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## Synthetic, Structural and Biological Studies on Cyclic 3',5'-Nucleotide Analogs and Derivatives

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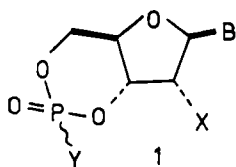
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## SYNTHETIC, STRUCTURAL AND BIOLOGICAL STUDIES ON CYCLIC 3',5'-NUCLEOTIDE ANALOGS AND DERIVATIVES

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Cyclic 3',5'-monophosphates (with the general formula I) of 5-alkylcytidines, 5-alkyl-2'-deoxyuridines, 5-halocytidines, 5-halouridines and 5-halo- and 5-(trifluoromethyl)-2'-deoxyuridine have been synthesized and evaluated for their anti-viral and antitumor properties.



Methods for the preparation of cyclic 3',5'-monophosphate P-O-alkyl (aralkyl) esters of 5-substituted-2'-deoxyuridines and ribonucleoside 3',5'-cyclic N-substituted phosphoramidates have also been elaborated. Analysing the  $^{13}\text{C}$  NMR data, correlations suitable for determining the specific geometry at the phosphorus atom in nucleoside 3',5'-cyclic monophosphate P-O-alkyl (aralkyl) esters and N-substituted phosphoramidates were observed. Enzymic studies (cAMP-dependent protein kinase type I) showed that pyrimidine ribonucleoside 3',5'-cyclic phosphates are also capable of interacting with the enzyme but to a much less extent than cyclic 3',5'-ribonucleotides with adenine ring. Comparative antiviral and antitumor evaluations showed the 5-fluoro and 5-trifluoromethyl analogs significantly active against DNA virus strains and in the growth inhibition of murine and human tumor cells. A certain group of the compounds exhibited remarkable activity against thymidine kinase deficient herpes simplex virus type 1.