*The Synthesis of Compounds with Potential Anti-folic Acid Activity. Part III.** 3 : 6-*Diaminoquinoxaline and Derived Compounds.*

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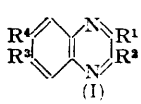
An unambiguous synthesis of 3 : 6-diaminoquinoxaline, and its 2-carboxylic acid and amide, from 2 : 4-diamino-1-nitrosobenzene is described. The corresponding 7-methyl derivatives have also been prepared.

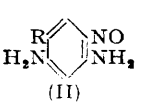
Acetylation of the 3-aminoquinoxaline-2-carboxyamides has been shown to give 3-acetamido-derivatives, which cyclise in dilute sodium hydroxide solution to 6 : 7-benzopteridines.

Four 2-aryl-substituted 3 : 6-diaminoquinoxalines have been prepared from nitrosobenzene derivatives and phenylacetonitrile and its substituted derivatives.

Quinoxaline (I; $R^1 = R^2 = R^3 = R^4 = H$) inhibits the growth of *S. lactis* R, the inhibition being reversed by folic acid (Hall, *Biochem. J.*, 1947, **41**, 294). Woolley and Pringle (*J. Biol. Chem.*, 1948, **174**, 327) found inhibition of *L. casei* in a quinoxaline derivative [I; $R^2 = R^3 = R^4 = H$, $R^1 = -CO{\cdot}NH{\cdot}C_6H_4{\cdot}CO{\cdot}NH{\cdot}CH(CO_2H){\cdot}[CH_2]_2{\cdot}CO_2H$] which showed structural analogies with folic acid. Horner, Schwenk, and Junghanns (*Annalen*, 1953, **579**, 212) have recently prepared a number of quinoxalines, isosteric with simple pteridine derivatives. Further the successful use of sulphanilamide derivatives of quinoxalines as antibacterial agents in animals indicates the pharmacological suitability of this nucleus (Smith and Robinson, *Proc. Soc. Exp. Biol. Med.*, 1944, **57**, 292; Seeler *et al.*, *J. Pharmacol.*, 1944, **82**, 357). And since in Part I (*J.*, 1954, 2887) it was shown that 6-aryl-2 : 4 : 7-triaminopteridines showed antifolic acid activity we wished to ascertain the effect of analogous substitution in the quinoxaline nucleus.

Hitherto all routes leading to quinoxalines involve condensation of *o*-phenylenediamine with structures containing the 1 : 2-dicarbonyl function. Clearly when both the dicarbonyl structure and the *o*-phenylenediamine are unsymmetrically substituted, the product


(I)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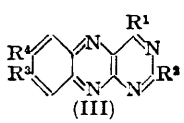
(III)

isolated will be a mixture of isomers or a single substance of ambiguous structure. Thus a glyoxylic acid (or ester) or alloxan and an unsymmetrically substituted *o*-phenylenediamine will yield a 2(or 3)-hydroxyquinoxaline, or an alloxazine of undetermined structure. The former type of product has been converted into 2(or 3)-aminoquinoxalines by replacement of hydroxyl by chlorine and reaction with ammonia (Weijlard, Tishler, and Erickson, *J. Amer. Chem. Soc.*, 1944, **66**, 1951; Wolf *et al.*, *ibid.*, 1949, **71**, 6); and the alloxazine by hydrolytic fission of the pyrimidine ring yields aminoquinoxalinecarboxylic acid or its derivatives (Kuhn and Bär, *Ber.*, 1934, **67**, 898; Weijlard and Tishler, U.S.P. 2,479,443;

* Part II, *J.*, 1954, 2895.

Wolf, Beutel, and Stevens, *J. Amer. Chem. Soc.*, 1948, **70**, 2572). Again, 2-aminoquinoxaline can be prepared by the condensation of *o*-phenylenediamine and formaldehyde cyanohydrin, ring closure of the product, and subsequent oxidation (Pfister, Sullivan, Weijlard, and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 4955), but ambiguous structures would be obtained from unsymmetrically substituted *o*-phenylenediamines.

