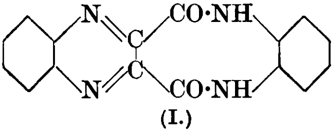
XCIII.—*The Action of* o-*Phenylenediamines upon Dihydroxytartaric Acid.*

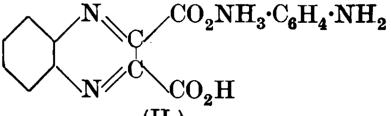
By Frederick Daniel Chattaway and William Gerald Humphrey.

In the course of his investigation of the quinoxalines, Hinsberg condensed *o*-phenylenediamine (*Ber.*, 1894, **27**, 2185) and 3 : 4-tolylenediamine (*Annalen*, 1887, **237**, 353) with sodium dihydroxytartrate and obtained, on acidification of the resulting solutions, quinoxaline-2 : 3-dicarboxylic acid and 6-methylquinoxaline-2 : 3-dicarboxylic acid respectively. Attempts to obtain the bases themselves from these acids by elimination of carbon dioxide were unsuccessful.

A reinvestigation of the course of this reaction has shown that it is not so simple as Hinsberg supposed. When sodium dihydroxytartrate is heated with an aqueous solution of *o*-phenylenediamine, two molecules of the diamine react with one molecule only of the salt, forming *quinoxaline*-2 : 3-*dicarboxy*-o-*phenylenediamide* (I); sodium dihydroxytartrate is only very sparingly soluble in water, and any excess above one molecular proportion remains in suspension unchanged. When the filtered alkaline solution is partly neutralised with hydrochloric acid, the diamide (I) separates as a colourless crystalline powder. It is stable in neutral solution, and dissolves readily in cold dilute aqueous alkali, from which it is reprecipitated on addition of a deficiency of acid. It dissolves in hot dilute hydrochloric acid (1 : 50), but on cooling, the o-*phenylenediamine* salt (II) of quinoxaline-2 : 3-dicarboxylic acid separates; whereas if it is dissolved in hot, moderately concentrated hydrochloric acid (1 : 1), quinoxaline-2 : 3-dicarboxylic acid separates on cooling, *o*-phenylenediamine hydrochloride remaining in solution. The salt (II) and the dicarboxylic acid may consequently be obtained directly from the original yellow condensation solution, the former by making the solution weakly acid with hydrochloric acid, and the latter by saturating it with gaseous hydrogen chloride.



(I.)

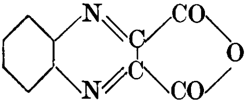


(II.)

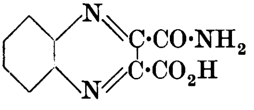
Attempts to acetylate or benzoylate the amide (I) by the usual methods also cause decomposition, with formation of the diacetyl or the dibenzoyl derivative of *o*-phenylenediamine.

Quinoxaline-2 : 3-dicarboxylic acid, when heated with acetic anhydride, is converted into *quinoxaline*-2 : 3-*dicarboxylic anhydride*

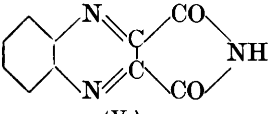
(III), and the action of dry ammonia upon this anhydride in benzene suspension yields the *ammonium* salt of *quinoxaline*-2 : 3-*dicarboxyamic acid* (IV), from which the *acid* itself may be obtained on acidification. This amic acid is converted into the corresponding *imide* (V) on being heated above its melting point, and into the *acetyl* derivative of the imide on boiling with acetic anhydride.



(III.)



(IV.)



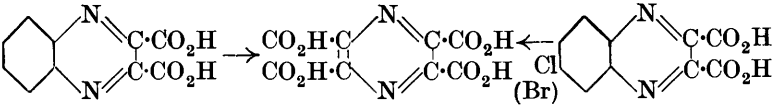
(V.)

