105. *Polycyclic Aromatic Hydrocarbons. Part XVII. Completion of the Synthesis of the Twelve Monomethyl-1 : 2-benzanthracenes.*

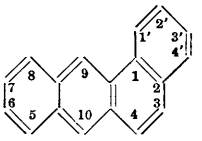
By J. W. Cook and (Mrs.) A. M. Robinson.

Several monomethyl derivatives of 1 : 2-benzanthracene have very pronounced cancer-producing properties, although the parent hydrocarbon is inactive. As part of an attempt to define the positions of substitution favourable for the development of carcinogenic activity in benzanthracene derivatives a study of these monomethyl compounds has been in progress for some years and the last two members of the series of twelve isomerides have now been synthesised. The condensation of anthracene with succinic anhydride by the Friedel–Crafts reaction has been carried out under such conditions that the pure β-keto-acid (I) is readily isolated, and this has been used for building up the 1 : 2-benzanthracene ring system with the introduction of a methyl group at position 1′ (V). The starting point in the synthesis of 8-methyl-1 : 2-benzanthracene was 3-acetylphenanthrene. This was condensed with ethyl succinate under the influence of sodium ethoxide to give a compound (XIII) having the requisite carbon chain; its reduction product underwent cyclisation in the anticipated manner to give a keto-acid related to 8-methyl-1 : 2-benzanthracene (XV), which was obtained from it in two simple stages. It has been established that a molecular rearrangement accompanies the cyclisation of 2-methyl-1 : 1′-dinaphthyl ketone (VIII) with a fused mixture of aluminium chloride and sodium chloride, for the resulting benzanthrone derivative gave on degradation, not 8-methyl-1 : 2-benzanthraquinone as was hoped, but the 3-methyl isomeride.

Twelve monomethyl derivatives of 1 : 2-benzanthracene are theoretically possible. Of these, ten have been described already, and we now report the synthesis of the two remaining members of the series with substituents at positions 8 and 1′.* For convenience of reference, the m. p.'s of the whole series of hydrocarbons, with those of their picrates and quinones, are given in the table, in which the corresponding constants of the parent hydrocarbon are also inserted.

Several of these methylbenzanthracenes have carcinogenic properties, in some cases to a high degree. The biological testing of the more recently synthesised members of the series is still at a comparatively early stage and it seems preferable to defer discussion of the contribution which this series makes to the question of the relation between carcinogenic action and molecular structure until the tests are complete.

* Since this paper was written the synthesis of 1′-methyl-1 : 2-benzanthracene by a different type of method has been described by Fieser and Seligman (*J. Amer. Chem. Soc.*, 1938, **60**, 170).



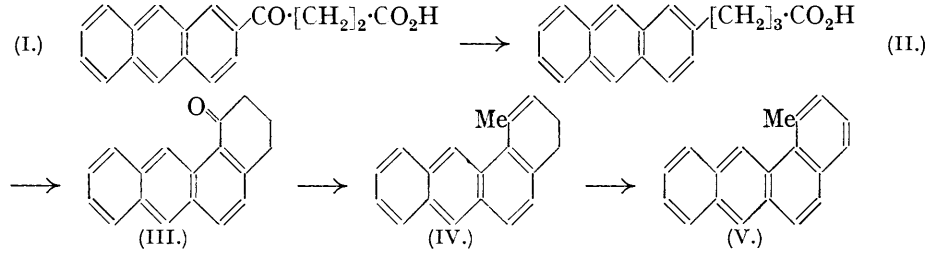
Position of methyl group.	M. p. of hydrocarbon.	picrate.	quinone.	Position of methyl group.	M. p. of hydrocarbon.	picrate.	quinone.
—	160°	142°	168°	9 [d,e]	138°	115°	—
3 [a]	155	153	179	10 [d,f]	140	172	—
4 [b]	125	150	168	1′	138	119 †	189°
5 [b]	158	163	174	2′ [c]	150	180	190
6 [c]	151	152	174	3′ [c]	160	144	168
7 [c]	182	— *	167	4′ [d]	194	139	220
8	107	161	191				

[a] Cook, J., 1930, 1087. [b] Cook, J., 1933, 1592 (compare Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 3742). [c] Cook, J., 1932, 456. [d] Cook, Robinson, and Goulden, J., 1937, 393. [e] Newman, *J. Amer. Chem. Soc.*, 1937, **59**, 1003. [f] Fieser and Newman, *ibid.*, 1936, **58**, 2376.

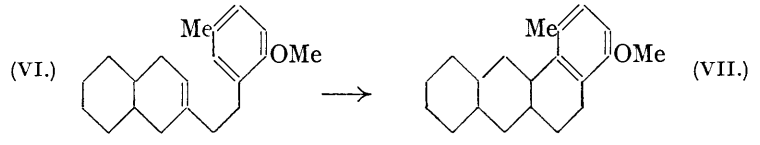
* The picrate of 7-methyl-1 : 2-benzanthracene was too readily dissociated for isolation to be possible.

† This is a dipicrate; the other picrates are all monopicrates.

Although the succinic anhydride condensation method has been widely used in recent years for building up an additional condensed ring to polycyclic structures, there appears to be no mention in the literature of the interaction of anthracene with succinic anhydride beyond a statement (Meister Lucius und Brüning, D.R.-P. 376,635) that in nitrobenzene solution this gave a keto-acid of m. p. 160°. Undoubtedly this was a mixture of isomerides. In our hands this reaction has given a mixture of acids, m. p. *ca.* 160°, from which β-2-*anthroylpropionic acid* (I), m. p. 220°, was readily isolated in 18% yield through the medium of its sparingly soluble sodium salt. This was the acid which was required for the synthesis of 1′-*methyl*-1 : 2-*benzanthracene* (V), and the remaining stages of the synthesis, represented by the following scheme, presented no difficulty. The isomeric anthroylpropionic acids present in the crude mixture have not yet been studied.



