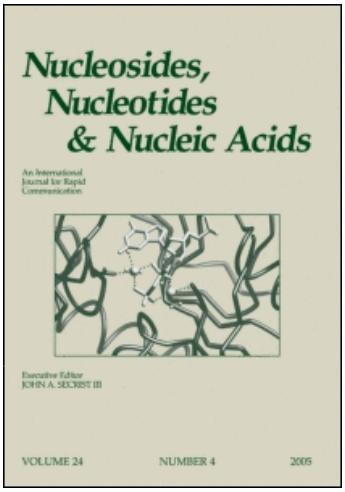

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Rapid Chemical Synthesis of Oligodeoxyribonucleotides by the Improved Phosphotriester Method

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RAPID CHEMICAL SYNTHESIS OF OLIGODEOXYRIBONUCLEOTIDES BY THE IMPROVED PHOSPHOTRIESTER METHOD

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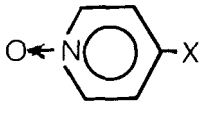
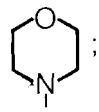
Summary. An efficient phosphotriester methodology based on the use of condensing agents in the presence of several new nucleophilic catalysts has been developed.

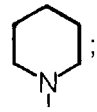
Earlier, we have developed the rapid variant of the phosphotriester approach based on the use of arylsulfonyl chlorides in the presence of N-methylimidazole as coupling reagents for internucleotide bond formation. Now, we report that using condensing agents in conjunction with more powerful nucleophilic catalysts, such as derivatives of pyridine N-oxide (I)-(V), leads to further increase of the rate of phosphotriester bond formation and minimizes the amount of by-products caused by the modification of heterocyclic bases. These catalysts allow to perform condensations in different organic solvents (acetonitrile, pyridine, dioxane, $CHCl_3$, CH_2Cl_2, $C_2H_4Cl_2$, etc.). In the



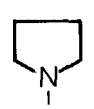
X= $-N(CH_3)_2$ (I); $-N(C_2H_5)_2$ (II);



(III)



(IV)



(V)

presence of (I)-(V), condensations in solution go to a completion in 0.75, 1.0 and 1.5 min under the action of mesitylenesulfonyl chloride, mesitylenesulfonyl 3-nitro-1,2,4-triazolide and triisopropylbenzenesulfonyl chloride,respectively. On polymer supports (pore glass or paper disks), the coupling reactions are complete in 2-4 min. Thus, the overall time for addition of each nucleotide to a growing chain on solid phase is about 10 min. Furthermore, these catalysts three times increase the rate of phosphotriester bond formation in the hydroxybenzotriazole approach.

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