

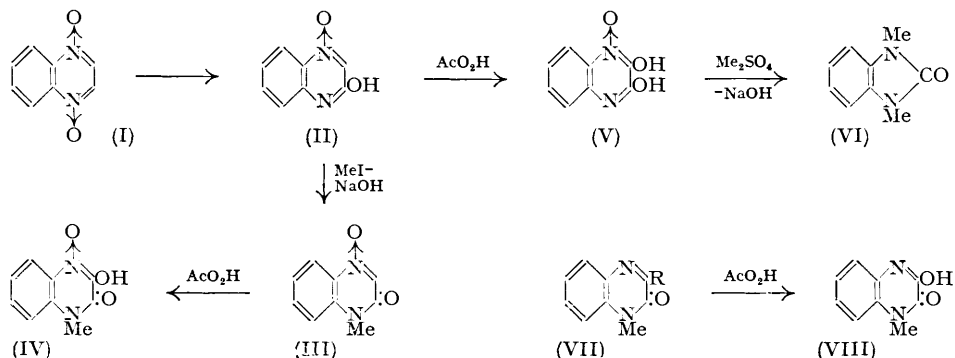
569. *Quinoxaline N-Oxides. Part III.\* Photochemical Decomposition of Quinoxaline Mono- and Di-N-oxides.*

By JUSTUS K. LANDQUIST.

Photochemical decomposition of quinoxaline 1-oxide affords 2-hydroxyquinoxaline. Quinoxaline 1:4-dioxide undergoes rapid photochemical decomposition in dilute solution, the course of the reaction being influenced by the solvent. In dilute hydrochloric acid the product is a chloroquinoxaline mono-*N*-oxide, and in water or dilute sulphuric acid 2-hydroxyquinoxaline 4-oxide is formed. Some 1-methylquinoxaline 4-oxides are described.

WHILE developing a spectrophotometric method for the determination of quinoxaline 1:4-dioxide (I) in biological materials Dr. A. Spinks (personal communication) found that the absorption spectrum of dilute solutions changed rapidly on exposure to light. At the same time it was found that the amœbicidal activity of solutions of (I) was lost on storage in clear glass bottles exposed to daylight or to ultra-violet light. Decomposition of 0.05% solutions in a silica cell 15" from a Hanovia ultra-violet lamp was complete in 10–30 minutes, the rate of reaction and the spectrum of the end products varying with the solvent. Numerous other quinoxaline di-*N*-oxides were examined, and all showed about the same degree of photochemical instability. McIlwain (*J.*, 1943, 322) found that the production of a blue product from 2-methylquinoxaline 1:4-dioxide in alkaline solution was greatly accelerated by light.

Quinoxaline 1-oxide in aqueous solution undergoes a slower photochemical decomposition than (I); the product was identified as 2-hydroxyquinoxaline. Irradiation of (I) in dilute hydrochloric acid gives a compound  $C_8H_5ON_2Cl$ , whose absorption spectrum and other physical properties resemble those of quinoxaline 1-oxide. It is not identical with any of the chloroquinoxaline mono-*N*-oxides described in Part I (*J.*, 1953, 2816). On prolonged irradiation it undergoes further decomposition.