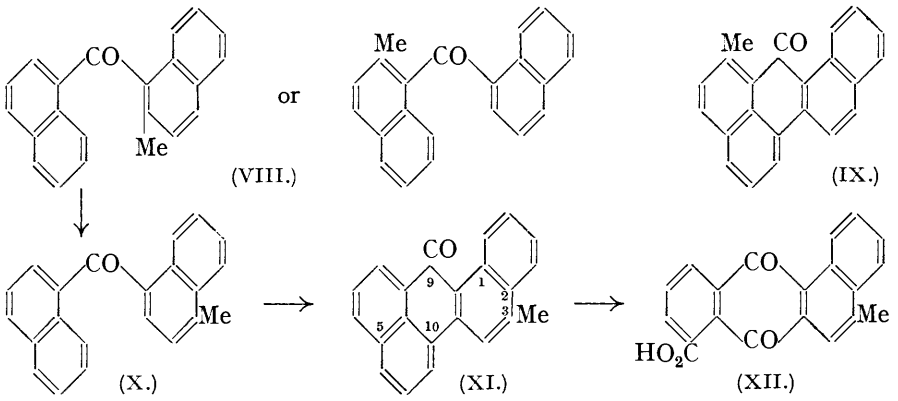
Another method by which we had attempted to synthesise 1′-methyl-1 : 2-benzanthracene was an adaptation of the benzanthracene synthesis of Cook and Hewett (J., 1934, 365). For this purpose *trans*-2-decalone was condensed with the Grignard compound of β-4-*methoxy*-m-*tolylethyl chloride* to give a *carbinol*, which was dehydrated to 2-β-(4′-*methoxy*-m-*tolyl*)*ethyl*-$\Delta^{2:3}$-*octalin* (VI). This was cyclised by aluminium chloride to 4′-*methoxy*-1′-*methyldodecahydro*-1 : 2-*benzanthracene* (VII).



The reason for the presence of the methoxyl group in (VI) was to prevent cyclisation at the *p*-position with respect to the methyl group in the aromatic nucleus, and it was hoped that the methoxyl group could be eliminated after cyclisation, a hope that was encouraged by the knowledge that there are several examples in the literature of the

expulsion of methoxyl groups during selenium dehydrogenation. However, the selenium dehydrogenation of (VII) at 300—310° gave a complex mixture of products, from which the only pure compound isolated, in small yield, was 1 : 2-benzanthracene.

We hoped to obtain 8-methyl-1 : 2-benzanthracene from the methyl-dibenzanthrone (IX) which might conceivably arise by the Scholl *peri*-ring-closure of 2-methyl-1: 1′-dinaphthyl ketone (VIII). It was subsequently shown, however, that this reaction was accompanied by migration of a methyl group exactly comparable with that observed by Mayer, Fleckenstein, and Günther (*Ber.*, 1930, **63**, 1464) in the analogous case of 1-benzoyl-2-methylnaphthalene, so that the product was 3-*methyl*-1 : 2 : 5 : 10-*dibenz*-9-*anthrone* (XI). The mechanism suggested requires that the same pentacyclic ketone should arise from the action of aluminium chloride on 4-*methyl*-1 : 1′-*dinaphthyl ketone* (X), which is regarded as an intermediate in the conversion of (VIII) into (XI). This was shown to be the case by Dr. de Worms, who was engaged in an investigation of (X) for another purpose.



The transformation of (VIII) into (X) is apparently an unusual example of *m*-migration of a methyl group, but we regard it as at least equally probable that the migration is a duplex process consisting of a *p*-migration of the α-naphthoyl group, together with an *o*-migration of methyl to the position which the naphthoyl radical vacates. We are planning experiments to test this hypothesis.

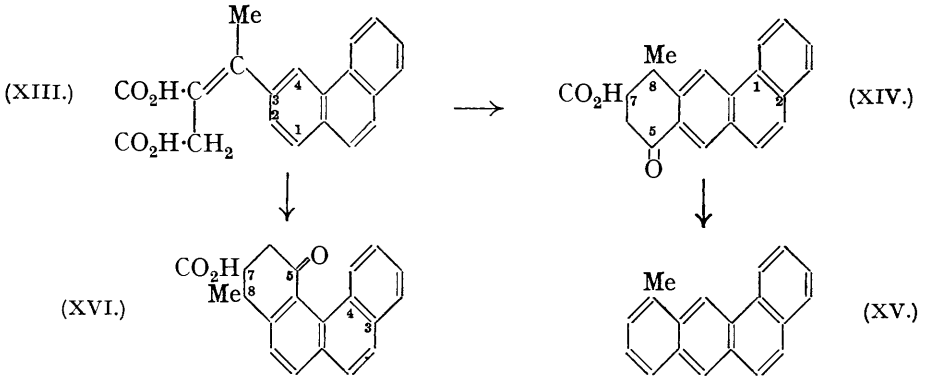
3-*Methyl*-1 : 2-*benzanthraquinone*-5-*carboxylic acid* (XII) was obtained by oxidation of the methyldibenzanthrone (XI) with chromic acid in acetic acid, and was reduced to 3-*methyl*-1 : 2-*benz*-5-*anthroic acid*, which on decarboxylation gave the known 3-methyl-1 : 2-benzanthracene. The identification was completed by comparison of the picrates and quinones, and by crystallographic examination of the two specimens of quinone by Dr. John Iball, who reports as follows :

" The two specimens crystallised from amyl acetate in clusters of needles which had identical appearance. *X*-Ray examination of single crystals of each specimen gave identical photographs and identical unit cell dimensions. The crystals are monoclinic with the *a* axis parallel to the length of the needle. In the case of each specimen the faces developed on the crystals were {011} with a very imperfect {001}. From these facts it can be concluded that both specimens are 3-methyl-1 : 2-benzanthraquinone." Identification of the final hydrocarbon as 3-methyl-1 : 2-benzanthracene provides conclusive proof of the structure (XI) assigned to the methyldibenzanthrone from which it was obtained.