We have therefore developed an unambiguous synthesis for 3 : 6-diaminoquinoxalines, both substituted and unsubstituted in the 2-position. We reported (*Chem. and Ind.*, 1954, 405) that *o*-aminonitrosobenzene derivatives react with cyanoacetic acid or its amide to yield quinoxaline derivatives. Part I (*loc. cit.*) described the formation of 6-aryl-7-aminopteridines from aminonitrosopyrimidines and substituted phenylacetonitriles and this reaction has now been extended to the preparation of several new 3 : 6-diamino-2-arylquinoxalines.

Readily available starting materials were 2 : 4-diamino- and 2 : 4-diamino-5-methyl-1-nitrosobenzene (II; R = H and Me) obtained by the nitrosation of *m*-phenylenediamine and *m*-tolylenediamine in hydrochloric acid solution with less than the theoretically required amount of sodium nitrite (Täuber and Walder, *Ber.*, 1900, **33**, 2118). On the reaction of (II; R = H or Me) with cyanoacetic acid in ethanol containing 2 mols. of sodium ethoxide, sodium 3 : 6-diaminoquinoxaline- and 3 : 6-diamino-7-methylquinoxaline-2-carboxylate (I; $R^2 = R^3 = NH_2$, R^4 = H or Me, $R^1 = CO_2Na$) were rapidly deposited in high yield. Lower yields were obtained when 1—2 mols. of sodium ethoxide were used. With 2-ethoxyethanol containing sodium 2-ethoxyethoxide there is more rapid reaction but greater contamination of the products. Both the quinoxalinecarboxylic acids were readily decarboxylated in hot quinoline. Both the resultant amines with hot acetic anhydride yielded the 3 : 6-diacetamido-derivatives.

2 : 4-Diamino-1-nitrosobenzene (II; R = H) with cyanoacetamide in ethanol containing 1 mol. of sodium ethoxide yielded 3 : 6-diaminoquinoxaline-2-carboxyamide (I; $R^1 = CO{\cdot}NH_2$, $R^2 = R^3 = NH_2$, R^4 = H), which with boiling acetic anhydride yielded the same compound, 3 : 6-diacetamidoquinoxaline-2-carboxyamide (I; $R^1 = CO{\cdot}NH_2$, $R^2 = R^3$ = NHAc, R^4 = H) after boiling for one or for sixty min. Warming this diacetamido-derivative in 0·5N-sodium hydroxide suspension caused rapid ring closure to 3′-acetamido-4-hydroxy-2-methyl-6 : 7-benzopteridine (III; R^1 = OH, R^2 = Me, R^3 = NHAc, R^4 = H). The diamino-amide with ethyl orthoformate in the presence of acetic anhydride (Albert, Brown, and Cheeseman, *J.*, 1951, 474) yielded a product to which structures (III; R^1 = OH, R^2 = H or Me, R^3 = NHAc or NH·CHO, R^4 = H) could be allotted, essentially depending on whether the 3-amino-group of the quinoxaline was acetylated or formylated before ring closure occurred. Hydrolysis of the cyclised product yielded 3′-amino-4-hydroxy-6 : 7-benzopteridine (III; R^1 = OH, R^2 = H, $R^3 = NH_2$, R^4 = H), showing that the initial compound must be 3′-acetamido-4-hydroxy-6 : 7-benzopteridine (III; R^1 = OH, R^2 = H, R^3 = NHAc, R^4 = H).

