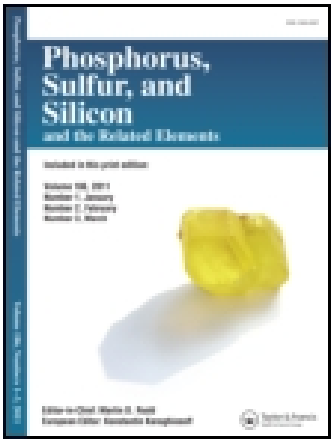

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Phosphorylacetic Acid Thioamides As Key Substances for Phosphorylated Heterocycles

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Published online: 21 Jun 2008.

To cite this article: V. A. Kozlov , I. L. Odinets , D. V. Aleksanyan , P. V. Petrovskii & T. A. Mastryukova (2008) Phosphorylacetic Acid Thioamides As Key Substances for Phosphorylated Heterocycles, Phosphorus, Sulfur, and Silicon and the Related Elements, 183:2-3, 683-684, DOI: 10.1080/10426500701807152

To link to this article: http://dx.doi.org/10.1080/10426500701807152

Phosphorus, Sulfur, and Silicon, 183:683–684, 2008

ISSN: 1042-6507 print / 1563-5325 online
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Phosphorylacetic Acid Thioamides As Key Substances for Phosphorylated Heterocycles

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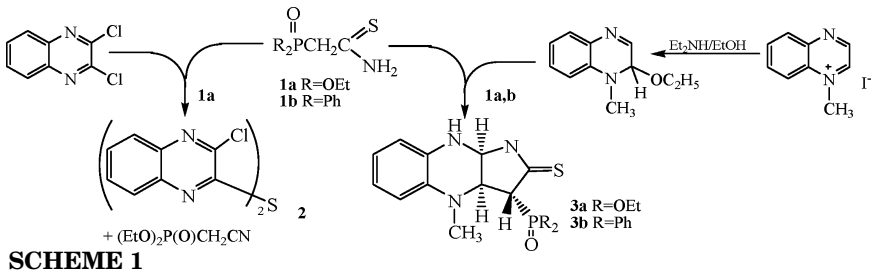
Diethoxyphosphorylthioacetamide in a reaction with 2,3-dichloroquinoxaline acted as a thionating reagent, giving diethoxyphosphorylacetonitrile and 2-chloro-3-[(3-chloro-2-quinoxalinyl)-thio]quinoxaline. Base-catalyzed reactions of phosphorylthioacetamides with N-methylquinoxalinium iodide proceeded stereoselectively to yield cis-3-phosphoryl-1,3,3a,4,9,9a-hexahydro-2H-pynola[2,3-b]quinoxaline-2-thiones.

Keywords 1,3,3a,4,9,9a-hexahydro-2H-pyrrolo[2,3-b]quinoxaline-2-thiones; 2,3-dichloroquinoxaline; annulation; N-methylquinoxalinium iodide; phosphorylthioacetamides

Thioamides served as building blocks to obtain heterocycles of pharmaceutical importance. Recently we elaborated the facile synthetic route to phosphorus-substituted carboxylic acid thioamides[1] (PTA) and demonstrated their application in regioselective heterocyclization with dimethyl acetylendicarboxylate leading to phosphorus containing thiazolidin-4-ones as potential drug candidates.[2] Since azines containing two or more heteroatoms undergo annelation with various bisnucleophilic reagents[3] leading to annulated heterocycles possessing biological activity, we investigated the ability of PTA to play a role as annelating agents in such reactions.

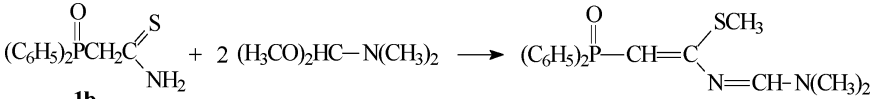


SCHEME 1

It was found that interacting with 2,3-dichloroquinoxaline thioamide **1a** served as thionation agent, resulting in bis(quinoxalinyl)sulfide **2** and phosphorylacetonitrile instead of the expected thiazolo[4,5-b]quinoxaline. The interaction of PTA with *N*-methylquinoxalinium iodide proceeded as annelation but resulted in 3-phosphorylated thiolactames, namely *cis*-1,3,3a,4,9,9a-hexahydro-2H-pyrrolo[2,3-b]quinoxaline-2-thiones **3a**, **b**, in contrast to the similar reactions of non-phosphorylated thioamides giving thiazole derivatives.

To compare the reactivity of phosphorylated acetic acid amides and thioamides we tried to accomplish a similar transformation using $(EtO)_2P(O)CH_2C(O)NH_2$. But CH-acidity of the latter was found to be insufficient for addition to the quinoxaline derivative, and the starting phosphorus containing substrate was retrieved from the reaction mixture.

Taking into account that derivatives of carboxylic acid thioamides are inclined to various hetrocyclizations similar to thioamides themselves, we attempted to obtain enamine that was useful for further synthesis of phosphorylated pyrimidinethione. However, treatment of **1b** with N(dimethoxymethyl)-N,N-dimethylamine resulted in S-alkylation product **4**, which does not react with phenyl hydrazine.



1b **4**

SCHEME 2

Therefore, research of phosphorylacetic acid thioamides' reactivity has revealed that these compounds can serve as thionating agents, C,N-, S,N-, or S-nucleophiles, depending on the substrate's structure.

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