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THE STRUCTURE OF THE LOSSEN REARRANGEMENT PRODUCT OF 2-METHYL-3-*N*-OXIDOQUINAZOLINE-4-HYDROXAMIC ACID

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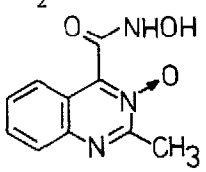
We have recently shown (*cf.* the preceding paper) that the reaction of *N*-acetylisatin with hydroxylamine leads to 2-methyl-3-*N*-oxidoquinazoline-4-hydroxamic acid (1) and not to the earlier reported *N*-acetylisatin-2,3-dioxime (2). Before the true structure was recognized we treated the reaction product with dicyclohexylcarbodiimide in refluxing dioxan in order to prepare 3. A product, A (m.p. 232-233°), with the correct composition ($C_{10}H_7N_3O_2$) was obtained, but the spectral data, which included a C=O stretching at 1 805 cm^{-1}, were in disagreement with the anticipated structure. The same product (A) was obtained by Takahashi[1] by heating the purported compound (2) with Ac_2O.



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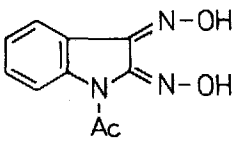

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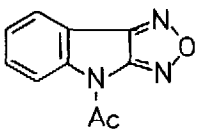

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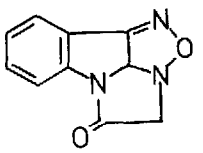

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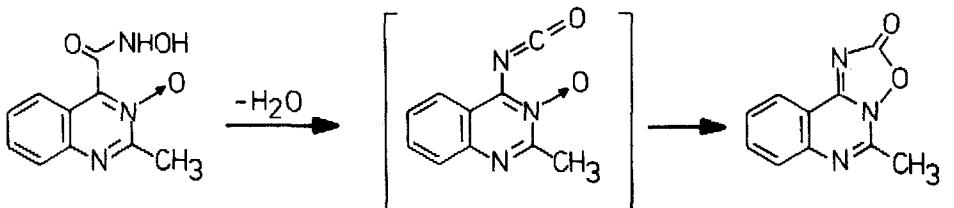
Takahashi[1] assigned it structure 4. Mild treatment of A with alkali gave an isomer B (m.p. 195-197°), which was assigned structure 3 by Takahashi.

Taking into account the reassignment of 2 and the intriguing isomerisation (A→B) we decided to investigate compound A by X-ray analysis, which gave conclusive evidence for structure (5).



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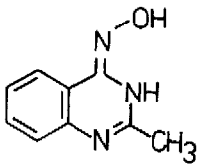

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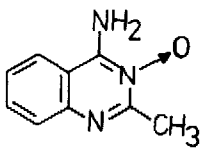

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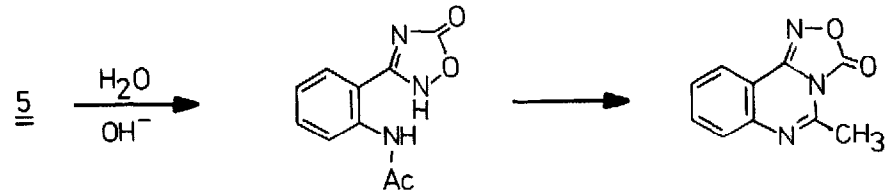
The transformation (1→5) is formulated as a Lossen rearrangement followed by an intramolecular cycloaddition. Once the structure was elucidated an alternate synthesis was developed. Thus treatment of the known[2] compound 7 with $COCl_2$ in pyridine gave 5 in good yield. By a similar route (treatment of 8[2] with $COCl_2$) the structure of compound B was established as 9. The isomerisation (5→9) is formulated as follows. The intermediate (10)[3] (m.p. 160-170° with cyclisation and crystallisation, 190-200°, and remelting 215-225°) could be isolated.



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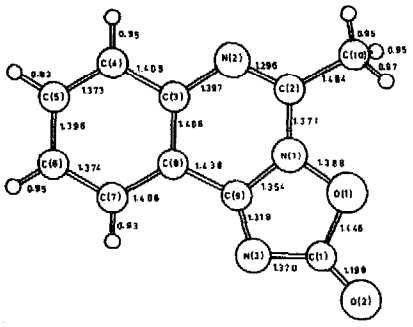
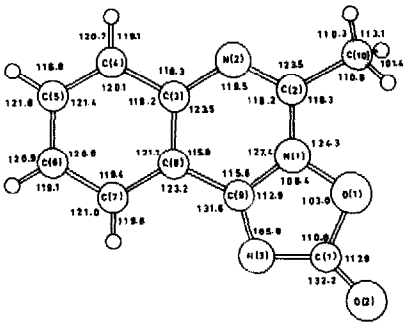
Conclusive evidence for structure 5 was obtained from X-ray analysis. The crystal is monoclinic, space group $P2_1/n$; unit cell dimensions: a = 12.686(8), b = 5.452(6), c = 13.304(1) Å; β = 103.51(6)°, V = 894.7 Å^3; D_{calc} = 1.493 g cm^{-3}. Bond distances and angles are shown in the figures.





References and Notes

1. Takahashi, M., *Bull. Chem. Soc. Japan, 43,* 2986 (1970).
2. Gonçalves, H., Mathis, F. and Foulcher, C., *Bull. Soc. Chim. France,* 2599 (1970).
3. a) The parent compound, 3-phenyl-1,2,4-oxadiazol-5-one, is known.[3b]
   b) Burakevich, J.V., Butler, R.S. and Volpp, G.P., *J. Org. Chem., 37,* 593 (1972).