

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

Amide Protection in Oligodeoxynucleotide Synthesis

Joachim W. Engels^a; Matthias Mag^a

^a Institut für Organische Chemie, Universität Frankfurt/M., Frankfurt/Main

To cite this Article Engels, Joachim W. and Mag, Matthias(1987) 'Amide Protection in Oligodeoxynucleotide Synthesis', *Nucleosides, Nucleotides and Nucleic Acids*, 6: 1, 473 — 475

To link to this Article: DOI: 10.1080/07328318708056261

URL: <http://dx.doi.org/10.1080/07328318708056261>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

AMIDE PROTECTION IN OLIGODEOXYNUCLEOTIDE SYNTHESIS

Joachim W. Engels and Matthias Mag
Institut für Organische Chemie, Universität Frankfurt/M.,
D-6000 Frankfurt/Main 50

Summary: Several O⁶-protected deoxyguanosine- as well as O⁴-protected thymidine-phosphoramidites were prepared according to the Mitsunobu reaction and Michael addition and were tested in a solid-phase automated DNA synthesizer.

During the last ten years some possible side reactions of the amide function of thymidine and deoxyguanosine, especially the phosphorylation by activated nucleotides, have been reported. In order to look into this problem we prepared several derivatives which can be cleaved by β -elimination. The nucleosides 2a-f were tried to synthesize via a Mitsunobu reaction, using the procedure developed by Pfleiderer et al. <1>, applying additionally the transient protection method of Jones et al. <2>. But only the

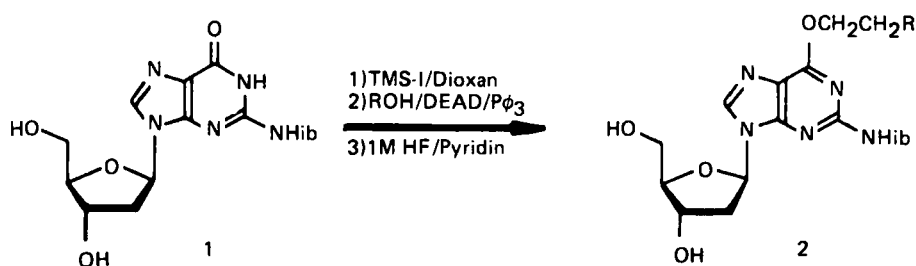


Fig.1 2a R = -C₆H₄NO₂, (NPE), 80%; 2b R = -S-C₆H₄NO₂, (NPTE), 40%; 2c R = -S-C₆H₅, 0%; 2d R = -SO₂-C₆H₄NO₂, 2,0%; 2e R = -SO₂-C₆H₅, 0%; 2f R = -CN, 0%

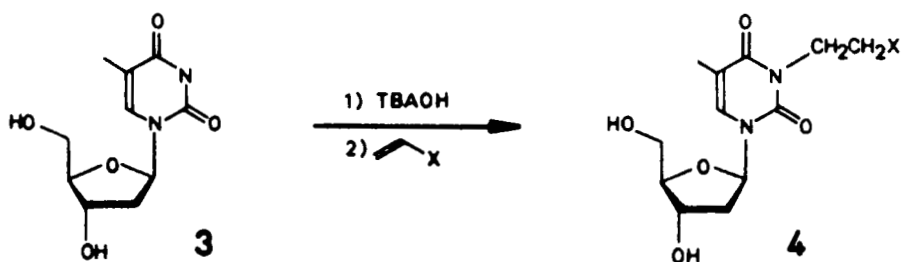


FIG.2 4a R = $-\text{SO}_2-\text{C}_6\text{H}_4\text{NO}_2$, 84%; 4b R = $-\text{SO}_2-\text{C}_6\text{H}_5$, 80%; 4c R = $-\text{SO}_2-\text{CH}_3$, 20%; 4d R = $-\text{CN}$, 45%



Fig.3

compounds 2a-b were obtained by using this transient protection/Mitsunobu alkylation sequence.

The NPE group can be cleaved by DBU in aprotic solvents while we had to oxidise the NPTE group to the sulfoxide before the cleavage by ammonia could be accomplished.

The appropriately protected thymidines were obtained by adding the Michael acceptors to a pyridine solution of dT in the presence of tetrabutyl ammonium hydroxyde (TBAOH) <3>. Structure assignments of 4a-c for N- or O-alkylation were done by 2-D-NMR in the COLOC-experiment <4> ¹³C-shift as well as ³J-coupling support the above assignment of N-alkylation.

The protected 2a and 4a were subsequently tritylated and converted to the phosphoramidites. These monomers were used for the syntheses of the sequences (Fig.3) with a ABI 380A DNA-synthesizer. After ammonia deprotection the crude mixtures were directly loaded on a 1mm 12%/7M urea polyacrylamide gel and visualized by uv-shadowing.

Conclusion: When using a long cycle (Ogilvie et al., <5>, coupling time 360s) O-6 protection seems to be advantageous, whereas shorter addition times (20s) do not seem to justify additional amide protection in this system.

REFERENCES

- <1> W. Pflleiderer et al., Tetrahedron 1, 59 (1984)
- <2> R. Jones et al., J.Org.Chem. 51, 755 (1986)
- <3> G.I. Tesser et al., Tetrahedron Lett. 32, 3859 (1985)
- <4> H. Kessler et al., J.Magn.Res. 57, 331, (1984)
- <5> K.K. Ogilvie et al., Nucleic Acids Res. 18, 6447 (1985)