511. *Heterocyclic* N-*Oxides. Part III.*[1] *Extensions of a Quinoxaline* N-*Oxide Synthesis.*

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When warmed with sodium ethoxide in ethanol, both the ester (I; R = R′ = H, R″ = CO_2Et) and the dianilide (V) afford a mixture of the quinoxaline *N*-oxides (II; R = H, R′ = H or CO_2Et). The *N*-methylanilide (I; R = Me, R′ = H, R″ = Ph) cyclises in high yield to the oxide (II; R = Me, R′ = Ph), in contrast to *o*-nitro-α-phenylacetanilide (I; R = R′ = H, R″ = Ph) which gives the oxide (II; R = H, R′ = Ph) in poor yield. Hydrolysis of the nitriles (II; R = H or Me, R′ = CN), formed by treating the anilides (I; R = H or Me, R′ = H, R″ = Cl or CN) with aqueous sodium cyanide, yields the hydroxy-compounds (II; R = H or Me, R′ = OH). Aqueous sodium hydroxide converts the anilide (I; R = H, R′ = Me, R″ = Bz), obtained by methylation of α-benzoyl-*o*-nitroacetanilide (I; R = R′ = H, R″ = Bz), into the oxide (II; R = H, R′ = Me).

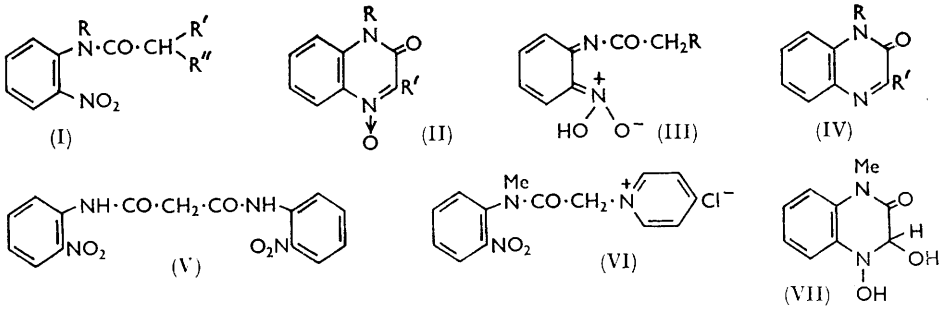
As was shown in Part I,[2] derivatives of *o*-nitroacetanilide (I; R = R′ = H), when warmed with aqueous alkali, afford 1,2-dihydro-2-oxoquinoxaline 4-oxides (II; R = H). A similar reaction is the base-catalysed cyclisation of *o*-nitrophenylurea to 3-hydroxy-1,2,4-benzotriazine *N*-oxide,[3] which belongs to a class of nitro-group side-chain interactions whose study has recently been undertaken by Loudon and his collaborators.[4] They propose a mechanism involving a direct aldol-type condensation between the nitro-group and the side-chain, rather than interaction preceded by the formation of an *aci*-nitro-intermediate (*e.g.*, III) as proposed by Arndt.[3] For this reason, it was of interest to attempt the cyclisation of the methylated anilides (I; R = Me, R′ = H) which lack the proton necessary for the formation of an *aci*-nitro-intermediate, and, if possible, extend the reaction to other *o*-nitroacetanilides.

[1] Part II, *J.*, 1964, 1986.
[2] Part I, *J.*, 1963, 2428.
[3] Arndt, *Ber.*, 1913, **46**, 3522.
[4] Loudon and Wellings, *J.*, 1960, 3462; Loudon and Tennant, *J.*, 1960, 3466.

Attempts to prepare the ester (I; R = R′ = H, R″ = CO_2Et) and the nitrile (I; R = R′ = H, R″ = CN) from *o*-nitroaniline and diethyl malonate or ethyl cyanoacetate by the Weissberger–Kibler method,[5] were unsuccessful. Using diethyl malonate, the only products isolated were the acid (I; R = R′ = H, R″ = CO_2H) and the dianilide (V), whilst ethyl cyanoacetate did not react. However, the anilides required were conveniently prepared by warming *o*-nitroaniline or its *N*-methyl derivative with the corresponding acid chloride in dry benzene.

Unlike α-acetyl- or α-benzoyl-*o*-nitroacetanilide,[2] the anilides (I; R = R′ = H, R″ = CO_2H, CO_2Et, or Ph) and the dianilide (V) were rapidly hydrolysed by warm aqueous alkali to *o*-nitroaniline. Poor yields of quinoxaline *N*-oxides were obtained when sodium ethoxide was the base in these reactions. Thus, the ester (I; R = R′ = H, R″ = CO_2Et) and the dianilide (V) gave a mixture of the oxide (II; R = H, R′ = CO_2Et) and 1,2-dihydro-2-oxoquinoxaline 4-oxide (II; R = R′ = H).[2] The latter was also formed by cyclisation of the acid (I; R = R′ = H, R″ = CO_2H). *o*-Nitro-α-phenylacetanilide (I; R = R′ = H, R″ = Ph), on the other hand, contains a relatively unreactive methylene group, and gave a low yield of the phenylquinoxaline (II; R = H, R′ = Ph). In contrast, the *N*-methylanilide (I; R = Me, R′ = H, R″ = Ph), warmed with aqueous alkali or sodium ethoxide in ethanol, afforded the oxide (II; R = Me, R′ = Ph), identical with the *N*-methyl derivative of the oxide (II; R = H, R′ = Ph), in high yield. Increased resistance to hydrolysis might account for the higher yield of the *N*-methyl derivative. When warmed with piperidine in methanol, the pyridine salt (VI) likewise gave the amine (II; R = Me, R′ = NH_2).[2] The structure of the oxides (II; R = H, R′ = CO_2Et or Ph) and (II; R = Me, R′ = Ph or NH_2) were established by reduction to the corresponding known quinoxalones.

