Purines, Pyrimidines, and Imidazoles. Part XLII.[1] Stereospecific Synthesis of Some D-Xylofuranosylimidazole Derivatives from Oxazoline Intermediates and Some Related Compounds derived from D-Ribofuranosylamine

By **David H. Robinson** and **Gordon Shaw,*** *School of Chemistry, University of Bradford, Bradford 7*

The reaction of 3,5-*O*-isopropylidene-D-xylofuranosylamine with ethyl formimidate (or acetimidate) or derived formamidines gave 3,5-*O*-isopropylidene-α-D-xylofuranoso[1,2-*d*]-Δ$^{2'}$-oxazoline (or the 2'-methyl derivative), which with α-amino(cyano)acetamide or ethyl α-amino(cyano)acetate gave stereospecifically the corresponding 5-amino-1-(3,5-*O*-isopropylidene-α-D-xylofuranosyl)imidazole-4-carboxylic acid derivatives, from which the isopropylidene groups were removed by acidic hydrolysis. D-Xylopyranosylamine with dimethylformamide dimethyl acetal produced an acyclic xylopyranosylformamidine from which 5-amino-1-D-xylopyranosylimidazole-4-carboxamide was prepared, but on acidic treatment the formamidine gave the corresponding xylofuranosyl derivative. 2,3-*O*-Isopropylidene-D-ribofuranosylamine with dimethylformamide dimethyl acetal gave an acyclic ribosylformamidine which with ethyl α-amino(cyano)acetate produced mainly a β-D-imidazole ribofuranoside. The structures assigned were confirmed by analytical and u.v., n.m.r., and mass spectral techniques.

THE preparation of the isopropylidene D-xylofuranosylamine (I) toluene-*p*-sulphonate and its use in the synthesis of pyrimidine nucleosides were described in Part XLI.[1] We have also recently described [1,2] two general routes to 5-aminoimidazole nucleosides, including D-ribose and D-mannose derivatives, (*a*) by condensation of a glycofuranosylamine with pre-formed complex imidates (IIa) or (IIb) and (*b*) by prior reaction of the glycofuranosylamine with ethyl formimidate hydrochloride and treatment of the resulting mixture of anomeric glycosyl formimidates (III) with ethyl α-amino(cyano)acetate or α-amino(cyano)acetamide. We now describe the results of the application of these two procedures to the D-xylofuranosylamine (I).[3]

In initial experiments, t.l.c. of the products of the reaction of (I) with the imidate (IIa) revealed the presence of two u.v. absorbing compounds, active in the Bratton–Marshall assay [4] for aromatic amines, which presumably were the α- and β-xylosylimidazoles (IVa) and (V), but these were not isolated in pure form. Reaction of (I) with ethyl formimidate hydrochloride in an attempt to produce a xylosyl formimidate of type (III) gave a high yield of a crystalline compound to which we assign the oxazoline structure (VIa). The structure was confirmed by elemental analysis, i.r. spectrum [absence of OH, strong band at 1620 cm^{-1} (C=N), and a doublet at 1380 cm^{-1} (CMe_2)], mass spectrum [weak peaks at *m/e* 199 (M^+) and 200 ($M^+ + 1$) and a strong peak at *m/e* 184 ($M^+ - CH_3$), a pattern characteristic of carbohydrate isopropylidene derivative [5]], and n.m.r. spectroscopy (Table 1). The same oxazoline was obtained in similar high yield by the reaction of (I) with formamidine acetate or dimethylformamide dimethyl acetal.

