FISCHER CYCLIZATION OF N,N-DIARYL- AND N-ARYL-N-HETARYLHYDRAZINES

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In connection with the fact that the mechanisms of the individual steps in the Fischer cyclization of arylhydrazones to indoles are currently under discussion (for example, see [1, 2]), we began a systematic study of the direction of indolization of N,N-disubstituted hydrazones $RR'NNH_2$ (I), where R and R' = aryls or hetaryls (R or R' may also be alkene residues), in the reaction with various ketones. The results of our first examples of the condensation of hydrazines I with cyclohexanone (II) and tetrahydro-4-thiopyrone (III) under the influence of acids are presented in Table 1.

The ratios of the indole compounds in the reaction mixtures were determined by means of PMR spectroscopy.† Electron-donating groups facilitate cyclization with respect to the benzene ring to which they are attached, despite the fact that these substituents occupy the meta position with respect to the C atom that participates in the formation of a new carbon–carbon bond. This phenomenon was also noted previously (for example, see [1-3]). However, our method of competitive closing of the indole ring makes it possible to form a direct judgement regarding the relative rates of the rearrangement reactions, i.e., the second step of the Fischer reaction. The first step is tautomerization of the hydrazone to an enehydrazine, and in this case is common to the formation of both isomers. In exactly the same manner, the rates of the third step – closing of the pyrrole ring with splitting out of the elements of ammonia – do not determine the relative yields of the final reaction products, i.e., the isomeric substituted indoles, in this variant of the study of the Fischer reaction.

The structure of the indoles obtained was proved by spectral methods or alternative syntheses by arylation of 1,2,3,4-tetrahydrocarbazoles.

TABLE 1

Starting ketone	$RR'NNH_2$		Relative yield (%) of indolization product with participation of R or R'	
	R	R'	R	R'
II	$4\text{-}CH_3C_6H_4$	$4\text{-}CH_3OC_6H_4$	24	76
II	$4\text{-}CH_3C_6H_4$	C_6H_5	60	40
II	$4\text{-}CH_3OC_6H_4$	C_6H_5	82	18
II	C_6H_5	4-Coumarinyl	64*	
II	C_6H_5	2-Pyridyl	74*	
III	C_6H_5	2-Pyridyl	61*	

* Preparative isolation; a second isomer was not detected.

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LITERATURE CITED

1. B. Robinson, Usp. Khim., 40, 1434 (1971).
2. I. I. Grandberg and V. I. Sorokin, Usp. Khim., 43, 266 (1974).
3. N. N. Suvorov, V. P. Mamaev, and V. M. Rodionov, RIMIOS [in Russian], Vol. 9, Izd. NTIKhL, Moscow (1959), p. 7.