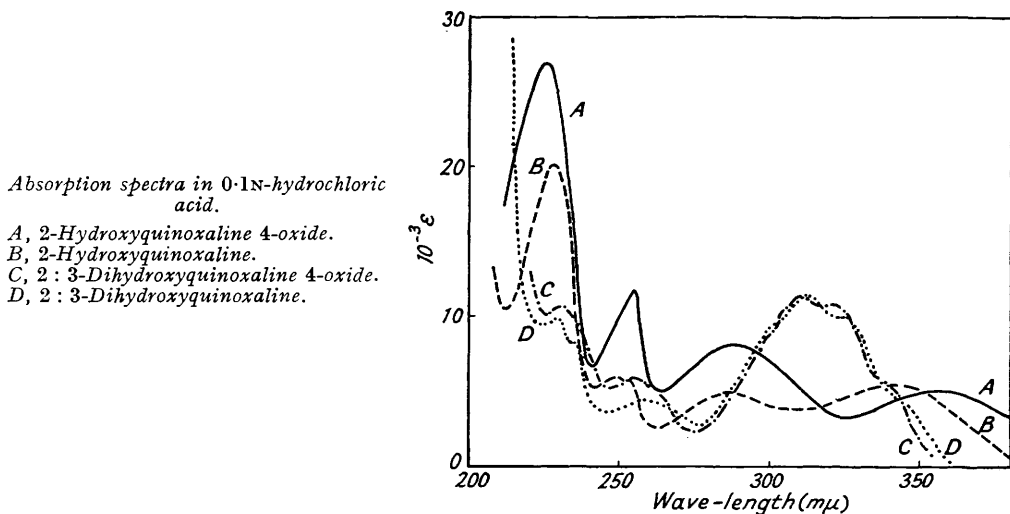


In chloroform and in aqueous alkali, (I) undergoes photochemical decomposition to end-products with indefinite absorption spectra which suggest complex mixtures, but in

\* Part II, preceding paper.

water or dilute sulphuric acid a single compound,  $C_8H_6O_2N_2$ , m. p.  $275^\circ$ , with an absorption spectrum resembling that of 2-hydroxyquinoxaline, is obtained. This does not show the reactions of a hydroxamic acid, and it was shown to be 2-hydroxyquinoxaline 4-oxide (II) by the following reactions: methylation with methyl iodide and sodium hydroxide afforded a methyl derivative (III), m. p.  $208-209^\circ$ , which contained no methoxyl groups, and this on oxidation with peracetic acid gave 3-hydroxy-1-methylquinoxal-2-one 4-oxide (IV), identical with material obtained by cyclisation of nitrosomalonic bis-*N*-methylanilide and subsequent hydrolysis (Usherwood and Whiteley, *J.*, 1923, 1069). Peracetic acid oxidation of (II) gave 2 : 3-dihydroxyquinoxaline 4-oxide (V), the absorption spectrum of which resembled that of 2 : 3-dihydroxyquinoxaline, and this compound on treatment with methyl sulphate and sodium hydroxide was degraded and methylated to 1 : 3-dimethylbenzimidazol-2-one (VI).

The methyl derivative (III) is 1-methylquinoxal-2-one 4-oxide, which Usherwood and Whiteley (*loc. cit.*) obtained from nitromalonic bis-*N*-methylanilide and described as melting



at  $192-194^\circ$ . Peracetic acid oxidation of 1-methylquinoxal-2-one (VII;  $R = H$ ), and of methyl 1 : 2-dihydro-1-methyl-2-oxo-3-quinoxalinyacetate (VII;  $R = CH_2 \cdot CO_2Me$ ) gave 3-hydroxy-1-methylquinoxal-2-one (VIII), but 1 : 3-dimethylquinoxal-2-one (VII;  $R = Me$ ) on oxidation gave a small yield of 1 : 3-dimethylquinoxal-2-one 4-oxide. Methylation of ethyl 2-hydroxy-3-quinoxalinyacetate with methyl sulphate in alkaline solution gave (VII;  $R = CH_2 \cdot CO_2Me$ ); the ethyl ester (VII;  $R = CH_2 \cdot CO_2Et$ ) was prepared from *N*-methyl-*o*-phenylenediamine and ethyl ethoxalylacetate, and the acid obtained on hydrolysis of the ester was unstable, yielding (VII;  $R = Me$ ) by decarboxylation at room temperature.

Some absorption spectra are shown in the Figure.

#### EXPERIMENTAL

*Isolation of Irradiation Products.*—(a) Quinoxaline 1-oxide (0.5 g.) in water (100 c.c.) was irradiated by a Hanovia ultra-violet lamp for 14 days and then by daylight for an equal time. 2-Hydroxyquinoxaline (0.1 g.) crystallised out, and after extraction with dilute sodium hydroxide solution, treatment with carbon, reprecipitation, and crystallisation from ethanol, it melted at  $262-264^\circ$ , alone or admixed with an authentic specimen.

