472. *Chemistry of Indanthrone. Part III.* The Cyclisation of 2-Amino-1 : 2′-dianthraquinonylamine.*

By William Bradley, Edward Leete, and Douglas S. Stephens.

Stannous chloride reduction of 2-nitro-1 : 2′-dianthraquinonylamine affords 2-amino-1 : 2′-dianthraquinonylamine and indanthrone. The latter product is formed when the former is heated alone, in air or carbon dioxide, in acetic acid, or in pyridine containing potassium hydroxide. A suspension of sodium hydroxide in cold pyridine converts the 2-amino-compound into a grey-green intermediate which is changed into indanthrone by heating it in quinoline. The intermediate is considered to be a hydroaromatic compound formed by linking the 2-amino-group to the 1-position of the adjacent nucleus. It is converted into indanthrone as a result of a prototropic change and dehydrogenation. The 2-methylamino-analogue cyclises with equal ease to form *N*-methylindanthrone but the conversion of 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine into *N*-methylindanthrone requires the use of alkalis.

Reduction of the nitro-compound by alkaline dithionite yields 2-aminoanthraquinone and 2-aminoanthraquinol. The result indicates that in the process of forming indanthrone the initial step by which the 2-anthraquinonylamine anion becomes linked to the 1-position of another molecule of 2-aminoanthraquinone is reversible.

The reversible character of the first step in the sequence of changes which lead ultimately to indanthrone is considered to explain the increasing importance of the direct hydroxylation of 2-aminoanthraquinone, which leads to alizarin, with reduction in the temperature of the alkali fusion.

The present communication is concerned with the properties of 2-amino-1 : 2′-dianthraquinonylamine (III) and their bearing on the formation of indanthrone (IV) when 2-aminoanthraquinone (I) is heated with fused alkali hydroxides. In Part I (*J.*, 1951, 2129) it

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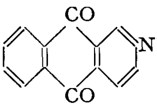
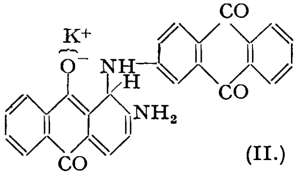
* Part II, preceding paper.

was shown that 2-aminoanthraquinone behaves as a weak acid towards strong alkalis, and also that the same compound and its *N*-aryl derivatives undergo substitution at the 1-position by the anions of certain weak acids, hydrogen being replaced. The facts support the view that (II), the adduct formed by the anion of the 2-anthraquinonylamine ion with 2-aminoanthraquinone represents an intermediate stage in the process of forming indanthrone from 2-aminoanthraquinone. Equally, the facts harmonize with the view first put forward by Barnett ("Anthracene and Anthraquinone," London, 1921, p. 344) that 2-amino-1 : 2′-dianthraquinonylamine (III) is an intermediate, since (III) can be derived from (II) by dehydrogenation by air, alkali nitrates, or the quinones, for example, 2-aminoanthraquinone, which are always present in the alkali melt.



(I.)



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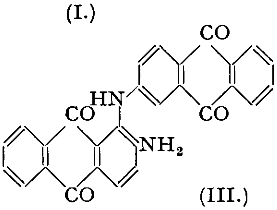
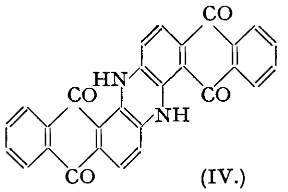


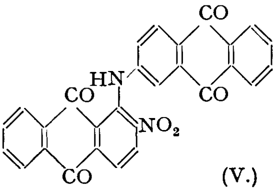
(III.)



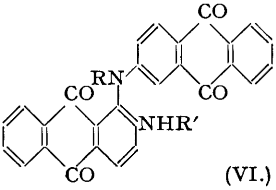
(IV.)

