Quinoxaline Derivatives. VI.[1] An Unusual Chlorine Substitution during the Reaction of 3-Hydroxy-2-phenylquinoxaline 1-Oxide with Acetyl Chloride

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During an attempted acetylation of 3-hydroxy-2-phenylquinoxaline 1-oxide[2] (Ia) with acetyl chloride, it was observed that, instead of the normal acetyl derivative, a compound X was obtained; it was analysed as $C_{14}H_9ClN_2O$. The parent compound ($C_{14}H_{10}N_2O_2$) had gained a chlorine atom at the expense of one hydrogen and one oxygen atom, and the chlorine in the molecule was in the non-ionic form. The same compound X was obtained if the *N*-oxide (Ia) was heated with a mixture of concentrated hydrochloric acid and acetic acid (1 : 1 by volume). The reactions seemed to be general ones, as 7-chloro-, 7-ethoxy-, 7-methoxy- derivatives (Ib—d) of 3-hydroxy-2-phenylquinoxaline 1-oxide behaved similarly and gave the corresponding chlorine-substituted compounds. Although the *N*-oxide function was lost during the transformation, electrophilic chlorination by the chlorine generated at the expense of the *N*-oxide function was ruled out, as in each case a uniform single-chlorinated compound was obtained in almost a quantitative yield.

1) Part V: Y. Ahmad, M. S. Habib, M. Iqbal and Ziauddin, This Bulletin, **38**, 562 (1965).

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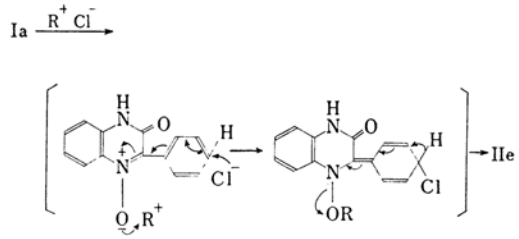
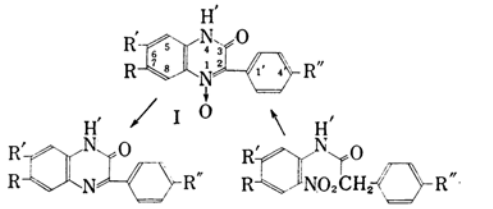
2) Y. Ahmad, M. S. Habib, Ziauddin and N. Bashir, *Tetrahedron*, **21**, 861 (1965).

The evidence presented in earlier papers[1,3,4] strongly indicated that the presence of an oxide function at $N_{(1)}$, coupled with an electron-withdrawing group on $C_{(2)}$ in the quinoxaline molecule, made $C_{(2)}$ strongly electrophilic. The acetylation (or protonation) of the *N*-oxide would further enhance this effect, making the nucleophilic chlorination of the molecule quite feasible. However, in the case of 3-hydroxy-2-phenylquinoxaline 1-oxide, this effect was not expected to remain localised at $C_{(2)}$; it could have been relayed further, through the mesomeric effect, making the 4′-position of the phenyl ring at $C_{(2)}$ liable to the attack by a nucleophile (in the present case a chloride anion). The reaction was expected to take the course indicated below:



(R=Ac or H)

To test the feasibility of this hypothesis, an authentic sample of 2-(*p*-chlorophenyl)-3-hydroxyquinoxaline (IIe) was synthesised in order to compare it with compound X, by the condensation of *o*-nitroaniline with *p*-chlorophenylacetyl chloride, and the resulting α-(*p*-chlorophenyl)-*o*-nitroacetanilide (IIIe) was cyclised with hot aqueous alkali to 2-(*p*-chlorophenyl)-3-hydroxyquinoxaline 1-oxide (Ie), which, on deoxygenation with sodium dithionite in aqueous ethanol, gave IIe. However, the infrared spectrum, melting point and other properties of compound X indicated it to be different from 2-(*p*-chlorophenyl)-3-hydroxyquinoxaline (IIe).

