CLXXXVI.—*The Action of Thionyl Chloride on Hydroxyanthraquinones. Part II. Quinizarin.*

By ALBERT GREEN.

THE action of quinizarin on boiling thionyl chloride is different from that of alizarin (J., 1924, **125**, 1450). One hydroxyl group of quinizarin is replaced by a chlorine atom, which is reactive, and the product consists of deep red needles. In these and other properties the compound differs from the known monochloro-monohydroxyanthraquinones.

Slight loss of chlorine (1—2%) occurs when the compound is heated at 100°, or is boiled with acetic acid, for 1 hour. When a solution in concentrated sulphuric acid is heated on the boiling water-bath, the chlorine is eliminated as hydrogen chloride, and after 1 hour quinizarin is obtained in quantitative yield. The same product results from treatment with aqueous alkalis, and also by heating the *chloro*-compound under pressure with absolute methyl or ethyl alcohol or with acetic acid.

Oxidation with alkaline permanganate yields phthalic acid.

When a solution of the chloro-compound in absolute alcohol containing 3% of hydrogen chloride is heated, a product is obtained

* Since this paper was written, these acids have been prepared by Hodgson (this vol., p. 150).

which is isomeric with the known monoethyl ether of quinizarin (Liebermann and Jellinek, *Ber.*, 1888, **21**, 1168). This product is converted into quinizarin by heating it with concentrated sulphuric acid at 100° for an hour.

Treatment of the chloro-compound with boiling acetic anhydride, alone or with concentrated sulphuric acid, converts it into diacetyl derivatives of quinizarin. Efforts to isolate a monoacetyl derivative were fruitless, as in all cases some decomposition occurred with loss of chlorine. Similarly the products of methylation with diazomethane were not uniform and contained varying amounts of chlorine, although the analyses pointed to the presence of one methoxyl group only.

The chloro-compound condenses rapidly with boiling aniline and *p*-toluidine with loss of hydrogen chloride and production of *monoaminomonohydroxy*-compounds; longer treatment in presence of boric acid gives *diaminoanthraquinones*. These derivatives are respectively isomeric with the mono- and di-amino-compounds obtained by the condensation of quinizarin with aromatic amines, and the different colours of the solutions in concentrated sulphuric acid afford a means of distinguishing the isomerides.

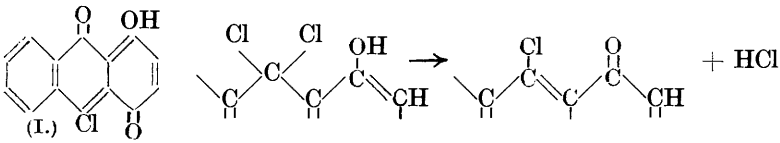
While the replacement of one hydroxyl group of quinizarin by chlorine would be expected to give 1-chloro-4-hydroxyanthraquinone, it is obvious that the properties of the compound under consideration are not consonant with those of a chlorohydroxyanthraquinone in which the halogen is in one of the outer rings. 1-Chloro-4-hydroxyanthraquinone separates from alcohol in golden-yellow needles melting at 193°. It is unaffected by heating its solution in concentrated sulphuric acid for 1 hour at 100°, and is converted into quinizarin only when it is heated for several hours at 140° with sulphuric and boric acids (Eckert and Steiner, *Monatsh.*, 1914, **35**, 1145).

The replacement of a hydroxyl group by a chlorine atom by means of thionyl chloride connotes an acidic hydroxyl, and this is a well-known method of preparing the acid chlorides of carboxylic acids. Properties similar to those of an acid chloride are shown by this new derivative of quinizarin; such are its rapid condensation with amines, and the tendency of the chlorine atom to react with diazomethane. The interaction of what may be called "normal" chloroanthraquinones with amines is slow even in the presence of catalysts (compare, among others, Harrop, Norris, and Weizmann, J., 1909, **95**, 1313). Meyer and Sander (*Annalen*, 1912, **396**, 145), however, have shown that halogen-substituted anthrones, in which the halogen atom is attached to a *meso*-carbon atom, react readily with amines, giving aminoanthrones.

