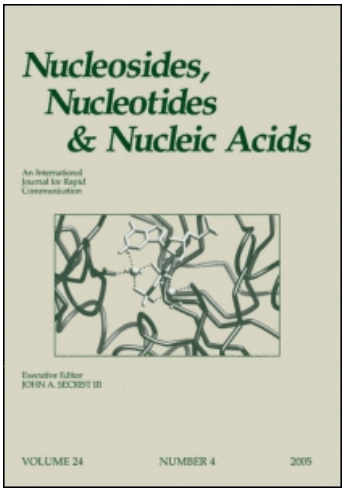

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SYNTHESIS OF 5'-SUBSTITUTED ANALOGUES OF CARBOCYCLIC 3-DEAZAADENOSINE AS POTENTIAL ANTIVIRALS

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ABSTRACT: Various 5'-substituted analogues of carbocyclic 3-deazaadenosine (**1a**), a potent antiviral agent, have been prepared and tested against nine viruses.

Carbocyclic 3-deazaadenosine (**1a**) has been shown to be a promising antiviral agent.[1,2] We therefore prepared a series of 5'-derivatives of **1a** which would have the following characteristics: 1) resemblance to adenine nucleosides, 2) little or no substrate activity for adenine deaminase or for nucleoside kinases.

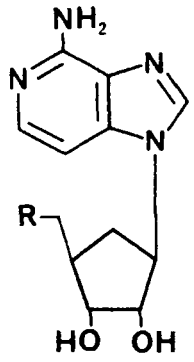
Compound **1b** was prepared by reacting **1a** with thionyl chloride in trimethyl phosphate. Compound **1c** was prepared by dechlorinating **1b** with tri-n-butyltin hydride in the presence of AIBN. Reaction of the mixture (**1b** + **1c**) with the sodium salt of isobutyl mercaptan produced a mixture of **1c** and **1d** where were separable by flash chromatography, providing **1c** in 72% yield.

Compound **2b** was prepared from **2a** under Mitsunobu conditions (Ph_3P, phthalimide, diethyl azodicarboxylate). Hydrolysis with 4N HCl removed the protecting group.

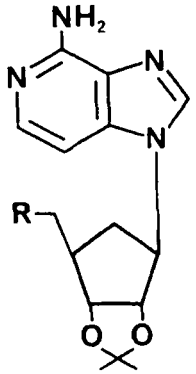
Compound **3b** was prepared from **3a** by reaction with tetra-n-butylammonium bromide in pyridine/dichloromethane. Reaction of **3b** with isobutyl mercaptan in the presence of sodium ethoxide provided **3c**. Compounds **3b** and **3c** were deblocked with 4N HCl.

Oxidation of **4a** (Pt, O_2, H_2O) followed by esterification with diazomethane in DMAC, reaction with hydrazine, and hydrogenation over Raney Nickel provided **4b**.

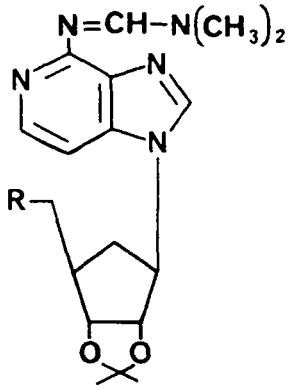
The 5'-Br and 5'-Me derivatives were active[3] against both vaccinia and vesicular stomatitis viruses. The 5'-NH_2 and 5'-Cl derivatives were marginally active against vaccinia.



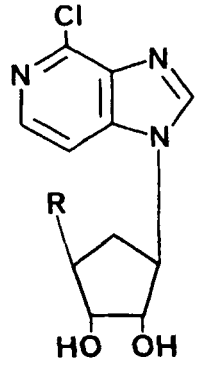
Compound	R
1a	OH
1b, 1c, 1d	Cl, CH_3, i BuS



Compound	R
2a	OH
2b	NH_2



Compound	R
3a	OT_f
3b, 3c	Br, i BuS



Compound	R
4a	CH_2OH
4b	$CONH_2$

Figure 1.

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3. Virus Ratings were calculated by the method of Hoffman and Sidwell *Appl. Micro.*, 22, 795 (1971).