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New Strategies for Chemical Synthesis of Phosphorodithioates Derived from 2'- or 3'- or 5'-Thionucleosides

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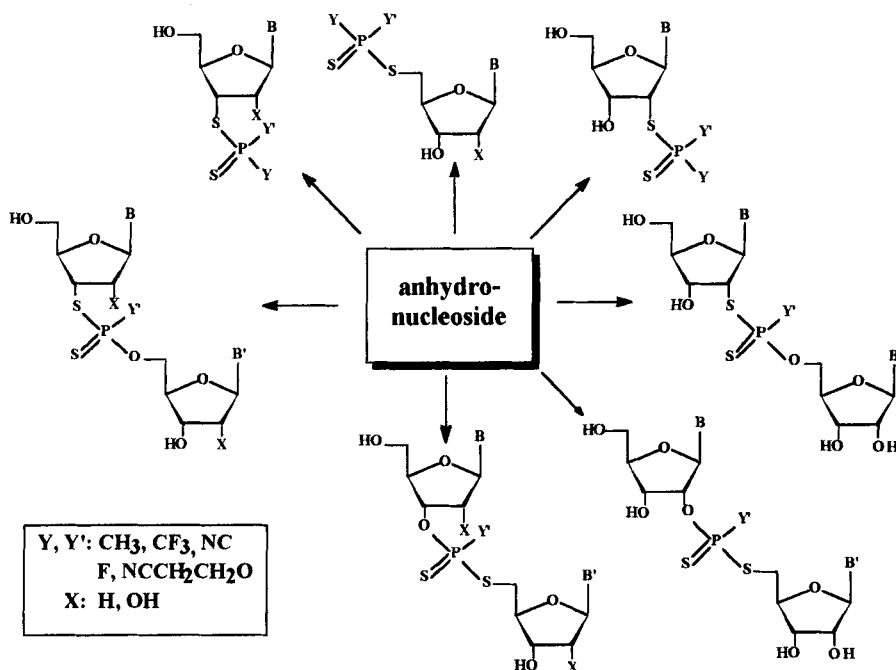
NEW STRATEGIES FOR CHEMICAL SYNTHESIS OF PHOSPHORODITHIOATES DERIVED FROM 2'- or 3'- or 5'-THIONUCLEOSIDES

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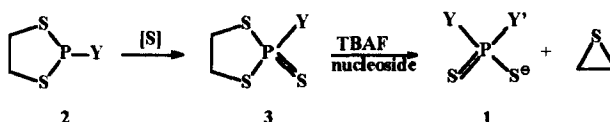
ABSTRACT: Various phosphorodithioates derived from thionucleosides were synthesized by the reaction of anhydronucleosides with phosphorodithioic acids.

(Oligo)nucleotide analogues containing phosphorothiolate linkages¹ are valuable for investigating the biochemistry of nucleic acids.² We have found that 2, 3'-anhydrothymidine reacts with phosphorus dithioacids to form phosphorodithioates derived from



3'-thiothymidine.³ Here we present generality and efficiency this method for the synthesis of nucleotides with internucleotide linkage P(S)-S-C

Our method required disclose the efficient synthesis of phosphorodithioic acids **1**. Therefore we have propose now a novel synthesis of the compounds **1** *via* 1,3,2-dithiaphospholane derivatives **2**. The roots of this approach was derived from dithiaphospholane methodology.⁴ The protocol we have developed involves two consecutive reactions: sulfurization of the compound **2** to form the compound **3** and finally the reaction with nucleophile to formation of the desired acid **1**.



Y: nucleosid-5'-yl, nucleosid-3'-yl, CH ₃ , CF ₃ , NC, (CF ₃) ₂ CHO, (CH ₃) ₃ CO	TBAF: Y' : F
Y: CH ₃ , CF ₃ , NC, citronellyl, cholesteryl, (CF ₃) ₂ CHO, (CH ₃) ₃ CO	nucleoside / DBU Y': nucleosid-5'-yl, nucleosid-3'-yl

General procedure: A solution of anhydronucleoside and phosphorodithioate **1** in MeCN was acidified with toluene-*p*-sulphonic acid. After 2-12 h at 20° C the reaction mixture was concentrated *in vacuo*. The product was isolated by silica gel chromatography.

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