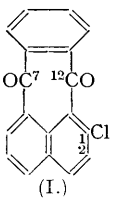
355. *Polycyclic Aromatic Amines. Part I.*

By G. M. Badger.

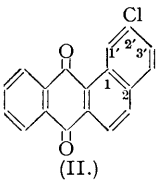
1-Chloropleiadene-7 : 12-dione (I) has been condensed with toluene-*p*-sulphonamide, and the product rearranged into 2′-*amino*-1 : 2-*benzanthraquinone*, which has been reduced to 2′-*amino*-1 : 2-*benzanthracene* (IV). The Friedel–Crafts reaction with 2-chloronaphthalene and phthalic anhydride has given two chloronaphthoylbenzoic acids, which have been cyclised to 2′-chloro-1 : 2-benzanthraquinone (II) and 3′-*chloro*-1 : 2-*benzanthraquinone*, respectively; (II) is evidently identical with the chlorobenzanthraquinone, described as 2′-chloro-2 : 3-benzanthraquinone (III), which Heller (*Ber.*, 1912, **45**, 665; 1913, **46**, 1497) obtained by the same series of reactions. 2′-Chloro-2 : 3-benzanthraquinone is still unknown.*

Experimental evidence that β-naphthylamine may be responsible for some of the cancers of the bladder to which operatives engaged in the manufacture of dye intermediates are somewhat liable has been provided by the production of such tumours in dogs by administration, over several years, of massive doses of β-naphthylamine. A variety of other types of tumour has also been produced in experimental animals by 2-aminofluorene, 2-acetamidofluorene, and 2-aminoanthracene (compare Bielschowsky, *Brit. Med. Bull.*, 1947, **4**, 382). It will be noted that in all these compounds the substituent is in a β-position of a fused-ring system. It seemed of interest to examine further compounds of this class, and in particular amino-derivatives of 1 : 2-benzanthracene, a hydrocarbon from which many of the known carcinogenic hydrocarbons are derived. The present communication describes the synthesis of 2′-*amino*-1 : 2-*benzanthracene* (IV).

1-Chloropleiadene-7 : 12-dione (I) is readily available (Fieser, *J. Amer. Chem. Soc.*, 1931, **53**, 3546), and may be rearranged, in good yield, by treatment with concentrated sulphuric acid, into 2′ chloro-1 : 2-benzanthraquinone (II) (Fieser and Fieser, *ibid.*, 1933, **55**, 3342). First attempts were therefore made to prepare the 2′-amino-compound from this chlorobenzanthraquinone by treatment with toluene-*p*-sulphonamide under conditions in which Ullmann and Fodor (*Annalen*, 1911, **380**, 317) converted 1-chloroanthraquinone into the corresponding toluene-*p*-sulphonamido-derivative, but no reaction occurred. Furthermore, 2′-*chloro*-1 : 2-*benzanthracene*, obtained from the quinone by reduction, was likewise recovered unchanged following the same treatment. 1-Chloropleiadene-7 : 12-dione, however, condensed readily with toluene-*p*-sulphonamide, 1-*toluene*-p-*sulphonamidopleiadene*-7 : 12-*dione* being isolated in satisfactory yield. Mild treatment with sulphuric acid gave 1-*aminopleiadene*-7 : 12-*dione*, the product of hydrolysis without rearrangement; but more vigorous treatment with concentrated sulphuric acid (compare B.P. 375,305) gave the deep purple 2′-*amino*-1 : 2-*benzanthraquinone*, the product of both hydrolysis and rearrangement. The constitution of this substance was proved by its conversion into the known 2′-hydroxy-1 : 2-benzanthraquinone (Fieser and Fieser, *loc. cit.*; Badger, *J.*, 1947, 940), by the method which Bachmann and Boatner (*J. Amer. Chem. Soc.*, 1936, **58**, 2194) used for the preparation of phenanthrols from the corresponding aminophenanthrenes. Reduction of the aminobenzanthraquinone with zinc dust and ammonia in the usual way gave the desired 2′-amino-1 : 2-benzanthracene (IV).



(I.)



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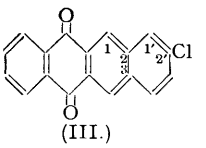

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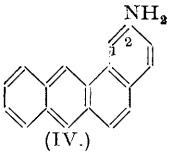


(IV.)

