80. *Quinoxaline Derivatives. Part V.* Decomposition of 3 : 4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-N-methylanilide 1-Oxide with Sulphuric Acid.*

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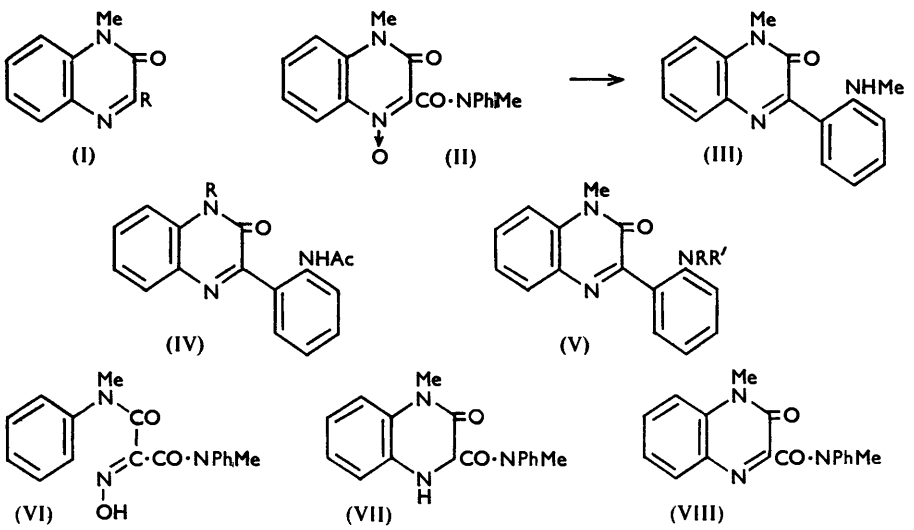
The structure of Usherwood and Whiteley's 3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide 1-oxide is confirmed by synthesis, and the product of its decomposition with sulphuric acid is shown to be 1 : 2-dihydro-1-methyl-3-*o*-methylaminophenyl-2-oxoquinoxaline.

Methylaniline reacts with 3-chloro-1 : 2-dihydro-1-methyl-2-oxoquinoxaline (I; R = Cl) to give the expected tertiary amine, 1 : 2-dihydro-1-methyl-3-methylphenylamino-2-oxoquinoxaline (I; R = NMePh), which differs from the isomer described as this compound by Usherwood and Whiteley. The authentic tertiary amine did not react with nitrous acid, whereas the compound prepared by Usherwood and Whiteley by adding



3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide 1-oxide (II) to sulphuric acid yielded a colourless nitroso-derivative,[1] which is clearly an *N*-nitroso-*sec.*-amine as it responded to the Liebermann nitroso-reaction. Unequivocal synthesis has established that Usherwood and Whiteley's compound is 1 : 2-dihydro-1-methyl-3-*o*-methylaminophenyl-2-oxoquinoxaline (III).

The amine (III) was prepared in 38% overall yield from *o*-phenylenediamine in the

* Part IV, preceding paper.

[1] Usherwood and Whiteley, *J.*, 1923, **123**, 1069.

following six stages. 1-Acetylisatin and *o*-phenylenediamine gave 3-*o*-acetamidophenyl-1 : 2-dihydro-2-oxoquinoxaline [2] (IV; R = H) which when methylated in acetone–potassium carbonate gave the 1-methyl derivative (IV; R = Me), and it is of interest that the *ortho*-substituted acetanilide was not methylated further even with an excess of methyl iodide and a longer reaction time. The product was hydrolysed and the toluene-*p*-sulphonyl derivative (V; R = H, R′ = *p*-$C_6H_4Me{\cdot}SO_2$) was then methylated to the dimethyl compound (V; R = Me, R′ = *p*-$C_6HMe{\cdot}SO_2$). Hydrolysis then gave the free amine (III) identical with that obtained by Usherwood and Whiteley.

