vol., p. 465). When this hydrocarbon was heated with platinum-black at 300°, dehydrogenation of the ring system was accompanied by hydrogenation of the side chain, so that the product was 5-n-*propyl*-1 : 2-*benzanthracene*. It thus seems likely that the tetracyclic ketone (IV) will be serviceable for the synthesis of other higher homologues of 1 : 2-benzanthracene with substituents at position 5, for which purpose 5-keto-5 : 6 : 7 : 8-tetrahydro-1 : 2-benzanthracene was unsuitable (Cook, J., 1933, 1593). In view of the marked carcinogenic activity of 5-methyl-1 : 2-benzanthracene (Barry, Cook, Haslewood, Hewett, Hieger, and Kennaway, *Proc. Roy. Soc.*, 1935, *B*, **117**, 318) a study of such compounds should be profitable.

There is as yet no evidence concerning the stereochemical configuration with respect to the points of attachment of the two condensed hydroaromatic rings present in many of the compounds now described.

Experimental.

* Denotes microanalysis by Dr. A. Schoeller. † Denotes microanalysis by Dr. G. Weiler.

β-6-as-*Octahydrophenanthroylpropionic Acid* (II).—The *as*-octahydrophenanthrene used in these experiments was prepared by F. Goulden by the action of aluminium chloride on β-phenylethyl-Δ^1-*cyclo*hexene in carbon disulphide (6 hours at room temperature). The distilled hydrocarbon (57 g.), cooled to 0°, was added during ½ hour to a solution of aluminium chloride (80 g.) and succinic anhydride (33 g.) in nitrobenzene (240 c.c.), the whole being cooled in a freezing mixture. The dark red solution was kept at 0° for 5 hours and then poured on ice and hydrochloric acid. The whole was extracted with ether, and the acidic reaction products removed from the extract by agitation with 10% potassium hydroxide solution. After washing with ether, the alkaline extract was acidified, and the liberated acids extracted with ether. The brown oil remaining after removal of the ether became crystalline when digested with methyl alcohol. Recrystallisation from benzene–ligroin gave colourless crystals (27 g.), m. p. 134—137°. For complete purification, the semicarbazone was prepared (m. p. 185—187°, decomp.), and hydrolysed by a boiling saturated solution of oxalic acid. β-6-as-*Octahydrophenanthroylpropionic acid* (II) crystallised from glacial acetic acid in colourless prisms, m. p. 140—141° (Found : C, 75·4; H, 8·0. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·75%). The mother-liquors from which the crude acid had been separated contained considerable amounts of other substances, but no pure isomeride could be isolated. Repeated crystallisation of the semicarbazones gave a fraction, m. p. 144—146° (decomp.), but the product of hydrolysis would not crystallise.

6-as-*Octahydrophenanthroic Acid*.—The keto-acid (II) (2 g.) was oxidised with a dilute alkaline solution of potassium permanganate (2·2 g.) at room temperature. The product, crystallised from methyl alcohol (charcoal), acetic acid, and then *cyclo*hexane, formed colourless prisms, m. p. 226—228° (slight decomp.) (*Found : C, 78·2; H, 7·8. $C_{15}H_{18}O_2$ requires C, 77·9; H, 7·85%). Dehydrogenation of this *octahydrophenanthroic acid* (0·4 g.) with selenium (1 g.) at 280—300° (24 hours) gave 3-phenanthroic acid, m. p. 268—270°, identified by direct comparison with an authentic sample.

