ANTHRAQUINONE AND ANTHRONE SERIES

Part XIII. Synthesis of 5-Substituted Benzanthrones

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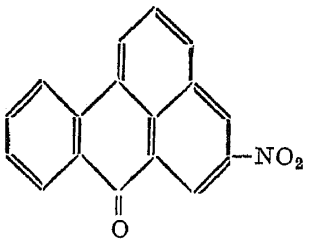
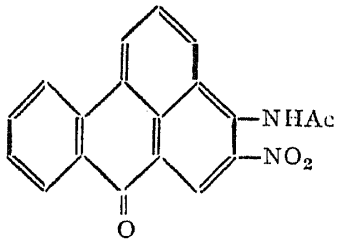
Received June 3, 1953

The only 5-monosubstituted benzanthrone derivative to which a reference can be found in the literature is 5-nitrobenzanthrone, prepared by Boyes, Grieve and Rule[1] by a tedious route. Methyl 8-bromo-3-nitro-1-naphthoate was condensed with methyl *o*-iodobenzoate to form methyl 3-nitro-8-(*o*-carbomethoxyphenyl)-1-naphthoate; cyclization with sulphuric acid gave 5-nitrobenzanthrone-11-carboxylic acid, which was finally decarboxylated to 5-nitrobenzanthrone. Boriani[2] has mentioned a benzanthrone sulphonic acid obtained by sulphonation of benzanthrone and he considered that the sulphonic group probably entered the 5-position. The monosulphonation of benzanthrone has been studied by Pritchard and Simonsen[3] and Ioffe and Pavlova,[4] who have shown that the main product is the 9-sulphonic acid, the 3-sulphonic acid being formed to a very small extent. According to a German patent[5] 5-hydroxybenzanthrone is produced when 2-hydroxyanthranol, prepared from 2-hydroxyanthraquinone by reduction with zinc dust and ammonia, is heated with sulphuric acid and glycerine; the product, however, was later shown by Perkin[6, 7] to be 4-hydroxybenzanthrone. Two disubstituted benzanthrones in which one substituent is in the 5-position have been described. Waldmann *et al.*[8] synthesized 4:5-dihydroxybenzanthrone from 2:3-dihydroxyanthraquinone (hystazarin); the 5:6-isomer was prepared by the Scholl cyclization of 2:3-dihydroxy-1-benzoylnaphthalene and also by the action of glycerol and sulphuric acid on alizarin.

5-Nitrobenzanthrone (I) has now been synthesized by taking advantage of the powerful directing influence of the acetamido group. Nitration of 4-acetamidobenzanthrone with fuming nitric acid in glacial acetic acid gave 4-acetamido-5-nitrobenzanthrone (II). Deacetylation of (II) with alcoholic sulphuric acid proceeded in quantitative yield, and the constitution of the product as 4-amino-5-nitrobenzanthrone was established by reduction with methanolic sodium sulphide to a diamine which condensed with phenanthraquinone to a quinoxaline. The adjacent orientation of the

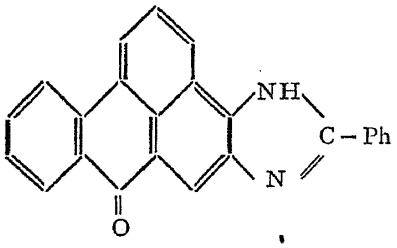


(I)



(II)

amino groups was also shown by the ready formation of the corresponding phenylimidazole (III) when the diamine was treated with benzoyl chloride.