2 : 4-Diamino-5-methyl-1-nitrosobenzene (II; R = Me) and cyanoacetamide yielded 3 : 6-diamino-7-methylquinoxaline-2-carboxyamide (I; $R^1 = CO{\cdot}NH_2$, $R^2 = R^3 = NH_2$, R^4 = Me), which when boiled with acetic anhydride for 1 min. yielded the 6-acetamido-derivative (I; $R^1 = CO{\cdot}NH_2$, $R^2 = NH_2$, R^3 = NHAc, R^4 = Me). That the product is not the isomeric 3-acetamido-derivative is shown by its being unchanged after 30 minutes' treatment with hot sodium hydroxide solution which would have cyclised the 3-acetamido-compound to a benzopteridine. Confirmation was afforded by the fact that the original amide (I; $R^1 = CO{\cdot}NH_2$, $R^2 = R^3 = NH_2$, R^4 = Me) was readily diazotised and coupled with R salt, while the acetylated product was unaffected. It was to be expected that the aromatic 6-amino-group would be diazotised rather than the 3-amino-group in the pyrazine ring and this is shown to be the case by the inability of the 3-amino-group in the compound (I; $R^1 = CO{\cdot}NH_2$, $R^2 = NH_2$, R^3 = NHAc, R^4 = Me) to react with nitrous acid. Reaction of the amide (I; $R^1 = CO{\cdot}NH_2$, $R^2 = R^3 = NH_2$, R^4 = Me) with boiling acetic anhydride for 1 hr. yielded the 3 : 6-diacetamidoamide together with a small amount of material $C_{16}H_{17}O_4N_5$, m. p. 245°. The structure (III; R^1 = OAc, $R^2 = R^4$ = Me, R^3 = NHAc), as the monohydrate, for this compound is supported by its infrared spectrum: in chloroform two absorption bands of approximately equal intensity were found in the

carbonyl region at 1679 and 1719 cm.$^{-1}$ and have been assigned to the secondary amide and the acetoxy-group respectively, and the total integrated intensity is close to that expected for these two groups (Richards and Burton, *Trans. Faraday Soc.*, 1949, **45**, 874; Jones, Ramsay, Keir, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 80); the intensity evidence excludes, in particular, the structure (I; R^1 = CO·NHAc, R^2 = R^3 = NHAc, R^4 = Me) which would absorb much more strongly in this region. No weight loss occurred on drying *in vacuo* at 180°; Gowenlock, Newbold, and Spring (*J.*, 1948, 517) suggested an analogous structure for one of the products from the reaction of 2-aminoquinoxaline-3-carboxyamide (I; R^1 = CO·NH_2, R^2 = NH_2, R^3 = R^4 = H) with acetic anhydride. Prolonged treatment of the diacetamido-derivative (I; R^1 = CO·NH_2, R^2 = R^3 = NHAc, R^4 = Me) with hot acetic anhydride yielded exclusively the material, m. p. 245°. Ring closure of the diacetamido-derivative (I; R^1 = CO·NH_2, R^2 = R^3 = NHAc, R^4 = Me) with warm dilute sodium hydroxide solution yielded 3′-acetamido-4-hydroxy-2 : 2′-dimethyl-6 : 7-benzopteridine (III; R^1 = OH, R^2 = R^4 = Me, R^3 = NHAc) which however remains unchanged by boiling acetic anhydride for 9 hr.

2 : 4-Diamino-1-nitrosobenzene (II; R = H) also reacted with *o*-chlorophenylacetonitrile and *p*-chlorophenylacetonitrile in ethanol containing sodium ethoxide to yield 3 : 6-diamino-2-*o*- and 3 : 6-diamino-2-*p*-chlorophenylquinoxaline (I; R^1 = Cl·C_6H_4, R^2 = R^3 = NH_2, R^4 = H) respectively. Similarly 2 : 4-diamino-5-methyl-1-nitrosobenzene with phenylacetonitrile and *o*-chlorophenylacetonitrile yielded 3 : 6-diamino-7-methyl-2-phenyl- and -2-*o*-chlorophenyl-quinoxaline.

Experimental

M. p.s were determined on an electrically heated copper block. Analyses are by Mr. P. R. W. Baker, Beckenham. Fluorescence (which was intense) refers to ultraviolet light. Temperatures in parentheses in analyses refer to drying *in vacuo*.

3 : 6-*Diaminoquinoxaline*-2-*carboxylic Acid*.—To a solution of sodium (0·5 g.) in 2-ethoxyethanol (25 ml.) were added 2 : 4-diamino-1-nitrosobenzene (1·37 g.) and cyanoacetic acid (0·95 g.), and the mixture was boiled under reflux for 15 min., during which a brown precipitate was deposited. This (2·2 g.) was crystallised several times from acetic acid, to yield 3 : 6-*diaminoquinoxaline*-2-*carboxylic acid* as yellow rods, m. p. 255° (effervescence) [Found (110°): C, 52·1; H, 4·0; N, 27·6. $C_9H_8O_2N_4$ requires C, 52·9; H, 3·95; N, 27·4%]. The acetic acid solution showed an intense green fluorescence.

