Vicinal Amino- and (N-Acetylamino)alkynylpyrazoles are Convenient Synthones for Preparing Potential Physiologically Active Compounds

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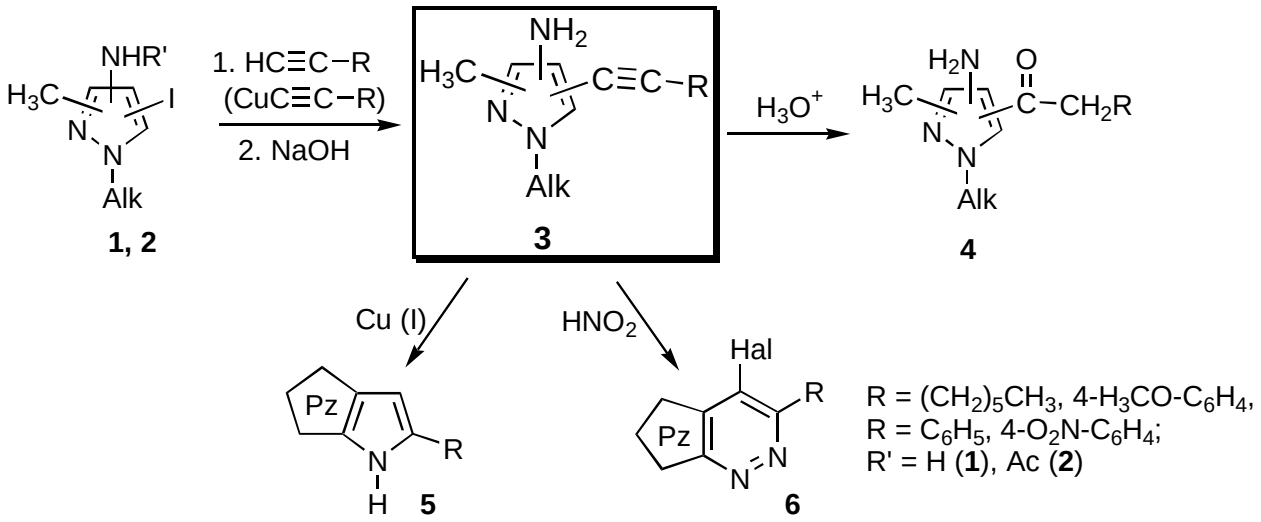
Substantial efforts have been directed over the last decade toward a development of methods of synthesis of *vic*-functionalized aryl- and hetarylacetylenes. Vicinal aminoalkynylpyrazoles are very perspective class of compounds for a search of medicines. It is known that aminoalkynylpyrazoles possess different biological activities [1].

In this connection, we have initiated the development of synthesis of vicinal aminoalkynylpyrazoles with all possible versions of the arrangement of functional groups (C≡C and NH_2). It is noteworthy, that the information about the synthesis of vicinal aminoalkynylpyrazoles is rather poor and the use of usual methods for introducing acetylenic substituents is not obviously due to a strong +M-effect of amino group.



In spite of the Pd/Cu- catalyzed cross-coupling of halogenoarenes with 1-alkynes is known about 25 years. For the first time we observe that the reaction of iodopyrazoles with 1-alkynes bearing the electron-releasing substituent is unsuitable for synthesis of alkynylpyrazoles. 3-, 5-Iodopyrazoles **1** (R = H) did not enter the reaction, but in the case of vicinal 4-iododerivatives **1** their reductive desiodination, accompanied by the homocoupling of 1-alkynes (up to 90%), was the only reaction. These complications were avoided by applying acetyl protection for amino group and acetylide method of cross-coupling. The condensation of (N-acetylamino)pyrazoles **2** with copper acetylides in pyridine at 110-115°C in argon atmosphere and the subsequent hydrolysis afford acetylaminoacetylenes **3** in 65-75% overall yields. Thus, the reaction of copper acetylides with amino- and (N-acetylamino)iodopyrazoles was established to be a common method for preparation of (N-acetylamino)alkynylpyrazoles.

Pyrazoles containing an acetylenic substituent and an amino group on the adjacent carbon atoms can be used to prepare of acylaminopyrazoles **4**, pyrrolopyrazole **5**, and pyrazolopyridazine **6** derivatives. Both condensed systems are the perspective compounds for the finding of new drugs.

References:

[1] A.K. Godad, B.S. Kittur, S.G. Kapsi, *Arzneim-Forsch.* **1996**, *46*, 1082.