

## Reduction of Anthraquinone Derivatives with Alkaline Dithionite.

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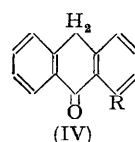
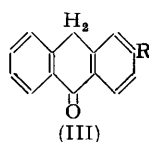
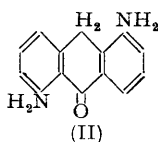
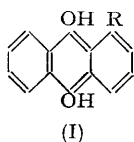
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Extension of the work of Grandmougin and of Battegay and Hueber has shown that when excess of alkaline dithionite is employed the nature of the reduction product from anthraquinone derivatives is influenced by the kind and number of nuclear substituents. 1-Piperidino- and 1-dimethylamino-anthraquinone afford derivatives of anthraquinol. 1-Amino-, 1-methylamino-, 1-benzylamino-, 1-hydroxy-, 2-amino-, 2-ethylamino-, 2-dimethylamino-, and 1 : 5-diaminoanthraquinone give derivatives of anthrone. 1 : 4-Diaminoanthraquinone gives ammonia and quinizarin as already reported. Generally only one form was readily isolable, even when two isomeric anthrones were possible in theory, and, except in the case of 1-hydroxyanthraquinone, it was the form having the substituent *ortho* or *para* to a carbonyl group. 2-Nitro-1 : 2'-dianthraquinonylamine undergoes fission with formation of 2-aminoanthr-10-one.

THE introduction of sodium dithionite (hydrosulphite) and an alkali as a means of reducing anthraquinone to anthraquinol (Grandmougin, *Ber.*, 1906, **39**, 3561) was followed by the recognition that the reduction could proceed further, anthrone being formed (Battegay and Hueber (*Bull. Soc. chim.*, 1923, **33**, 1097). In the present communication the effect of alkaline dithionite solutions on a range of anthraquinone derivatives is described.

Both 1-dimethylamino- and 1-piperidino-anthraquinone were easily reduced by the reagent, deep red solutions resulting, and these remained unchanged even after prolonged heating with an excess of reagent. Aeration of the product quickly restored the starting material in good yield. In these instances the anthraquinols (I; R = NMe<sub>2</sub> or NC<sub>5</sub>H<sub>10</sub>) were the end products of reduction.

With 1 : 5-diaminoanthraquinone the end product was an anthrone (II). No ammonia was detected in this reaction. 1 : 4-Diaminoanthraquinone behaved otherwise: after its reduction to give a deep red solution ammonia was freely evolved and on aeration 1 : 4-dihydroxyanthraquinone was formed. The similar behaviour of 1-amino-4-hydroxyanthraquinone and some related aminohydroxy-compounds is recorded in G.P. 436,526, and the reduction of 1 : 4-diaminoanthraquinone to a dihydro-derivative which yields quinizarin when heated with an acid is described in G.P. 207,668.



2-Dimethylaminoanthraquinone was reduced to a relatively stable yellow anthrone. Oxidation in air regenerated 2-dimethylaminoanthraquinone, and treatment with acetic anhydride in pyridine gave the acetyl derivative of the enol form. The anthrone differed from 3-dimethylaminoanthr-10-one (Weitz, *Annalen*, 1918, **418**, 30); it must therefore have been 2-dimethylaminoanthr-10-one (III; R = NMe<sub>2</sub>). 2-Ethylaminoanthraquinone similarly afforded a relatively stable anthrone (III; R = NHEt) which formed the *N*-acetyl derivative with acetic anhydride and sulphuric acid. 2-Aminoanthraquinone gave an anthrone, but this was too unstable in air to permit analysis. By analogy, it was 2-aminoanthr-10-one (III; R = NH<sub>2</sub>). Acetylation with acetic anhydride and sulphuric acid gave the *NN*-diacetyl derivative.

