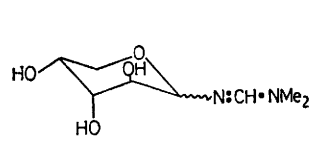
Synthesis of a Novel Acyclic D-Arabinose Nucleoside

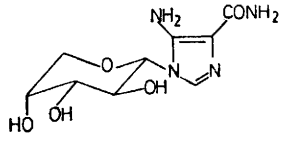
By GRAHAME MACKENZIE and GORDON SHAW
(*School of Chemistry, University of Bradford, Bradford* BD7 1DP)

Summary D-Arabinopyranosylamine and (dimethoxymethyl)dimethylamine produce *N*-dimethylaminomethylene-D-arabinopyranosylamine, heating of which with methanolic acetic acid and reaction of the product with α-amino-α-cyanoacetamide produces a mixture of 5-amino-1-α- and -β-D-arabinopyranosylimidazole-4-carboxamides, together with the acyclic nucleoside (IV).

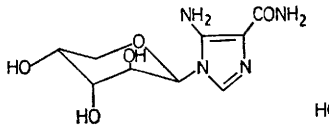
REACTION of D-arabinopyranosylamine with $Me_2NCH(OMe)_2$ gave the crystalline (from acetonitrile) glycosyl formamidine derivative (I) of unknown anomeric configuration. A similar D-xylosyl derivative has been prepared and converted into a 5-amino-1-α-D-xylofuranosylimidazole-4-carboxamide by



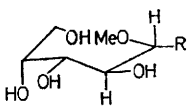
(I)

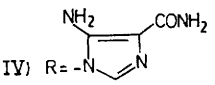


(II)

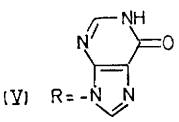


(III)





(IV) R = -



(V) R = -

reaction of the acid-treated product with α-amino-α-cyanoacetamide.[1] In the hope of achieving a similar sequence of reactions in the arabinose case, compound (I) was heated with methanolic acetic acid for 45 min and the solution then treated with α-amino-α-cyanoacetamide.

From the reaction mixture, by chromatography on Amberlite CG-400 (OH^- form), were isolated the two arabinopyranosyl imidazole derivatives (II) and (III). Their structures were confirmed by conversion with HCO_2Et and NaOEt into the corresponding known arabinopyranosyl hypoxanthines.[2] A third crystalline compound, m.p. 189°, was isolated from the chromatographic separation of (II) and (III) in a yield of *ca.* 20%. We suggest the novel acyclic structure (IV) for this compound.† The configuration about C–1 in (IV) was established by comparison of its ^1H n.m.r. data (δ; $J_{1',2'}$/Hz) (5·08; < 1) with those of the arabinopyranosylimidazoles (II) (4·92; 9) and (III) (5·78; < 1) and the corresponding arabinopyranosylhypoxanthine derivatives[2] (5·30; 9) and (6·03; < 1) respectively in $(CD_3)_2SO$. Compound (IV) had a u.v. absorption spectrum very similar to that of typical 1-substituted glycosyl imidazoles of this type and in addition could be diazotised and the product coupled with α-naphthylethylenediamine to produce a coloured dyestuff with an absorption spectrum characteristic of the glycosyl aminoimidazoles.[3] In addition, reaction of (IV) with HCO_2Et and NaOEt produced the corresponding crystalline acyclic hypoxanthine derivative (V), m.p. 193°, the structure of which was further confirmed by periodate titration (exactly 3 equiv. absorbed), and a u.v. absorption spectrum very similar to that of inosine and related 9-glycosylhypoxanthines.

This route to the novel acyclic structures (IV) and derived purine nucleosides such as (V) and related adenines or mercaptopurines could be of value both in general synthesis and also as providing potential slow release precursors *in vivo* of known active drugs such as Ara-A.[4]

(*Received*, 28*th October* 1974; *Com.* 1316.)

† Satisfactory analytical, tlc and spectral data were obtained for all new compounds.

[1] D. H. Robinson and G. Shaw, *J.C.S. Perkin I*, 1974, 774.
[2] A. P. Martinez and W. W. Lee, *J. Org. Chem.*, 1969, **34**, 416.
[3] N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg, and G. Shaw, *J.C.S. Perkin I*, 1973, 1720.
[4] R. J. Suhadolnik, 'Nucleoside Antibiotics' Wiley-Interscience, London and New York, 1970.