(b) Quinoxaline 1 : 4-dioxide (0.5 g.) in 0.5N-hydrochloric acid (50 c.c.) was irradiated by a Hanovia lamp until the absorption spectrum indicated that decomposition was complete (about 2 weeks). The filtered solution was concentrated under reduced pressure to about 5 c.c. and the crystalline solid (0.2 g.) collected, washed with water, dried, and extracted with

cyclohexane, leaving a trace of high-melting solid, probably 2:3-dihydroxyquinoxaline (similar absorption spectrum). The *chloroquinoxaline 1-oxide* crystallised from cyclohexane in long colourless needles, m. p. 114° (Found: C, 53.2; H, 2.6; N, 15.1; Cl, 19.9.  $C_8H_8ON_2Cl$  requires C, 53.2; H, 2.8; N, 15.5; Cl, 19.65%).

(c) Quinoxaline 1:4-dioxide (7.5 g.) was dissolved in water (500 c.c.) by warming and the solution was left in full daylight (direct sunlight when possible) in a glass flask. The product began to separate after 2–3 hr., together with some quinoxaline 1:4-dioxide which was re-dissolved by warming. After 2 weeks the solid (3.0 g.) was collected, dissolved in dilute sodium hydroxide solution, clarified with carbon, and precipitated with acetic acid. 2-Hydroxyquinoxaline 4-oxide crystallised from glacial acetic acid in buff prisms, m. p. 274–275° (Found: C, 59.0; H, 3.8; N, 17.6.  $C_8H_6O_2N_2$  requires C, 59.3; H, 3.7; N, 17.3%).

1-Methylquinoxal-2-one 4-Oxide.—2-Hydroxyquinoxaline 4-oxide (2.0 g.), dissolved in 4% sodium hydroxide solution (30 c.c.) and methanol (30 c.c.), was shaken with methyl iodide (6 c.c.) for 5 hr., and the product (1.1 g.) was collected next day and crystallised from benzene, forming pale buff needles, m. p. 208–209° (Found: C, 61.4; H, 4.5; N, 16.2; OMe, 0. Calc. for  $C_9H_8O_2N_2$ : C, 61.3; H, 4.55; N, 15.9%).

3-Hydroxy-1-methylquinoxal-2-one 4-Oxide.—1-Methylquinoxal-2-one 4-oxide (0.5 g.) and 1.2M-peracetic acid (5 c.c.) were heated overnight at 50°. The product crystallised out in needles, m. p. 253–255° alone or admixed with 3-hydroxy-1-methylquinoxal-2-one 4-oxide, m. p. 257°, prepared by Usherwood and Whiteley's method.

2:3-Dihydroxyquinoxaline 4-Oxide.—2-Hydroxyquinoxaline 4-oxide (2.5 g.), glacial acetic acid (100 c.c.) and 30% hydrogen peroxide (50 c.c.) were heated at 50° overnight, cooled, and diluted with water. The product separated in white globular aggregates of crystals which changed to pale brown rhomboidal tablets of the *hydrate* (Found: C, 49.0; H, 3.9; N, 14.4.  $C_8H_6O_3N_2 \cdot H_2O$  requires C, 49.0; H, 4.1; N, 14.3%), which at 100° fell to a white powder of 2:3-dihydroxyquinoxaline 4-oxide, m. p. 290° (decomp.) (Found: C, 53.5; H, 3.2; N, 15.4.  $C_8H_6O_3N_2$  requires C, 53.9; H, 3.4; N, 15.7%).