On being heated above its melting point, quinoxalinedicarboxylic acid decomposes, evolving carbon dioxide and yielding a small quantity (10%) of quinoxaline; better yields (30%) of this base are obtained by heating the ammonium salt of the acid. In common with other nitrogen bases, quinoxaline forms a stable, well-crystallised *mono-tetrachloroiodide*.

p-Chloro-*o*-phenylenediamine (2 mols.) reacts similarly with sodium dihydroxytartrate (1 mol.), forming first 6-*chloroquinoxaline*-2 : 3-*dicarboxy*-p-*chloro*-o-*phenylenediamide*, from which the p-*chloro*-o-*phenylenediamine* salt of 6-chloroquinoxaline-2 : 3-dicarboxylic acid, and 6-*chloroquinoxaline*-2 : 3-*dicarboxylic acid* (VI) are obtained by heating with dilute and with concentrated hydrochloric acid respectively. *p*-Bromo-*o*-phenylenediamine reacts similarly to give the corresponding *bromo*-compounds. These halogen-substituted derivatives are considerably less soluble than the unsubstituted compounds, and are therefore more readily prepared and purified; otherwise their reactions are analogous. 6-Chloro- and 6-bromo-quinoxaline-2 : 3-dicarboxylic acid melt with decomposition and yield 6-*chloro*- and 6-*bromo-quinoxaline* respectively; as with the unsubstituted acid, better yields are obtained by heating the ammonium salts.

The oxidation of quinoxaline derivatives was attempted by Hinsberg (*Annalen*, 1887, **237**, 353) but without success; Gabriel and Sonn, however, succeeded in oxidising quinoxaline with alkaline permanganate to pyrazine-2 : 3-dicarboxylic acid (*Ber.*, 1907, **40**, 4850); it has been found that quinoxaline-2 : 3-dicarboxylic acid, and also 6-chloro- and 6-bromo-quinoxaline-2 : 3-dicarboxylic acids are similarly oxidised, yielding pyrazinetetracarboxylic acid (VII). This acid was prepared by Wolff (*Ber.*, 1893, **26**, 721) by the oxidation of tetramethylpyrazine, but no details or analyses are given; some difficulty was evidently experienced in preparing it, and Kalischer (*Ber.*, 1895, **28**, 1516) failed to isolate it in a pure condition from the products of oxidation of dimethyldiethylpyrazine.

Pyrazinetetracarboxylic acid forms a sparingly soluble, well-crystallised *dipotassium dihydrogen* salt and a *tetraethyl* ester.



(VII.) (VI.)

EXPERIMENTAL.

Quinoxaline-2 : 3-*dicarboxy*-o-*phenylenediamide* (I).—A fine suspension of 7 g. of sodium dihydroxytartrate (1 mol. + excess) in a solution of 5·4 g. of *o*-phenylenediamine (2 mols.) in 50 c.c. of water was heated at 90° for ½ hour, and the hot yellow filtered solution was partly neutralised by the slow addition of 2·5 c.c. of concentrated hydrochloric acid (1 mol.) with vigorous stirring. The *diamide* (I), which separated on cooling, crystallised from boiling water (animal charcoal), in which it was very easily soluble, in glistening, colourless, rhombic plates, m. p. 184° (decomp.); yield, 3 g. (Found: C, 66·1; H, 3·2; N, 19·3. $C_{16}H_{16}O_2N_4$ requires C, 66·2; H, 3·4; N, 19·3%).

o-*Phenylenediamine Salt of Quinoxaline*-2 : 3-*dicarboxylic Acid* (II).—In an experiment similar to the above, the hot filtered solution was cooled and acidified with 10 c.c. of concentrated hydrochloric acid (4 mols.); the thick pulp of the o-*phenylenediamine* salt of quinoxaline-2 : 3-dicarboxylic acid obtained was recrystallised from boiling water (animal charcoal), in which it was very easily soluble, separating in lemon-yellow, compact prisms, m. p. 186° (decomp.); yield, 5 g. (Found: C, 59·2; H, 4·4; N, 17·0. $C_{16}H_{14}O_4N_4$ requires C, 58·9; H, 4·3; N, 17·2%). This salt is also readily prepared by mixing aqueous or alcoholic solutions of quinoxalinedicarboxylic acid and *o*-phenylenediamine.