The only structure which appears to account adequately for the properties of the new compound is that of 10-*chloro*-1-*hydroxy*-4 : 9-*anthraquinone* (I). This formula *necessitates* an ortho-quinonoid grouping, and in this connexion the deep red colour of the compound is noteworthy, and is not found in " normal " monohydroxy-9 : 10-anthraquinones, which are yellow.

Probably 10-chloro-1-hydroxy-4 : 9-anthraquinone is formed from quinizarin in one of two ways. (1) Quinizarin may exist in a reactive ortho-quinonoid state in which the two hydroxyl groups are in the 1 : 10 positions instead of the 1 : 4 as usually formulated. α-Hydroxyl groups of hydroxyanthraquinones react with methylating and acylating agents much less rapidly than similar groups in β-positions. This fact and others have given rise to suggestions both of co-ordination between the hydrogen atoms of the α-hydroxyls and the neighbouring carboxyl oxygen atoms (Dimroth and Faust, *Ber.*, 1921, **54**, 3020; Sidgwick and Callow, J., 1924, **125**, 527), and also of isomeric structures in which the hydrogens of the α-hydroxyl groups are attached to the *meso*-oxygen atoms (Perkin, J., 1899, **75**, 453; Georgievics, *Monatsh.*, 1911, **32**, 329), to give ortho-quinonoid formulæ. There is, however, no recorded instance of a hydroxy-9 : 10-anthraquinone reacting in such an isomeric form.

(2) The reaction may occur in two stages. The first stage may be represented by the replacement of a carbonyl oxygen atom by two chlorine atoms—a reaction of this type occurs between benzaldehyde and thionyl chloride to give benzal chloride (Loth and Michaelis, *Ber.*, 1894, **27**, 2548). The second stage would then consist of the union of one of these chlorine atoms and the



hydrogen atom of the neighbouring hydroxyl group, giving hydrogen chloride and 10-chloro-1-hydroxy-4 : 9-anthraquinone. It is intended to test this theory of the mechanism of the reaction by an examination of the action of thionyl chloride on the ethers of quinizarin.

Both the above interpretations leave unexplained why only one of the carbonyl groups of quinizarin appears to take part in the reaction.

In the preparation of pure quinizarin for this investigation it was observed that the diacetyl derivative exists in two polymorphic forms with different melting points.

EXPERIMENTAL.

Quinizarin.—Pure diacetylquinizarin (see p. 1435) was heated with concentrated sulphuric acid (6 parts) at 100° for 30 minutes, and the solution was then stirred into cold water. After boiling for 10 minutes, the mixture was filtered, the quinizarin washed with boiling water until free from acid, and dried at 100°. It assumed a dark metallic lustre at 183° and melted at 197—198°.

10-*Chloro*-1-*hydroxy*-4 : 9-*anthraquinone.*—When 30 g. of quinizarin were boiled with 120 c.c. of recently distilled thionyl chloride, solution occurred rapidly with evolution of sulphur dioxide and hydrogen chloride. After 8—30 hours, the deep red liquid was concentrated to half bulk. On cooling in a dry atmosphere, it deposited dark red, fine needles (26 g.), m. p. 225—226° (even after recrystallisation from methyl or ethyl alcohol or benzene); a further 4 g. were obtained by concentrating the filtrate. The product was washed free from thionyl chloride with dry benzene and ether and dried in a vacuum over fused calcium chloride and soda lime (Found : C, 65·0; H, 2·8; Cl, 13·7; *M*, cryoscopic in naphthalene, 265, 260. $C_{14}H_7O_3Cl$ requires C, 65·0; H, 2·7; Cl, 13·7%; *M*, 258·5). It gave a bright red colour with alcoholic ferric chloride and when warmed with pyridine formed a dirty brown solution which slowly deposited a black, apparently amorphous powder.