1:3-Dimethylbenziminazol-2-one.—(a) Benziminazolone (1 g.), dissolved in 2N-sodium hydroxide (10 c.c.), was shaken with methyl sulphate (3 c.c.) for 2–3 hr., and the product was collected, washed with a little cold water, dried, and crystallised from light petroleum (b. p. 100–120°), forming needles which gradually changed to shorter prisms, m. p. 107–108°. (b) 2:3-Dihydroxyquinoxaline 4-oxide (1.0 g.) in 2N-sodium hydroxide (15 c.c.) was treated with methyl sulphate (2.5 c.c.), further additions of methyl sulphate (1.5 c.c.) and sodium hydroxide being made after 3 days and after 1 week. On long storage stout needles of 1:3-dimethylbenziminazolone (0.45 g.) separated and, crystallised from water (carbon) and then from light petroleum (b. p. 100–120°), had m. p. and mixed m. p. 107° (Found: C, 66.4; H, 6.3; N, 17.2. Calc. for  $C_9H_{10}ON_2$ : C, 66.6; H, 6.2; N, 16.8%).

Methyl 1:2-Dihydro-1-methyl-2-oxo-3-quinoxalinyllacetate.—Crude ethyl 2-hydroxy-3-quinoxalinyllacetate (29 g.) was dissolved in 1.5N-sodium hydroxide (200 c.c.) and methanol (50 c.c.) and shaken at 0–5° with methyl sulphate (30 c.c.). The *product* (7.0 g.; m. p. 155–157°) crystallised slowly, and formed orange needles, m. p. 164–166°, from ethanol (Found: C, 61.7; H, 5.2; N, 12.0.  $C_{12}H_{12}O_3N_2$  requires C, 62.05; H, 5.2; N, 12.1%).

Ethyl 1:2-Dihydro-1-methyl-2-oxo-3-quinoxalinyllacetate.—N-Methyl-*o*-phenylenediamine (2.25 g.), ethyl ethoxalylacetate sodium salt (4.5 g.), and 10% acetic acid (50 c.c.) were heated on the steam-bath for 30 min. The oil which separated rapidly and then hardened was collected when cold, washed with water and crystallised from ethanol (carbon), giving ethyl 1:2-dihydro-1-methyl-2-oxo-3-quinoxalinyllacetate as yellow platelets or hair-like needles, m. p. 140–142° (Found: C, 63.1; H, 5.4; N, 11.6.  $C_{13}H_{14}O_3N_2$  requires C, 63.4; H, 5.7; N, 11.4%).

Hydrolysis. The foregoing ester (0.9 g.) was boiled under reflux for 30 min. with 2N-sodium hydroxide, and the warm solution was acidified with acetic acid. There was a prolonged effervescence, and 1:3-dimethylquinoxal-2-one crystallised slowly (m. p. and mixed m. p. 86–87°).

1:3-Dimethylquinoxal-2-one 4-Oxide.—1:3-Dimethylquinoxal-2-one (17.6 g.) and 1.2M-peracetic acid (280 c.c.) were heated at 50° overnight, evaporated under reduced pressure to 60–70 c.c., and neutralised with 40% sodium hydroxide solution and ice. The aqueous layer was decanted from tar and extracted with chloroform, and the extract dried ( $Na_2SO_4$ ) and evaporated. Four crystallisations of the residue from ethanol (carbon) gave 1:3-dimethylquinoxal-2-one 4-oxide (0.3 g.) as faintly pink needles, m. p. 200–202° (Found: C, 63.0; H, 5.25; N, 14.4.  $C_{10}H_{10}O_2N_2$  requires C, 63.15; H, 5.25; N, 14.75%). A further 0.25 g. was recovered from the tar by repeated crystallisation from benzene and then ethanol.

*Other Oxidations.*—Peracetic acid, heated overnight at 50° with 1-methylquinoxal-2-one or methyl 1 : 2-dihydro-1-methyl-2-oxo-3-quinoxalinylnylacetate, gave 30—50% yields of 1-methyl-3-hydroxyquinoxal-2-one, m. p. and mixed m. p. 284—286°.

I am indebted to Dr. A. Spinks for measurements of absorption spectra, and for observations on the rate of photochemical decomposition of the substances examined.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, DYESTUFFS DIVISION,  
HEXAGON HOUSE, BLACKLEY, MANCHESTER, 9.

[Received, May 16th, 1953.]

---