The oxazoline (VIa) reacted smoothly with ethyl α-amino(cyano)acetate or α-amino(cyano)acetamide to produce stereospecifically the aminoimidazole α-nucleosides (IVa) and (IVb), respectively, as crystalline solids in good yield. The structure of each compound was confirmed by elemental analysis, mass and u.v. spectra (Table 2), and the formation of a coloured dyestuff in the Bratton–Marshall assay. In each case only one nucleoside isomer was isolated, and t.l.c. failed to reveal other isomers. The α-configuration is assigned on the basis of the mode of synthesis and of the similarity of the carbohydrate $J_{1,2}$ values of the oxazoline and the derived nucleosides (Table 1). The α-nucleoside (IVa) obtained was identical (t.l.c.) with one of the aforementioned two products formed by the first of the two general methods involving preformed imidates; this helps confirm the postulated identity of this pair of compounds. The imidazole nucleoside (IVb) readily gave a pure, crystalline picrate. The isopropylidene nucleosides (IVa and b) were readily hydrolysed by aqueous acid to the nucleosides (VIIa and b), respectively; hydrolysis is complete in *ca.* 15 min (*cf. ca.* 3·5 h for the analogous α-ribose nucleoside). In a similar manner the xylofuranosylamine (I) with ethyl acetimidate hydrochloride gave the 2-methyloxazoline (VIb) in high yield as a crystalline solid, the structure of which was confirmed by elemental analysis and mass and n.m.r. spectroscopy (Table 1). The methyloxazoline with ethyl α-amino(cyano)acetate or α-amino(cyano)-acetamide gave the corresponding α-nucleoside (IVc or d), identified by elemental analysis, mass and u.v.

TABLE 1

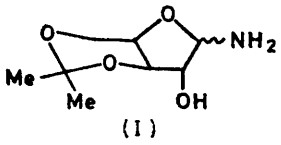
N.m.r. data * for some xylofuranosylimidazoles and xylofuranosyloxazolines

Compound	Solvent	H-1′ ($J_{1',2'}$/Hz)	H-2
(VIa)	$CDCl_3$	6·17 (6·0 ± 0·5)	7·00 (s)
(IVa)	D_2O	6·13 (4·0 ± 0·5)	7·44 (s)
(VIb)	$CDCl_3$	6·12 (6·0 ± 0·5)	
(IVc)	$(CD_3)_2SO$	5·98 (4·0 ± 0·5)	

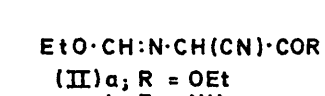
* δ Values; internal Me_4Si standard.

[1] Part XLI, N. J. Cusack, D. H. Robinson, P. W. Rugg, G. Shaw, and R. Lofthouse, *J.C.S. Perkin I*, 1974, 73.
[2] N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg, and G. Shaw, *J.C.S. Perkin I*, 1973, 1720.
[3] Preliminary account, D. H. Robinson and G. Shaw, *Experientia*, 1972, **28**, 763.
[4] C. Bratton and E. K. Marshall, *J. Biol. Chem.*, 1939, **128**, 537.
[5] P. Brown, G. R. Pettit, and R. K. Robins, *Org. Mass Spectrometry*, 1969, **2**, 521; J. J. Dolhun and J. L. Wiebers, *ibid.*, 1970, **3**, 669.

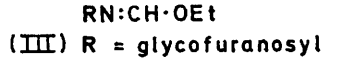
spectra (Table 2), and the Bratton–Marshall assay (Table 2).



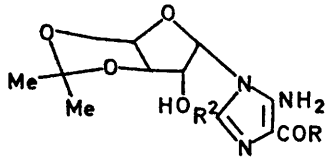
(I)



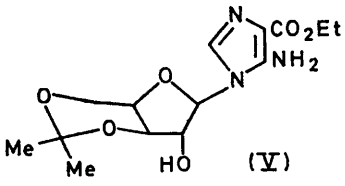
(II) a; R = OEt
b; R = NH_2



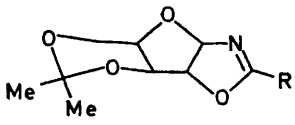
(III) R = glycofuranosyl



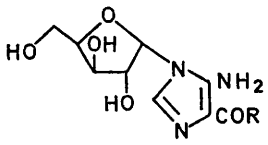
(IV) a; R^1 = OEt, R^2 = H
b; R^1 = NH_2, R^2 = H
c; R^1 = OEt, R^2 = Me
d; R^1 = NH_2, R^2 = Me



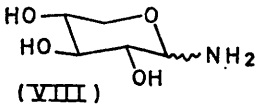
(V)



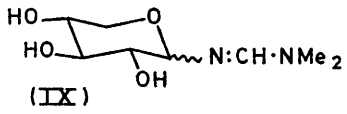
(VI) a; R = H
b; R = Me



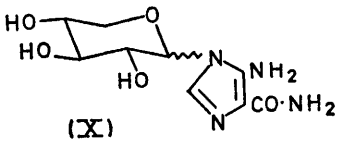
(VII) a; R = OEt
b; R = NH_2



(VIII)



