

New reactions of 2-nitroaryl carbanions and their nitrogen analogs with selected electrophilic reagents leading to the formation of nitrogen heterocyclic compounds

Magdalena Walewska-Królikiewicz, M.Sc.

Supervisor: dr hab. Zbigniew Wróbel, prof. IChO PAN

Abstract

Heterocyclic compounds containing a nitrogen atom in their structure are very important compounds. Many of them are drugs, but their role is not limited to biomedical chemistry. They are successfully used in many fields of chemistry and industry. In organic chemistry, we encounter them as substrates or catalysts for many important reactions. Despite the vast literature available on methods for obtaining heterocyclic compounds, I believe that this important field requires further research efforts. For this reason, I focused my attention on the development of new syntheses, distinguished by their simplicity and economic approach, of some of the most important representatives of heterocyclic compounds, such as indoles, benzimidazoles and quinolines. To achieve this, I focused on the use of *ortho*-substituted nitrobenzene derivatives. For this purpose, I used easily available and inexpensive *ortho*-substituted nitrobenzene derivatives, characterized by multidirectional reactivity.

The synthesis of 2-trifluoromethylindole was planned in two stages and was inspired by Reissert's method. The first step involved the acylation of the methyl group of an appropriately substituted *o*-nitrotoluene under basic conditions, while the second involved the reductive cyclization of the intermediate product using an appropriate reducing agent (Zn/AcOH or sodium dithionite).

The preparation of quinolines substituted in position 4 with an electron withdrawing group (EWG) was based on a three-step synthesis consisting of Knoevenagel-type condensation of activated *o*-nitrotoluene derivatives with acetaldehyde, cyclocondensation and reduction of quinoline *N*-oxide to the corresponding quinoline at the last stage of the synthesis. The complete synthesis was successful (with the selection of individual reaction conditions) for derivatives with cyano, sulfonate and ester groups. The cyclization of the condensation products of carbonyl compounds failed, and *o*-nitrotoluene activated with a nitro group did not give the proper product even at the Knoevenagel condensation stage.

The third concept allowing for the preparation of a number of benzimidazole derivatives was based on the transformation of *o*-nitroaniline derivatives. In the first stage, under the influence of phosphine, the nitro group is transformed into a nucleophilic nitrogen center in the form of an iminophosphate, which is then reacted with an appropriate electrophilic agent. In this way, various 2-functionalized benzimidazole derivatives have been synthesized, such as benzimidazolones, benzimidazolthiones, 2-amino-2-alkyl- and 2-arylbenzimidazoles. Particular attention was paid to the synthesis of compounds containing a 2-trifluoromethyl group. A separate problem that was successfully solved was the synthesis of 2-functionalized benzimidazoles with an alkyl substituent at the nitrogen atom.