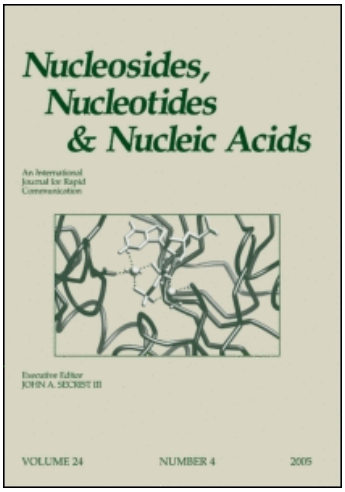

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Investigation of the Synthesis of 2-Carbamoylmethyl-6-D-Ribofuranosylpyridine

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INVESTIGATION OF THE SYNTHESIS OF 2-CARBAMOYLMETHYL-6-D-RIBOFURANOSYLPYRIDINE

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During the course of our study on the synthesis of new pyridine-C-nucleosides with potential anti-viral and/or anti-tumoural properties, the preparation of 2-carbamoylmethyl-6-β-D-ribofuranosylpyridine **1**, by means of a lithiation reaction on 2-(2,3-O-isopropylidene-β-D-ribofuranosyl)-6-methylpyridine **2**, was investigated (Scheme I). The latter compound was prepared by treating 6-methyl-2-(β-D-ribofuranosyl)pyridine[1] **2** with 2,2-dimethoxypropane in the presence of p-toluenesulphonic acid.

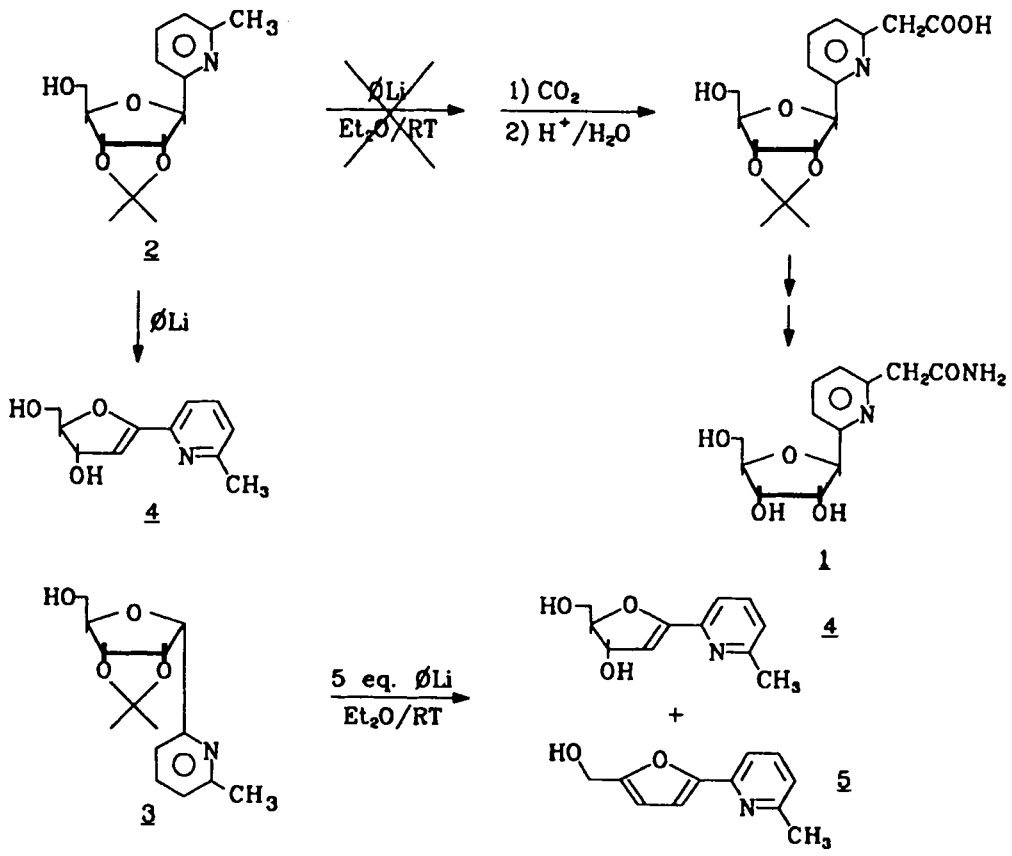
However, the metallation of 2-(2,3-O-isopropylidene-β-D-ribofuranosyl)-6-methylpyridine **2** with the aid of phenyllithium at RT, followed by carboxylation with dry CO_2, did not result in the formation of the expected compound.

Instead an unknown compound was isolated which was identified as 2-(2-deoxy-1,2-didehydroribofuranosyl)-6-methylpyridine **4** (21%). The same compound was obtained from the reaction of phenyllithium with the α-isomer **3** (32%). The use of lithiumtetramethylpiperidide (LTMP) in dimethoxyethane at -78°C did not alter the course of the reaction.

Noteworthy is the fact that the unsaturated nucleoside showed a slow dehydration at RT to the corresponding furanderivative **5**.

A single attempt to improve the yield of the reaction was performed on the α-isomer **3** with 5 eq phenyllithium. This resulted in 28% of the elimination product **4** as well as 38% of the dehydrated compound **5**.

The stability of **4** in phosphate buffer at pH 7.5 at 37°C was studied with HPLC using a solvent mixture MeOH/H_2O 1/1. The results indicated that the nucleoside is unstable, having half-live time of about three days.



Scheme I.

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