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## Nucleosides, Nucleotides and Nucleic Acids

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### Synthesis of 3-Deazaclitocwe [2-Amino-3-nitro-4-( $\beta$ -D-ribofuranosylamino)pyridine] as Cytotoxic Agent

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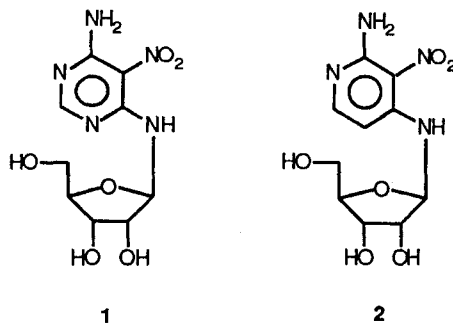
SYNTHESIS OF 3-DEAZACLITOCINE [2-AMINO-3-NITRO-4-( $\beta$ -D-RIBOFURANOSYLAMINO)PYRIDINE] AS CYTOTOXIC AGENT.

Palmarisa Franchetti\*, Loredana Cappellacci, Gloria Cristalli,  
Mario Grifantini and Sauro Vittori

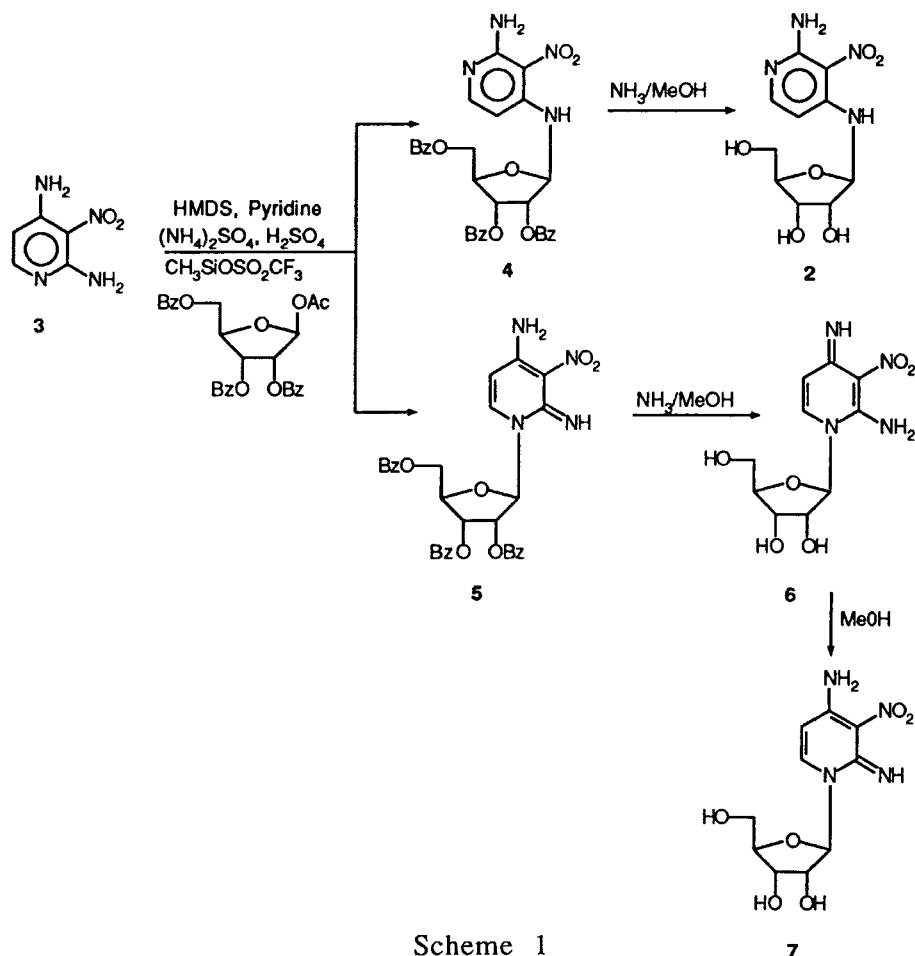
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**ABSTRACT:** The 2-amino-3-nitro-4-( $\beta$ -D-ribofuranosylamino)pyridine (**2**) was synthesized by glycosylation of 2,4-diamino-3-nitropyridine with 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribofuranose. The 4-amino-3-nitro-1-( $\beta$ -D-ribofuranosyl)-2(1H)pyridinimine (**6**) and its tautomer **7** were also obtained. *In vitro* antitumor activity of compounds **2** and **7** was evaluated.

In order to investigate the structure-activity relationships of clitocine (**1**), an antitumor exocyclic nucleoside isolated from *Clitocybe inversa*,<sup>1a,b</sup> we have synthesized its 3-deazaanalogue (**2**) starting from 2,6-diamino-3-nitropyridine<sup>2</sup> (**3**) (Scheme 1).



Compound **3** was silylated and then directly glycosylated with 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribofuranose to give a complex mixture of glycosylated products. Chromatographic separation of this mixture yielded the blocked nucleosides **4** and **5**.



Scheme 1

Deprotection of compounds 4 and 5 with a saturated solution of ammonia in methanol gave 2-amino-3-nitro-4-( $\beta$ -D-ribofuranosyl-amino)pyridine (2) and 4-amino-3-nitro-1-( $\beta$ -D-ribofuranosyl)-4-(1H)pyridinimine (6). Compound 6 was easily converted to the tautomer 7 upon crystallization from methanol.

Compounds 2 and 7 have been evaluated *in vitro* for their ability to inhibit the growth of *murine leukemia* P388 and *human promyelocytic leukemia* HL60. Compound 2 was found to be less active than clitocine ( $\text{ID}_{50}$ ,  $8.8 \times 10^{-5}$  M and  $7.5 \times 10^{-5}$  M).

Compound 7 (a 3-deazacytosine derivative) appears to be more active against both the tumoral cell lines ( $\text{ID}_{50}$ ,  $2.8 \times 10^{-5}$  M and  $8.5 \times 10^{-6}$ ).

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