1-Aminoanthraquinone afforded a relatively stable anthrone which gave a yellow *N*-acetyl derivative with acetic anhydride and sulphuric acid and a red derivative with acetic anhydride and boroacetic anhydride. The last reaction indicates that the reduction product is 4-aminoanthr-10-one (IV; R = NH<sub>2</sub>), and the same compound results on reduction with aluminium and sulphuric acid (G.P. 201,542). Oxidation with ferric chloride in acetic acid gave 1-acetamidoanthraquinone, an indication that acetylation occurs on

the nitrogen when the catalyst is sulphuric acid. 4-Aminoanthr-10-one and alkaline hydrogen peroxide afford a 40% yield of 1-aminoanthraquinone. Coffey (Soc. Chem. Ind. Ann. Meeting, 1953) has reported that 1-aminoanthr-10-one can also be obtained by the reduction of 1-aminoanthraquinone. 1-Methylaminoanthraquinone gave the somewhat less stable 4-methylaminoanthr-10-one (IV; R = NHMe) together with methylamine. It gave a positive (yellow-red) boroacetic anhydride reaction. When a smaller proportion of dithionite is used reduction to the anthraquinol occurs and this is hydrolysed to methylamine and a reduction product of 1-hydroxyanthraquinone. 1-Benzylaminoanthraquinone gave a relatively unstable anthrone, oxidised rapidly in air to the starting material. By analogy it was 4-benzylaminoanthr-10-one (IV; R = NHCH<sub>2</sub>Ph).

In all the reactions referred to, when more than one form of an anthrone could result the product obtained was a vinylogue (Fuson, *Chem. Reviews*, 1935, 16, 1; Bradley and Geddes, *J.*, 1952, 1636) of an amide, and for this reason would be expected to possess enhanced stability and to exist in the keto(anthrone)-form.

1-Hydroxyanthraquinone gives 1-hydroxyanthr-10-one, identical with the product obtained by Cross and Perkin (*J.*, 1930, 292) by reducing 1-acetoxyanthraquinone with stannous chloride. Zahn and Koch (*Ber.*, 1938, 71, 172) found that reduction of 1-hydroxyanthraquinone with hydrogen and nickel gave 4-hydroxyanthr-10-one, probably owing to chelation between the hydroxyl substituent and the neighbouring carbonyl group. Similarly, the formation of 4-amino- and 4-alkylamino-derivatives of anthrone is probably a consequence of chelation of the amino- and the substituted amino-groups with the neighbouring carbonyl group.

Bradley, Leete, and Stephens (*J.*, 1951, 2158) recorded the fission of 2-nitro-1 : 2'-dianthraquinonylamine by hot alkaline sodium dithionite, 2-aminoanthraquinone being obtained after crystallisation of the reduction product. The fission has now been confirmed and we have established that the product before crystallisation is 2-aminoanthr-10-one. This compound could have resulted by the reduction of 2-aminoanthraquinone or 2-aminoanthraquinol formed at an earlier stage, or by reduction of the dianthraquinonylamine to a anthraquinol-anthrone or to a 2-amino-1 : 2'-dianthronylamine.

#### EXPERIMENTAL.

*Reduction of 1-Piperidinoanthraquinone.*—1-Piperidinoanthraquinone (2 g.) was ground into a paste with alcohol (12 c.c.), then added to a solution of sodium hydroxide (2 g.) and sodium dithionite (4 g.) in water (60 c.c.) and heated to gentle boiling in a flask fitted with a Bunsen valve. This device was used in all the reduction experiments. A deep red solution formed immediately and the colour remained unchanged throughout the experiment. The cooled solution, acidified with acetic acid, gave a bright yellow precipitate, and this on exposure to air very rapidly re-formed 1-piperidinoanthraquinone, m. p. and mixed m. p. 116°.

1-Dimethylaminoanthraquinone, m. p. 135° was similarly recovered after 5 g. in alcohol (30 c.c.) had been heated for 1 hr. with sodium hydroxide (10 g.) and sodium dithionite (20 g.) in water (200 c.c.) and the product had been aerated.

*2-Dimethylaminoanthr-10-one.*—2-Dimethylaminoanthraquinone (5 g.) was made into a paste with alcohol (10 c.c.) and heated with sodium hydroxide (10 g.) and sodium dithionite (20 g.) in water (200 c.c.), affording a red solution from which a yellow solid separated. After 10 min. the product was cooled, and the solid was collected, washed, and then dried *in vacuo*. 2-Dimethylaminoanthr-10-one (m. p. 148°, 4 g.) crystallised from alcohol in the form of golden rods (3.6 g.), m. p. 149—150° (Found: C, 80.6; H, 6.4; N, 6.0. C<sub>16</sub>H<sub>15</sub>ON requires C, 81.0; H, 6.3; N, 5.9%). It exhibited an intense golden fluorescence in ultra-violet light, dissolved in warm aqueous potassium hydroxide forming a yellow solution and slowly became orange in air.

