Purines, Pyrimidines, and Imidazoles. Part XLI.[1] Glycofuranosylamines Derived from D-Xylose, D-Glucose, D-Mannose, and L-Rhamnose and their use in the Synthesis of Pyrimidine and Imidazole Nucleosides

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3,5-O-Isopropylidene-D-xylofuranosylamine, 5,6-*O*-isopropylidene-D-glucofuranosylamine, 2,3-*O*-isopropylidene-L-rhamnofuranosylamine, and 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine toluene-*p*-sulphonates have been prepared in good yield by reactions of the corresponding pyranosylamines with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid. Reaction of the glycofuranosylamines with α-acetyl-, α-cyano-, or *N*-methyl-α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamides gave the corresponding 5-substituted uracil α- or β-glycofuranosides. Furanose structures were confirmed by periodate titration or periodate oxidation. Assignments of anomeric configurations were in most cases confirmed by n.m.r. spectroscopy. The anomeric structures of the glycofuranosylamines in various solvents were studied by means of n.m.r. spectroscopy and optical rotation measurements. A bis(di-isopropylidenemannofuranosyl)amine of unknown anomeric structure was obtained as a by-product in one reaction. The isopropylidenemannofuranosylamine either with ethyl *N*-[ethoxycarbonyl- or carbamoyl(cyano)methyl]formimidates, or with ethyl formimidate hydrochloride [to give a mixture of ethyl *N*-1-(2,3:5,6-di-*O*-isopropylidene-α- and -β-D-mannofuranosyl)formimidates] followed by ethyl amino(cyano)acetate, gave 2,3:5,6-di-*O*-isopropylidene-α- and -β-5-amino-4-ethoxycarbonyl or -carbamoyl-imidazole D-mannofuranosides, from which the isopropylidene groups could be removed by aqueous acid. Structures of the aminoimidazole mannofuranosides were confirmed by means of periodate oxidation, n.m.r. and c.d. studies, and conversion of the esters into the corresponding amides.

PART XL[1] described the reaction of D-ribopyranosylamine with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid to give, in high yield, the crystalline isopropylideneribofuranosylamine toluene-*p*-sulphonate which could be used to prepare a wide variety of pyrimidine and aminoimidazole (and hence purine) ribonucleosides. This reaction should in principle be usefully applicable to all sugars which form pyranosylamines (virtually all the common monosaccharides), the structures of which would not hinder the formation of furanose cyclic acetal derivatives (including those, like xylose, where the derived cyclic acetal contains a six-membered ring). These criteria are satisfied by all the common hexoses and all the common pentoses except arabinose. Similar structural concepts apply to ketoses. We now record the preparation of derivatives of these types derived from D-xylose, D-glucose, D-mannose, and L-rhamnose, and some applications to the synthesis of nucleosides.[2]

Reactions of the appropriate pyranosylamines (each prepared crystalline from the corresponding sugar and methanolic ammonia) with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid gave in good yield the highly crystalline 3,5-*O*-isopropylidenexylofuranosylamine (I), 5,6-*O*-isopropylideneglucofuranosylamine (II), 2,3:5,6-di-*O*-isopropylidenemannofuranosylamine (III), and 2,3-*O*-isopropylidene-L-rhamnofuranosylamine (IV), respectively, as toluene-*p*-sulphonates. The structures of these compounds (apart from anomeric configuration) followed from elemental analysis, mild acidic hydrolysis to acetone, i.r. spectra [characteristic doublet at 1380 cm^{-1} (CMe_2)], n.m.r. spectra, and subsequent chemical reactions.

