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7-Deaza Analogues of Carbovir. Synthesis and Antiviral Evaluation

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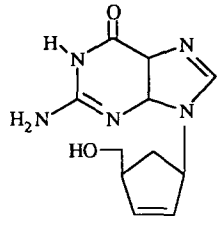
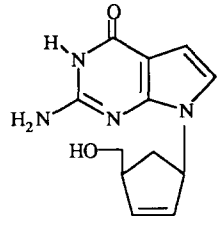
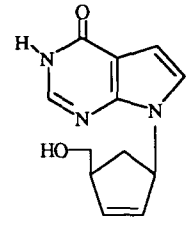
Carbovir (**1**) has emerged as the first carbocyclic nucleoside analogue with potential as a therapeutic agent for the treatment of AIDS. Therefore we have been interested to synthesize some deaza analogues of **1** in order to evaluate their antiviral activitie(s).



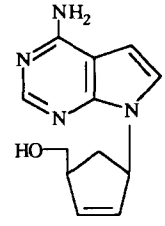
CARBOVIR (1)



(2)



(3)



(4)

The synthesis of **2**, **3** and **4** will be presented as well as their antiviral activities.

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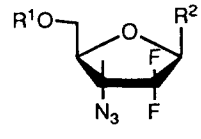
Synthesis and Anti-Viral Activity of 3'-Azido-2',3'-Dideoxy-2', 2-Difluoro-ß-D-Ribofuranosyl Nucleosides, C. J. Paget, M. T. Reamer, M. A. Winter, C. D. Jones, R. E. Holmes, T. S. Chou, J. Tang, J. Colacino, L. W. Hertel, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana, USA

A number of 2',3'-dideoxynucleosides have been shown to be potent anti-retroviral agents in vitro, with possible utility in the chemotherapy of AIDS. AZT (3'-azido-2',3'-dideoxythymidine) was the first of these compounds to be tested clinically and was found to reduce the morbidity and mortality associated with severe HIV infections. AZU (3'-azido-2',3'-dideoxyuridine) is currently in Phase I clinical trials. In our research on 2',2'-difluoronucleosides, a series of 3'-azido-2',3'-dideoxy-2',2'-difluoro-D-ribofuranosyl nucleosides (1) was synthesized and evaluated for anti-HIV activity. The synthesis of the 3-azido-2,3-dideoxy-2,2-difluororibofuranose intermediate (2) from the similarly protected 2-deoxy-2,2-difluoro-ribofuranose was accomplished by the inversion of configuration of C-3 utilizing an oxidation-reduction sequence. Conversion of the inverted 2-deoxy-2,2-difluoroxylofuranose to the triflate was followed by azide displacement yielding (2), which was then deprotected and coupled to the appropriate base. The synthetic details and anti-viral activity of this series will be presented.



(1) $R^1 = H$, $R^2 = Base$

(2) $R^1 = Bz$, $R^2 = O\text{-}Si$