Whereas warm aqueous sodium cyanide converted the anilides (I; R = H or Me, R′ = H, R″ = CN) into the nitriles (II; R = H or Me, R′ = CN), cyclisation in warm aqueous alkali, yielded the hydroxy-compounds (II; R = H or Me, R′ = OH) which were also formed by refluxing the nitriles with acid or alkali. Sodium ethoxide in ethanol, however, cyclised the anilide (I; R = R′ = H, R″ = CN) to the oxide (II; R = H, R′ = CN), but reacted with the *N*-methylanilide (I; R = Me, R′ = H, R″ = CN) to give the hydroxy-compound (II; R = Me, R′ = OH). The nitrile (II; R = Me, R′ = CN) is a



probable intermediate in the latter reaction since it is similarly converted into the hydroxy-compound. Fusco and Rossi [6] cyclised the nitrile (I; R = R′ = H, R″ = CN) to the oxide (II; R = H, R′ = CN) using aqueous barium hydroxide, sodium ethoxide in ethanol, or sodamide in benzene. The hydroxy-compounds (II; R = H or Me, R′ = OH) were identified by comparison with authentic samples,[2,7] and, in the case of the oxide (II; R = Me, R′ = OH), by the formation of an acetate showing an infrared band at 1800

[5] Weissberger and Kibler, *Org. Synth.*, 1945, **25**, 7.
[6] Fusco and Rossi, *Chimica e Industria*, 1963, **45**, 834.
[7] Landquist, *J.*, 1953, 2830.

cm.$^{-1}$ (cyclic :N·OAc,[4] which gave the quinoxalone (IV; R = Me, R′ = OH) [7] on hydrogenolysis. The oxides (II; R = H or Me, R′ = CN) were also formed by warming the chloroanilides (I; R = H or Me, R′ = H, R″ = Cl) with aqueous sodium cyanide, and, on reduction with sodium dithionate in acetic acid, gave poor yields of the expected nitriles (IV; R = H or Me, R′ = CN), the major products being the quinoxalones (IV; R = H or Me, R′ = H). This is not unexpected since, under similar conditions, the nitriles are reduced to the quinoxalones.[1] In contrast, reduction of the oxide (II; R = H, R′ = CN) with zinc and acetic acid gives a mixture of the nitrile (IV; R = H, R′ = CN) and 1,4-dihydro-2-hydroxyquinoxaline.[6] Hydrolysis with hot polyphosphoric acid to the amides (II; R = H or Me, R′ = $CONH_2$) which on reduction afforded the quinoxalones (IV; R = H or Me, R′ = $CONH_2$),[8] established the structure of the nitriles (II; R = H or Me, R′ = CN). Like the oxides (II; R = H or Me, R′ = Ac or Bz),[2] the amides (II; R = H or Me, R′ = $CONH_2$), warmed with aqueous sulphuric acid in acetic acid, gave the hydroxyquinoxalones (IV; R = H or Me, R′ = OH). However, warm aqueous alkali converted the amide (II; R = H, R′ = $CONH_2$) into the oxide (II; R = R′ = H), but reacted with the *N*-methyl compound (II; R = Me, R′ = $CONH_2$) to give a mixture of the oxide (II; R = Me, R′ = OH),[7] the quinoxalone (IV; R = Me, R′ = OH),[7] and the acid (IV; R = Me, R′ = CO_2H).[9] In contrast, warming of the amide (II; R = Me, R′ = $CONH_2$) with aqueous sodium cyanide gave only the hydroxy-compound (IV; R = Me, R′ = OH). The oxide (II; R = Me, R′ = H) is a possible intermediate in these reactions since it also reacted with aqueous sodium cyanide to give the hydroxy-compound,[1] and with warm aqueous alkali it afforded the oxide (II; R = Me, R′ = OH) and the quinoxalone (IV; R = Me, R′ = H). Formation of the oxide (II; R = Me, R′ =OH might occur, either by displacement of hydride ion at the 2-position in the *N*-oxide (II; R = Me, R′ = H) or by dehydrogenation of the adduct (VII) obtained by reaction of the oxide with hydroxide ion. The hydrogen liberated would then be available for formation of the reduction products also isolated.