3 : 6-*Diaminoquinoxaline*.—3 : 6-Diaminoquinoxaline-2-carboxylic acid (1·33 g.) was boiled under an air-condenser with quinoline (50 ml.) for 30 min. during which a clear solution was obtained. The solution was filtered and the bulk of the quinoline was removed under reduced pressure on the pump. Addition of ether to the residue deposited a yellow precipitate, which after drying was sublimed twice at 180°/0·1 mm. Crystallisation from water yielded 3 : 6-*diaminoquinoxaline* as pale yellow silky needles, m. p. 204° (Found: C, 59·6; H, 4·9; N, 35·1. $C_8H_8N_4$ requires C, 60·0; H, 5·0; N, 35·0%).

Treatment of the base with hot acetic anhydride yielded 3 : 6-*diacetamidoquinoxaline* as fine white needles (from water), m. p. 302° [Found (150°): C, 58·9; H, 5·1; N, 23·0. $C_{12}H_{12}O_2N_4$ requires C, 59·0; H, 4·95; N, 22·9%].

The base and aqueous picric acid gave the *picrate*, orange rods (from water), m. p. 200° (decomp.) (Found: C, 43·4; H, 2·8; N, 24·6. $C_{14}H_{11}O_7N_7$ requires C, 43·2; H, 2·8; N, 25·2%).

3 : 6-*Diamino*-7-*methylquinoxaline*-2-*carboxylic Acid*.—2 : 4-Diamino-5-methyl-1-nitrosobenzene (3·0 g.) and cyanoacetic acid (2·0 g.) were added to a solution of sodium (1·2 g.) in ethanol (100 ml.), and the mixture was boiled under reflux for 1 hr. The precipitated salt was removed, washed with ether, and dried. Several crystallisations from glacial acetic acid yielded 3 : 6-*diamino*-7-*methylquinoxaline*-2-*carboxylic acid* as irregular yellow prisms, m. p. 248° (effervescence) (Found: C, 50·9; H, 5·3; N, 19·9. $C_{10}H_{10}O_2N_4,CH_3{\cdot}CO_2H$ requires C, 51·4; H, 5·75; N, 20·0%). The acetic acid solution showed a green fluorescence.

3 : 6-*Diamino*-7-*methylquinoxaline*.—3 : 6-Diamino-7-methylquinoxaline-2-carboxylic acid (1·0 g.) and nitrobenzene (10 ml.) were boiled under air-condenser for 1 hr. during which a clear solution was obtained. The hot solution was filtered through a warm funnel. Brown crystals were gradually deposited. After addition of ether and light petroleum (b. p. 40—60°) the crystalline precipitate was filtered off and dried (0·58 g.). Several crystallisations from water

yielded 3 : 6-*diamino*-7-*methylquinoxaline* as yellow rods, m. p. 221° (Found : C, 62·4; H, 5·9; N, 32·0. $C_9H_{10}N_4$ requires C, 62·05; H, 5·8; N, 32·2%).

Hot acetic anhydride (15 min.) yielded 3 : 6-*diacetamido*-7-*methylquinoxaline* as white silky needles, m. p. 310° (Found : C, 60·3; H, 5·55; N, 22·7. $C_{13}H_{14}O_2N_4$ requires C, 60·45; H, 5·5; N, 21·7%). 3 : 6-*Diamino*-7-*methylquinoxaline picrate* formed deep orange rods (from water), m. p. 288° (decomp.), softening at 250° (Found : C, 44·9; H, 3·4; N, 23·5. $C_{15}H_{13}O_7N_7$ requires C, 44·7; H, 3·25; N, 24·3%).