A mixture of 40 c.c. of 10% aqueous potassium hydroxide, 2 g. of the quinone, and 100 c.c. of 10% potassium permanganate solution was boiled for 2 hours, and the excess of permanganate destroyed by alcohol; from the colourless acidified filtrate ether extracted 0·8 g. of impure phthalic acid (identified in the form of the anhydride, from which fluorescein was prepared).

Conversion into quinizarin. (1) *By sulphuric acid.* A solution (reddish-purple) of 0·86 g. of 10-chloro-1-hydroxy-4 : 9-anthraquinone in 20 c.c. of concentrated sulphuric acid was heated on a boiling water-bath for 1 hour and then poured into water, the suspension boiled, and the light red precipitate (0·79 g., theoretical) collected and dried (Found : C, 69·8; H, 3·3. Calc.; C, 70·0; H, 3·3%). It melted at 197° alone and when mixed with pure quinizarin, and when acetylated in pyridine gave a diacetyl derivative in prisms, m. p. 206—208°.

(2) *By acetic acid.* A mixture of 0·9 g. of the quinone and 2 c.c. of acetic acid was heated, with or without 0·3 g. of freshly-fused potassium acetate, in a sealed tube for 3 hours at 180°. The product, on recrystallisation from 20 c.c. of boiling acetic acid (bone charcoal), gave 0·3—0·4 g. of red needles which, alone or

mixed with pure quinizarin, melted at 197° (Found: C, 69·8; H, 3·4%).

(3) *By methyl alcohol.* When 0·85 g. of the quinone was heated in a sealed tube at 200° for 2 hours with 2 c.c. of absolute methyl alcohol, and the product recrystallised from methyl alcohol (bone charcoal), 0·4 g. of quinizarin, m. p. 196—197°, was obtained (Found: C, 70·0; H, 3·4%).

(4) *By ethyl alcohol.* When the experiment was repeated with absolute ethyl alcohol, 0·3 g. of quinizarin was obtained (Found: C, 69·7; H, 3·3%).

(5) *By sodium or potassium hydroxide.* A paste of the quinone (3 g.) and an excess of concentrated aqueous sodium or potassium hydroxide was boiled with water for 5 minutes and stirred into an excess of boiling dilute hydrochloric acid. The reddish-brown solid (2·5 g.) produced crystallised from acetic acid in red needles of quinizarin, m. p. 195—197° (alone and mixed) (Found: C, 69·7; H, 3·3%), which was converted into its diacetyl derivative, m. p. 206—208°.

Acetylation. (1) *Acetic anhydride alone.* 10-Chloro-1-hydroxy-4 : 9-anthraquinone (4 g.) was boiled with 40 c.c. of acetic anhydride until fumes of hydrogen chloride (due to decomposition, by atmospheric moisture at the top of the condenser, of acetyl chloride produced in the reaction) were no longer observed (4 hours). The original dark red colour became dark green, and from the filtered, cooled solution small, olive-green crystals (4·2 g.), m. p. 204°, separated. These were repeatedly crystallised from acetic anhydride (bone charcoal) and finally twice from pyridine; the characteristic yellow prisms of diacetylquinizarin were then obtained which, alone or mixed with an authentic specimen, melted at 207—208°. A quantitative experiment showed that the substance did not contain chlorine [Found: C, 66·7; H, 3·6; CH_3·CO, 26·7; *M*, in freezing naphthalene, 310, 315. Calc. for $C_{14}H_6O_4(CO\cdot CH_3)_2$: C, 66·7; H, 3·7; CH_3·CO, 26·7%; *M*, 324].

Hydrolysis of this acetyl derivative by an alcoholic solution of sulphuric acid yielded quinizarin, m. p. 198° (Found: C, 69·9; H, 3·3%).

