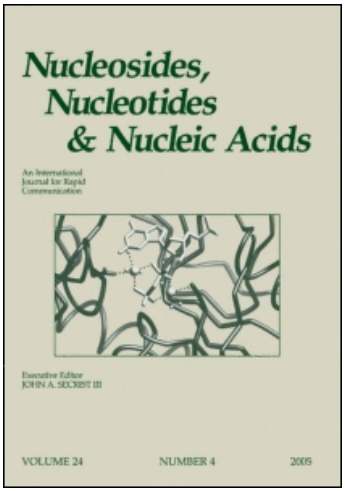

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Glycosylation of 5-Hydroxy-4-cyanoimidazole

Fatma Ibrahim-lodgemann[a]; Grahame Mackenzie[a]; Gordon Shaw[ab]
[a] School of Science, Humberside College of Higher Education, Hull [b] School of Chemistry, University of Bradford, Bradford, W. Yorkshire, (U.K.)

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GLYCOSYLATION OF 5-HYDROXY-4-CYANOIMIDAZOLE

Fatma Ibrahim-Lodgemann[+], Grahame Mackenzie[+] and Gordon Shaw[+ ø]
[+]School of Science, Humberside College of Higher Education, Hull, HU6 7RT and [ø]School of Chemistry, University of Bradford, Bradford, W. Yorkshire, BD7 1DP (U.K.)

Summary: The sodium derivative of 5-hydroxy-4-cyanoimidazole with 2,3,5-tri-O-benzoylribofuranosyl bromide gave 5-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)oxy-4-cyanoimidazole whereas with 2,3,5-tri-O-benzyl-α/β-D-arabinofuranosyl)-4-cyanoimidazole was produced. The compounds were characterised by ^{1}H-n.m.r. and mass spectrometry.

Bredinin[1](1) is a novel imidazole nucleoside isolated from Eupenicillium brefeldianum M-2166 and possess potent immunosuppressive activity and selective cytotoxicity against L5187 Y cells derived from a malignant lymphoma of the mouse. It also inhibits the growth of vaccinia virus but apart from its inhibitory action on Candida albicans in vitro it shows little antibacterial or antifungal activity. It has been synthesised[2] by the reaction of the trimethylsilyl derivative of 5-hydroxy-4-carbamoylimidazole with either 1-O-acetyl-2,3,5-tri-O-benzoyl-D-ribofuranose or 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose in the presence of titanium tetrachloride and deblocking of the intermediate triacyl derivatives. X-ray crystal analysis indicates that Bredinin has the dipolar structure (1).

We have been interested to make the nitrile corresponding to Bredinin as a potential intermediate in the synthesis of a variety of analogues of the antibiotic. Attempts to prepare the compound either by an extension of the latter or by heating the mercury salt with 2,3,5-tri-O-benzoyl-D-ribofuranosyl chloride proved unsuccessful. However, a suspension of the sodium derivative of the hydroxy nitrile (2) in acetonitrile reacted with 2,3,5-tri-O-benzoyl-D-ribofuranosyl

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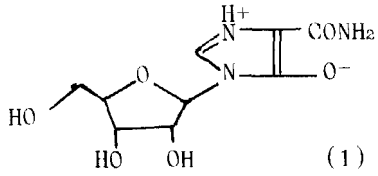
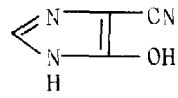
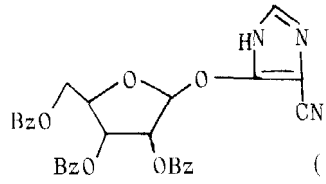
bromide to produce a single product which was readily obtained crystalline after chromatography on silica gel and had the elemental composition of the required nucleoside derivative.



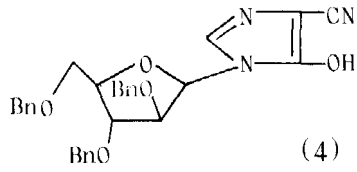
(1)



(2)



(3)



(4)

However, attempts to debenzoylate the nucleoside with methanolic ammonia or sodium methoxide led to rapid formation of the aglycone (2) and ribose. The lability of the compound to bases, a property not possessed by Bredinin tri-O-benzoate, suggested that it is the O-glycoside (3). ^{1}H-n.m.r., spectroscopy supported this evidence and the β-configuration for the compound seems likely from the observed zero coupling constant ($J_{1',2'}$). In addition, attempts to rearrange the O-nucleoside (3) by heating with mercuric bromide using a method which had proved successful[3] for conversion of O-to N- glycosyl cytosines in our case resulted in no change in the starting material.

Similarly reaction of the sodium salt of (2) with 2,3,5-tri-O-benzyl-α-D-arabinofuranosyl chloride in acetonitrile gave a single product which was readily isolated in crystalline form and possessed the elemental composition of the expected nucleoside. The product appeared stable under mild basic conditions and showed similar spectroscopic characteristics (^{1}H-n.m.r. and m.s.) to that of Bredinin and was, therefore, assigned as the N-glycoside (4).

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