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A ONE-STEP SYNTHESIS OF NICOTINE FROM CYCLOPROPYL 3-PYRIDYL KETONE*

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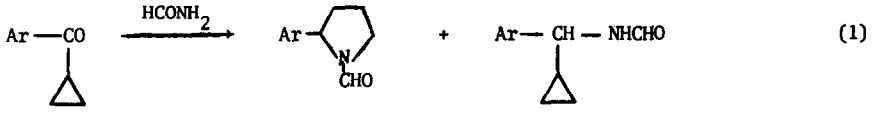
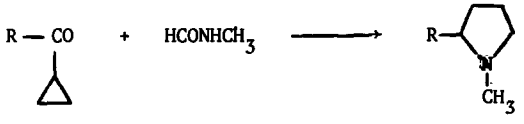
We have recently reported [1] that reactions of aryl cyclopropyl ketones with formamide give predominantly the corresponding 1-formyl-2-aryl pyrrolidines, along with the expected reaction products (equation 1) [2].



(1)

In the present communication we wish to describe the results of reactions of N-methylformamide with some cyclopropyl ketones. We found that the reaction of phenyl cyclopropyl ketone (1a) with N-methylformamide proceeds somewhat slower than that with formamide, but even in the absence of Lewis acids it leads exclusively to the formation of N-methyl-2-phenyl pyrrolidine (2a), b.p. 105-108° at 20 mm, $n_D^{24.5}$ 1.5209, picrate, m.p. 145°, literature [3] b.p. 106 at 20 mm, picrate m.p. 145°-146°. 2a could most conveniently be obtained in nearly quantitative yield by refluxing 1a with N-methylformamide and magnesium chloride in a 1:6:0.1 molar ratio in a N_2 atmosphere for 24 hours.



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a, R=phenyl

b, R=3-pyridyl

* Reactions of cyclopropane derivatives with nitrogen compounds, II.

Under similar conditions, reaction of 3-pyridyl cyclopropyl ketone (1b) with N-methylformamide gave an oily product, isolated by gas-chromatography, which was identified as dl-nicotine (2b) (30%). Its identification was based on comparison of its nmr spectrum with that published [4]. It was further characterized as the dipicrate, m.p. 218°, lit. m.p. 218° [5]. Mixed m.p. with dipicrate prepared from authentic sample of dl-nicotine showed no depression.

The rearrangement of some cyclopropyl ketimines to pyrrolines has recently been applied to the synthesis of some alkaloids [6,7,8]. The uniqueness of our method is that three consecutive steps : the formation of the ketimine, its rearrangement to pyrroline, and the reduction to pyrrolidine, can be carried out in one process.

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