We are indebted to Dr. C. L. Hewett for a suggestion which led to the elaboration of a successful method for the synthesis of 8-methyl-1 : 2-benzanthracene. For this, 3-acetylphenanthrene was condensed with ethyl succinate, and the product hydrolysed to a *methyl*-3-*phenanthrylitaconic acid* (XIII), which after reduction was cyclised to 5-*keto*-8-*methyl*-5 : 6 : 7 : 8-*tetrahydro*-1 : 2-*benz*-7-*anthroic acid* (XIV). Clemmensen reduction of this keto-acid, followed by dehydrogenation–decarboxylation with platinum-black, gave the desired 8-*methyl*-1 : 2-*benzanthracene* (XV).

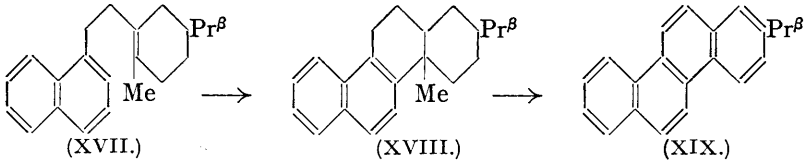
A minor product of the cyclisation of the saturated acid obtained by reduction of (XIII) was 5-*keto*-8-*methyl*-5 : 6 : 7 : 8-*tetrahydro*-3 : 4-*benz*-7-*phenanthroic acid* (XVI), in

which the carbonyl group was inert towards semicarbazide. Ring-closure of a derivative of γ-3-phenanthrylbutyric acid at position 4 has not hitherto been observed, although



Bachmann and Kloetzel (*J. Amer. Chem. Soc.*, 1937, **59**, 2207) have shown that cyclisation of β-3-phenanthrylpropionic acid takes place almost exclusively at position 4. These relationships furnish additional illustration of the difficulty of formation of the ring system of 3 : 4-benzphenanthrene (compare Hewett, J., 1936, 596).

The present communication provides a convenient opportunity to record the synthesis of 4-iso*propylchrysene* (XIX), the carcinogenic inactivity of which has been reported elsewhere (Bachman *et al.*, *Proc. Roy. Soc.*, 1937, *B*, **123**, 363). This was obtained by selenium dehydrogenation of the *methyl*iso*propyloctahydrochrysene* (XVIII) resulting from cyclisation of 2-*methyl*-1-(β-1′-*naphthylethyl*)-5-iso*propyl*-Δ^1-cyclo*hexene* (XVII), which in its turn was prepared by dehydration of the crude carbinol resulting from interaction of β-1-naphthylethylmagnesium chloride with tetrahydrocarvone.



An attempt to prepare a methyl*iso*propylchrysene from tetrahydrocarvone was frustrated by the failure of the potassio-compound of *ethyl* 6-*methyl*-3-iso*propyl*cyclo*hexanone*-2-*carboxylate* to condense with β-1-naphthylethyl bromide.

Experimental.

1′-*Methyl*-1 : 2-*benzanthracene*.

β-2-*Anthroylpropionic Acid* (I).—Succinic anhydride (100 g.) was dissolved in nitrobenzene (1 l.) at 60—70°, the solution cooled to 20° and finely powdered anhydrous aluminium chloride (133 g.) gradually added. The mechanically stirred mixture was cooled to 5°, treated slowly with powdered anthracene (178 g.), and kept at 5—10° for 72 hours. The product was diluted with dry benzene (500 c.c.) and the precipitate was collected. This consisted mainly of anthracene (70 g.) together with a little of the acidic condensation product (5 g.), which was extracted with dilute sodium carbonate solution. The benzene and nitrobenzene were removed from the filtrate by steam distillation; the residue was collected after cooling, dissolved in dilute sodium carbonate solution (1 l.), and filtered hot. The sodium salt which crystallised on cooling was collected, and the free acid liberated (35 g.). β-2-*Anthroylpropionic acid* (I) crystallised from ethyl acetate in yellow prismatic needles, m. p. 220—221° (Found : C, 77·7; H, 5·1. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%). The *methyl* ester formed pale yellow leaflets (from alcohol), m. p. 144·5—145·5° (Found : C, 78·0; H, 5·5. $C_{19}H_{16}O_3$ requires C, 78·05; H, 5·5%). The orientation of this keto-acid was shown by its oxidation to anthraquinone-2-carboxylic acid. This was carried out in two stages, the first with sodium dichromate in boiling glacial acetic acid, and the second with dilute alkaline permanganate solution. The product crystallised from concentrated

nitric acid in soft yellowish needles, m. p. 287—288°, not depressed by authentic anthraquinone-2-carboxylic acid, but depressed to 250° by anthraquinone-1-carboxylic acid.