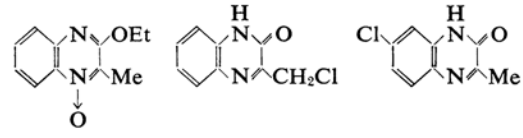


II III

	R	R′	R″		R	R′	R″
(a)	H	H	H	(g)	H	Cl	H
(b)	Cl	H	H	(h)	Cl	Cl	H
(c)	EtO	H	H	(i)	EtO	Cl	H
(d)	MeO	H	H	(j)	MeO	Cl	H
(e)	H	H	Cl	(k)	H	Cl	Cl
(f)	Cl	H	Cl	(l)	Cl	Cl	Cl

7-Chloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline 1-oxide (If) was obtained by a similar sequence of reactions: [*p*-chlorophenylacetyl chloride + 4-chloro-2-nitroaniline → 4-chloro-α-(*p*-chlorophenyl)-2-nitroacetanilide (IIIf) → If]. Ie and If, derivatives of 3-hydroxyquinoxaline 1-oxide, had, at position 2, a phenyl ring, in which the *p*-position was already blocked. Even these compounds, on being heated with acetyl chloride, lost the *N*-oxide and gained an extra chlorine atom in the molecule. These observations indicated that probably the point of the attack of the chloride anion was not in the phenyl ring at position 2 of these quinoxaline derivatives, but at position 5, 6 or 8 of the molecule. Position 7 was excluded, as 2-phenyl-7-chloro-3-hydroxyquinoxaline (IIb), the synthesis of which has already been reported in Part IV,[2] was different (infrared spectra and melting point) from the compound X.

A survey of the literature brought to our notice a similar case. Nowbold and Spring,[5] on heating 3-ethoxy-2-methylquinoxaline 1-oxide (IV) with ethanolic hydrochloric acid, obtained a chlorine substituted quinoxaline, to which they assigned the 2-chloromethyl-3-hydroxyquinoxaline (V) structure, obviously on considerations similar to those above and on some spectroscopic evidence. Later,[6] when they synthesised 2-chloromethyl-3-hydroxyquinoxaline by an unambiguous route, it turned out

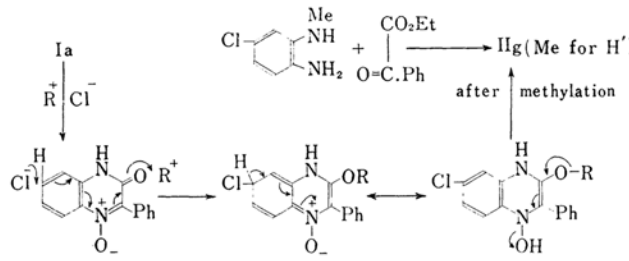


IV V VI

to be different from their earlier chloro-derivative, which they then proved to be 6-chloro-3-hydroxy-2-methyl quinoxaline (VI) through another synthesis. Spring et al.[5,6] had proposed no mechanism for this unusual chlorination, which they had earlier considered to have taken place on the methyl at position 2 and had later found to replace $C_{(6)}$ of the quinoxaline molecule.

In view of the above observation, 6-chloro-3,4-dihydro-4-methyl-3-oxo-2-phenylquinoxaline (IIg, Me for H′) was synthesised by two different routes: (a) 5-chloro-2-nitro-*N*-methylaniline with phenylacetyl chloride gave 5-chloro-*N*-methyl-2-nitro-α-phenylacetanilide

3) Y. Ahmad, M. S. Habib and Ziauddin, ibid., **20**, 1107 (1964).
4) M. S. Habib and C. W. Rees, *J. Chem. Soc.*, **1960**, 3371, 3384, 3386.
5) G. T. Newbold and F. S. Spring, ibid., **1948**, 519.
6) W. Dawson, G. T. Newbold and F. S. Spring, ibid., **1949**, 2579.



(IIIg, Me for H'), which, with hot aqueous alkali, cyclised to 6-chloro-3,4-dihydro-4-methyl-3-oxo-2-phenylquinoxaline 1-oxide (Ig, Me for H'), and its deoxygenation with sodium dithionite in boiling aqueous ethanol gave IIg (Me for H'). (b) 2-Amino-5-chloro-*N*-methylaniline, on condensation with ethyl phenylglyoxalate, gave IIg (Me for H'). The chloro-base (IIg, Me for H') as prepared by either of the methods was identical (infrared spectra and mixed melting point) with the product of the methylation of the compound X.

The dichloro-compound obtained by heating 7-chloro-3-hydroxy-2-phenylquinoxaline 1-oxide (Ib) with acetyl chloride in a sealed tube was identical (infrared spectra and mixed melting point) with 6, 7-dichloro-3-hydroxy-2-phenylquinoxaline (IIh), which was synthesised by the condensation of 4, 5-dichloro-*o*-phenylenediamine with ethyl phenylglyoxalate. The trichloro-compound, which resulted when 7-chloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline 1-oxide (If) and acetyl chloride were heated together in a sealed tube, was identical (infrared spectra and mixed melting point) with 6, 7-dichloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline (III), an authentic sample of which, for the sake of comparison, was prepared by following sequence of reactions: [4, 5-dichloro-2-nitroaniline + *p*-chlorophenylacetyl chloride → 4, 5-dichloro-α-(*p*-chlorophenyl)-2-nitroacetanilide (IIII), which cyclised with alkali → 6, 7-dichloro-2-(*p*-chlorophenyl-3-hydroxyquinoxaline 1-oxide (II), which on deoxygenation gave → III].