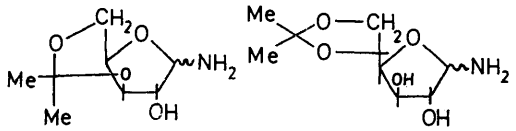
Reaction of 3,5-*O*-isopropylidene-D-xylofuranosylamine (I) toluene-*p*-sulphonate with the acyclic acryloylurethane (Va) readily gave a mixture of two anomeric 5-acetyl-(3,5-*O*-isopropylidenexylofuranosyl)uracils, (VIa) and (VIIa), identified on the basis of elemental analysis and mass and n.m.r. spectra (Table 1). Hydrolysis with aqueous acetic acid readily gave the α- and β-xylosyluracils (IXa) and (VIII), respectively, identified by mass and n.m.r. spectra (Table 1) and by periodate titration (in each case one molecule of periodate was absorbed and no formic acid was produced). In a similar manner the amine (I) toluene-*p*-sulphonate with the acrylamide (Vb) gave the *N*-methyl-5-cyanouracil derivative (VIb) or (VIIb) but in this case only one anomer was isolated.

The anomers (VIa) and (VIIa) were readily differentiated by n.m.r. spectroscopy, and the results provide a useful frame of reference for assignment of other xylofuranosyl derivatives (Table 1). In $(CD_3)_2SO$ the α-anomer (VIIa) shows the anomeric (*cis*) proton signal as a doublet ($J_{1.2}$ 3 Hz) at lower field (δ 6·10) than the

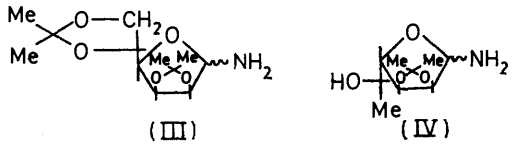
[1] Part XL, N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg, and G. Shaw, *J.C.S. Perkin I*, 1973, 1720.

[2] Preliminary communication, N. J. Cusack, P. W. Rugg, and G. Shaw, *Chem. Comm.*, 1971, 190.

singlet corresponding to the β-anomeric (*trans*) proton of (VIa) (δ 5·66) (see Part XL [1] for a summary of assign-



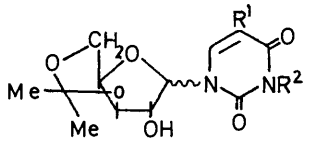
(I) (II)



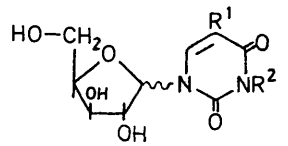
(III) (IV)

$R^1C(:CH\cdot OEt)\cdot CO\cdot NR^2\cdot CO_2Et$

(V)a; R^1=Ac, R^2=H
b; R^1=CN, R^2=Me
c; R^1=CN, R^2=H



(VI)a; R^1=Ac, R^2=H, β-anomer
b; R^1=CN, R^2=Me, β-anomer
(VII)a; R^1=Ac, R^2=H, α-anomer
b; R^1=CN, R^2=Me, α-anomer



(VIII) R^1=Ac, R^2=H, β-anomer
(IX)a; R^1=Ac, R^2=H α-anomer
b; R^1=CN, R^2=Me, α-anomer

ments in carbohydrate derivatives from consideration of coupling constants and chemical shifts). A further aid to structural assignment appears to be the separation of the signals produced by the 3,5-*O*-isopropylidene methyl groups (0·13 p.p.m. for the α-anomer and 0·21 p.p.m. for the β-anomer). In the case of the sole isolated isomer of the 5-cyano-3-methyluracil derivative [(VIb) or (VIIb)] the separation 0·13 p.p.m. is the same as that for the α-anomer (VIIa), implying that the cyano-derivative can also be assigned the α-configuration (VIIb) [as can also the derived nucleoside (IXb), the structure of which was supported by the results of periodate titration and by mass and n.m.r. spectra (Table 1)]. This is confirmed by a doublet (4 Hz) in the anomeric region (δ 6·04). The n.m.r. spectrum of the isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate itself (Table 2) in $(CD_3)_2SO$ shows a separation of $Me_2C<$ signals of 0·13 p.p.m. and a doublet (3·5 Hz) at δ 5·10, suggesting that the α-anomer is the main species. However there is also a singlet at higher field (δ 4·81), suggesting the presence of some β-anomer (less than 20%); nevertheless there are only two $Me_2C<$ signals. The spectrum of a solution in D_2O shows both a doublet δ 5·61 ($J_{1,2}$ 4 Hz) and a singlet δ 5·25 (αβ-ratio 4 : 3), and in this case three signals arise for the $Me_2C<$ group (δ 1·48, 1·42, and 1·39).