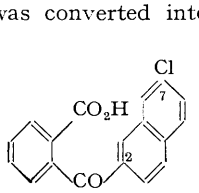
Fieser and Fieser (*loc. cit.*) have suggested that the chlorobenzanthraquinone which Heller (*loc. cit.*) obtained by cyclisation of the chloronaphthoylbenzoic acid resulting from the Friedel–Crafts reaction between 2-chloronaphthalene and phthalic anhydride, is not 2′-chloro-2 : 3-benzanthraquinone (III) but 2′-chloro-1 : 2-benzanthraquinone (II). At first Heller (*Ber.*, 1912, **45**, 665) considered his product to be 4-chloro-1 : 2-benzanthraquinone, but (*Ber.*, 1913, **46**, 1497) retracted this when he found that it gave an anthraquinonedicarboxylic acid on oxidation. Heller supposed this acid to be the 2 : 3-derivative but Fieser and Fieser (*loc.*

* *Added October 18th*, 1948.—Marschalk and Dassigny (*Bull. Soc. chim.*, 1948, **15**, 812), in a paper dated April 28th, 1948, have also studied the Friedel–Crafts reaction between 2-chloronaphthalene and phthalic anhydride. Their results (without experimental details) are similar to those reported here.

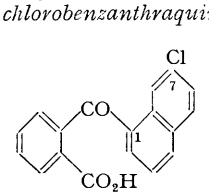
cit.) pointed out that the evidence given does not exclude the 1 : 2-dicarboxylic acid. In order to clarify this position the reaction between 2-chloronaphthalene and phthalic anhydride has been reinvestigated.

When carried out either in *s*-tetrachloroethane or in benzene solution a mixture of acids was obtained. Following the work of Heller, one of these was readily isolated in a fairly pure condition by recrystallisation of the crude product from acetic acid, the isomeric acids remaining in solution. In the present instance, further purification was achieved by the conversion of the acid into the *acetoxy-lactone*, followed by hydrolysis. This acid must be either 7-chloro-2-naphthoyl-*o*-benzoic acid (V) or 7-chloro-1-naphthoyl-*o*-benzoic acid (VI), for on cyclisation it gave 2′-chloro-1 : 2-benzanthraquinone (II), identical with a specimen prepared by rearrangement of 1-chloropleiadene-7 : 12-dione with concentrated sulphuric acid by the method of Fieser and Fieser (*loc. cit.*). It must be concluded therefore that Heller was in error in attributing the structure (III) to his product. It is of some interest that cyclisation of this chloronaphthoylbenzoic acid (V or VI) with molten aluminium chloride–sodium chloride also gave 2′-chloro-1 : 2-benzanthraquinone, for Weizmann, Bergmann, and Bergmann (*J.*, **1935**, 1367) found that 1-*o*-naphthoylbenzoic acid rearranges under these conditions to give naphthacenequinone.

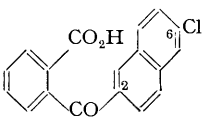
Heller (*loc. cit.*) isolated only one chloronaphthoylbenzoic acid from the mixture of crude acids, for attempts to purify the acids by recrystallisation of the free acid, or of its salts, were unsuccessful. In the present work the crude mixture obtained after the removal of the above isomeric acid was treated with acetic anhydride and pyridine, and a pure *acetoxy-lactone* was easily obtained by recrystallisation. Hydrolysis gave a *chloronaphthoylbenzoic acid*, which was converted into a *chlorobenzanthraquinone*. Only four chlorobenzanthraquinones could



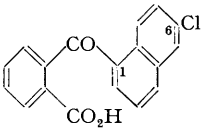
(V.)



(VI.)



(VII.)



(VIII.)

theoretically be obtained from 2-chloronaphthalene and phthalic anhydride. One is 2′-chloro-2 : 3-benzanthraquinone (III), and there are three 1 : 2-benzanthraquinones, namely, the 2′-, 3′-, and 4-chloro-derivatives. As the chlorobenzanthraquinone gave an alkaline vat without difficulty, and as the *chlorobenzanthracene* obtained from it by reduction was found to be colourless, 2′-chloro-2 : 3-benzanthraquinone would appear to be excluded, although evidence for its formation in small quantity, as a by-product of the cyclisation, was obtained. The 2′-chloro-1 : 2-benzanthraquinone structure was excluded by comparison with an authentic specimen. It was therefore concluded that the chlorobenzanthraquinone must be either the 3′- or the 4-chloro-isomer. It was found that no reaction took place with toluene-*p*-sulphonamide; the 4-isomer might be expected to react, for 1-chloroanthraquinone readily undergoes this reaction (Ullmann and Fodor, *loc. cit.*). In order to exclude the 4-isomer completely, the chlorobenzanthracene, obtained from the quinone by reduction, was converted into the corresponding *cyanobenzanthracene*, and hydrolysed to the *carboxybenzanthracene* by Newman and Orchin's method (*J. Amer. Chem. Soc.*, **1939**, **61**, 244). This carboxybenzanthracene, and the *carboxybenzanthraquinone* obtained from it by oxidation, were found to differ from 1 : 2-benz-4-anthroic acid and 1 : 2-benzanthraquinone-4-carboxylic acid (Cook, *J.*, **1931**, 2524). It must therefore be concluded that cyclisation of the second acid, which must have the structure (VII) or (VIII), gave 3′-chloro-1 : 2-benzanthraquinone.