(IX)



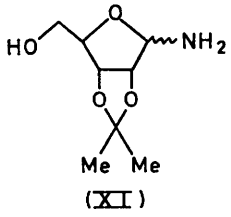
(X)

Oxazolines of the foregoing types are novel although analogous 2-amino-derivatives derived from ribose and arabinose have been described [6] and shown to react with cyanoacetylene to produce pyrimidine nucleosides. Preliminary experiments in our hands have indicated that such amino-oxazolines have little tendency to react with compounds such as α-amino(cyano)acetamide to produce imidazole nucleosides.

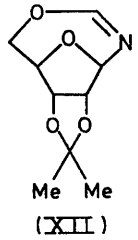
[6] R. A. Sanchez and L. E. Orgel, *J. Mol. Biol.*, 1970, **47**, 531.
[7] Z. Arnold and M. Karnilov, *Coll. Czech. Chem. Comm.*, 1966, **29**, 645.

In an attempt to convert the D-xylopyranosylamine (VIII) into a furanoso-oxazoline it was treated with dimethylformamide dimethyl acetal;[7] however, the product was the acyclic derivative (IX), isolated as a crystalline solid in good yield and identified by elemental analysis and i.r. spectra [strong band at 1640 cm^{-1} (C=N)]. Also the product reacted readily with α-amino(cyano)acetamide in the presence of acetic acid to produce the xylopyranosylimidazole (X), which was isolated and characterised as a crystalline picrate. The product (X) was identical with that obtained by direct condensation of (VIII) with the more complex imidate (IIb). However if (IX) was first heated with acetic acid mutarotation occurred. When the resulting mixture was condensed with α-amino(cyano)acetamide t.l.c. revealed two major strongly absorbing Bratton–Marshall active spots, one of which corresponded to the xylopyranosyl derivative (X) and the other, more intense spot to the xylofuranosylimidazole (VIIb). Also treatment of the crude mixture with toluene-*p*-sulphonic acid and acetone gave the isopropylidene derivative (IVb), which was isolated as a crystalline picrate and shown to be identical (m.p., mixed m.p., t.l.c., and i.r.) with the material prepared directly from the oxazoline (VIa).

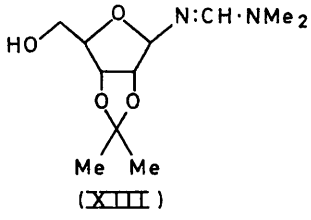
The results obtained with the xylose derivatives and the stereospecificity of nucleoside formation from oxazoline precursors prompted us to examine the possibility of synthesis from the isopropylideneribosylamine (XI) of an analogous compound (XII), which might be expected to be a source of β-ribonucleosides. The ring system in (XII) exists in analogous cyclonucleosides derived from 5-*p*-tolylsulphonyluridine.[8]



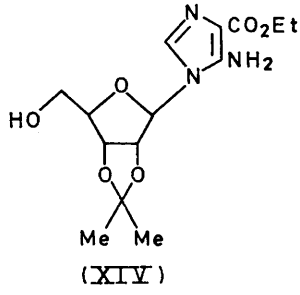
(XI)



(XII)



(XIII)



(XIV)

Treatment of (XI) with ethyl formimidate hydrochloride has already been shown [2] to produce a non-crystalline

[8] W. W. Zorbach and R. S. Tipson, 'Synthetic Procedures in Nucleic Acid Chemistry,' Interscience, New York, 1968.

TABLE 2

Optical rotation, light absorption, and R_F values of some xylosylaminoimidazole derivatives

Nucleoside	$[\alpha]_D^{20}$ (°) (*c* in Me_2SO)	$\lambda_{max.}$/nm (ε) (in MeOH)	λ_{max} /nm of dyestuff produced in Bratton–Marshall assay	R_F (B)	R_F (A)
(IVa)	−24 (0·4)	266 (12,640)	513	0·53	0·47
(V)				0·54	0·48
(IVb)	−56 (1·3)	267 (12,800)	527	0·49	0·23
(VIIa)	−24 (1)	268 (12,610)	528	0·45	0·09
(VIIb)	−19 (0·5)	267 (12,350)	527	0·41	0·01
(IVc)	−21 (0·4)	272 (11,370)	530	0·48	0·51
(IVd)	−22 (1·3)	271 (12,400)	528	0·52	0·17
(X)	−16 (2)			0·36	

mixture of ribofuranosyl formimidates (III; R = ribofuranosyl). A similar reaction of (XI) with dimethylformamide dimethyl acetal however gave the crystalline glycosylformamidine (XIII), the β-configuration of which was suggested by its reaction with ethyl α-amino(cyano)acetate to give almost entirely the β-nucleoside (XIV).