γ-2-Anthrylbutyric Acid (II).—A mixture of β-2-anthroylpropionic acid (10 g.), glacial acetic acid (100 c.c.), concentrated hydrochloric acid (100 c.c.), toluene (20 c.c.), and amalgamated zinc (30 g.) was boiled under reflux for 20 hours, further portions of concentrated hydrochloric acid (20 c.c.) being added hourly during the first 8 hours. The toluene was removed in steam, the residual solid collected and purified through its sparingly soluble sodium salt, and the regenerated acid twice recrystallised from glacial acetic acid (yield, 6·6 g.) and then from benzene. *γ-2-Anthrylbutyric acid* (II) formed colourless rectangular plates, m. p. 194—195° (Found: C, 81·9; H, 6·2. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

1′-Keto-1′ : 2′ : 3′ : 4′-tetrahydro-1 : 2-benzanthracene (III).—(a) This was obtained in 65% yield when γ-2-anthrylbutyric acid was heated at 100° for 1½ hours with anhydrous stannic chloride (1·5 c.c. per g.). The product, freed from stannic chloride by repeated extraction with concentrated hydrochloric acid, was twice recrystallised from alcohol, sublimed at 0·2 mm., and finally crystallised from alcohol. *1′-Keto-1′ : 2′ : 3′ : 4′-tetrahydro-1 : 2-benzanthracene* (III) formed pale yellow plates, m. p. 114—114·5° (Found: C, 87·9; H, 5·75. $C_{18}H_{14}O$ requires C, 87·8; H, 5·7%).

(b) Phosphorus pentachloride (4·5 g.) was added to a suspension of γ-2-anthrylbutyric acid (5 g.) in benzene (50 c.c.), and the solution heated to boiling, and then cooled to 5°, with stirring. Anhydrous aluminium chloride (6·5 g.) was then gradually added, and stirring continued for 6 hours at room temperature. The product was decomposed with ice and hydrochloric acid, the benzene removed in steam, and the ketone (III) freed from unchanged acid (0·7 g.) and recrystallised from alcohol. The yield was 3 g.

1′-Methyl-3′ : 4′-dihydro-1 : 2-benzanthracene (IV).—The aforesaid ketone (4 g.) was slowly added to a Grignard solution prepared from methyl iodide (8·5 g.) and magnesium turnings (1·4 g.) in anhydrous ether (100 c.c.). The mixture was boiled for 3 hours and decomposed with ice and ammonium chloride, and the resulting crude carbinol was dehydrated by ½ hour's boiling in alcoholic solution (30 c.c.) with picric acid (4 g.). The *picrate* of 1′-methyl-3′ : 4′-dihydro-1 : 2-benzanthracene (7 g.), which crystallised on cooling, formed purplish-black clusters of needles, m. p. 120—121° (Found: C, 63·5; H, 4·2. $C_{19}H_{16},C_6H_3O_7N_3$ requires C, 63·4; H, 4·05%). *1′-Methyl-3′ : 4′-dihydro-1 : 2-benzanthracene*, obtained from this picrate by shaking with benzene and dilute sodium carbonate solution, was distilled at 0·001 mm., and twice recrystallised from ligroin; it then formed pale yellow, laminated needles, m. p. 74—75° (Found: C, 93·1; H, 6·4. $C_{19}H_{16}$ requires C, 93·4; H, 6·6%).

1′-Methyl-1 : 2-benzanthracene (V).—The crude dihydro-compound (3 g.) was rapidly dehydrogenated when heated at 250° with platinum-black (0·3 g.) in an atmosphere of carbon dioxide. After an hour at this temperature the product was crystallised from a little benzene, sublimed at 0·1 mm., and recrystallised from ethyl acetate. *1′-Methyl-1 : 2-benzanthracene* (V) formed almost colourless leaflets, m. p. 137·5—138·5°, which gave the characteristic 1 : 2-benzanthracene colour reaction with concentrated sulphuric acid (Found: C, 94·0; H, 6·0. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%). The m. p. was not changed after regeneration from the purified *dipicrate*, which formed scarlet needles (from benzene), m. p. 119° (Found: C, 53·4; H, 3·1. $C_{19}H_{14},2C_6H_3O_7N_3$ requires C, 53·1; H, 2·9%). The crude quinone obtained by oxidation of the hydrocarbon with sodium dichromate in boiling acetic acid was purified by reduction with zinc dust and boiling dilute sodium hydroxide, followed by aerial oxidation of the filtered blood-red solution. The precipitate was collected, dried, and sublimed at 0·05 mm., and the sublimate was recrystallised from ethyl acetate. *1′-Methyl-1 : 2-benzanthraquinone* formed orange needles, m. p. 188·5—189·5° (Found: C, 83·8; H, 4·5. $C_{19}H_{12}O_2$ requires C, 83·8; H, 4·4%).

β-4-Methoxy-m-tolylethyl Chloride.—Ethylene oxide (25 g.) was added slowly to a well-cooled Grignard solution prepared from 3-bromo-4-methoxytoluene (86 g.) (Schall and Dralle, *Ber.*, 1884, **17**, 2531; compare Anderson, *J. Biol. Chem.*, 1916, **26**, 393) and magnesium turnings (10·3 g.) in dry ether (400 c.c.). After the mixture had been kept overnight at room temperature, the ether was removed by distillation, and the residue was heated on a boiling water-bath for 1½ hours and then decomposed with ice and hydrochloric acid. The resulting *β-4-methoxy-m-tolylethyl alcohol* (b. p. 150—160°/18 mm.; 37 g.) crystallised from ligroin in colourless prismatic needles, m. p. 45—46° (Found: C, 72·4; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·2; H, 8·5%). *β-4-Methoxy-m-tolylethyl chloride*, obtained in the usual way by the action of thionyl chloride on the alcohol, in dimethylaniline, formed a colourless liquid, b. p. 126—127°/12 mm. (Found: C, 64·85; H, 7·2. $C_{10}H_{13}OCl$ requires C, 65·0; H, 7·1%).

