This article was downloaded by: [University of California Santa Cruz] On: 17 December 2014, At: 15:18 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

V. A. Kozlov $^{\rm a}$, I. L. Odinets $^{\rm a}$, D. V. Aleksanyan $^{\rm a}$,

P. V. Petrovskii ^a & T. A. Mastryukova ^a

^a A. N. Nesmeyanov Institute of Organoelement compounds RAS , Moscow, Russia 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: <u>10.1080/10426500701807152</u>

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

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or

indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions



Phosphorylacetic Acid Thioamides As Key Substances for Phosphorylated Heterocycles

V. A. Kozlov, I. L. Odinets, D. V. Aleksanyan, P. V. Petrovskii, and T. A. Mastryukova

A. N. Nesmeyanov Institute of Organoelement compounds RAS, Moscow, Russia

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 phosphorythioacetamides with N-methylquinoxalinium iodide proceeded stereoselectively to yield cis-3-phosphoryl-1,3,3a,4,9,9a-hexahydro-2H-pynola[2,3-b]quinoxaline-2thiones.

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

Thioamides served as building blocks to obtain heterocycles of pharmaceutical importance. Recently we elaborated the facile synthetic route to phosphorus-substituted carboxylic acid thioamides¹ (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 reagents³ leading to annulated heterocycles possessing biological activity, we investigated the ability of PTA to play a role as annelating agents in such reactions.



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[4,5b]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[2,3b]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.

$$\begin{array}{c} O \\ \parallel \\ (C_6H_5)_2PCH_2C \\ NH_2 \end{array} + 2 (H_3CO)_2HC - N(CH_3)_2 \longrightarrow (C_6H_5)_2P - CH = C \\ 1b \\ \textbf{SCHEME 2} \end{array}$$

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.

REFERENCES

- V. A. Kozlov, I. L. Odinets, K. A. Lyssenko, S. G. Churusova, S. V. Yarovenko, P. V. Petrovskii, and T. A. Mastryukova, *Izv. AN, Ser. khim.*, 4, 887 (2004) [*Russ. Chem. Bull.*, 53, 925 (2004)].
- [2] V. A. Kozlov, I. L. Odinets, K. A. Lyssenko, S. G. Churusova, S. V. Yarovenko, P. V. Petrovskii, and T. A. Mastryukova, *Heteroatom. Chem.*, 2, 159 (2005).
- [3] V. N. Charushin, O. N. Chupakhin, and Henk C. van der Plas. Adv. In Hc. Chem., 43, 301 (1988).