EXPERIMENTAL

Evaporations were carried out with a Büchi rotary evaporator under water pump vacuum with a flask temperature ⩽40° unless otherwise stated. U.v. absorption spectra were measured with a Unicam SP 800 spectrophotometer, i.r. spectra with a Perkin-Elmer 157 spectrophotometer, n.m.r. spectra with a JEOL-MH-100 spectrometer (tetramethylsilane or 3-trimethylsilylpropane-1-sulphonic acid as internal standard), mass spectra with an A.E.I. MS 902 spectrometer, and optical rotations with a Perkin-Elmer 141 polarimeter. Silica gel (0·05—0·20 mm; 315—70 mesh) from Machery Nagel and Co. was used for column chromatography, and silica gel $60F_{254}$ 0·25 mm precoated glass plates from Merck were used for t.l.c., with (A) $CHCl_3$–MeOH (9 : 1), and (B) n-butanol–acetic acid–water (12 : 3 : 5) as development systems.

Ethyl 5-Amino-1-(3,5-O-isopropylidene-α-D-xylofuranosyl)imidazole-4-carboxylates (IVa) *and* (V).—A solution of ethyl α-amino(cyano)acetate [9] (1·5 g) and triethyl orthoformate (1·8 ml) in acetonitrile (30 ml) was boiled under reflux for 45 min, cooled, and added to a mixture of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate [1] (2·9 g) and ethanolic sodium ethoxide (50 ml containing 8 mmol of sodium). The resulting mixture was set aside at room temperature overnight. T.l.c. [system (A)] then showed two Bratton–Marshall active spots (R_F 0·48 and 0·47) and much aglycone (R_F 0·29).

3,5-O-*Isopropylidene-α-D-xylofuranoso*[1,2-d]-$\Delta^{2'}$-*oxazoline* (VIa).—(*a*) A suspension of ethyl formimidate hydrochloride (1·2 g) in a solution of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (3·6 g) and triethylamine (1·4 ml) in acetonitrile (60 ml) was shaken at room temperature for 20 min; the crystalline hydrochloride was replaced by an amorphous precipitate of ammonium chloride. The mixture was filtered and the filtrate evaporated to a gum. A solution of this in chloroform (50 ml) was washed with water (30 ml), dried (Na_2SO_4), and evaporated to a waxy crystalline solid. The *oxazoline* (1·26 g, 63%) was collected and recrystallised from a small volume of ethyl acetate to give rods, m.p. 120—121°, $[\alpha]_D^{20}$ +9° (*c* 2·7 in Me_2SO) (Found: C, 54·25; H, 6·85; N, 6·9%; *m/e* 200. $C_9H_{13}NO_4$ requires C, 54·25; H, 6·6; N, 7·05%; *M*, 199).

(*b*) A solution of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (3·6 g), freshly dried (P_2O_5) formamidine acetate (1·04 g), and triethylamine (2·8 ml) in methanol (100 ml) was heated under reflux for 2 h, cooled, and evaporated to a gum. A solution of this in chloroform (30 ml) was washed with water (20 ml), dried (Na_2SO_4), and evaporated to a waxy crystalline residue (0·92 g, 46%). Crystallisation from ethyl acetate gave the oxazoline, identical (m.p., mixed m.p., i.r., and n.m.r.) with that formed in (*a*).

(*c*) A solution of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (3·6 g), dimethylformamide dimethyl acetal (1·5 g), and trimethylamine (1·4 ml) in acetonitrile (50 ml) was heated under reflux for 1 h. The resulting solution was cooled and evaporated to a gum, which gave the oxazoline, identical (m.p., mixed m.p., and i.r.) with that formed in (*a*).