In an attempt to prepare the *N*-methylanilide (I; R = Me, R′ = H, R″ = Bz), α-benzoyl-*o*-nitroacetanilide [2] was treated with methyl iodide and potassium carbonate, in acetone. The resulting monomethyl derivative cyclised in warm aqueous alkali, giving an alkali-soluble quinoxaline *N*-oxide which formed an *N*-methyl derivative. Reduction of the *N*-oxide and of its *N*-methyl derivative to the quinoxalones (IV; R = H, R′ = Me) [10] and (IV; R = R′ = Me) [11] established the structure of the oxide as 1,2-dihydro-3-methyl-2-oxoquinoxaline 4-oxide (II; R = H ,R′ = Me), and the anilide as the *C*-methyl derivative (I; R = H, R′ = Me, R″ = Bz). The scope of this reaction is being investigated.

Experimental

Infrared spectra were measured for Nujol suspensions, using a Perkin-Elmer Infracord spectrophotometer; bands were either strong or very strong unless specified (w), as weak.

α-Cyano-o-nitroacetanilide (I; R = R′ = H, R″ = CN) *and its* N-*Methyl Derivative* (I; R = Me, R′ = H, R″ = CN).—Cyanoacetic acid (13·0 g.) in anhydrous ether (120·0 ml.) was treated in one portion at room temperature with phosphorus pentachloride (34·0 g.), and the mixture stirred for 15 min. Removal of the benzene and phosphorus oxychloride *in vacuo* gave cyanoacetyl chloride as a pale yellow oil, which was dissolved in dry benzene (75·0 ml.) and warmed at 100° for 2·0 hr. with *o*-nitroaniline (20·0 g.). The anilide was collected from the cooled mixture and combined with material recovered from the benzene mother-liquor by concentration, dilution with chloroform, and evaporation of the washed (dilute sulphuric acid then sodium hydrogen carbonate) and dried extract, to give α-cyano-*o*-nitroacetanilide as

[8] Clark-Lewis, *J.*, 1957, 422.
[9] King and Clark-Lewis, *J.*, 1951, 3379.
[10] Hinsberg, *Annalen*, 1896, **292**, 245.
[11] Cook and Perry, *J.*, 1943, 394.

colourless needles (25·0 g.), m. p. 154° (from acetic acid) (lit.,[6] 149°) (Found: C, 52·7; H, 3·7; N, 20·2. Calc. for $C_9H_7N_3O_3$: C, 52·7; H, 3·4; N, 20·5%). Similarly, *N*-methyl-*o*-nitroaniline (22·0 g.) gave *α-cyano*-N-*methyl*-o-*nitroacetanilide*, colourless needles (22·0 g.), m. p. 133° (from ethanol) (Found: C, 54·7; H, 4·4; N, 19·4. $C_{10}H_9N_3O_3$ requires C, 54·8; H, 4·1; N, 19·2%).

o-*Nitro*-α-*phenylacetanilide* (I; R = R′ = H, R″ = Ph) *and its* N-*Methyl Derivative* (I; R = Me, R′ = H, R″ = Ph).—Phenylacetyl chloride (6·7 ml.) was warmed with *o*-nitroaniline (6·9 g.) or *N*-methyl-*o*-nitroaniline (7·6 g.) in dry benzene (25·0 ml.) at 100° for 2·0 hr. Removal of the solvent and the excess of acid chloride *in vacuo* afforded a gum which crystallised on rubbing, to give o-*nitro*-α-*phenylacetanilide* as cream needles (12·0 g.), m. p. 84° (from methanol) (Found: C, 65·3; H, 4·4; N, 11·0. $C_{14}H_{12}N_2O_3$ requires C, 65·6; H, 4·7; N, 10·9%), or N-*methyl*-o-*nitro*-α-*phenylacetanilide* (12·5 g.), m. p. 80° (from methanol) (Found: C, 66·5; H, 5·4; N, 10·4. $C_{15}H_{14}N_2O_3$ requires C, 66·7; H, 5·2; N, 10·4%).

When warmed for 10—15 min. with 2N-sodium hydroxide, the anilide (I; R = R′ = H, R″ = Ph) gave *o*-nitroaniline (85%), m. p. and mixed m. p. 72°, and phenylacetic acid (80%), m. p. and mixed m. p. 76°.

Ethyl o-*Nitrophenylcarbamoylacetate* (I; R = R′ = H, R″ = CO_2Et).—Ethyl chloroformylacetate [12] (3·4 g.), treated in dry benzene (18·0 ml.) with *o*-nitroaniline (4·0 g.) at 100° for 2·0 hr. as above, gave the *ester* (3·5 g.), m. p. 49° [from benzene–light petroleum (b. p. 40—60°)] (Found: C, 52·3; H, 4·8; N, 11·1. $C_{11}H_{12}N_2O_5$ requires C, 52·4; H, 4·8; N, 11·1%). On refluxing with 2N-sodium hydroxide in methanol for 0·5 hr., the ester gave *o*-nitroaniline (75%).

