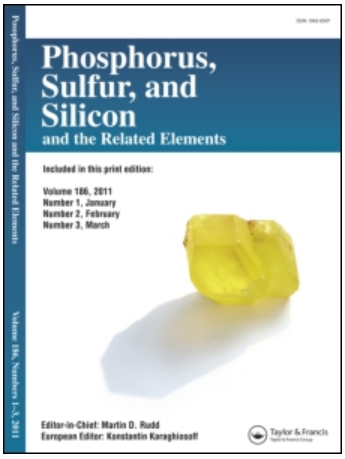

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Synthesis of N -Phosphonamidothionate Derivatives of Nucleoside

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SYNTHESIS OF *N*-PHOSPHONAMIDOTHIONATE DERIVATIVES OF NUCLEOSIDE

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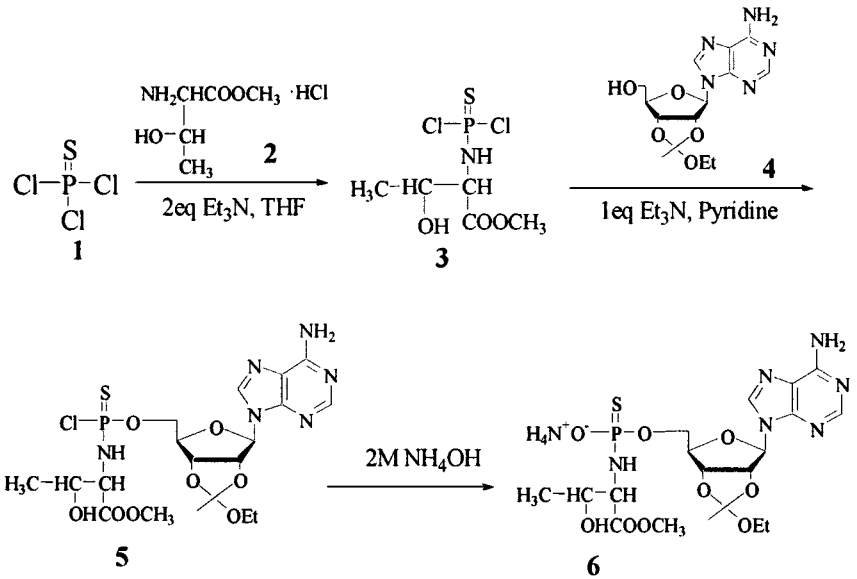
N-Phosphonamidothionate derivatives of nucleoside analogues have been prepared as potential pro-drugs of the big-active free phosphate forms. The relative metabolic stability of nucleoside 5′-phosphorothioates is well-documented. AMP-S is relatively resistant to enzymatic transformations.[1] We now report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



SCHEME 1

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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 NH_4OH, **6** was obtained in 72% yield by chromatography on silica gel. Compound **6** was check by its ^{1}H, ^{13}C, ^{31}P NMR, and ESI-MS spectral data.

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