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Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

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Base Labile Protecting Groups for Hydroxyl Functions in Ribonucleosides and Deoxyribonucleosides

H. Schirmeister^a; W. Pfeleiderer^a

^a Fakultät für Chemie, Universität Konstanz, Konstanz

To cite this Article Schirmeister, H. and Pfeleiderer, W.(1987) 'Base Labile Protecting Groups for Hydroxyl Functions in Ribonucleosides and Deoxyribonucleosides', *Nucleosides, Nucleotides and Nucleic Acids*, 6: 1, 501 — 503

To link to this Article: DOI: 10.1080/07328318708056269

URL: <http://dx.doi.org/10.1080/07328318708056269>

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BASE LABILE PROTECTING GROUPS FOR HYDROXYL FUNCTIONS IN
RIBONUCLEOSIDES AND DEOXYRIBONUCLEOSIDES

H. Schirmeister and W. Pfleiderer

Fakultät für Chemie, Universität Konstanz, D-7750 Konstanz

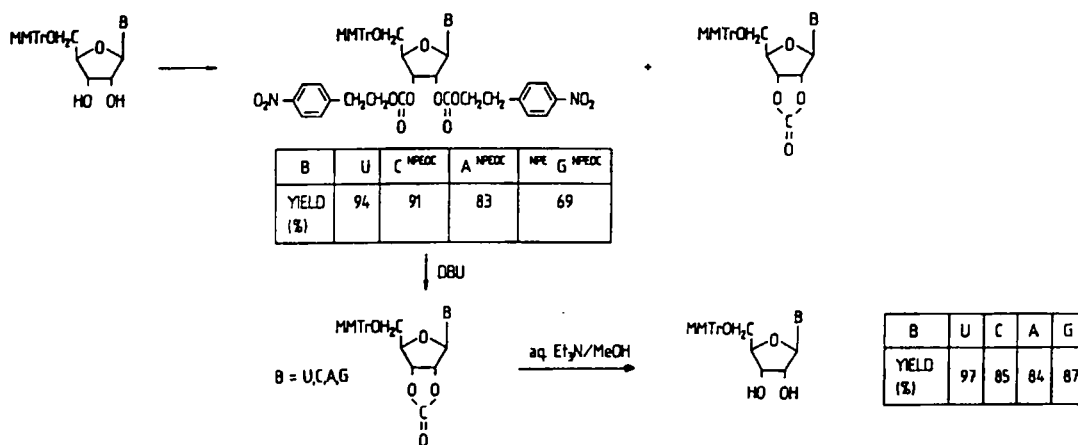
Summary: The use of the base labile 2-(p-nitrophenyl)-ethoxycarbonyl (NPEOC), 2-(2,4-dinitrophenyl)-ethoxycarbonyl (DNPEOC) and 2-cyanoethoxycarbonyl (CEOC) group for hydroxyl protection of the sugar moiety in ribonucleosides and deoxyribonucleosides are described and discussed.

The protection of sugar hydroxyl functions represents an important step in designing a strategy for a multistep chemical synthesis of oligonucleotides (1). The striking features of the p-nitrophenylethyl (NPE) and 2-(p-nitrophenyl)-ethoxycarbonyl (NPEOC) protecting group for various functions (2,3,4) prompted us to use the latter base labile group for blocking the hydroxyl groups in ribo- and deoxyribonucleosides respectively.

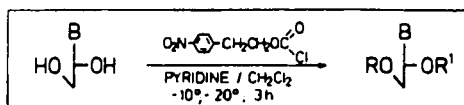
Treatment of 5'-O-MMTr-ribonucleosides proceeds in high yields with 1-methyl-3-p-nitrophenylethoxycarbonylimidazolium chloride in presence of 4-dimethylaminopyridine in dry CH_2Cl_2 within 2 h to the corresponding 2',3'-di-O-carbonates and formation of little 2',3'-cyclic carbonate derivatives (Scheme 1).

The NPEOC groups as well as the 2-(2,4-dinitrophenyl)-ethoxycarbonyl (DNPEOC) group are also suitable for selective protection of the 5'-hydroxy position in deoxyribonucleosides. Dropwise addition of the 2-(4-nitrophenyl)-ethyl chloroformate and 2-(2,4-dinitrophenyl)-ethyl chloroformate respectively to the deoxyribonucleosides in dry pyridine at -10°C resulted after few hours in high yields of the corresponding 5'-O-protected deoxyribonucleoside derivatives (Schemes 2,3).

The NPEOC group is removable quantitatively at 20°C by action of 0.5 M DBU in dry pyridine whereas the DNPEOC group can be cleaved under relatively mild reaction conditions by

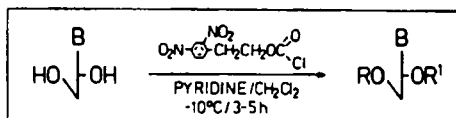


SCHEME 1



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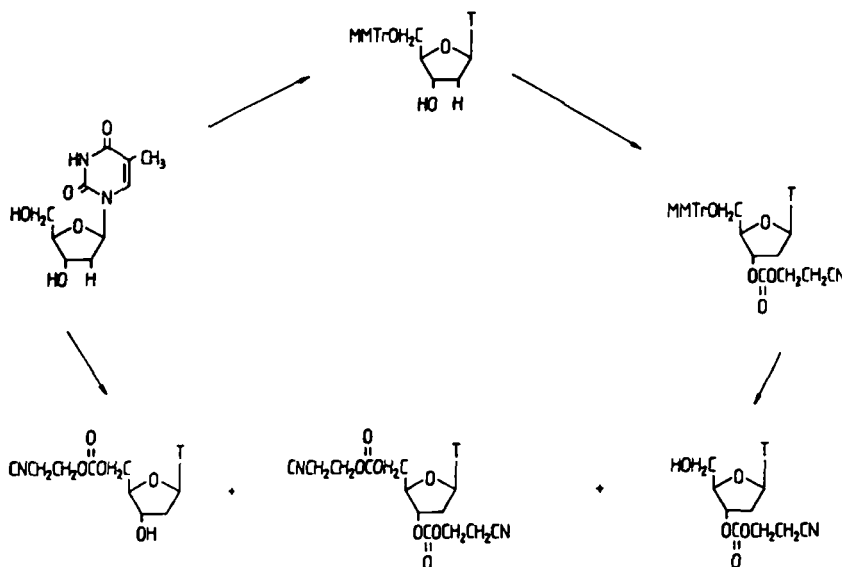
SCHEME 2



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SCHEME 3

2 - CYANOETHOXYCARBONYL - PROTECTING



SCHEME 4

triethylamine to unmask the 5'-OH function (5). The experimental details will be published soon.

Another easily accessible reagent, the 2-cyanoethyl chloroformate (6) can also conveniently be used for the protection of hydroxy functions at the sugar moiety of ribo- and deoxyribonucleosides respectively (Scheme 4).

For instance, the reaction of thymidine with CEOCOC1 leads to the desired 5'-O-(2-cyanoethoxycarbonyl)-thymidine in satisfactory yield and the selective cleavage was possible by treatment with aqueous triethylamine within few minutes.

R E F E R E N C E S

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