γ-6-as-*Octahydrophenanthrylbutyric Acid* (III).—The keto-acid (II) (15 g.) was boiled for 6 hours with amalgamated zinc (from 45 g. of granulated zinc) and hydrochloric acid (22·5 c.c. of concentrated acid and 45 c.c. of water), a further 7·5 c.c. of concentrated acid being added at the end of each hour. The product was extracted with ether, the extract cautiously washed with sufficient sodium carbonate solution to remove hydrochloric acid, and the dried ethereal solution distilled. γ-6-as-*Octahydrophenanthrylbutyric acid* (12·2 g.), b. p. 198°/0·15 mm., was crystallised from light petroleum, then from aqueous alcohol, and finally from light petroleum, forming small, colourless, hexagonal prisms, m. p. 81—83° (Found : C, 79·1; H, 9·1. $C_{18}H_{24}O_2$ requires C, 79·3; H, 8·9%).

5-*Ketododecahydro*-1 : 2-*benzanthracene* (IV).—The reduced acid (III) (9 g.) was heated at 100° for an hour with a mixture of concentrated sulphuric acid (36 c.c.) and water (9 c.c.).

After dilution with water, the product was extracted with ether, washed free from acid, and the residue remaining after removal of the ether was recrystallised from methyl alcohol. The tetracyclic *ketone* (IV) (6·5 g.) formed colourless needles, m. p. 120—121°, from ligroin (Found : C, 85·0; H, 8·8. $C_{18}H_{22}O$ requires C, 85·0; H, 8·7%).

Dodecahydro-1 : 2-*benzanthracene* was obtained by reduction of this ketone by Clemmensen's method, the product being distilled at 180°/0·2 mm. and then recrystallised from light petroleum. It formed colourless needles, m. p. 87—88° (*Found : C, 89·5; H, 9·95. $C_{18}H_{24}$ requires C, 89·9; H, 10·1%).

Dodecahydro-1 : 2-*benzanthryl*-5-*acetic Acid.*—Ethyl bromoacetate (3·8 c.c.) was added to a mixture of 5-ketododecahydro-1 : 2-benzanthracene (IV) (8·7 g.), pure benzene (25 c.c.), anhydrous ether (25 c.c.), and magnesium (0·82 g.). After addition of a trace of iodine a vigorous reaction set in on warming, and the whole boiled spontaneously for 20 minutes. The mixture was kept at room temperature for 20 hours, and then treated again with magnesium and ethyl bromoacetate, exactly as described above. After a further 20 hours at room temperature the reddish-brown solution was treated with dilute hydrochloric acid, the solvents removed from the washed ethereal extract, and the residue hydrolysed by boiling alcoholic potassium hydroxide (100 c.c. of 10% solution). After extraction of the acidic products, 3—4 g. of unchanged ketone were isolated. The acid fraction was purified by esterification (methyl-alcoholic hydrogen chloride), distillation of the esters (b. p. 195—212°/0·2 mm.; 2·6 g.), followed by hydrolysis. When the crude resinous acids were digested with *cyclo*hexane, a crystalline unsaturated *acid* (V or VI) was isolated in small yield. This crystallised from benzene in small colourless plates, m. p. 226—232° (efferv.) (†Found : C, 81·2; H, 8·2. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%).

The resinous mixture of acids from which this crystalline material had been isolated (4·8 g., from several batches), purified as described above, was hydrogenated by shaking its ethereal solution (100 c.c.) for 3 hours with hydrogen and palladium-black (1·2 g.). The resulting *dodecahydro*-1 : 2-*benzanthryl*-5-*acetic acid* crystallised from benzene–ligroin in colourless microscopic needles (2 g.), and had m. p. 163—165° after several recrystallisations (*Found : C, 80·7; H, 8·9. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%). The same acid resulted from the hydrogenation of the crystalline unsaturated acid (V or VI).

By heating with platinum-black at 300° for 9 hours, both dodecahydrobenzanthrylacetic acid and the mixture of unsaturated acids (V and VI) suffered dehydrogenation and decarboxylation, the resulting 5-methyl-1 : 2-benzanthracene being identified by direct comparison with an authentic sample (Cook, J., 1933, 1596). An attempt was made to avoid decarboxylation by heating the methyl ester of dodecahydrobenzanthrylacetic acid with selenium at 290—300°. Hydrolysis gave a small amount of an acid which, after sublimation in a vacuum, was purified through its dark red picrate (m. p. 170—173°). Picric acid was removed by reduction with stannous chloride, and the product was crystallised from *cyclo*hexane. This substance, m. p. 160—162°, was undoubtedly 1 : 2-benzanthryl-5-acetic acid, but the amount was too small for further purification.

