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### Synthesis of N -Phosphonamidothionate Derivatives of Nucleoside

Zhi-Wei Miao<sup>a</sup>; Hua Fu<sup>a</sup>; Bo Han<sup>a</sup>; Yu-Fen Zhao<sup>a</sup>

<sup>a</sup> Tsinghua University, China

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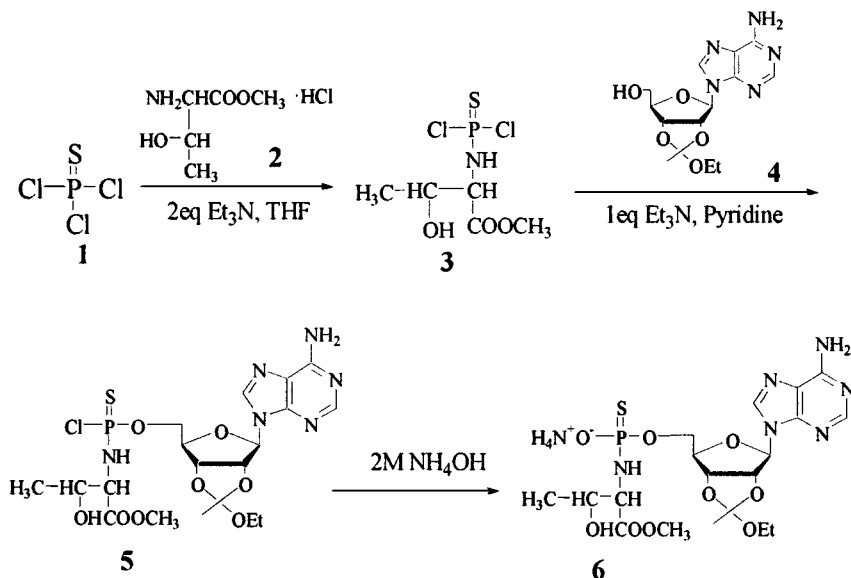
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## SYNTHESIS OF N-PHOSPHONAMIDOTHIONATE DERIVATIVES OF NUCLEOSIDE

Zhi-Wei Miao, Hua Fu, Bo Han, and Yu-Fen Zhao  
 Tsinghua University, China

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N-Phosphonamidothionate derivatives of nucleoside analogues have been prepared as potential pro-drugs of the big-active free phosphate forms. The relative metabolic stability of nucleoside 5'-phosphorothioates is well-documented. AMP-S is relatively resistant to enzymatic transformations.<sup>1</sup> We now report on the synthesis of 2',3'-O-ethoxymethylidene adenosine 5'-thiophosphor-amidates, which was



SCHEME 1

Address correspondence to Yu-Fen Zhao, Bioorganic Phosphorus Chemistry Laboratory, Department of Chemistry, School of Life Science and Engineering, Tsinghua University, Beijing 100084, P. R. China. E-mail: tp-dch@mail.tsinghua.edu.cn

prepared by 1 equiv of threonine amino acid methyl ester **2** with **1** equiv of thiophosphoryl chloride **1** in THF at room temperature under nitrogen. A solution of **1** equiv of 2', 3'-O-ethoxymethylidene adenosine **4** and triethylamine in pyridine was added to the reaction mixture. The solution was stirred overnight, filtered, and concentrated in vacuo. After hydrolysis in  $\text{NH}_4\text{OH}$ , **6** was obtained in 72% yield by chromatography on silica gel. Compound **6** was checked by its  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR, and ESI-MS spectral data.

## REFERENCE

- [1] A. W. Murray and M. R. Atkinson, *Biochemistry*, **11**, 4023 (1968).