The above reactions clearly establish that 3-hydroxy-2-phenylquinoxaline 1-oxide and its derivatives, when heated with acetyl chloride or a mixture (1 : 1) of concentrated hydrochloric acid and acetic acid, undergoes chlorination at position 6 with simultaneous deoxygenation. By analogy, the chloro compounds similarly obtained from 2-(*p*-chlorophenyl)-3-hydroxyquinoxaline 1-oxide (Ie) and 7-ethoxy- and 7-methoxy- derivatives (Ic and Id) of Ia should be formulated as IIk, IIi and IIj respectively. In this reaction, powerful electron-withdrawing properties of the *N*-oxide function at $N_{(1)}$, augmented by the interaction of an Ac^+ (or H^+)*2 with the oxygen function at $C_{(3)}$ of quinoxaline molecule, made position 6 prone to nucleophilic attack by the chloride anion (as shown below), particularly so if position 2 was already occupied. The presence of an oxygen function at position 3 of the quinoxaline 1-oxides seemed to be essential for directing this nucleophilic chlorination to position 6. Otherwise[8] either the chlorination did not take place at all under the conditions of this reaction, or, if it did take place, it was directed to the substituent at position 2.

This mechanism† satisfactorily accounted for the cases of chlorination with the simultaneous deoxygenation of quinoxaline *N*-oxide derivatives reported above, and also for all such cases reported earlier by other workers.[5,6,9]

On the other hand, when 3-hydroxy-2-phenylquinoxaline 1-oxide (Ia) was heated with fuming hydrobromic acid, the product isolated, instead of being 6-bromo-3-hydroxy-2-phenylquinoxaline (IIg, Br for Cl), was the halogen-free deoxygenated base, i. e., 3-hydroxy-2-phenylquinoxaline (IIa). This was not entirely unexpected, as Loudon et al.[10,11] had obtained chlorinated quinoline derivatives when they

*2 Acetyl chloride, when used as a reaction medium, has been shown[7] to ionise as $CH_3COCl \rightleftarrows CH_3CO^+ + Cl^-$. Therefore, hydrochloric acid and acetyl chloride can be considered to follow the same course of reaction, to effect the nucleophilic chlorination reaction in the present investigation.

7) K. K. Desai and B. C. Halder, *J. Indian Chem. Soc.*, **41**, 116 (1964).

8) Y. Ahmad et al., unpublished work.

† We do not wish to imply that the initial attack of the reagent on the *N*-oxide is to be excluded here. This probably takes place and helps in further enhancing the electron-withdrawing properties of the *N*-oxide. However, this alone does not seem to direct the attack of the nucleophile (Cl^-) to position 6 of the quinoxaline molecule. It is the attack (or simultaneous attack) of the reagent at the oxygen function at $C_{(3)}$ which seems to control it. For the sake of brevity, the attack of the reagent on the *N*-oxide is, therefore, not shown in the mechanism.

9) J. W. Clark-Lewis and G. F. Katekar, *J. Chem. Soc.*, **1959**, 2825.

10) J. D. Loudon and I. Wellings, ibid., **1960**, 3470.

11) J. D. Loudon and G. Tennant, ibid., **1962**, 3092.

reacted *o*-nitrobenzaldehyde with compounds containing an active methylene group in the presence of hydrogen chloride. However, when they replaced hydrogen chloride by hydrogen bromide, the compounds isolated, although similar in structure, were free from halogen.

Further work is in progress.

Experimental*3

α-(*p*-Chlorophenyl)-2-nitroacetanilide (IIIe). — *o*-Nitroaniline (0.1 mol.) and *p*-chlorophenylacetyl chloride[12] (0.12 mol.) dissolved in minimum quantity of dry benzene were heated together under reflux for 25—30 min. More benzene was then added and, the solution was washed with 5% aqueous hydroxide and with water and then dried (sodium sulphate). The residue obtained after the removal of the solvent under reduced pressure was crystallised from light petroleum as yellow plates of the anilide (IIIe) in 80% yield, m. p. 91—92°C.

