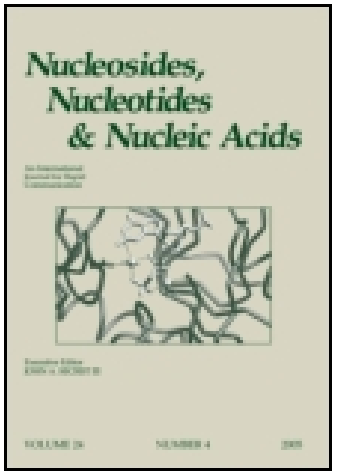

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The 9-Fluorenylmethoxycarbonyl (Fmoc) Group and Its Use in Oligonucleotide Synthesis

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THE 9-FLUORENYLMETHOXYCARBONYL (Fmoc) GROUP AND ITS USE IN OLIGONUCLEOTIDE SYNTHESIS

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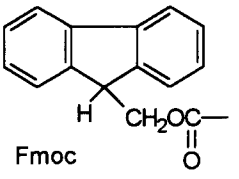
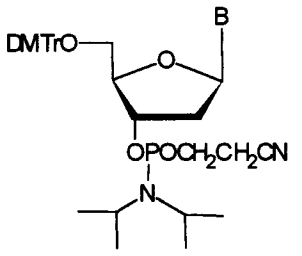
ABSTRACT: The introduction of the base-labile 9-fluorenylmethoxycarbonyl (Fmoc) group into the exocyclic amino function of 2'-deoxynucleosides and their dimethoxytritylation and phosphitylation is described. The resulting key intermediates were investigated in the built-up of different oligodeoxyribonucleoside phosphate and thiophosphate chains which were deprotected under mild basic conditions leading to crude oligomers of high purity.

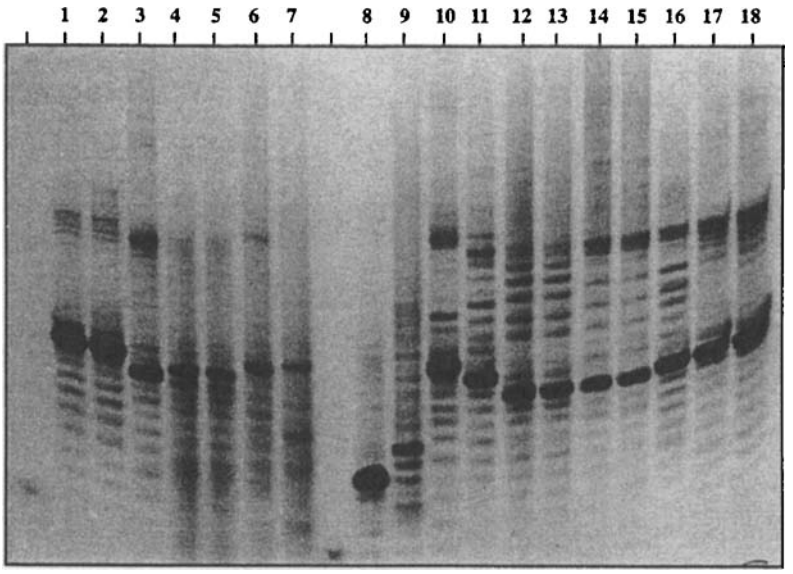
The synthesis of the fluorenylmethoxycarbonyl-protected 2'-deoxyribonucleoside phosphoramidites follows the common techniques introducing first the base labile protecting group [1-4] into the exocyclic amino functions of the 2'-deoxyadenosine, 2'-deoxycytidine and 2'-deoxyguanosine, then dimethoxytritylation at 5'-OH and subsequent phosphitylation in 3'-OH position. Due to the base-labile characteristic of the fmoc group careful purification of each derivative is crucial to obtain pure and stable compounds.





B
Ade^{fmoc}
Ade$^{fmoc}_2$
Cyt^{fmoc}
Gua^{fmoc}
Gua$^{fmoc}_2$
Gua$^{npe}_{fmoc}$

The corresponding phosphoramidites and the fmoc-protected solid support material can be used in the usual manner in machine-controlled oligonucleotides cycles without



PAGE of synthesized oligonucleotides: 5'-d(CGTGGGTGATGGGAT)$_{P=O}$-3' (**1,2**); 5'-d(ACTTGGATACGCACG)$_{P=O}$-3' (**3**); 5'-d(ACTTGGATACGCACG)$_{P=S}$-3' (**4,5**); 5'-d(GGAAGATGTCGCAGT)$_{P=S}$-3' (**6**); 5'-d(CGTGGGTGATGGGAT)$_{P=S}$-3' (**7**); 5'-d(A$_{10}$)$_{P=O}$-3' (**8**); 5'-d(A$_{12}$)$_{P=O}$-3' (**9**); 5'-d(CGTCGTTGGATGCTGC)$_{P=O}$-3' (**10**); 5'-d(GTAACTTATGCGGGC)$_{P=O}$-3' (**11**); 5'-d(CAGCCCCCAAGGTAC)$_{P=O}$-3' (**12, 13**); 5'-d(GCACCCACTACCCTA)$_{P=O}$-3' (**14,15**); 5'-d(TAAACCTTACTGAAC)$_{P=O}$-3' (**16**); 5'-d(CATTGAATACGCCCG)$_{P=O}$-3' (**17,18**)

harming the nucleobase protecting groups. The final deprotection steps of the resulting oligonucleoside phosphates and thiophosphates were carried out under weakly basic conditions (e.g. 0.05 M DBU in CH_3CN) to split off the fmoc and cyanoethyl groups *via* β-elimination and followed by treatment with ammonia to cleave the synthesized oligonucleotide from the solid support. HPLC-analysis and polyacrylamide gelelectrophoresis documented good quality of the crude oligomers which do not need further purification.

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