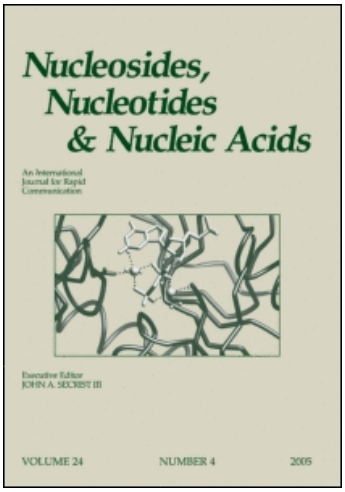


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis and Antimalarial Activity of Novel N^6-Substituted Adenosine Derivatives

P. H. Heidler[a]; C. Herforth[a]; A. Link[ab]
[a] Faculty of Pharmacy, University of Marburg, Marburg, Germany [b] Universität Hamburg, Institut für Pharmazie, Hamburg, Germany

Online publication date: 09 August 2003

To cite this Article Heidler, P. H. , Herforth, C. and Link, A.(2003) 'Synthesis and Antimalarial Activity of Novel N^6-Substituted Adenosine Derivatives', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 977 — 979
To link to this Article: DOI: 10.1081/NCN-120022717
URL: http://dx.doi.org/10.1081/NCN-120022717

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 977–979, 2003

Synthesis and Antimalarial Activity of Novel N^6-Substituted Adenosine Derivatives

P. H. Heidler, C. Herforth, and A. Link*

Faculty of Pharmacy, University of Marburg, Marburg, Germany

Substituted adenosine analogues were previously obtained as hits in a screening program focussed on the identification of novel drug leads for antimalarial chemotherapy.[1]

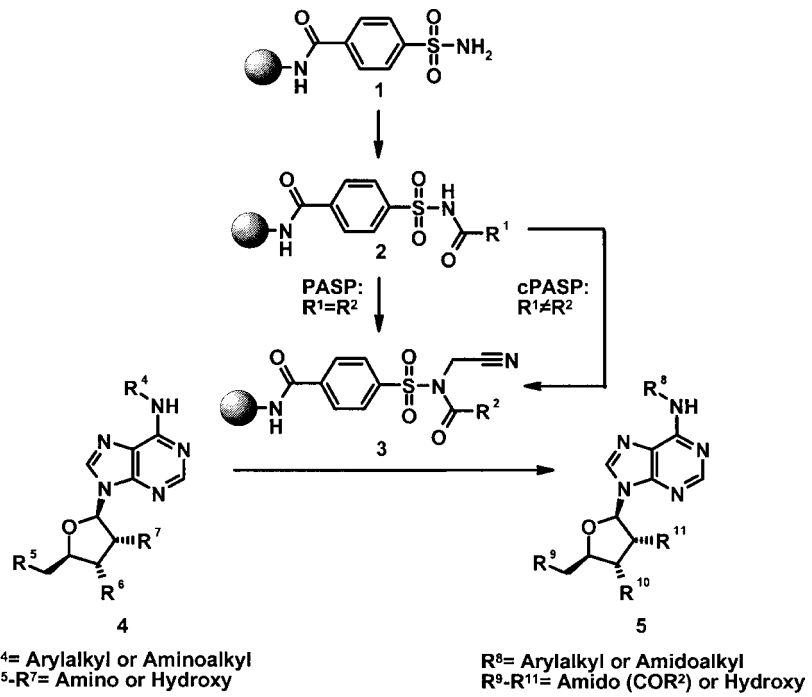
Continuing these efforts, we have investigated the in vitro antimalarial activity of a new series of adenosine derivatives **5** combining available information on favourable substitution patterns.

The results show that e.g., N^6-(1-naphthylmethyl)-5′-deoxy-5′-(amido)-adenosines as well as N^6-(4-phenylbenzyl)-5′-deoxy-5′-(amido)adenosines display significant activity against the malaria causing parasites, with the sterically demanding bisubstituted species reported being active in most cases in the low-micro molar range.

*Correspondence: A. Link, Universität Hamburg, Institut für Pharmazie, Bundesstrasse 45, Hamburg D-20146, Germany; Fax: +49 404 2838 6573; E-mail: andreas.link@chemie.uni-hamburg.de.

DOI: 10.1081/NCN-120022717
1525-7770 (Print); 1532-2335 (Online)

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



Scheme 1. Scaffold derivatization yielding a library of adenosine derivatives **5**.

The novel compounds were obtained applying an efficient convergent polymer-assisted solution phase (cPASP) synthesis protocol. The nucleoside building blocks were assembled in solution via multi-step synthesis and treated with an excess of polymer-supported carboxylic acid equivalents in parallel leading to chemoselective, practically quantitative conversion of the amines to the desired amides, as described.[2,3]

Work-up consisted of filtration and removal of the solvent, yielding the target compounds in sufficient purity, ready for biological evaluation.

In addition to amino deoxy modification of the ribose moiety, N^6-alkylamino functionalised derivatives could be shown to be distinctly suited for the introduction of diversity elements into the molecular regions of interest.

REFERENCES

1. Golisade, A.; Herforth, C.; Quirijnen, L.; Maes, L.; Link, A. Improving an antitrypanosomal lead applying nucleophilic substitution on a safety catch linker. Bioorg. Med. Chem. **2002**, *10*, 159–165.
2. Golisade, A.; Wiesner, J.; Herforth, C.; Jomaa, H.; Link, A. Anti-malarial activity of N^6-substituted adenosine derivatives. Part I. Bioorg. Med. Chem. **2002**, *10*, 769–777.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

3. Herforth, C.; Wiesner, J.; Franke, S.; Golisade, A.; Jomaa, H.; Link, A. Antimalarial activity of N^6-substituted adenosine derivatives (Part 2). J. Comb. Chem. **2002**, *4*, 302–314.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016