Found: N, 9.4. Calcd. for $C_{14}H_{11}ClN_2O_3$: N, 9.6%. The same procedure was followed for the preparation of the anilides described below.

4-Chloro-α-(*p*-chlorophenyl)-2-nitroacetanilide (IIIf).—4-Chloro-2-nitroaniline,[13] when treated by the above method, gave, in a 86% yield, yellow plates (from benzene-light petroleum) of the dichloroanilide (IIIf), m. p. 127—128°C.

Found: C, 51.9; H, 3.3; Cl, 21.2; N, 7.9. Calcd. for $C_{14}H_{10}Cl_2N_2O_3$: C, 51.7; H, 3.1; Cl, 21.8; N, 7.7%.

4,5-Dichloro-α-(*p*-chlorophenyl)-2-nitroacetanilide (IIII).—4,5-Dichloro-2-nitroaniline[14] gave, in 78% yield, yellow needles (from benzene) of the trichloroanilide (IIII), m. p. 150—151°C.

Found: Cl, 30.2; N, 7.6. Calcd. for $C_{14}H_9Cl_3N_2O_3$: Cl, 29.6; N, 7.8%.

5-Chloro-*N*-methyl-2-nitro-α-phenylacetanilide (IIIg; H′=Me). — 5-Chloro-2-nitro-*N*-methylaniline,[15] on being allowed to react with phenylacetyl chloride[16] as described above, gave, in 83% yield, yellow microneedles (from benzene-light petroleum) of the 5-chloro-*N*-methylanilide (IIIg; H′=Me), m. p. 140—141°C.

Found: N, 8.9. Calcd for $C_{15}H_{14}ClN_2O_3$: N, 9.2%.

2-(*p*-Chlorophenyl)-3-hydroxyquinoxaline 1-Oxide (Ie).—A solution of the anilide (IIIe) (4.0 g.) in pyridine (20 ml.) was heated with 20% aqueous potassium hydroxide (20 ml.) on a water bath for 1 hr. The reaction mixture, after dilution with water and acidification with dilute hydrochloric acid, gave a solid which crystallised from ethanol as yellow needles of the *N*-oxide (Ie) in 65% yield, m. p. 316—318°C (decomp.).

Found: N, 10.1. Calcd. for $C_{14}H_9ClN_2O_2$: N, 10.3%.

These needles, on being heating with an excess of sodium dithionite in 50% aqueous ethanol, was deoxygenated, and, on removal of the excess solvent, gave a solid which crystallised from benzene as yellow needles of *2-(p-chlorophenyl)-3-hydroxyquinoxaline (IIe)* in 82% yield, m. p. 291—292°C.

Found: N, 10.5. Calcd. for $C_{14}H_9ClN_2O$: N, 10.9%.

The *N*-oxides described below were obtained and deoxygenated by the procedures outlined above.

7-Chloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline 1-Oxide (If).—The compound IIIf when treated by the above method, gave yellow microneedles (from dimethylformamide-ethanol) of the dichloro-*N*-oxide (If) in 62% yield, m. p. 333°C (decomp.).

Found: C, 54.4; H, 2.9; N, 8.9. Calcd. for $C_{14}H_8Cl_2N_2O_2$: C, 54.7; H, 2.6; N, 9.1%; these microneedles, on reduction with sodium dithionite in 50% aqueous acetic acid, gave pale yellow microneedles (from benzene) of *7-chloro-2-(p-chlorophenyl)-3-hydroxyquinoxaline (IIf)* in quantitative yield, m. p. 220—222°C.

Found: C, 57.0; H, 2.8; N, 9.8. Calcd. for $C_{14}H_8Cl_2N_2O$: C, 57.7; H, 2.7; N, 9.6%.

6,7-Dichloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline 1-Oxide (Il). — The anilide (IIII) gave, in 64% yield, yellow needles (from ethanol) of the trichloro *N*-oxide (Il), m. p. 310°C (decomp.).

Found: Cl, 30.5; N, 8.2. Calcd. for $C_{14}H_7Cl_3N_2O_2$: Cl, 31.2; N, 8.2%.

6,7-Dichloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline (III).—a) The *N*-oxide (Il), on reduction with sodium dithionite in 50% aqueous ethanol, gave, in good yield, pale yellow microneedles (from ethanol) of the trichloroquinoxaline (III), m. p. 320—323°C.

