

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>

## **Novel Analogues of the Nucleoside Antibiotics Coroyepin**

Vasu Nalr<sup>a</sup>; David F. Purdy<sup>a</sup>; Arthur G. Lyons<sup>a</sup>

<sup>a</sup> Department of Chemistry, The University of Iowa Iowa City, Iowa, U. S. A.

**To cite this Article** Nalr, Vasu , Purdy, David F. and Lyons, Arthur G.(1991) 'Novel Analogues of the Nucleoside Antibiotics Coroyepin', *Nucleosides, Nucleotides and Nucleic Acids*, 10: 1, 497 — 498

**To link to this Article:** DOI: 10.1080/07328319108046506

**URL:** <http://dx.doi.org/10.1080/07328319108046506>

**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.

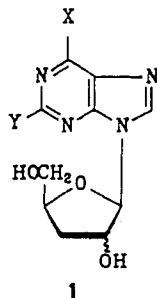
The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any 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.

### NOVEL ANALOGUES OF THE NUCLEOSIDE ANTIBIOTIC, CORDYCEPIN

Vasu Nair\*, David F. Purdy and Arthur G. Lyons  
Department of Chemistry, The University of Iowa  
Iowa City, Iowa 52242, U. S. A.

**Abstract.** The syntheses of novel compounds of the cordycepin family including stereochemically modified analogues are described. Hypoxanthine counterparts of these compounds have also been obtained.

The nucleoside antibiotic, cordycepin (3'-deoxyadenosine), was originally isolated from *Cordyceps militaris* and *Aspergillus nidulans*.<sup>1</sup> Cordycepin is known to have antiviral activity against a number of RNA viruses.<sup>2</sup> The biochemical basis for this mechanism of action is thought to be a result of the inhibition of the viral RNA polymerase activity by cordycepin 5'-triphosphate. Analogues of cordycepin would therefore be of potential antiviral interest. However, very few examples of compounds related to this nucleoside antibiotic have been described. This paper reports on the synthesis of some novel compounds of the cordycepin family. Synthesis of analogues of the hypoxanthine counterpart of cordycepin as well as stereochemically modified analogues have also been investigated. The target compounds can be illustrated by the general structure 1 where X



may be  $\text{NH}_2$  or  $\text{OH}$  and  $Y$  represents a variety of functional groups such as  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-\text{CHO}$ ,  $-\text{CONH}_2$ ,  $-\text{CH}=\text{CH}_2$ ,  $-\text{C}\equiv\text{CH}$ , and others.

The strategy for the syntheses involved starting with readily available natural guanosine, tailoring it to an appropriate precursor, sequentially modifying the carbohydrate and base moieties, and finally elaborating the immediate product. A key intermediate for the cordycepin analogues in this sequence of reactions was protected 2-iodo-3'-deoxyadenosine, synthesized from 2-amino-6-chloropurine nucleoside in five steps involving the following reactions and positions: bis-silylation (2',5'), deoxygenation (3'), iodination (2), and nucleophilic displacement with ammonia (6). Introduction of specific functionality at the 2-position and their elaboration were carried out by metal mediated functionalizations, photochemical reactions, and ozonolysis.<sup>3,4</sup> Hypoxanthine nucleoside counterparts were synthesized by related methodologies. Cordycepin analogues where the stereochemistry is inverted (i.e.  $\beta$ ) at the 2'-position have also been investigated. Confirmation of structures of intermediate regioisomers and stereoisomers and products were made using high-field  $^1\text{H}$  and  $^{13}\text{C}$  NMR data including COSY NMR data.

**Acknowledgment.** We thank the U. S. Army Medical Research and Development Command for support of this research.

#### REFERENCES

1. Cunningham, K. G.; Hutchinson, S. A.; Manson, W.; Spring, F. S. J. Chem. Soc. 1951, 2299.
2. Suhadolnik, R. J. "Nucleosides as Biological Probes," Wiley: New York, 1979, pp 118-135.
3. Nair, V.; Buenger, G. A. J. Am. Chem. Soc. 1989, **111**, 8502.
4. Nair, V.; Lyons, A. G. Tetrahedron 1989, **45**, 3653.