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 A P(V) Platform for Oligonucleotide Synthesis
Science **2021**, 373, 1265–1270, DOI: 10.1126/science.abi9727.

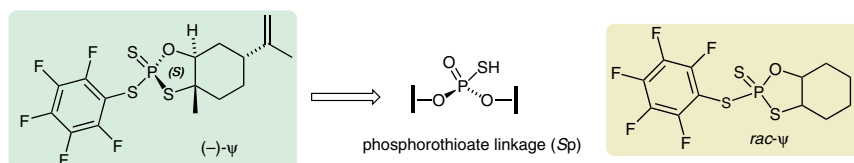
Category

Chemistry in
 Medicine and
 Biology

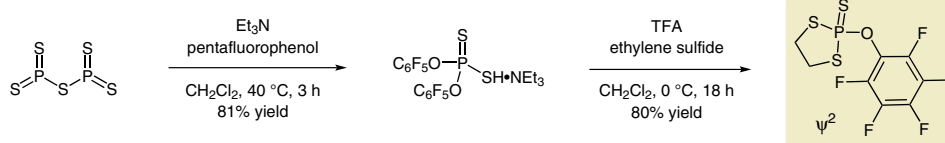
Key words

P(V) chemistry
 phosphate-based
 linkages
 phosphorothioates
 phosphorodithioates
 phosphate diesters

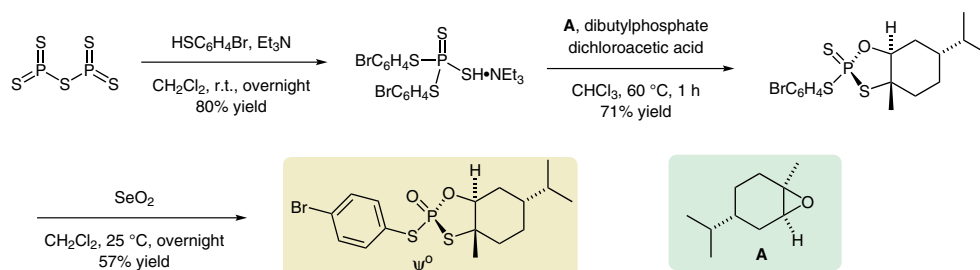
On-Demand Synthesis of Modified Oligonucleotides



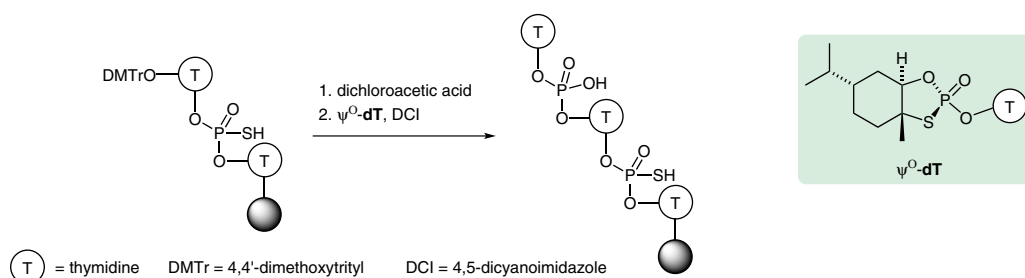
Synthesis of ψ^2 reagent:



Synthesis of ψ^0 reagent:



Synthesis of phosphorothioate/phosphodiester oligonucleotide:



Significance: Oligonucleotides with unnatural phosphate linkages have emerged as promising drug candidates due to their desirable pharmacological properties. Accordingly, many FDA approvals have been issued for therapeutic oligonucleotides in the last years. Their synthesis, however, is challenging using existing methods.

Comment: Based on the phosphorous sulfur incorporation (PSI or ψ) reagent for the synthesis of optically pure phosphorothioates (*Science* **2018**, 361, 1234), the researchers developed three new reagents for the synthesis of racemic phosphorothioates (*rac-ψ*), phosphorodithioates (ψ^2), and phosphate diester (ψ^0) linkages.

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Synfact
 of the
 Month

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