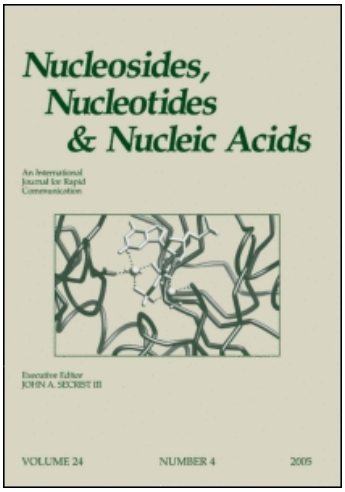

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Synthesis and Biological Activity of Certain 4-Substituted Imidazo[4,5-d]Pyridazine Nucleosides

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF CERTAIN 4-SUBSTITUTED IMIDAZO[4,5-d]PYRIDAZINE NUCLEOSIDES

BY

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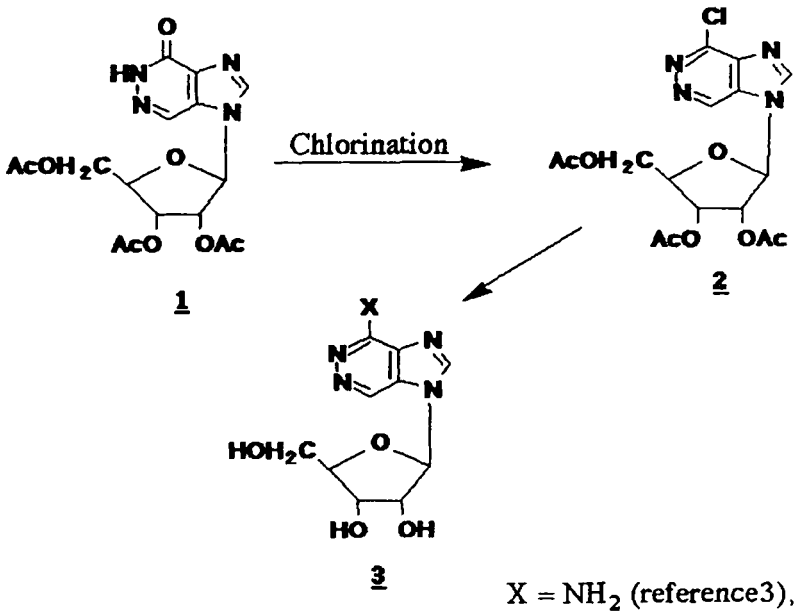
Purine analogues and derivatives exhibit a broad range of pharmaco - logical activities and are used in the chemotherapy of cancer, parasitic and viral infections, and for the suppression of immune responses. Un - doubtedly, this wide range of biological activities reflect an equally wide number of biochemical sites of action, one of which is the purine de novo pathway. New agents which can either serve as inhibitors of enzymes involved in this pathway or as substrates are continually sought. The unique series of nucleosides described herein should meet these desired needs.

The synthesis of 1 involved glycosylation of a suitably 4,5-disubsti - tuted imidazole and subsequent cyclization of the imidazole nucleo - side so formed to the imidazo[4,5-d]pyridazine nucleoside. Such methodology was successfully employed [1,2] in the preparation of certain 4,7-disubstituted imidazo[4,5-d]pyridazine nucleosides. Chlorination of 1 furnished 4-chloro-1-(2,3,5-tri-O-acetyl-β-D-ribo- furanosyl)imidazo[4,5-d]pyridazine (2) in 80% yield. This versatile intermediate can now serve as a precursor to a variety of 4-substi - tuted imidazo[4,5-d]pyridazine nucleosides.

In the present study, we focused our attention on amino bearing substituents at the C4 position. The synthetic methodology leading to the nucleosides 3 as well as their biological activity will be discussed.



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REFERENCES AND NOTES

1. Tapiero, C.; Imbach, J.-L.; Panzica, R.P.; Townsend, L.B. J. Carbohydr. Nucleosides, Nucleotides, 1976, 3, 191.

2. Cook, P.D.; Dea, P.; Robins, R.K. J. Heterocyclic Chem. 1978, 15, 1.

3. For alternate synthesis of 4-amino-1-(β-D-ribofuranosyl)imidazo-[4,5-d] pyridazine, see a) Carbon, J.A. J. Org. Chem. 1960, 25, 579 and b) Gagnier, R.P.; Halat, M.J.; Otter, B.A. J. Heterocyclic Chem. 1984, 21, 481.