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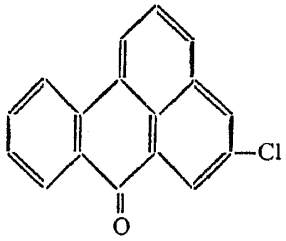

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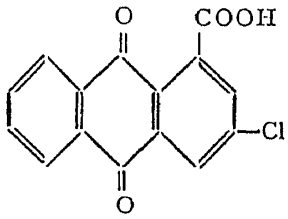

(V)

On diazotizing 4-amino-5-nitrobenzanthrone with sulphuric acid and sodium nitrite and refluxing the diazonium sulphate with alcohol, deamination took place to give 5-nitrobenzanthrone (I). Reduction of (I) with methanolic sodium sulphide gave 5-aminobenzanthrone from which 5-chlorobenzanthrone (IV) was prepared by the Sandmeyer reaction. Oxidation of this chlorobenzanthrone with chromic anhydride in acetic acid led to 3-chloroanthraquinone-1-carboxylic acid (V), identical with an authentic sample synthesized by an unambiguous route.[9] Oxidation of 5-nitrobenzanthrone gave 3-nitroanthraquinone-1-carboxylic acid.

EXPERIMENTAL

4-Acetamido-5-nitrobenzanthrone

4-Hydroxybenzanthrone was prepared by the action of potassium hydroxide and potassium chlorate on benzanthrone in the presence of anthraquinone according to the procedure described by Bradley and Jadhav.[10] Ammonolysis of 4-hydroxybenzanthrone according to Perkin and Spencer[7] gave 4-aminobenzanthrone, which was crystallized from chlorobenzene. Acetylation of 4-aminobenzanthrone was effected by heating the finely powdered substance (20 g.) with acetic anhydride (60 c.c.) on a low flame for 2 mins.; a yellow crystalline compound separated, which was washed with ether and dried (22 g.). The m.p. (264–65°) agreed with the m.p. cited for the monoacetyl derivative by Perkin.[7]

4-Acetamidobenzanthrone (20 g.) was heated on a water-bath with glacial acetic acid (1100 c.c.) under stirring. A solution of fuming nitric acid (d. 1·49; 12 c.c.) in glacial acetic acid (30 c.c.) was quickly added and stirring continued for 20 mins., when yellow needles (18·3 g.) separated. This substance was filtered off while the mixture was hot, and washed with hot acetic acid. On crystallization from nitrobenzene, 4-acetamido-5-nitrobenzanthrone was obtained as yellow needles, m.p. 312° (Found: C, 68·8; H. 3·6; N, 8·6. $C_{19}H_{12}N_2O_4$ requires C, 68·7; H, 3·6; N, 8·4%).

4-*Amino-5-nitrobenzanthrone*

A solution of 4-acetamido-5-nitrobenzanthrone (15 g.) in conc. sulphuric acid (150 c.c.) and 95% alcohol (750 c.c.) was refluxed for 4 hours and diluted with water. The precipitate was collected, washed free from acid and dried (13 g.). On crystallization from nitrobenzene 4-amino-5-nitrobenzanthrone was obtained as golden yellow silky needles, m.p. 347–48° (Found: C, 70·2; H, 3·4; N, 9·5. $C_{17}H_{10}N_2O_3$ requires C, 70·3; H, 3·5; N, 9·7%).

4 : 5-*Diaminobenzanthrone*

Finely powdered 4-amino-5-nitrobenzanthrone (5 g.) was refluxed under stirring with 10% alcoholic sodium sulphide (110 c.c.) for 6 hours. A deep red crystalline mass separated and was filtered, washed with hot water and dried (4·2 g.). Two crystallizations from *o*-dichlorobenzene gave deep red shining needles which decomposed without melting at 257–58° (Found: C, 78·6; H, 4·5; N, 10·7. $C_{17}H_{12}N_2O$ requires C, 78·4; H, 4·6; N, 10·8%).

4 : 5-*Diacetamidobenzanthrone*

To a clear solution of 4: 5-diaminobenzanthrone (0·2 g.) in hot glacial acetic acid (7 c.c.) acetic anhydride (0·8 c.c.) was added and the solution refluxed for 30 mins. On cooling minute yellow needles separated (0·2 g.). Crystallization from nitrobenzene gave microscopic yellow needles, m.p. 332–33° (*dec.*) (Found: C, 73·8; H, 4·6; N, 8·7. $C_{21}H_{16}N_2O_3$ requires C, 73·3; H, 4·6; N, 8·3%).