In the preparation of (III), 2-acetamido-1-chloroanthraquinone was heated with 2-aminoanthraquinone, potassium acetate, and a copper catalyst in nitrobenzene. Dehalogenation occurred, 2-acetamidoanthraquinone being formed. Kopetschni and Wiesler (*Monatsh.*, 1922, **43**, 92) similarly found that 2-amino-1-chloroanthraquinone yielded 2-aminoanthraquinone when it was heated in dimethylaniline with cupric acetate.

1-Chloro-2-nitroanthraquinone, prepared by Kopetschni's method (G.P. 363,930) and also by the procedure described in Part I (*loc. cit.*), was condensed with 2-aminoanthraquinone as described in G.P. 581,439, to form 2-nitro-1 : 2′-dianthraquinonylamine (V). Reduction with stannous chloride in acetic acid afforded both the related amine (III) and indanthrone (IV). The conversion of the amine (III) into indanthrone was described in G.P. 544,919—by heating the amine in 1-nitronaphthalene or by passing a rapid current of air through its solution in α-chloronaphthalene. The present experiments have shown, however, that added oxidants are not essential for cyclisation, which takes place readily under a variety of conditions. It occurs when the amine is heated alone at 290°, or suspended in paraffin at this temperature. It does not occur in boiling pyridine, but it takes place readily when potassium hydroxide is added to a solution of the amine in cold pyridine. Indanthrone is also formed when the amine is heated with glacial acetic acid; in this respect 2-amino-1 : 2′-dianthraquinonylamine differs from both 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine (VI; R = Me, R′ = H) and its methyl derivative (VI; R = R′ = Me) which require the use of alkalis for their cyclisation to methylindanthrones. That the *tertiary* methyl group contributes to the different behaviour of the two methyl derivatives is shown by the properties of 2-methylamino-1 : 2′-dianthraquinonylamine (VI; R = H, R′ = Me) which cyclises to form *N*-methylindanthrone even in acid solution (preceding paper).

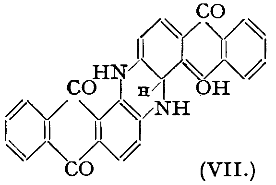


(V.)

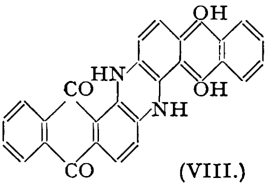


(VI.)

Lithium hydroxide, added to a solution of 2-amino-1 : 2′-dianthraquinonylamine in pyridine, had almost no action. Addition of powdered sodium hydroxide caused the rapid formation of a grey-green substance (A). This product was not an alkali salt. It was insoluble in water, but sparingly soluble in *o*-dichlorobenzene with a greenish-yellow colour; it formed a reddish-brown solution in concentrated sulphuric acid, from which it was precipitated unchanged by water. It dissolved in pyridine with a dull green colour; on addition of methanolic potassium hydroxide a deep green colour resulted. A deep green colour with the same reagent is also given by the three isomeric dianthraquinonylamines and certain other –NH– compounds, including 2-anilinoanthraquinone (*J.*, 1951, 2133). Indanthrone was formed merely by heating (A) with boiling quinoline (cf. Fig.), an indication that (A) is not an anthrone or anthranol; compounds belonging to these types are oxidised to indanthrone only with difficulty. Warming (A) with alkaline dithionite (hydrosulphite) dissolved it, forming the blue alkali salt of dihydroindanthrone and subsequent aeration of the solution caused the separation of indanthrone. These properties suggest that (A), the composition of which approximated closely to that of a dihydroindanthrone, is a compound having the constitution (VII), which is capable of a prototropic change in the



(VII.)

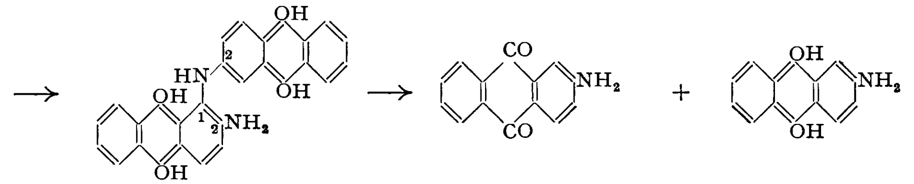


(VIII.)

