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Efficient and Selective Enzymatic Acylation Reaction: Separation of Furanosyl and Pyranosyl Nucleosides

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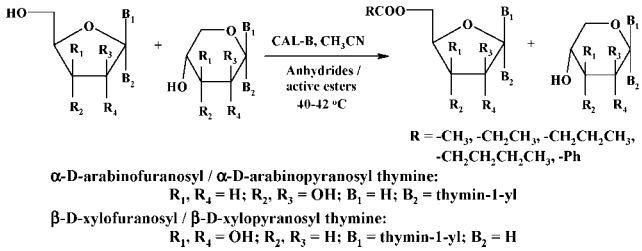

Candida antarctica lipase-B (CAL-B) immobilized on lewatite selectively acylated the primary hydroxyl group of the furanosyl nucleoside in a mixture of 1-(α-D-arabinofuranosyl)thymine and 1-(α-D-arabinopyranosyl)thymine. This selective biocatalytic acylation of furanosyl nucleoside has enabled us an easy separation of arabinofuranosyl thymine from an inseparable mixture with arabinopyranosyl thymine. The primary hydroxyl selective acylation methodology of arabinonucleoside has also been successfully used for the separation of 1-(β-D-xylofuranosyl)thymine and 1-(β-D-xylopyranosyl)thymine from a mixture of the two, which demonstrate the generality of the enzymatic methodology for separation of furanosyl and pyranosyl nucleosides.

Modified nucleosides of arabinofuranosyl moiety have attracted much attention as antiviral,[1] anticancer,[2] antimicrobial,[3] antitumor,[4] antihepatitis B virus,[5,6] antimycobacterial,[7] and cytostatic agents.[8]

Arabinonucleosides with pyranosyl configuration have been used as nucleoside monomers in the synthesis of oligonucleotides for the evaluation of their importance in etiology of nucleic acid structure.[9] In one of our research programs we aimed to synthesize α-D-arabinofuranosyl nucleosides but all our efforts of condensation of tetraacetylated arabinose with thymine led to the formation of an inseparable mixture of α-D-arabinofuranosyl and α-D-arabinopyranosyl nucleosides in varying proportions depending on the temperature of the reaction.

Imbach and co-workers[10] have generalized Guthrie−Smith[11] methodology for the synthesis of tetraacetate of five-membered aldofuranose sugars. They synthesized α- and β-anomers of tetra-*O*-acetyl-D-aldopentofuranosides starting from D-ribose, D-arabinose, D-xylose, and D-lyxose by their methanolysis, acetylation, and acetolysis protocol with an overall yield of ∼70%.

Contrary to this, Bristow and Lythgoe[12] pointed out that the preparative procedure for 1,2,3,5-tetra-*O*-acetylribofuranosyl starting from D-ribose cannot be applied in its entirety to other pentoses such as D-arabinose and D-xylose, possibly because of the existence of the sugar mainly in one cyclic form over the other at equilibrium in solution.

Further, during the synthesis of α- and β-D-xylofuranosyl nucleosides of the five naturally occurring bases, Imbach and co-workers[13] have also reported the existence of furanosyl sugar tetraacetate and the corresponding nucleosides with pyranose forms and found it very difficult to separate them on a preparative scale in contrast to their earlier report.[10] Thus far, no methodology exists for the efficient separation of mixtures of furanosyl and pyranosyl nucleosides.

During the synthesis of α-D-arabinofuranosyl thymine from D-arabinose following literature procedure,[10] we obtained an anomeric mixture of 1,2,3,5-tetra-*O*-acetylarabinofuranoside (**6a**,**b**)[10] and 1,2,3,4-tetra-*O*-acetylarabinopyranoside (**7a**,**b**). The Vorbruggen's coupling[14] of thymine with the anomeric mixtures of furanosides **6a**,**b** and pyranosides **7a**,**b** afforded a mixture of 1-(2′,3′,5′-tri-*O*-acetyl-α-D-arabinofuranosyl)thymine (**8**)[15] and 1-(2′,3′,4′-tri-*O*-acetyl-α-D-arabinopyranosyl)thymine (**9**),

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