

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>

Synthesis of Modified Thymidine Dimers

S. Farkas^a; W. Pfeleiderer^a

^a Fakultät für Chemie, Universität Konstanz, Konstanz

To cite this Article Farkas, S. and Pfeleiderer, W.(1987) 'Synthesis of Modified Thymidine Dimers', *Nucleosides, Nucleotides and Nucleic Acids*, 6: 1, 509 — 511

To link to this Article: DOI: 10.1080/07328318708056271

URL: <http://dx.doi.org/10.1080/07328318708056271>

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.

SYNTHESIS OF MODIFIED THYMIDINE DIMERS

S. Farkas and W. Pfeleiderer

Fakultät für Chemie, Universität Konstanz, D-7750 Konstanz

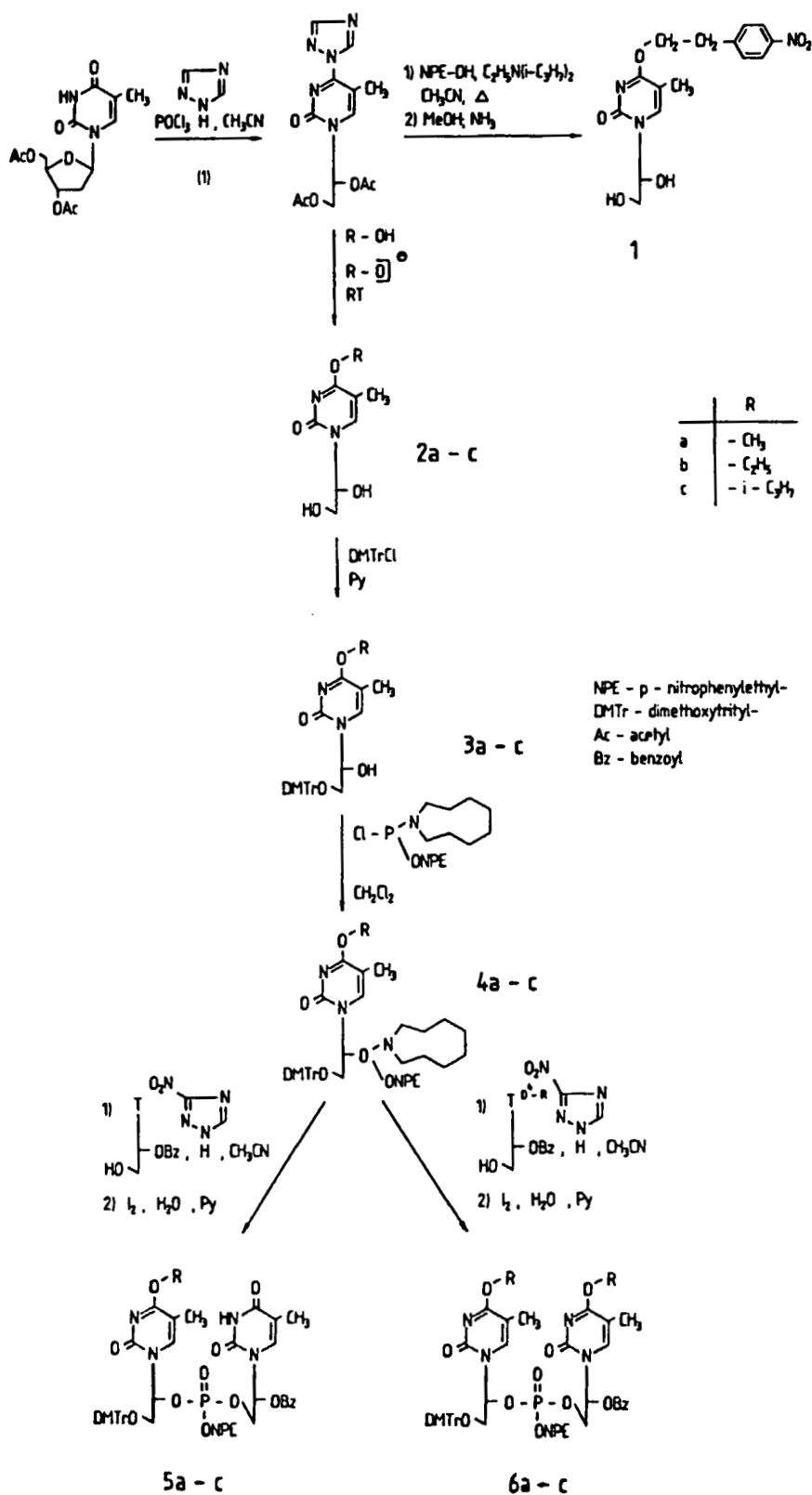
Alkylating agents are mutagenic and carcinogenic substances due to reaction with the pyrimidine and purine bases of the various nucleic acids. The thymine base can be alkylated at N³-, O²- or O⁴-position. Their behaviour during transcription and replication is unknown (1).

The direct synthesis of O⁴-alkylthymidine (2a-c) by normal alkylating agents is difficult, but the preparation can be achieved in good yields if 5-methyl-2-oxo-1-(3,5-di-O-acetyl-2-deoxyribofuranosyl)-4-(1,2,4-triazol-1-yl)-1,2-dihydropyrimidine (2) is treated with sodium methoxide, ethoxide, and isopropoxide respectively.

The 5'-O-dimethoxy-O⁴-alkylthymidines (3a-c) and the corresponding phosphoramidites, O⁴-alkyl-5'-O-dimethoxytrityl-3'-O-[(p-nitrophenylethoxy, N-octa-hydroazonino)phosphino]-thymidine, were prepared by analogous procedures according to the literature (3) in good yields. The phosphoramidites can be purified by silica gel chromatography and the resulting solid foam is quite stable and can be stored at room temp. for several months without decomposition.

The phosphoramidites (4a-c) were condensed with 3'-O-benzoylthymidine and 3'-O-benzoyl-O⁴-alkylthymidine respectively to the corresponding dimers (5a-c) and (6a-c).

The introduction of the p-nitrophenylethyl group into O⁴-position of thymidine was performed from 5-methyl-2-oxo-1-(3,5-di-O-acetyl-2-deoxyribofuranosyl)-4-(1,2,4-triazol-1-yl)-1,2-dihydropyrimidine with p-nitrophenylethanol in presence of Hünig's base followed by deacylation with ammonia in methanol to give the required O⁴-p-nitrophenylethylpyrimidine in good yield.



R E F E R E N C E S

1. B. Singer, J.T. Kusmierek, *Ann.Rev.Biochem.* 52, 655 (1982);
2. C.B. Reese, P.A. Skone, *J.Chem.Soc., Perk.Trans. I*, 6, 1263 (1984);
3. M.W. Schwarz, W. Pfeleiderer, *Tetrahedron Lett.* 1984, 5513.