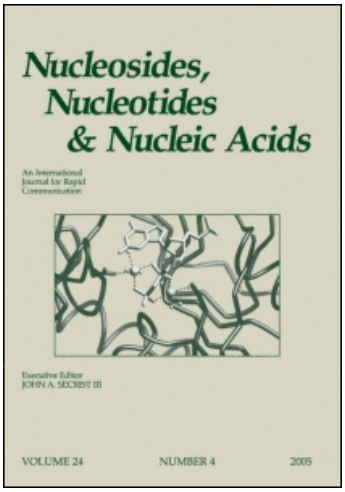

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SYNTHESIS OF SOME PYRIDINE-C-NUCLEOSIDES

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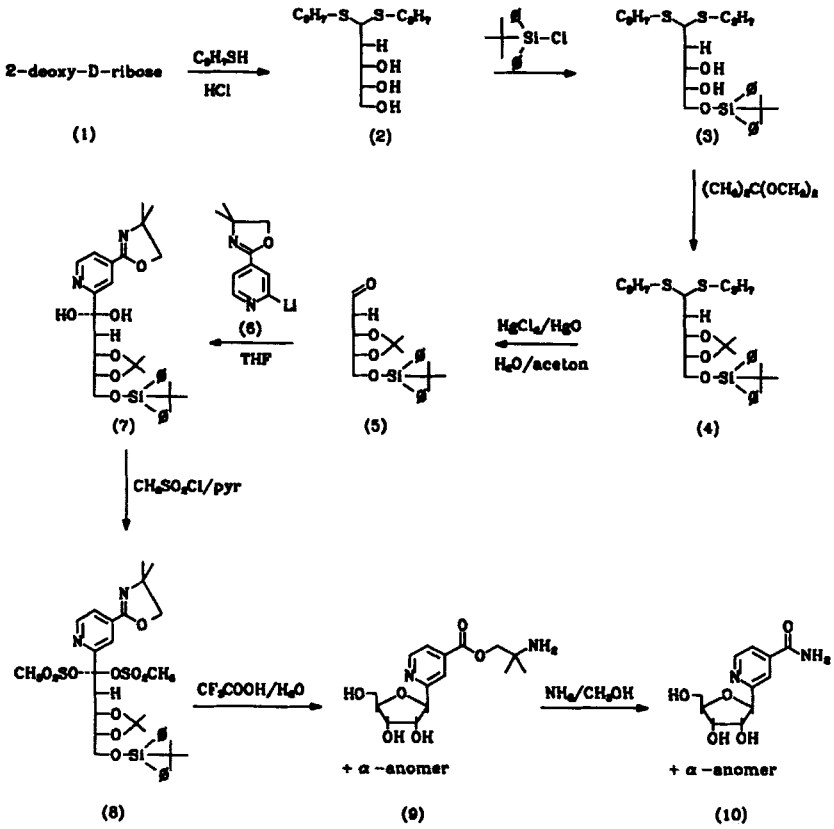
Abstract : The synthesis of 4-carbamoyl-2-(2'-deoxy-ß-D-ribofuranosyl)pyridine (10ß) was accomplished using a new sugar derivative and the appropriate lithiopyridine derivative.

In a program aiming at the synthesis of new pyridine-C-nucleosides, modified in the sugar moiety, 4-carbamoyl-2-(2'-deoxy-ß-D-ribofuranosyl)pyridine (10ß) was synthesised (SCHEME 1). The synthesis of this 2'-deoxy-C-nucleoside is interesting in view of the anti-tumor activity of 4-carbamoyl-2-ß-D-ribofuranosylpyridine[1].

Prior to the synthesis of (10) a new sugar derivative had to be synthesised. 2-Deoxy-D-ribose was treated with propanethiol/HCl according to Zinner[2] and afforded (2) in 95% yield. The thioacetal (2) was protected in the 5-position with *tert*-butyldiphenylsilylchloride[3,4], giving the 5'-O-protected thioacetal (3) in 76% yield as a colorless syrup. The isopropylidene derivative of (3) was synthesised according to Fromageot[5] and yielded a yellow syrup (4) (50% from (3)). Removal of the thioacetal protecting group was accomplished with $HgCl_2$/HgO in acetone/H_2O and gave the protected 2-deoxy sugar as a colorless syrup in 60% yield (from (4)).

Treatment of 2-bromo-4-(4,4-dimethyloxazolin-2-yl)pyridine with BuLi in THF at -78°C resulted in the formation of the 2-lithio derivative (6) which was quenched after 3 min. with 0.9 eq of 5-O-*tert*-butyldiphenylsilyl-2-deoxy-3,4-O-isopropylidene-aldehydo-D-ribose (5). This resulted in the formation of the adducts (7), which were isolated in 50% yield. Mesylation of (7) with methanesulphonylchloride in pyridine yielded the 1'-O-mesyl derivative (8) in 80% yield. Cyclisation with CF_3COOH/H_2O (4/1) at room temperature and subsequent ammonolysis in CH_3OH at 50°C gave the 2'-deoxy nucleoside in 50% yield from (8). The α/ß-anomers were separated by HPLC on a LICHROSORB 10 RP 8-column using H_2O/CH_3OH (85/15) as the eluant. A more detailed paper including the evaluation of antiviral and cytostatic activity is in preparartion.



SCHEME 1

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