381. *Heterocyclic N-Oxides. Part II.*[1] *Nucleophilic Reactions of 1,2-Dihydro-2-oxoquinoxaline 4-Oxide.*

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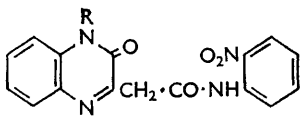
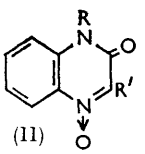
The compound formed when α-acetyl-*o*-nitroacetanilide is warmed with aqueous sodium hydroxide is shown to have the structure (I; R = H). 1,2-Dihydro-2-oxoquinoxaline 4-oxide and its *N*-methyl derivative (II; R = Me, R′ = H) condense with compounds containing a reactive methylene group in the presence of piperidine, yielding alkylated quinoxalines (IV). The oxide (II; R = R′ = H), when warmed with aqueous potassium cyanide, affords 2-cyano-3,4-dihydro-3-oxoquinoxaline, whereas the *N*-methyl compound (II; R = Me, R′ = H), treated similarly, gives the hydroxyquinoxalinone (VII; R = Me, R′ = OH).

WARM aqueous sodium hydroxide converts α-acetyl-*o*-nitroacetanilide (III; R = Ac) into several products, among which the oxide (II; R = H, R′ = Ac) and a yellow compound predominate.[1] The latter is also formed when either of the oxides (II; R = R′ = H) or (II; R = H, R′ = Ac) is warmed with the anilides (III; R = Ac or Bz) and piperidine, and its properties and transformations show it to have the structure (I; R = H). Condensation of the oxides (II; R = H or Me, R′ = H) with reactive methylene compounds in piperidine–ethanol provides a general route to alkylated quinoxalines (IV), and reaction with aqueous potassium cyanide affords the hitherto unknown nitriles (VII; R = H, R′ = CN) and (VII; R = Me, R′ = CN).



(I)



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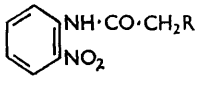

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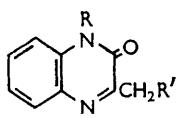


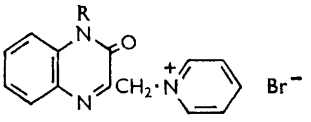
(IV)

The yellow compound, $C_{16}H_{12}N_4O_4$, was formed when either of the oxides (II; R = H, R′ = H or Ac) was warmed with the anilides (III; R = Ac or Bz) and piperidine in ethanol. It was insoluble in dilute mineral acid and in dilute alkali, but dissolved slowly when shaken with cold 20% aqueous potassium hydroxide. Bands characteristic of amide and nitro-groups were present in the infrared spectrum. Hydrolysis of the compound and of its *N*-methyl derivative yielded *o*-nitroaniline, and 1,2-dihydro-3-methyl-2-oxoquinoxaline (IV; R = R′ = H)[2] and 1,2-dihydro-1,3-dimethyl-2-oxoquinoxaline (VII; R = R′ = Me),[3] respectively, whilst oxidation afforded the hydroxy-compounds (VII; R = H, R′ = OH)[4] and (VII; R = Me, R′ = OH).[5] Structure (I; R = H) for the yellow compound was finally confirmed by its synthesis from ethyl 1,2-dihydro-2-oxoquinoxalin-3-ylacetate (IV; R = H, R′ = CO_2Et) and *o*-nitroaniline by the method of

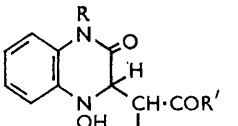
[1] Part I, *J.*, 1963, 2428.
[2] Hinsberg, *Annalen*, 1896, **292**, 245.
[3] Cook and Perry, *J.*, 1943, 394.
[4] Newbold and Spring, *J.*, 1948, 519.
[5] Landquist, *J.*, 1953, 2830.

Weissberger and Kibler.[6] The *N*-methyl compound (I; R = Me) was likewise prepared from the ester (IV; R = Me, R′ = CO_2Et).

