

241. Polycyclic Aromatic Hydrocarbons. Part XVIII. A General Method for the Synthesis of 3 : 4-Benzphenanthrene Derivatives.

By C. L. HEWETT.

3 : 4-Benzphenanthroic acid has been synthesised by the elimination of hydrogen bromide, by means of fused potassium hydroxide, from α -2'-(1'-bromonaphthyl)-cinnamic acid. 6-, 7-, and 8-Methyl-3 : 4-benzphenanthrenes, 1 : 2 : 5 : 6-dibenzphenanthrene, and 1 : 2-(1' : 2'-naphth)anthracene have been obtained from their corresponding carboxylic acids, prepared in a similar manner.

THE introduction of a methyl group into the 2-position of the 3 : 4-benzphenanthrene molecule (Hewett, J., 1936, 596) has the effect of increasing the cancer-producing activity of the latter so that it approaches that of methylcholanthrene and 3 : 4-benzpyrene (Bachmann *et al.*, *Proc. Roy. Soc.*, 1937, B, 123, 358). It is of interest, therefore, to determine if this considerable increase in the activity of 3 : 4-benzphenanthrene is due to substitution solely in position 2 or whether substitution in other parts of the molecule would produce a similar effect.

There is no synthesis of 3 : 4-benzphenanthrene in the literature which is readily adaptable to the production of a variety of alkyl derivatives, the existing methods either being limited to special cases (such as 8-methyl-2-isopropyl-3 : 4-benzphenanthrene; Adelson and Bogert, *J. Amer. Chem. Soc.*, 1937, 59, 1776) or requiring so many stages as to restrict the practical importance of the method (Cook, J., 1931, 2524; Newman and Joshel, *J. Amer. Chem. Soc.*, 1938, 60, 485; Fieser, Fieser, and Hershberg, *ibid.*, 1936, 58, 1463; Hewett, *loc. cit.*).

The method now described is based on the production of 9-phenanthroic acid from α -*o*-chlorophenylcinnamic acid by refluxing in quinoline solution with caustic potash (I. G. Farbenindustrie, *Brit. Pat.* 459,108; *Brit. Chem. Abs.*, 1937, B, 215), a reaction which has proved readily adaptable to the production of a variety of derivatives of 3 : 4-benz-10-phenanthroic acid.



α -2'-(1'-Bromonaphthyl)cinnamic acid (I; R = H) was obtained by a Perkin condensation between the easily accessible sodium 1-bromo-2-naphthylacetate (Mayer and Sieglitz, *Ber.*, 1922, 55, 1858) and benzaldehyde. Cyclisation of this acid to 3 : 4-benz-10-phenanthroic acid (II; R = H) (yield, 60%) was effected by fusion with potassium hydroxide at 230–240°.

By using *o*-, *m*-, and *p*-tolualdehyde in the Perkin reaction in place of benzaldehyde, the three corresponding α -2'-(1'-bromonaphthyl)- β -tolylacrylic acids were obtained. These acids on cyclisation by means of fused potassium hydroxide gave 8-, 7-, and 6-methyl-3 : 4-benz-10-phenanthroic acid respectively, in yields of about 40%. Decarboxylation to

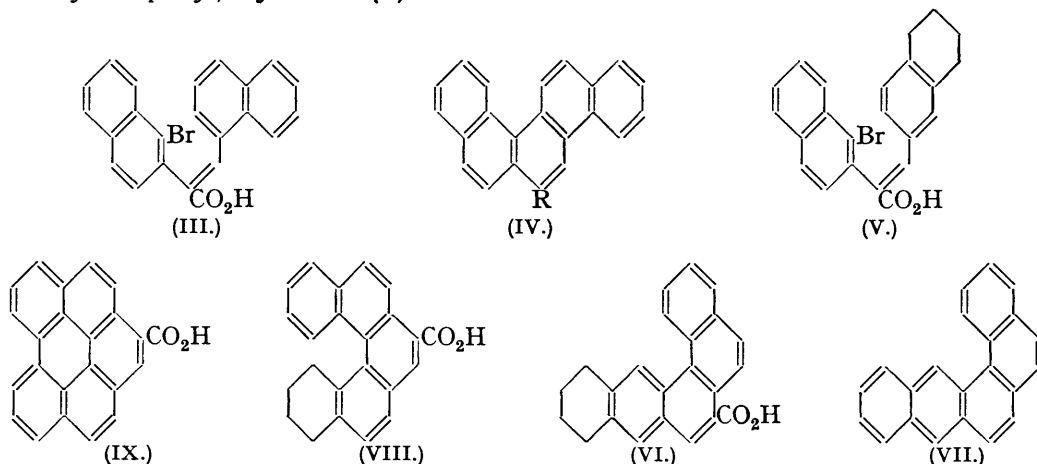
the corresponding 8-, 7-, and 6-methyl-3 : 4-benzphenanthrenes with copper-bronze in boiling quinoline proceeded smoothly; the hydrocarbons were purified through their *picrates*.

