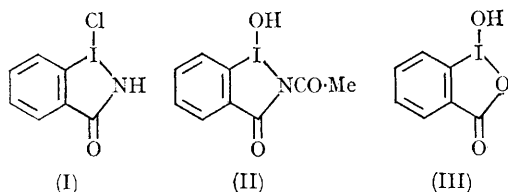


Benziodazole: A New Heterocyclic Ring System¹

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WE report here the first examples of compounds of the benziodazole series containing a new heterocyclic ring with iodine and nitrogen as heteroatoms. They are 1-chloro-1,3-dihydro-3-oxo-1,2-benziodazole (I) and 2-acetyl-1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodazole (II). Evidence for the heterocyclic nature of the oxygen analogue of (I) was previously given,^{2,3} in accord also with the



recent study of F. G. Mann and co-workers.⁴ While a substantial contribution of an open-chain iodonium-carboxylate dipolar-ion structure to 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole (III) was considered unlikely on the basis of the *pK* values of selected examples of this series,² it could be argued that the ionic character of the iodine-oxygen bond could nevertheless help to stabilize the benziodoxole ring. Replacement of oxygen by a less electronegative atom such as nitrogen would make such stabilization due to a dipolar-ion contribution even less likely; hence the possibility of synthesizing such a ring system would confirm the more general ability of polyvalent iodine to act as a hetero-atom.

Dry chlorine gas passed through a solution of *o*-iodobenzamide in dry chloroform at 0°, caused precipitation of a yellow crystalline solid, presumably the *o*-iododichlorobenzamide, m.p. 131–133° (uncorr.) insoluble in the usual organic solvents. Trituration with water gave a white microcrystalline powder⁵ (I) m.p. 124–126° (uncorr.). Infrared spectra show major bands at 3364, 1635, 1610, 1453, 1440, 1355, and 740 cm.⁻¹. The product was insoluble in cold water, the usual organic

solvents, and alkalis, but soluble in dimethyl sulphoxide. Treatment of (I) with hot water caused loss of the polyvalent iodine function, rather than replacement of the chlorine by a hydroxyl, as in the benziodoxole series.

In an attempt to obtain a 1-hydroxybenziodazole derivative, peracetic oxidation⁶ was tried. To a slurry of *o*-iodobenzamide with glacial acetic acid, 40% peracetic acid was added slowly, with stirring, at 30°. After the mixture was held at room temperature for 30 minutes, it was treated with water, filtered, and dried. The dry product was extracted with ether to give a white powder (II) d. 140°. Compound (II) is insoluble in the usual organic solvents, sparingly soluble in concentrated hydrochloric acid, and soluble in alkali. Infrared spectra show major bands at 3100, 1666, 1618, 1440, 1370, and 733 cm.⁻¹

The assignment of structures (I) and (II) is based on the chemical and analytical properties and infrared spectra. Thus, 1-chloro-1,3-dihydro-3-oxobenziodazole (I) has a single chlorine, nonhydrolyzable with water, a carbonyl absorption comparable to that of 1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodoxole (1625 cm.⁻¹) and a single N-H band at 3364 cm.⁻¹, compared to the 3175–3350 cm.⁻¹ doublet of *o*-iodobenzamide. It is also very different from its isomer, *N*-chloro-2-iodobenzamide, m.p. 176–177°, unstable in hydrochloric acid and alkali.⁷

2-Acetyl-1,3-dihydro-1-hydroxy-3-oxo-1,2-benziodazole (II) is soluble in dilute alkali, and the presence of a hydroxyl group is confirmed by a broad absorption band centred at 3100 cm.⁻¹; also, no N-H bands could be detected. Two carbonyl absorption bands occur at 1618 and 1666 cm.⁻¹, in good agreement with the similar bands observed at 1615 and 1660 cm.⁻¹ for 1-acetoxy-1,3-dihydro-3-oxo-1,2-benziodoxole.⁴

Studies of these and other types of heterocyclic compounds of polyvalent iodine are being continued.

(Received, August 23rd, 1965; Com. 532.)

¹ Previous paper, *J. Pharm. Sci.*, 1965, **54**, 329.

² W. Wolf and L. Hsu, Abstracts of Papers 54C, 146th Meeting, American Chemical Society, Denver, Colorado, 1964.

³ E. Shefter and W. Wolf, *J. Pharm. Sci.*, 1965, **54**, 104.

⁴ G. P. Baker, F. G. Mann, N. Sheppard, and A. J. Tetlow, *J. Chem. Soc.*, 1965, 3721.

⁵ The stoichiometry of the reaction $\text{RIO} + 2\text{I}^- + 2\text{H}^+ \rightarrow \text{I}_2 + \text{RI} + \text{H}_2\text{O}$, requires for compounds having a single iodoso-function, molecular weight = 2 × equivalent weight. All new compounds reported gave satisfactory elemental analyses.

⁶ J. S. Sharefkin and H. Saltzman, *Analyt. Chem.*, 1963, **35**, 1428.

⁷ B. Altenkirk and S. S. Israelstam, *J. Org. Chem.*, 1962, **27**, 4532.