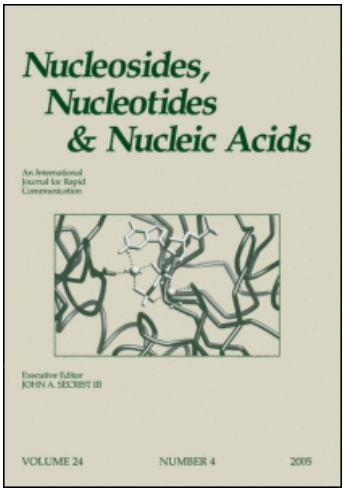

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

A Regiospecific and Stereoselective Rearrangement of a 1-β-D-Ribofuranosyl-5-aminoimidazole to a 4-β-D-Ribofuranosylaminoimidazole

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To cite this Article Ewing, David F. , Mackenzie, Graharne , Rouse, Sean P. N. and Scrowston, Richard M.(1995) 'A Regiospecific and Stereoselective Rearrangement of a 1-β-D-Ribofuranosyl-5-aminoimidazole to a 4-β-D-Ribofuranosylaminoimidazole', Nucleosides, Nucleotides and Nucleic Acids, 14: 3, 367 — 368
To link to this Article: DOI: 10.1080/15257779508012384
URL: http://dx.doi.org/10.1080/15257779508012384

NUCLEOSIDES & NUCLEOTIDES, 14(3-5), 367-368 (1995)

A REGIOSPECIFIC AND STEREOSELECTIVE REARRANGEMENT OF A 1-β-D-RIBOFURANOSYL-5-AMINOIMIDAZOLE TO A 4-β-D-RIBOFURANOSYLAMINOIMIDAZOLE

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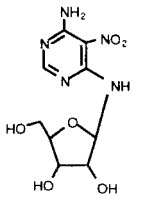
Abstract

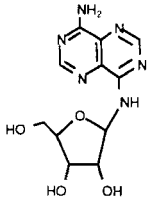
Ethyl 1-methyl-4-(β-D-ribofuranosylamino)imidazole-5-carboxylate **8** was synthesized from ethyl 5-amino-1-(5-*O*-trityl-2,3-*O*-isopropylidene-β-D-ribofuranosyl)imidazole-4-carboxylate **4** by quaternization and subsequent base-catalysed ring-opening and closure.

Clitocine [6-amino-5-nitro-4-(β-D-ribofuranosylamino)pyrimidine] **1** is an exocyclic amino nucleoside which was first isolated from the mushroom *Clitocybe inversa* in 1986 by Kubo *et al.*[1]. Clitocine exhibits a range of biological properties, which include strong insecticidal activity against the pink bollworm *Pectinophora gossypiella*[1] and *in vitro* inhibition of L1210 cells and adenosine kinase[2]. Chemical synthesis of clitocine was achieved in 1988[2,3] and was soon followed by the preparation of carbocyclic analogues[4,5]. Other exocyclic amino nucleosides include 4-amino-8-(β-D-ribofuranosylamino)pyrimido[5,4-*d*]pyrimidine **2**, which was synthesized by Robins *et al.*[6]. Analogous exocyclic amino nucleosides which contain an imidazole moiety have not been previously reported.

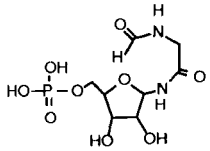


1

Clitocine



2



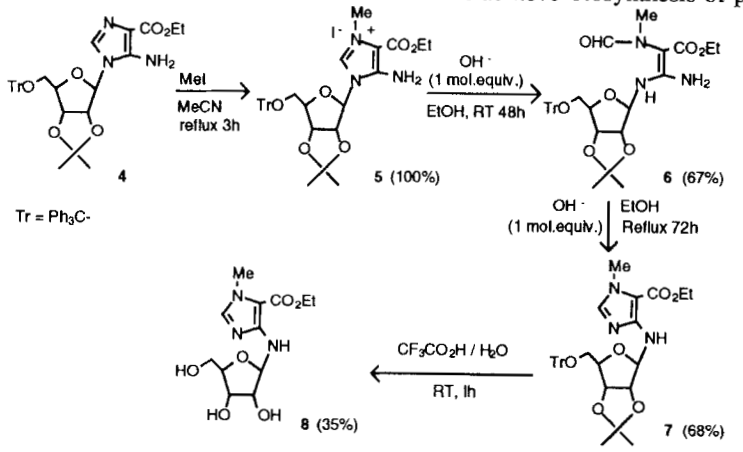
3

FGAR

In previous studies[7,8] imidazoles were quaternized at the N-3 position by use of methyl iodide and the resulting quaternary compounds were found to be labile to base-catalysed ring-opening[8] but the nature of the products was not established. We have now investigated the reaction in greater detail and are able to report the regiospecific and stereoselective

synthesis of the exocylic amino nucleoside **8** from the protected nucleoside **4**[9,10] in 16% overall yield.

Quaternization of the nucleoside **4** with MeI in refluxing MeCN gave **5** in quantitative yield. The acyclic intermediate **6** was the sole product of the action of base (1 mol. equiv.) on the 3-*N*-methylimidazole quaternary salt **5** at room temperature. Interestingly, this is an analogue of FGAR **3**, which is an intermediate in the *de novo* biosynthesis of purines.



Ring closure of compound **6** was effected by heating under reflux with a further mol. equiv. of base to give **7** exclusively. Deprotection of **7** was achieved by use of aqueous trifluoroacetic acid (50%) at room temperature to yield the free nucleoside **8.** Structures of all compounds were established by ^{1}H NMR spectroscopy and mass spectrometry. The β-anomeric configuration of compounds **7** and **8** was confirmed by ^{1}H NMR spectroscopy[11].

ACKNOWLEDGEMENT

We thank the EPSRC for financial support (to SPNR) and Dr R. W. Humble for providing a sample of compound **4**.

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