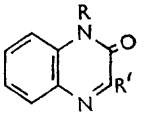
The quinoxaline derivative (I; R = H) is presumably obtained from the oxide (II; R = R′ = H) by way of an intermediate of type (VI). A similar reaction is the alkylation of quinoline *N*-oxide by reactive methylene compounds and benzoyl chloride.[7] The oxides (II; R = R′ = H) and (II; R = Me, R′ = H) likewise condensed with a series of reactive methylene compounds in the presence of piperidine, to give alkylated quinoxalines (IV). The structures of these products were established by hydrolysis to the quinoxalones (IV; R = R′ = H) or (VII; R = R′ = Me), oxidation to the hydroxy-compounds (VII; R = H or Me, R′ = OH), and comparison with synthetic samples. In this way, the esters (IV; R = H, R′ = CO_2Et) [8] and (IV; R = Me, R′ = CO_2Et) [5] were obtained from the oxides (II; R = R′ = H) and (II; R = Me, R′ = H) and ethyl acetoacetate, ethyl benzoylacetate, or diethyl acetonedicarboxylate, whilst the oxide (II; R = Me, R′ = H) and α-benzoyl-*o*-nitroacetanilide (III; R = Bz) gave the anilide (I; R = Me). Benzoylacetonitrile and phenacylpyridinium bromide similarly yielded the nitriles (IV; R = H or Me, R′ = CN) and the pyridine salts (V; R = H or Me). Acetylacetone, however, condensed with the oxide (II; R = R′ = H), yielding the known ketone (IV; R = H, R′ = Ac),[9] but reacted with the oxide (II; R = Me, R′ = H) to give a yellow compound different from the ketone formed on methylation of 2-acetonyl-3,4-dihydro-3-oxoquinoxaline (IV; R = H, R′ = Ac). The methylation product is assigned the structure (IV; R = Me, R′ = Ac) from its conversion on hydrolysis and oxidation into the quinoxalones (VII; R = R′ = Me) and (VII; R = Me, R′ = OH). The structure of this yellow compound is being investigated. The amide (IV; R = H, R′ = $CONH_2$), formed by warming the nitrile (IV; R = H, R′ = CN) with polyphosphoric acid, was identified by analysis, and by hydrolysis and oxidation to the known quinoxalones (IV; R = R′ = H) and (VII; R = H, R′ = OH).



(V)



(VI)



(VII)

Though 1,2-dihydro-2-oxoquinoxaline 4-oxide is stable to hot 20% aqueous potassium hydroxide,[1] it reacted rapidly with warm aqueous potassium cyanide to give an acidic compound, $C_9H_5N_3O$, with a weak infrared band at 2200 cm.$^{-1}$ (C≡N). Stepwise alkaline hydrolysis to the known amide (VII; R = H, R′ = $CONH_2$) [10] and the acid (VII; R = H, R′ = CO_2H),[11] and thence by decarboxylation to 1,2-dihydro-2-oxoquinoxaline, identified this nitrile as 2-cyano-3,4-dihydro-3-oxoquinoxaline (VII; R = H, R′ = CN). The formation of this compound from the oxide (II; R = R′ = H) is analogous to the preparation of cyanoquinolines [12] and cyanoquinazolines [13] from quinoline and quinazoline *N*-oxides. The oxide (II; R = Me, R′ = H) also reacted with aqueous potassium cyanide, but yielded the hydroxy-compound (VII; R = Me, R′ = OH) and not the expected nitrile (VII; R = Me, R′ = CN), though the latter was isolated in poor yield when the reaction was carried out at room temperature. This result is not unexpected since the nitrile (VII; R = Me, R′ = CN), prepared by methylation of 2-cyano-3,4-dihydro-3-oxoquinoxaline, is rapidly converted by warm aqueous sodium carbonate or potassium cyanide

[6] Weissberger and Kibler, *Org. Synth.*, 1945, **25**, 7.
[7] Hamata and Yamazaki, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 415.
[8] L'Italien and Banks, *J. Amer. Chem. Soc.*, 1951, **73**, 3246.
[9] Schöpf and Ross, *Annalen*, 1941, **546**, 1; Fatutta and Stener, *Gazzetta*, 1958, **88**, 89.
[10] Clark-Lewis, *J.*, 1957, 422.
[11] Gowenlock, Newbold, and Spring, *J.*, 1945, 622.
[12] Montanari and Pentimalli, *Gazzetta*, 1953, **83**, 273.
[13] Higashino, *J. Pharm. Soc. Japan*, 1959, **79**, 699; *Chem. and Pharm. Bull.* (*Japan*), 1961, **9**, 635.

