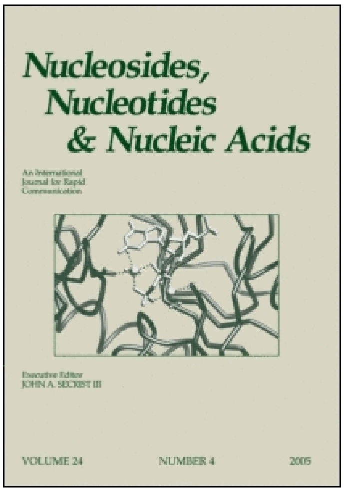

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CHEMICAL AND ENZYMATIC SYNTHESIS AND ANTIVIRAL PROPERTIES OF 2'-DEOXY-2'-FLUOROGUANOSINE

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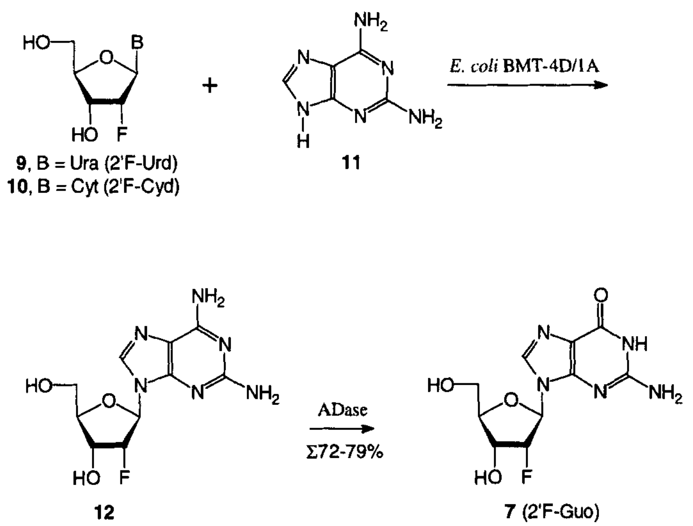
ABSTRACT: Chemical and enzymatic methods were employed for the synthesis of the title compound, 2'F-Guo **7**. High antiviral activity of 2'F-Guo was established in chick embryo cells infected with influenza virus FPV/Rostock/34 (H7N1) and herpes simplex virus (HSV) type I (1C strain).

As a part of our continuing interest in fluorodeoxy nucleosides and nucleotides,[1] here we present the synthesis of 2'F-Guo (*cf.*, *e.g.*[2,3]) *via* chemical and enzymatic methods and data on its activity against influenza virus (*cf.*, *e.g.*[2,4]) and HSV (type I) as well.

The condensation of 1-O-acetyl-2-deoxy-2-fluoro-3,5-di-O-benzoyl-β-D-ribofuranose (**1**)[1] with trimethylsilylated N^2-palmitoylguanine (**2**) in the presence of TMS-Tfl in anhydrous acetonitrile or 1,2-dichloroethane under reflux for 3-5 h afforded a mixture of the N^7-β-D-glycoside **3** as principal product along with the formation of the N^9-β- and -α-D-anomers **5** and **6**, respectively (**3/5/6** ratio *ca.* 5:2:1 according to the ^{1}H NMR data; 44-54%, combined). Deblocking of the above nucleosides gave the free N^7-β-D-glycoside **4**, 2'F-Guo **7** and its α-D-anomer **8**, respectively.

An enzymatic transglycosylation of 2,6-diaminopurine (**11**) using the glutaraldehyde-treated whole cells of *E. coli* BMT-4D/1A as a biocatalyst[5] and 2'-deoxy-2'-fluoro-uridine (**9**) or -cytidine (**10**) as a donor of the glycosyl moiety followed by an enzymatic deamination of intermediate 2,6-diaminopurine glycoside **12** afforded the title compound 2'F-Guo **7** in 72-79% combined yield.



Antiviral activity of 2'F-Guo was tested in chick embryo cells infected with influenza virus FPV/Rostock/34 (H7N1) and herpes simplex virus (HSV) type I (1C strain). The 50% inhibitory concentration (IC_{50}) of 2'F-Guo was found to be 0.42 μg/mL for FPV and 0.027 μg/mL for HSV. Rimantadine (xHCl), ribavirin (both against FPV) and acycloguanosine (HSV) were tested simultaneously for comparison and their IC_{50} values were <0.1, 3.54 and 0.018 μg/mL, respectively.

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REFERENCES

1 Mikhailopulo, I.A.; Poopeiko, N.E.; Sivets, G.G.; Khripach, N.B. *Carbohyd. Res.* **1995**, *278*, 71-89.

2 Tuttle, J.V.; Tisdale, M.; Krenitsky, T.A. *J. Med. Chem.* **1993**, *36*, 119-125.

3 Thomas, H.J.; Tiwari, K.N.; Clayton, S.J.; Secrist III, J.A.; Montgomery, J.A. *Nucleosides Nucleotides* **1994**, *13*, 309-323.

4 Tisdale, M.; Ellis, M.; Klumpp, K.; Court, S.; Ford, M. *Antimicrob. Agents Chemther.* **1995**, *39*, 2454-2458, and references therein.

5 Zinchenko, A.I.; Barai, V.N.; Bokut, S.B.; Kvasyuk, E.I.; Mikhailopulo, I.A. *Appl. Microbiol.Biotechnol.* **1990**, *32*, 658-661.