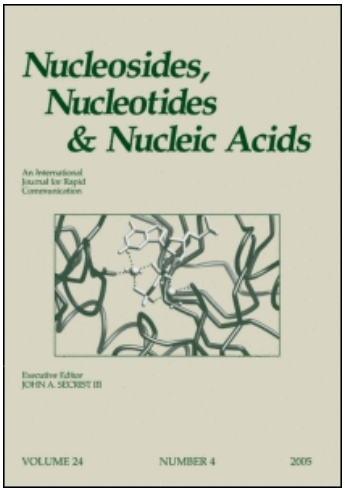

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Synthesis of Some 2',3'-Didehydro-2',3'-dideoxynucleosides and 2',3'-dideoxynucleosides

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SYNTHESIS OF SOME 2',3'-DIDEHYDRO-2',3'-DIDEOXYNUCLEOSIDES AND 2',3'-DIDEOXYNUCLEOSIDES

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Abstract. 2',3'-Didehydro-2',3'-dideoxyformycin A (4), 2',3'-dideoxyformycin A (11), 2',3'-dideoxytubercidin (12) and 2',3'-dideoxy-3-deazaadenosine (19) were synthesised via a free radical β-elimination of bromo and phenoxythiocarbonyl groups or by deoxygenation of appropriate 2' and 3'-deoxy counterparts.

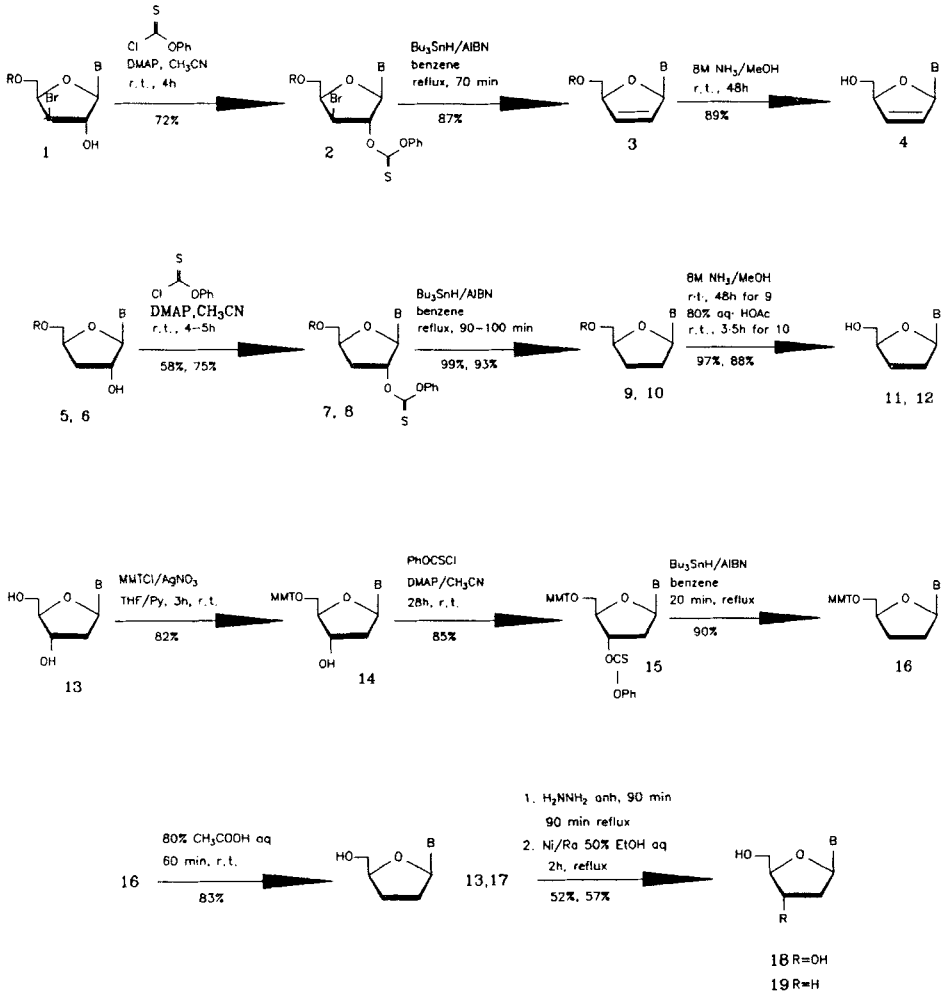
Some of the 2',3'-dideoxynucleosides displayed activity against HIV.[1] With the aim of examining their biological properties several 2',3'-dideoxy nucleoside analogues were synthesised.

7-Amino-3-[5-O-(2-acetoxyisobutyryl)-3-bromo-3-deoxy-β-D-xylofuranosyl]-1-H-pyrazolo[4,3-d]pyrimidine (1) was acylated with O-phenylchlorothionoformate to give 7-amino-3-[5-O-(2-acetoxyisobutyryl)-3-bromo-3-deoxy-2-O-phenoxy (thiocarbonyl)]-1H-pyrazolo[4,3-d]pyrimidine (2). Reaction of 2 with tributyltin hydride afforded 5'-O-(2-acetoxyisobutyryl)-2',3'-didehydro-2',3'-dideoxyformycin A (3) and subsequent removal of 2-acetoxyisobutyryl group from 3 with methanolic ammonia, yielded 2,3'-didehydro-2',3'-dideoxyformycin A (4).

Acylation of 5'-O-(2-acetoxyisobutyryl)-3'-deoxyformycin A (5) with O-phenylchlorothionoformate and deoxygenation of the resulting 7-amino-3-[5-O-(2-acetoxyisobutyryl)-3-deoxy-2-O-phenoxy(thiocarbonyl)-β-D-ribofuranosyl]-1H-pyrazolo[4,3-d]pyrimidine (7) with tributyltin hydride gave 5'-O-(2-acetoxyisobutyryl)-2',3'-dideoxyformycin A (9). Removal of the 2-acetoxyisobutyryl group from 9 afforded 2',3'-dideoxyformycin A (11) 2',3'-Dideoxytubercidin (12) was prepared in a similar fashion starting from 5'-O-(4-methoxytrityl)-3'-deoxytubercidin (6).[2]

4-Chloro-1-(2-deoxy-β-D-erythropentofuranosyl)-1H-imidazo[4,5-c]pyridine (13) was obtained via glycosylation of 4-chloro-1H-imidazo[4,5-c]-pyridine under solid liquid phase transfer conditions.[3] Deoxygenation

of 13 gave 4-chloro-1-(2,3-dideoxy-β-D-glyceropentofuranosyl)-1H-imidazo[4,5-c]pyridine (17). Finally, amination of 13 and 17 afforded 2'-deoxy-3-deazaadenosine (18) and 2',3'-dideoxy-3-deazaadenosine (17) respectively.[4]



1-5, 7, 9, 11; B = 7-aminopyrazolo[4,3-d]pyrimidin-3-yl
R = 2-acetoxyisobutyryl
6, 8, 10, 12; B = 4-aminopyrrolo[2,3-d]pyrimidin-7-yl
R = 4-methoxytrityl
13-17 B = 4-chloroimidazo[4,5-c]pyridin-1-yl
18, 19 B = 4-aminoimidazo[4,5-c]pyridin-1-yl

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