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Dedicated to the 115th anniversary of B.A. Arbuzov's birth

Synthesis of New Phosphorylated 1,2,4-Triazole-3-thiones. N,S-Functionalization Methods

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Abstract—New phosphorylated 1,2,4-triazole-3-thiones have been synthesized, and the possibility of their N,S-functionalization has been demonstrated. The direction of alkylation of 1,2,4-triazole-3-thiones with ethyl acrylate has been shown to depend on the substituent on the N⁴ atom.

Keywords: 1,2,4-triazole-3-thione, N,S-functionalization, alkylation, phosphorylated 1,2,4-triazole-3-thiones

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1,2,4-Triazole-3-thiones exhibit a broad spectrum of biological activity [1, 2]; therefore, synthesis of new structures based thereon, in particular of those containing a pharmacophoric phosphoryl group, seems to be promising. There are published data on the synthesis of some phosphorylated bis-1,2,4-triazole-3-thiones [3] in which two 1,2,4-triazole heterocycles are separated by a phosphorus-containing ethylidene or ethylene fragments. However, these are the only known examples of research in the field of phosphorylated triazolethiones.

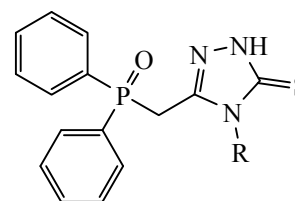
We previously described the synthesis of new phosphorylated 1,2,4-triazole-3-thiones **1a** and **1b** [4] by heterocyclization of the corresponding phosphorylated thiosemicarbazides based on Fosfenazid (diphenylphosphorylacetic acid hydrazide) which is a neurotropic drug [5] (Scheme 1). In continuation of these studies, we have synthesized new phosphorylated 1,2,4-triazole-3-thione **1c** (Scheme 2).

Triazolethione molecules possess two nucleophilic centers, which provides the possibility of their modification at the sulfur or nitrogen atom [6, 7]. The synthesis of ethyl triazolylsulfanylacetates by S-alkylation of triazoles **1a** and **1b** with ethyl bromoacetate and

subsequent hydrazinolysis with the goal of obtaining the corresponding hydrazides were described by us in [4]. Herein we report the synthesis of ethyl triazolylsulfanylacetate **3** (the product of alkylation of triazole **1c** with ethyl bromoacetate) and triazolylsulfanylacetohydrazide **4** (Scheme 3).

Triazolethiones can be alkylated with α,β -unsaturated compounds [8, 9] such as ethyl acrylate. It is known that the alkylation of triazolethiones with ethyl acrylate involves the N² atom as nucleophilic center [8, 9]. We have found that both nitrogen and sulfur atoms could be nucleophilic centers in the alkylation of

Scheme 1.



1a-1c

R = H (**a**), Ph (**b**), All (**c**).