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1-Deazapurine derivatives: a new class of antiviral compounds.

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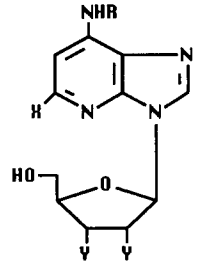
1-Deazaadenosine has been shown to possess cytotoxic activity and to inhibit adenosine deaminase and platelet aggregation (1). Furthermore, introduction of chlorine atoms and substitution of the N^6 amino group led to compounds endowed with biological activity (2). Moreover, deoxynucleosides are good tools for inhibition of HIV replication. On this basis a series of 1-deazaadenosine derivatives, outlined in the figure, were synthesized and evaluated in several antiviral tests. Synthesis was accomplished starting from 5,7-dichloro-imidazo[4,5-b]pyridine, which was glycosilated using the appropriate protected sugar. Substitution of chlorine in 7 position with several amines and reduction of the other chlorine with Raney Nichel gave the desired compounds. Preliminary results showed that substitutions on the amino group increases antiviral potency. The presence of a chlorine atom on the heterocyclic moiety enhances the anti-HIV activity.



R = Alkyl or alkylaryl

X = H or Cl

Y = H or OH

1) Cristalli, G et al. *J. Med. Chem.* **1984**, *27*, 274 and ibid. **1987**, *30*, 1686.
2) Cristalli, G et al., *J. Med. Chem.* **1988**, *31*, 1179 and ibid. **1991**, *34*, 2226.

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Synthesis and *in Vitro* Antiviral Activity of 8-Aza-analogues of the Potent Antiviral Agents 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA) and 9-[2-(Phosphonomethoxy)ethyl]guanine (PMEG).

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9-[2-Phosphonomethoxy)ethyl]adenine (PMEA) and 9-[2-phosphonomethoxy)-ethyl]guanine (PMEG) are potent and selective inhibitors of a broad-spectrum of DNA viruses and retroviruses, including human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) *in vitro* and *in vivo*. We report here on the syntheses of 8-aza-analogues of such acyclic nucleotides. 9-Phosphonomethoxyethylation of 8-azaadenine and 8-azaguanine with 2-[1-(diethylphosphonomethoxy)ethyl] p-toluensulfonate in DMF in the presence of sodium hydride, gave a mixture of regioisomers which were separated and readily distinguished by spectroscopic data. Deprotection of the phosphonate esters with TMSBr gave the desired compounds. *In vitro* antiviral activities of the title compounds will be reported and discussed.

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