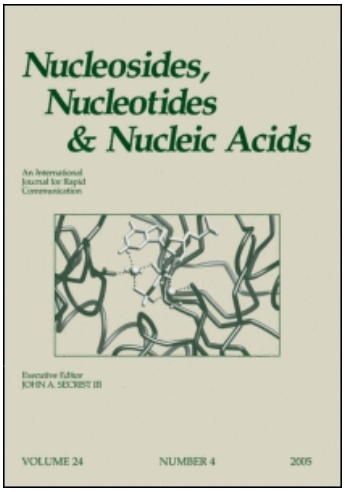

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L-$R_{ibonucleosides\ for}$ R_{acemic} RNA

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L-RIBONUCLEOSIDES FOR RACEMIC RNA

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ABSTRACT: Two L-ribosyl donors were synthesised from L-xylose, then submitted to a glycosidation reaction according to *Vorbrüggen*'s conditions to furnish L-ribonucleosides in high yield.

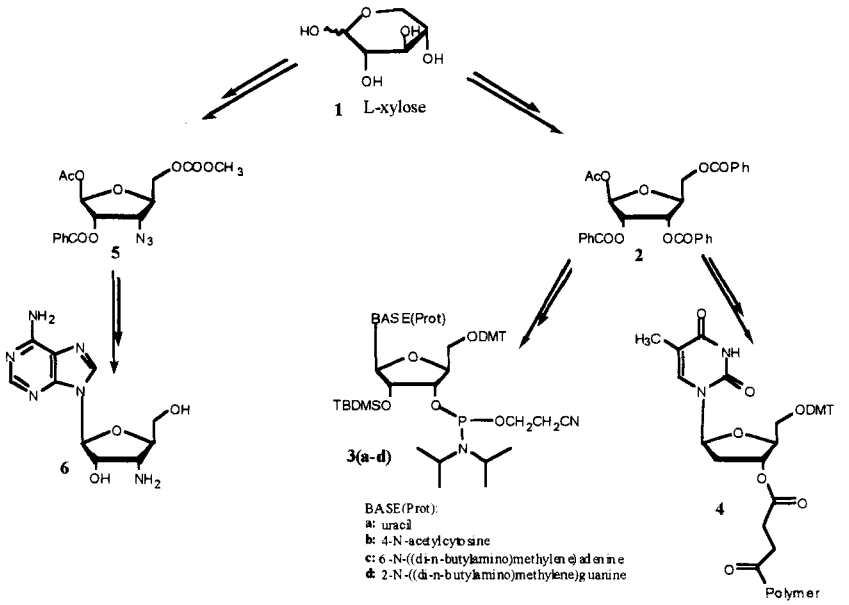
RNA crystal structure solving gained much interest in recent years. But it is impossible to predict whether a particular RNA sequence will crystallise orderly or not. According to *Wallach*'s rules,[1] racemic crystals may be more stable and denser than their enantiomeric counterparts. And also, racemic compounds should crystallise in centrosymmetric unit cells simplifying the procedure of structure solving. The D-nonamer r(GCUUCGGC)dT has already been studied.[2] Its crystallisation occurs in the presence of $Rh(NH_3)_6Cl_3$ and its crystal structure has been elucidated. With this knowledge, we wish to synthesise the enantiomer, the L-nonamer r(GCUUCGGC)dT, and attempt to crystallise D- and L-forms together using established crystallisation procedures, in order to solve the crystal structure of the racemate. The next step in our study will be to chemically synthesise D-aminoacyl-L-RNA strands, which will be stoichiometrically mixed with their enantiomers, in order to obtain the required racemate, then study if the crystallisation occurs. Therefore, we established an efficient synthesis of the four L-ribonucleosides and synthesised the L-phosphoramidites **3 (a-d)**. We also performed the synthesis of an anchoring nucleoside derivatives **4** (in D- and L-forms) for the oligonucleotide synthesis on solid support and the total synthesis of 3'-amino-3'-deoxy-L-adenosine **6**, an intermediate for an aminoacyl anchoring derivative (Fig.).

The ribosyl donor **2** has been synthesised, starting from the L-xylose (**1**), via a six-step synthesis (overall yield of 24 %). The glycosidation reaction according to *Vorbrüggen*[3] using the four protected bases (uracil, 4-N-acetylcytosine, 6-N-benzoyladenine, 2-N-acetyl-6-O-diphenylcarbamoylguanine) afforded the four protected L-ribonucleosides in 89%, 86%, 84% and 70% yield, respectively.[4] After deprotection, the synthesis of the corresponding L-phosphoramidites **3 (a-d)** was carried out following standard procedures.

In both D- and L-series, a thymidine derivative linked to a polymer **4** for oligonucleotide synthesis on solid support has been synthesised. Starting from the ribosyl donor **2**, the glycosidation reaction was carried out (92%), followed by 2'-deoxygenation[5] (88%), dimethoxytritylation and linkage to the solid support.

Proceeding from L-xylose (**1**), 3'-amino-3'-deoxy-L-adenosine (**6**) was obtained via glycosidation reaction. L-Azido-ribosyl donor **5** was synthesized via a seven-step synthesis with an overall yield of 17% and submitted to *Vorbrüggen*'s reaction conditions with 6-chloropurine (81%), deprotected and base-aminated (73%) and then converted to the corresponding amino compound (67%).[6]

FIGURE. Synthetic pathway to L-nucleosides.



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