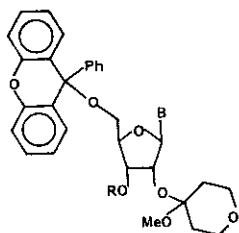


CHEMICAL SYNTHESIS OF AN UNDECARIBONUCLEOSIDE DECAPHOSPHATE CONSTITUTING THE 3'-TERMINAL ACCEPTOR STEM SEQUENCE OF YEAST tRNA^{Phe}.M. Kwiatkowski¹, J. Heikkilä¹, S. Björkman¹, H. Seliger² and Jyoti Chattopadhyaya¹¹ Department of Microbiology, The Biomedical Center, Box 581, University of Uppsala, S-751 23 Uppsala, Sweden.² Sektion Polymere, Universität Ulm, Oberer Eselsberg, D-7900 Ulm, West Germany.

The preparation of 5'-r(HO-ApUpUpCpGpCpApCpCpA-OH)^{3'}, by the phosphotriester approach, is described using fully protected tri- and tetra-ribonucleotide blocks. The salient features include the employment of 9-phenylxanthin-9-yl (Pixyl)¹ as a 5'-protecting group, 4-methoxytetrahydropyranyl- (MTHP)² as a 2'-protecting group and fluoren-9-methyl-(FM)³ as a 3'-terminal phosphate protecting group. Thus, successful employment of fluoren-9-methyl as a phosphate protecting group has enabled us to carry out a block synthesis strategy leading to oligoribonucleotides in high overall yields.

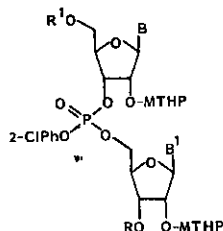
The key ribonucleoside building blocks, (general formula: (1)), were prepared starting from 3',5'-di-O-1,1,3,3-tetraisopropylidisiloxane-1,3-d-yl⁴ derivatives of the corresponding-N-protected ribonucleosides and uridine. They were then converted⁵ to the 2-chlorophenylphosphodiester salts, (general formula: (2)). These phosphodiester salts were then regioselectively⁶ condensed with a 3', 5'-dihydroxy ribonucleoside block to obtain partially protected (3' 5')-diribonucleotide blocks, (general formula: (3)), or a fully protected mononucleotide block (4). (3) could be easily converted to (5) with the help of 2-chlorophenylphosphorobis-(1,2,4-triazolide) in an usual way⁵. The phosphodiester salts, (general formula: (5)) could be used as a 5'-protected component for a further condensation with a 5'-hydroxy block. The 5'-hydroxy blocks were prepared by selective removal of the pixyl group by ZnBr₂ in CH₂Cl₂ at 0°C when the MTHP group was completely stable. (5) could also be employed in the preparation of the 5'-hydroxy blocks, (general formula: (7)), after the protection of the 3'-phosphodiester at the level of a triester with the help of fluoren-9-methyl-(FM) group. The fully protected phosphotriesters, (4) and (6), were completely stable under the conditions of normal manipulations during the synthesis; yet the FM group could be conveniently deprotected selectively to generate the phosphodiester salts within an hour at 20°C with the help of Et₃N (10 equiv.) in dry pyridine solution. The 5'-protected phosphodiester salts were then coupled to the appropriate 5'-hydroxy blocks to give the fully protected tri- and tetra- oligoribonucleotide blocks. They were then subsequently assembled to obtain the undecaribonucleotide, which was eventually deprotected to obtain the target sequence.



(1) R = H.

(2) R = PHOSPHODIESTER;

(4) R = PHOSPHOTRIESTER.



(3) R = H; R' = PIXYL;

(5) R = PHOSPHODIESTER

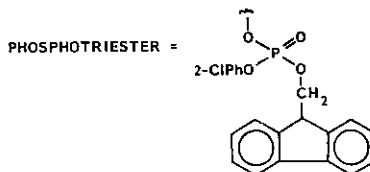
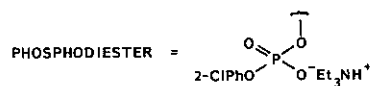
R' = PIXYL;

(6) R = PHOSPHOTRIESTER

R' = PIXYL;

(7) R = PHOSPHOTRIESTER

R' = H.



References:

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5. These two papers show the application of the FM group in DNA synthesis
6. W.T. Markiewicz, J. Chem. Res.(S) 24 (1979)
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