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## Nucleosides, Nucleotides and Nucleic Acids

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### Synthesis and Anti-HIV Activity of Dideoxycytidine Analogues Containing a Pyranose Carbohydrate Moiety

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SYNTHESIS AND ANTI-HIV ACTIVITY OF DIDEOXYCYTIDINE ANALOGUES CONTAINING  
A PYRANOSE CARBOHYDRATE MOIETY

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**Abstract.** Dideoxycytidine analogues with a trideoxy-D-hexopyranosyl or hexenopyranosyl moiety were synthesized starting from 2-deoxyglucosyl bromide or tri-O-acetyl-D-glucal.

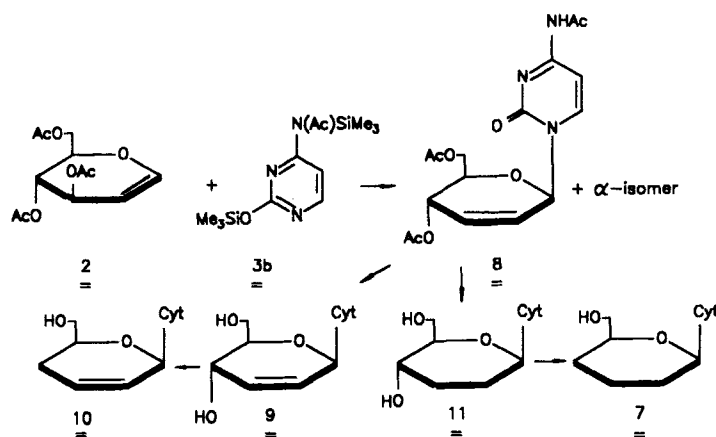
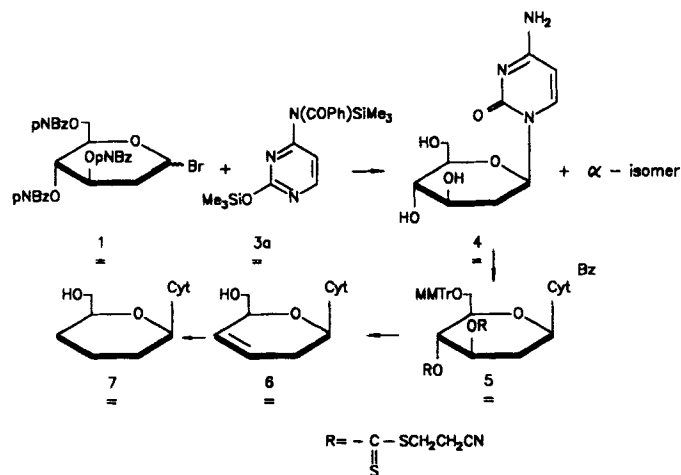
NGPB-21,<sup>1</sup> a dideoxycytidine analogue with sulfur replacing the 3'-carbon atom, has been reported to be a potent and selective inhibitor of HIV (human immunodeficiency virus) replication *in vitro*. Considering the isosterism between a sulfur atom and vinyl group, we prepared a variety of dideoxycytidine analogues containing a pyranosyl moiety with or without a double bond at either the C3'-C4' or C2'-C3' position.

Synthesis of the desired nucleoside analogues containing a trideoxy-D-hexopyranosyl moiety started from either p-nitrobenzoylated 2-deoxyglucosyl bromide (1) or tri-O-acetyl-D-glucal (2). The protected sugar derivatives were coupled with N-protected silylated cytosine (3a,3b) in the presence of trimethylsilyl triflate.

Following protection of 4, reaction with carbon disulfide in DMSO-NaOH 8 N (2:1), followed by addition of  $\beta$ -bromopropionitrile, afforded the bis(dithiocarbonate) 5. Heating with tributyltin hydride and AIBN, followed by deprotection, gave the hexenopyranosyl nucleoside 6. Hydrogenation in the presence of Pd/C afforded 7.

Deprotection of 8, obtained after reaction with glucal, afforded 9, which was deoxygenated to 10. Hydrogenation of 8, followed by treatment with base, gave 11 which could be transformed to 7 by

deoxygenation. Thus, the synthesis of the latter compound was achieved by two independent routes. None of these nucleoside analogues or their  $\alpha$ -anomers showed any significant anti-HIV activity ( $\alpha$  anomer of 10 not evaluated yet).



#### REFERENCE

1. M.A. Wainberg, M. Stern, R. Martel, B. Belleau and B. Soudeyns, Vth Intern. Conference on AIDS, Montreal, 1989, Abstracts, p. 552.