

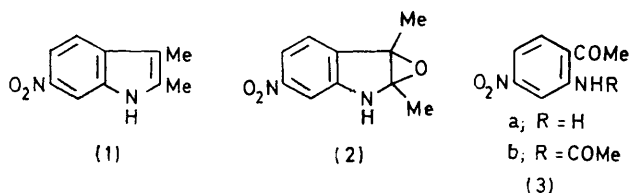
Oxidation of 2,3-Dimethyl-6-nitroindole by Chromic Acid–Aqueous Formamide: a Correction

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The product previously identified as 2,3-dimethyl-6-nitroindole 2,3-epoxide is shown to be a mixture of the title indole and *N*-(2-acetyl-5-nitrophenyl)acetamide.

CLAIMS to the isolation of indole 2,3-epoxides have often appeared,¹ but no such claim has yet survived re-investigation.² Atkinson *et al.* reported³ that oxidation of the nitroindole (1) with chromic anhydride gave an orange substance to which they assigned the epoxide structure (2). It was reported that acidic hydrolysis of this 'epoxide' gave 2-amino-4-nitroacetophenone (3a) and acetaldehyde, identified as its dimedone derivative. Despite the 'mechanism' suggested,³ we felt that this behaviour was not consistent with structure (2). Furthermore, other workers had shown⁴ that oxidation of the indole (1) with chromic anhydride, in a different

solvent, gave *N*-(2-acetyl-5-nitrophenyl)acetamide (3b). These considerations, together with recent interest in the possible intermediacy of indole 2,3-epoxides in



oxidative transformations of indoles,⁵ prompted us to reinvestigate the 'epoxide' of Atkinson *et al.*³

Oxidation of the indole (1) with chromic anhydride

¹ P. Chabrier, *Ann. Chim. (France)*, 1942, **17**, 353; W. C. Sumpter, *J. Amer. Chem. Soc.*, 1942, **64**, 1736; R. Goutarel, M. M. Janot, V. Prelog, and W. I. Taylor, *Helv. Chim. Acta*, 1950, **33**, 150; H. J. Teuber and L. Vogel, *Chem. Ber.*, 1970, **103**, 3302.

² J. M. Muchowski, *Canad. J. Chem.*, 1970, **48**, 422; B. Witkop, and A. Ek, *J. Amer. Chem. Soc.*, 1951, **73**, 5664; B. Witkop, *ibid.*, 1950, **72**, 2311.

³ C. M. Atkinson, J. C. E. Simpson, and A. Taylor, *J. Chem. Soc.*, 1954, 165.

⁴ K. Schofield and R. S. Theobald, *J. Chem. Soc.*, 1949, 797.

⁵ M. Nakagawa, T. Kaneko, and H. Yamaguchi, *J.C.S. Chem. Comm.*, 1972, 603.

and work-up as described by Atkinson *et al.* gave an orange crystalline substance, m.p. 134—135°, which we believe to be the 'epoxide,' m.p. 134°, previously described.³ T.l.c. and spectroscopic studies demonstrated that this substance was a mixture of the starting material (1) and *N*-(2-acetyl-5-nitrophenyl)acetamide (3b)* in the molar ratio 9:11 (¹H n.m.r.). This interpretation was confirmed by separation (preparative t.l.c.) and identification of the two components in the usual way (Experimental section). After isolation of the orange substance, the mother liquors were similarly shown to contain the nitroindole (1) with traces of the keto-amide (3b). No other compounds were present in significant quantity.

The results of acidic hydrolysis of the orange 'epoxide'³ require comment in the light of this re-investigation. It is now clear that the amine (3a) arose from hydrolysis of the amide (3b), a reaction which had been observed previously.⁴ However the reported³ isolation of acetaldehyde as its dimedone derivative is difficult to understand. When we repeated the acidic hydrolysis of the orange substance, we detected no trace of acetaldehyde; thus no significance is attached to the earlier result.³

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. data were determined at 60 MHz for solutions in deuteriochloroform with tetramethylsilane as internal reference.

Oxidation of 2,3-Dimethyl-6-nitroindole (cf. ref. 3).—A solution of chromic anhydride (680 mg) in water (1 ml) was

* Atkinson *et al.* described³ their 'epoxide' as non-ketonic but no evidence was presented for this statement.

added during 15 min to a stirred suspension of the indole (1.01 g) in formamide (10 ml) at 0°. The suspension was allowed to warm to room temperature and stirring was continued for 3 days. The suspension was then diluted with water and extracted with chloroform. The material obtained (1.03 g) was crystallised from the minimum quantity of warm chloroform by addition of ether. The product (202 mg) was recrystallised from ethanol to give an orange substance (135 mg), m.p. 134—135°. Preparative t.l.c. on silica gel G (elution twice with benzene) gave the indole (1), *R_F* 0.45, as orange-red prisms (from ethanol), m.p. and mixed m.p. 141.5—142.5° (lit.,⁴ 141—142°), τ 1.8 (exchangeable with D₂O, NH), 1.90 (d, *J* 2 Hz, 7-H), 2.14 (dd, *J* 2 and 9 Hz, 5-H), 2.66 (d, *J* 9 Hz, 4-H), 7.61 (Me), and 7.80 (Me); and *N*-(2-acetyl-5-nitrophenyl)acetamide (3b), *R_F* 0.2, as pale yellow needles (from ethanol), m.p. 128—129° (lit.,⁴ 126—127°), ν_{\max} (Nujol) 3230 and 3140 (H-bonded NH), 1685 (Amide I band), 1670 (aryl ketone), 1600 (aromatic C=C), and 1540br cm⁻¹ (Amide II band), ν_{\max} (CCl₄) 3270, 3120, 1715 (Amide I), 1670 (aryl ketone), 1600, and 1530 cm⁻¹, τ -1.65 (exchangeable with D₂O, H-bonded NH), 0.45 (d, *J* 2 Hz, 6-H), † 1.95 (d, *J* 9 Hz, 3-H), 2.09 (dd, *J* 2 and 9 Hz, 4-H), 7.26 (Me), and 7.75 (Me).

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† This proton is strongly deshielded by the amide carbonyl group in conformation (A), which is stabilised by an intramolecular hydrogen bond.

