SYNTHESIS OF LEPIDINE AND ITS DERIVATIVES FROM AROMATIC AMINES AND MANNICH BASES

B. I. Ardashev, E. Sh. Kagan, and N. F. Ovchinnikov

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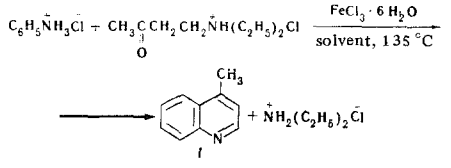
The synthesis of lepidine from aniline and 4-diethyl-amino-2-butanone has been carried out in two separate stages under the optimum conditions for each stage.

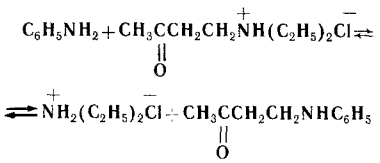
We have previously [1–3] described the synthesis of lepidine (I) by the following route:



The reaction can be carried out in ethanol under pressure or by using a high-boiling solvent such as nitrobenzene. In the latter case, it is necessary to eliminate from the reaction medium the water introduced with the ferric chloride. These circumstances complicate the performance of the synthesis of I.

In the present paper we propose a more convenient method for obtaining lepidine which enables the whole process to be carried out at 70–80° C.

In the synthesis of lepidine from aniline and 4-diethylamino-2-butanone, 4-anilino-2-butanone is formed as an intermediate:



For the successful performance of this reaction, one component must be taken in the form of a salt and the other in the form of the free amine. In this case the equilibrium is shifted to the right, since the more basic amine retains the proton catalyzing the exchange reaction [4].

Since the cyclization of 4-anilino-2-butanone will take place only in an acid medium whereas the preparation of 4-anilino-2-butanone must be carried out at a strictly defined ratio of acid of 4-diethylamino-2-butanone to aniline, it is desirable to carry out the two stages separately. Under these conditions, compound I and its derivatives are formed under mild conditions in good yields.

EXPERIMENTAL

Lepidine (I). A mixture of 71.5 g (0.5 mole) of 4-diethylamino-2-butanone, 65 g (0.5 mole) of aniline hydrochloride, and 200 ml of ethanol was heated in the water bath for 1 hr. The resulting solution, containing 4-anilino-2-butanone and diethylamine hydrochloride, was added in drops over 1–1.5 hr with stirring to a mixture of 270 g of ferric chloride hexahydrate, 12.9 g of aniline hydrochloride, 2 g of zinc chloride, and 500 ml of ethanol heated to 65–75° C. After this, the reaction was continued for another 4 hr. The solvent was distilled off in vacuum, the residue was made alkaline with caustic soda solution, and the I was distilled off with steam. The first portions of the distillate contained practically all the diethylamine liberated. The I was extracted from the distillate with ether, the extract was dried with anhydrous sodium sulfate, the ether was driven off, and the residue was fractionated in vacuum. This gave aniline (10 g), bp 60–63° C (2 mm), n_D^{20} 1.5860, and lepidine (46 g, or 62%), bp 105–107° C (2 mm), n_D^{20} 1.6170; picrate, mp 212° C.

In a similar manner, 4,6-dimethylquinoline was obtained from p-toluidine, yield 55%, bp 136° C (12 mm) picrate, mp 237° C; and 4,8-dimethylquinoline was obtained from o-toluidine with a yield of 65%, mp 56° C, picrate mp 220° C.

REFERENCES

1. B. I. Ardashev and E. Sh. Kagan, ZhOKh, 34, 2228, 1964.

2. E. Sh. Kagan and B. I. Ardashev, ZhOKh, 35, 303, 1965.

3. B. I. Ardashev and E. Sh. Kagan, Methods for Preparing Chemical Reagents and Products [in Russian], no. 2, IREA, p. 63, 1964.

4. J. C. Craig, M. Moyle, and L. F. Gohnson, J. Org. Chem., 29, 410, 1964.

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