489. *Electrophilic Substitution. Part X.* Nitration of Quinoxaline.*

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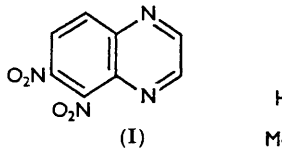
Quinoxaline has been shown to be mononitrated in the 5-position and dinitrated in the 5 : 6-positions.

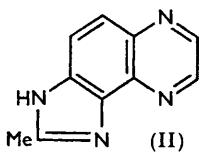
Apart from the formation of yellow crystals from quinoxaline by concentrated nitric acid which Hinsberg [1] suggested might be those of a nitro-derivative, no work has been reported on the nitration of quinoxaline. This base has always been assumed to be feebly reactive with electrophilic reagents, in view of the strong deactivating effect of the two nitrogen atoms. After several failures under milder conditions we found a mixture of oleum and nitric acid at 90° to give a mononitro- (1·5%) and a dinitro-quinoxaline (I) (24%). The former, m. p. 94—95°, must be 5-nitroquinoxaline, for which Schultz [2] gives m. p. 95—96°, since the only other isomer (6-) which could reasonably be formed

* Part IX, *J.*, 1957, 944.

[1] Hinsberg, *Ber.*, 1884, **17**, 320.
[2] Schultz, *J. Amer. Chem. Soc.*, 1950, **72**, 3824.

has m. p. 177°.[3] The compound (I) must therefore be a 5 : *x*-dinitroquinoxaline. This structure was confirmed by reduction with hydrazine hydrate and palladised charcoal, followed by acetylation : the only product isolated was 5-acetamidoquinoxaline.[4] Since the acetylation of the diaminoquinoxaline was shown to proceed smoothly, the extra nitro-group must have been lost during the reduction.


(I)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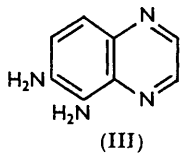
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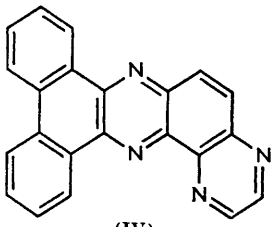
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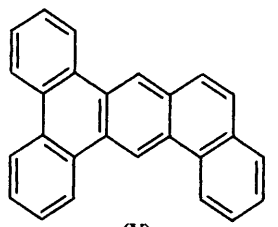
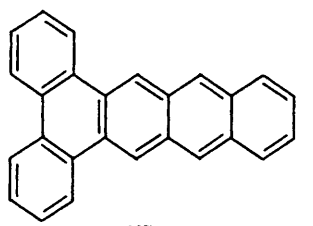

(V)


(VI)

Reduction with iron powder and glacial acetic acid, followed immediately by acetylation, gave a methylquinoxalinoglyoxaline (II), suggesting that the two original nitro-groups (assuming no molecular rearrangement had occurred) were *ortho* to each other. The reduction was then repeated and the products were separated at the amine stage by chromatography into a small amount of the tricyclic compound (II) and the crude diamine (III). The last, with phenanthraquinone, formed a condensation product which with sulphuric acid gave the red colour typical of dibenzophenazine derivatives; its analysis was that of the expected compound (IV). The spectrum of this compound (IV) in carbon tetrachloride does not agree exactly with that of 1 : 2-3 : 4-5 : 6-tribenzanthracene [5a] (V), in contrast to the frequent correspondence observed between heterocycles and isoconjugate hydrocarbons; [6] nevertheless the bands in compound (IV) at 401, 390, 379·5, 359·5, and 322 mμ correspond quite closely to the bands in the hydrocarbon (V) at 387·5, 377, 368, 345, and 303 mμ. Allowing for the difference in intensity of the various peaks, a bathochromic shift of *ca.* 13 mμ for the hydrocarbon would make the spectra superimposable. This is a much closer correspondence than that between the compounds (IV) and (VI).[5b]

Reductive acetylation of the dinitro-compound (I) in the presence of excess of acetic anhydride gave a diacetamidoquinoxaline. It was not possible to convert this into the glyoxaline (II) by treatment with hydrochloric acid, the starting material being recovered unchanged. Aqueous alkali destroyed the molecule.