Condensation of 4: 5-*diaminobenzanthrone with phenanthraquinone*

A solution of 4: 5-diaminobenzanthrone (2·5 g.) and phenanthraquinone (2 g.) in alcohol (350 c.c.) was refluxed for 30 mins. The quinoxaline (3·8 g.) crystallized from nitrobenzene in yellow needles, m.p. 403–4° (Found: C, 85·9; H, 3·7; N, 6·5. $C_{31}H_{16}N_2O$ requires C, 86·1; H, 3·7; N, 6·5%).

Conversion of 4: 5-*diaminobenzanthrone into imidazole* (*III*)

Method (*a*).—The diamine (0·2 g.) was refluxed with benzoyl chloride (3 c.c.) for 15 minutes. A change in colour from red to yellow occurred.

The mixture was cooled, dropped into crushed ice and kept overnight. The yellow precipitate was filtered, washed with dilute ammonia, and dried (0·26 g.). Crystallization from nitrobenzene (30 c.c.) gave golden yellow needles, m.p. 417° (Found: C, 82·7; H, 4·5; N, 8·5. $C_{24}H_{14}N_2O$ requires C, 83·2; H, 4·1; N, 8·1%).

Method (*b*).—The diamine (0·2 g.) was dissolved in dry distilled dimethylaniline (4 c.c.) at the boil and the solution was cooled to about 80°. Benzoyl chloride (0·3 c.c.) was added, when a golden yellow crystalline precipitate separated immediately. On cooling, ether (40 c.c.) was added and the precipitate filtered, washed with ether and dried (0·25 g.). Crystallization from nitrobenzene gave golden yellow needles, m.p. 417°, identical with the substance obtained by method (*a*).

5-*Nitrobenzanthrone*

4-Amino-5-nitrobenzanthrone (10 g.) was dissolved in conc. sulphuric acid (200 c.c.) and cooled in ice and salt. Sodium nitrite (4 g.) was gradually added under vigorous stirring during one hour. Crushed ice (350 g.) was added from time to time, so that the temperature was not allowed to rise above 20°. After stirring for one hour longer the reaction mixture was poured into 95% alcohol (400 c.c.). Vigorous evolution of nitrogen took place and the colour changed from bluish violet to yellowish brown. On refluxing for 2 hours and cooling, the precipitate was collected, washed free from acid and dried (8 g.). Crystallization from 500 parts of glacial acetic acid or 50 parts of acetic anhydride or 10 parts of nitrobenzene gave light brown needles, m.p. 281° (Boyes, *et al.*, cite m.p. 287°) (Found: C, 74·4; H, 3·4; N, 5·2. $C_{17}H_9NO_3$ requires C, 74·2; H, 3·5; N, 5·1%).

3-*Nitroanthraquinone*-1-*carboxylic acid*

To a boiling suspension of 5-nitrobenzanthrone (1 g.) in acetic acid (40 c.c.), chromium trioxide (2·5 g.) in 50% acetic acid (10 c.c.) was added during 3 hours. Refluxing was further continued for 3 hours. The mixture was then poured into water (200 c.c.) and left overnight. The precipitate was filtered, washed, dissolved in hot dilute ammonia, and filtered. The ammoniacal solution was acidified with hydrochloric acid, and the precipitate collected, washed and dried (0·36 g.). Crystallization from acetic acid gave pale pink plates, m.p. 270° (Found: C, 60·7; H, 2·5; N, 4·9. $C_{15}H_7NO_6$ requires C, 60·6; H, 2·7; N, 4·7%).

5-*Aminobenzanthrone*

5-Nitrobenzanthrone (5 g.) was suspended in methanol (200 c.c.) and treated with fused sodium sulphide (10 g.) in water (10 c.c.). After stirring

under reflux for 6 hours, methanol was distilled off, the bright red residue washed with water and dried (4 g.). On crystallization from chlorobenzene bright red shining needles were obtained, m.p. 235° (Found: C, 83·5; H, 4·6; N, 6·0. $C_{17}H_{11}NO$ requires C, 83·2; H, 4·8; N, 5·7%).