The cyclisation of the acid (I; R = Me) resulted in a mixture from which a pure acid was isolated by sublimation and crystallisation. To this acid is assigned the structure 7-methyl-3 : 4-benz-10-phenanthroic acid (II; R = Me), although there is no evidence that ring closure has not taken place in the alternative position to give 5-methyl-3 : 4-benz-10-phenanthroic acid. This structure is based on the assumption that cyclisation is unlikely to take place to any considerable extent in an *o*-position to a methyl group when a free *p*-position is available; also it would be expected that the formation of the 5-methyl derivative would be very difficult on account of steric hindrance, a view which is supported by the failure of Haworth and Sheldrick (J., 1934, 1950) to obtain the similarly constituted 4 : 5-dimethylphenanthrene.

Attempts are being made to obtain 2-substituted derivatives of 3 : 4-benzphenanthrene by the condensation of ethyl 1-bromo-2-naphthylacetate with phenyl alkyl ketones, and 1-substituted alkyl derivatives by the condensation of ethyl phenylacetate with 1-bromo-2-acylnaphthalene.

The two pentacyclic aromatic hydrocarbons which have not yet been described are both derivatives of 3 : 4-benzphenanthrene and since 1 : 2 : 3 : 4-dibenzphenanthrene (Hewett, this vol., p. 193) has proved to have carcinogenic activity (private communication from Professor E. L. Kennaway) interest in these two compounds has been stimulated. They have now been prepared by an extension of the foregoing method. α -2-(1-Bromonaphthyl)- β -1'-naphthylacrylic acid (III), obtained from sodium 1-bromo-2-naphthylacetate and 1-naphthaldehyde, underwent cyclisation by means of fused caustic potash to give 1 : 2 : 5 : 6-dibenz-9-phenanthroic acid (IV; R = CO₂H), decarboxylation of which gave 1 : 2 : 5 : 6-dibenzphenanthrene (IV; R = H): this did not depress the melting point of the same hydrocarbon synthesised by Bergmann by another method (following paper).

For the synthesis of 1 : 2-(1' : 2'-naphthyl)anthracene (VII) 1 : 2 : 3 : 4-tetrahydro-6-naphthaldehyde was necessary in order to promote ring closure in the β -position of the naphthalene nucleus. The methods recorded in the literature (Moldaenke, Dirlam, and Gruber, *Ber.*, 1922, 55, 1708; Fleischer and Feldmeier, *ibid.*, p. 3290) are not suitable for preparing the aldehyde in quantity and a new method has been devised. 6-Acetyltetraalin (Scharwin, *Ber.*, 1902, 35, 2511; Barbot, *Bull. Soc. chim.*, 1930, 47, 1314) was oxidised to 1 : 2 : 3 : 4-tetrahydro-6-naphthoic acid in good yield by means of sodium hypochlorite solution. The anilide of this acid was converted by means of phosphorus trichloride into the iminochloride, which was reduced with stannous chloride in an ethereal solution of hydrogen chloride. The resulting stannichloride complex of the anil gave on hydrolysis 1 : 2 : 3 : 4-tetrahydro-6-naphthaldehyde. The Perkin condensation between this aldehyde and sodium 1-bromo-2-naphthylacetate yielded α -2-(1-bromonaphthyl)- β -6'-(1' : 2' : 3' : 4'-tetrahydronaphthyl)acrylic acid (V).



Cyclisation of this acid gave a resinous acid which, on trituration with benzene, sublimation, and crystallisation from xylene, gave a small amount of 3 : 4-benz-5 : 6-tetra-methylene-10-phenanthroic acid (VIII), m. p. 280°. The main bulk of the acid, recovered from the xylene liquor, was 5 : 6 : 7 : 8-tetrahydro-1 : 2-(1' : 2'-naphtha)-3-anthroic acid (VI), m. p. 238—240°.