A product isolated on nitration of quinoxaline with nitric acid and trifluoracetic anhydride gave analyses for a hydroxynitroquinoxaline, but did not correspond to any of the known isomers.

Experimental

Microanalyses were by the Microanalytical Laboratory, Imperial College of Science and Technology, London. The spectrum of the compound (IV) was measured in "AnalaR" carbon tetrachloride on a Unicam S.P. 500 spectrophotometer.

[3] Beilstein's "Handbuch der organischen Chemie," Vol. XXIII, p. 177.
[4] Landquist, *J.*, 1953, 2816.
[5] Clar, "Aromatische Kohlenwasserstoffe," Springer Verlag, Berlin, 1952, 2nd Edn., pp. (*a*) 205, (*b*) 242.
[6] Badger *et al.*, *J.*, 1951, 3199; 1956, 122.

Nitration of Quinoxaline.—To a solution of quinoxaline [7] (11 g.) in sulphuric acid (50 ml.) was added (*a*) a mixture of nitric acid (*d* 1·5; 25 ml.) and sulphuric acid (50 ml.) and (*b*) oleum (65% of SO_3; 50 ml.). Solutions were made with strong cooling, usually in acetone–solid carbon dioxide. The final mixture was heated on a steam-bath at 85—90° for 24 hr., then allowed to cool to room temperature and hydrolysed by being poured on ice (2 kg.) whereupon a sticky orange solid separated. (Addition of alkali caused this solid to dissolve, the solution becoming deep red; the original solid could not then be recovered on acidification.) The solid was extracted with chloroform containing acetone (20% v/v; 10 × 200 ml.); evaporation of the dried extract left a tar (12 g.), which was taken up in the minimum amount of acetone (30 ml.), boiled with charcoal, filtered, and allowed to crystallise. Recrystallisation gave yellow prisms (5·1 g.), m. p. 172—173°, of 5 : 6-*dinitroquinoxaline* (Found : C, 43·0; H, 2·0; N, 25·6; *M*, 225. $C_8H_4O_4N_4$ requires C, 43·6; H, 1·8; N, 25·5%; *M*, 220). The mother-liquors were evaporated to dryness and the residue was chromatographed on alumina in benzene to give a yellow solution. Evaporation and recrystallisation gave the same compound (I) (0·2 g.) and 5-*nitroquinoxaline* (0·3 g.), m. p. 80—85°. This crystallised from aqueous alcohol in pale yellow needles, which after vacuum-sublimation had m. p. 95—96° (Found : C, 54·4; H, 3·2; N, 23·8%. Calc. for $C_8H_5N_3O_2$: C, 54·8; H, 2·8; N, 24·0%). Only a small amount of quinoxaline (0·4 g.) was recovered by neutralising the original solution.

Orientation of the 5 : x-*Dinitroquinoxaline.*—(a) *Reduction with hydrazine hydrate.* Hydrazine hydrate (3 ml.) and 10% palladised charcoal (50 mg., in portions, during 10 min.) were added to a solution of the nitro-compound (I) (0·9 g.) in ethanol (40 ml.) at 70°. After 30 min. the solution was filtered and evaporated. The product was warmed for 5 min. with acetic anhydride (10 ml.) and concentrated sulphuric acid (0·1 ml.) on a steam-bath. The mixture was neutralised and extracted with chloroform, and the extract chromatographed on alumina in 1 : 1 benzene–chloroform to give a yellow solid (0·1 g.). After recrystallisation from aqueous alcohol and vacuum-sublimation this had m. p. 130—131° alone or mixed with 5-acetamidoquinoxaline (Found : C, 64·5; H, 4·8; N, 22·6. Calc. for $C_{10}H_9ON_3$: C, 64·2; H, 4·8; N, 22·5%).