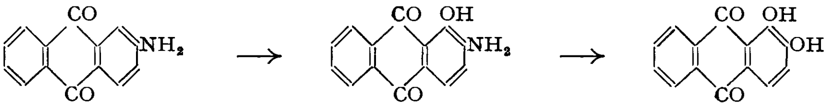
presence of bases to form dihydroindanthrone (VIII). Indanthrone is very readily derived from (VIII) by dehydrogenation. It is probable that other instances will be encountered in the present group of compounds in which a hydroaromatic nucleus results from the attachment of an electron-donating group, present in a side chain, to an aromatic nucleus, the process being analogous to the formation of *pseudo*-bases by the action of alkalis on heterocyclic 'onium salts.

Heating 2-amino-1 : 2′-dianthraquinonylamine at 290° in an atmosphere of carbon dioxide gave indanthrone but no alkali-soluble product. A similar result was obtained when 2-amino-1 : 2′-dianthraquinonylamine was heated with potassium hydroxide in pyridine containing methyl alcohol.

When the related nitro-compound (V) was reduced with alkaline dithionite, the initial product decomposed, yielding 2-aminoanthraquinone and 2-aminoanthraquinol. The reaction involves the elimination of the 2-anthraquinonylamino-substituent from the 1-position of the 2-aminoanthraquinol nucleus to which it is attached. The result is important for the present theory of formation of indanthrone which postulates the occurrence of a reduced form (II) of 2-amino-1 : 2′-dianthraquinonylamine as an intermediate. It indicates the weakness of the bond linking the secondary nitrogen to the 1-position of the aminated nucleus; it establishes further that the formation of the bond is a reversible process.



The reversible character of the initial substitution step, as a result of which the 2-anthraquinonylamine anion becomes linked to the 1-position of another molecule of 2-aminoanthraquinone, probably explains the observation, made first by Bohn (G.P. 129,845), that indanthrone is formed most abundantly when the temperature of the alkali fusion is 200—300°. At lower



temperatures alizarin is formed in notable amount; at 180° it forms 18% of the product (Liebermann, *Annalen*, 1882, **212**, 63). The direct hydroxylation of 2-aminoanthraquinone leading first to 2-amino-1-hydroxyanthraquinone and then to alizarin is not a reversible process, and below 200° it represents an important side-reaction. At higher temperatures the rate of substitution by hydroxyl and by 2-anthraquinonylamine anions increases and indanthrone formation becomes favoured because of the stability of the end-product and the rate at which it is formed.

The simultaneous formation of alizarin and indanthrone by the alkali fusion of 2-aminoanthraquinone recalls the simultaneous formation of 4- and 6-hydroxy*meso*benzanthrones together with violanthrone when *meso*benzanthrone is submitted to alkali fusion. These processes are considered to involve two simultaneous reactions : (*a*) the direct hydroxylation of *meso*benzanthrone by hydroxyl ions, and (*b*) substitution into *meso*benzanthrone by the 4-*meso*-benzanthronyl ion, hydrogen being replaced.

EXPERIMENTAL.

2-*Acetamido*-1-*chloroanthraquinone. Dehalogenation.*—A mixture of 2-acetamido-1-chloroanthraquinone (3 g.) (Junghans, *Annalen*, 1913, **399**, 320), potassium acetate (3 g.), copper bronze (0·1 g.), and cupric acetate (0·1 g.) in nitrobenzene (40 c.c.) was heated under reflux for 6 hours. The solvent was distilled in steam and the residue extracted by acetic acid. On cooling, the brown extract afforded 1·2 g. of an amorphous solid, m. p. 250—260°. Sublimed at 200° (bath)/0·5 mm. this afforded yellow needles (0·3 g.), m. p. 264—265°, not depressed on admixture with 2-acetamidoanthraquinone. When it was warmed with concentrated sulphuric acid and the resulting solution added to water the product yielded 2-aminoanthraquinone, m. p. 301—302°. There was no indication of the formation of a derivative of 1 : 2′-dianthraquinonylamine when 2-acetamido-1-chloroanthraquinone was heated with 2-aminoanthraquinone in naphthalene or quinoline.