Condensation of o-*Nitroaniline with Diethyl Malonate.*—*o*-Nitroaniline (14·0 g.) was added in portions during 0·5 hr. to a stirred solution of diethyl malonate (48·0 ml.) in xylene (30·0 ml.) at 220°, and the mixture stirred at this temperature for a further 2·0 hr. Dilution of the cooled mixture with ether gave a yellow solid which was combined with material recovered by evaporation from the washed (2N-sodium hydroxide) and dried (Na_2SO_4) organic filtrate, to give the *dianilide* (V) (2·5 g.), m. p. 186° (from acetic acid) (Found: C, 52·2; H, 3·4; N, 15·9. $C_{15}H_{12}N_4O_6$ requires C, 52·3; H, 3·5; N, 16·2%). The *acid* (I; R = R′ = H, R″ = CO_2H), recovered from the alkaline washings by acidification, formed yellow needles (9·0 g.), m. p. 152° (from water) (Found: C, 47·9; H, 3·5; N, 12·1. $C_9H_8N_2O_5$ requires C, 48·2; H, 3·6; N, 12·5%). Warming of the dianilide or the acid with 2N-sodium hydroxide afforded *o*-nitroaniline (80—85%).

The above reaction was repeated using ethyl cyanoacetate (5·4 ml.) and *o*-nitroaniline (6·9 g.) in xylene (15·0 ml.) at 220° for 2·0 hr. *o*-Nitroaniline (6·5 g.) was recovered.

Ethyl 3,4-*Dihydro*-3-*oxoquinoxaline*-2-*carboxylate* 1-*Oxide* (II; R = H, R′ = CO_2Et).—The ester (I; R = R′ = H, R″ = CO_2Et) or the dianilide (V) (0·002 mole), dissolved or suspended in dry ethanol (10·0 ml.), was refluxed (0·5 hr.) with 0·4M-sodium ethoxide in ethanol (10·0 ml.). Concentration of the cooled mixture, dilution with water, and recovery in chloroform gave *o*-nitroaniline. Acidification of the aqueous layer, extraction with chloroform, and evaporation of the dried (Na_2SO_4) extract gave a gum which, treated with hot benzene, left the insoluble oxide (II; R = R′ = H) [2] (0·05 g.), m. p. and mixed m. p. 276°. On cooling, the benzene extract afforded the *ester* (II; R = H, R′ = CO_2Et) (0·15 g.) as cream needles, which, after drying for 24·0 hr. at 100° *in vacuo*, had m. p. 193°, $\nu_{max.}$ 2700sh, 1725, and 1650 cm.$^{-1}$ (Found: C, 56·1; H, 4·5; N, 12·1. $C_{11}H_{10}N_2O_4$ requires C, 56·4; H, 4·3; N, 12·0%). On refluxing with sodium dithionite in acetic acid, the ester gave ethyl 3,4-dihydro-3-oxoquinoxaline-2-carboxylate (IV; R = H, R′ = CO_2Et), m. p. 177° (Found: C, 60·7; H, 4·9. Calc. for $C_{11}H_{10}N_2O_3$: C, 60·6; H, 4·6%), identical (mixed m. p. and infrared spectrum) with an authentic sample.[13]

1,2-*Dihydro*-2-*oxoquinoxaline* 4-*oxide* (II; R = R′ = H).—The acid (I; R = R′ = H, R″ = CO_2H) (0·45 g.) in dry ethanol (10·0 ml.) was refluxed with 0·4M-sodium ethoxide in ethanol (10·0 ml.) for 0·5 hr. The mixture was worked up as for the above ester, to give the oxide (0·15 g.), m. p. and mixed m. p. 276° (from acetic acid) (Found: C, 59·4; H, 3·4; N, 17·2. Calc. for $C_8H_6N_2O_2$: C, 59·3; H, 3·7; N, 17·2%), identical (infrared spectrum) with an authentic sample,[2] together with *o*-nitroaniline (0·12 g.).

1,2-*Dihydro*-2-*oxo*-3-*phenylquinoxaline* 4-*Oxide* (II; R = H, R′ = Ph).—The anilide (I;

[12] Snyder and Robison, *J. Amer. Chem. Soc.*, 1952, **74**, 5945.
[13] Gowenlock, Newbold, and Spring, *J.*, 1945, 622.

R = R′ = H, R″ = Ph) (3·0 g.) in dry ethanol (30·0 ml.) was refluxed for 0·5 hr. with 0·4M-sodium ethoxide in ethanol (50·0 ml.), to give *o*-nitroaniline (1·3 g.), and the *oxide* (0·2 g.), m. p. 285° (from acetic acid), $\nu_{max.}$ 2700sh and 1650 cm.$^{-1}$ (Found: C, 70·7; H, 4·3; N, 11·6. $C_{14}H_{10}N_2O_2$ requires C, 70·6; H, 4·2; N, 11·8%). Treatment in acetone at 100° for 3·0 hr. with methyl iodide and anhydrous potassium carbonate afforded the *N*-methyl derivative (II; R = Me, R′ = Ph) (80%), identical (m. p., mixed m. p., and infrared spectrum) with a sample prepared as below. On being refluxed with sodium dithionite (0·2 g.) for 2·0 hr. in acetic acid (2·5 ml.) the oxide (II; R = H, R′ = Ph) (0·12 g.) gave, on evaporation of the filtered mixture and treatment with water, 1,2-dihydro-2-oxo-3-phenylquinoxaline (0·09 g.), m. p. 257° (from ethanol) (Found: N, 12·4. Calc. for $C_{14}H_{10}N_2O$: N, 12·6%), identical (mixed m. p. 257° and infrared spectrum) with an authentic sample.[14]

