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# Synthesis of new thiazoles based on the reaction of *N*-aryl-*N'*-(quinazoline-2-yl) amidinothioureas with α-halocarbonyl compounds

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## Abstract

Biological activity of heterocyclic systems containing quinazoline and thiazole cycles widely studied. In this regard the synthesis of polyheterocyclic compounds with those cycles is an important problem to research novel biologically active substances. The purpose of this work is the synthesis of new quinazolyl-2-yl amidinothioureas and study of their reactions with alpha-haloketones: phenacyl bromide, ethyl monochloroacetate, 2-chloroacetoacetate and 3-chloroacetylacetone. Structures of the obtained compounds are confirmed by $^1$H NMR spectrometry and elemental analysis. Probability of obtaining a bioactivity to inhibit 2-gluconate dehydrogenase virtually determined.

A two-step synthesis of heterocyclic systems with thiazole and quinazoline rings based on interaction of substituted amidinothioureas with α-halocarbonyl compounds such as phenacyl bromide, ethyl monochloracetate, 3-chloroacetylacetone 2-chloroacetoacetate was studied. The optimal conditions for the reactions investigated: synthesis starting *N*-aryl-*N'*-quinazolyl 2-yl-thioureas was carried out at continuous stirring at room temperature in dimethylacetamide. Optimal conditions of interaction of α-halocarbonyl compounds with *N*-aryl-*N'*-quinazolylamidinothioureas is boiling in alcoholic medium followed by treatment with an aqueous alkali solution.

It is found that the reaction with phenacyl bromide, ethyl monohloracetate, 3-chloroacetylacetone selectively proceed with thioamide moiety of quinazolyl-2-yl amidinothioureas. The first step of this process is the *S*-alkylation according to the mechanism described for the first time by Hantzsch. In the second step proceeds thiazole ring closure by nucleophilic addition with amino-group of formed intermediate. Nucleophilicity of the nitrogen atom linked to the aromatic system reduced due to the bias of electron density of the benzene ring, that's why secondary amino-group of guanidine moiety involved in the cyclization. Interaction of 2-quinazolylamidinothioureas with 2-chloroacetoacetate occurs not so definitely and may lead to the formation of two alternative products. It is shown that heterocyclization with ethyl-2-chloroacetoacetate affects carbonyl group and result in formation of ethyl 2-[($R_1$-phenyl)imino]-3-{imino[(6-$R_2$-4-methyl-quinazolin-2-yl)-amino]methyl}-2,3-dihydro-1,3-thiazole-5-carboxylates.

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