Usherwood and Whiteley [1] obtained the *N*-oxide (II) by chromic acid oxidation of hydroxyiminomalonbis-*N*-methylanilide (VI), and deduced its structure from considerable degradative evidence and from its reduction to 1 : 2 : 3 : 4-tetrahydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide (VII). These structures are now confirmed by unequivocal syntheses from 3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide [3] (VIII) which was oxidised to the *N*-oxide (II) by hydrogen peroxide and reduced with zinc–acetic acid to the tetrahydroquinoxaline (VII), identical with that produced by similar reduction of the *N*-oxide. Usherwood and Whiteley inferred that formation of the *N*-oxide (II) from the hydroxyimino-compound (VI) occurred by cyclisation of nitromalonbis-*N*-methylanilide (*aci*-form), and this is supported by the stability of the methylanilide (VIII) towards chromic acid under similar conditions, so that (VIII) cannot be an intermediate in the oxidation of the hydroxyimino-compound (VI).

The interesting decomposition of the *N*-oxide (II) with sulphuric acid, apparently a novel type of *N*→*ortho*-rearrangement with loss of the elements of carbon dioxide, gave the secondary amine (III) in 75% yield, and may therefore have preparative value. It appears likely that it occurs by an intramolecular mechanism, but this aspect and the scope of the reaction have not yet been investigated.

Experimental

1 : 2-*Dihydro*-1-*methyl*-3-N-*methylanilino*-2-*oxoquinoxaline* (I; R = NMePh).—3-Chloro-1 : 2-dihydro-1-methyl-2-oxoquinoxaline [4] (1 g.), methylaniline (0·55 c.c.), and a little methanol were heated at 100° for 30 min. without a condenser. The solid product was washed with water, and crystallisation of the residue (1·3 g., 95%), m. p. 138—140°, from methanol (120 c.c.) yielded the N-*methylanilino-compound* in yellow needles (0·75 g.), m. p. 145—146°; concentration of the mother-liquors gave a further 0·235 g., m. p. 145—146° (Found : C, 72·9; H, 5·8; N, 16·0. $C_{16}H_{15}ON_3$ requires C, 72·4; H, 5·7; N, 15·7%). The compound was recovered (95%) after the addition of nitrous acid to a solution of the amine in 2N-hydrochloric acid.

Hydroxyiminomalonbis-N-*methylanilide* (VI).—Malondiamide (37·8 g.) was converted into malonbismethylanilide (87 g., 83%) by the method of Freund, and of Vorländer and Herrmann,[5] except that the amide was merely boiled with methylaniline until evolution of ammonia ceased. Nitrosyl chloride [6] was passed into a solution of malonbismethylanilide (54 g.) in dry chloroform (100 c.c.) at 0° for 1½ hr. and the solution was allowed to evaporate to a thick liquid (5 hr.) and hydroxyiminomalonbismethylanilide methanol solvate (50 g., 76%), m. p. 104—105° (decomp.), was precipitated by addition of methanol and collected after 1½ hr. A further quantity (4·3 g., total 83%) was recovered from the mother-liquors, and recrystallisation from methanol raised the m. p. to 105—106° (decomp.) (Found : C, 63·5; H, 6·1; N, 12·2. Calc. for $C_{17}H_{17}O_3N_3,CH_3{\cdot}OH$: C, 63·0; H, 6·2; N, 12·2%). It did not give the colour reactions with alkali and with alkaline ferrous sulphate described as characteristic by Whiteley.[7] In a similar experiment with 42 g. of the bismethylanilide where the chloroform solution was allowed to evaporate during 14 hr. the yield of hydroxyimino-compound was (23 g., 45%), m. p. 105° (decomp.), and dilution of the methanolic filtrate with water gave mesoxalbismethylanilide [7] (3·1 g., 7%), yellow prisms, m. p. 170°.

[2] Schunck and Marchlewski, *Ber.*, 1896, **29**, 197; Buraczewski and Marchlewski, *Ber.*, 1901, **34**, 4008.
[3] Clark-Lewis, Part III, *J.*, 1957, 422.
[4] Cheeseman, *J.*, 1955, 1804.
[5] Freund, *Ber.*, 1884, **17**, 137; Vorländer and Herrmann, *Ber.*, 1898, **31**, 1826.
[6] Morton and Wilcox, *Inorg. Synth.*, 1953, **4**, 48.
[7] Whiteley, *J.*, 1903, **83**, 24.

