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## **Nucleosides, Nucleotides and Nucleic Acids**

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## **Acyclonucleoside Inhibitors of Uridine Phosphorylase**

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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.<sup>1</sup> 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  $\mu\text{M}$  for 1-(1',3'-dihydroxypropoxymethyl)-5,6-tetramethylenuracil and 10  $\mu\text{M}$  for 1-(2'-hydroxyethoxymethyl)-5-ethyluracil. The overall results will be compared with those for crude mammalian enzymes<sup>1</sup>, and examined in relation to the finding that phosphorolysis of natural ribonucleosides proceeds *via* an intermediate with the *syn* conformation about the glycosidic bond.<sup>2</sup>

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