3 : 6-*Diaminoquinoxaline*-2-*carboxyamide*.—2 : 4-Diamino-1-nitrosobenzene (2·74 g.) was added to a solution of sodium (0·15 g.) in ethanol (50 ml.), followed by cyanoacetamide (1·85 g.). The mixture was boiled under reflux for 5 min. during which a yellow precipitate was deposited. After chilling in ice-water the precipitate was removed and dried at 110° (yield, 3·5 g.). Several crystallisations from water (charcoal) yielded 3 : 6-*diaminoquinoxaline*-2-*carboxyamide* as yellow needles, m. p. 295° (decomp.) [Found (150°) : C, 53·4; H, 4·8; N, 34·5. $C_9H_9O_2N_5$ requires C, 53·2; H, 4·5; N, 34·5%]. The aqueous solution showed a yellowish-green fluorescence.

This amide (1·0 g.) gave a solution in boiling acetic anhydride (25 ml.) in 1 min., which then immediately deposited yellow crystals. The mixture was immediately chilled and the precipitate removed and dried (1·24 g.). Several crystallisations from *n*-butanol afforded 3 : 6-*diacetamidoquinoxaline*-2-*carboxyamide* as yellow heart-shaped plates showing a high degree of twinning, slowly softening above 260° [Found (180°) : C, 54·55; H, 4·3; N, 24·2. $C_{13}H_{13}O_3N_5$ requires C, 54·35; H, 4·55; N, 24·4%]. One hour's boiling gave identical material (crystal form; fluorescence) (Found : N, 24·4%). The solution in *n*-butanol showed a blue fluorescence.

3′-*Acetamido*-4-*hydroxy*-2-*methyl*-6 : 7-*benzopteridine*.—3 : 6-Diacetamidoquinoxaline-2-carboxyamide (1·0 g.) was warmed in 0·5N-sodium hydroxide (40 ml.) until a clear solution was obtained (3—4 min.). The solution was filtered and acidified with glacial acetic acid, buff-coloured crystals being obtained. After cooling in ice-water, the precipitate was removed and dried (0·87 g.). Several crystallisations from *n*-butanol yielded 3′-*acetamido*-4-*hydroxy*-2-*methyl*-6 : 7-*benzopteridine* as small yellow rectangular rods, slow decomp. >280° [Found (180°) : C, 58·5; H, 4·6; N, 25·4. $C_{13}H_{11}O_2N_5$ requires C, 58·0; H, 4·1; N, 26·0%]. The solution in *n*-butanol showed a yellowish-green fluorescence.

3′-*Acetamido*-4-*hydroxy*-6 : 7-*benzopteridine*.—3 : 6-Diaminoquinoxaline-2-carboxyamide (1·0 g.) was boiled under reflux with ethyl orthoformate (10 ml.) and acetic anhydride (10 ml.) for 2·25 hr. or 15 min. (Albert, Brown, and Cheeseman, *loc. cit.*). After cooling in ice, the precipitate was removed and dried (1·3 g.). Several crystallisations from dimethylformamide (charcoal) yielded 3′-*acetamido*-4-*hydroxy*-6 : 7-*benzopteridine* as orange platelets or stubby needles, m. p. >300° [Found (180°) : C, 56·05, 56·2; H, 3·75, 3·8; N, 27·0. $C_{12}H_9O_2N_5$ requires C, 56·5; H, 3·55; N, 27·4%]. The material was completely soluble in dilute sodium hydroxide solution and showed a salmon-pink fluorescence.

Hydrolysis of 3′-*Acetamido*-4-*hydroxy*-6 : 7-*benzopteridine*.—This amide (250 mg.) and 6N-hydrochloric acid (10 ml.) were boiled under reflux for 30 min., giving first a deep red solution and then a brown precipitate. After neutralisation with sodium carbonate solution, the precipitate was removed. Several crystallisations from water (some scarlet insoluble material was present) yielded 3′-*amino*-4-*hydroxy*-6 : 7-*benzopteridine* as deep orange needles, m. p. >340° [Found (180°) : C, 55·55; H, 3·7. $C_{10}H_7ON_5$ requires C, 56·3; H, 3·3%]. The alternative hydrolysis product, 3′-amino-4-hydroxy-2-methyl-6 : 7-benzopteridine, $C_{11}H_9ON_5$, would require C, 58·2; H, 4·0%.