Dehydrogenation of the acid (VI) with sulphur yielded 1 : 2-(1' : 2'-naphtha)-3-anthroic acid; this on decarboxylation gave 1 : 2-(1' : 2'-naphth)anthracene (VII). Oxidation of (VII) with sodium dichromate in acetic acid solution led to a quinone which gave the Liebermann anthraquinol reaction with zinc dust and caustic soda, thus establishing the presence of an anthracene system in the hydrocarbon.

Dehydrogenation of the acid (VIII) with sulphur in quinoline solution resulted in the loss of 6 hydrogen atoms, giving 1 : 12-benzperylene-1'-carboxylic acid (IX), the decarboxylation of which yielded 1 : 12-benzperylene, the properties of which agreed with those recorded by Clar (*Ber.*, 1932, 65, 857), who obtained this hydrocarbon by decarboxylation-dehydrogenation of the adduct of perylene and maleic anhydride.

EXPERIMENTAL.

α -2'-(1'-Bromonaphthyl)cinnamitrile.—1-Bromo-2-naphthylacetoneitrile (11.5 g.) was added to a solution of sodium (0.3 g.) in ethyl alcohol (4 c.c.), and benzaldehyde (5.5 g.) slowly added. The whole, heated on a water-bath, with stirring, for a few minutes, became clear and then gelatinous. After cooling, water was added, and the product extracted with ether, washed, dried, and distilled, b. p. 235—245°/0.8 mm. (12 g.). The nitrile crystallised from alcohol in long, silky, colourless needles, m. p. 105—105.5° (Found : C, 68.8; H, 4.0. $C_{19}H_{12}NBr$ requires C, 68.25; H, 3.6%). Hydrolysis with boiling 50% sulphuric acid (10 parts) for 5 hours or with alcoholic potassium hydroxide gave poor yields of α -2'-(1'-bromonaphthyl)-cinnamic acid (I), identical with the acid described later.

The nitrile (5 g.) was slowly added to fused potassium hydroxide (25 g.) at 250—260°; after 5 minutes the mixture was cooled and extracted with water. The tarry product could not be crystallised or distilled. A similar product was obtained by using quinoline as a solvent.

The general method for the synthesis of 3 : 4-benzphenanthrene derivatives is as follows :

Perkin Condensation.—All the Perkin condensations were carried out under similar conditions. Sodium 1-bromo-2-naphthylacetate (1 mol.) (which separated in fine needles when a solution of 1 atom of sodium in alcohol was added to a solution of 1 mol. of the acid in hot alcohol), the appropriate aldehyde (1 mol.), and acetic anhydride (15 mols.) were heated at 130—140° for 7 hours and then poured into a large volume of water. After 18 hours the clear aqueous layer was decanted, and the resinous residue digested several times with $N/2$ -sodium carbonate. The combined alkaline extracts were boiled with charcoal, filtered, and acidified. The acids thus obtained were crystallised from acetic acid. The product obtained by using α -naphthaldehyde gave a very sparingly soluble sodium salt and was worked up in a different manner.

Ring closure. In each case the acid from the Perkin condensation (1 part) was added to fused potassium hydroxide (5 parts) at 230—240° and stirred for 5 minutes; a vigorous reaction then set in and the potassium salt separated as a black oil. After cooling slightly, the still molten potassium hydroxide was poured off from the potassium salt, which was extracted with water (charcoal), the solution filtered and acidified, and the crude acid collected.

Decarboxylation. The 3 : 4-benz-10-phenanthroic acid derivative (1 part) was dissolved in quinoline (10 parts) and heated in an oil-bath at 250—260° for 1 hour with copper bronze (0.5 part). The cooled solution was diluted with ether, filtered, washed with dilute hydrochloric acid and dilute sodium carbonate solution, dried, and evaporated, giving the hydrocarbon in a crude state.

α -2'-(1'-Bromonaphthyl)cinnamic acid (I; R = H), prepared from benzaldehyde and sodium 1-bromo-2-naphthylacetate, separated from acetic acid in colourless needles, m. p. 206—207° (Found : C, 64.8; H, 3.9. $C_{19}H_{13}O_2Br$ requires C, 64.6; H, 3.7%). Yield, 34%.

3 : 4-Benz-10-phenanthroic acid (II, R = H) was obtained in 60% yield by cyclisation of the foregoing acid with fused potassium hydroxide. After purification through the sparingly soluble sodium salt and crystallisation from acetic acid, it formed light yellow needles, m. p. 244—245°, not depressed by an authentic specimen.

