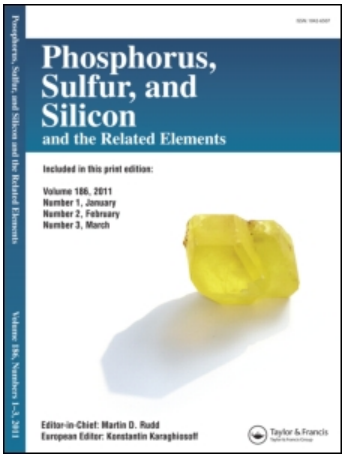

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Synthesis and Anti-HIV-1 Reverse Transcriptase Activity of Triphosphates of Penciclovir and β-D-Dioxolane-Guanine

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SYNTHESIS AND ANTI-HIV-1 REVERSE TRANSCRIPTASE ACTIVITY OF TRIPHOSPHATES OF PENCICLOVIR AND β-D-DIOXOLANE-GUANINE

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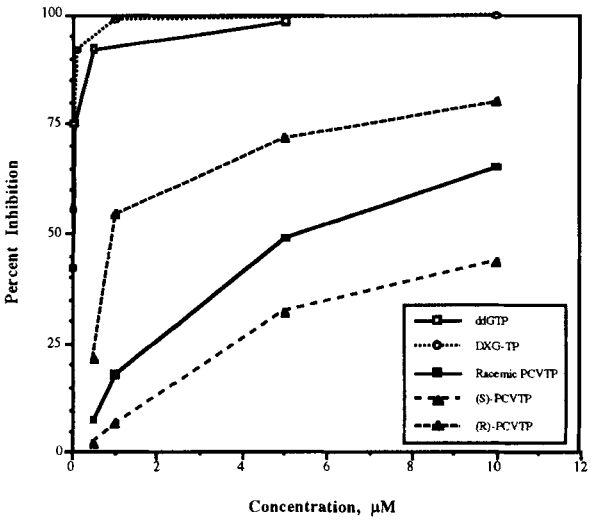
Abstract The synthesis of *R*- and *S*-9-(4-Hydroxy-3-hydroxymethyl-but-1-yl)guanine (PCV) and (-)-β-D-dioxolane-guanine (DXG) triphosphate and their enzyme inhibitory activity is descibed.

Penciclovir (PCV) and (-)-β-D-dioxolane-guanine (DXG) are selective antiviral agents against certain herpesviruses and human immunodeficiency viruses (HIV), respectively. The triphosphate forms inhibit viral replication by acting as substrates for viral polymerases.[1] To test the activity of nucleotide analogues against HIV-1 reverse transcriptase (RT) *in vitro*, the suitable triphosphates were synthesized.



Phosphorylation of *O*-monoisobutyryl-PCV (*R*-, *S*- or racemic form) with 2-chloro-4*H*-1,2,3-dioxaphosphorin-4-one followed by reaction with tri-*n*-butylammonium pyrophosphate, oxidation,[2] and removal of isobutyryl protection produced the desired PCV-triphosphates. Similarly DXG-triphosphate was synthesized. Enzymatic assays using a poly(rC)$_n$.oligo(dG)$_{12\text{-}18}$ template primer revealed potent activity of PCV- and DXG-triphosphates against HIV-1 RT.

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