A solution of 0.2 g. of the anthrone in alcohol (20 c.c.) was left in contact with air for 7 days and then evaporated. The resulting orange solid, dissolved in benzene and chromatographed on alumina, gave a single, deep violet band. This was eluted with benzene, and the extract evaporated to small volume and then mixed with light petroleum (b. p. 60—80°). A red, crystalline solid (0.18 g.) separated, m. p. 185°, not depressed by mixing with an authentic sample of 2-dimethylaminoanthraquinone.

The compound, m. p. 149—150° (1.4 g.), was refluxed with acetic anhydride (5 c.c.) and pyridine (4.5 c.c.) for 4 hr., and then further heated for 30 min. after the addition of acetic

anhydride (3 c.c.). On the addition of water 10-acetoxy-2-dimethylaminoanthracene separated; this was washed, dried, crystallised twice from alcohol (charcoal), and thus obtained as golden, elongated leaflets (0.6 g.), m. p. 165—166° (Found: C, 77.5; H, 6.1; N, 5.0.  $C_{18}H_{17}O_2N$  requires C, 77.4; H, 6.1; N, 5.0%).

**4-Methylaminoanthr-10-one.**—A paste of 1-methylaminoanthraquinone (2.5 g.) in alcohol (5 c.c.) was boiled for 15 min. with sodium hydroxide (5 g.) and sodium dithionite (10 g.) in water (200 c.c.). The resulting deep red solution was cooled, and the yellow solid collected and dried *in vacuo* (1.7 g.). Crystallisation from chlorobenzene gave 4-methylaminoanthr-10-one (1.2 g.) as golden needles, m. p. 111—113° (Found: C, 80.5; H, 5.7; N, 6.4.  $C_{15}H_{13}ON$  requires C, 80.7; H, 5.8; N, 6.3%). The product became brown on exposure to air, was sparingly soluble in boiling water forming a yellow solution, and dissolved in warm, 5% potassium hydroxide solution with a yellow colour which changed to orange. The yellow solution in acetic anhydride became red on the addition of boroacetic anhydride.

In a second experiment 1-methylaminoanthraquinone (1 g.), alcohol (5 c.c.), sodium hydroxide (5 g.), sodium dithionite (1 g.), and water (200 c.c.) were heated under reflux for 30 min. and the volatile products passed into a solution of 1-chloro-2:4-dinitrobenzene in alcohol. A yellow solid separated from the latter after 12 hr., and crystallisation from alcohol gave 1-methylamino-2:4-dinitrobenzene, m. p. 174—175°, not depressed by mixing with an authentic sample. The deep red solution of the non-volatile reduction product was aerated for several hours, and the precipitate was collected, washed, dried, and chromatographed from benzene on alumina. A small band of 1-methylaminoanthraquinone passed through the column. A strongly adsorbed yellow band was eluted with alcohol; evaporation of the extract gave 1-hydroxyanthraquinone (0.05 g.), m. p. 194—195°, not depressed on mixing with an authentic sample, and further characterised by its absorption spectrum in sulphuric acid.

**2-Ethylaminoanthr-10-one.**—2-Ethylaminoanthraquinone (2.8 g.), alcohol (10 c.c.), potassium hydroxide (5 g.), sodium dithionite (10 g.), and water (100 c.c.) were heated to boiling (Bunsen valve) for 15 min. and the product was then cooled. The material which separated was collected, dried *in vacuo*, and finally crystallised from benzene. It gave 1.8 g. of yellow 2-ethylaminoanthr-10-one, m. p. 155—157° (Found: C, 81.2; H, 6.3; N, 5.7.  $C_{16}H_{15}ON$  requires C, 81.0; H, 6.3; N, 5.9%). This dissolved in warm aqueous potassium hydroxide with a yellow colour, changed to orange on exposure to air.

The foregoing product (1 g.) was gently warmed with acetic anhydride (5 c.c.) and a drop of concentrated sulphuric acid until a clear solution resulted. This was added to ice and the resulting brown, oily precipitate was dissolved by warming and then adding just sufficient methyl alcohol to give a clear solution. During 3 days crystals separated and these were collected, washed with aqueous methanol, and dried (0.2 g.). Crystallisation from benzene—light petroleum (b. p. 60—80°) gave *N*-ethyl-2-acetamidoanthr-10-one as a yellow solid, m. p. 125—127° (Found: C, 77.4; H, 6.1; N, 5.2.  $CH_3CO$ , 15.1.  $C_{18}H_{17}O_2N$  requires C, 77.4; H, 6.1; N, 5.0;  $CH_3CO$ , 15.4%).