5-*Acetamidobenzanthrone*

5-Aminobenzanthrone (0·2 g.) was dissolved in boiling glacial acetic acid (7 c.c.). The clear solution was cooled to 90° and acetic anhydride (0·5 c.c.) added, when a yellow crystalline precipitate immediately separated. The mixture was heated on a boiling water-bath for ten minutes and the product filtered and dried (0·22 g.). Crystallization from nitrobenzene gave yellow needles, m.p. 313° (Found: N, 5·1; $C_{19}H_{13}NO_2$ requires N, 4·9%).

5-*Benzamidobenzanthrone*

5-Aminobenzanthrone (0·2 g.) was refluxed with benzoyl chloride (2 c.c.) for 15 minutes and the mixture was dropped with stirring into crushed ice. The precipitate was collected, washed with ammonia and dried (0·26 g.). Crystallization from chlorobenzene gave small yellow needles, m.p. 266° (Found: N, 4·2. $C_{24}H_{15}NO_2$ requires N, 4·0%).

5-*Chlorobenzanthrone*

A solution of 5-aminobenzanthrone (1·5 g.) in conc. sulphuric acid (6 c.c.) was added gradually to a stirred solution of sodium nitrite (0·7 g.) in conc. sulphuric acid (5 c.c.) during half an hour, the temperature being kept below 10°. After one hour the mixture was poured over crushed ice. The yellow precipitate was collected, washed with a little water, and made into a paste with conc. hydrochloric acid (10 c.c.) and added to a well-stirred solution of freshly prepared cuprous chloride (1·5 g.) in 18% hydrochloric acid (25 c.c.). The mixture was stirred at room temperature till the evolution of nitrogen ceased (2 hours). The yellow precipitate was collected, washed free from acid, and purified by dissolving in boiling glacial acetic acid (30 c.c.), filtering and adding a few drops of water. Clusters of microscopic needles separated, m.p. 198–99°. Crystallization from benzene gave shining yellow needles, m.p. 205–6° (Found C, 77·6; H, 3·4; Cl, 13·1. $C_{17}H_9ClO$ requires C, 77·2; H, 3·4; Cl, 13·4%).

3-*Chloroanthraquinone*-1-*carboxylic acid*

A solution of 5-chlorobenzanthrone (0·5 g.) in boiling acetic acid (10 c.c.) was slowly treated during 3 hours with a solution of chromium trioxide (1·2 g.) in 50% acetic acid (3 c.c.). After refluxing for 3 hours and pouring

into water (100 c.c.), the precipitate was collected, washed, dissolved in dilute aqueous ammonia and reprecipitated with acid. The light yellow crystalline mass (0·23 g.) crystallized from dilute acetic acid in light yellow needles, m.p. 274°, unchanged on admixture with an authentic sample of 3-chloroanthraquinone-1-carboxylic acid prepared from 1-amino-3-chloroanthraquinone.

SUMMARY

5-Nitrobenzanthrone has been synthesized by nitration of 4-acetamidobenzanthrone, hydrolysis to 4-amino-5-nitrobenzanthrone and subsequent deamination. The adjacent orientation of the amino and nitro groups was shown by reduction to a diamine, which formed a quinoxaline with phenanthraquinone and an imidazole with benzoyl chloride. Reduction of 5-nitrobenzanthrone gave 5-aminobenzanthrone which was converted to 5-chlorobenzanthrone. Oxidation of 5-chlorobenzanthrone gave 3-chloroanthraquinone-1-carboxylic acid, identical with the acid prepared from 1-amino-3-chloroanthraquinone.

ACKNOWLEDGMENT

We are greatly indebted to the Council of Scientific and Industrial Research for a Fellowship awarded to one of us (S. S. M.) and to Dr. T. S. Gore for the microanalyses.

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