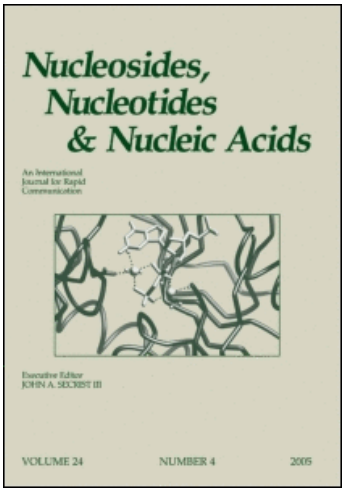

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Synthesis and Biological Evaluation of 4-Amino-1-β-D-Ribofuranosylpyrrolo[3,2-c]Pyriding (3-Deazatubercidin)

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SYNTHESIS AND BIOLOGICAL EVALUATION OF 4-AMINO-1-β-D-RIBOFURANOSYLPYRROLO[3,2-c]PYRIDINE (3-DEAZATUBERCIDIN)

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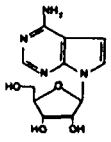
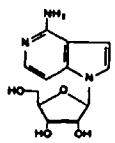
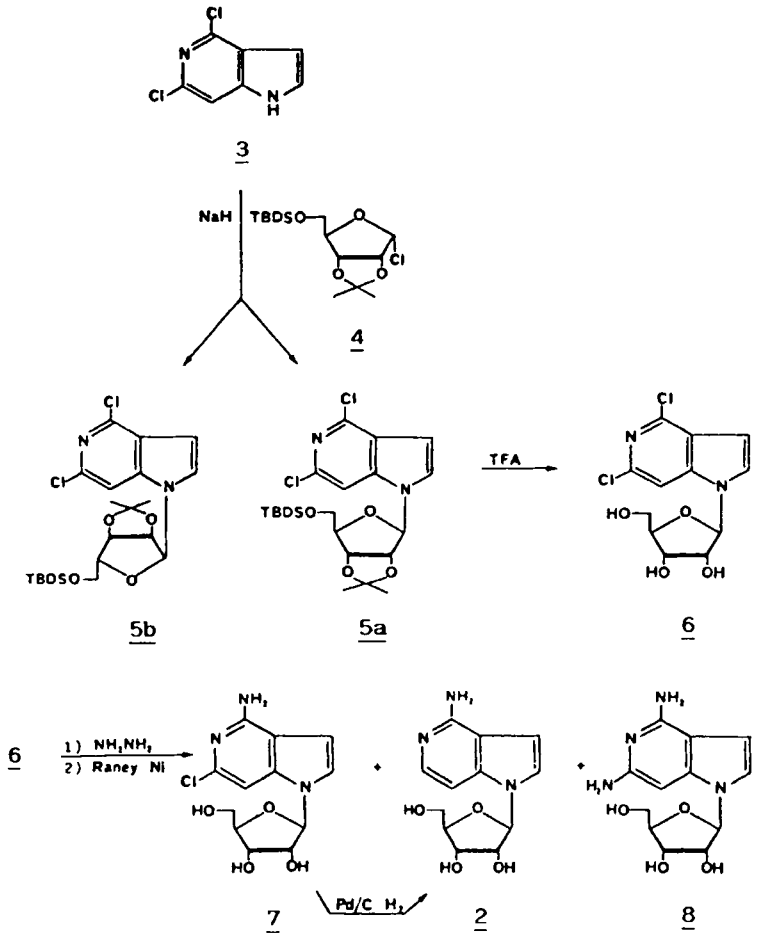
Abstract. 4-Amino-1-β-D-ribofuranosylpyrrolo[3,2-c]pyridine (3-deazatubercidin) has been synthesized in four steps by glycosylation of the anion of the 4,6-dichloro-1H-pyrrolo[3,2-c]pyridine with 1-chloro-2,3-O-isopropylidene-5-O-(t-butyl)dimethylsilyl-α-D-ribofuranose. 3-Deazatubercidin was found devoid of antitumor activity in vitro.

The antitumor, antibacterial and antiviral activity of tubercidin (1) a natural nucleoside, has been widely investigated.[1] We now wish to report on the synthesis of 4-amino-1-β-D-ribofuranosylpyrrolo[3,2-c]pyridine (2), the 3-deaza-analogue of tubercidin, starting from 4,6-dichloro-pyrrolo[3,2-c]pyridine (3).





Reaction of the sodium salt of 3 with 1-chloro-2,3-O-isopropylidene-5-O-(t-butyl)dimethylsilyl-α-D-ribofuranose (4) gave a mixture of the corresponding blocked nucleosides with β- and α-configuration (5a and 5b). Deprotection of 5a with aqueous trifluoroacetic acid gave 4,6-dichloro-1-β-D-ribofuranosylpyrrolo[3,2-c]pyridine (6). Treatment of 6 with hydrazine hydrate, followed by reduction of the resulting 4-hydrazino compound with Raney nickel gave a mixture of 2, 4-amino-6-chloro-1-β-D-ribofuranosylpyrrolo[3,2-c]pyridine (7) and a small amount of 4,-6-diamino-1-β-D-ribofuranosylpyrrolo[3,2-c]pyridine (8). Compounds 2 and 7 have been evaluated in vitro for their ability to inhibit the



growth of murine leukemia P-388 and found inactive. Compound 8 was found to be active in the same test with an ID_{50} of 7.2×10^{-6}M. The inactivity of 3-deazatubercidin and 1-deazatubercidin[2] proves that the nitrogen atoms at positions 1 and 3 of the pyrimidine ring of tubercidin are both essentials for the antitumor activity.

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