Found: C, 51.3; H, 2.2; N, 8.5. Calcd. for $C_{14}H_7Cl_3N_2O$: C, 51.6; H, 2.15; N, 8.6%.

b) The *N*-oxide (If) (0.5 g.) and acetyl chloride (30 ml.) were heated together in a sealed tube at 100°C for 72 hr. The excess solvent was then removed, and the residue was washed with water and the crystallised from ethanol as pale yellow microneedles of the trichloroquinoxaline (III) in 75% yield, m. p. 322—323°C. This was identical (infrared spectra and mixed melting point) with the sample described under a).

6-Chloro-3,4-dihydro-4-methyl-3-oxo-2-phenylquinoxaline 1-Oxide (Ig; H′=Me). — The anilide (IIIg; H′=Me) cyclised in 58% yield as pale yellow plates (from methanol) of the 6-chloro-dihydro *N*-oxide (Ig; H′=Me), m. p. 191—192°C.

Found: Cl, 12.0; N, 9.9. Calcd. for $C_{15}H_{11}ClN_2O_2$: Cl, 12.3; N, 9.75%.

6-Chloro-3,4-dihydro-4-methyl-3-oxo-2-phenylquinoxaline (IIg; H′=Me). — a) The above *N*-oxide, on reduction with sodium dithionite in 50% aqueous ethanol, gave, in a good yield, pale yellow microneedles (from ethanol) of the 6-chloro-dihydroquinoxaline (IIg; H′=Me), m. p. 123°C.

Found: Cl, 13.3; N, 10.2. Calcd. for $C_{15}H_{11}ClN_2O$: Cl, 13.1; N, 10.35%.

*3 All melting points are uncorrected. Infrared spectra were measured in Nujol mull. Light petroleum used was of 60—80°C boiling range.

12) E. Friedmann and C. Masse, *Biochem. Z.*, **27**, 97 (1910).

13) M. K. Bose, *J. Indian Chem. Soc.*, **22**, 169 (1945).

14) F. Beilstein and A. Kurbatow, *Liebig's Ann.*, **196**, 214 (1879).

15) F. Kehrmann and H. Muller, *Ber. Dtsch. Chem. Ges.*, **34**, 1095 (1901).

16) F. M. Hamer, *J. Chem. Soc.*, **1956**, 1480.

b) 5-Chloro-2-nitro-*N*-methylaniline[15] (1.0 g.) in benzene (40 ml.) was reduced with hydrogen over Pd-C. The catalyst was then filtered off, and the solvent from the dried (sodium sulphate) solution was completely removed under reduced pressure. The residue in a minimum of ethanol was heated with ethyl phenylglyoxalate[17] (1.2 g.) under reflux for 3 hr. The solid obtained on cooling was crystallised from ethanol as colourless microneedles of IIg (H′=Me), m. p. 122—123°C. It was identical (infrared spectrum and mixed melting point) with the product obtained under a).

6-Chloro-3-hydroxy-2-phenylquinoxaline (IIg).— 3-Hydroxy-2-phenylquinoxaline 1-oxide[2] (Ia) (1.0 g.) and acetyl chloride (40 ml.) or a mixture of hydrochloric acid and acetic acide (1 : 1) were heated under reflux for 6—8 hr. The excess solvent was then removed under reduced pressure, and the residue was washed with water and then crystallised from ethanol as pale yellow microneedles of the 6-chloroquinoxaline (IIg) in 88% yield, m. p. 274—275°C.

Found: C, 65.55; H, 3.9; Cl, 13.5; N, 10.7. Calcd. for $C_{14}H_9ClN_2O$: C, 65.5; H, 3.5; Cl, 13.8; N, 10.9%.

This, on being methylated with methyl sulphate in the presence of anhydrous sodium carbonate in acetone, gave, in a good yield, colourless microneedles (from ethanol) of the 6-chloro-3,4-dihydro-4-methyl-3-oxo-2-phenylquinoxaline (IIg; H′=Me), m. p. 123—124°C; these microneedles were identical (infrared spectra and mixed melting point) with the sample prepared under a) and b) above.

6, 7 - Dichloro - 3 - hydroxy - 2 - phenylquinoxaline (IIh). — a) A mixture of 7-chloro-3-hydroxy-2-phenylquinoxaline 1-oxide[2] (Ib) (1.0 g.) and acetyl chloride (40 ml.) was heated in a sealed tube at 100°C for 72 hr. After the acetyl chloride had then been removed, the residue was washed with water. The solid thus obtained (in a quantitative yield) was crystallised from ethanol as yellow needles of the dichloroquinoxaline (IIh), m. p. 305—306°C.

