The Preparation of 2-Substituted Benzimidazoles and 2-Phenylnaphtho-[1, 2-d]imidazole from *N*-Arylamidines

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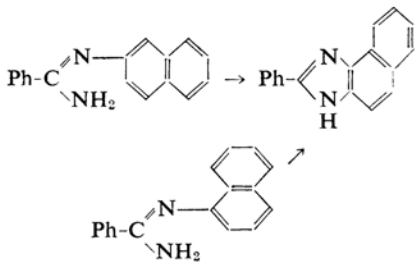
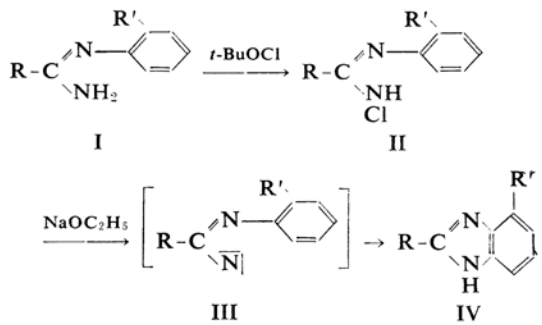
Grenda et al.[1] have recently reported the preparation of benzimidazoles from *N*-aryl-*N'*-haloamidines in an aqueous solvent. Independently of them, we also discovered an analogous method for the preparation of substituted benzimidazoles and 2-phenylnaphtho-[1, 2-d]imidazole during the course of a research program into the preparation and the reactivity of *N*-haloamidines. In our case, the benzimidazole derivatives and 2-phenylnaphtho[1, 2-d]-imidazole were obtained by the treatment of *N*-aryl-*N'*-chloroamidines with an equivalent amount of sodium ethoxide in benzene-ethanol.

To 3.9 g. (0.02 mol.) of *N*-phenylbenzamidine in 15 ml. of dry benzene and 15 ml. of absolute ethanol, there was added 2.3 g. of *t*-butyl hypochlorite at 0——5°C. After the mixture had been stirred at the same temperature for two hours, 0.9 g. of sodium in 10 ml. of absolute ethanol was added; the mixture was then refluxed for three hours. When the mixture was cooled and poured into ice water, brown precipitates were obtained. Recrystallization from aqueous ethanol gave 3.1 g. (80% yield) of a pure product, m. p. 289—290°C. This compound was identified as 2-phenylbenzimidazole by means of infrared and ultraviolet spectroscopic measurements, and by a mixed melting point test with an authentic sample which had been prepared according to the method described in the literature.[2]

By the same procedure, *N*-(*o*-tolyl)benzamidine was converted to 4-methyl-2-phenylbenzimidazole in a 76% yield, and *N*-phenylphenylacetamidine, to 2-benzylbenzimidazole in a 35% yield. However, the attempt to convert *N*-phenylacetamidine to 2-methylbenzimidazole was unsuccessful. Both *N*-(α-naphthyl)benzamidine and *N*-(β-naphthyl)benzamidine afforded the same product, 2-phenylnaphtho-[1, 2-d]imidazole, in 24% and 64% yields respectively.



Our proposed mechanism for this reaction is as follows:



I II III IV

a; R=C_6H_5, R'=H
b; R=C_6H_5, R'=CH_3
c; R=$C_6H_5CH_2$, R'=H

Amidines react with *t*-butyl hypochlorite to give *N*-chloroamidines (II), which are isolated as discrete intermediates. The reaction of sodium ethoxide with *N*-haloamidines would produce the nitrene intermediate (III), which attacks the benzene nucleus to give the benzimidazole ring.

The usual syntheses of the benzimidazole ring system utilize *o*-phenylenediamine or *o*-nitroaniline as starting materials.[3] In either case, the cyclization involves a coupling at the *o*-phenylene nitrogens. It is interesting to note that the benzimidazole ring can be prepared without using *o*-phenylenediamine derivatives.

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1) V. J. Grenda, R. E. Jones, G. Gale and M. Sletzinger, *J. Org. Chem.*, **30**, 259 (1965).
2) B. A. Porai-Koshits, O. F. Ginzburg and L. S. Eflos, *J. Gen. Chem.* (*U. S. S. R.*), **17**, 1768 (1947).
3) K. Hoffman, "Heterocyclic Compounds. Imidazoles and Derivatives," Part I, Interscience Publishers, New York (1953), pp. 258—273.