The compound was easily soluble in dilute sodium hydroxide solution and this solution showed an orange fluorescence.

3 : 6-*Diamino*-7-*methylquinoxaline*-2-*carboxyamide*.—2 : 4-Diamino-5-methyl-1-nitrosobenzene (6·0 g.) and cyanoacetamide (4·0 g.) were added to a solution of sodium (1·0 g.) in dry ethanol (150 ml.) and the mixture was boiled for 1 hr. A thick yellow precipitate was deposited after 30 min. After cooling in ice-water, the precipitate was removed (7·8 g.). Several crystallisations from water (charcoal) yielded 3 : 6-*diamino*-7-*methylquinoxaline*-2-*carboxyamide* as long yellow silky needles, m. p. 245° [Found (110°) : C, 55·8; H, 5·05; N, 32·4. $C_{10}H_{11}ON_5$ requires C, 55·3; H, 5·1; N, 32·2%]. The aqueous solution showed an intense green fluorescence. Diazotisation and coupling with R salt gave a brilliant scarlet colour.

6-*Acetamido*-3-*amino*-7-*methylquinoxaline*-2-*carboxyamide*.—3 : 6-Diamino-7-methylquinoxaline-2-carboxyamide (1·0 g.) and acetic anhydride (25 ml.) were boiled under reflux for 1—2 min.; a bright yellow precipitate was formed. The mixture was immediately cooled in ice and the precipitate was washed with ether and dried in the air (1·1 g.). Several crystallisations from water (750 ml.) yielded 6-*acetamido*-3-*amino*-7-*quinoxaline*-2-*carboxyamide* as yellow

rectangular plates, m. p. 315° (slow decomp.) [Found (180°; loss, 7·1%) : C, 54·9; H, 4·6; N, 27·1. $C_{12}H_{13}O_2N_5$ requires C, 55·6; H, 5·05; N, 27·0; $C_{12}H_{13}O_2N_5,H_2O$ requires H_2O, 6·5%]. The aqueous solution showed a green fluorescence visible both in daylight and in ultraviolet light.

3 : 6-*Diacetamido-7-methylquinoxaline-2-carboxyamide.*—3 : 6-Diamino-7-methylquinoxaline-2-carboxyamide (4 g.) was boiled under reflux for 1 hr. with acetic anhydride (100 ml.). A bright yellow, thick precipitate was first formed which was rapidly transformed into a denser pale yellow material. After cooling in ice-water, the precipitate was washed with ether and dried in the air (3·84 g.). Two crystallisations from *n*-butanol afforded 3 : 6-*diacetamido-7-methylquinoxaline-2-carboxyamide* as yellow rods, m. p. >300° [Found (180°) : C, 55·8; H, 4·9; N, 23·0. $C_{14}H_{15}O_3N_5$ requires C, 55·8; H, 5·0; N, 23·25%].

The acetic anhydride mother-liquors were evaporated to dryness under reduced pressure to yield a pale yellow precipitate (0·74 g.). Several crystallisations from *n*-butanol afforded microscopic pale yellow needles, m. p. 244—245° [Found (110°) : C, 55·8; H, 4·8; N, 20·5. $C_{16}H_{17}O_4N_5$ requires C, 56·0; H, 5·0; N, 20·4%]. On the basis of the analysis and because in $CHCl_3$ infrared max. were found at 1719 (OAc) and 1679 (NHAc) cm.$^{-1}$ the tentative structure 3′-*acetamido*-4-*acetoxy*-2 : 2′-*dimethyl*-6 : 7-*benzopteridine monohydrate* is assigned to this compound.

When the diacetamidoquinoxaline was boiled under reflux with acetic anhydride for a further 3 hr. it dissolved and, on working up, again yielded the material, m. p. 245°, which had a greenish-blue fluorescence.