Ethyl 5-Amino-1-(3,5-O-isopropylidene-α-D-xylofuranosyl)-imidazole-4-carboxylate (IVa).—A solution of the oxazoline (VIa) (2 g) and ethyl α-amino(cyano)acetate (1·4 g) in acetonitrile (50 ml) was heated under reflux for 0·5 h. T.l.c. [system (A)] showed one major Bratton–Marshall-active spot at R_F 0·47. The solution was evaporated to a gum which was dissolved in ethyl acetate and stored at 0° overnight to produce a crystalline solid, R_F 0·47 [system (A)]. The *ester* (IVa) crystallised from ethyl acetate as spars (2·3 g, 70%), m.p. 177—179° (Found: C, 51·5; H, 6·6; N, 12·55%; M^+, 327. $C_{14}H_{21}N_3O_6$ requires C, 51·35; H, 6·45; N, 12·85%; *M*, 327).

5-Amino-1-(3,5-O-isopropylidene-α-D-xylofuranosyl)imidazole-4-carboxamide (IVb).—A solution of the oxazoline (VIa) (2 g) and α-amino(cyano)acetamide [10] (1·0 g) in acetonitrile (50 ml) was heated under reflux for 0·5 h. T.l.c. [system (A)] showed the presence of one major Bratton–Marshall-active spot at R_F 0·23. The solution was evaporated to a foam and a solution of this in 30% ethanolic chloroform was applied to a silica gel column (1·5 × 30 cm). The major Bratton–Marshall-active product was eluted with 10% ethanolic chloroform. A solution in 10% ethanolic ethyl acetate (5 ml) soon gave the *carboxamide* (IVb) as a crystalline solid, which formed solvated needles (1·4 g, 43%), m.p. 212—213° (from 10% ethanolic ethyl acetate) (Found: C, 49·9; H, 6·45; N, 17·15%; M^+, 298. $C_{12}H_{18}N_4O_5$,0·5EtOAc requires C, 49·20; H, 6·5; N, 16·4%; *M*, 298). The *picrate*, prepated in methanol, had m.p. 157° (decomp.) (Found: C, 40·65; H, 4·1; N, 17·9. $C_{22}H_{18}N_4O_5$,$C_6H_3N_3O_7$ requires C, 41·0; H, 4·0; N, 18·6%).

Ethyl 5-Amino-1-(α-D-xylofuranosyl)imidazole-4-carboxylate (VIIIa).—A solution of the ester (IVa) (500 mg) in 20% aqueous acetic acid (10 ml) was heated at 100° for 15 min.

[9] D. H. Robinson and G. Shaw, *J.C.S. Perkin I*, 1972, 1715.
[10] L. H. Smith and P. Yates, *J. Amer. Chem. Soc.*, 1954, **76**, 6080.

T.l.c. [system (A)] showed the absence of the isopropylideneimidazole (R_F 0·47) and the presence of a new Bratton–Marshall-active spot (R_F 0·09). The cooled solution was evaporated and the residue re-evaporated with water (2 × 10 ml). A solution of the residual gum in water (5 ml) soon produced the crystalline *imidazole nucleoside*, which formed plates (390 mg, 92%), m.p. 207—208° (from aqueous alcohol) (Found: C, 46·3; H, 6·05; N, 14·65%; M^+, 287. $C_{11}H_{17}N_3O_6$ requires C, 45·95; H, 5·95; N, 11·6%; *M*, 287).

5-*Amino*-1-(α-D-*xylofuranosyl*)*imidazole*-4-*carboxamide* (VIIb).—A solution of the amide (IVb) (500 mg) in 20% aqueous acetic acid (10 ml) was heated at 100° for 15 min, cooled, and evaporated. The residue was re-evaporated with water (2 × 10 ml) to give the crystalline *imidazole nucleoside* which formed needles (380 mg, 87%), m.p. 222—223° (decomp.) (from aqueous ethanol) (Found: C, 41·55; H, 5·5; N, 21·55%; M^+, 258. $C_{19}H_{14}N_4O_5$ requires C, 41·85; H, 5·45; N, 21·7%; *M*, 258).