α -2'-(1'-Bromonaphthyl)- β -p-tolylacrylic acid, prepared from p-tolualdehyde, crystallised

from acetic acid in fine colourless needles, m. p. 234—235° (Found : C, 65.1; H, 4.2. $C_{20}H_{15}O_2Br$ requires C, 65.4; H, 4.1%). Yield, 33%.

6-Methyl-3 : 4-benz-10-phenanthroic acid. A solution of the crude acid, obtained by cyclisation of the foregoing acid, in acetic acid, was boiled with charcoal, filtered, and concentrated. The acid, which separated on cooling, was sublimed at 250°/0.5 mm.; it then crystallised from acetic acid in bright yellow needles, m. p. 274—275° (Found : C, 83.7; H, 5.0. $C_{20}H_{14}O_2$ requires C, 83.9; H, 4.9%). Yield, 35%.

6-Methyl-3 : 4-benzphenanthrene. The crude hydrocarbon obtained from the above acid (2.4 g.) was distilled from an air-bath at 200°/0.4 mm., forming a yellow glass (1.65 g.) which easily solidified. The picrate separated from methyl alcohol in vermilion needles, m. p. 118—118.5° (Found : C, 63.7; H, 3.7. $C_{19}H_{14}, C_8H_3O_7N_3$ requires C, 63.7; H, 3.6%). Pure 6-methyl-3 : 4-benzphenanthrene, regenerated from the picrate, separated from ethyl alcohol in colourless plates, m. p. 80—81° (Found : C, 94.3; H, 5.8. $C_{19}H_{14}$ requires C, 94.0; H, 6.0%).

α -2'-(1'-Bromonaphthyl)- β -m-tolylacrylic acid (I; R = Me) was obtained from m-tolualdehyde as a sticky solid which, after trituration with and crystallisation from acetic acid, formed small colourless tablets, m. p. 204—205° (Found : C, 65.3; H, 4.2%). Yield, 39%.

7-Methyl-3 : 4-benz-10-phenanthroic acid (II; R = Me) obtained by cyclisation was purified in the same way as the 6-methyl compound; it formed pale yellow needles, m. p. 243—244° (Found : C, 83.8; H, 5.0%). Yield, 28.5%.

7-Methyl-3 : 4-benzphenanthrene. Decarboxylation of the foregoing acid (1 g.) gave a gum, which was distilled from an air-bath at 180°/0.2 mm., giving a colourless viscous oil (0.8 g.). The picrate separated from ethyl alcohol in vermilion needles, m. p. 134—134.5° (Found : C, 63.9; H, 3.8%). 7-Methyl-3 : 4-benzphenanthrene, regenerated from the picrate, crystallised from ethyl alcohol in slender silky needles, m. p. 54—54.5° (Found : C, 94.1; H, 6.1%).

α -2'-(1'-Bromonaphthyl)- β -o-tolylacrylic acid, prepared from o-tolualdehyde, separated from acetic acid as a microcrystalline powder, m. p. 233—235° (Found : C, 65.1; H, 4.1%).

8-Methyl-3 : 4-benz-10-phenanthroic acid, obtained by cyclisation, formed a sparingly soluble sodium salt, which separated from water in colourless plates. The pure acid, regenerated from the salt, crystallised from acetic acid in pale yellow needles, m. p. 269—270° (Found : C, 83.7; H, 4.9%). Yield, 38%.

8-Methyl-3 : 4-benzphenanthrene. The distilled hydrocarbon (0.95 g.) obtained from the foregoing acid (1.3 g.) was converted into the picrate, which separated from ethyl alcohol in long, bright red needles, m. p. 107—108° (Found : C, 63.8; H, 3.7%). Pure 8-methyl-3 : 4-benzphenanthrene, recovered from the picrate and distilled from an air-bath at 200°/0.3 mm., crystallised from alcohol in colourless plates, m. p. 65—66° (Found : C, 94.2; H, 5.9%).

α -2-(1-Bromonaphthyl)- β -1'-naphthylacrylic acid (III). The resin arising from the Perkin condensation with α -naphthaldehyde was dissolved in ether and filtered from an insoluble neutral substance, which separated from acetic acid in long colourless needles, m. p. 187—188° (Found : C, 58.9; H, 3.6%). This substance has not yet been identified; it was recovered unchanged after boiling for 5 hours with alcoholic potassium hydroxide solution and also after fusion with potassium hydroxide at 230—240°. The ethereal solution was shaken with sodium carbonate solution; the very sparingly soluble sodium salt of the acid then separated. The regenerated acid crystallised from acetic acid, in which it was very sparingly soluble, in yellow tablets, m. p. 267—268° (Found : C, 68.3; H, 3.85. $C_{23}H_{15}O_2Br$ requires C, 68.5; H, 3.75%). Yield, 24%.

