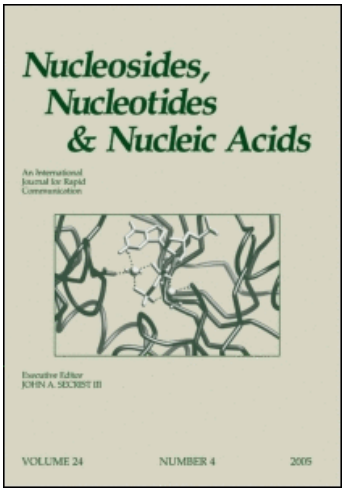

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Novel Acyclic Analogues of Purine Nucleosides: 2,3-Dihydroxy-1-Methoxypropyl and 3-Hydroxy-1-Methoxypropyl Derivatives

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NOVEL ACYCLIC ANALOGUES OF PURINE NUCLEOSIDES: 2,3-DIHYDROXY-1-METHOXYPROPYL AND 3-HYDROXY-1-METHOXYPROPYL DERIVATIVES

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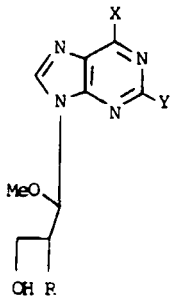
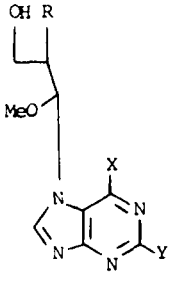
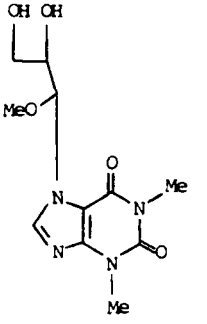
Summary Novel purine nucleoside analogues in which the N-9 ribosyl moiety is replaced by a 2,3-dihydroxy-1-methoxypropyl or 3-hydroxy-1-methoxypropyl substituent and their N-7 substituted isomers have been synthesized and tested for antiviral activity.



	X	Y	R
1	NH_2	H	OH
2	NH_2	H	H
3	OH	H	OH
4	OH	H	H
5	OH	NH_2	OH
6	OH	NH_2	H
7	NH_2	NH_2	OH



	X	Y	R
8	NH_2	H	OH
9	OH	NH_2	OH
10	OH	NH_2	H



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Synthesis of the purine derivatives (1-11) was achieved by reaction of either 1,2,3-triacetoxy-1-methoxypropane or 1,3-diacetoxy-1-methoxypropane with pertrimethylsilylated 6-N-benzoyladenine, hypoxanthine, 2-N-acetylguanine, 2,6-diacetamidopurine and theophylline in acetonitrile in the presence of stannic chloride. Acetyl and benzoyl protecting groups were removed subsequently with either ammonia in

aqueous methanol or hydrazine hydrate in ethanol. Reaction of 1,2,3-triacetoxy-1-methoxypropane with 2,6-diacetamidopurine resulted in selective N-9 substitution and with theophylline in only N-7 substitution. Reaction of either 1,2,3-triacetoxy-1-methoxypropane or 1,3-diacetoxy-1-methoxypropane with 6-N-benzoyladenine, hypoxanthine and 2-N-acetylguanine afforded both N-9 and N-7 substitution products, but only N-9 substituted hypoxanthines could be isolated. The ^{1}H and ^{13}C nmr spectra of the 2,3-dihydroxy-1-methoxypropyl derivatives indicated that in each case a mixture of diastereoisomers was obtained.

None of these acyclonucleosides was significantly active when tested against influenza A virus, parainfluenza virus 1 or herpes simplex virus 1 in cell culture.