3 : 4-*Dihydro*-4-*methyl*-3-*oxoquinoxaline*-2-*carboxy*-N-*methylanilide* 1-*Oxide* (II).—(*a*) Oxidation of hydroxyiminomalonbismethylanilide methanol solvate (10 g.) with chromic acid [1] afforded the *N*-oxide (II) (3·3 g., 37%), m. p. 187° raised to 191° by recrystallisation (elongated leaflets) from ethanol (Found: C, 66·3; H, 5·1; N, 13·9. Calc. for $C_{17}H_{15}O_3N_3$: C, 66·0; H, 4·9; N, 13·6%).

(*b*) 3 : 4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide [3] (1 g.), acetic acid (5 c.c.), and 30% hydrogen peroxide (1 c.c.) were heated at 56° and two further quantities of hydrogen peroxide (0·5 c.c. each) were added after 24 and 48 hr. After the solution had been kept at 56° for 72 hr. it was diluted with water (2 vol.), and the crystalline *N*-oxide (0·5 g., *ca.* 50%) was collected after 24 hr.; chloroform extraction of the filtrate gave a further 0·05 g. The crude oxide had m. p. and mixed m. p. 188°, raised to 191° by recrystallisation from ethanol. Light absorption: max. 230 (ε 26,000), 309 (ε 7000), and 360 mμ (ε 5700); min. 214 (ε 14,000), 270 (ε 3600), and 336 mμ (ε 4800). Oxidation of the methylanilide with peracetic acid [8] (1·2M) at room temperature and at 56° gave a black tar. The methylanilide was recovered (70%) after treatment with chromic acid under conditions similar to those employed for the oxidation of the hydroxyimino-compound to the *N*-oxide [method (*a*)].

1 : 2 : 3 : 4-*Tetrahydro*-4-*methyl*-3-*oxoquinoxaline*-2-*carboxy*-N-*methylanilide* (VII).—3 : 4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxy-*N*-methylanilide [3] (1 g.) in acetic acid (20 c.c.) was reduced by the gradual addition of zinc dust (1 g.). The mixture was filtered after 15 min. and the tetrahydroquinoxaline derivative (0·7 g., 70%) crystallised from the filtrate after dilution with water (2 vol.), in needles, m. p. 187° unchanged by recrystallisation from ethanol (lit.,[1] m. p. 185°) (Found: C, 69·2; H, 6·1. Calc. for $C_{17}H_{17}O_2N_3$: C, 69·1; H, 5·8%). The product was identical (m. p. and mixed m. p.) with that obtained by similar reduction of the *N*-oxide (II) as described by Usherwood and Whiteley.[1] Light absorption: max. 227 (ε 30,000) and 300 mμ (ε 3400); min. 277 mμ (ε 2000).

3-o-*Aminophenyl*-1 : 2-*dihydro*-1-*methyl*-2-*oxoquinoxaline* (V; R = R′ = H).—3-*o*-Acetamidophenyl-2-hydroxyquinoxaline [2] (15 g.) (91% from *o*-phenylenediamine and 1-acetylisatin [9]), dimethyl sulphate (11 c.c.), anhydrous potassium carbonate (20 g.), and acetone (150 c.c.) were heated under reflux for 7 hr., the cooled suspension was filtered, and the solid washed with water. The residue dissolved in boiling acetic acid (*ca.* 25 c.c. per g.) and crystallisation afforded 3-o-*acetamidophenyl*-1 : 2-*dihydro*-1-*methyl*-2-*oxoquinoxaline* as a felted mat of needles (10 g., 64%), m. p. 202—204° unchanged by two recrystallisations from ethanol (Found: N, 14·6; NMe, 7·5; OMe, 0. $C_{17}H_{15}O_2N_3$ requires N, 14·3; NMe, 9·9%). The acetyl compound (2 g.) was heated with ethanol (100 c.c.) and 12N-hydrochloric acid (100 c.c.) at 100° for several hours, and the solution was concentrated to small bulk under reduced pressure before being poured into aqueous ammonia. The orange precipitate (1·6 g., 94%) of 3-o-*aminophenyl*-1 : 2-*dihydro*-1-*methyl*-2-*oxoquinoxaline* crystallised from ethanol in yellow rods, m. p. 185—186° (Found: C, 72·2; H, 5·2; N, 16·9. $C_{15}H_{13}ON_3$ requires C, 71·7; H, 5·2; N, 16·7%). The diazonium chloride gave a dark red azo-compound with 2-naphthol.