into the hydroxy-compound (VII; R = Me, R′ = OH). In contrast, the nitrile (VII; R = H, R′ = CN) was unaffected by these reagents. Elimination of the cyano-group in the nitriles (VII; R = H, R′ = CN) and (VII; R = Me, R′ = CN) occurs when they are refluxed with sodium dithionite in acetic acid, yielding, respectively, 1,2-dihydro-2-oxoquinoxaline (VII; R = R′ = H) [14] and the quinoxalone (VII; R = Me, R′ = H).[15] Since both nitriles are stable to refluxing acetic acid, this reaction probably occurs by reduction to a 1,2-dihydro-derivative [16] and elimination of hydrogen cyanide, rather than by hydrolysis to the corresponding acid and decarboxylation. The reactions of the nitriles (VII; R = H, R′ = CN) and (VII; R = Me, R′ = CN) in acid are also interesting. Under relatively anhydrous conditions (polyphosphoric acid, or hydrogen chloride in acetic acid), the amides (VII; R = H, R′ = $CONH_2$) [10] and (VII; R = Me, R′ = $CONH_2$) [10] were formed in good yield, whereas in aqueous acid displacement of the cyano-group occurred to give the hydroxy-compounds (VII; R = H, R′ = OH) and (VII; R = Me, R′ = OH).

Further experiments on the reactions of the oxides (II; R = R′ = H) and (II; R = Me, R′ = H), and their derivatives, with nucleophilic reagents are in progress.

Experimental

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

Alkylated Quinoxalines (IV; R = H).—(*a*) The general procedure consisted in refluxing 1,2-dihydro-2-oxoquinoxaline 4-oxide (0·01 mole) and the reactive methylene compound (0·01 mole) with piperidine (3·0 ml.) in ethanol (75·0 ml.) for 0·5 hr. The product, which usually separated from the hot mixture, was collected after cooling, and combined with material recovered from the filtrate by evaporation. In some cases, complete evaporation of the ethanol mother-liquor, treatment of the residue with water, and neutralisation, gave a third crop. The crude quinoxaline was further purified by washing with dilute sodium hydrogen carbonate [or, in the case of the salt (V; R = H), with chloroform], drying *in vacuo*, and recrystallising from a suitable solvent.

(*b*) 1,2-*Dihydro*-3-o-*nitrophenylcarbamoylmethyl*-2-*oxoquinoxaline* (I; R = H). This was obtained by condensing either of the oxides (II; R = H, R′ = H or Ac) with the anilides (III; R = Ac or Bz); it formed orange needles, m. p. 258° (from acetic acid) (yield 50—96%), $\nu_{max.}$ 3300w, 2700sh, 1670, 1625w, 1495, and 1340 cm.$^{-1}$ (Found: C, 58·9; H, 3·9; N, 17·2. $C_{16}H_{12}N_4O_4$ requires C, 59·2; H, 3·7; N, 17·3%), identical (mixed m. p. and infrared spectrum) with a sample prepared as described below. When warmed with methyl iodide and potassium carbonate in acetone at 100° for 3 hr., the anilide (I; R = H) yielded the *N*-methyl derivative (I; R = Me), m. p. 207° (from acetic acid) (yield 88% after recovery of starting material), and, on oxidation with 30% hydrogen peroxide in acetic acid at 50° for 15 hr., afforded 2,3-dihydroxyquinoxaline, m. p. >360°, identical (infrared and ultraviolet spectra) with a synthetic sample.[4] Hydrolysis of the anilide (I; R = H) with refluxing 20% w/v aqueous sulphuric acid in acetic acid, concentration of the mixture, and recovery in chloroform gave 1,2-dihydro-3-methyl-2-oxoquinoxaline (70%), m. p. and mixed m. p. 255° (from ethanol), and *o*-nitroaniline (70%), m. p. and mixed m. p. 72°.

(*c*) Ethyl 1,2-dihydro-2-oxoquinoxalin-3-ylacetate (IV; R = H, R′ = CO_2Et) (82—90%), identical (mixed m. p. and infrared spectrum) with an authentic specimen,[8] was prepared from the oxide (II; R = R′ = H) and ethyl acetoacetate, ethyl benzoylacetate, or diethyl acetonedicarboxylate. It had m. p. 214° (from aqueous acetic acid), $\nu_{max.}$ 2700sh, 1680, and 1640 cm.$^{-1}$ (Found: C, 62·0; H, 5·4; N, 12·2. Calc. for $C_{12}H_{12}N_2O_3$: C, 62·1; H, 5·2; N, 12·1%). With methyl iodide and potassium carbonate in acetone, it afforded the *N*-methyl derivative (IV; R = Me, R′ = CO_2Et) (86%), m. p. 128° (from ethanol).