Quinoxaline-2 : 3-*dicarboxylic Acid*.—14 G. of sodium dihydroxytartrate (1 mol.) were dissolved in a hot solution of 11 g. of *o*-phenylenediamine (2 mols.) in 100 c.c. of water, and the filtered solution was saturated with hydrogen chloride. Quinoxaline-2 : 3-dicarboxylic acid, which separated as a crystalline powder, was recrystallised from boiling water (animal charcoal), in which it was moderately easily soluble, separating in long colourless prisms containing two molecules of water (yield, 8·5 g. or 70%). This water is lost at 110°; the anhydrous acid melts at 190° (decomp.). Half of the *o*-phenylenediamine is inevitably lost as the hydrochloride.

The *ethyl* ester prepared by boiling the acid with alcohol containing 2% of hydrogen chloride, separated from alcohol, in which it was very easily soluble, in small, slender, colourless prisms, m. p. 83° (Found : N, 10·1. $C_{14}H_{14}O_4N_2$ requires N, 10·2%).

The *ammonium* salt separated as a white pulp when a few drops of aqueous ammonia (*d* 0·880) were added to an alcoholic solution of the acid. It is very easily soluble in water, but is rather sparingly soluble in glacial acetic acid, from which it crystallises in long, slender, colourless prisms (Found : C, 47·3; H, 4·5. $C_{10}H_{12}O_4N_4$ requires C, 47·6; H, 4·75%); these blacken and decompose at 220—230°, yielding quinoxaline.

Quinoxaline-2 : 3-*dicarboxylic anhydride* (III) separated in very pale yellow, long prisms when a solution of 2 g. of the acid in 20 c.c. of acetic anhydride was cooled (Found: N, 13·9. $C_{10}H_4O_3N_2$ requires N, 14·0%). It decomposes and chars at 250—260°.

Quinoxaline-2 : 3-*dicarboxyamic Acid* (IV).—Dry ammonia was passed for several hours through a fine suspension of 8 g. of the anhydride (II) in 150 c.c. of benzene. The anhydride gradually dissolved and the ammonium salt of the amic acid, which separated as a white crystalline powder, was filtered off and dissolved in cold water, and the *acid* (IV) precipitated by addition of dilute hydrochloric acid. It crystallised from alcohol, in which it was moderately easily soluble, in small, colourless, rhombic prisms, m. p. 190—195° (decomp.) (Found : C, 55·1; H, 3·1; N, 19·4. $C_{10}H_7O_3N_3$ requires C, 55·3; H, 3·2; N, 19·35%).

This acid crystallises from acetic acid, in which it is very easily soluble, in colourless, compact, hexagonal prisms containing one molecule of acetic acid; if heated slowly, the crystals evolve acetic acid at about 100°, and melt identically with the acid crystallised from alcohol; the crystals slowly effloresce and become opaque on exposure to air (Found : loss at 120°, 21·8. $C_{10}H_7O_3N_3,C_2H_4O_2$ requires loss, 21·65%).

Quinoxaline-2 : 3-*dicarboxyimide* (V) was prepared by heating the above acid at 185° (oil-bath) for 20 minutes and finally at 205°. The resulting brown mass crystallised from acetic acid (animal charcoal), in which it was rather sparingly soluble, in very pale yellow, rhombic prisms, decomp. about 260° (Found : C, 60·2; H, 2·3; N, 21·2. $C_{10}H_5O_2N_3$ requires C, 60·3; H, 2·5; N, 21·1%).

The *acetyl* derivative of the above imide, prepared by crystallising 3 g. of the acid (IV) from 100 c.c. of boiling acetic anhydride, separated in colourless, irregular leaflets, decomp. about 220° (Found : C, 59·7; H, 3·0; N, 17·4. $C_{12}H_7O_3N_3$ requires C, 59·75; H, 2·9; N, 17·4%).

Preparation of Quinoxaline from Quinoxaline-2 : 3-*dicarboxylic Acid*.—The ammonium salt (5 g.) of the acid was heated at 220—240° (oil-bath) for ½ hour, and the product distilled in steam. Addition of concentrated aqueous caustic potash to the distillate gave quinoxaline in colourless, feathery needles, m. p. 27°, b. p. 225—226° (yield, 30%).

