20

Synthesis of 2-amino-9-(3'-azido-2',3'-dideoxy-beta-D-erythro-pentofuranosyl)-6-methoxy-9H purine (AzddMAP) and AzddGuo

M. R. Almond, J. L. Collins, B. E. Reitter, J. L. Rideout, G. A. Freeman, and M. H. St Clair
Burroughs-Wellcome Co., 3030 Cornwallis Rd., R. T. P., N. C. 27709 U. S. A.

A novel synthesis of AzddMAP and AzddGuo is described. The key step in the synthesis involves the replacement of a diphenyl carbamoyl protecting group by methanol. The furanose derivative 1,2-di-O-acetyl-3-O-mesyl-5-O-methoxycarbonyl-D-xylofuranose **1** was treated with 2-N-acetyl-6-O-diphenylcarbamoylguanine **2** according to the method of Robins (1). The product **3** was treated with methanolic HCl and 2-amino-9-(3'-O-mesyl-5'-O-(methoxycarbonyl)-beta-D-xylofuranosyl)-6-methoxy-9H-purine **4** was isolated in an 80% yield. Compound **4** was deoxygenated according to the method of Saito (2). The product **5** was treated with lithium azide and deblocked to generate AzddMAP **6**. Compound **6** was treated with bovine adenosine deaminase yielding AzddGuo.

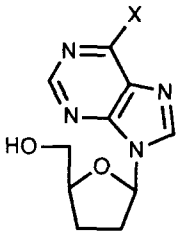
References
1) R. Zou and M. J. Robins. Can. J. Chem., 65, 1436-7 (1987).
2) I. Saito et al., J. Am. Chem. Soc., 108, 3115-7 (1986).

21

SHORT AND STEREOSELECTIVE SYNTHESIS OF A NEW BIOISOSTER OF 2',3'- DIDEOXY ADENOSINE MONOPHOSPHATE

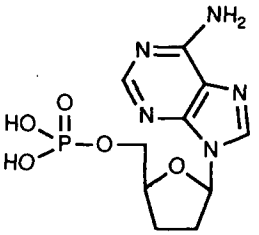
S. HALAZY , dept of chemistry , MARION MERRELL DOWRESEARCH INSTITUTE, STRASBOURG , FRANCE.

ddI (1) and ddA (1') have proven to be effective agents to prevent HIV replication *in vitro* and *in vivo* ; both of these compounds are believed to be intracellularly transformed into ddATP which is a potent inhibitor of reverse transcriptase.ddAMP (2) has been identified as a common key intermediate in these metabolic processes required for antiviral activity.

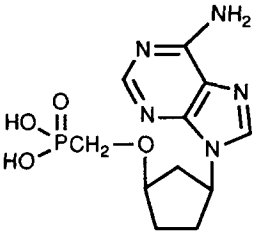


1: ddI : X=OH

1': ddA : X=NH_2



2: ddAMP



3

The carbocyclic nucleoside phosphonate 3 has been designed as a stable bioisoster of ddAMP (2). A new , short and stereoselective synthesis of 3 will be presented and discussed.