(*d*) 2-Acetonyl-3,4-dihydro-3-oxoquinoxaline (IV; R = H, R′ = Ac) (64%), m. p. 267° (yellow prisms from aqueous acetic acid), $\nu_{max.}$ 2700sh, 1680, and 1570 cm.$^{-1}$ (Found: C, 65·6;

[14] Perkin and Riley, *J.*, 1923, **123**, 2399.
[15] Cheeseman, *J.*, 1955, 1804.
[16] Habib and Rees, *J.*, 1960, 3384.

H, 5·3; N, 14·2. Calc. for $C_{11}H_{10}N_2O_2$: C, 65·4; H, 5·0; N, 13·9%), was obtained from 1,2-dihydro-2-oxoquinoxaline 4-oxide and acetylacetone. The ketone (IV; R = H, R′ = Ac) was further identified, by mixed m. p. (267°) and infrared spectrum, with a sample prepared as described below, and by oxidation with hydrogen peroxide in acetic acid to 2,3-dihydroxyquinoxaline, m. p. >360°, identical (ultraviolet and infrared spectra) with an authentic specimen.[4] The ketone (IV; R = H, R′ = Ac) (0·2 g.) in acetone (10·0 ml.), with methyl iodide (0·1 ml.) and potassium carbonate (0·2 g.) at 100° for 3 hr., gave the *N*-methyl derivative (IV; R = Me, R′ = Ac) as yellow needles (0·17 g.), m. p. 200° (from ethanol) (lit.,[9] 187°), $\nu_{max.}$ 1660 and 1580 cm.$^{-1}$ (Found: C, 66·4; H, 5·9; N, 13·2. Calc. for $C_{12}H_{12}N_2O_2$: C, 66·7; H, 5·6; N, 13·0%), which was oxidised by hydrogen peroxide in acetic acid to the quinoxalone (VII; R = Me, R′ = OH), m. p. and mixed m. p. 298°.[5]

(*e*) 2-Cyanomethyl-3,4-dihydro-3-oxoquinoxaline (IV; R = H, R′ = CN) (86%), identical (mixed m. p. and infrared spectrum) with a sample prepared as described below, was obtained from the oxide (II; R = R′ = H) and benzoylacetonitrile as yellow prisms, m. p. 302° (decomp.) (from dimethylformamide), $\nu_{max.}$ 2700sh, 2200, 1670, and 1640 cm.$^{-1}$ (Found: C, 64·6; H, 4·0; N, 22·5. Calc. for $C_{10}H_7N_3O$: C, 64·9; H, 3·8; N, 22·7%). When warmed with methyl iodide and potassium carbonate, it yielded the *N*-methyl derivative (IV; R = Me, R′ = CN) (88%), m. p. 208° (from acetic acid).

(*f*) 1-(1,2-Dihydro-2-oxoquinoxalin-3-ylmethyl)pyridinium bromide (V; R = H) (75%) was obtained from the oxide (II; R = R′ = H) and phenacylpyridinium bromide as colourless needles, m. p. 272° (from aqueous ethanol) (Leese and Rydon,[17] and Green and Delaby,[17] record m. p.s 245 and 255°, respectively). It had $\nu_{max.}$ 2700sh and 1670 cm.$^{-1}$ (Found: C, 52·9; H, 4·0; N, 13·0. Calc. for $C_{14}H_{12}BrN_3O$: C, 52·8; H, 3·8; N, 13·2%), and was identical (mixed m. p. and infrared spectrum) with an authentic sample.[17] With 30% hydrogen peroxide, or chromium trioxide, in acetic acid, the salt (V; R = H) afforded 2,3-dihydroxyquinoxaline, m. p. >360°, identical (infrared and ultraviolet spectra) with an authentic sample.[4]

1,2-*Dihydro*-3-o-*nitrophenylcarbamoylmethyl*-2-*oxoquinoxaline* (I; R = H).—Ethyl 1,2-dihydro-2-oxoquinoxalin-3-ylacetate (IV; R = H, R′ = CO_2Et) (0·2 g.) in xylene (15·0 ml.) was treated in portions at 220° with *o*-nitroaniline (0·2 g.), and kept at this temperature for a further 2 hr. The anilide (I; R = H), which separated on cooling, was collected and crystallised from acetic acid (0·15 g.), m. p. 258°.