2-β-(4′-Methoxy-m-tolyl)ethyl-$\Delta^{2:3}$-octalin (VI).—*trans*-2-Decalone (18·5 g.) was added to an

ice-cold Grignard solution prepared from the foregoing chloride (22 g.) and magnesium turnings (2 g.) in ether (120 c.c.) and anisole (40 c.c.). After ½ hour at 0° the mixture was boiled for 1½ hours and decomposed with ice and ammonium chloride, and the tertiary carbinol isolated by distillation. It formed a glassy solid, b. p. 175—185°/0·3 mm., and gave a 3 : 5-*dinitrobenzoate*, m. p. 117—117·5° (from alcohol) (Found : C, 65·3; H, 6·6. $C_{27}H_{32}O_7N_2$ requires C, 65·3; H, 6·5%). 2-β-(4′-*Methoxy*-m-*tolyl*)*ethyl*-$\Delta^{2:3}$-*octalin* (VI), obtained from the carbinol by heating with potassium hydrogen sulphate (1½ parts) at 170—180° for 2 hours, formed a colourless liquid, b. p. 178—180°/0·5 mm., after distillation over sodium (Found : C, 84·0; H, 10·15. $C_{20}H_{28}O$ requires C, 84·45; H, 9·9%).

4′-*Methoxy*-1′-*methyldodecahydro*-1 : 2-*benzanthracene* (VII).—A mixture of the octalin (VI) (10 g.), carbon disulphide (100 c.c.), and aluminium chloride (14 g.) was kept at 0° for 4 hours and then at room temperature overnight. The solution was decanted, washed, and fractionated. The fraction (7 g.), b. p. 175—185°/0·5 mm., solidified when triturated with methyl alcohol, and the resulting 4′-*methoxy*-1′-*methyldodecahydro*-1 : 2-*benzanthracene* (VII) (4·5 g.) crystallised from methyl alcohol in long colourless needles, m. p. 80·5—81° (Found : C, 84·1; H, 10·1. $C_{20}H_{28}O$ requires C, 84·45; H, 9·9%).

3-*Methyl*-1 : 2-*benzanthracene from* 2-*Methyl*-1 : 1′-*dinaphthyl Ketone*.

3-*Methyl*-1 : 2 : 5 : 10-*dibenz*-9-*anthrone* (XI).—(a) An intimate mixture of 2-methyl-1 : 1′-dinaphthyl ketone (Clar, *Ber.*, 1929, **62**, 350) (35 g.), anhydrous aluminium chloride (140 g.), and sodium chloride (35 g.) was stirred mechanically in a bath gradually heated to 110°. At this temperature the mass began to liquefy and a vigorous reaction ensued. The temperature was then maintained at 80—90° for 1½ hours, stirring being continued, and the product was poured on ice and hydrochloric acid. After 12 hours the solid was collected and recrystallised from glacial acetic acid. The resulting 3-*methyl*-1 : 2 : 5 : 10-*dibenz*-9-*anthrone* (XI) (18 g.) was almost pure; a sample for analysis, sublimed at 160—200°/0·05 mm. and crystallised from glacial acetic acid, formed fine golden-yellow needles, m. p. 221—222° (Found : C, 89·6; H, 5·05. $C_{22}H_{14}O$ requires C, 89·8; H, 4·8%).

(b) * Finely powdered aluminium chloride (20 g.) was added during ½ hour to an ice-cold mixture of 1-methylnaphthalene (20 g.), 1-naphthoyl chloride (23 g.), and carbon disuphide (65 c.c.). After 5½ hours with occasional shaking, the product was decomposed with ice and hydrochloric acid, the carbon disulphide and the excess of methylnaphthalene removed in steam, naphthoic acid extracted with dilute sodium carbonate solution, and the residual crude ketone distilled (b. p. 275—280°/0·6 mm.). The distillate was recrystallised from glacial acetic acid and then from alcohol. 4-*Methyl*-1 : 1′-*dinaphthyl ketone* (X) formed colourless octahedra, m. p. 100—101·5° (Found : C, 88·9; H, 5·4. $C_{22}H_{16}O$ requires C, 89·15; H, 5·4%), and its *picrate* crystallised from alcohol in yellow rosettes, m. p. 86—87·5° (Found : C, 63·95; H, 3·85. $C_{22}H_{16}O,C_6H_3O_7N_3$ requires C, 64·0; H, 3·65%). The constitution assigned to this ketone (X) was confirmed by its preparation from 1-naphthonitrile and the Grignard compound of 4-bromo-1-methylnaphthalene, the structure of which rests on fairly secure foundation (see Mayer and Sieglitz, *Ber.*, 1922, **55**, 1835).

Cyclisation of 4-methyl-1 : 1′-dinaphthyl ketone to 3-methyl-1 : 2 : 5 : 10-dibenz-9-anthrone (XI) by an aluminium chloride–sodium chloride melt was effected as described under (a). The product had m. p. 221—222°, not depressed by the compound prepared from 2-methyl-1 : 1′-dinaphthyl ketone (VIII).