2-*Amino*-1 : 2′-*dianthraquinonylamine.*—2-Nitro-1 : 2′-dianthraquinonylamine (2·0 g.; G.P. 581,439; *J.*, 1951, 2139) was finely powdered and then added to a boiling solution of AnalaR stannous chloride (4·0 g.) in glacial acetic acid (40 c.c.). After 5 minutes the solution was cooled, and the reddish-brown needles (1·9 g.) were collected and chromatographed in chlorobenzene on alumina. Development by the same solvent afforded three main zones. The most strongly adsorbed was violet-blue; eluted by means of quinoline this afforded indanthrone. The least strongly adsorbed was orange; elution with acetone yielded 0·2 g. of unchanged 2-nitro-1 : 2′-dianthraquinonylamine. The intermediate zone was violet; extraction by ethyl acetate yielded a red solution from which reddish-brown needles of 2-*amino*-1 : 2′-*dianthraquinonylamine* (0·9 g.) (Found : C, 75·1, 7·50; H, 4·0, 3·8; N, 6·5, 6·4. $C_{28}H_{16}O_4N_2$ requires C, 75·7; H, 3·6; N, 6·3%) separated on evaporation. 2-Amino-1 : 2′-dianthraquinonylamine is red when powdered, dissolves in alkaline dithionite with a brown colour, and decomposes at 290°, without melting.

Reduction of 2-*Nitro*-1 : 2′-*dianthraquinonylamine. Formation of* 2-*Aminoanthraquinone.*—Sodium hydroxide (4 g.) and sodium dithionite (9 g.) in water (120 c.c.) at 65° were added to a paste of the finely divided nitro-compound (1·4 g.) and alcohol (10 c.c.). The mixture was heated to boiling for 30 minutes in a flask provided with a Bunsen valve. A red solution formed but this became yellow and a yellow precipitate separated. The solid was collected, washed with water, and recrystallised from acetic acid. Needles, m. p. 302°, not depressed by authentic 2-aminoanthraquinone, were obtained.

Cyclisation of 2-*Amino*-1 : 2′-*dianthraquinonylamine. Formation of Indanthrone and an Intermediate Product.*—(*a*) A red solution of the amine (0·05 g.) in glacial acetic acid (5 c.c.) became almost colourless after 3 hours' boiling; meanwhile violet needles of indanthrone separated.

(*b*) A similar change from red to blue occurred when the amine was heated to 320° in liquid paraffin.

(*c*) The amine (0·1 g.) was recovered unaltered after 10 hours' boiling with pyridine (5 c.c.).

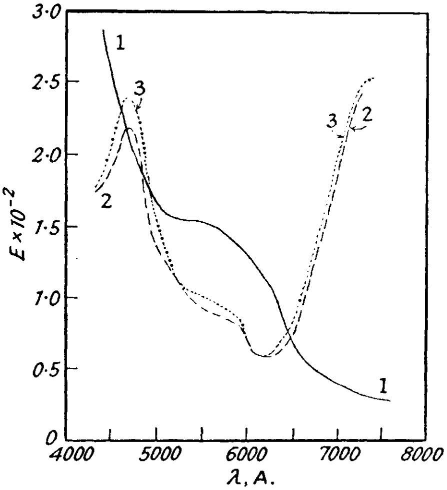
(*d*) The amine (0·2 g.) was dissolved in pyridine (5 c.c.). Powdered lithium hydroxide was added and the suspension shaken occasionally during 10 days at the room temperature. Only a trace of indanthrone was formed; the bulk of the amine was recovered.