2-*Acetonyl*-3,4-*dihydro*-3-*oxoquinoxaline* (IV; R = H, R′ = Ac).—Solutions of *o*-phenylenediamine (1·1 g.) in ethanol (5·0 ml.), and the sodium salt of ethyl acetopyruvate [18] (1·6 g.) in water (3·0 ml.), were mixed and warmed at 100° with acetic acid (2·0 ml.) for 10 min. The product was collected from the cooled mixture and recrystallised from aqueous acetic acid (charcoal), to give the ketone as yellow prisms (0·6 g.), m. p. 267° (Schöpf and Ross,[9] and Fatutta and Stener,[9] record m. p. 257°).

2-*Cyanomethyl*-3,4-*dihydro*-3-*oxoquinoxaline* (IV; R = H, R′ = CN).—The sodium salt of ethoxalylacetonitrile [19] (1·4 g.) in water (3·0 ml.), warmed at 100° for 10 min. with *o*-phenylenediamine (1·1 g.) in ethanol (5·0 ml.) and acetic acid (2·0 ml.), afforded the nitrile (IV; R = H, R′ = CN) (1·0 g.) as yellow prisms, m. p. 302° (decomp.) (from dimethylformamide) (lit.,[19] 285—290°).

1,2-*Dihydro*-2-*oxoquinoxalin*-3-*ylacetamide* (IV; R = H, R′ = $CONH_2$).—2-Cyanomethyl-3,4-dihydro-3-oxoquinoxaline (0·2 g.) was warmed with polyphosphoric acid (5·0 ml.) at 110° for 3 hr. The mixture was cooled, and diluted with water, and the *amide* was collected from the filtered, neutralised solution, and crystallised, to give buff-coloured prisms (0·12 g.), m. p. 288° (decomp.) (from acetic acid), $\nu_{max.}$ 3400, 3200, 1680, 1640, and 1550 cm.$^{-1}$ (Found: C, 58·8; H, 4·6; N, 20·3. $C_{10}H_9N_3O_2$ requires C, 59·1; H, 4·4; N, 20·6%). The amide was refluxed with 20% aqueous potassium hydroxide for 0·5 hr., yielding 1,2-dihydro-3-methyl-2-oxoquinoxaline (75%), m. p. and mixed m. p. 255°, identical (infrared spectrum) with a synthetic sample.[2] When warmed with chromium trioxide in 70% aqueous acetic acid at 100° for 0·5 hr., the amide (IV; R = H, R′ = $CONH_2$) afforded 2,3-dihydroxyquinoxaline, m. p. >360°, identical (ultraviolet and infrared spectra) with a synthetic sample.[4]

Alkylated Quinoxalones (IV; R = Me).—(*a*) The oxide (II; R = Me, R′ = H) (0·001

[17] Leese and Rydon, *J.*, 1955, 303; Green and Delaby, *Bull. Soc. chim. France*, 1955, 704.
[18] Marvel and Dreger, *Org. Synth.*, Coll. Vol. I, 233.
[19] Vul'fson, Davydova, and Lukashina, *Organ. Poluprod. i Krasiteli, Nauchn.-Issled. Inst. Organ. Poluprod Krasitelei, Sb. Statei*, 1959, No. 1, 222 (*Chem. Abs.*, 1961, **55**, 18,748).

mole) and the methylene compound (0·001 mole) were refluxed in ethanol (10·0 ml.) and piperidine (0·3 ml.) for 0·5 hr., and the mixture was worked up as for the quinoxalines (IV; R = H).