Ketododecahydrocholanthrene (VII).—A mixture of dodecahydro-1 : 2-benzanthryl-5-acetic acid (2 g.), concentrated sulphuric acid (8 c.c.), and water (2 c.c.) was heated at 100° for an hour. The resulting *ketone* (VII), washed free from acid, crystallised from methyl alcohol in long colourless needles (1·3 g.) which, after recrystallisation from ligroin, had m. p. 114—116° (*Found : C, 85·7; H, 8·9. $C_{20}H_{24}O$ requires C, 85·65; H, 8·6%). This ketone (1·2 g.) was reduced by Clemmensen's method to *dodecahydrocholanthrene* (VIII), which, after distillation, crystallised from alcohol–ligroin in small colourless needles, m. p. 62—63° (*Found : C, 90·3; H, 9·8. $C_{20}H_{26}$ requires C, 90·2; H, 9·8%).

Cholanthrene.—The foregoing hydrocarbon (VIII) (0·2 g.) was heated in an atmosphere of carbon dioxide at 290—310° for 7 hours with platinum-black (50 mg.). Cholanthrene, m. p. 167·5—168·5° (picrate, m. p. 167—168·5°), was obtained in good yield, being purified by vacuum sublimation and then recrystallisation from benzene–alcohol.

5-n-*Propyl*-1 : 2-*benzanthracene.*—Allylmagnesium bromide (compare Gilman and McGlumphy, *Bull. Soc. chim.*, 1928, **43**, 1322) was prepared by addition during 45 minutes, with continuous agitation, of a solution of allyl bromide (6 g.) in anhydrous ether (28 c.c.) to magnesium turnings (7·2 g.), suspended in ether (20 c.c.). The Grignard solution, decanted from the excess of magnesium, was treated with 5-ketododecahydro-1 : 2-benzanthracene (IV) (6·35 g.), suspended in ether (80 c.c.). After an hour at room temperature, the mixture was boiled for 2 hours and then kept at room temperature for 20 hours. The crude resinous carbinol, isolated after decomposition with ice and ammonium chloride, was dehydrated by

heating at 155—160° for 10 minutes. The resulting hydrocarbon (IX) was twice distilled, and had b. p. 174°/0·1 mm. The bromine absorption value (pyridine sulphate dibromide reagent) was in agreement with that required by formula (IX), and was completely unaffected by two treatments with sodium in boiling amyl alcohol.

This hydrocarbon (IX) (1·5 g.) was heated with platinum-black (0·4 g.) for 9 hours at 295—300° in an atmosphere of carbon dioxide. The resulting 5-n-*propyl*-1 : 2-*benzanthracene* was purified by crystallisation from benzene of its dark red *picrate*, m. p. 131·5—132·5° (†Found : N, 8·5. $C_{21}H_{18},C_6H_3O_7N_3$ requires N, 8·4%). The regenerated hydrocarbon crystallised from alcohol in colourless fluorescent needles, m. p. 91—91·5° (†Found : C, 93·3; H, 6·7; *M*, Rast method, 280. $C_{21}H_{18}$ requires C, 93·3; H, 6·7%; *M*, 270), and was oxidised by sodium dichromate (5 parts) in boiling acetic acid to 5-n-*propyl*-1 : 2-*benzanthraquinone*, which, crystallised from alcohol and then from ligroin, formed orange-yellow needles, m. p. 104—105·5° (†Found : C, 83·8; H, 5·3. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·4%).

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[*Received, April 17th,* 1935.]