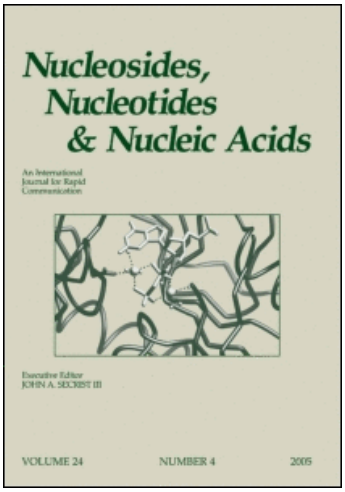

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis of 2'-O-p-Nitrophenylethylsulfonyl-Ribonucleosides

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To cite this Article Pfister, M. and Pfleiderer, W.(1987) 'Synthesis of 2'-O-p-Nitrophenylethylsulfonyl-Ribonucleosides', Nucleosides, Nucleotides and Nucleic Acids, 6: 1, 505 — 507
To link to this Article: DOI: 10.1080/07328318708056270
URL: http://dx.doi.org/10.1080/07328318708056270

NUCLEOSIDES & NUCLEOTIDES, 6(1&2), 505-507 (1987)

SYNTHESIS OF 2'-O-p-NITROPHENYLETHYLSULFONYL-RIBONUCLEOSIDES

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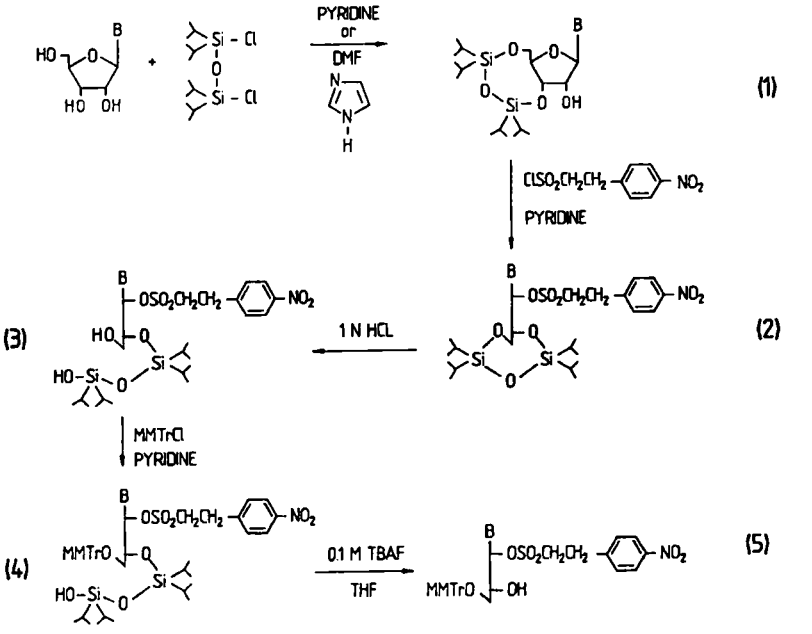
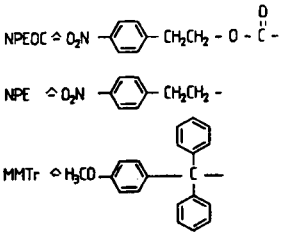
The appropriate protection of the 2'-OH group in ribonucleosides is the crucial point of oligoribonucleotide synthesis. The use of the tetrahydropyranyl (1), 4-methoxytetrahydropyranyl (2), tert.butyldimethylsilyl (3) and o-nitrobenzyl group (4) respectively has its limitations in the acid sensitivity or the problems arising during the deprotection steps. A more stable blocking group is needed, which is stable towards acid and base treatment but can be cleaved selectively under different conditions.

The striking features of the p-nitrophenylethyl (NPE) and p-nitrophenylethoxycarbonyl (NPEOC) group (5,6) as universal protecting groups of various functionalities prompted us to develop the p-nitrophenylethylsulfonyl (NPES) group to block the 2'-hydroxy function in ribonucleosides. The common advantage of these three similar protecting groups is seen in the relatively stable ester bonds against mild hydrolyses but the clean and easy cleavage by a ß-elimination process in aprotic solvents. The low reactivity of 2'-sulfonate esters of carbohydrates in general towards nucleophilic displacements (7) and their high stability regarding intremolecular migration favours the NPES group in every respect over the commonly used blocking groups.

The synthesis of the 2'-O-p-nitrophenylethylsulfonyl-ribonucleosides was achieved starting from the 3',5'-O-(tetraisopropyldisiloxane-1,3-diyl)-ribonucleosides (8). The 2'-hydroxy function was then protected by treatment with p-nitrophenylethylsulfonyl chloride in dry pyridine at room temp. for about 2 h. The 3',5'-disiloxane bridge can regioselectively be opened to release the 5'-OH group by acid hydrolysis (1 M HCl in dry dioxane, room temp., 1-2 h). Protection at this part of the molecule was done by monomethoxytritylation. The 3'-O-silyl groups was then removed by action of tetra-n-butylammonium fluoride in dry THF at $0^{o}C$ for 1-2 min and

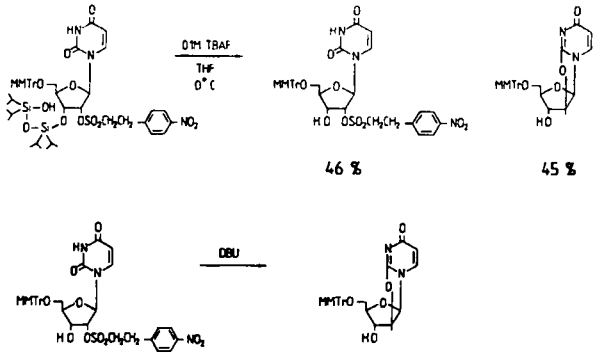


B	1	2	3	4	5
A^{NPEOC}	76%	94%	88%	94%	98%
$^{NPE}G^{NPEOC}$	74%	82%	91%	91%	67%
C^{NPEOC}	86%	67%	87%	63%	58%
U	97%	75%	99%	75%	46%



proceeded well with the corresponding derivatives of adenosine, guanosine, and cytidine respectively.

A side reaction was only noticed with 5'-O-monomethoxytrityl-2'-O-p-nitrophenylethylsulfonyl-3'-O-tetraisopropyldisiloxane-3-ol-1-yl-uridine on fluoride ion treatment forming the 2,2'-anhydro-5'-O-monomethoxytrityl-uridine, which resulted also by treatment of 5'-O-monomethoxytrityl-2'-O-p-nitrophenylethylsulfonyl-uridine. Migration of the NPES group could so far not be observed.



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