(*b*) 1,2-*Dihydro*-1-*methyl*-3-o-*nitrophenylcarbamoylmethyl*-2-*oxoquinoxaline* (I; R = Me) (83%) was formed as orange-red needles, m. p. 207° (from acetic acid), $\nu_{max.}$ 3300w, 1670, 1640, 1570, 1490, and 1340 cm.$^{-1}$ (Found: C, 60·4; H, 4·1; N, 16·9. $C_{17}H_{14}N_4O_4$ requires C, 60·4; H, 4·1; N, 16·6%), from the oxide (II; R = Me, R′ = H) and α-benzoyl-*o*-nitroacetanilide (III; R = Bz).[1] The anilide (I; R = Me) was identical (mixed m. p. and infrared spectrum) with a sample prepared as below, and on oxidation with 30% hydrogen peroxide in acetic acid at 50° for 15·0 hr., gave 1,2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (VII; R = Me, R′ = OH), m. p. 298°, identical (mixed m. p. and infrared spectrum) with an authentic specimen.[5] Hydrolysis of the anilide with 20% w/v aqueous sulphuric acid in acetic acid gave 1,2-dihydro-1,3-dimethyl-2-oxoquinoxaline (VII; R = R′ = Me),[3] m. p. and mixed m. p. 86°, and *o*-nitroaniline, m. p. and mixed m. p. 72°.

(*c*) Ethyl 1,2-dihydro-1-methyl-2-oxoquinoxalin-3-ylacetate (IV; R = Me, R′ = CO_2Et) (61%), m. p. 128° (yellow needles from ethanol), $\nu_{max.}$ 1660sh and 1650 cm.$^{-1}$ (Found: C, 63·5; H, 5·9; N, 11·2. Calc. for $C_{13}H_{14}N_2O_3$: C, 63·4; H, 5·7; N, 11·4%), prepared from the oxide (II; R = Me, R′ = H) and ethyl acetoacetate, was identical (mixed m. p. and infrared spectrum) with a sample prepared as above.

(*d*) 2-*Cyanomethyl*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* (IV; R = Me, R′ = CN) (50%), identified by its mixed m. p. and infrared spectrum with a sample prepared as above, was obtained from the oxide (II; R = Me, R′ = H) and benzoylacetonitrile as yellow needles, m. p. 208° (from acetic acid), $\nu_{max.}$ 2200, 1660sh, and 1640 cm.$^{-1}$ (Found: C, 66·2; H, 4·7; N, 20·8. $C_{11}H_9N_3O$ requires C, 66·3; H, 4·5; N, 21·1%).

(*e*) 1-(1,2-*Dihydro*-1-*methyl*-2-*oxoquinoxalin*-3-*ylmethyl*)*pyridinium bromide* (V; R = Me) (60%), m. p. 213° (colourless needles from ethanol), $\nu_{max.}$ 1660 cm.$^{-1}$ (Found: C, 53·8; H, 4·5; N, 12·6. $C_{15}H_{14}BrN_3O$ requires C, 54·2; H, 4·2; N, 12·7%), was prepared from the oxide (II; R = Me, R′ = H) and phenacylpyridinium bromide, and identified (mixed m. p. and infrared spectrum) with a sample prepared as below. On oxidation with chromium trioxide or hydrogen peroxide, in acetic acid, it afforded the quinoxalone (VII; R = Me, R′ = OH), m. p. 298°, identical (infrared spectrum and mixed m. p.) with a synthetic sample.[5]

1,2-*Dihydro*-1-*methyl*-3-o-*nitrophenylcarbamoylmethyl*-2-*oxoquinoxaline* (I; R = Me).—The ester (IV; R = Me, R′ = CO_2Et) (0·24 g.), warmed with *o*-nitroaniline (0·2 g.) in xylene (15·0 ml.) at 220° for 2·5 hr., as for the anilide (I; R = H) above, gave the quinoxalone (I; R = Me) (0·15 g.), m. p. 207° (from acetic acid).

2-*Bromomethyl*-3,4-*dihydro*-4-*methyl*-3-*oxoquinoxaline* (IV; R = Me, R′ = Br).—1,2-Dihydro-1,3-dimethyl-2-oxoquinoxaline (VII; R = R′ = Me)[3] (0·7 g.) and anhydrous sodium acetate (0·28 g.), in warm acetic acid (5·0 ml.), were treated dropwise, with shaking, with a solution of bromine (0·2 ml.) in acetic acid (2·0 ml.) and the mixture was heated at 100° for 10 min. The yellow solid which separated was collected, washed with acetic acid and water, and dried *in vacuo*. The *bromo-compound* crystallised from acetic acid (charcoal) as cream needles (0·6 g.), m. p. 198°, $\nu_{max.}$ 1650 cm.$^{-1}$ (Found: C, 47·1; H, 3·8; N, 11·1. $C_{10}H_9BrN_2O$ requires C, 47·4; H, 3·6; N, 11·1%). The bromo-compound (0·11 g.) was warmed with pyridine (2·5 ml.) for 5 min.; the mixture was concentrated, and treated with ether, and the solid was collected and washed with chloroform, to give the salt (V; R = Me) (0·1 g.) as colourless needles, m. p. 213° (from ethanol).