The product obtained on reduction of the crude chlorobenzanthraquinone was bright yellow. This colour was evidently due to the presence of a small quantity of 2′-chloro-2 : 3-benzanthracene, for it was readily removed by a short treatment with maleic anhydride. Furthermore, the absorption spectrum of the crude product showed a band associated with a substituted 2 : 3-benzanthracene (see Clar, " Aromatische Kohlenwasserstoffe," Springer, **1941**).

Experimental.

1-*Toluene*-p-*sulphonamidopleiadene*-7 : 12-*dione*.—A mixture of 1-chloropleiadene-7 : 12-dione (10 g., Fieser and Fieser, *loc. cit.*), toluene-*p*-sulphonamide (10 g.), anhydrous potassium carbonate (8 g.), copper acetate (0·4 g.), copper bronze (0·2 g.), and nitrobenzene (75 c.c.) was heated at 180—190° for 3½ hours. The nitrobenzene was removed in steam, and the residue recrystallised from acetic acid. 1-*Toluene*-p-*sulphonamidopleiadene*-7 : 12-*dione* (10·2 g.) formed small yellow plates, m. p. 211—213° (Found: C, 70·2; H, 4·1. $C_{25}H_{17}O_4NS$ requires C, 70·3; H, 4·0%).

1-*Aminopleiadene*-7 : 12-*dione*.—A mixture of the above toluene-*p*-sulphonamido-compound (1 g.) and concentrated sulphuric acid (10 c.c.) was kept at 30—40° for 1 hour, then poured into water; the product was collected and recrystallised from alcohol. 1-*Aminopleiadene*-7 : 12-*dione* (0·6 g.) formed orange-yellow prisms, m. p. 193—195° (Found: C, 79·3; H, 4·1. $C_{18}H_{11}O_2N$ requires C, 79·1; H, 4·0%).

2′-*Amino*-1 : 2-*benzanthraquinone*.—The above toluene-*p*-sulphonamido-compound (5 g.) was heated at 160° with concentrated sulphuric acid (50 c.c.) for ¼ hour, and the solution poured into water. The yellow salt was collected and washed on the filter with dilute sodium hydroxide until it had all been converted into the purple base. 2′-*Amino*-1 : 2-*benzanthraquinone* formed long, shining, deep purple needles, from toluene, m. p. 204—205° (Found: C, 79·1; H, 4·0. $C_{18}H_{11}O_2N$ requires C, 79·1; H, 4·0%). The quinone gave a dark red-brown solution in concentrated sulphuric acid, and it readily gave a red-brown vat with alkaline hydrosulphite (dithionite).

Proof of constitution. A solution of 2′-amino-1 : 2-benzanthraquinone (2 g.) in pyridine (20 c.c.) was added dropwise, with stirring, to a mixture obtained by adding sodium nitrite (1·5 g.) to a mixture of water (7·5 c.c.) and sulphuric acid (15 c.c.). The temperature was kept below 5° during the addition. After 2 hours the mixture was diluted with a large volume of water, urea was added, and the whole heated until gas evolution ceased. The product was collected, sublimed at 230°/0·1 mm., and recrystallised from alcohol. It formed red crystals, m. p. 251°, not depressed by admixture with an authentic specimen of 2′-hydroxy-1 : 2-benzanthraquinone.