Quinoxaline Mono-tetrachloroiodide.—A solution of tetrachloroiodic acid (excess), prepared by passing chlorine through a fine suspension of 1·5 g. of iodine in 20 c.c. of concentrated hydrochloric acid, was added to 0·5 g. of quinoxaline in 2 c.c. of concentrated hydrochloric acid. The *tetrachloroiodide*, which separated immediately, crystallised from acetic acid (containing a little tetrachloroiodic acid), in which it was moderately easily soluble, in bright yellow, rhombic plates, m. p. 125—130° (decomp.) (Found: Cl, 35·7. $C_8H_6N_2,HICl_4$ requires Cl, 35·5%). It does not lose halogen on keeping and can be dried in a desiccator over calcium chloride.

6-*Chloroquinoxaline*-2 : 3-*dicarboxy*-p-*chloro*-o-*phenylenediamide* and 6-*bromoquinoxaline*-2 : 3-*dicarboxy*-p-*bromo*-o-*phenylenediamide* (formulæ as I), prepared in a similar manner to the corresponding unsubstituted compound, crystallise from water, in which they are rather sparingly soluble, in colourless irregular plates, m. p. 207° (decomp.) (Found: N, 15·7; Cl, 19·9. $C_{16}H_8O_2N_4Cl_2$ requires N, 15·6; Cl, 19·8%), and 198° (decomp.) (Found: N, 12·35; Br, 35·8. $C_{16}H_8O_2N_4Br_2$ requires N, 12·5; Br, 35·7%), respectively.

The p-*chloro*-o-*phenylenediamine* salt of 6-chloroquinoxaline-2 : 3-dicarboxylic acid and the p-*bromo*-o-*phenylenediamine* salt of 6-bromoquinoxaline-2 : 3-dicarboxylic acid (formulæ as II), prepared in a similar manner to the corresponding unsubstituted compound, crystallise from water, in which they are rather sparingly soluble, in lemon-yellow, elongated, rhombic plates, m. p. 205° (decomp.) (Found: N, 13·9; Cl, 18·0. $C_{16}H_{12}O_4N_4Cl_2$ requires N, 14·2; Cl, 18·0%), and 199° (decomp.) (Found: C, 39·9; H, 2·6; N, 11·3; Br, 33·1. $C_{16}H_{12}O_4N_4Br_2$ requires C, 39·7; H, 2·5; N, 11·6; Br, 33·1%), respectively.

6-*Chloroquinoxaline*-2 : 3-*dicarboxylic acid* (VI) was prepared in a similar manner to the corresponding unsubstituted compound. It crystallises from water, in which it is moderately easily soluble, in small, slender, colourless prisms containing two molecules of water, which are lost at 110° (Found: loss, 12·8. $C_{10}H_5O_4N_2Cl,2H_2O$ requires loss, 12·5%); the anhydrous acid melts at 175° (decomp.) (Found: C, 47·7; H, 2·0; N, 10·9; Cl, 13·9. $C_{10}H_5O_4N_2Cl$ requires C, 47·5; H, 2·0; N, 11·1; Cl, 14·05%).

The *anhydride* (formula as III), prepared by crystallising 2 g. of the acid from 20 c.c. of boiling acetic anhydride, separates in very faintly yellow, rhombic plates, decomp. 235—240° (Found: Cl, 15·15. $C_{10}H_3O_3N_2Cl$ requires Cl, 15·15%).

The *ethyl hydrogen* ester, prepared by dissolving 2 g. of the anhydride in 5 c.c. of boiling alcohol, separates on addition of water in colourless, long, slender prisms, m. p. 159° (Found: Cl, 12·6. $C_{12}H_9O_4N_2Cl$ requires Cl, 12·65%). The *ethyl* ester, prepared by boiling 2 g. of the anhydride with 5 c.c. of alcohol, containing hydrogen chloride, for 8 hours, crystallises from 25% aqueous alcohol, in which it is moderately easily soluble, in small, colourless, rhombic plates, m. p. 60° (Found: Cl, 11·4. $C_{14}H_{13}O_4N_2Cl$ requires Cl, 11·5%).

The *ammonium* salt, which separates as a white pulp when aqueous ammonia (*d* 0·880) is added to an alcoholic solution of the acid, crystallises from acetic acid, in which it is rather sparingly soluble, in hair-like needles, decomp. 215—225° (Found: Cl, 12·3. $C_{10}H_{11}O_4N_4Cl$ requires Cl, 12·4%).