(*e*) In a similar experiment powdered potassium hydroxide (0·2 g.) was added to a solution of the amine (0·2 g.) in pyridine (5 c.c.); a green colour developed immediately. After 10 days at the room temperature methyl alcohol was added and the bluish-green product (0·195 g.) collected. This was dissolved in alkaline dithionite, and the solution passed through a column of cellulose, the method described in Part II (preceding paper) being used. The most strongly adsorbed zone was blue; it yielded indanthrone when eluted by alkaline dithionite and oxidised in air. There was also a weakly adsorbed brown zone. Similar treatment of this afforded *ca.* 0·005 g. of unchanged 2-amino-1 : 2′-dianthraquinonylamine, identified by its deep violet colour in concentrated sulphuric acid.

(*f*) In a similar experiment in which powdered sodium hydroxide (0·2 g.) was used instead of potassium hydroxide, the solution became green immediately and a green mass formed during 10 days at the room temperature. Methyl alcohol was added, the pale green product was collected, washed with water, and dried in air (yield, 0·16 g.) (Found : C, 73·4; H, 3·3; N, 6·3. $C_{28}H_{16}O_4N_2$ requires C, 75·7; H, 3·6; N, 6·3%). Heating this product (0·05 g.) with quinoline (30 c.c.) at the b. p. for 5 minutes changed the brown colour of the solution to greenish-blue; on cooling the characteristic curved needles of indanthrone (0·045 g.) separated. The pale green product dissolved in *o*-dichlorobenzene with a greenish-yellow colour. It formed a reddish-brown solution in concentrated sulphuric acid (see figure); addition of water precipitated the pale green product unaltered. When kept it became bluer. It dissolved in alkaline dithionite with a deep blue colour; oxidation by air gave indanthrone in quantitative yield. The grey-green product dissolved in pyridine with a dull green colour; on addition of methanolic potassium hydroxide the solution became deep green.

(*g*) A few mg. of 2-amino-1 : 2′-dianthraquinonylamine were heated in an atmosphere of carbon dioxide at 300° for 15 minutes. The blue product was cooled in a stream of the gas and then added to 0·5 c.c. of 10% sodium hydroxide solution which had been boiled to expel air. There was no indication of the presence of an alkali-soluble product or of unchanged amine; the product contained indanthrone.

Products in concentrated sulphuric acid.



1, *Product obtained by the ring closure of* 2-*amino*-1 : 2′-*dianthraquinonylamine with sodium hydroxide in pyridine.*
2, *Product obtained by refluxing that of* (1) *with quinoline.*
3, *Indanthrone, max. at* 4650 Å. (E = 240), *min. at* 6150 Å. (E = 61).

(*h*) In the experiments recorded in the Table 2-amino-1 : 2′-dianthraquinonylamine was added to pyridine containing 3% (by vol.) of water. Powdered potassium hydroxide was added, and the containing vessels were evacuated until the medium boiled, and then closed. The reactants were shaken at the temperatures stated for the times recorded and then opened under warm, boiled-out water. In no instance was there evidence of the presence of a reduced (anthraquinol) form of indanthrone, which is known to dissolve in warm dilute sodium hydroxide with a deep blue colour. The resulting suspension was filtered off, washed with water, and dried. It was then extracted by hot pyridine (100 c.c.), and the undissolved material washed with hot pyridine and alcohol. The residue consisted of indanthrone; the extracts consisted mainly of unchanged amine and small amounts of indanthrone.

Temp.	16°	25°	35°	45°	70°	80°
2-Amino-1 : 2′-dianthraquinonylamine (g.)	0·4	0·4	0·4	0·4	0·4	0·4
Aqueous pyridine (c.c.)	20	20	20	20	30	40
KOH (g.)	2·0	2·0	2·0	2·0	4·0	6·0
Indanthrone (g.)	0·3	0·3	0·35	0·38	0·4	0·4
Products sol. in C_5H_5N (g.)	0·1	0·1	0·05	0·02	—	—
Reaction time (hrs.)	8	6	4	3	1	0·5

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