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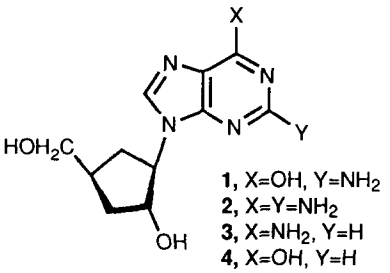
The Anti-HCMV Potential of Carbocyclic 3'-Deoxypurine Nucleosides. S.W. Schneller and W. F. Frick, Department of Chemistry, University of South Florida, Tampa, FL 33620-5250 and P.G. Medveczky, Department of Medical Microbiology and Immunology, College of Medicine, University of South Florida, Tampa, FL 33612-4799

The literature* describes the synthesis and antiviral activity for the carbocyclic nucleosides (±)-**1** and (±)-**2**. Lacking is the anti-HCMV properties for these two derivatives. This paper will present (i) a convenient synthesis of (±)-**1** and (±)-**2** and related derivatives (including (±)-3'-deoxyaristeromycin (**3**) and its hypoxanthine analogue **4**) and (ii) the anti-HCMV data for these compounds. (This work has been supported by NO1-AI-72645 and NO1-AI-72644 from the DHHS.)



1, X=OH, Y=NH_2
2, X=Y=NH_2
3, X=NH_2, Y=H
4, X=OH, Y=H

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Anti-herpes Activity of Fatty Acid Nucleoside Derivatives.

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The antiviral activity of mono and polyunsaturated fatty acids has been known for over a decade. They are active against a number of enveloped viruses and are thought to work in part by physical disruption of the virus particle. A number of clinical advantages could be obtained by the use of virucidal agents in combination with inhibitors of replication. The antiviral activity of a number of compounds, produced by the covalent addition of polyunsaturated fatty acid molecules to known antiviral nucleoside analogues, has been determined. Several of these compounds retain the ability of the polyunsaturated moiety to inactivate viruses and also retain the activity of the parental nucleoside analogue to inhibit virus replication. Indeed the hybrid molecules in some cases exceeds the activity of both parental molecules. Three compounds of interest are:- the 5' ester linoleic acid derivative of acyclovir (AK6), the 6-guanine linoleic amide derivative of acyclovir (AK13) and the di-substituted acyclovir containing both ester and amide linkages (AK11). AK11 and AK13 are potent inactivators of herpes simplex virus (HSV). At a concentration of 1-5µg/ml they are capable of destroying 90% of virus in suspension in 30 minutes. AK6 does not inactivate virus at concentrations up to 50µg/ml. AK13 has the equivalent replication inhibiting ability of acyclovir while AK6 and AK11 may be slightly less potent. The considerable lipophilicity of these compounds will increase the percutaneous absorption, cellular uptake and metabolism. Further studies are in progress to ascertain their suitability for clinical applications.