3-*Methyl*-1 : 2-*benzanthraquinone*-5-*carboxylic Acid* (XII).—A solution of chromic anhydride (35 g.) in 80% acetic acid (70 c.c.) was added dropwise during an hour to a boiling suspension of 3-methyl-1 : 2 : 5 : 10-dibenz-9-anthrone (9·4 g.) in glacial acetic acid (200 c.c.). Boiling was continued for another hour, and the green solution was concentrated in a vacuum on the water-bath until no more acetic acid distilled. The residue was extracted with water, treated with excess of sodium carbonate, boiled, and filtered hot. The chromium hydroxide sludge was extracted three times with a large volume of boiling dilute sodium carbonate solution. The combined alkaline liquors were acidified and the precipitated acid was collected and dried (yield, 5·35 g.). Purification was effected by crystallisation of the sparingly soluble sodium salt from water. 3-*Methyl*-1 : 2-*benzanthraquinone*-5-*carboxylic acid* (XII) crystallised from a large volume of glacial acetic acid in small orange needles, m. p. 305—306° (Found : C, 75·8; H, 3·9. $C_{20}H_{12}O_4$ requires, C, 75·9; H, 3·8%).

3-*Methyl*-1 : 2-*benz*-5-*anthroic Acid*.—A solution of stannous chloride (13·5 g.) in concentrated

* These experiments were carried out by Dr. C. G. M. de Worms.

hydrochloric acid (40 c.c.) was added to a suspension of the quinone-acid (XII) (3·25 g.) in glacial acetic acid (500 c.c.), and the mixture boiled for an hour. After cooling, the crystalline anthranol acid was collected and reduced further by 9 hours' boiling with zinc dust (20 g.) in N-sodium hydroxide (300 c.c.). The cooled suspension of sodium salt and excess of zinc was filtered off, and the solid digested with hydrochloric acid until the zinc was dissolved. The residual 3-*methyl*-1 : 2-*benz*-5-*anthroic acid* crystallised from a large volume of glacial acetic acid as a yellow crystalline powder, m. p. 320—322° (decomp.) (Found : C, 83·3; H, 5·0. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%). The *methyl* ester formed lemon-yellow irregular plates (from ethyl acetate), m. p. 170—171° (Found : C, 83·5; H, 5·6. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·4%).

3-*Methyl*-1 : 2-*benzanthracene*.—This was obtained by decarboxylation of 3-methyl-1 : 2-benz-5-anthroic acid (1·2 g.) with copper-bronze (0·5 g.) in boiling quinoline (25 c.c.) (2 hours). The hydrocarbon was sublimed at 160°/0·1 mm. and recrystallised from benzene–alcohol, forming colourless plates, m. p. 155° (Found: C, 94·2; H, 5·9. Calc.: C, 94·2; H, 5·8%); it gave a *picrate*, m. p. 153° (from benzene) (Found : C, 63·7; H, 3·8. $C_{19}H_{14},C_6H_3O_7N_3$ requires C, 63·7; H, 3·6%). The quinone obtained by oxidation had m. p. 177° (Found : C, 83·6; H, 4·5. Calc.: C, 83·8; H, 4·4%). These three compounds gave no depression of m. p. when mixed with authentic specimens prepared from phthalic anhydride and 1-methylnaphthalene (Scholl and Tritsch, *Monatsh.*, 1911, **32**, 997; Cook, J., 1930, 1087). The constitution of the intermediate 4-methyl-*o*-1-naphthoylbenzoic acid was confirmed by the preparation of the same acid, m. p. 169°, from phthalic anhydride and 4-methyl-1-naphthylmagnesium bromide, the technique of Weizmann, Bergmann, and Bergmann (J., 1935, 1367) being used.

8-*Methyl*-1 : 2-*benzanthracene*.

Methyl-3-*phenanthrylitaconic Acid* (XIII).—Absolute ethyl alcohol (15·4 g.) was added to fine sodium wire (7·7 g.) covered with anhydrous ether, and the suspension kept for 24 hours. Most of the ether was distilled off, the temperature raised to 60—70°, and a warm ethereal solution of 3-acetylphenanthrene (Mosettig and van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704) (37 g.) and ethyl succinate (29·6 g.) slowly added. A vigorous reaction set in. The ether and alcohol were removed by distillation, water added to the residue, and insoluble material extracted with ether. The aqueous solution was refluxed for 6 hours after addition of sodium hydroxide (20 g.). It was then cooled and the sodium salt which crystallised was collected, dissolved in water, and acidified. The precipitate was recrystallised from acetic acid and gave 3 g. of acid, m. p. 191—192°. The alkaline liquors were acidified and extracted with ether. The ether was removed from the extract, and the residue triturated with benzene. The undissolved residue was recrystallised from acetic acid and gave another 22 g. of the same acid, m. p. 191°. For analysis, *methyl*-3-*phenanthrylitaconic acid* (XIII) was purified through its anhydride and crystallised from ethyl acetate; it then formed colourless prisms, m. p. 192—193° (Found : C, 75·0; H, 5·0. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

The *anhydride*, obtained by boiling with acetyl chloride, formed a microcrystalline colourless powder (from chloroform), m. p. 203° (Found : C, 79·0; H, 4·8. $C_{20}H_{14}O_3$ requires C, 79·45; H, 4·7%).

