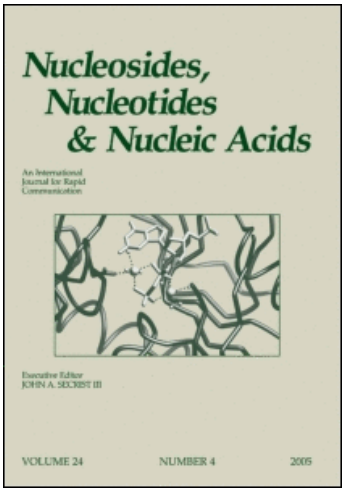

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2,3-Dideoxy-3-Phthalimidopentoses in the Synthesis of 3'-Amino-2',3'-Dideoxynucleosides

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2,3-DIDEOXY-3-PHTHALIMIDOPENTOSES IN THE SYNTHESIS OF 3'-AMINO-2',3'-DIDEOXYNUCLEOSIDES

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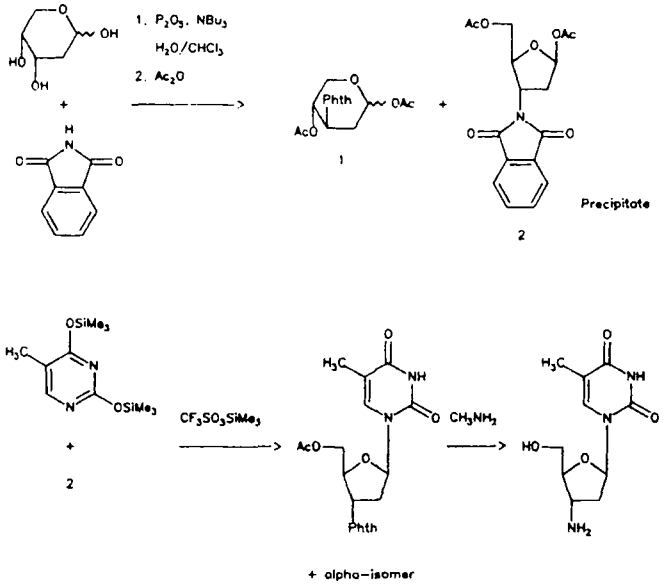
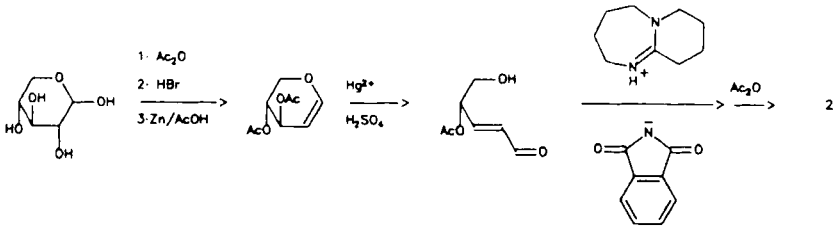
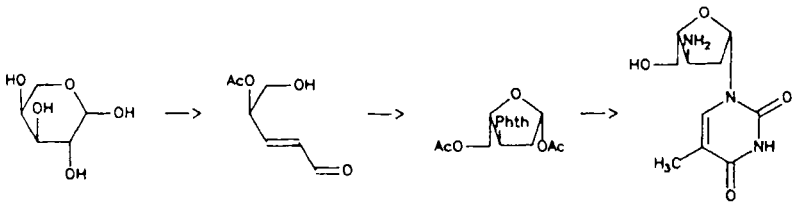
3'-Amino-3'-deoxythymidine is a very effective drug *in vivo* against L 1210 leukemia. It gives 144% increase in lifespan with very little drug-induced toxicity[1]. Therefore, it was attractive to synthesize a large series of analogues, but unfortunately, such compounds are only achievable through a linear synthesis via the corresponding nucleoside which typically is transformed into the 3'-azido derivative and finally reduced.



Scheme 1



Scheme 2



Scheme 3

We have now developed a new strategy (Scheme 1) for synthesis of 3'-amino-2,3-dideoxynucleosides using 2,3-dideoxy-3-phthalimido-D-erythro-pentofuranose **2** as an easily available starting material which was synthesized in one pot by direct coupling of unprotected 2-deoxy-D-ribose with phthalimide. **2** is obtained as a precipitate after acetylation and washing of the coupled product whereas the corresponding threo derivative **1** precipitates from the mother liquid on standing in a refrigerator.

In order to make α,β-unsaturated aldehydes likely as intermediates, 4-O-acetyl-2,3-dideoxy-aldehydo-D-glycero-trans-pent-2-enose was prepared according to standard procedures[2], as shown in Scheme 2, and reacted with the DBU salt of phthalimide to give **2**. This opens up a route for preparation of nucleosides with unnatural configurations and structures of the carbohydrate moiety as exemplified in Scheme 3 showing the first synthesis of a 3'-amino-2,3-dideoxy nucleoside with L-configuration.

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