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## Nucleosides, Nucleotides and Nucleic Acids

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### Studies on Disaccharide Nucleoside Synthesis. Mechanism of the Formation of Trisaccharide Purine Nucleosides

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**STUDIES ON DISACCHARIDE NUCLEOSIDE SYNTHESIS. MECHANISM OF THE FORMATION OF TRISACCHARIDE PURINE NUCLEOSIDES**

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Klaus Rothenbacher<sup>b</sup>, Eveline Lescrinier<sup>b</sup>, Piet Herdewijn<sup>b</sup>

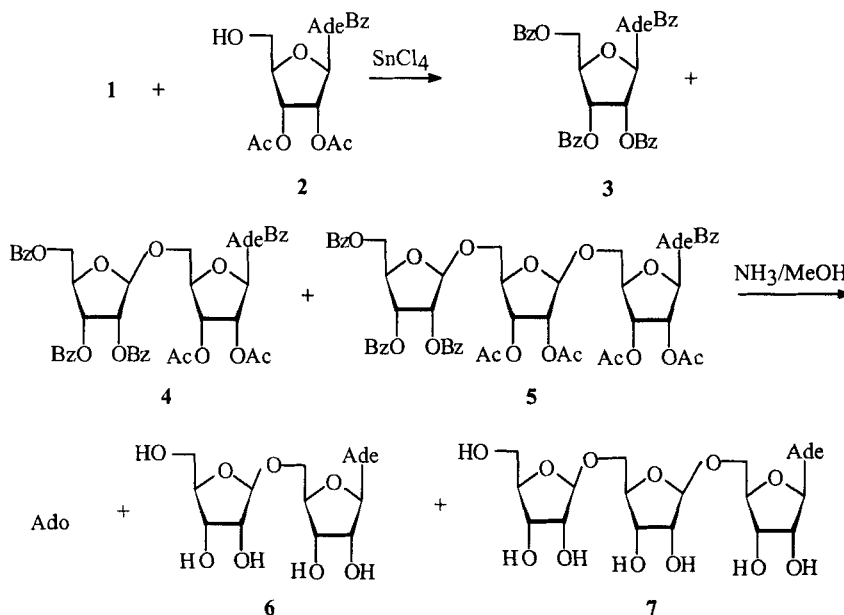
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**ABSTRACT:** The unexpected formation of trisaccharide nucleosides during synthesis of purine 5'-*O*-β-D-ribofuranosylnucleosides in the presence of Lewis acids was observed.

Purine nucleosides having a D-ribofuranosyl substituent bonded to the 2'-hydroxyl function of the nucleoside sugar moiety have been isolated from tRNA<sup>1</sup>. Recently we have developed general route for the preparation of 2'-*O*-β-D-ribofuranosylnucleosides by condensation of partially protected nucleosides with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**1**) in the presence of tin tetrachloride<sup>2</sup>. This reaction was further extended to the synthesis of pyrimidine 5'-*O*-β-D-ribofuranosylnucleosides<sup>3</sup>.

The application of this reaction to the preparation of purine 5'-*O*-β-D-ribofuranosylnucleosides gave a complex mixture of products<sup>4</sup>. Thus condensation of **2** with slight excess of **1** in the presence of 1.2 eq. of SnCl<sub>4</sub> in dichloroethane (0°C, 2 hr, under nitrogen) produced a mixture of compounds **3**, **4** and **5** which was separated on silica gel column (yields 18%, 29% and 17% respectively). Further deprotection of **3**, **4** and **5** with ammonia in methanol gave adenosine, **6** and **7**. The structures of **4-7** were proven by NMR and mass spectroscopy. The formation of trisaccharide **7** as a main by-product was evidently due to the instability of glycosidic bond of adenine nucleosides in the presence of

Lewis acid. Nucleoside **2** was treated with tin tetrachloride for 16 h at 0° C, after usual work-up and saponification, the mixture of adenine, adenosine and **6** was separated by HPLC. It should be mentioned that the formation of disaccharide in this case without acceptor of nucleic base **1** is much slower.



It may be concluded that purine nucleoside is the source of additional ribose moiety in **7**. To exclude the formation of by-products another substrate with more stable glycosidic bond should be used. The alternative route to **6** was proposed starting from 2',3'-O-isopropylidenenucleosides.

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