Isatogens; 9. The Synthesis of Isatogens by the Oxidation of 2-Substituted 1-Hydroxyindoles

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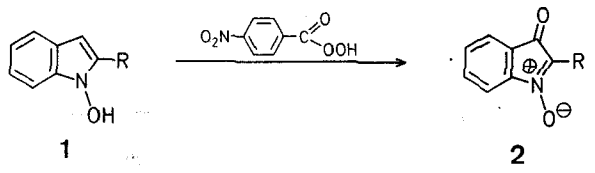
Isatogens (**2**) are usually prepared from 2-nitrostilbenes, or 1-(2-nitrophenyl)-2-substituted acetylenes[1], or pyridinium ethanol derivatives[2]. No method for the synthesis of isatogens from compounds containing a preformed indole ring have been described, although 2-phenylisatogen has been obtained as a minor product from the oxidation of 1-hydroxy-2-phenylindole (**1a**) with a variety of oxidising agents including amyl nitrite[3], lead(IV) acetate[4], and air[5]. We now wish to report the preparation of the isatogens **2a–c**, in high yield, by the oxidation of the corresponding 1-hydroxyindoles **1a–c** with 4-nitrobenzoperoxoic acid.



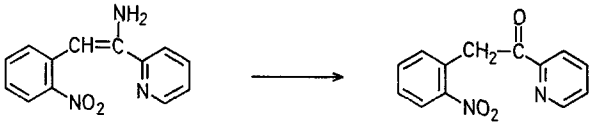
1 **2**

a R =  98% yield

b R =  76%

c R = $-COOCH_3$ 80%

The hydroxyindole **1a** was prepared by the method of Fischer and Hutz[6] and the ester **1c**[7] was obtained by esterification of the acid (**1**; R = COOH)[8]. The 2-pyridyl derivative **1b** was prepared by slightly modifying the procedure of Patterson[9]. Amino compound **3** was obtained as an analytically pure compound by the method of Kröhnke and Vogt[10] and careful treatment with nitrous acid gave ketone **4** which was reduced by sodium borohydride and palladised charcoal[8] to the hydroxyindole **1b**[9].



3 **4**

Attempts to prepare the 3- and 4-pyridyl ketones by this route were unsuccessful and oxidation of the carboxylic acid (**1**; R = COOH)[8] gave only an intractable tar. No characterisable material was obtained when the reported literature methods[11,12] for the preparation of the parent compound (**1**; R = H) were attempted. The exploitation of this facile oxidation reaction awaits the development of further routes to 2-substituted 1-hydroxyindoles. Possible routes to these compounds are being investigated in these laboratories.

Oxidation of 1-Hydroxyindoles with 4-Nitrobenzoperoxoic Acid: The 1-hydroxy-2-substituted indoles (**1**; 0.005 mol) and 4-nitrobenzoperoxoic acid (0.01 mol) were stirred at room temperature in ethanol (10 ml/g of indole) for 4 h. The solutions became orange-red in colour and the precipitated 4-nitrobenzoic acid was removed. The solvent was evaporated and the product recrystallised (**2a**). In the preparation of **2b,c** an oil was obtained which was dissolved in acetone (5 ml) and subjected to preparative T.L.C. (Kieselgel PF_{254} (Merck), 1 mm, 50:50 benzene/ethyl acetate). The orange bands (**1b**: R_F 0.33, **1c**: R_F 0.54) were eluted with acetone. The products (**2a–c**) were identical (mixture m.p., superimposable I.R. spectra) with authentic samples[1,13,14].

1-Amino-2-(2-nitrophenyl)-1-(2-pyridyl)-ethylene (3): 1-(2-Nitro-ω-pyridylstyryl)-pyridinium bromide (3.0 g, prepared according to the method of Kröhnke and Vogt[10]) and piperidine (30 ml) were heated on a water bath for 5 min. The solution turned red and was poured on to ice (300 g); yield: 1.75 g (93%); orange crystals, m.p. 96–97% (from ethanol). The compound was unstable and had to be stored under nitrogen.

$C_{13}H_{11}N_3O_2$	calc.	C 64.71	H 4.56	N 17.43
	found	64.57	4.50	17.37

M.S. (M^+, *m/e*): calc. 241.0851 found 241.0848

I.R. (Nujol): ν_{max} = 3400, 3300 (NH_2), 1630 (C=C), 1525 and 1360 (NO_2), 880, 760 cm^{-1}.

2-Nitrobenzyl 2-Pyridyl Ketone (4): A solution of 1-amino-2-(2-nitrophenyl)-1-(2-pyridyl)-ethylene (0.3 g) in dilute hydrochloric acid (10 ml) was stirred at 0° during the addition of sodium nitrite (0.3 g) in water (5.0 ml). Excess nitrous acid was removed by the addition of urea. The clear solution was stirred at room temperature for 30 min and made alkaline with 2*N* sodium hydroxide solution to give the ketone; yield: 0.27 g (90%); colourless prisms, m.p. 84–85° (from ethanol). Identical (mixture m.p. and superimposable I.R.) with an authentic sample[9].

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