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SYNTHESIS OF L-THREO- AND D-ERYTHRO-
APIOFURANOSYLCYTIDINES

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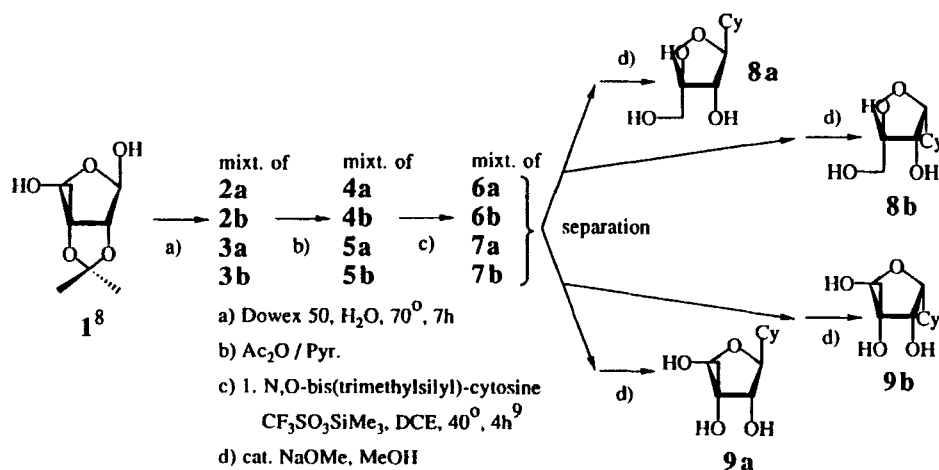
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ABSTRACT: The synthesis of β -L-threo-, α -L-threo, β -D-erythro and α -D-erythro-apiofuranosylcytidine and their biochemical properties are reported.

Apiose, a branched chain sugar, occurs in its D-erythro-form as an important component of various natural glycosides ¹. This was obviously the reason to prepare apiofuranosyl-nucleoside analogues with adenine ^{2a,b; 3,4}, thymine, uracil, Br-uracil and I-Uracil ⁴ in order to investigate their behaviour towards viruses ⁴ and bacteria ³. Some immunochemical studies were also performed ⁴. With respect that free apiose is existing in the D-erythro- as well as L-threo-form as α - and β -anomers we decided to synthesize simultaneously the mixture of all possible apio-cytidines.

2,3-O-Isopropylidene- β -D-apiofuranose (1)^{5,6} was transformed to a mixture of two anomeric pairs of L- threo- and D- erythro-apiofuranoses (2a/2b = β -L / α -L threo as well as 3a/3b = β -D / α -D erythro) in a ratio of 10 : 1 : 2 : 3, which were peracetylated to 4a/4b and 5a/5b. (70%). This mixture gave by the silyl-Hilbert-Johnson ⁷ procedure the expected mixture of the apio-derivatives (54% Scheme I). Separation of the compounds was achieved by a three stage chromatography process. Yields of pure compounds: 6a 28%, 6b 3%, 7a 9%, 7b 14%. Zemplen saponification led to the title compounds



SCHEME 1

8a 3C-Hydroxymethyl- β -L-threofuranosyl-cytidine, **8b** 3C-Hydroxymethyl- α -L-threofuranosyl-cytidine, **9a** 3C-Hydroxymethyl- β -D-erythrofuransyl-cytidine and **9b** 3C-Hydroxymethyl- α -D-erythrofuransyl-cytidine. Derivatisation of the title compounds was performed for further spectroscopical characterisation. Thus the stereochemistry was assigned by NOE - experiments. None of the compounds proved effective as inhibitor of HLV replication in MT-4 cells at subtoxic concentrations. The ED₅₀^a and CD₅₀^b values of all title compounds were over 200 μ g/ml.

^a50% effective dose, or dose required to inhibit HLV cytopathogenicity in MT-4 cells

^b50% cytotoxic dose, or dose required to reduce the viability by 50%

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