**4-Aminoanthr-10-one.**—1-Aminoanthraquinone (10 g.), alcohol (50 c.c.), potassium hydroxide (20 g.), sodium dithionite (40 g.), and water (500 c.c.) were heated to gentle boiling. The deep red solution which formed at first soon became less intense and after 15 min. the product was rapidly cooled, and the precipitated solid was quickly collected, washed, and finally dried *in vacuo* (5.2 g.; m. p. 110—113°). Crystallisation from chlorobenzene gave yellow needles of 4-aminoanthr-10-one, m. p. 113—115° (Found: C, 79.9; H, 5.5; N, 7.0.  $C_{14}H_{11}ON$  requires C, 80.3; H, 5.3; N, 6.7%). The product, though sparingly soluble in boiling water to a yellow solution, was insoluble in cold 5% potassium hydroxide. It dissolved on warming, the yellow solution rapidly becoming orange, then brown. Solutions in ethyl alcohol and acetic acid were yellow with a bluish-green fluorescence. The compound gave a yellow solution in acetic anhydride, unchanged after heating at the b. p. for a few minutes, but rendered red immediately on the addition of boroacetic anhydride.

A suspension of the product (1 g.) in acetic anhydride (5 c.c.) was warmed with a drop of concentrated sulphuric acid. The resulting brown solution gave a yellow solid on cooling. The whole was added to ice and after 5 min. the solid was collected, washed, and dried. Crystallisation from alcohol gave 1.1 g. of 4-acetamidoanthr-10-one as yellow rods, m. p. 143—145° (Found: C, 76.4; H, 5.5; N, 5.9.  $C_{16}H_{13}O_2N$  requires C, 76.5; H, 5.2; N, 5.6%), which were insoluble in cold 5% aqueous potassium hydroxide; on warming a golden-yellow solution was formed. The colour in sulphuric acid was green.

The reduction product (1 g.) was ground in a mortar for 5 min. with a hot mixture of 5% sodium hydroxide solution (25 c.c.) and 20-volume hydrogen peroxide (25 c.c.). The solid was

collected and similarly treated with four further portions of alkaline hydrogen peroxide. The red product was collected, washed with water, dried, then dissolved in benzene and chromatographed on alumina. The more mobile red band was eluted with acetone, and the extract concentrated to small volume and then mixed with light petroleum. A red solid (0.4 g.) crystallised, having m. p. 250°, not depressed on mixing with an authentic sample of 1-aminoanthraquinone.

A solution of hydrated ferric chloride (1.7 g.) in water (10 c.c.) was added dropwise to a boiling solution of the acetyl compound (0.9 g.) in acetic acid (10 c.c.). After 15 min. water (10 c.c.) was added to the brown solution, the small tarry precipitate was filtered off, and the filtrate concentrated to small volume and then mixed with light petroleum. A red solid (0.4 g.) crystallised from alcohol (charcoal) as a yellow solid (0.015 g.), m. p. 215—218° (Found: N, 5.4%. Calc. for  $C_{16}H_{11}O_3N$ : N, 5.3%).

*2-Aminoanthr-10-one.*—2-Aminoanthraquinone (9 g.), alcohol (50 c.c.), sodium hydroxide (7.5 g.), and sodium dithionite (20 g.) in water (300 c.c.) were heated; before the b. p. was reached the red solution formed initially gave place to a dense mass of yellow crystals. After a few minutes' heating at the b. p. the product was cooled quickly, and the crystals were collected, washed, and dried *in vacuo* (7.5 g.). The product, which was too unstable for satisfactory analysis, dissolved in acetic acid forming a yellow solution with a green fluorescence; exposure to air changed the yellow colour to orange. A solution in chlorobenzene, chromatographed on alumina, gave a single bright orange zone from which acetone eluted 2-aminoanthraquinone.