(2) *Acetic anhydride and sulphuric acid.* When 2·2 g. of 10-chloro-1-hydroxy-4 : 9-anthraquinone were heated to boiling with 10 c.c. of acetic anhydride containing 2 drops of concentrated sulphuric acid, the red solution rapidly became yellow-green. The filtered solution slowly deposited 1·4 g. of very fine, pale yellow rods identical with those obtained by acetylating quinizarin under similar conditions (see under). The product of one recrystallisation from acetic anhydride containing sulphuric acid changed colour from yellow to light orange at about 120° and melted at 200—201°

(Found: C, 66·5; H, 3·8; CH_3·CO, 26·6%). This diacetyl derivative separated from pyridine in small, yellow prisms, m. p. 207—208°.

Numerous experiments were carried out with a view to acetylating the single hydroxyl group. The chloro-compound was heated with acetyl chloride and potassium acetate under ordinary pressure, in benzene solution, and in sealed tubes at 90—100°. The products, however, were mixtures containing in some cases as little as 4% of chlorine. Attempted acetylations in pyridine with one molecular proportion of acetic anhydride yielded black amorphous products which would not crystallise and in which the chlorine content also varied.

Methylation of 10-*chloro*-1-*hydroxy*-4 : 9-*anthraquinone*. Since methylation in alkaline media was impossible, diazomethane was used. In every experiment chlorine was lost (4% in one experiment), and the products were not uniform. Nevertheless analyses clearly indicated the presence of one hydroxyl group.

In a typical experiment a suspension of 1·0 g. of the finely powdered dry compound in 30 c.c. of absolute ether at 5° was treated with an excess of diazomethane (from 2 g. of nitrosomethylurethane and 6 c.c. of 70% aqueous potassium hydroxide) in 60 c.c. of dry ether during ½ hour. Stirring was continued for 3 hours, and the red product (1 g.) collected after 12 hours. After darkening at about 190°, it melted to a black paste between 270° and 280° (Found: Cl, 12·1; OMe, 11·1. $C_{14}H_6O_2$·OMe requires Cl, 13·0; OMe, 11·4%).

Condensations with amines. (1) *Anilino-derivative*, $C_{14}H_7O_3$·NH·C_6H_5.

A solution of 1·5 g. of 10-chloro-1-hydroxy-4 : 9-anthraquinone in 8 c.c. of freshly distilled aniline was boiled for 5 minutes, the red colour changing to brown. The hot solution was stirred into an excess of dilute hydrochloric acid and boiled. The black precipitate was filtered off hot, washed free from acid and dried (1·9 g.). It separated from tetrachloroethane in black, microscopic crystals after the addition of a little ether. The product, which contained no chlorine, formed a paste at 272—274° and decomposed at 290°. It dissolved in concentrated sulphuric acid with a deep amethyst colour and in boiling sodium hydroxide to a very pale purple solution (Found: N, 4·3. $C_{20}H_{13}O_3N$ requires N, 4·4%).

(2) *Dianilino-derivative*, $C_{14}H_6O_2(NH{\cdot}C_6H_5)_2$. A mixture of 1 g. of the chloro-compound, 0·5 g. of boric acid (dried at 120° for 4 hours), and 10 c.c. of freshly-distilled aniline was boiled for 6 hours, the purple colour becoming dark brown. It was stirred while hot into an excess of dilute hydrochloric acid, and the pre-

cipitate treated as in the previous experiment. The product consisted of black crystals (1·6 g.) which did not melt below 310°. It gave a golden-brown solution in concentrated sulphuric acid, but was insoluble in hot aqueous caustic soda (Found : N, 7·2. $C_{26}H_{18}O_2N_2$ requires N, 7·2%).

The dianilino-derivative from quinizarin, prepared similarly, formed blue-black crystals from tetrachloroethane. These dissolved in sulphuric acid to a blue-black solution and were insoluble in boiling caustic soda solution (Found : N, 7·1%).

(3) *Mono-*p*-toluidino-derivative*, $C_{14}H_7O_3{\cdot}NH{\cdot}C_6H_4Me$. This was prepared in a similar manner to the monoanilino-derivative. The product, which was free from chlorine (Carius), crystallised from acetic acid in microscopic, very dark brown needles which softened at 280° and showed no further change up to 310°. Its solution in sulphuric acid was amethyst and in caustic soda light purple (Found : N, 4·1. $C_{21}H_{15}O_3N$ requires N, 4·3%).

