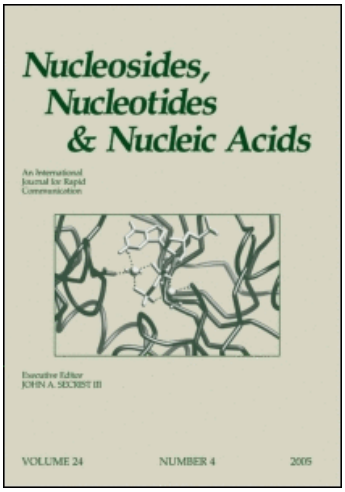

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Synthesis of L-Threo- and D-Erythro-apiofuranosylcytidines

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

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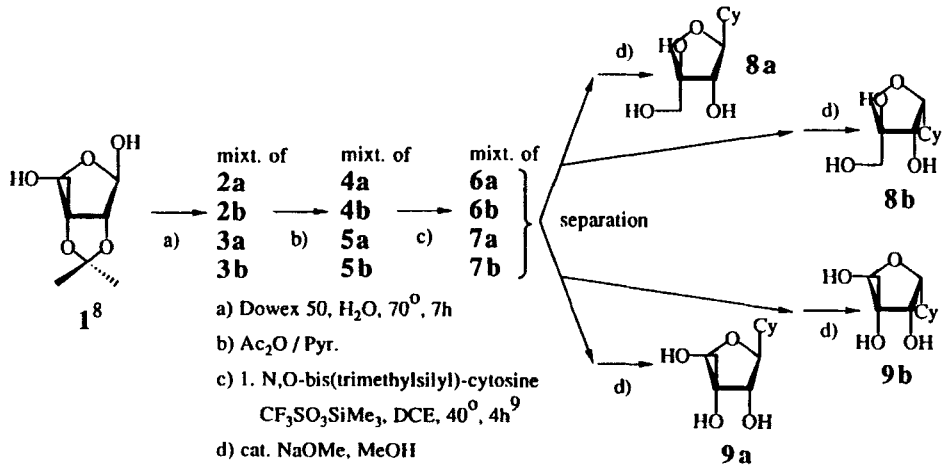
ABSTRACT: The synthesis of β-L-threo-, α-L-threo, β-D-erythro and α-D-erythro-apiofuranosylcytidine and their biochemical properties are reported.

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 adenin [2a,b; 3,4], thymin,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 simultanenously 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 acchieved 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-erythrofuranosyl-cytidine and **9b** 3C-Hydroxymethyl-α-D-erythrofuranosyl-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 ED_{50}[a] and CD_{50}[b] values of all title compounds were over 200 µg/ml.

[a] **50% effective dose**, or dose required to inhibit HLV cytopathogenicity in MT-4 cells

[b] **50% cytotoxic dose**, or dose required to reduce the viability by 50%

References:

1) R. R. Watson and N. S. Orenstein *Adv. in Carbohydr. Chem. and Biochem.* **31**, 135 (1975)

2a) J. M. J. Tronchet and J. Tronchet *JCarbohydr. Res.* **34**, 263 (1974)

2b) J. M. J. Tronchet, J. M. Bourgeois, J. M. Chalet, R. Graf, R. Gurny and J. Tronchet *Helv. Chim. Acta* **54**, 687 (1971)

3) J. M. J. Tronchet and J. Tronchet *Helv. Chim. Acta* **54**, 1466 (1971)

4) D. K. Parikh and R. R. Watson *J. Med. Chem.* **27/7**, 707 (1978)

5) Pak Tsun Ho *Can. J. Chem.* **57**, 381 (1979)

6) P. Hettinger and H. Schildknecht *L. Ann. Chem.* **1984**, 1230

7) H. Vorbrüggen, K. Krolikiewicz and B. Bennua *Chem. Ber.* **114**, 1234 (1981)