1,2-*Dihydro*-1-*methyl*-2-*oxo*-3-*phenylquinoxaline* 4-*Oxide* (II; R = Me, R′ = Ph).—On being refluxed for 0·5 hr. with N-sodium hydroxide (4·0 ml.) in methanol (10·0 ml.), or treated (1·0 hr.) with 0·4M-sodium ethoxide in ethanol (10·0 ml.) at room temperature with stirring, the anilide (I; R = Me, R′ = H, R″ = Ph) (0·54 g.) afforded a yellow precipitate which was collected and combined with material recovered by working-up the mother-liquor, to give the oxide (0·43 g.), yellow needles, m. p. 196° (from acetic acid), $\nu_{max.}$ 1640 and 1575 cm.$^{-1}$ (Found: C, 71·4; H, 4·9; N, 11·2. $C_{15}H_{12}N_2O_2$ requires C, 71·4; H, 4·8; N, 11·1%). Reduction with sodium dithionite in acetic acid yielded the quinoxalone (IV; R = Me, R′ = Ph) (96%), m. p. and mixed m. p. 138° (from methanol) (Found: C, 76·3; H, 4·8; N, 11·7. Calc. for $C_{15}H_{12}N_2O$: C, 76·3; H, 5·1; N, 11·9%), identical (infrared spectrum) with an authentic sample.[15]

1-(N-*Methyl*-o-*nitrophenylcarbamoylmethyl*)*pyridinium Chloride* (VI).—The chloroanilide (I; R = Me, R′ = H, R″ = Cl) [16] (2·0 g.) was warmed with pyridine (20·0 ml.) for 5 min., and the red solution cooled, concentrated, and diluted with ether, to give the crude *salt* (2·0 g.), colourless needles, m. p. 157° (from ethanol–ethyl acetate) (Found: C, 54·2; H, 5·0; N, 13·5. $C_{14}H_{14}ClN_3O_3$ requires C, 54·5; H, 4·5; N, 13·6%). Concentration of the ether residues gave starting material (0·5 g.). On being refluxed for 1·0 hr. with piperidine (6·0 ml.) in methanol (9·0 ml.), the salt (0·9 g.) gave a precipitate of the amine (II; R = Me, R′ = NH_2),[2] which was collected and combined with material recovered by concentration of the filtrate (total 0·3 g.), m. p. 314° (decomp.) (from methanol) (Found: C, 56·7; H, 4·9; N, 22·0. Calc. for $C_9H_9N_3O_2$: C, 56·5; H, 4·7; N, 21·9%), identified with an authentic sample [2] by mixed m. p. 314° and infrared spectrum, and by reduction with sodium dithionite in acetic acid to 2-amino-3,4-dihydro-4-methyl-3-oxoquinoxaline (IV; R = Me, R′ = NH_2), m. p. 276° (from aqueous acetic acid) (Found: C, 61·8; H, 5·0; N, 23·8. Calc. for $C_9H_9N_3O$: C, 61·7; H, 5·1; N, 24·0%), identical (mixed m. p. and infrared spectrum) with an authentic sample.[17]

2-*Cyano*-3,4-*dihydro*-3-*oxoquinoxaline* 1-*Oxide* (II; R = H, R′ = CN).—The cyano-oxide was formed (*a*) by warming α-chloro-*o*-nitroacetanilide (7·0 g.),[2] in water (40·0 ml.) at 60° for 2·0 hr., with stirring, with solid sodium cyanide (2·0 g.) and sodium carbonate (1·6 g.), followed by acidification of the aqueous filtrate after removal of starting material (5·3 g.) from the cooled mixture (yield 1·0 g.), or (*b*) from α-cyano-*o*-nitroacetanilide (I; R = R′ = H, R″ = CN) (2·0 g.), treated in ethanol (25·0 ml.) dropwise with stirring at 50—60° for 0·5 hr. with a solution of sodium cyanide (2·0 g.) in water (10·0 ml.), or refluxed (0·5 hr.) with 0·4M-sodium ethoxide in ethanol (50·0 ml.). Concentration of the mixture (containing an orange solid), dilution with water, and recovery in chloroform gave *o*-nitroaniline (0·4 g.). The aqueous layer was acidified, to give the *oxide*, golden yellow plates (0·8—1·0 g.), m. p. 282° (decomp.) (from aqueous dimethylformamide) (lit.,[6] 265°), $\nu_{max.}$ 2700sh, 2200, and 1650 cm.$^{-1}$ (Found: C, 57·8; H, 2·8; N, 22·8. $C_9H_5N_3O_2$ requires C, 57·8; H, 2·7; N, 22·5%). When shaken at room temperature for 0·5 hr. with 2N-sodium hydroxide (1·3 ml.) and dimethyl sulphate (0·2 ml.), the oxide (0·1 g.) afforded the *N*-methyl derivative (II; R = Me, R′ = CN) (0·05 g.), m. p. 223° alone or mixed with a sample prepared as below. The oxide (0·4 g.) in acetic acid (30·0 ml.) was refluxed with sodium dithionite (0·8 g.) for 2·0 hr. Concentration of the filtered mixture and dilution with water gave the nitrile (IV; R = H, R′ = CN) [1] (0·05 g.), identical [m. p.