1 : 2 : 5 : 6-Dibenz-9-phenanthroic acid (IV; R = CO_2H). The crude acid from the cyclisation of the foregoing acid was sublimed at 300°/0.4 mm. and crystallised from acetic acid, the pure acid separating in light yellow needles, m. p. 309—310° (Found : C, 85.2; H, 4.4. $C_{23}H_{14}O_2$ requires C, 85.3; H, 4.5%). Yield, 46%.

1 : 2 : 5 : 6-Dibenzphenanthrene. The crude hydrocarbon from the decarboxylation was distilled (yield, 1.5 g. from 1.9 g. of the acid) and converted into the picrate, which after two crystallisations from acetic acid containing picric acid formed reddish-orange needles, m. p. 126.5—127° (Found : C, 66.3; H, 3.5. $C_{22}H_{14}, C_8H_3O_7N_3$ requires C, 66.25; H, 3.4%). The picrate dissociated when dissolved in 80% acetic acid and the hydrocarbon separated in colourless needles which, after a further crystallisation from glacial acetic acid, had m. p. 126—127° (Found : C, 94.8; H, 5.3. $C_{22}H_{14}$ requires C, 94.9; H, 5.1%).

1 : 2 : 3 : 4-Tetrahydro-6-naphthaldehyde. 6-Acetyltetralin (Scharwin, *loc. cit.*) (38.2 g.) was boiled for 6 hours with a solution of sodium hypochlorite prepared from sodium hydroxide (110 g.) in water (1.5 l.) and chlorine (from 78 g. of potassium permanganate). After cooling,

unchanged acetyltetralin was extracted with ether, and the alkaline solution acidified. The unchanged material was again treated with sodium hypochlorite, and a further amount of acid obtained. Combined yield, 74%. The acid chloride (126 g.), obtained by refluxing the acid (115.5 g.) with thionyl chloride (300 c.c.), was converted, by treatment with aniline (126 g.) in chloroform (450 c.c.), into the anilide (153 g.) which formed colourless needles (from methyl alcohol), m. p. 146—147° (Scharwin, *loc. cit.*, p. 2902, gives m. p. 141°) (Found: C, 81.3; H, 7.2. Calc. for $C_{17}H_{17}ON$: C, 81.2; H, 6.8%).

The anilide (75 g.) was converted into the iminochloride by heating with phosphorus pentachloride (109.5 g.) in tetrachloroethane (330 c.c.) at 150° for $\frac{1}{2}$ hour. After removal of phosphorus oxychloride and the solvent, the residue was dissolved in a little tetrachloroethane and added to a solution of stannous chloride (240 g.) in a saturated solution of hydrogen chloride in ether (1.5 l.), cooled in ice. After remaining for 4 hours in ice and for 16 hours at the ordinary temperature, the ether and tetrachloroethane were removed with steam, and the residue hydrolysed with dilute hydrochloric acid. The crude aldehyde was extracted with ether, purified through its bisulphite compound, and steam-distilled; b. p. 150°/13 mm. (29.2 g.). Its semicarbazone, m. p. 228° (lit., 223°), separated from ethyl alcohol, in which it was sparingly soluble, in small needles.

α -2-(1-Bromonaphthyl)- β -6'-(1' : 2' : 3' : 4'-tetrahydronaphthyl)acrylic acid (V). The acid arising from the Perkin condensation with the foregoing aldehyde formed a white microcrystalline powder, m. p. 206—207°, after crystallisation from acetic acid (Found: C, 67.8; H, 4.7. $C_{23}H_{19}O_2Br$ requires C, 67.8; H, 4.7%). Yield, 22%.

