ONE-POT SYNTHESIS OF 3-ALKYLTHIO AND 3-AMINO-SUBSTITUTED 5-AMINO-4-R-SULFONYL-*1H*-PYRAZOLES

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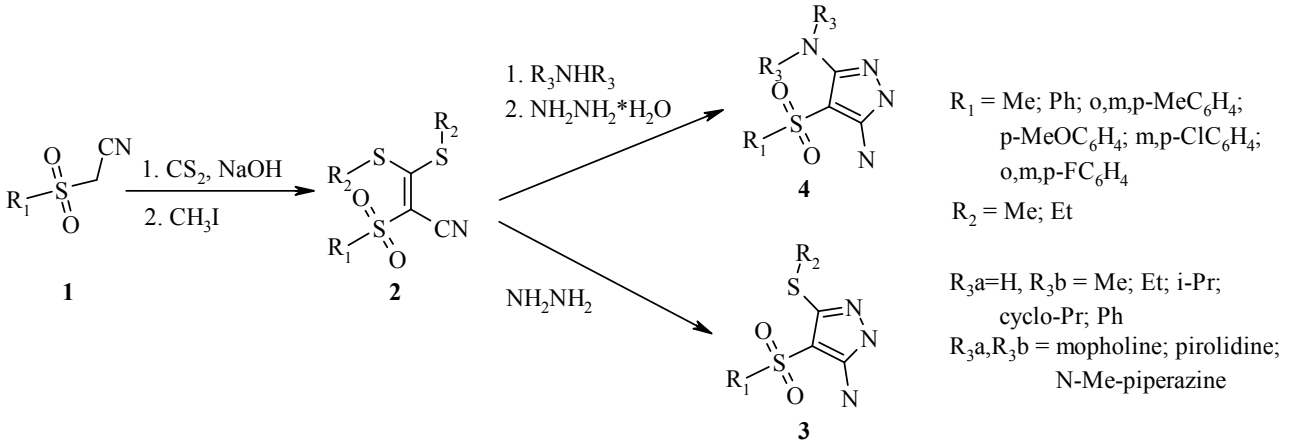
Development of the new synthetic methods and search for biological active compounds among the aminopyrozoles is obvious interested, as evidenced by the wide range of pharmacological properties of some derivatives of pyrazoles. The most known drugs for cancer treatment, as Binukleyin 2 (metanymidamin), Barasertib (AZD-1152), Tozasertib (MK-0457), are derivatives of aminopyrozole. This pharmacophore system is characterized by antimicrobial, antifungal, antiviral, antiparasitic and anti-inflammatory activity. We focused on purposeful combination of two pharmacophores in the one molecule — sulfonyl group and 3- aminopyrazole cycle.

Traditionally this reaction is conducted in three stages for the 3-*S*-derivatives and in four stages for 3-*N*-alkyl-substituted pyrazole derivatives. We have developed a one-pot method of synthesis of the corresponding aminopyrazoles **3** and **4** on the base of the methylene active cyanomethylarylsulfones **1** as starting reagents. The proposed scheme has been implemented in the laboratory version (in the Erlenmeyer flask in the mixture of dioxane : water 5:1) and scaled (ScaleLab) on 25 g batch. The resulting compounds had a high purity (> 95%) and did not require further purification.



The obtained compounds appear as promising building-blocks to build the combinatorial libraries for directional biological screening.