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Synthesis and antimicrobial activity of new phosphorus-containing pyridine derivatives

© **Pavel A. Volkov**,[1] **Nina I. Ivanova**,[1] **Anton A. Telezhkin**,[1] **Ksenia O. Khrapova**,[1] **Lyudmila A. Belovezhets**,[1] **Konstantin A. Apartsin**,[2] **Viktoriya V. Kireeva**,[2] and **Nina K. Gusarova**[1]*[+]

[1] *A.E. Favorsky Irkutsk Institute of Chemistry. Siberian Branch of the Russian Academy of Sciences. Favorsky St., 1. Irkutsk, 664033. Russia. Phone: +7 (395-2) 42-24-36. E-mail: gusarova@irioch.irk.ru*

[2] *Irkutsk Scientific Center. Siberian Branch of the Russian Academy of Sciences. Lermontov St., 134. Irkutsk, 664033. Russia. Phone: +7 (395-2) 45-30-80. E-mail: director@isc.irk.ru*

*Supervising author; [+]Corresponding author

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Abstract

The directed synthesis of new pharmacophoric molecules is one of the urgent tasks of organic chemistry. A special place in this area is occupied by vital nitrogen-containing heterocycles and their derivatives, on the basis of which new promising precursors of drugs are created. For example, pyridinium salts are part of such well-known drugs as pyridoxine, mexidol and metadoxine. Phosphorus-containing pyridine derivatives, among which compounds with cytotoxic and antimicrobial properties have been identified, are also being actively studied now. Thus, the development of convenient approaches for obtaining new functional phosphorus-containing pyridine derivatives is an important and timely task. Special attention is paid to synthetic methods that correspond to the PASE (pot, atom and step economy) paradigm. Using this approach, we have synthesized hydrochlorides and tosylates of 4-bis(2-phenylethyl)chalcogenophosphoryl-pyridine, not described previously, by practically quantitative interaction of the available 4-bis(2-phenylethyl)chalcogenophosphorylpyridines with hydrochloric or 4-methylbenzenesulfonic acids at room temperature or slight heating (40-45 °C). The reaction proceeds regioselectively on the nitrogen atom of the base pyridine. The second reaction center in the 4-bis(2-phenylethyl)chalcogenophosphorylpyridine molecule, chalcogenophosphoryl group, does not participate in the studied process, even when using an excess of hydrochloric acid. The starting 4-bis(2-phenylethyl)chalcogenophosphorylpyridines are easily obtained on the basis of the original reaction of pyridine with secondary phosphine chalcogenides with the assistance of electron-deficient acetylenes. Using the example of microorganisms of different taxonomic groups: *Bacillus subtilis* B-406, *Enterococcus durans* B-603, *Penicillium citreo-viride* F-1777, *Escherichia coli* B-1238, we have found that the target hydrochlorides and tosylates of 4-bis(2-phenylethyl)chalcogenophosphorylpyridine exhibit pronounced antimicrobial activity against non-spore gram-positive microorganisms.

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