1 : 2-*Dihydro*-1-*methyl*-3-o-*methylaminophenyl*-2-*oxoquinoxaline* (III).—(*a*) The aminophenylquinoxalone (4·3 g.), toluene-*p*-sulphonyl chloride (4 g.), and pyridine (10 c.c.) were heated at 100° for 2 hr., then poured into water and acidified. The precipitated 1 : 2-*dihydro*-1-*methyl*-2-*oxo*-3-o-(*toluene*-p-*sulphonamido*)*phenylquinoxaline* (6·4 g., 92%), m. p. 148° after crystallisation from ethanol, was collected, washed with water, and dried (Found: C, 65·6; H, 4·8. $C_{22}H_{19}O_3N_3S$ requires C, 65·2; H, 4·7%). Methylation of the sulphonanilide (6·2 g.) with methyl iodide (5 c.c.) and anhydrous potassium carbonate (10 g.) in acetone (100 c.c.) for 14 hr. afforded the *toluene*-p-*sulphon*-N-*methylanilide* (5·5 g., 86%) which crystallised from aqueous acetic acid and from methanol in needles, m. p. 195° (Found: C, 66·5; H, 5·1; N, 10·1. $C_{23}H_{21}O_3N_3S$ requires C, 65·9; H, 5·0; N, 10·0%). The toluene-*p*-sulphonmethylanilide (4·5 g.) was heated for 1 hr. at 100° with a mixture (10 c.c.) of acetic acid (45 c.c.) and sulphuric acid (100 c.c.), and the solution then added to water and basified with sodium hydroxide to precipitate the product (2·5 g., 88%), m. p. 132—133°. The 1 : 2-*dihydro*-1-*methyl*-3-o-*methylaminophenyl*-2-*oxoquinoxaline* (2 g.) was dissolved in methanol (*ca.* 150 c.c.) and crystallisation afforded orange prisms (1·6 g.), m. p. 135° (Found: C, 73·0; H, 5·7; N, 16·0. $C_{16}H_{15}ON_3$ requires C, 72·4; H, 5·7; N, 15·8%). The compound exhibited the characteristic dimorphism formerly ascribed [1] to the 3-*N*-methylanilino-isomer. The N-*nitroso-derivative* crystallised

[8] Byers and Hickinbottom, *J.*, 1948, 286; cf. Landquist, *J.*, 1953, 2816.
[9] Suida, *Ber.*, 1878, **11**, 585.

from methanol in colourless prisms, m. p. 199° (decomp.) (Found: N, 19·5. $C_{16}H_{14}O_2N_4$ requires N, 19·0%).

(*b*) 3 : 4-Dihydro-4-methyl-3-oxoquinoline-2-carboxymethylanilide 1-oxide (II) (1·5 g., m. p. 187°) was finely powdered and stirred gradually into 92% sulphuric acid (5 c.c.) cooled in ice–salt and, when dissolution of the compound and evolution of gas were complete, the solution was poured into water (250 c.c.) and filtered. Basification of the filtrate gave an orange precipitate of 1 : 2-dihydro-1-methyl-3-*o*-methylaminophenyl-2-oxoquinoxaline (0·97 g., 75%), m. p. 131—133° not depressed by admixture with the compound, m. p. 135°, prepared by method (*a*). The *N*-nitroso-derivative had m. p. and mixed m. p. 199° (decomp.).

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