2′-*Amino*-1 : 2-*benzanthracene*.—Finely divided 2′-amino-1 : 2-benzanthraquinone (1 g.) was reduced by 12 hours' boiling with zinc dust (3 g.), ammonium hydroxide (*d* 0·880; 15 c.c.), and water (60 c.c.). The insoluble material was dried, and sublimed from the zinc at 180°/0·1 mm. In some runs the sublimate was purple, owing to unchanged quinone. This was removed by treatment with a boiling solution of sodium hydroxide–sodium hydrosulphite (dithionite), followed by rapid filtration. The residue was then washed, dried, and recrystallised from benzene. 2′-*Amino*-1 : 2-*benzanthracene* (0·6 g.) formed yellow plates, from benzene, m. p. 162·5—164·5° (Found: C, 88·8; H, 5·25. $C_{18}H_{13}N$ requires C, 88·9; H, 5·35%). Solutions of the amine were strongly fluorescent in daylight, and rapidly became dark if exposed to light and air.

Chloronaphthoylbenzoic Acids.—A mixture of 2-chloronaphthalene (12 g.), phthalic anhydride (11 g.), aluminium chloride (22 g.), and *s*-tetrachloroethane (100 c.c.) was allowed to stand in ice, with shaking, for 3 hours, and then at room temperature for 24 hours. Finally, the mixture was heated on a steam-bath for 1 hour. After decomposition with ice and hydrochloric acid in the usual way, the product was extracted with warm dilute sodium carbonate (charcoal), and the crude acid (23·6 g.) precipitated with hydrochloric acid. Recrystallisation from acetic acid (charcoal) gave *o*-7-chloro-1(or 2)-naphthoylbenzoic acid (V or VI) (3·6 g.), m. p. 216—218° (Heller gives m. p. 225—227° for the pure acid). A sample of the acid (1·4 g.) was converted into the *acetoxy-lactone* by heating on the steam-bath for 2 hours with pyridine (9 c.c.) and acetic anhydride (3·5 c.c.). It formed colourless prisms from alcohol, m. p. 168—170° (Found: C, 68·4: H, 3·7. $C_{20}H_{13}O_4Cl$ requires C, 68·1; H, 3·7%). The pure acid was obtained by hydrolysis of the lactone with alcoholic sodium hydroxide, followed by recrystallisation from acetic acid.

The liquors from the first acetic acid crystallisation of the crude product gave, on addition of water, a gummy acid which, after drying, was treated with pyridine (120 c.c.) and acetic anhydride (40 c.c.) for 2 hours on the steam-bath. After being poured into water, a brown gum was obtained, which crystallised on treatment with a little alcohol and benzene. After being washed with alcohol, the solid was recrystallised from alcohol (charcoal) and gave almost colourless crystals, m. p. 130—131° (7·4 g.). After further recrystallisation from alcohol and from benzene, the pure *acetoxy-lactone* formed colourless elongated prisms, m. p. 132—134° (Found: C, 68·3; H, 3·7. $C_{20}H_{13}O_4Cl$ requires C, 68·1; H, 3·7%). Hydrolysis of this acetoxy-lactone followed by recrystallisation from benzene gave o-6-*chloro*-2 (or 1)-*naphthoylbenzoic acid*, (VII) or (VIII), as colourless prisms, m. p. 174—175·5° (Found: C, 69·6; H, 3·7. $C_{18}H_{11}O_3Cl$ requires C, 69·6; H, 3·5%). Similar results were obtained when the Friedel–Crafts reaction was carried out in benzene solution.

2′-*Chloro*-1 : 2-*benzanthraquinone*.—A mixture of the above acid (m. p. 218°, 0·5 g.) and concentrated sulphuric acid (5 c.c.) was heated at 60—70° for 6 hours. The product, obtained as a bright yellow powder on pouring into water, was extracted with boiling sodium carbonate, washed, and recrystallised from acetic acid. 2′-Chloro-1 : 2-benzanthraquinone formed bright yellow needles, m. p. 235—236°, alone, or mixed with an authentic specimen prepared by Fieser and Fieser's method (*loc. cit.*). It readily gave a red vat with alkaline hydrosulphite. The same quinone was also obtained when the acid (1 g.) was cyclised by heating with aluminium chloride (10 g.) and sodium chloride (2 g.) for 1 hour at 140°.

2′-*Chloro*-1 : 2-*benzanthracene*.—A mixture of the quinone (5·2 g.), stannous chloride (5 g.), acetic acid (100 c.c.), and concentrated hydrochloric acid (30 c.c.) was refluxed for 1 hour, cooled, diluted with water, and the solid filtered off; it was refluxed with 2N-sodium hydroxide (100 c.c.) and zinc dust (10 g.) for 3 hours (Badger and Cook, *J.*, 1939, 802). 2′-*Chloro*-1 : 2-*benzanthracene* (4·02 g.) formed colourless plates from acetic acid, m. p. 161·5—162·5° (Found: C, 82·35; H, 4·3. $C_{18}H_{11}Cl$ requires C, 82·3; H, 4·2%).

