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Acyclic Nucleoside and Nucleotide Analogues Derived from 1-Deaza and 3-Deazaadenine.

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Acyclic analogues of adenine nucleosides and nucleotides have attracted attention as antivirals. While 9-(S)-2,3-dihydroxypropyl) adenine (DHPA) is a broad-spectrum antiviral, 9-(2-phosphonylmethoxyethyl) adenine (PMEA) and 9-(S)-3-hydroxy-2-phosphonylmethoxypropyl) adenine (HPMPA) are potent inhibitors of DNA viruses. 1-Deaza- and 3-deazaadenine analogues of DHPA and PMEA were synthesized by condensation of appropriate synthons with the corresponding deazaadenines, the (S)-enantiomers of deaza-HPMPA were obtained from the deaza-DHPA derivatives by treatment with $ClCH^2P(O)Cl^2$ followed by methanolysis and $BrSiMe^3$ treatment. Of all the compounds tested, only 3-deaza-HPMPA exhibits high activity against CMV and VZV which is comparable with HPMPA. However, its in vitro selectivity index is less favorable.

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Antiviral Activity and Metabolism of 7-Isomer Derivatives of the Purine Nucleoside Analogue HOE 602. I. Winkler, M. Helsberg, T. Scholl, C. Meichsner, G. Jähne, M. Rösner. PGE: Antiinfektiva, Hoechst AG, P.O. Box 80 03 20, D-6230 Frankfurt 80, FRG.

HOE 602 (2-amino-9-[1.3-bis(isopropoxy)-2-propoxymethyl]purine) is an oral prodrug of ganciclovir, which shows excellent therapeutic efficacy in mice against systemic infections with Herpes simplex virus 1 (HSV 1), Herpes simplex virus 2 (HSV 2) and murine cytomegalovirus (MCMV). Unexpectedly, the 7-isomer of HOE 602 was also active against HSV 1 in mice when administered parenterally or orally. In contrast the corresponding guanine derivative is almost inactive in vivo. In vitro studies as well as metabolic studies in mice reveal that the 7-isomer of HOE 602 is not metabolized to ganciclovir. A new compound with excellent activity against HSV 1 and HSV 2 in cell culture was found to be the ultimate metabolite which causes the in vivo antiviral activity of the 7-isomer in mice.