1,2-*Dihydro*-3-*methyl*-2-*oxoquinoxaline and its* N-*Methyl Derivative*.—Solutions of the quinoxalines (IV; R = H, R′ = CO_2Et, Ac, or CN), or their *N*-methyl derivatives (IV; R = Me, R′ = CO_2Et, Ac, or CN) (0·001 mole), in acetic acid (5·0 ml.) and 20% w/v aqueous sulphuric acid (2·5 ml.), were refluxed for 1 hr. Concentration, dilution with water, and recovery in chloroform yielded 1,2-dihydro-3-methyl-2-oxoquinoxaline (IV; R = R′ = H) (80—90%),[2] m. p. 255° (from ethanol) (Found: C, 67·5; H, 5·3; N, 17·8. Calc. for $C_9H_8N_2O$: C, 67·5; H, 5·0; N, 17·5%), or its *N*-methyl derivative (VII; R = R′ = Me)[3] (80—90%), m. p. 86° (from methanol). Both compounds were identical (mixed m. p. and infrared spectra) with authentic samples.[2,3]

2-*Cyano*-3,4-*dihydro*-3-*oxoquinoxaline* (VII; R = H, R′ = CN).—1,2-Dihydro-2-oxoquinoxaline 4-oxide (II; R = R′ = H) (5·4 g.), suspended in water (22·0 ml.), was treated in portions, with shaking, with solid potassium cyanide (3·0 g.). Heat was evolved, and the mixture was warmed at 100° for 15 min., cooled, acidified, and the precipitate collected, washed

with water, and dried *in vacuo*, to give the crude *nitrile* (5·0 g.). Recrystallised, it formed buff needles (4·8 g.), m. p. 298° (from acetic acid), $\nu_{max.}$ 2700sh, 2200w, and 1680 cm.$^{-1}$ (Found: C, 62·8; H, 3·0; N, 24·5. $C_9H_5N_3O$ requires C, 63·1; H, 2·9; N, 24·6%). Refluxed (1 hr.) with sodium dithionite (0·17 g.) in acetic acid (10·0 ml.), then with more sodium dithionite (0·17 g.) for a further 1 hr., the nitrile (VII; R = H, R′ = CN) (0·17 g.) yielded, after recovery from the filtered reaction mixture by concentration, dilution with water, and extraction with chloroform, 1,2-dihydro-2-oxoquinoxaline (VII; R = R′ = H), m. p. 272° (from acetic acid) (0·13 g.) (Found: C, 66·1; H, 4·0; N, 19·0. Calc. for $C_8H_6N_2O$: C, 65·8; H, 4·1; N, 19·1%), identical (mixed m. p. and infrared spectrum) with an authentic specimen.[14] When the nitrile (VII; R = H, R′ = CN) was refluxed with acetic acid and 20% w/v aqueous sulphuric acid for 0·5 hr., it afforded 2,3-dihydroxyquinoxaline (90%), m. p. >360° (colourless needles from acetic acid) (Found: C, 59·1; H, 3·8; N, 17·5. Calc. for $C_8H_6N_2O_2$: C, 59·2; H, 3·7; N, 17·3%), identical (infrared and ultraviolet spectra) with a synthetic sample.[4] 2-Cyano-3,4-dihydro-3-oxoquinoxaline (VII; R = H, R′ = CN) was recovered unchanged after being refluxed for 1 hr. with aqueous 2N-sodium carbonate, or acetic acid, and afforded starting material (80% recovery) on attempted oxidation, in acetic acid, with hydrogen peroxide or chromium trioxide.