[14] Burton and Shoppee, *J.*, 1937, 546.
[15] Cheeseman, *J.*, 1961, 1246.
[16] Clark and Hams, *Biochem. J.*, 1953, **55**, 839.
[17] Cheeseman, *J.*, 1955, 1804.

mixed m. p. 298° (from acetic acid), and infrared spectrum] with an authentic sample.[1] 1,2-Dihydro-2-oxoquinoxaline (0·2 g.), m. p. and mixed m. p. 272° (from acetic acid), was recovered from the aqueous filtrate by extraction with chloroform, and identified by comparison of its infrared spectrum with that of an authentic sample.[18] The nitrile (II; R = H, R′ = CN) was quantitatively recovered after heating with 30% hydrogen peroxide in acetic acid at 50° for 15·0 hr.

2,3-*Dihydroxyquinoxaline* 1-*Oxide* (II; R = H, R′ = OH).—The oxide was formed in 84% yield by refluxing the anilide (I; R = R′ = H, R″ = CN) or the nitrile (II; R = H, R′ = CN) for 0·5 hr. with N-sodium hydroxide or 20% aqueous potassium hydroxide. It was also prepared by refluxing the oxide (II; R = H, R′ = CN) (0·2 g.) in acetic acid (10·0 ml.) with 20% (w/v) aqueous sulphuric acid (4·0 ml.) for 5·0 hr. (yield 50% after recovery of starting material). The oxide formed colourless needles, m. p. 290° (decomp.) (from aqueous acetic acid) (Found: C, 53·6; H, 3·4; N, 16·0. Calc. for $C_8H_6N_2O_3$: C, 53·9; H, 3·4; N, 15·7%), identical (mixed m. p. 290° and infrared spectrum) with an authentic sample.[2]

3,4-*Dihydro*-3-*oxoquinoxaline*-2-*carboxyamide* 1-*Oxide* (II; R = H, R′ = $CONH_2$).—The nitrile (II; R = H, R′ = CN) (0·4 g.) was warmed with polyphosphoric acid (10·0 ml.) at 110° for 1·0 hr., cooled, and treated with water, to give the amide as pale yellow needles (0·38 g.), m. p. 259° (decomp.) (from dimethylformamide) (lit.,[6] 247°), $\nu_{max.}$ 3350, 3100sh, 2700sh, and 1660 $cm.^{-1}$ (Found: C, 52·6; H, 3·8; N, 20·4. Calc. for $C_9H_7N_3O_3$: C, 52·7; H, 3·4; N, 20·5%). Reduction with sodium dithionite in acetic acid gave 3,4-dihydro-3-oxoquinoxaline-2-carboxyamide (IV; R = H, R′ = $CONH_2$) (50%), m. p. and mixed m. p. 308°, identical (infrared spectrum) with an authentic sample.[8] When refluxed with 20% (w/v) aqueous sulphuric acid (1·3 ml.) in acetic acid (2·5 ml.) for 0·5 hr., the amide (0·1 g.) yielded, on dilution of the concentrated mixture, 2,3-dihydroxyquinoxaline (0·06 g.), m. p. >360°, identical (ultraviolet and infrared spectra) with an authentic sample.[19] Warming the amide for 0·5 hr. with 20% aqueous potassium hydroxide afforded the oxide (II; R = R′ = H), m. p. and mixed m. p. 276° (from acetic acid).

2-*Cyano*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* 1-*Oxide* (II; R = Me, R′ = CN).—(*a*) α-Chloro-*N*-methyl-*o*-nitroacetanilide [16] (2·3 g.) in ethanol (12·0 ml.) was treated dropwise with stirring at 60° for 0·5 hr. with a solution of sodium cyanide (0·6 g.) and sodium carbonate (0·5 g.) in water (12·0 ml.), to give the oxide (1·2 g.) and starting material (0·5 g.).

