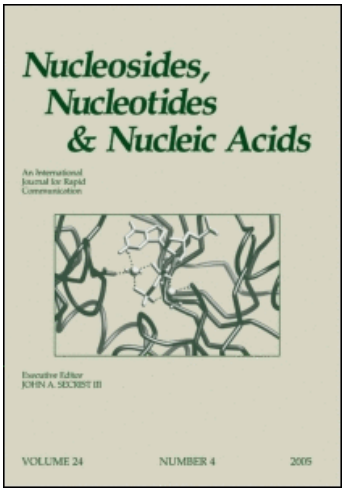


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# Novel Acyclic Analogues of Pyrimidine Nucleosides: 1-Methoxy-2, 3-Dihydroxypropyl and 1-Methoxy-3-hydroxypropyl Derivatives

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# NOVEL ACYCLIC ANALOGUES OF PYRIMIDINE NUCLEOSIDES: 1-METHOXY-2,3-DIHYDROXYPROPYL AND 1-METHOXY-3-HYDROXYPROPYL DERIVATIVES.

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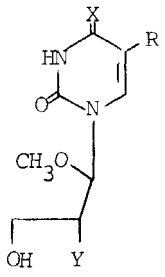
Summary The preparation of a series of novel pyrimidine nucleoside analogues in which the N-1 ribosyl moiety is replaced by 1-methoxy-2,3-dihydroxypropyl and 1-methoxy-3-hydroxypropyl substituents is described.



| | R | X | Y | | R | X | Y | | R | X | Y |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | H | O | OH | 7 | $CF_3$ | O | OH | 13 | H | O | H |
| 2 | $CH_3$ | O | OH | 8 | CN | O | OH | 14 | $CH_3$ | O | H |
| 3 | F | O | OH | 9 | $NO_2$ | O | OH | 15 | F | O | H |
| 4 | Cl | O | OH | 10 | $CH=CH_2$ | O | OH | 16 | Br | O | H |
| 5 | Br | O | OH | 11 | C≡CH | O | OH | 17 | I | O | H |
| 6 | I | O | OH | 12 | H | NH | OH | 18 | $NO_2$ | O | H |
| | | | | | | | | 19 | H | NH | H |

Synthesis of the uracil derivatives (1-11, 13-18) was achieved by reaction of the appropriate bis-trimethylsilylated pyrimidine base with either 2,3-diacetoxy-1,1-dimethoxypropane or 1,3-diacetoxy-1-methoxypropane in the presence of stannic chloride and subsequent removal of the O-acetyl groups with methanolic ammonia or sodium methoxide in methanol. Cytosine derivatives (12, 19) were prepared under similar conditions from the trimethylsilylated 4-N-acetyl base. Attempted deprotection of 1-(1-methoxy-2,3-diacetoxypropyl)-5-trifluoromethyluracil with methanolic ammonia gave the 5-cyanouracil 8 in high yield. With 1,3-diacetoxy-1-methoxypropane, 1,3-bis-substituted pyrimidines were sometimes obtained but, under the conditions used for deprotection of hydroxyl groups, these also yielded the required 1-monosubstituted pyrimidines. The $^{13}C$ and $^{1}H$ nmr spectra of the 1-methoxy-2,3-dihydroxypropyl derivatives (1-12) indicated that in each case a mixture of diastereoisomers was obtained.

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





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