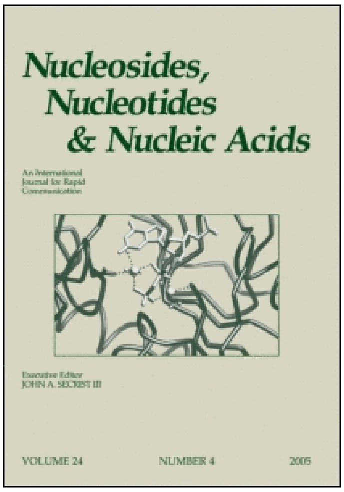

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SYNTHESIS AND ANTI-HIV ACTIVITY OF DIDEOXYCYTIDINE ANALOGUES CONTAINING A PYRANOSE CARBOHYDRATE MOIETY

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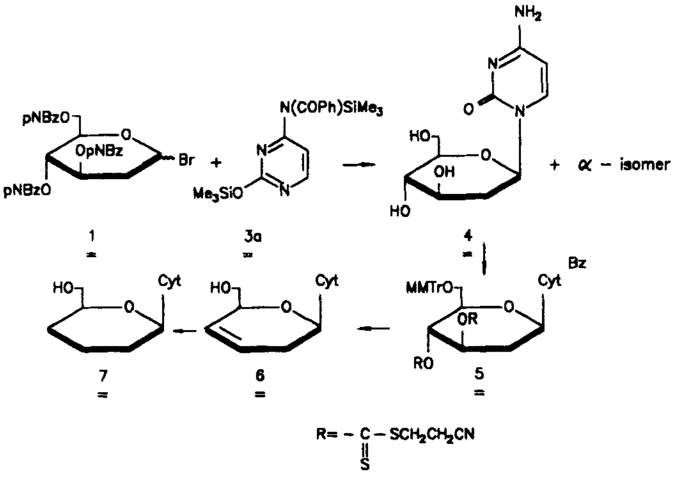
Abstract. Dideoxycytidine analogues with a trideoxy-D-hexopyranosyl or hexenopyranosyl moiety were synthesized starting from 2-deoxyglucosyl bromide or tri-O-acetyl-D-glucal.

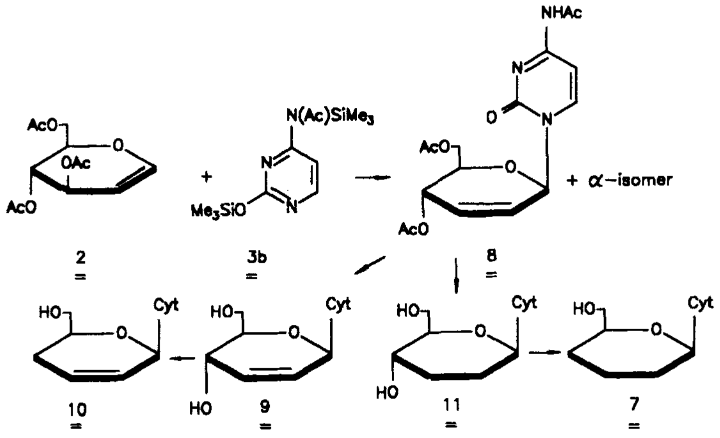
NGPB-21,[1] a dideoxycytidine analogue with sulfur replacing the 3'-carbon atom, has been reported to be a potent and selective inhibitor of HIV (human immunodeficiency virus) replication *in vitro*. Considering the isosterism between a sulfur atom and vinyl group, we prepared a variety of dideoxycytidine 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 β-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 α-anomers showed any significant anti-HIV activity (α anomer of 10 not evaluated yet).





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