3,4-Dihydro-3-oxoquinoxaline-2-carboxyamide (VII; R = H, R′ = $CONH_2$).—The amide (VII; R = H, R′ = $CONH_2$) was prepared from 2-cyano-3,4-dihydro-3-oxoquinoxaline (VII; R = H, R′ = CN): (*a*) by refluxing it with 0·5N-sodium hydroxide for 0·5 hr. (yield 25%), together with the acid (VII; R = H, R′ = CO_2H), m. p. and mixed m. p.[11] 265°; (*b*) by warming it with polyphosphoric acid at 110° for 1 hr. (yield 50%); and (*c*) by treating it with hydrogen chloride in acetic acid at room temperature for 24 hr. (yield 85%). It formed buff-coloured needles m. p. 308° (decomp.) (Found: C, 57·5; H, 4·0; N, 22·2. Calc. for $C_9H_7N_3O_2$: C, 57·2; H, 3·7; N, 22·2%), identified with a synthetic sample [10] by mixed m. p. and infrared spectrum, and by conversion in warm aqueous sulphuric and acetic acids into the acid (VII; R = H, R′ = CO_2H), m. p. and mixed m. p.[11] 265°, which afforded 1,2-dihydro-2-oxoquinoxaline, m. p. and mixed m. p. 272°, on decarboxylation.

2-Cyano-3,4-dihydro-4-methyl-3-oxoquinoxaline (VII; R = Me, R′ = CN).—2-Cyano-3,4-dihydro-3-oxoquinoxaline (VII; R = H, R′ = CN) (0·68 g.), in acetone (20·0 ml.), was warmed with methyl iodide (0·4 ml.) and anhydrous potassium carbonate (0·8 g.) at 100° for 3 hr., and the filtered mixture evaporated, to yield the *nitrile* (VII; R = Me, R′ = CN) as yellow needles (0·55 g.), m. p. 211° (from ethanol), $\nu_{max.}$ 2200w and 1670 cm.$^{-1}$ (Found: C, 64·6; H, 3·8; N, 23·0. $C_{10}H_7N_3O$ requires C, 64·9; H, 3·8; N, 22·7%). When warmed (10 min.) with 2N-sodium carbonate solution or aqueous-ethanolic potassium cyanide at 100°, or refluxed (0·5 hr.) with 20% w/v aqueous sulphuric acid in acetic acid, this nitrile gave 1,2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (VII; R = Me, R′ = OH) (70%), m. p. 298° (from acetic acid) (Found: C, 61·7; H, 4·6; N, 15·6. Calc. for $C_9H_8N_2O_2$: C, 61·4; H, 4·5; N, 15·9%), identical (mixed m. p. and infrared spectrum) with a synthetic sample.[5] The nitrile (VII; R = Me, R′ = CN) was recovered unchanged from refluxing acetic acid, or after treatment in acetic acid with 30% hydrogen peroxide or chromium trioxide (recovery 80%). Reduced with sodium dithionite in acetic acid as for 2-cyano-3,4-dihydro-3-oxoquinoxaline above, the *N*-methyl compound (VII; R = Me, R′ = CN) afforded 1,2-dihydro-1-methyl-2-oxoquinoxaline (75%), m. p. and mixed m. p.[15] 122°.

3,4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxyamide (VII; R = Me, R′ = $CONH_2$).—The amide (VII; R = Me, R′ = $CONH_2$), obtained from the nitrile (VII; R = Me, R′ = CN) (*a*) by treating it for 24 hr. at room temperature with hydrogen chloride in acetic acid, or (*b*) by warming it with polyphosphoric acid at 110° for 1·0 hr., formed yellow needles (70%), m. p. 256° (from hot water) (Found: C, 58·8; 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. and infrared spectrum) with a synthetic sample.[10]

1,2-Dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (VII; R = Me, R′ = OH).—(*a*) The oxide (II; R = Me, R′ = H) (0·18 g.), in ethanol (10·0 ml.) and water (2·0 ml.), was treated with solid potassium cyanide (0·1 g.), and the suspension stirred at room temperature for 0·5 hr. The precipitate was collected, washed with water, and recrystallised from ethanol, giving the nitrile (VII; R = Me, R′ = CN) (0·04 g.), m. p. 211° alone or mixed with a sample prepared as above. The ethanol filtrate was concentrated, diluted with water, acidified, and extracted with chloroform, to give 1,2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (VII; R = Me, R′ = OH) (0·07 g.), m. p. 298°, identical (mixed m. p. and infrared spectrum) with a synthetic sample.[5]

(*b*) Reaction (*a*) was repeated at 100° for 0·5 hr. The crystalline solid which separated on

cooling was collected, dissolved in water, acidified, and the cream precipitate combined with material recovered by working up the ethanol mother-liquor, to give the quinoxalone (VII; R = Me, R′ = OH) (68%), m. p. and mixed m. p. 298°.

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