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LETTERS TO THE EDITOR

UNEXPECTED CHLORINATION DURING THE DIAZOTIZATION PROCESS OF 2-ETHOXYCARBONYL-7-AMINOINDOLE

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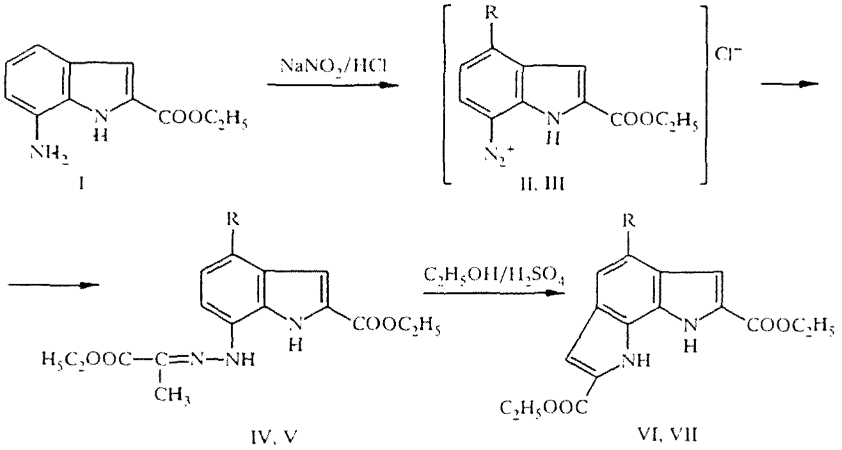
In an attempt to obtain hydrazone IV by the Japp–Klingemann method, while carrying out the diazotization of 7-aminoindole I at 40°C in the presence of a 50% aqueous solution of HCl, we have unexpectedly isolated 4-chlorohydrazone V (M^+ 351/353) in a yield of 10% in a mixture with small amounts of two unidentified chlorine-containing compounds with M^+ 321/323 and 379/381.



II, IV, VI R = H; III, V, VII R = Cl

Since it is known that the Japp–Klingemann reaction for aminoindole I, when carried out under the same conditions, but at 0°C, leads directly to hydrazone IV [1], it becomes clear that the chlorination may occur at the first stage at elevated temperature. Chlorinating agents may comprise the decomposition products of nitrosyl chloride (NOCl), which is formed in the reaction of HNO_2 with conc. HCl.

Thus, an aqueous solution of 0.33 g (5 mmoles) of $NaNO_2$ was added at room temperature to a suspension of 1.17 g (4.9 mmoles) of the hydrochloride of amine I in 6 ml of 50% HCl, the temperature was raised to 40°C, and the mixture was stirred for 30 min. The reaction mixture was cooled and 1 ml (7 mmoles) of methyl acetoacetate and 2.5 ml of a 50% KOH in 7.5. ml of ethanol were added at 0-5°C. The mixture was stirred for 1 h and allowed to stand for 24 h. It was then extracted with ether, the extract was dried over $CaCl_2$ and evaporated. The remaining viscous red mass was chromatographed on a column with silica gel in benzene. From the fraction with R_f 0.49 (benzene–ether 10:1) 0.19 g (10%) of yellow-brown crystals

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of 2-ethoxycarbonyl-4-chloroindolyl-7-hydrazone of ethyl pyruvate (V) were isolated, mp 142-143°C. IR spectrum (mineral oil): 3410, 3290 (NH), 1730, 1700 (CO of ester), 1640 cm^{-1} (CN). UV spectrum (ethanol), λ_{max} (log ε): 206 (4.44), 2.42 (4.35), 303 (4.10), 365 nm (4.10).

The presence in the PMR spectra* of compound V of signals at 10.3 (NH of hydrazone, s), 11.73 (d, NH of pyrrole), 7.11 (d, J_{13} = 2.4 Hz, 3-H), 7.02 (d, J_{56} = 8.4 Hz, 5-H) and 7.14 ppm (d, 6-H) confirms the presence of chlorine in the 4-position.

The indolization of hydrazone V, which was accompanied by a strong resinification, gave us 4-chloropyrroloindole VII. Thus, a few drops of conc. H_2SO_4 were added to a solution of 1 g (3 mmoles) of hydrazone V in 50 ml of ethanol, and the mixture was boiled for 25 h. The solution was evaporated to a volume of 20 ml and diluted with water. The precipitate was filtered off and chromatographed on a column with silica gel. From the fraction with R_f 0.48 (benzene:ether, 5:1) 0.07 g (8%) of white crystals of 4-chloro-2,7-diethoxycarbonyl-1H,6H-pyrrolo[3,2-g]indole (VII) was isolated, M$^+$ 334/336, mp 270-272°C. IR spectrum (mineral oil): 3350, 3290 (NH), 1720, 1690 cm^{-1} (CO of ester). UV spectrum (ethanol), λ_{max} (log ε): 208 (4.4), 270 (4.53), 385 nm (3.95).

In the PMR spectrum of the asymmetric pyrroloindole VII two sets of signals of pyrrole ring protons are observed: 11.86 and 11.65 (NH); 1.39 and 1.34 ($\underline{CH_3}CH_2$); 4.40 and 4.35 ($CH_3\underline{CH_2}$). The 5-H proton signal appears in the form of a singlet at 7.37 ppm.

The fragmentation schemes of the molecular ions of compounds V and VII by the action of electron impact are not contrary to the proposed structures.

The elemental analysis results of compounds V and VII correspond to the calculated data.

REFERENCES

1. H. A. Katti and S. Siddappa, Ind. J. Chem., **22B**, 1205 (1983).

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