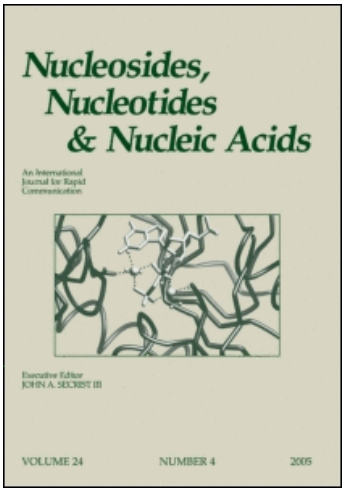

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Acyclonucleoside Inhibitors of Uridine Phosphorylase

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To cite this Article Draminski, M. , Zgit-wroblewska, A. , Drabikowska, A. and Shugar, D.(1985) 'Acyclonucleoside Inhibitors of Uridine Phosphorylase', Nucleosides, Nucleotides and Nucleic Acids, 4: 1, 293
To link to this Article: DOI: 10.1080/07328318508077895
URL: http://dx.doi.org/10.1080/07328318508077895

NUCLEOSIDES & NUCLEOTIDES, 4(1&2), 293 (1985)

ACYCLONUCLEOSIDE INHIBITORS OF URIDINE PHOSPHORYLASE

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Summary: Various acyclonucleoside analogues have been examined as inhibitors of highly purified, and electrophoretically homogeneous, bacterial uridine phosphorylase.

In a follow-up on the finding of Niedzwicki et al.[1] that some 1-(2'-hydroxyethoxymethyl)pyrimidines are inhibitors of uridine phosphorylase, we have synthesized some new analogues and examined their inhibitory properties *vs* a highly purified, homogeneous in SDS-gel electrophoresis, enzyme from *E.coli*. The analogues synthesized included, as heterocyclic bases, 5- or /and 6- substituted uracils and 5,6-tri- and tetra-methylene uracils. The acyclic moieties included, amongst others, 2-hydroxyethoxymethyl, 2-hydroxypropyl, 2,3-dihydroxypropyl and 1,3-dihydroxypropoxymethyl. None of the compounds was a substrate for phosphorolysis, and most were competitive inhibitors. Typical K_i values for inhibition of phosphorolysis are 3.6 μM for 1-(1',3'-dihydroxypropoxymethyl)-5,6-tetramethyleneuracil and 10 μM for 1-(2'-hydroxyethoxymethyl)-5-ethyluracil. The overall results will be compared with those for crude mammalian enzymes [1], and examined in relation to the finding that phosphorolysis of natural ribonucleosides proceeds *via* an intermediate with the *syn* conformation about the glycosidic bond.[2]

Supported by Polish Cancer Research Program (PR-6, 2201).

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0732-8311/85/0401-0293$3.50/0