3′-*Acetamido*-4-*hydroxy*-2 : 2′-*dimethyl*-6 : 7-*benzopteridine.*—3 : 6-Diacetamido-7-methylquinoxaline-2-carboxyamide (1·0 g.) was warmed in 0·5N-sodium hydroxide (40 ml.) until dissolved (3—4 min.). The solution was filtered and acidified with acetic acid, giving a pale buff-coloured precipitate. After cooling, this was removed (0·9 g.). Several crystallisations from a large volume of water yielded 3′-*acetamido*-4-*hydroxy*-2 : 2′-*dimethyl*-6 : 7-*benzopteridine* as microscopic bundles of needles, m. p. >300° [Found (180°) : C, 59·6; H, 4·4; N, 24·8; O, 11·75. $C_{14}H_{13}O_2N_5$ requires C, 59·35; H, 4·6; N, 24·7; O, 11·30%]. The compound was easily soluble in sodium hydroxide solution which had an orange fluorescence. An acetic acid solution had a yellow fluorescence. The compound was unchanged by boiling acetic anhydride for 9 hr. [Found (180°) : C, 59·0; H, 4·85; N, 24·4; O, 11·9%].

3 : 6-*Diamino*-2-o-*chlorophenylquinoxaline.*—2 : 4-Diamino-1-nitrosobenzene (1·37 g.) and *o*-chlorophenylacetonitrile (1·6 ml.) were boiled under reflux for 4 hr. with a solution of sodium (0·3 g.) in ethanol (100 ml.). On cooling in ice, a crystalline material was deposited, which was removed (2·35 g.). Several crystallisations from 50% aqueous ethanol followed by one from ethanol yielded 3 : 6-*diamino*-2-o-*chlorophenylquinoxaline* as pale buff needles, m. p. 230—231° [Found (110°) : C, 61·3; H, 4·1; N, 20·6. $C_{14}H_{11}N_4Cl$ requires C, 62·1; H, 4·1; N, 20·7%]. The solution in ethanol showed a green fluorescence.

A similar mixture containing *p*-chlorophenylacetonitrile (1·6 ml.) was boiled for 1 hr. The bulk of the ethanol was removed and the residue was cooled in ice-water; a yellow precipitate was deposited (2·2 g.) which on several crystallisation from aqueous ethanol yielded 3 : 6-*diamino*-2-p-*chlorophenylquinoxaline* as yellow needles, m. p. 212—213° [Found (110°) : C, 62·2; H, 4·2; N, 21·2; Cl, 12·4. $C_{14}H_{11}N_4Cl$ requires C, 62·1; H, 4·1; N, 20·7; Cl, 13·1%]. The solution in ethanol showed a green fluorescence.

3 : 6-*Diamino-7-methyl-2-phenylquinoxaline.*—To a solution of sodium (0·3 g.) in dry ethanol (100 ml.) were added 2 : 4-diamino-5-methyl-1-nitrosobenzene (1·5 g.) and benzyl cyanide (1·2 ml.), and the mixture was boiled under reflux for 8 hr. After removal of the ethanol, the residue was triturated with water to give a buff precipitate, which was removed and dried in the air (2·25 g.). Several crystallisations from ethanol yielded 3 : 6-*diamino-7-methyl-2-phenylquinoxaline* as light brown plates, m. p. 174° [Found (110°) : C, 72·0; H, 5·5; N, 22·9. $C_{15}H_{14}N_4$ requires C, 72·0; H, 5·6; N, 22·4%]. The solution in ethanol showed a blue-green fluorescence.

3 : 6-*Diamino*-2-o-*chlorophenyl*-7-*methylquinoxaline.*—2 : 4-Diamino-5-methyl-1-nitrosobenzene (1·5 g.) and *o*-chlorophenylacetonitrile (1·6 ml.), reacting as above, gave 3 : 6-*diamino*-2-o-*chlorophenyl*-7-*methylquinoxaline* as colourless soft needles, m. p. 236° [Found (110°) : C, 63·1; H, 4·6; N, 19·9; Cl, 12·0. $C_{15}H_{13}N_4Cl$ requires C, 63·25; H, 4·6; N, 19·7; Cl, 12·45%]. The solution in ethanol showed a pale blue fluorescence.

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