α-(α′-3-*Phenanthrylethyl*)*succinic Acid*.—A solution of the unsaturated acid (XIII) (17 g.) in water (1700 c.c.) and sodium hydroxide (5·1 g.) was heated at 60—70° for 120 hours, during which five portions of 2·5% sodium amalgam (170 g.) were added. The solution was cooled and the sodium salt which crystallised (13·5 g.) was collected. The acid obtained from this was combined with a little more obtained from the liquors and recrystallised from aqueous acetic acid, yielding 13·5 g. of saturated acid, m. p. 178—179°. For analysis, a specimen was recrystallised from ethyl acetate and then aqueous methyl alcohol. α-(α′-3-*Phenanthrylethyl*)*succinic acid* formed colourless leaflets, m. p. 183° (Found : C, 74·3; H, 5·7. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%).

The *anhydride* was obtained by refluxing a suspension of this acid (5 g.) in acetyl chloride (30 c.c.) for 4 hours. The cooled solution was filtered, the acetyl chloride removed under reduced pressure, and the residue recrystallised from benzene–light petroleum; it then had m. p. 142—143°. A specimen of this anhydride crystallised from *cyclo*hexane in colourless needles, m. p. 145° (Found : C, 78·9; H, 5·3. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

5-*Keto*-8-*methyl*-5 : 6 : 7 : 8-*tetrahydro*-1 : 2-*benz*-7-*anthroic Acid* (XIV).—A solution of α-(α′-3-phenanthrylethyl)succinic anhydride (10 g.) in nitrobenzene (50 c.c.) was added dropwise during ½ hour to an ice-cold solution of anhydrous aluminium chloride (10 g.) in nitrobenzene (50 c.c.). The blood-red solution was kept at 0° for 20 hours and then decomposed with ice and hydrochloric acid and freed from nitrobenzene by steam distillation. The residual solid was

collected and dissolved in hot dilute sodium carbonate solution, and the filtered solution cooled. The sodium salt which crystallised was collected; it gave the desired keto-acid (XIV) (6 g.), which crystallised from aqueous acetic acid in colourless plates, m. p. 214—215°. For analysis, a specimen was purified through its *semicarbazone*, which formed colourless silky needles, m. p. 275° (decomp.), too sparingly soluble to be recrystallised (Found: N, 11·15. $C_{21}H_{19}O_3N_3$ requires N, 11·6%). This semicarbazone was largely unattacked after being heated at 180—190° for 17 hours with alcoholic sodium ethoxide. *5-Keto-8-methyl-5 : 6 : 7 : 8-tetrahydro-1 : 2-benz-7-anthroic acid* (XIV), obtained by hydrolysis of the semicarbazone, was sublimed at 200°/0·01 mm. and recrystallised from benzene, in which it was very sparingly soluble. It formed a colourless microcrystalline powder, m. p. 214—215° (Found: C, 78·6; H, 5·4. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

The alkaline mother-liquors, from which the sparingly soluble sodium salt of this acid had been separated, were acidified and the precipitate was recrystallised from aqueous acetic acid. The product (1·7 g.) was sublimed at 210°/0·01 mm., and the sublimate was treated with semicarbazide in boiling aqueous alcoholic solution. A small amount of sparingly soluble semicarbazone was separated; the bulk of the material had not reacted with semicarbazide and was recrystallised twice from alcohol and then from toluene. This keto-acid (yield, 0·5 g.), which was much more soluble than its isomeride (XIV), was undoubtedly *5-keto-8-methyl-5 : 6 : 7 : 8-tetrahydro-3 : 4-benz-7-phenanthroic acid* (XVI), formed by cyclisation at the alternative position 4 of the phenanthrene ring system. It formed colourless prismatic needles, m. p. 177—178°, and its failure to react with semicarbazide is readily explicable on stereochemical grounds (Found: C, 79·1; H, 5·45. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%).

The keto-acid (XIV) was also obtained, in less satisfactory yield, by cyclisation of the succinic anhydride derivative with stannic chloride at 100°. The sample prepared by this method had m. p. 217°.

8-Methyl-5 : 6 : 7 : 8-tetrahydro-1 : 2-benz-7-anthroic Acid.—This was obtained by Clemmensen reduction of the keto-acid (XIV). To this end the keto-acid (5 g.) was boiled under reflux for 24 hours with acetic acid (15 c.c.), water (25 c.c.), concentrated hydrochloric acid (30 c.c.), toluene (10 c.c.), and amalgamated granulated zinc (15 g.). At the end of each of the first 5 hours additional concentrated hydrochloric acid (10 c.c.) was added. Examination of the product indicated that it probably still contained some of the sparingly soluble keto-acid, and the whole was submitted anew to the above treatment, boiling being prolonged for 48 hours. The product was isolated, and esterified with methyl-alcoholic hydrogen chloride, and the methyl ester distilled at 0·1 mm. from a bath gradually heated from 220° to 280°. The viscous distillate (3·5 g.) was hydrolysed with boiling aqueous alcoholic alkali, and the acid recrystallised from aqueous acetic acid. *8-Methyl-5 : 6 : 7 : 8-tetrahydro-1 : 2-benz-7-anthroic acid* (2·9 g.) formed colourless needles, m. p. 215—217°, unaltered by recrystallisation from toluene and then benzene (Found: C, 82·7; H, 6·3. $C_{20}H_{18}O_2$ requires C, 82·7; H, 6·3%).