(b) *Reduction with iron powder.* (i) Iron powder (1 g.) was added gradually to a solution of the nitro-compound (I) (0·95 g.) in boiling acetic acid (10 ml.) and the solution refluxed for ½ hr., then hydrolysed, neutralised, and extracted with chloroform. Evaporation of the extract gave a black tar which was acetylated. Chromatography of the product gave 2′-*methylglyoxalino*(4′ : 5′-5 : 6)*quinoxaline* (0·25 g., 31%), which after vacuum-sublimation had m. p. 249—249·5° (Found : C, 66·0; H, 4·0; N, 30·1. $C_{10}H_8N_4$ requires C, 65·2; H, 4·3; N, 30·4%).

(ii) The reduction product, obtained as in (i), was chromatographed in chloroform–benzene (1 : 1) on alumina. A colourless band (a), faintly yellow in solution, came through rapidly, followed by a bright green fluorescent band (b) which gave a brown solution. Evaporation of the solution (a) gave the glyoxaline (II) (0·14 g., 16%), whereas (b) gave a very dark red amorphous solid, presumed to be the diamine (III) (0·2 g., 36%).

Phenanthraquinone (0·15 g.) in hot acetic acid (1 ml.) was warmed with the diamine (0·14 g.) in ethanol (1 ml.), then poured into water; the yellow 1 : 2-3 : 4-*dibenzopyrazino*(2′ : 3′-6 : 7)-*phenazine* (IV), recrystallised from nitromethane, had m. p. >300° (0·2 g., 80%) (Found : C, 79·1; H, 3·6; N, 16·7. $C_{22}H_{12}N_4$ requires C, 79·5; H, 3·6; N, 16·9%).

(c) *Reductive acetylation.* Iron powder (0·5 g.) was added gradually to a solution of the nitro-compound (I) (0·5 g.), acetic anhydride (3 ml.), and acetic acid (2 ml.), and the whole refluxed for 30 min. The product was chromatographed on alumina in chloroform–benzene (1 : 1) to give a pale yellow solid. Vacuum-sublimation and crystallisation from aqueous alcohol gave white needles, m. p. 232—233°, of 5 : 6-*diacetamidoquinoxaline* (0·45 g., 83%) (Found : C, 58·4; H, 5·1; N, 22·9. $C_{12}H_{12}O_2N_4$ requires C, 59·0; H, 4·9; N, 22·9%). Attempts to hydrolyse this material failed. After being heated for 30 min. with 5N-hydrochloric acid it was recovered. The solution in hydrochloric acid did not give a positive diazo-reaction even after prolonged boiling. Only tars resulted from hydrolysis by 5N-sodium hydroxide.

Nitration of Quinoxaline in Trifluoracetic Anhydride.—A solution of quinoxaline (1·0 g.) in trifluoracetic anhydride (12 ml.) and nitric acid (*d* 1·5; 0·5 ml.) was left for 88 hr. at room temperature. After the excess of anhydride had been distilled off, the residue was hydrolysed, neutralised, and extracted with chloroform. Evaporation of the extract and chromatography in benzene on alumina gave a yellow *hydroxynitroquinoxaline* (0·43 g., 28%), which crystallised

[7] *Org. Synth.*, 1950, **30**, 86.

from acetone in colourless prisms, m. p. 182—183° (Found: C, 50·5; H, 2·9; N, 22·5. $C_8H_5O_3N_3$ requires C, 50·3; H, 2·6; N, 22·0%).

We thank D.S.I.R. for a maintenance grant (to P. M. M.) and Dr. J. K. Landquist of Imperial Chemical Industries Limited, Dyestuffs Division, for a sample of 5-acetamidoquinoxaline.

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