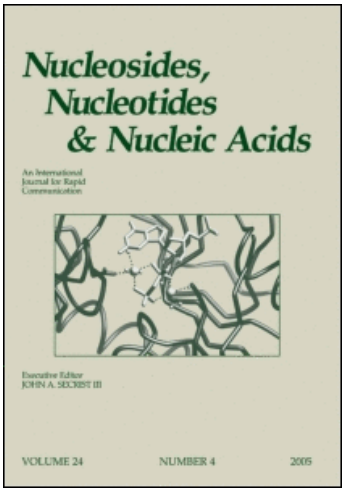

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Synthesis of Novel Carbocyclic Nucleosides with a Modified Cyclopentane Ring and Evaluation of Their Antiviral Activity

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SYNTHESIS OF NOVEL CARBOCYCLIC NUCLEOSIDES WITH A MODIFIED CYCLOPENTANE RING AND EVALUATION OF THEIR ANTIVIRAL ACTIVITY

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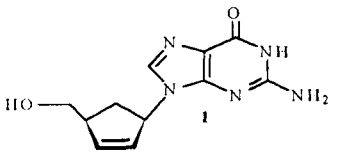
Abstract: New carbocyclic nucleosides with purine (compounds **2a-2c**), 8-azapurine (compounds **2d** and **2e**) or pyrimidine (compound **3**) as base were prepared and assayed for *in vitro* activity.

The discovery of carbocyclic nucleosides with antiviral activity, such as carbovir (**1**),[1] prompted us to search for congeners with a modified cyclopentane moiety. Here work we descibe the synthesis of carbocyclic nucleosides **2** and **3**, and report their antiviral activity.



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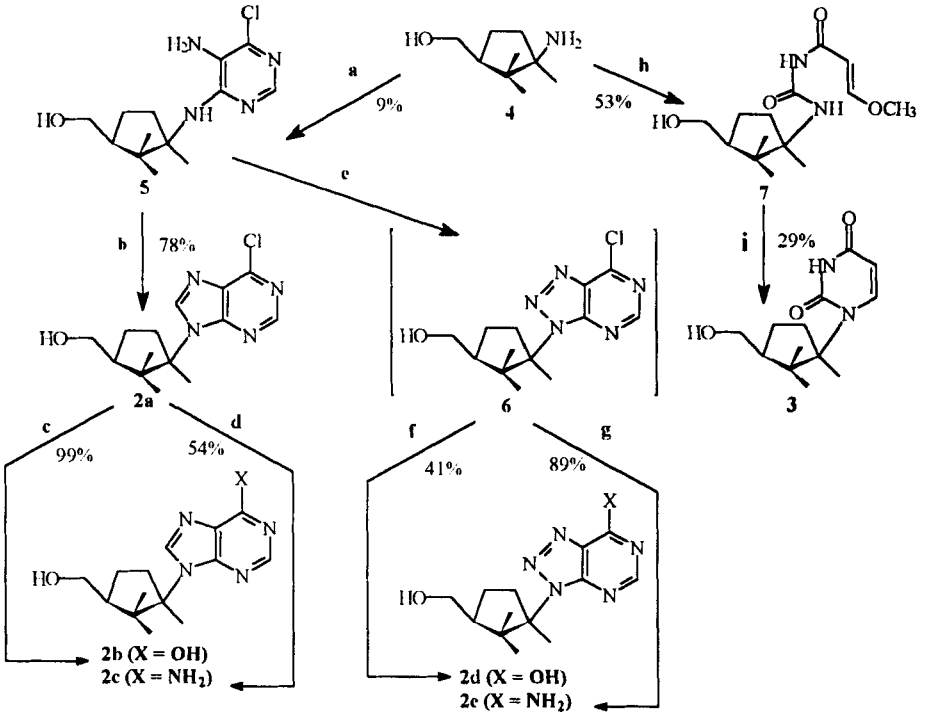
(1*S*,3*R*)-3-Amino-2,2,3-trimethylcyclopentylmethanol (**4**) identified as a convenient starting compound for the synthesis of **2** and **3**, was prepared from (+)-camphoric acid.[2] Standard methods[3,4] were then used to construct purine or pyrimidine about the amino group.

Compounds **2b-2e** and **3** were tested in E_6SM cell cultures for their broad spectrum antiviral activity[5] against herpes simplex virus-1 (KOS), herpes simplex virus-2 (G), vaccinia virus, vesicular stomatitis virus, thymidine kinase-deficient herpes simplex

virus-1 TK⁻ (B2006) and herpes simplex virus-1 TK⁻ (VMW1837); in HeLa cell cultures against vesicular stomatitis virus, Coxsackie virus B4 and respiratory syncytial virus; in



a) 5-Amino-4,6-dichloropyrimidine, Et_3N, n-butanol, reflux, 72 h; b) $CH(OEt)_3$, 12N HCl, r.t., 72 h; c) 0.33 N NaOH, reflux, 6 h; d) 14M NH_4OH, reflux 18 h; e) $NaNO_2$, AcOH, or 1N HCl; f) H_2O, r.t., 18 h; g) 14M NH_4OH, reflux, 5 min; h) methyl 3-methoxiacriloyl isocianate, C_6H_6, DMF, r.t., overnight; i) 2N H_2SO_4, reflux, 3.5 h.

Vero cell cultures against *parainfluenza*-3 virus, *reovirus*-1, *Sindbis* virus, *Coxsackie* virus B4 and *Punta Toro* virus; and in HEL cell cultures against varicella-zoster virus (strains OKA,YS, 07/1 and YS/R) and cytomegalovirus. No specific antiviral activity was obtained with any of the compounds at subtoxic concentrations.

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