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METHOD FOR ARYLATION OF THE AMINO GROUP IN N-AMINOAZOLES

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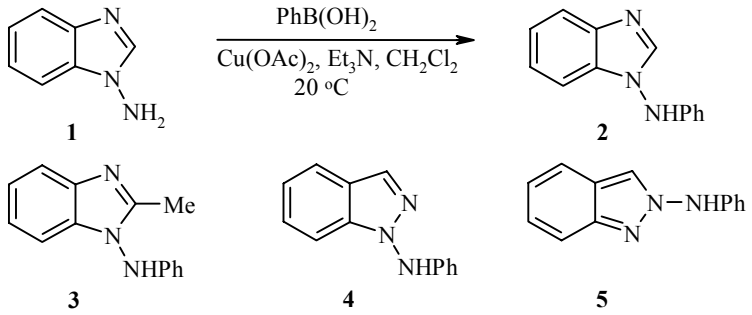
The direct arylation of the N-amino group in N-aminoazoles proceeds much less readily than the corresponding alkylation reaction [1-3]. All the reported examples of such arylation reactions have involved the use of aryl halides activated by strong electron-withdrawing groups such as NO_2 or CN. Thus, in particular, some 2-(arylamino)benzotriazoles [4], 1-(arylamino)benzimidazoles [5], and 1-(arylamino)-1,2,4-triazoles were obtained [6]. Following the recent report of the N-arylation of arylamines using arylboric acids by a modification of the Suzuki reaction [7], we studied the use of such a procedure for N-aminoazoles. The amino groups in arylamines and N-aminoazoles differ in their geometry and interaction with the aromatic π-system [1]. Thus, it was impossible to predict the result of these experiments.

The reaction of 1-aminobenzimidazole (**1**) with phenylboric acid in the presence of $Cu(OAc)_2$ and Et_3N gave previously unreported 1-phenylaminobenzimidazole (**2**) in 18% yield. Analogously, 2-methyl-1-phenylaminobenzimidazole (**3**) as well as 1- (**4**) and 2-phenylaminoindazoles (**5**) were obtained from the corresponding amines. Despite the low yields (16-29%), this method appears useful since there are presently no other methods for the preparation of N-phenylaminoazoles. For example, we were unable to obtain **2** by the arylation of amine **1** through the Ullmann reaction or heating the potassium salt of 1-formylaminobenzimidazole with halobenzenes. On the other hand, the Suzuki reaction is probably limited to N-aminoazoles. Thus, only the starting amine was obtained in an attempt to arylate 1-aminobenzotriazole by phenylboric acid.



1 **2** **3** **4** **5**

General Method for the Synthesis of N-Phenylaminoazoles. A sample of anhydrous cupric acetate (0.182 g, 1 mmol), phenylboric acid (0.244 g, 2 mmol), and Et_3N (0.14 ml, 1 mmol) were added to a solution of N-aminoazole (1 mmol) in a minimal amount of CH_2Cl_2 (3-10 ml). The mixture was stirred at 20°C for 17-96 h until the starting compound disappeared as indicated by thin-layer chromatography. The solvent was distilled

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off and the dry residue was extracted with 10 ml chloroform. The extract was passed through a 25-cm alumina column (d = 1.5 cm), collecting the fraction with R_f 0.4-0.6. Evaporation of the chloroform gave white crystalline N-phenylaminoazoles.

1-Phenylaminobenzimidazole (2) was obtained in 18% yield after 70 h; mp 203-205°C (ethyl acetate). IR spectrum in vaseline mull, ν_{NH}, cm^{-1}: 3166. ^1H NMR spectrum ($CDCl_3$, 250 MHz), δ, ppm: 6.59 (2H, m, 2'-, 6'-H); 6.87 (1H, br. s, NH); 6.95 (1H, m, 4'-H); 7.26 (5H, m, 4-, 5-, 6-, 3'-, 5'-H); 7.74 (1H, m, 7-H); 8.05 (1H, s, 2-H).

2-Methyl-1-phenylaminobenzimidazole (3) was obtained in 27% yield after 96 h; mp 225-227°C (acetonitrile). IR spectrum in vaseline mull, ν_{NH}, cm^{-1}: 3193. ^1H NMR spectrum ($CDCl_3$, 250 MHz), δ, ppm: 2.55 (3H, s, CH_3); 6.54 (2H, m, 2'-, 6'-H); 6.63 (1H, br. s, NH); 6.94 (1H, m, 4'-H); 7.20 (5H, m, 4', 5', 6'-, 3'-, 5'-H); 7.70 (1H, m, 7-H).

1-Phenylaminoimidazole (4) was obtained in 29% yield after 17 h; mp 139-140°C (octane). IR spectrum in vaseline mull, ν_{NH}, cm^{-1}: 3190. ^1H NMR spectrum ($CDCl_3$, 250 MHz), δ, ppm: 6.48 (2H, m, 2'-, 6'-H); 6.92 (1H, m, 4'-H); 7.10 (1H, br. s, NH); 7.19 (3H, m, 5-, 3'-, 5'-H); 7.41 (1H, m, 6-H); 7.52 (1H, m, 4-H); 7.74 (1H, m, 7-H); 8.03 (1H, d, J = 0.66 Hz, 2-H).

2-Phenylaminoindazole (5) was obtained in 16% yield after 17 h; mp 140-142°C (octane). IR spectrum in vaseline mull, ν_{NH}, cm^{-1}: 3180. ^1H NMR spectrum ($CDCl_3$, 250 MHz), δ, ppm: 6.51 (2H, m, 2'-, 6'-H); 6.95 (1H, m, 4'-H); 7.16 (3H, m, 5-, 3'-, 5'-H); 7.33 (1H, m, 6-H); 7.68 (2H, m, 4-, 7-H); 7.72 (1H, br. s, NH); 8.12 (1H, d, J = 0.77 Hz, 2-H).

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