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NUCLEOSIDE DERIVATIVES OF 2-MERCAPTO-5,6-DICHLOROBENZIMIDAZOLE: SYNTHESIS AND ANTIVIRAL EVALUATION

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2-Mercapto-5,6-dichlorobenzimidazole ß-D-ribofuranonucleosides have been synthesized by condensing commercially available 1-O-acetyl-2,3,5-tri-O-benzoyl-ß-D-ribofuranose with 2-mercapto-5,6-dichlorobenzimidazole. Depending on the glycosylation procedure employed, the ß-D-*N*-1 isomer (along with the *N,N-bis*-riboside) or the ß-D-S^2 isomer was obtained. After deprotection, the ß-D-*N*-1 isomer was deoxygenated to the corresponding 2',3'-didehydro-2',3'-dideoxy derivative *via* formation of a 2,2'-anhydro intermediate. The α and ß 2',3'-dideoxy nucleoside anomers were synthesized by a different route.

All the compounds prepared were tested for their activity against a variety of DNA and RNA viruses including HIV. The results will be discussed.

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CYTOSOLIC DELIVERY OF ANTI-HIV NUCLEOSIDE MONOPHOSPHATES HAVING ENZYME-LABILE TRANSIENT PHOSPHATE PROTECTING GROUPS

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For many years numerous attempts have been made to deliver mononucleotides intracellularly in order to bypass the first phosphorylation step in the activation of nucleosides. Among the approaches employed, those based on the use of neutral phosphotriester derivatives substituted with bioreversible protecting groups seem most promising.

Here we report new enzyme-labile phosphate protecting groups, that are selectively removed by carboxyesterase or reductase enzymes. Using three nucleoside models, ddU (an inactive nucleoside), PMEA (a compound with low bioavailability) and AZT (inactive in TK^- cells), it will be shown that the 5'-phosphotriesters possessing dithioethanol or S-acetylthioethanol protecting groups fulfill the requirements for cytosolic delivery of the mononucleotides, with the expected biological consequences.