(*b*) α-Cyano-*N*-methyl-*o*-nitroacetanilide (I; R = Me, R′ = H, R″ = CN) (2·2 g.) in ethanol (12·0 ml.) and water (12·0 ml.) at 100° was treated with sodium cyanide (1·0 g.) in one portion, and, after the initial vigorous reaction had subsided, was heated for a further 10 min. at 100°, to give the *oxide* (1·4 g.), yellow needles, m. p. 223° (from acetic acid), $\nu_{max.}$ 2200, 1640, and 1570 $cm.^{-1}$ (Found: C, 59·5; H, 3·5; N, 20·8. $C_{10}H_7N_3O_2$ requires C, 59·7; H, 3·5; N, 20·9%). The oxide was recovered unchanged (80%) after warming at 50° for 15·0 hr. with 30% hydrogen peroxide in acetic acid. When refluxed with sodium dithionite (0·8 g.) in acetic acid (20·0 ml.) for 2·0 hr. the oxide (0·4 g.) gave, after recovery in chloroform from the concentrated and diluted (water) mixture, a crude gum, which was separated by extraction with light petroleum (b. p. 60—80°) into the insoluble nitrile (IV; R = Me, R′ = CN) (0·05 g.), m. p. 211° alone or mixed with an authentic sample,[1] and 1,2-dihydro-1-methyl-2-oxoquinoxaline (IV; R = Me, R′ = H) (0·25 g.), m. p. 122°, identical (mixed m. p. and infrared spectrum) with an authentic sample.[17]

1,2-*Dihydro*-3-*hydroxy*-1-*methyl*-2-*oxoquinoxaline* 4-*Oxide* (II; R = Me, R′ = OH).—The oxide was formed from the anilide (I; R = Me, R′ = H, R″ = CN) or the nitrile (II; R = Me, R′ = CN) (0·001 mole) (*a*) by refluxing a suspension in ethanol (5·0 ml.) with 0·4M-sodium ethoxide in ethanol (5·0 ml.), for 0·5 hr., or (*b*) by refluxing with 20% aqueous potassium hydroxide or N-sodium hydroxide (5·0 ml.) for 0·5 hr., followed by acidification and recovery in chloroform, as colourless needles (50%), m. p. 253° (decomp.) (from ethanol) $\nu_{max.}$ 2700sh, 1670, and 1620 $cm.^{-1}$ (Found: C, 56·5; H, 4·5; N, 15·1. Calc. for $C_9H_8N_2O_3$: C, 56·3; H, 4·2; N, 14·6%). The oxide was also formed (60% after recovery of starting material) by refluxing the nitrile (II; R = Me, R′ = CN) with 20% (w/v) aqueous sulphuric acid in acetic acid for 0·5 hr. When warmed with acetic anhydride it gave the *acetate*, m. p. 177° (from methanol), $\nu_{max.}$ 1800, 1725, and 1680 $cm.^{-1}$ (Found: C, 56·1; H, 4·1; N, 11·7. $C_{11}H_{10}N_2O_4$ requires C,

[18] Perkin and Riley, *J.*, 1923, **123**, 2399.
[19] Newbold and Spring, *J.*, 1948, 519.

56·4; H, 4·3; N, 11·9%) which was hydrogenolysed in ethanol over palladium–charcoal to 1,2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (IV; R = Me, R′ = OH), m. p. and mixed m. p. 298°, identical (infrared spectrum) with an authentic sample.[7]

3,4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxyamide 1-Oxide (II; R = Me, R′ = $CONH_2$).—The nitrile (II; R = Me, R′ = CN) (1·0 g.) was warmed at 110° for 1·0 hr., with polyphosphoric acid (25·0 ml.), and the cooled mixture diluted with water, to give the *amide* (1·0 g.), m. p. 228° (from dimethylformamide), $\nu_{max.}$ 3350, 3150, 1680, and 1575 $cm.^{-1}$ (Found: C, 55·0; H, 4·4; N, 19·3. $C_{10}H_9N_3O_3$ requires C, 54·8; H, 4·1; N, 19·2%). The amide was reduced with sodium dithionite in acetic acid, to give the quinoxalone (IV; R = Me, R′ = $CONH_2$) (75%), m. p. 256° (from aqueous ethanol) (Found: C, 59·2; H, 4·5; N, 21·0. Calc. for $C_{10}H_9N_3O_2$: C, 59·1; H, 4·4; N, 20·7%), identical (mixed m. p. 256° and infrared spectrum) with an authentic sample.[8] When refluxed for 0·5 hr. with 20% (w/v) aqueous sulphuric acid (1·3 ml.) in acetic acid (2·5 ml.), or with sodium cyanide (0·1 g.) in water (5·0 ml.), the amide (0·11 g.) gave 1,2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (IV; R = Me, R′ = OH) (0·07 g.), m. p. and mixed m. p. 298°.

