SYNTHESIS AND PHYSICOCHEMICAL PROPERTIES OF TRIAZOLE AND THIAZOLE CONTAINING XANTHINE DERIVATIVES

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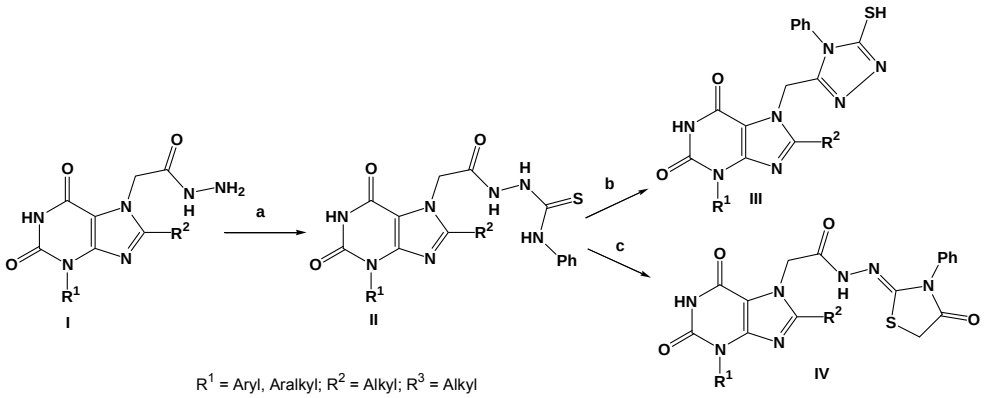
Heterocycle containing compounds (xanthines, triazoles, thiazoles etc) represent very important structural units in drug discovery. A survey of literature reveals the biological properties of these substances including hypoglycemic, anticancer, antioxidant, anti-inflammatory, bronchodilator and xanthine oxidase inhibitory effects. In our opinion, combination of several heterocyclic systems in one molecule could improve pharmacological properties. Aim of our work was a development of method of thiazole and triazole containing xanthine derivative synthesis.

As initial substances we used hydrazides of 3-aryl(aralkyl)-8-alkylxanthinyl-7-acetic acids **I**, which had been synthesized earlier on the department of Biological chemistry of Zaporozhye State Medical University. At the first stage we obtained N-phenylthiosemicarbazides **II** by the interaction of hydrazides **I** with phenylisothiocyanate in the aqueous dioxane.



R^1 = Aryl, Aralkyl; R^2 = Alkyl; R^3 = Alkyl

a) PhSCN, dioxane, H_2O, t; b) NaOH, H_2O, t; c) $ClCH_2COOH$, CH_3COOH, CH_3COONa

Reflux of compounds **II** in the solution of sodium hydroxide led to the cyclisation of triazole cycle **III**. Carrying out reaction in glacial acetic acid with presence of calculated amounts of chloroacetic acid and sodium acetate caused formation of thiazole ring **IV**. As result of these reactions we obtained number of 5-(xanthinyl-7-methyl)-4-phenyl-3-thio-1,2,4-triazoles **III** and xanthinyl-7-acetic acids 4-oxo-3-phenylthiazolydine-2-ylidenhydrazides **IV**.

The structures of all obtained compounds were proved by the elemental analysis, IR- and ^{1}H NMR-spectroscopy.