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## Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

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### Synthetic Strategies Towards the Synthesis of 1-(2,4-Dideoxy-4-C-hydroxymethyl- $\alpha$ -L-Lyxopyranosyl)base Nucleosides.

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**To cite this Article** Turner, S. J. and Herdewijn, P.(1998) 'Synthetic Strategies Towards the Synthesis of 1-(2,4-Dideoxy-4-C-hydroxymethyl- $\alpha$ -L-Lyxopyranosyl)base Nucleosides.', *Nucleosides, Nucleotides and Nucleic Acids*, 17: 9, 2085 — 2086

**To link to this Article:** DOI: 10.1080/07328319808004750

**URL:** <http://dx.doi.org/10.1080/07328319808004750>

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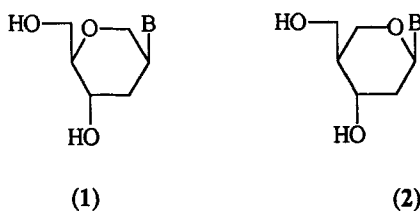
**SYNTHETIC STRATEGIES TOWARDS THE SYNTHESIS OF 1-(2,4-DIDEOXY-4-C-HYDROXYMETHYL- $\alpha$ -L-LYXOPYRANOSYL)BASE NUCLEOSIDES.**

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**Abstract:** A synthetic strategy towards the synthesis of 1-(2,4-dideoxy-4-C-hydroxymethyl- $\alpha$ -L-lyxopyranosyl)thymine by the formation and opening of a 3,4-anhydropentopyranose sugar is described.

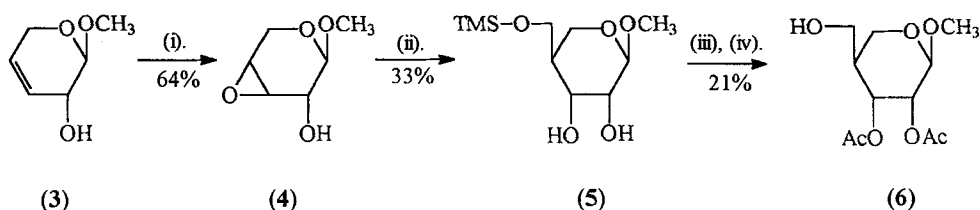
1,5-Anhydrohexitol nucleosides (1) in which the natural furanosyl sugar has been replaced by a six membered ring are promising antiviral agents<sup>1,2</sup>. To investigate the structure activity relationship and effect upon the strong hybridisation properties observed by 1',5'-anhydrohexitol nucleic acids incorporated within oligonucleotides<sup>3</sup>, a series of 1-(2,4-dideoxy-4-C-hydroxymethyl- $\alpha$ -L-lyxopyranosyl)nucleosides (2) were desired.



B = Heterocyclic Base eg thymine or adenosine.

The key to this synthesis involves the introduction of a hydroxymethyl moiety onto the C4-carbon of a pyranose sugar. This has previously been achieved by displacement of a C4-O-triflate group by the sodium salt of diethylmalonate<sup>4</sup> and via the formation of a C4-exocyclic vinylic intermediate by either a Peterson olefination or Wittig reaction upon the C4-ketone<sup>4</sup>. In this synthesis the use of an epoxide intermediate was investigated.

Reaction of the 3,4-vinyl-pentapyranoside (3) with meta-chloroperoxybenzoic acid resulted in the formation of a mixture of the  $\beta$ -D- (4) and  $\alpha$ -L-methyl-3,4-anhydropentapyranoses in a ratio of 6:2 respectively. These isomers could be separated by column chromatography. The methyl 3,4-anhydro- $\beta$ -D-anhydropentopyranose (4) upon reaction with the higher order cuprate of trimethylsilylmethyl lithium ( $(\text{TMS-Si})_2\text{Cu}(\text{CN})\text{Li}_2$ ) gave the desired methyl-4-deoxy-4-trimethylsilylmethyl- $\alpha$ -L-lyxopyranoside (5) in moderate yield. Methyl-3-deoxy-3-trimethylsilylmethyl- $\beta$ -D-xylopyranoside and unreacted starting material were also recovered. Upon protection, bromination followed by oxidative cleavage of the silyl group gave the desired 4-deoxy-4-hydroxymethyl- $\alpha$ -L lyxopyranoside structure (6) which can be further converted into the nucleoside.



Reagents: i. mCPBA,  $\text{CH}_2\text{Cl}_2$ . ii.  $(\text{CH}_3)_3\text{SiCH}_2)_2\text{Cu}(\text{CN})\text{Li}_2$ ,  $\text{Ti}(\text{OiPr})_4$ , THF;  $\text{H}_2\text{O}$ . iii.  $\text{Ac}_2\text{O}$ , Pyr. iv. KBr, AcO-OH, AcOH;  $\text{HClO}_4$ .

In summary, this paper reports a strategy for the introduction of a hydroxymethyl moiety onto the C4-position of an  $\alpha$ -L-lyxopyranoside sugar by means of an epoxide. These methods have not yet been fully optimised, full results and procedures will be published at a future date.

## REFERENCES

1. Verheggen, I.; Van Aerschot, A.; Van Meervelt, L.; Rozenski, J.; Wiebe, L.; Snoeck, R.; Andrei, G.; Balzarini, J.; Claes, P.; De Clercq, E.; Herdewijn, P. *J. Med. Chem.* **1995**, *38*, 826-835.
2. Verheggen, I.; Van Aerschot, A.; Toppet, S.; Snoeck, R.; Janssen, G.; Balzarini, J.; De Clercq, E.; Herdewijn, P. *J. Med. Chem.* **1993**, *36*, 2033-2040.
3. Van Aerschot, A.; Verheggen, I.; Hendrix, C.; Herdewijn, P. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1338-1339.
4. Doboszewski, B.; Herdewijn, P. *Nucleosides Nucleotides* **1996**, *15*, 1495-1518.