Reaction of the Oxides (II; R = Me, R′ = H or $CONH_2$) *with Alkali.*—(*a*) The amide (II; R = Me, R′ = $CONH_2$) (1·0 g.) was refluxed with 2N-sodium hydroxide (10·0 ml.) for 0·5 hr. Acidification of the cooled mixture gave a precipitate which was collected, washed with water and chloroform, and dried *in vacuo*, to give the oxide (II; R = Me, R′ = OH) (0·15 g.), m. p. 253° (from ethanol) alone or mixed with an authentic sample.[7] Extraction of the aqueous filtrate with the chloroform washings, and evaporation of the washed (dilute sodium hydrogen carbonate) and dried (Na_2SO_4) extract, afforded 1,2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline [7] (0·05 g.), m. p. and mixed m. p. 298° (from acetic acid). Neutralisation of the sodium hydrogen carbonate extract and recovery in chloroform yielded the acid (IV; R = Me, R′ = CO_2H) (0·4 g.), m. p. 166° (from water) (Found: C, 58·9; H, 4·2; N, 13·9. Calc. for $C_{10}H_8N_2O_3$: C, 58·8; H, 3·9; N, 13·7%), identical (mixed m. p. 166° and infrared spectrum) with an authentic sample.[9] When refluxed with sulphuric acid in ethanol, the acid gave the ester (IV; R = Me, R′ = CO_2Et), m. p. 126° (Found: C, 61·9; H, 5·1; N, 11·8. Calc. for $C_{12}H_{12}N_2O_3$: C, 62·1; H, 5·2; N, 12·1%), identified with a sample prepared by methylation of ethyl 3,4-dihydro-3-oxoquinoxaline-2-carboxylate [13] with methyl iodide and anhydrous potassium carbonate, by mixed m. p. 126° and infrared spectrum.

(*b*) 1,2-Dihydro-1-methyl-2-oxoquinoxaline 4-oxide (II; R = Me, R′ = H) [7] (0·18 g.) in methanol (5·0 ml.) was refluxed with 20% aqueous potassium hydroxide (2·5 ml.) for 0·5 hr. Concentration of the red solution, dilution with water, extraction with chloroform, and evaporation of the dried (Na_2SO_4) extract gave the quinoxalone (IV; R = Me, R′ = H) (0·06 g.), m. p. and mixed m. p. 122° [from light petroleum (b. p. 100—120°)]. Acidification of the aqueous layer and recovery in chloroform gave the oxide (II; R = Me, R′ = OH) (0·05 g.), m. p. and mixed m. p. 253° (from ethanol).

α-Benzoyl-α-methyl-o-nitroacetanilide (I; R = H, R′ = Me, R″ = Bz).—α-Benzoyl-*o*-nitroacetanilide [2] (5·2 g.) was warmed with potassium carbonate (4·0 g.) and methyl iodide (1·0 ml.) in acetone (100·0 ml.) at 100° for 8·0 hr. Evaporation of the filtered mixture and treatment of the residue with water afforded the *anilide*, more of which was recovered from the aqueous filtrate by extraction with chloroform (total 5·7 g.), m. p. 145° (from ethanol) (Found: C, 64·1; H, 4·8; N, 9·7. $C_{16}H_{14}N_2O_4$ requires C, 64·4; H, 4·7; N, 9·4%).

1,2-Dihydro-3-methyl-2-oxoquinoxaline 4-Oxide (II; R = H, R′ = Me).—The anilide (I; R = H, R′ = Me, R″ = Bz) (0·9 g.) was refluxed with 2N-sodium hydroxide (5·0 ml.) for 15 min., cooled, acidified, and the solid collected, washed with dilute sodium hydrogen carbonate and water, and dried *in vacuo*, to give the *oxide* (0·5 g.), m. p. 250° (from ethanol), $\nu_{max.}$ 2700sh and 1650 $cm.^{-1}$ (Found: C, 61·3; H, 4·8; N, 15·9. $C_9H_8N_2O_2$ requires C, 61·4; H, 4·5; N, 15·9%). Neutralisation of the sodium hydrogen carbonate washings and extraction with chloroform gave benzoic acid (0·3 g.), m. p. and mixed m. p. 122°. When treated in acetone (30·0 ml.) with anhydrous potassium carbonate (0·3 g.) and methyl iodide (0·18 ml.) at 100° for 3·0 hr., the oxide (II; R = H, R′ = Me) (0·3 g.) gave, after evaporation of the filtered mixture and dilution with water, the N-*methyl derivative* (II; R = R′ = Me) (0·27), m. p. 207° (from ethanol), $\nu_{max.}$ 1630 and 1580 $cm.^{-1}$ (Found: C, 63·0; H, 5·6; N, 14·5. $C_{10}H_{10}N_2O_2$ requires C, 63·2; H, 5·3; N, 14·7%). Reduction of the oxide and of its *N*-methyl derivative in acetic acid with sodium dithionite afforded, respectively, 1,2-dihydro-3-methyl-2-oxoquinoxaline (IV; R = H, R′ = Me) (94%), m. p. 253°, identical (mixed m. p. and infrared spectrum)

with an authentic sample,[10] and 1,2-dihydro-1,3-dimethyl-2-oxoquinoxaline (IV; R = R′ = Me) (60%), m. p. and mixed m. p. 86° (lit.,[17] 85°), identical (infrared spectrum) with an authentic sample.[11]

Thanks are offered to Miss H. Gilmour for the microanalyses recorded. This work was carried out during the tenure of an Imperial Chemical Industries Limited Fellowship.

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