I-38

Synthesis of HOE 602 and Analogues. New Acyclic Nucleoside Derivatives with Antiviral Activity.

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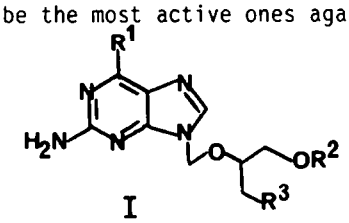
The synthesis and anti-herpetic activity of HOE 602, a new acyclic nucleoside derivative of the DHPG type is presented. Compounds of the general formular I are prepared by reaction of a suitably substituted silylated purine with a preformed 2-chloromethoxy-1,3-disubstituted glycerol. Structure-activity relationships will be discussed. Unexpectedly, compounds bearing an isopropyl ether linkage in the side chain or 6-position turned out to be the most active ones against HSV-1.



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I-39

Selective Inhibition of Human Cytomegalovirus Replication by Oxetanocin G.
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Recently, a novel nucleoside, 9-[(2R,3R,4S)-3,4-bis(hydroxymethyl)-2-oxetanyl] adenine (OXT-A), was isolated from a culture filtrate of Bacillus megaterium. This compound was the first natural product having an oxetanosyl-N-glycoside. We have evaluated for the anti-herpesvirus activities of OXT-A and its derivatives, and found that OXT-G had very potent and selective activity against human cytomegalovirus (HCMV). The selectivity index, based on the ratio of the ID_{50} for cell growth of human diploid fibroblasts to the ID_{50} for HCMV plaque formation, was more than 300. The synthesis of HCMV-induced late polypeptides such as 150K capsid and 68K major matrix proteins was strongly suppressed when OXT-G (5 ug/ml) was added to the cultures at the beginning of infection. At this concentration of OXT-G, the amount of HCMV DNA detected in the drug-treated infected cells was less than 1/10 of that detected in infected control cells. The results suggest that the mode of action of OXT-G is inhibition of viral replication by impairing the viral DNA synthesis.