3,5-O-*Isopropylidene*-2′-*methyl*-α-D-*xylofuranoso*[1,2-d]-Δ²′-*oxazoline* (VIb).—A suspension of powdered ethyl acetimidate hydrochloride (1·34 g) in a solution of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (3·6 g) and triethylamine (1·4 ml) in acetonitrile (60 ml) was shaken at room temperature for 1 h. The amorphous precipitate was removed and the filtrate evaporated to a gum. A solution of the gum in chloroform (30 ml) was washed with water (20 ml), dried (Na_2SO_4), and evaporated to a waxy, crystalline residue. Recrystallisation from a small amount of ethyl acetate gave the *methyloxazoline* as spars (1·4 g, 65%), m.p. 199—200°, $[\alpha]_D^{20}$ +10° (*c* 2·7 in Me_2SO) (Found: C, 56·3; H, 7·2; N, 6·6%; *m/e*, 214. $C_{10}H_{15}NO_4$ requires C, 56·3; H, 7·1; N, 6·55%; *M*, 213).

Ethyl 5-*Amino*-1-(3,5-O-*isopropylidene*-α-D-*xylofuranosyl*)-2-*methylimidazole*-4-*carboxylate* (IVc).—A solution of the methyloxazoline (VIb) (2·13 g) and ethyl α-amino(cyano)-acetate (1·4 g) in acetonitrile (20 ml) was heated under reflux for 1 h. T.l.c. [system (A)] showed the presence of one major Bratton–Marshall-active spot at R_F 0·51. The mixture was evaporated, the residue dissolved in chloroform (30 ml), and the solution washed with 2N-sodium hydroxide (10 ml), dried (Na_2SO_4), and evaporated to a gum; this when dissolved in ethyl acetate (2 ml) soon gave the crystalline *methylimidazole nucleoside*, which formed prisms (1·6 g, 47%), m.p. 264—265° (decomp.) (from ethanol) (Found: C, 52·65; H, 6·95; N, 12·1%; M^+, 341. $C_{15}H_{23}N_3O_6$ requires C, 52·8; H, 6·8; N, 12·2%; *M*, 341).

5-*Amino*-1-(3,5-O-*isopropylidene*-α-D-*xylofuranosyl*)-2-*methylimidazole*-4-*carboxamide* (IVd).—A solution of the methyloxazoline (VIb) (2·13 g) and α-amino(cyano)acetamide (1·1 g) in acetonitrile (50 ml) was heated under reflux for 3 h. T.l.c. [system (A)] showed one Bratton–Marshall-active spot (R_F 0·17). The cooled mixture was evaporated and the residue dissolved in 10% ethanolic chloroform (4 ml) and applied to silica gel column. The major u.v.-absorbing fraction was eluted by 10% ethanolic chloroform. This fraction was evaporated to a gum, which immediately gave a crystalline solid on trituration with 10% aqueous methanol. The *carboxamide monohydrate* crystallised from water as prisms (1·0 g, 46%), m.p. 212—214° (Found: C, 47·1; H, 6·8; N, 16·7%; M^+, 312. $C_{13}H_{20}N_4O_5,H_2O$ requires C, 47·25; H, 6·7; N, 16·95%; *M*, 312).

N-[(*Dimethylamino*)*methylene*]-D-*xylopyranosylamine* (IX).—A suspension of D-xylopyranosylamine [1] (3 g) in a solution of dimethylformamide dimethyl acetal (3 g) in methanol (150 ml) was stirred under reflux for 1 h; dissolution was then complete. The mixture was evaporated and the residue was triturated with ethanol (20 ml); the solution was filtered and evaporated. Trituration of the residue under cold ether soon induced crystallisation. The *xylopyranosylformamidine* (3·5 g, 85%) crystallised from ethanol as prisms, m.p. 149—150° (Found: C, 46·8; H, 7·75; N, 13·6. $C_8H_{16}N_2O_4$ requires C, 47·05; H, 7·9; N, 13·75%), $\nu_{max.}$ 1640s cm^{-1} (C=N).

5-*Amino*-1-(D-*xylopyranosyl*)*imidazole*-4-*carboxamide* (X).—A suspension of the amidine (IX) (2·04 g) and α-amino(cyano)acetamide (1 g) in acetic acid (0·8 g) and methanol (20 ml) was stirred at room temperature overnight. T.l.c. [system (B)] showed the presence of one major Bratton–Marshall-active spot (R_F 0·36). The mixture was evaporated to a gum which was re-evaporated with methanol (3 × 10 ml). An excess of methanolic picric acid was added to a solution of the residue in methanol (20 ml). After 2 h at 0° the precipitate of the *imidazole picrate* (2·4 g, 50%) was collected and recrystallised from much methanol to give yellow fluffy needles, m.p. 206—207° (decomp.) (Found: C, 36·3; H, 3·45; N, 19·8. $C_9H_{14}N_4O_4,C_6H_3N_3O_8$ requires C, 37·0; H, 3·5; N, 20·1%).

