SHORT COMMUNICATIONS

A Novel Synthesis of 1-Acylindole Derivatives

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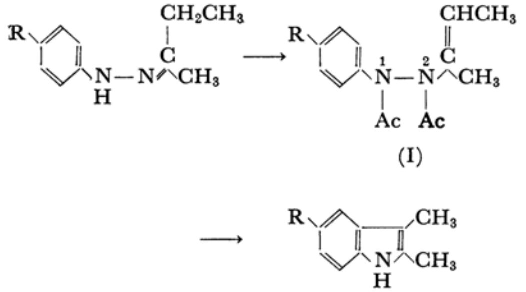
Acyl groups in 1-acylindole derivatives are so easily hydrolyzed by acid or alkali that it had been considered to be impossible to obtain 1-acylindole derivatives directly from the corresponding N^1-acylated phenylhydrazine derivatives by Fischer indole syntheses.

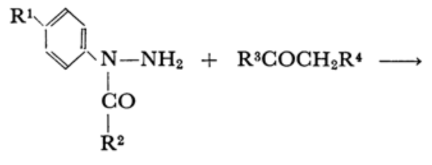
Suvorov *et al.*[1,2] have, however, recently reported that an important requirement for indole (II) formation is the deacylation of the N^1-acyl group of the hydrazine derivative (I), which frees a p-electron pair on the N^1-nitrogen atom.



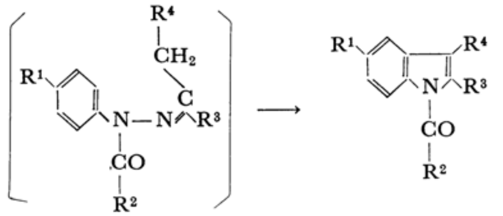
(I)

(II)

However, we have found that 1-acylindole derivatives can be directly synthesized by heating N^1-acylated phenyl hydrazines and ketones in acetic acid.



(III) (IV)



For example, 1 mole of the N^1-acylphenylhydrazine derivative (III, R^1=$-OCH_3$, R^2=$-CH_3$) and 1.2 moles of levulinic acid (IV, R^3=$-CH_3$, R^4=$-CH_2COOH$) were heated at 75—85°C with stirring in acetic acid for 3 hr. After cooling, crystals of 1-acyl-2-methyl-5-methoxy-3-indolylacetic acid were obtained in a good yield.

It was observed that the acyl group in the 1-acylindole derivative (V) can be very easily hydrolyzed at pH values lower than 1 or higher than 9.

As a 1-acyl derivative (VI) of II is also deacylated to II under the reaction conditions which Suvorov *et al.*[2] used for obtaining an indole derivative from a corresponding hydrazine compound, it can be assumed that VI must be produced as an intermediate in this reaction, although no definite evidence of this was obtained.

The results of these experiments show that deacylation from the N^1-nitrogen atom is not necessary for indole cyclization, and that the p-electron pair hardly participates in the formation of the new C–C bond.

Studies of this new process are proceeding; they will be reported in detail later.

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[1] N. N. Suvorov and N. P. Sorokina, *Doklady Acad. Nauk S. S. S. R.*, **136**, 840 (1961): *Chem. Abstr.*, **55** 17621 (1961).

[2] N. N. Suvorov, N. P. Sorokina and I. N. Sheinker, *J. Gen. Chem. U. S. S. R.*, **28**, 1058 (1958).