CYCLIZATION OF 2-INDOYLHYDRAZONES TO DIHYDROPYRROLO[3,4-b]INDOLE DERIVATIVES AND THEIR ISOMERIZATION TO PYRIDAZINO[4,5-b]INDOLES

N. A. Kogan and M. I. Vlasova

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When 2-indoylhydrazones of aromatic aldehydes are heated at 120°C for 3-5 min in amyl alcohol saturated with HCl, they cyclize to give 1-aryl-2-amino-1,2-dihydropyrrolo[3,4-b]indol-3-ones (I-VI) (see Table 1) in 60-85% yields.

In contrast to the starting hydrazones, I-VI do not undergo acid and alkaline hydrolysis with cleavage of an aldehyde. Their IR spectra show the presence of a 3-amino group (a narrow band at 3350 cm^{-1}). Also in contrast to the starting hydrazones, the PMR spectra of I-VI contain a singlet at 5.4 ppm due to a proton in the 1-position. The exocyclic position of the amino group in I-VI is confirmed by the reaction with aldehydes, which gives hydrazones XI. All I-VI have λ_{max} 298-302 nm(ε $1.6 \cdot 10^4$).

When I-VI are heated above 50° in ethanol or amyl alcohol, they isomerize to 1-aryl-1,2,3,4-tetrahydropyridazino[4,5-b]indol-4-ones (VII-X) (see Table 1). Bases I-VI are isomerized only at temperatures above 80° and when 11 > pH > 2. The rate of isomerization of bases I-VI to VII-X follows a first-order equation. On treatment with $POCl_3$, VII is converted into the 4-chloro derivative (XIII). The IR spectra of VII-X do not contain the absorption of a free NH_2 group. Compounds VII-X have λ_{max} at 255-260 nm.

The reduction of I and VII with Raney nickel gives the amide of 3-benzylindole-2-carboxylic acid (XIV). Treatment of hydrazone XI under the same conditions gives the N-unsubstituted dihydropyrrolo-[3,4-b]indol-3-one (XII).

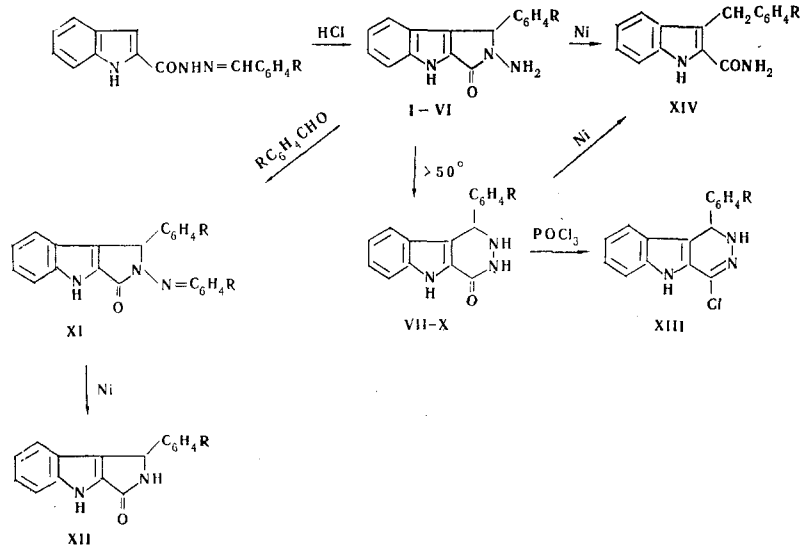

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TABLE 1. Characteristics of the Compounds Obtained

Compound	R	Mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
I	H	250	$C_{16}H_{13}N_3O$	72,8	5,0	16,0	73,0	4,9	16,0	60
II	*p*-CH_3	242	$C_{17}H_{15}N_3O$	73,6	5,3	15,0	73,6	5,4	15,2	85
III	*p*-OCH_3	218	$C_{17}H_{15}N_3O_2$	69,5	5,2	14,2	69,6	5,1	14,3	70
IV	*p*-Cl	238	$C_{16}H_{12}ClN_3O$	64,4	4,0	14,1	64,5	4,0	14,1	65
V	*o*-Cl	290	$C_{16}H_{12}ClN_3O$	64,3	4,0	14,1	64,5	4,0	14,1	65
VI	*p*-OH, *m*-OCH_3	265	$C_{17}H_{15}N_3O_3$	65,9	4,8	13,5	66,0	4,8	13,6	70
VII	H	348—350	$C_{16}H_{13}N_3O$	73,2	4,8	15,6	73,0	4,9	16,0	70
VIII	*p*-CH_3	350	$C_{17}H_{15}N_3O$	73,5	5,0	15,1	73,6	5,4	15,2	90
IX	*p*-OCH_3	320	$C_{17}H_{15}N_3O_2$	69,1	5,3	14,3	69,6	5,1	14,3	80
X	*p*-Cl	320—322	$C_{16}H_{12}ClN_3O$	64,6	4,4	14,0	64,5	4,0	14,1	65
XI	H	290	$C_{23}H_{17}N_3O$	78,7	4,9	11,9	78,6	4,8	12,0	60
XII	H	238	$C_{16}H_{12}N_2O$	77,6	4,8	11,3	77,4	4,8	11,3	74
XIII	H	297	$C_{16}H_{12}ClN_3$	68,6	4,2	14,8	68,2	4,3	14,9	65
XIV	H	188	$C_{16}H_{14}N_2O$	76,8	5,7	11,1	76,8	5,6	11,2	68

EXPERIMENTAL

1-Phenyl-2-amino-1,2-dihydropyrrolo[3,4-b]indol-3-one Hydrochloride (I). A stream of HCl was passed through 0.5 g (1.9 mmole) of benzaldehyde 2-indoylhydrazone in 5 ml of amyl alcohol at 120° for 3 min. The hydrazone dissolved, and I began to precipitate. Base I was isolated by treatment of an aqueous suspension of it with pyridine.

1-Phenyl-1,2-dihydropyridazino[4,5-b]indol-4-one (VII). A 0.5 g (1.6 mmole) sample of I in 20 ml of amyl alcohol was refluxed for 2 h. The mixture was then cooled to precipitate VII, which was crystallized from alcohol.