8-Methyl-1 : 2-benzanthracene.—The foregoing acid (2·8 g.) was heated with platinum-black (0·5 g.) at 300—310° for 5 hours in an atmosphere of carbon dioxide. The product was extracted with ether and washed with dilute sodium carbonate solution, which removed 0·6 g. of unchanged acid. The neutral fraction from the ethereal extract was distilled from an air-bath at 145—155°/0·02 mm. The distillate was recrystallised from alcohol, and gave 1·45 g. of crude hydrocarbon, m. p. 102—114°. This was purified through its *s-trinitrobenzene complex*, which crystallised from alcohol in long scarlet needles, m. p. 164—165° (Found: C, 66·2; H, 4·1. $C_{19}H_{14},C_6H_3O_6N_3$ requires C, 65·9; H, 3·8%). To recover the hydrocarbon, a boiling alcoholic suspension of this complex was treated with a solution of stannous chloride in concentrated hydrochloric acid, boiling being continued for a few minutes. The resulting 8-methyl-1 : 2-benzanthracene (m. p. 107—109°) was further purified by crystallisation of its picrate from benzene. This *picrate*, recrystallised for analysis from alcohol, formed reddish-brown needles, m. p. 161—162° (Found: C, 63·8; H, 3·8. $C_{19}H_{14},C_6H_3O_7N_3$ requires C, 63·7; H, 3·6%). The hydrocarbon regenerated from the picrate was sublimed at 150°/0·01 mm., and then recrystallised from alcohol. *8-Methyl-1 : 2-benzanthracene* formed colourless leaflets, m. p. 107°, and gave the series of colours in concentrated sulphuric acid characteristic of the benzanthracene hydrocarbons (Found: C, 94·2; H, 5·8. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%).

8-Methyl-1 : 2-benzanthraquinone was obtained by oxidation of the hydrocarbon with sodium dichromate (2 parts) in glacial acetic acid, and was purified as described for the 1′-methyl compound (p. 509). It formed long canary-yellow needles (from ethyl acetate), m. p. 191—192°, and gave large depressions of m. p. when mixed with 1′-methyl- or 2′-methyl-1 : 2-benzanthraquinone (Found: C, 83·7; H, 4·5. $C_{19}H_{12}O_2$ requires C, 83·8; H, 4·4%).

4-iso*Propylchrysene.*

2-*Methyl*-1-(β-1′-*naphthylethyl*)-5-iso*propyl*-Δ^1-cyclo*hexene* (XVII).—Tetrahydrocarvone (31 g.)* was added slowly to an ice-cold Grignard solution prepared from β-1-naphthylethyl chloride (47 g.), magnesium turnings (6 g.), and anhydrous ether (125 c.c.). The mixture was then boiled for 24 hours and decomposed with ice and ammonium chloride, the crude distilled carbinol (b. p. 217—218°/0·8 mm.; 10 g.) dehydrated with potassium hydrogen sulphate at 160—180°, and the product purified by crystallisation from alcohol of its easily soluble picrate. 2-*Methyl*-1-(β-1′-*naphthylethyl*)-5-iso*propyl*-Δ^1-cyclo*hexene* (XVII) formed a colourless viscous liquid, b. p. 160—165°/0·15 mm. (Found : C, 90·4; H, 9·65. $C_{22}H_{28}$ requires C, 90·35; H, 9·65%).

4-iso*Propylchrysene* (XIX).—Cyclisation of the unsaturated hydrocarbon (XVII) (5 g.) with aluminium chloride (6 g.) in carbon disulphide (30 c.c.) at 0° was complete in 24 hours. The distilled product (b. p. 195°/0·2 mm.) gave crystals of *methyl*iso*propyloctahydrochrysene* (XVIII), which formed colourless rectangular plates, m. p. 108° after recrystallisation from alcohol (Found : C, 89·8; H, 9·7. $C_{22}H_{28}$ requires C, 90·35; H, 9·65%). This was dehydrogenated by selenium at 320° (24 hours) to 4-iso*propylchrysene* (XIX), which crystallised from alcohol in colourless plates, m. p. 227° (Found : C, 93·0; H, 6·75. $C_{21}H_{18}$ requires C, 93·3; H, 6·7%), and gave a 2 : 7-*dinitroanthraquinone complex*, m. p. 241—242° (Found : C. 74·2; H, 4·3. $C_{21}H_{18},C_{14}H_6O_6N_2$ requires C, 74·5; H, 4·3%).

Ethyl 6-*Methyl*-3-iso*propyl*cyclo*hexanone*-2-*carboxylate*.—Tetrahydrocarvone was converted by the procedure of Simonsen, Bradfield, and Jones (J., 1935, 315) into α-methyl-δ-*iso*propylpimelic acid and this was esterified with alcoholic hydrogen chloride. The *ethyl* ester formed a colourless liquid, b. p. 110°/0·5 mm. (Found : C, 66·0; H, 10·45. $C_{15}H_{28}O_4$ requires C, 66·1; H, 10·4%). The Dieckmann cyclisation of this ester (12 g.) was effected by heating it for 6 hours at 120—130° with sodium (1·7 g.) in dry toluene (30 c.c.) (compare Cornubert and Borrel, *Bull. Soc. chim.*, 1930, **47**, 301). After fractionation, the resulting *ethyl* 6-*methyl*-3-iso*propyl*-cyclo*hexanone*-2-*carboxylate* formed a colourless liquid, b. p. 100°/0·2 mm. (Found : C, 69·5; H, 10·2. $C_{13}H_{22}O_3$ requires C, 69·0; H, 9·8%), and gave no condensation product when its potassio-compound was heated under reflux in benzene solution for 8 days with β-1-naphthylethyl bromide.

We are indebted to the International Cancer Research Foundation for a grant which has enabled one of us (A. M. R.) to participitate in this work, and to the British Empire Cancer Campaign for grants which have supported this investigation.

RESEARCH INSTITUTE OF THE ROYAL CANCER HOSPITAL (FREE),
LONDON, S.W. 3.

[*Received, March 17th*, 1938.]