SYNTHESIS OF 4-AZAINDOLES

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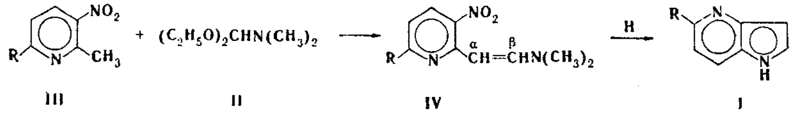
We have developed a convenient method for the preparation of 4-azaindoles (I) by condensation of dimethylformamide diethylacetal (II) with 3-nitropicoline (IIIa) or its derivatives and subsequent reductive cyclization of the resulting nitro enamines IV. All of the synthesized substances were characterized by complete elementary analysis.



I, III, IV a R=H; b R=Cl

A solution of 1.19 g of picoline IIIa and 1.91 g of acetal II in 4 ml of anhydrous dimethylformamide (DMF) was heated at 80-90°C for 1 h, after which it was vacuum evaporated to give 1.66 g (100%) of nitro enamine IVa as red crystals with mp 70-71°C (from benzene and heptane). PMR spectrum (ppm, 100 MHz, $CDCl_3$): 2.99 s [$N(CH_3)_2$], 6.12 d (α-H), 6.72 q (5-H), 8.03 d (β-H), 8.13 q (4-H), and 8.37 q (6-H). A similar procedure was used to obtain dark-red crystals of nitro enamine IVb, with mp 105-106°C (from alcohol), from IIIb. PMR spectrum: 3.40 s [$N(CH_3)_2$], 6.16 d (α-H), 6.56 d (5-H), 8.03 d (β-H), and 8.11 d (4-H). A 0.3-g sample of nitro enamine IVa was hydrogenated in 70 ml of ethanol with 0.3 g of 6% Pd/C at room temperature and an excess hydrogen pressure of 20-30 cm (water column). Separation of the catalyst and evaporation of the alcohol solution gave 0.18 g (100%) of 4-azaindole (Ia) with mp 122-123°C. The product was found to be identical to a genuine sample with respect to its IR spectrum and a mixed-melting-point determination. Hydrogenation of nitro enamine IVb under the same conditions gave a mixture of azaindoles Ia and Ib. Complete dehalogenation of Ib is achieved by hydrogenation with excess Pd catalyst, and the yield of azaindole Ia is practically quantitative.

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