6-*Chloroquinoxaline*.—6-Chloroquinoxaline-2 : 3-dicarboxylic acid decomposes on being heated to 190°, giving a 20% yield of 6-chloroquinoxaline. An improved yield is obtained by heating the corresponding ammonium salt, the method being similar to that employed in the preparation of quinoxaline; the 6-*chloroquinoxaline* was isolated by steam distillation and separated from the distillate in fine colourless needles, m. p. 60° (Found: C, 58·6; H, 3·1; N, 17·3; Cl, 21·6. $C_8H_5N_2Cl$ requires C, 58·4; H, 3·0; N, 17·0; Cl, 21·6%).

The following bromo-compounds were prepared in a similar manner to the corresponding chloro-compounds.

6-*Bromoquinoxaline*-2 : 3-*dicarboxylic acid* (VI) is moderately easily soluble in water, from which it separates in small, colourless, slender prisms containing two molecules of water which are lost at 110° (Found: loss, 11·0; Br, 24·05. $C_{10}H_5O_4N_2Br,2H_2O$ requires loss, 10·8; Br, 24·0%). The anhydrous acid melts at 172° (decomp.).

The *anhydride* (formula as III) crystallises from acetic anhydride in very pale yellow, small, flattened prisms, decomp. 235—245° (Found: Br, 28·6. $C_{10}H_3O_3N_2Br$ requires Br, 28·7%).

The *ethyl hydrogen* ester is very easily soluble in alcohol, from which it separates in very small, colourless, compact, rhombic prisms, m. p. 161° (Found: Br, 24·5. $C_{12}H_9O_4N_2Br$ requires Br, 24·6%). The *ethyl* ester is moderately easily soluble in 25% aqueous alcohol, from which it separates in colourless, long, flattened prisms, m. p. 69° (Found: Br, 22·5. $C_{14}H_{13}O_4N_2Br$ requires Br, 22·7%).

The *ammonium* salt is rather sparingly soluble in acetic acid, from which it separates in long, slender, colourless prisms, decomp. 235—240° (Found: Br, 23·9. $C_{10}H_{11}O_4N_4Br$ requires Br, 24·2%).

6-*Bromoquinoxaline* is easily soluble in water, from which it separates in fine colourless needles, m. p. 56° (Found: Br, 38·2. $C_8H_5N_2Br$ requires Br, 38·3%).

Oxidation of Quinoxaline-2 : 3-dicarboxylic Acid with Formation of Pyrazinetetracarboxylic Acid (VII).—A solution of 5 g. of quinoxaline-2 : 3-dicarboxylic acid dihydrate (1 mol.) in 60 c.c. of *N*-potassium hydroxide (3 mols.) was heated for 6 hours on a water-bath with 1000 c.c. of 2% potassium permanganate solution (6 mols.), manganese dioxide slowly separating. The small excess of permanganate was destroyed by a few drops of alcohol, and the solution was filtered, concentrated to about 80 c.c., and made just acid with hydrochloric acid (about 20 c.c.). *Dipotassium dihydrogen pyrazinetetracarboxylate* separated as a colourless crystalline precipitate; after being washed with boiling alcohol (to remove any trace of the acid), it crystallised from water, in which it was rather sparingly soluble, in compact, rhombic prisms (4 g.) (Found : K, 23·6. $C_8H_2O_8N_2K_2$ requires K, 23·5%).

Pyrazinetetracarboxylic acid was obtained from the acid potassium salt by crystallisation from 20% hydrochloric acid. It was recrystallised from water, in which it was easily soluble, separating in colourless, rhombic plates containing two molecules of water; the anhydrous acid melts with decomposition at 205° (Found : C, 33·2; H, 2·9; N, 9·4. Calc. for $C_8H_4O_8N_2,2H_2O$: C, 32·9; H, 2·75; N, 9·6%).

The *tetraethyl* ester was prepared by boiling 2 g. of the acid with 10 c.c. of alcohol, saturated with hydrogen chloride, for 8 hours. On addition of water, the ester separated as a colourless crystalline solid. It was recrystallised from alcohol, in which it was easily soluble, separating in long, colourless, rhombic prisms, m. p. 104° (Found : N, 7·5. $C_{16}H_{20}O_8N_2$ requires N, 7·6%).

THE QUEEN'S COLLEGE, OXFORD. [*Received, January 25th*, 1929.]