Ring closure. The crude acid arising from the ring closure of the foregoing acid (16 g.) was dissolved in hot aqueous sodium carbonate, the solution filtered and cooled, and the sodium salt, which separated as a brown, almost gelatinous mass, collected. This was dissolved in water (charcoal), the filtered solution acidified, and the precipitate extracted with ether. The washed and dried extract was evaporated to dryness, the residue triturated with benzene, and the solid which separated filtered off and sublimed at 260°/3 mm. (4.3 g.). Crystallisation from xylene gave 0.6 g. of light yellow needles, m. p. 286—287°, which were shown to be 3 : 4-benz-5 : 6-tetramethylene-10-phenanthroic acid (VIII) (Found: C, 83.9; H, 5.4. $C_{23}H_{18}O_2$ requires C, 84.6; H, 5.6%). The xylene liquor of this acid was evaporated to dryness, and the residue crystallised once from acetic acid; m. p. 238—240°, clear at 243° (3.5 g.). Repeated crystallisation from acetic acid failed to improve the m. p. This was shown to be essentially 5 : 6 : 7 : 8-tetrahydro-1 : 2-(1' : 2'-naphtha)-3-anthroic acid (VI) (Found: C, 84.9; H, 5.5. $C_{23}H_{18}O_2$ requires C, 84.6; H, 5.6%).

1 : 2-(1' : 2'-Naphth)anthracene (VII). 5 : 6 : 7 : 8-Tetrahydro-1 : 2-(1' : 2'-naphtha)-3-anthroic acid (2.6 g.) was dehydrogenated with sulphur (0.6 g.) at 270° for $1\frac{1}{2}$ hours. The cooled mass was dissolved in warm dilute aqueous sodium carbonate, the filtered solution acidified, and the crude acid collected and dried. After sublimation at 300°/0.2 mm. and crystallisation from xylene the acid formed bright yellow needles (0.7 g.), m. p. 284—285° (Found: C, 85.45; H, 4.3. $C_{23}H_{14}O_2$ requires C, 85.3; H, 4.5%).

Decarboxylation gave a solid crude hydrocarbon, which was distilled at 200—210°/0.2 mm. (0.5 g.) and converted into the dipicrate, m. p. 147—148°, in acetic acid, from which the hydrocarbon, m. p. 135—136°, was regenerated. Oxidation of the hydrocarbon (50 mg.) with sodium dichromate (100 mg.) in boiling acetic acid (2 c.c.) (1 hour) gave a quinone, which was purified by reduction with zinc and boiling dilute sodium hydroxide solution to a deep red vat, from which the quinone was regenerated by shaking with air. 1 : 2-(1' : 2'-Naphth)anthraquinone was sublimed at 250°/0.3 mm.; it then crystallised from xylene in yellow needles, m. p. 273—274° (Found: C, 85.4; H, 4.0. $C_{22}H_{12}O_2$ requires C, 85.7; H, 3.8%). The pure quinone was reduced by the two-stage method of Cook (J., 1932, 468) to 1 : 2-(1' : 2'-naphth)anthracene, which separated from acetic acid in long, slightly yellow needles, m. p. 137—138° (Found: C, 95.0; H, 5.0. $C_{22}H_{14}$ requires C, 94.9; H, 5.1%). The pure dipicrate separated from acetic acid in deep purplish-red needles, m. p. 148—149° (Found: C, 55.7; H, 2.9. $C_{22}H_{14}, 2C_6H_5O_7N_3$ requires C, 55.4; H, 2.75%).

3 : 4-Benz-5 : 6-tetramethylene-10-phenanthroic acid (0.4 g.) was dehydrogenated with sulphur (0.1 g.) in quinoline (1 c.c.) at 240° for 3 hours. The cooled solution was boiled with dilute hydrochloric acid and filtered, the product boiled with dilute sodium carbonate solution, and the very sparingly soluble sodium salt, which was the main product, collected. The regenerated acid was sublimed at 300°/0.3 mm., a trace of material which came off at 250°/0.2 mm. being rejected. The sublimate was boiled with xylene to remove colouring matter and then formed a yellow powder (0.13 g.). 30 Mg., recrystallised from 200 c.c. of acetic acid, formed yellow

microscopic needles, m. p. 357—358° (Found : C, 85.5; H, 4.0. $C_{23}H_{12}O_2$ requires C, 86.2; H, 3.8%), of 1 : 12-benzperylene-1'-carboxylic acid (IX). Decarboxylation of the acid yielded 1 : 12-benzperylene; this separated from benzene in yellow plates, m. p. 269—270°, which gave an emerald-green colour with concentrated sulphuric acid (cf. Clar, *loc. cit.*). Its picrate separated from benzene in purplish needles, m. p. 266—267° (Found : C, 66.8; H, 3.0. Calc. : C, 66.5; H, 3.0%). Clar gives m. p. 267°.

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

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