PREPARATION OF 2-ARYLBENZIMIDAZOLES FROM o-NITROANILINES AND AROMATIC ALDEHYDES

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The possibility of obtaining 2-arylbenzimidazoles by heating o-nitroanilines and aromatic aldehyde in various solvents with simultaneous removal by distillation of the water formed is demonstrated.

2-Phenylbenzimidazole was isolated in 20% yield along with other compounds in a study of the reaction of benzaldehyde with o-nitroaniline [1].

It seemed to us that this sort of method (with refinement) for obtaining benzimidazoles may be of interest because of its simplicity. With this end in mind we investigated the effect of the synthesis conditions on the benzimidazole yields. In the case of the preparation of 2-phenylbenzimidazole we studied the effect of the ratio of o-nitroaniline and benzaldehyde on the yield of reaction product (Table 1).

The data in Table 1 indicate that when the o-nitroaniline: benzaldehyde ratio is greater than 0.33 the reaction proceeds with the quantitative formation of 2-phenylbenzimidazole. We assume that the formation of benzimidazoles under the conditions described above proceeds via the following scheme:

 $o-NO_2ArNH_2 + 3ArCHO - Ar + 2ArCOOH + H_2O$

A confirmation of this is the fact that the amount of water evolved as a result of the reaction was close to that calculated in accordance with the equation presented above, and the corresponding benzoic acid was always found in the reaction products. However, as for the mechanism of this reaction, the formation of 2-phenylbenzimidazole most likely occurs via formation of an azomethine which subsequently undergoes reduction and cyclization. Since attempts to obtain 1-methyl-2(p-methoxyphenyl)benzimidazole from o-nitro-N-methylaniline and anisaldehyde was unsuccessful, this fact can be considered to be an indirect proof of the participation of an azomethine in the formation of the benzimidazole under the conditions described above. Thus, in this method for the preparation of benzimidazoles, the aromatic aldehyde is simultaneously the cyclizing agent and the reducing agent.

The reaction of benzaldehyde with o-nitroaniline proceeds in benzene, toluene, p-xylene, and mesitylene. Substituted benzaldehydes react in higher-boiling solvents, for example, tetralin.

The experimental results on the synthesis of various 2-phenylbenzimidazole derivatives are presented in Table 2.

EXPERIMENTAL

The syntheses were carried out in a round-bottomed flask equipped with a Dean-Stark adapter. The conditions used to obtain the benzimidazoles are presented in Table 2. The completion of the reaction was monitored by analysis of the reaction mass by thin-layer chromatography.

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o-Nitroaniline:benzaldehyde, mole	0,33	0,25	0,20	0,10 .
Yield,%	49	79	83	94

TABLE 1. Effect of the Reagent Ratio on the Yield of 2-Phenylbenzimidazole

TABLE 2.



2-Phenylbenzimidazole (I). o-Nitroaniline [6.91 g (0.05 mole)] was heated with 53.1 g (0.5 mole) of benzaldehyde in 10 ml of p-xylene. At the end of the reaction the reaction mass was cooled, and the resulting precipitate was filtered and washed on the filter with ether to give 9.1 g (94%) of I. A mixture of this product with an authentic sample of 2-phenylbenzimidazole did not give a melting-point depression.

Compounds II-VI. These compounds were isolated by a different method. The Dean-Stark adapter was replaced by a Claisen adapter, and the solvent and excess aldehyde were removed by vacuum distillation. The reaction products were extracted from the resinous reaction mass thus obtained by repeated extraction with hot, concentrated hydrochloric acid. The solution was clarified with activated charcoal and diluted with water. The solid reaction product precipitated, and II-VI were extracted from it with aqueous alkali. These compounds were precipitated from the aqueous alkaline solution by neutralization. One to two recrystallizations from aqueous ethanol were sufficient to further purify the compounds.

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