The mono-*p*-toluidino-derivative * from quinizarin melted at 190—192°, and dissolved in concentrated sulphuric acid with a brilliant green colour (Found : N, 4·2%).

(4) *Di-*p*-toluidino-derivative*, $C_{14}H_6O_2(NH{\cdot}C_6H_4Me)_2$. This was prepared similarly to (2) above, and crystallised from alcohol in bluish-black, microscopic needles which decomposed at 305° with previous sintering. The solution in sulphuric acid was dark honey-coloured (Found : N, 6·7. $C_{28}H_{22}O_2N$ requires N, 6·7%).

The isomeric compound prepared from quinizarin gave a blue-black solution in concentrated sulphuric acid (Found : N, 6·8%).

10-*Ethoxy*-1-*hydroxy*-4 : 9-*anthraquinone*.—10-Chloro-1-hydroxy-4 : 9-anthraquinone (2·5 g.) was boiled with absolute ethyl alcohol (200 g.) containing 3% of dry hydrogen chloride for 3½ hours, the red solution becoming dark green and fluorescent. From the filtered, concentrated, cooled solution clusters of reddish-brown needles separated (2·1 g.), m. p. 135°, after recrystallisation from ethyl alcohol (Found : C, 71·3; H, 4·3; OEt, 16·3. $C_{14}H_7O_3{\cdot}OEt$ requires C, 71·6; H, 4·5; OEt, 16·9%).

This ether was very soluble in cold benzene and less soluble in cold ethyl alcohol. In concentrated sulphuric acid, its solution was similar to that given by quinizarin. When this solution was heated at 100° for 1 hour and then stirred into water, quinizarin (m. p. 195—197°) was obtained in quantitative yield (Found : C, 70·0; H, 3·4%).

1-*Chloro*-4-*acetoxyanthraquinone*.—Commercial 1-chloro-4-hydroxyanthraquinone † was boiled with an excess of acetic anhydride

* Kindly presented by the British Alizarine Co., Ltd., Manchester.

† Kindly presented by the Scottish Dyes, Ltd., Carlisle.

and a few drops of pyridine for ½ hour. The crude acetyl derivative was repeatedly crystallised from pyridine containing a little anhydride, until the melting point remained constant at 176—177°, the pure 1-*chloro*-4-*acetoxyanthraquinone* forming fine, pale primrose needles (Found : Cl, 11·8; CH_3·CO, 14·4. $C_{14}H_6O_3Cl$·CO·CH_3 requires Cl, 11·8; CH_3·CO, 14·3%).

1-*Chloro*-4-*hydroxyanthraquinone*.—The pure acetyl derivative (2 g.) was hydrolysed by boiling for 2 hours with 140 c.c. of absolute alcohol containing 3 c.c. of concentrated sulphuric acid. On cooling, the hydroxy-compound separated in golden-yellow needles, m. p. 192—193°, unchanged by further recrystallisation (Found : Cl, 13·8. Calc. for $C_{14}H_7O_3Cl$: Cl, 13·7%). The alcoholic solution of 1-chloro-4-hydroxyanthraquinone gave a pale red colour with ferric chloride.

Treatment of 1-*Chloro*-4-*hydroxyanthraquinone with Sulphuric Acid*.—A solution of 3 g. in 50 c.c. of concentrated sulphuric acid was heated at 100° for 1 hour. The hot liquid was then stirred into 200 c.c. of cold water, the mixture boiled for 10 minutes, and the yellow product filtered off, washed with boiling water until acid-free, and dried at 100° (2·8 g.). The substance melted at 192°, alone and when mixed with an authentic specimen of 1-chloro-4-hydroxyanthraquinone (Found : Cl, 13·7%).

Diacetylquinizarin.—Liebermann and Giesel (*Ber.*, 1875, **8**, 1648) describe diacetylquinizarin as " gelbe Saulchen " melting at 200°.

