In contrast to 1-amino- and 1-alkylaminobenzimidazoles, 1-di-alkylaminobenzimidazoles are metallated by n-butyl-lithium in absolute ether at the 2-position. The subsequent treatment of the lithium derivatives by electrophilic reagents, in which role benzophenone and iodine were used, leads to the formation of the corresponding 2-R-1-dialkylaminobenzimidazoles, which are difficult to obtain by other methods. The possibility was studied of using the N-dialkylamino group as a protective function.

Despite the fact that interest has increased in the last few years in N-aminoazoles [1], their metallation remains uninvestigated up to the present time. It is very difficult to predict beforehand the result of this reaction, since the N-amino group may be eliminated by the action of strong bases [2], while its ionization with the formation of an N-anion [3] may hinder the C-metallation of the hetero ring — the most desirable path of the reaction from the synthetic point of view. In the present work we studied this problem taking N-aminoazoles as an example.

We selected 1-amino- (I), 1-methylamino- (IV) and also 1-dimethylamino- and 1-diethylaminobenzimidazoles (Va,b) as the starting compounds. To prepare compound IV we have developed a more convenient method than that known before [4], consisting in the methylation of the sodium salt of 1-formylaminobenzimidazole (II) by methyl iodide in acetone, followed by the removal of the formyl group. The yields at both stages exceed 80%. 1-Dialkylaminobenzimidazoles Vа,b were synthesized in a yield of 57 and 36%, respectively, by the action of methyl iodide or ethyl iodide on amine I in liquid ammonia in the presence of potassium amide. It is interesting to note that in all of the experiments, not even traces of the formation of 1-alkylaminobenzimidazoles were detected. A similar phenomenon was also observed during the alkylation of C-aminoazoles under the same conditions [5, 6].
We were also unable to carry out the C-metallation of compounds I and IV by n-butyl-lithium in absolute ether at temperatures from $-20^\circ$C to $-100^\circ$C; in all cases, after the addition of benzophenone to the reaction mixture, the starting compound was isolated instead of the expected 1-amino(methylamino)-2-α-hydroxybenzhydrylbenzimidazole. In contrast to this, the experiments with 1-dialkylaminobenzimidazoles gave positive results. First, we have carried out the reactions at $-20^\circ$C, setting two experiments in parallel: with 1-methylaminobenzimidazole and 1-dimethylaminobenzimidazole. In both cases, the attempts to record the formation of the organolithium compounds by adding benzophenone into the reaction mixture were unsuccessful, and led only to the separation of the starting compounds. It is possible that the 1-R-2-lithium-benzimidazoles are unstable under these conditions. In fact, by decreasing the temperature of the reaction mixture to $-100^\circ$C, we obtained in the case of 1-methylbenzimidazole the already known [7] 1-methyl-2-α-hydroxybenzhydrylbenzimidazole, and in the case of compounds Va,b — the alcohols VIIa and VIId. The yields of the latter compounds were 74% and 30%, respectively. In a similar way, in treatment of 1-dimethylamino-2-lithiumbenzimidazole (VIIa) with iodine, 1-dimethylamino-2-iodobenzimidazole (VIIb) was obtained in a 42% yield. In an attempt to methylate the lithium-derivative VIIa with methyl iodide, a mixture of the starting compound Va and 1-dimethylamino-2-methylbenzimidazole (VIIc) was obtained, which, however, could not be separated because of the similarity of the chromatographic mobility and other properties. Judging from the IR spectrum of this mixture, the yield of compound VIIc did not exceed 20%.

It was of interest to study the possibility of using the N-dimethylamino group as a protective function for the organometallic synthesis of 2-substituted benzimidazoles not containing a substituent in the 1-position. Most of the known methods of elimination of the N-amino group (for example, action of nitrous acid) [1] are inapplicable here, because they require the presence of free N–H bonds in the amino group. We therefore tested the reducing methods and the action of strong bases. It was found that the dimethylamino group in compound Va is eliminated both by the action of excess sodium (potassium) in liquid ammonia (the reducing method), and by the action of potassium amide, but the process is slow and cannot be brought to completion. Thus, as the result of stirring compound Va with two equivalents of KNH₂ in liquid ammonia, only 17% of benzimidazole was obtained and about 75% of the starting compound was regenerated. The yield of benzimidazole was higher (40%) by the action of excess sodium in liquid ammonia on compound Va, but also in this case a large portion of the starting compound remained unchanged. Approximately the same results were obtained as a result of the reductive elimination of the dimethylamino group in alcohol VIIa. The starting alcohol, VIIa (35%), 2-α-hydroxybenzhydrylbenzimidazole (VIII) (30%) and also the product of the reduction of the hydroxyl group in the latter compound — 2-benzhydrylbenzimidazole (IX) (35%) were isolated from the reaction mixture.

In contrast to the dimethylamino group, the elimination of the N-amino group in compound I, both by the action of metallic sodium and potassium amide in liquid ammonia, proceeds very readily and the yields of benzimidazole reach 70 and 85%, respectively, it is very likely that three possible elimination mechanisms are realized under these conditions: the reducing mechanism (path a), nucleophilic (b) and fragmentation of the anion (c):

\[
\begin{align*}
\text{a) } & \quad \begin{array}{l}
\text{NR}_2^- \quad \xrightarrow{2 \text{ e}^-} \quad N \quad + \quad R_2\text{N}^+ \\
n \quad \text{or Na} \quad \xrightarrow{\text{NH}_2^-} \quad \xrightarrow{\text{NH}^-} \quad N \quad + \quad [\text{NH}] \\
\end{array} \\
\text{b) } & \quad \begin{array}{l}
\text{NR}_2^- \quad \xrightarrow{\text{NH}_2^-} \quad N \quad + \quad R_2\text{NNH}_2 \\
n \quad \text{or Na} \quad \xrightarrow{\text{NH}_2^-} \quad \xrightarrow{\text{NH}^-} \quad N \quad + \quad [\text{NH}] \\
\end{array} \\
\text{c) } & \quad \begin{array}{l}
\text{NR}_2^- \quad \xrightarrow{\text{NH}_2^-} \quad N \quad + \quad R_2\text{NH}_2 \\
n \quad \text{or Na} \quad \xrightarrow{\text{NH}_2^-} \quad \xrightarrow{\text{NH}^-} \quad N \quad + \quad [\text{NH}] \\
\end{array}
\end{align*}
\]