Found: Cl, 24.3; N, 9.75. Calcd. for $C_{14}H_8Cl_2N_2O$: Cl, 24.4; N, 9.6%.

It was identical (infrared spectra and mixed melting point) with an authentic sample synthesised as described below.

b) A solution of 4,5-dichloro-*o*-phenylenediamine (obtained in situ by reduction with hydrogen of 4,5-dichloro-2-nitroaniline[14] (1.0 g.) in ethanol over Pd-C) and ethyl phenylglyoxalate[17] (1.2 g.) in ethanol (about 10 ml.) was heated under reflux for 3 hr. The solid obtained on cooling was crystallised from ethanol (in a quantitative yield) as yellow needles of 6,7-dichloro-3-hydroxy-3-phenylquinoxaline (IIh), m. p. 305—306°C.

6-Chloro-7-ethoxy-3-hydroxy-2-phenylquinoxaline (IIi). — 7-Ethoxy-3-hydroxy-2-phenylquinoxaline 1-oxide[2] (Ic) (1.0 g.) and a mixture of concentrated hydrochloric acid and acetic acid (1 : 1) (40 ml.) were heated under reflux for 6 hr. The mixture, after the excess acetic acid had been removed, was diluted with water and chilled overnight; a solid was thereby obtained (yield 70%) which crystallised from ethanol as yellow needles of the chloroethoxyquinoxaline (IIi), m. p. 283—284°C.

Found: Cl, 11.5; N, 9.4. Calcd. for $C_{16}H_{13}ClN_2O_2$: Cl, 11.8; N, 9.3%.

6-Chloro-7-methoxy-3-hydroxy-2-phenylquinoxaline (IIj). — 7-Methoxy-3-hydroxy-2-phenylquinoxaline 1-oxide[2] (Id), on being heated with acetyl chloride under reflux for 15 hr. (and being worked up as usual) gave, in a quantitative yield, yellow needles (from ethanol) of the chloromethoxyquinoxaline (IIj), m. p. 260—261°C.

Found: Cl, 12.3; N, 10.2. Calcd. for $C_{15}H_{11}ClN_2O_2$: Cl, 12.4; N, 9.8%.

6-Chloro-2-(*p*-chlorophenyl)-3-hydroxyquinoxaline (IIk).—2-(*p*-Chlorophenyl)-3-hydroxyquinoxaline 1-oxide (Ie) (1.0 g.), on being heated under reflux for 12 hr. with a mixture of concentrated hydrochloric acid and acetic acid (1 : 1) (40 ml.) (an additional 5 ml. of concentrated hydrochloric acid was added every hour) and on being worked up as usual, gave a solid which crystallised from ethanol as pale yellow microneedles (yield 95%) of the dichlorophenylquinoxaline (IIk), m. p.>325°C.

Found: Cl, 22.9; N, 9.1. Calcd. for $C_{14}H_8Cl_2N_2O \cdot H_2O$: Cl, 23.0; N, 9.1%.

The Action of Hydrobromic Acid on 3-Hydroxy-2-phenylquinoxaline 1-Oxide (Ia). — The *N*-oxide[2] (Ia) (1.0 g.), on being heated with a mixture of fuming hydrobromic acid and acetic acid (1 : 1) (40ml.) at 100°C for 12 hr., gave after the excess acids had been removed and it had been washed with water, a product which crystallised from ethanol as pale yellow microneedles (yield 60%) of the 3-hydroxy-2-phenylquinoxaline (IIa), m. p. 243—245°C. It was identical (infrared spectrum) with an authentic sample prepared[2] by the condensation of *o*-phenylenediamine with ethyl phenylglyoxalate.

Summary

3-Hydroxy-2-phenylquinoxaline 1-oxide (Ia), on being heated with acetyl chloride, instead of giving the acetyl derivative, gives a chloro compound (IIg), with a simultaneous loss of its *N*-oxide function. Ia, on being refluxed with a mixture of concentrated hydrochloric acid and acetic acid, undergoes the same transformation. Other derivatives (Ib—f) of Ia behave similarly and give the corresponding chlorine-substituted bases (IIh—l), the structure of which has been established by authentic syntheses.

A nucleophilic mechanism of this chlorination has been proposed, in which the presence of an oxygen function a position 3 of the 2-substituted quinoxaline 1-oxides seems to direct the chlorine substitution to position 6.

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17) J. Vene, *Bull. soc. chim. France*, **12**, 506 (1945).

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