Tetrahedron Letters No.47, pp. 4851–4854, 1968. Pergamon Press. Printed in Great Britain.

A REVISED STRUCTURE FOR METHYLQUINOXALINE ORANGE

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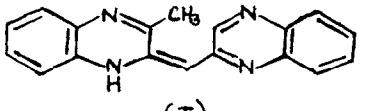
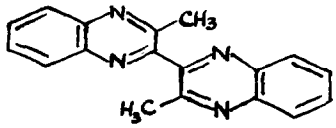
(Received in UK 25 July 1968; accepted for publication 16 August 1968)

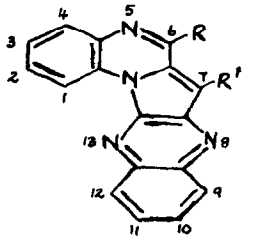
There are two reports (1,2) in the literature of the conversion of 2-methylquinoxaline into a high melting orange crystalline solid. In the first (1), the change was effected with dilute hydrochloric acid. The product designated methylquinoxaline orange, was formulated as compound (I) by analogy with the structure assigned previously to methylpteridine red (3). In the second (2), the conversion was brought about by heating at 200°, preferably in the presence of a palladium on carbon catalyst. The product was formulated as 3,3'-dimethyl-2,2'-biquinoxaline (II), because quinoxaline itself was converted into 2:2'-biquinoxaline under similar conditions, whereas 2,3-dimethylquinoxaline failed to react. We have proved that the same compound is formed in each of the above reactions and suggest that methylquinoxaline orange is 6-methyl-pyrrolo-[1,2-a:4,5-b']diquinoxaline (IIIa) rather than compound (I) or (II).



(I)



(II)



(IIIa ; R = CH_3, R' = H)

(IIIb ; R = H, R' = CN)

(IIIc ; R = R' = H)

A previous example of this ring system, namely the 7-cyano derivative (IIIb) has been reported although this compound was not fully characterised (4).

In our investigation, methylquinoxaline orange was prepared either by heating a solution

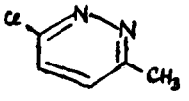
of 2-methylquinoxaline in concentrated hydrochloric acid at 95°, or by heating a fused mixture of 2,3-dimethylquinoxaline and 2-chloroquinoxaline in the presence of a little concentrated hydrochloric acid at about 100°. In each case, the product was obtained as the hydrochloride; the free base was liberated by treatment with sodium hydrogen carbonate. Crystallisation from dimethyl sulphoxide followed by sublimation at 200°/0.2mm. gave orange needles, m.p. 257-258° (Found: C, 75.9; H, 4.3; N, 20.2. Calc. for $C_{18}H_{12}N_4$: C, 76.0; H, 4.25; N, 19.7%). λ_{max} (EtOH) 495i (3.67), 470 (3.77), 449i (3.67), 385 (4.25), 368 (4.17), 354i (3.92), 275 (4.71), 272.5i(4.70), 241.5i mμ($\log_{10}\varepsilon$ 4.17).

We were able to eliminate the possibility that methylquinoxaline orange had structure (II) because 3,3'-dimethyl-2,2'-biquinoxaline (II) has been independently synthesised from o-phenylenediamine and acetylformoin $CH_3CO.CH(OH)CO.COCH_3$; it is reported to be a colourless compound, m.p. 182° (5). The u.v. spectrum of methylquinoxaline orange did not enable us to distinguish between structures (I) and (IIIa), but the p.m.r. spectrum was in much better accord with the pentacyclic structure (IIIa). This showed the 6-methyl resonance as a singlet at 7.18τ, H-7 as a sharp singlet at 2.85τ and a low field quartet at 0.09τ assigned to H-1. The τ values are closely similar to our previous assignments for the corresponding protons in the pyrrolo [1,2-a] quinoxaline ring system (6), we attribute the de-shielding of H-1 to the proximity of N-13. The mass spectrum of methylquinoxaline orange showed a base peak at 284 and only a small peak at 286. This is consistent with a molecular formula $C_{18}H_{12}N_4$ required for structure (IIIa) rather than a molecular formula $C_{18}H_{14}N_4$ required for structure (I). The small peak at 286 is due presumably to heavy isotopes of carbon, hydrogen and nitrogen and its intensity is consistent with their expected natural abundance.

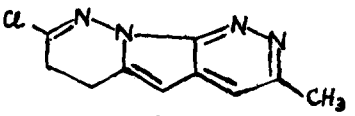
The parent heterocycle (IIIc) was formed in small yield when a solution of 2-methylquinoxaline in 2N-hydrochloric acid was added to a boiling solution of excess of 2-chloroquinoxaline in the same solvent. The product was isolated by chromatography on alumina and purified by vacuum sublimation. It formed deep orange needles, m.p. 244-245° (Found: C, 75.7; H, 3.5; N, 20.4. $C_{17}H_{10}N_4$ requires C, 75.5; H, 3.7; N, 20.7%). λ_{max} (EtOH) 503i (3.66), 467 (3.77), 452i (3.65), 388 (4.26), 371 (4.19), 357i (3.92), 277i (4.70), 273 (4.73), 225.5i mμ ($\log_{10}\varepsilon$ 4.61). The n.m.r. spectrum showed a singlet at 2.90τ assigned to H-7; a singlet at 1.00τ assigned to H-6; and a low field quartet at 0.32τ assigned to H-1. The u.v. and p.m.r. spectra of methylquinoxaline orange (IIIa) and the parent heterocycle (IIIc) are thus

very similar, with the notable difference that the singlet assigned to the 6-methyl group in the p.m.r. spectrum of (IIIa) is replaced in the spectrum of (IIIc) by an additional low field singlet due to H-6. The mass spectrum of (IIIc) showed the expected base peak at 270 due to the molecular ion.

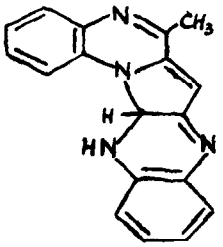
The formation of (IIIa) and (IIIc) from 2,3-dimethyl- and 2-methyl-quinoxaline and 2-chloroquinoxaline, respectively, is analogous to the formation of the dihydro compound (V) on treatment of 3-chloro-6-methylpyridazine (IV) with boiling phosphoryl chloride. In the latter case the initial step appears to be quaternisation, the fully aromatic compound corresponding to (V) is also formed to a minor extent (7,8).



(IV)



(V)



(VI)

In our case, we favour initial C-C bond formation partly because of the formal similarity of this reaction and the reaction of 2,3-dimethylquinoxaline and maleic anhydride (9), also because diquinolylmethanes are formed by the reaction of methylquinolines and 2-chloroquinoline (10). In our opinion compound (I) (or a tautomer) is an intermediate in the formation of (IIIa), ring closure then leads to the pentacyclic dihydroquinoxaline (VI), and this is finally oxidised to the fully aromatic structure (IIIa). We have detected spectroscopically an intermediate in the reaction of 2,3-dimethylquinoxaline and 2-chloroquinoxaline when the reaction is carried out under nitrogen. This intermediate which may well be compound (VI), has λ_{max}(EtOH)517 and 484mμ and its rapid conversion to methylquinoxaline orange can be followed in the spectrophotometer.

We are directing our future efforts to establishing the scope of the ring closure reaction and also investigating the chemistry of the novel ring systems produced.

We thank Professor L. Crombie for providing facilities for this research.

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