5-*Amino*-1-(3,5-O-*isopropylidene*-α-D-*xylofuranosyl*)*imidazole*-4-*carboxamide* (VIIb).—A solution of the amidine (IX) (2·04 g) and acetic acid (0·6 g) in dry methanol was heated under reflux for 1 h, then cooled. α-Amino(cyano)-acetamide (1·0 g) was added and the mixture was set aside at room temperature overnight. T.l.c. [system (B)] showed a Bratton–Marshall-active spot at R_F 0·36 (purple) which corresponded to the foregoing xylopyranosylimidazole, and a further intense spot at R_F 0·41 (red) which corresponded to an authentic sample of the xylofuranosylimidazole (VIIb).

The reaction mixture was evaporated to a gum. A solution of this and dry toluene-*p*-sulphonic acid monohydrate (3 g) in dry acetone was stirred at room temperature for 4 h. T.l.c. [system (A)] showed one major Bratton–Marshall-active spot at R_F 0·23, which corresponded to an authentic sample of 5-amino-1-(3,5-*O*-isopropylidene-α-D-xylofuranosyl)imidazole-4-carboxamide. The solution was added dropwise with stirring to cold M-sodium hydrogen carbonate solution (100 ml). The resulting mixture was evaporated to a solid, which was re-evaporated with dry benzene (3 × 30 ml). The solid residue was extracted with boiling chloroform (3 × 10 ml; 10 min allowed for each extraction) and the extracts were combined and evaporated to a gum. An excess of methanolic picric acid was added to a solution of the gum in methanol (10 ml). After 2 h at 0° the precipitate (320 mg, 7%) was collected and recrystallised from methanol to give yellow needles, m.p. 157°. The product was identical (m.p., mixed m.p., t.l.c., and i.r.) with an authentic specimen of the carboxamide (VIIb) picrate prepared from the isopropylidenexylofuranosyloxazoline.

N-[(*Dimethylamino*)*methylene*]-2,3-O-*isopropylidene*-D-*ribofuranosylamine* (XIII).—A solution of 2,3-*O*-isopropylidene-D-ribofuranosylamine toluene-*p*-sulphonate [2] (7·2 g), triethylamine (2·8 ml), and dimethylformamide dimethyl acetal (4·3 g) in dry methanol (80 ml) was boiled under reflux for 1·25 h, cooled, and evaporated to a gum. A solution of the gum in chloroform (30 ml) was washed with water (20 ml), dried (Na_2SO_4), and evaporated to a crystalline residue. The N-*substituted ribofuranosylamine* (2·1 g,

44%) separated from ethyl acetate–ether (1 : 1) as large prisms, m.p. 106—107°, $[\alpha]_D^{20}$ −57° (*c* 2·1 in Me_2SO) (Found: C, 54·3; H, 8·35; N, 11·4%; M^+, 244. $C_{11}H_{20}N_2O_4$ requires C, 54·1; H, 8·25; N, 11·5%; *M*, 244), $\nu_{max.}$ 1640s cm^{-1} (C=N).

Ethyl 5-Amino-1-(2,3-O-isopropylidene-β-D-ribofuranosyl)-imidazole-4-carboxylate (XIV).—A solution of the foregoing amidine (2·4 g), ethyl α-amino(cyano)acetate (1·9 g), and acetic acid (0·6 ml) in acetonitrile was boiled under reflux for 15 min. T.l.c. [system (A)] showed one major Bratton–Marshall-active product (R_F 0·55) which corresponded to an authentic sample of the title imidazole. A trace of the corresponding α-anomer was detected (R_F 0·39). The solution was evaporated to a gum; the product (1·8 g, 55%) isolated after chromatography on silica gel was identical (t.l.c., m.p. and mixed m.p. 180—182°) with an authentic sample of the β-nucleoside.

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