The reduction product (1 g.) was made into a paste with glacial acetic acid (1 c.c.), and acetic anhydride (5 c.c.) was added followed by a drop of concentrated sulphuric acid. An exothermic reaction occurred, a brown solution resulted, and when this was cool it was added to ice. The solid was collected, washed, and then dried *in vacuo* (1.1 g.; m. p. 220°). After two crystallisations from alcohol (charcoal) pale greenish-yellow needles (0.6 g.) of 2-diacetamidoanthr-10-one resulted, having m. p. 224—225° (Found: C, 73.4; H, 5.1; N, 5.2.  $C_{18}H_{15}O_2N$  requires C, 73.6; H, 5.1; N, 4.8%). This derivative exhibited a strong blue fluorescence in alcohol. It gave a pale yellow solution in concentrated sulphuric acid.

*1:4-Diaminoanthraquinone.*—A paste of the diamine (1 g.) and alcohol (5 c.c.) was boiled for 1 hr. with a solution of sodium hydroxide (5 g.) and sodium dithionite (1 g.) in water (150 c.c.). Ammonia was liberated freely. Water (400 c.c.) was then added, the solution was aerated, filtered from a trace of insoluble matter, then acidified. The resulting precipitate dried to a red-brown solid (0.52 g.), m. p. 193—195°, not depressed on admixture with quinizarin.

*1:5-Diaminoanthr-10-one.*—1:5-Diaminoanthraquinone (5 g.), alcohol (25 c.c.), sodium hydroxide (5 g.), sodium dithionite (10 g.), and water (150 c.c.) were heated to boiling for 1 min. and then quickly cooled. A crystalline mass separated and this was collected, washed, and dried *in vacuo* (4 g.).

*1:5-Diaminoanthr-10-one* crystallised from *n*-butanol in golden-yellow needles, m. p. 216—218° (Found: C, 75.2; H, 5.3; N, 11.9.  $C_{14}H_{12}ON_2$  requires C, 75.0; H, 5.4; N, 12.5%). It was sparingly soluble in hot water forming a yellow solution. It was insoluble in cold, dilute potassium hydroxide, but dissolved on warming to give a yellow solution which became orange-yellow in air. It dissolved in concentrated sulphuric acid to form a colourless solution which rapidly became red.

On addition of the product (1 g.) to acetic anhydride (5 c.c.) containing a drop of concentrated sulphuric acid, rise in temperature occurred and a brown solution resulted. After cooling, addition to ice gave 1:5-diacetamidoanthr-10-one as a solid which crystallised from *n*-butanol in fine, yellow needles (0.8 g.). These decomposed, without melting, at 270° (Found: C, 70.1; H, 5.2; N, 9.1.  $C_{18}H_{16}O_3N_2$  requires C, 70.0; H, 5.2; N, 9.1%).

*1-Hydroxyanthr-10-one.*—A paste of 1-hydroxyanthraquinone (4 g.) in alcohol (10 c.c.) was heated to boiling with sodium hydroxide (6 g.), sodium dithionite (15 g.), and water (300 c.c.). A deep red solution formed and after 2.5 hr. this was filtered and the filtrate acidified. The resulting greenish-yellow precipitate was washed with a small volume of water, then dried (3.5 g.; m. p. 180—210°) and crystallised from chlorobenzene (m. p. 203—208°). Sublimation *in vacuo* gave two bands. The more volatile fraction (m. p. 160—170°) gave 1-hydroxyanthraquinone after crystallisation from chlorobenzene. The less volatile crystallised from toluene (charcoal) in colourless needles, m. p. 238—240°, not depressed by 1-hydroxyanthr-10-one. It dissolved in warm, dilute potassium hydroxide to give a yellow solution which rapidly became red in air. The yellow solution in acetic anhydride remained unchanged on the addition of boroacetic anhydride.

*Reduction of 2-Nitro-1:2'-dianthraquinonylamine.*—A paste of the nitro-compound (0.5 g.)

with alcohol (5 c.c.) was heated to boiling with potassium hydroxide (1 g.) and sodium dithionite (2 g.) in water (30 c.c.). In 5 min. the red colour formed initially had become less intense. After cooling quickly, the yellow solid which separated was collected, washed, and then dried *in vacuo*. Exposed to air it rapidly re-formed 2-aminoanthraquinone. It exhibited the same properties as 2-aminoanthr-10-one, and on acetylation with acetic anhydride gave 2-diacetyl-aminoanthr-10-one, m. p. and mixed m. p. 220—222°.

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