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A NEW PROCEDURE FOR THE CYCLIZATION OF 2-INDOLE- AND 3-INDOLE CARBOHYDRAZONES TO 5H-PYRIDAZINO[4,5-b]INDOLE DERIVATIVES.

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As a continuation of previous studies on the cyclization of 2-(or-3) indolecarbohydrazones to derivatives of 5H-pyridazino [4,5-b] indole, we describe here a new procedure for the cyclization of 2-indolecarbohydrazones to derivatives of 1,2,3,4 -tetrahydro-4-oxo-5H-pyridazino[4,5-b] indole and of the 3-indole carbohydrazones to derivatives of 1,2,3,4-tetrahydro-1-oxo-1-oxo-5H-pyridazino[4,5-b] indole.

The derivatives of 5H-pyridazino[4,5-b] indole are generally obtained by any of the following procedures: a) Cyclization with hydrazines of 3-acyl, 3-hydroxymethyl, 3-acethoxymethyl or 3-halomethyl derivatives of indoles, with suitable substituents in position 2; 2-carbethoxyindoles are generally used, which leads to the 4-oxo derivatives; b) Condensation of 2-indolemethyl hydrazines or 3-indolemethylhydrazines with aldehydes; c) Intramolecular reductive cyclization of 4-(o-nitrophenyl) pyridazines; d) Acid catalyzed intramolecular cyclization of 2-indolecarbohydrazones or acid catalyzed condensation of 2-indolecarbohydrazides with aldehydes of ketones.

We have already described that the intramolecular cyclization of 2-indolecarbohydrazones with 12-14 N HCl in ethanol or dioxane leads (80%) to the respective derivatives of 4-oxo-5H-pyridazino[4,5-b]indole when R_1=H, R_2=aryle (C_6H_5, p-HO-C_6H_4), but the hydrazone breaks under those conditions to give the hydrochloride of 2-(1-methyl-5-ethoxyindole) carbohydrazide, when R_1=H, CH_3 and R_2=alkyle. On the other hand, the condensation of 2-indolecarbohydrazones with benzaldehyde or methylethylketo-

ne led satisfactorily (56-76%) to the corresponding derivatives of the pyridazinoindole, even if the reaction failed with alyphatic aldehydes because their polimerization under those conditions.

In this paper a new method is described, which seems to be a general one, for the cyclization of 2-indolecarbohydrazones to derivatives of 1,2,3,4-tetrahydro-4-oxo-5H-pyridazino[4,5-b] indole and the cyclization of 3-indolecarbohydrazones to derivatives of 1,2,3,4-tetrahydro-1-oxo-5H-pyridazino[4,5-b] indole, for the treatmen of the corresponding carbohydrazones with an acylhalide (acetyl or benzoyl chlorides) and triethylamine in ethyl acetate or chloroform, respectively, as solvents. The reaction was carried out at temperature below 40°C, by slow and gradual addition of the acyl halide (40-70 mmoles) to solutions or suspension of the carbohydrazides (3 mmoles) in the referred solvent containing triethylamine. The reaction takes place in about 0,5-3 h.

All the compounds described are new and the ir, ^{1}H-nmr, uv mass and ^{13}C-nmr spectra are discussed.