Quinizarin supplied by the British Dyestuffs Corporation, Ltd., was acetylated by boiling for 15 minutes with acetic anhydride containing a few drops of concentrated sulphuric acid. The product on purification was obtained in two polymorphic forms :

Form A. (1) Small, twinned, six-sided, yellow prisms from quickly chilled solutions in hot pyridine [Found : C, 66·6; H, 3·7; CH_3·CO, 26·8; *M*, cryoscopic in naphthalene, 325.

$$C_{14}H_6O_4(CO{\cdot}CH_3)_2$$

requires C, 66·7; H, 3·7; CH_3·CO, 26·7%; *M*, 324]. (2) Long, flat, six-sided, yellow plates by recrystallisation from acetic anhydride alone (Found : C, 66·4; H, 3·6; CH_3·CO, 26·6%; *M*, 330). (3) Very thin, pale yellow needles from alcohol (Found : C, 66·7; H, 3·6; CH_3·CO, 26·9%; *M*, 26·9). All three forms melted at 207—208°.

Form B. Sheaves of yellow needles or fine rods, which became light orange at about 120° and melted at 200—201° (Found : C, 66·6; H, 3·6; CH_3·CO, 26·2%; *M*, 320). This form was converted into A by recrystallisation from pyridine, acetic anhydride, or alcohol, and hot solutions of *A* in acetic anhydride containing a few drops of sulphuric acid always deposited crystals of B only.

Solubility Determinations.—The two forms of the diacetyl derivative have identical solubilities in benzene and in chloroform at 25°. This may be accounted for by the long time required for saturation. Benzene, for example, was still unsaturated with respect to A after 15 hours' shaking at 25°.

In Table I the figures represent g. of solute per 100 g. of solution.

TABLE I.

Sub-	Benzene.				Chloroform.			
stance.	20 hrs.	30 hrs.	55 hrs.	Mean.	40 hrs.	55 hrs.	65 hrs.	Mean.
A 1	0·693	0·699	0·694	0·70	5·01	5·05	5·01	5·0
A 2	0·698	—	0·699	0·70	—	5·00	—	5·0
A 3	0·698	—	0·697	0·70	—	—	—	—
B	0·694	0·700	0·699	0·70	—	5·03	5·03	5·0
A + B	—	—	0·701	0·70	—	—	—	—

Benzene was freed from thiophen, washed, dried over calcium chloride, fractionated, and distilled from sodium before use. A uniform sample was used throughout.

" Pure " chloroform was washed with alkali, acid, and water, dried over calcium chloride, and twice distilled, and a constant boiling fraction was used.

The sealed solubility tubes were attached to a large paddle stirrer, which was rotated continuously in an electrically heated thermostat (25° ± 0·025°). Samples were taken, after settling, in 50 c.c. pipettes fitted with short removable glass tubes plugged with cotton wool.

The weighing bottles were dried to constant weight at 90°. Constant weighings (± 0·0002 g.) were obtained by allowing the bottles, when removed from the oven, to stand in a desiccator over sulphuric acid for precisely 30 minutes, and by taking the final readings after the bottles had been on the balance for 2 minutes.

Cryoscopic Measurements.—In applying the test suggested by Sidgwick (J., 1915, **107**, 672) for distinguishing between polymorphic, isomeric and tautomeric substances, solvents with low freezing points such as benzene and nitrobenzene could not be used, owing to the small solubilities of the acetyl derivatives in them and also to the long time required for saturation. Naphthalene was used and saturated solutions were obtained in a few minutes at a degree or two above its freezing point. Table II shows the results of these experiments.

TABLE II.

Substance.	Weight of solvent (g.).	Maximum depression.
A 1 alone	7·785	1·95°
After addition of B	,,	1·90
B alone	7·780	1·95
After addition of A 1	,,	1·92

The determinations were carried out in a small Beckmann apparatus fitted with a thermometer graduated in tenths of a degree This could be read to the nearest fortieth of a degree with ease.

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