NEW METHOD FOR THE SYNTHESIS OF INDOLO[3,2-b]INDOLE DERIVATIVES

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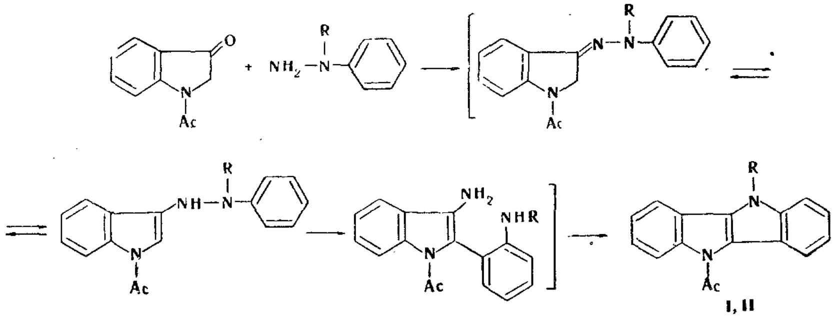
The corresponding 1-alkyl-6-acetylindolo[3,2-b]indoles are formed in the reaction of N-acetylindoxyl with N-methyl- and N-benzyl-N-phenylhydrazines in acetic acid. The structures of the compounds were confirmed by alternative synthesis and by the UV, PMR, and mass spectra.

It is known that arylhydrazones of coumaranones, thioindoxyls, γ-piperidones, quinolones, etc. undergo indolization to give condensed heterocycles [1]. However, the literature does not contain information regarding the Fischer reaction with arylhydrazones of indoxyl and its derivatives.

We have previously obtained N-acetylindoxyl arylhydrazones [2]; however, Fischer indolization was not observed when they were treated with acidic agents. When N-acetylindoxyl arylhydrazones were heated in acetic acid in the presence of acetic anhydride, they were converted to 12-acetamidoindolo[1,2-c]quinazoline derivatives [2].

In the present research we studied the reaction of N-acetylindoxyl with N-alkyl-N-phenylhydrazines and found that 1-alkyl-6-acetylindolo[3,2-b]indoles (I, II) are formed in ~40% yields when the reaction is carried out in acetic acid.



I, II

I $R=CH_3$; II $R=CH_2C_6H_5$

The initial products are evidently arylhydrazones, which are converted through a step involving the tautomeric hydrazine form to indolo[3,2-b]indole derivatives. Consequently, the presence of an alkyl substituent in the phenylhydrazine molecule hinders the formation of indolo[1,2-c]quinazoline derivatives.

The structures of the substances obtained were confirmed by data from the mass spectra, in which molecular-ion peaks, the m/z values of which correspond to the molecular masses of these compounds, are observed.

In addition, indolo[3,2-b]indole structure I is confirmed by the absence of a melting-point depression of a mixture of this compound with a sample obtained by acetylation of the known 1-methylindolo[3,2-b]indole [3] with acetic anhydride in the presence of sodium acetate.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of I and II were recorded with a Perkin-Elmer spectrometer. The UV spectra were recorded with a Perkin-Elmer 575 spectrophotometer. The PMR spectra were measured with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard. The mass spectra were obtained with a Varian MAT-112 mass spectrometer (70 eV) by

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direct introduction of the samples into the ion source. The course of the reaction and the individuality of the substances were monitored on Silufol UV-254 in plates in a benzene—methanol system (9:2) with development in UV light.

1-Methyl-6-acetylindolo[3,2-b]indole (I). A) A 1.22-g (0.01 mole) sample of N-methyl-N-phenylhydrazine was added to a suspension of 1.75 g (0.01 mole) of N-acetylindoxyl in 5 ml of glacial acetic acid, and the mixture was refluxed for 10 min. It was then cooled, and the precipitate was removed by filtration and washed with acetic acid and methanol to give 1.15 g (44%) of a product with mp 175-176°C (from methanol). IR spectrum (thin layer): 1690 cm^{-1} (C=O). IV spectrum (in alcohol), λ_{max} (log ε): 224 (4.54), 248 (4.67), 316 (4.42) shoulder, 324 (4.47), and 345 nm (4.18) shoulder. PMR spectrum ($CDCl_3$): 2.73 (s, $COCH_3$), 3.85 (s, CH_3), and 7.58-8.24 ppm (aromatic ring protons). Found: C 77.9; H 5.4; N 10.6%; M^+ 262. $C_{17}H_{14}N_2O$. Calculated: C 77.8; H 5.4; N 10.7%; M 262.

B) A mixture of 0.22 g (0.001 mole) of 1-methylindolo[3,2-b]indole, 5 ml of acetic anhydride, and 0.38 g (0.006 mole) of fused sodium acetate was refluxed for 2.5 h, after which it was cooled and poured into water. The resulting precipitate was removed by filtration and washed with water and methanol to give 0.18 g (69%) of a product with mp 174-175°C (from methanol). No melting-point depression was observed for a mixture of I obtained by method B with a sample obtained by method A, and their IR, UV, and PMR spectra were identical.

1-Benzyl-6-acetylindolo[3,2-b]indole (II). A 1.98-g (0.01 mole) sample of N-benzyl-N-phenylhydrazine was added to a suspension of 1.75 g (0.01 mole) of N-acetylindoxyl in 10 ml of glacial acetic acid, and the mixture was refluxed for 10 min. It was then cooled, and the resulting precipitate was removed by filtration and washed with acetic acid and methanol to give 1.5 g (44%) of a product with mp 193-194°C [from dimethylformamide—methanol (1:1)]. IR spectrum (thin layer): 1675 cm^{-1} (C=O). UV spectrum (in alcohol), λ_{max} (log ε): 212 (4.58), 220 (4.53) shoulder, 243 (4.61), 317 (4.36) shoulder, 322 (4.41), and 345 nm (4.13). PMR spectrum ($CDCl_3$): 1.95 (s, $COCH_3$), 5.26 (s, CH_2), and 7.00-8.28 ppm (aromatic ring protons). Found: C 81.9; H 5.4; N 8.4%; M^+ 338. $C_{23}H_{18}N_2O$. Calculated: C 81.6; H 5.4; N 8.3%; M 338.

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