The *picrate*, prepared in acetic acid with excess of picric acid, dissociated on attempted recrystallisation from acetic acid, but was recrystallised from benzene. It formed red needles, m. p. 166·5—167° (Found: C, 58·7; H, 2·7. $C_{24}H_{14}O_7N_3Cl$ requires C, 58·6; H, 2·85%).

3′-*Chloro*-1 : 2-*benzanthraquinone*.—A mixture of *o*-6-chloro-2 (or 1)-naphthoylbenzoic acid (m. p. 175°, 0·5 g.) was heated at 95° with concentrated sulphuric acid (5 c.c.) for 3 hours. Recrystallised from acetic acid, and from benzene, 3′-*chloro*-1 : 2-*benzanthraquinone* (0·35 g.) formed fine yellow needles, m. p. 213—215° (Found: C, 73·9; H, 3·15. $C_{18}H_9O_2Cl$ requires C, 73·9; H, 3·1%). It readily formed a red vat with alkaline hydrosulphite. A mixed m. p. with 2′-chloro-1 : 2-benzanthraquinone was *ca.* 180°.

3′-*Chloro*-1 : 2-*benzanthracene*.—The above chlorobenzanthraquinone (3·0 g.) was reduced by the stannous chloride–zinc and alkali method as described for the 2′-isomer. The crude product (1·9 g.) formed bright yellow plates from acetic acid, and showed a brilliant green-yellow fluorescence in ultra-

violet light, but its solution in benzene was not fluorescent. A semi-quantitative examination of the absorption spectrum showed an absorption band at 4775 A., as might be expected from a 2 : 3-benzanthracene derivative. The crude product, however, was readily decolourised by a few minutes' boiling with a little maleic anhydride in xylene solution, followed by the removal of the xylene with steam in the presence of dilute sodium hydroxide. There was no significant loss of material by this purification process. The pure *3'-chloro-1 : 2-benzanthracene* formed colourless plates from acetic acid, m. p. 175—177° (Found : C, 82·25; H, 4·2. $C_{18}H_{11}Cl$ requires C, 82·3; H, 4·2%).

3'-Cyano-1 : 2-benzanthracene.—A mixture of 3'-chloro-1 : 2-benzanthracene (0·9 g.), cuprous cyanide (0·5 g.), acetonitrile (1 c.c.), and pyridine (3 c.c.) was heated in a sealed tube at 230—240° for 48 hours. The neutral product was purified by sublimation at 180°/0·1 mm. and formed fawn needles, m. p. 181·5—182·5° from acetic acid (yield 0·47 g.) (Found : C, 89·9; H, 4·6. $C_{19}H_{11}N$ requires C, 90·1; H, 4·4%). Its solutions showed an intense blue fluorescence in daylight. Oxidation of this *cyanobenzanthracene* (0·1 g.) with sodium dichromate (0·5 g.) in acetic acid (10 c.c.) gave *3'-cyano-1 : 2-benzanthraquinone* as fine yellow needles, m. p. 307—308°, from acetic acid (Found : C, 80·6; H, 3·1. $C_{19}H_9O_2N$ requires C, 80·6; H, 3·2%).

3'-Carboxy-1 : 2-benzanthracene.—A solution of the above 3'-cyano-1 : 2-benzanthracene (0·25 g.) in acetic acid (35 c.c.) and 70% sulphuric acid (7 c.c.) was refluxed for 6 hours. The *acid* separated from acetic acid, or from xylene, as a microcrystalline powder, m. p. 290°, after darkening (Found : C, 83·7; H, 4·3. $C_{19}H_{12}O_2$ requires C, 83·3; H, 4·4%). A mixed m. p. with 1 : 2-benz-4-anthroic acid (m. p. 281°; Cook *J.*, 1931, 2524) was 240—250°. Oxidation of this carboxybenzanthracene (0·1 g.) with sodium dichromate (0·5 g.) in acetic acid (10 c.c.) gave *3'-carboxy-1 : 2-benzanthraquinone*, as yellow microprisms, from tetrahydrofurfuryl alcohol, m. p. 345°, after darkening and sintering (Found : C, 75·3; H, 3·3. $C_{19}H_{10}O_4$ requires C, 75·5; H, 3·3%) [4-carboxy-1 : 2-benzanthraquinone has m. p. 292—293° (decomp.); Cook, *loc. cit.*].

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