This apparent solvent effect on the anomeric equilibrium is confirmed by comparison of equilibrium optical rotations in these solvents (Figure 1). The rotations of the protonated and non-protonated forms of the isopropylidene-D-xylofuranosylamines (Figure 1) suggest that in the latter the neighbouring 2-OH group tends to favour the α-form by hydrogen bonding whereas in the protonated form, repulsion by the 2-OH favours the β-configuration. The values for solutions in Me_2SO suggest that the protonated amine forms a complex involving the solvent and the 2-OH group, so that the rotation is similar to that of the unprotonated form in the α-configuration. Interaction of the 2-hydroxy-group in (I) with imidate systems derived from the 1-amino-group has been found to produce oxazolines, which in turn are a stereospecific source of aminoimidazole α-nucleosides.[3]

The 5,6-*O*-isopropylidene-D-glucofuranosylamine (II) toluene-*p*-sulphonate similarly reacted with the acrylamide (Vc) to give a mixture of anomeric nucleosides (Xb) and (XI), but with the *N*-methyl acrylamide (Vb) only one anomer (Xa) was isolated. Identification of these compounds was confirmed by elemental analyses

TABLE 1

Chemical shifts and coupling constants of some xylofuranosyl nucleosides [δ values; solvent $(CD_3)_2SO$]

	6-H	1′-H	2′-OH	3′-OH	5′-OH	2′—5′-H				5- or 3-Me	CMe_2
(VIIa)	8·22	6·12(d, 3 Hz)	5·93			4·35	4·27	4·10(d, 4 Hz)	4·01(q)	2·47	1·42, 1·30
(IXa)	8·24	6·08(d, 2 Hz)	5·73(d)	5·41(d)	4·73(t)	4·32(m)	4·10	3·68	3·63	2·50	
(VIa)	8·75	5·66	6·15				4·17(m)			2·47	1·44, 1·23
(VIII)	8·64	5·67	5·86	5·32	4·80	4·14(m)	4·06	3·95(d, 2 Hz)	3·80(d, 5 Hz)	2·46	
(VIIb)	8·51	6·04(d, 4 Hz)	5·79(d, 4 Hz)			4·41	4·33	4·0(m)		3·18	1·43, 1·30
(IXb)	8·39	6·03(d, 4 Hz)	5·63(d, 4 Hz)	5·36(d, 4 Hz)	4·62(t)	4·43(m)	4·11(m)		3·64(t)	3·20	

[3] D. H. Robinson and G. Shaw, *Experientia*, 1972, **28**, 763.

TABLE 2

Chemical shifts (δ values) and coupling constants of some isopropylideneglycofuranosylamine toluene-*p*-sulphonates

	Solvent *	H-1 α	H-1 β	CMe_2	ArMe
(I)	$(CD_3)_2SO$	5·10(d, 3·5 Hz)	4·81	1·40, 1·27	2·31
	D_2O	5·61(d, 4 Hz)	5·25	1·48, 1·42, 1·39	2·37
(II)	$(CD_3)_2SO$ (+drop D_2O)	5·03(d, 3 Hz)	4·75	1·36, 1·32	2·32
	D_2O	5·42(d, 4 Hz)	5·2	1·45, 1·38	2·36
(III)	$(CD_3)_2SO$	(5·03, 4·80) [a]		1·48, 1·38, 1·33, 1·28	2·28
	D_2O	(5·36, 5·24) [b]		1·62, 1·58, 1·53, 1·49, 1·46	2·37
(IV)	$(CD_3)_2SO$	(5·01, 4·80) [a]		1·46, 1·42, 1·37, 1·27	2·28
	D_2O	(5·34, 5·00) [b]		1·49, 1·41, 1·38	2·39

* Internal standard tetramethylsilane [$(CD_3)_2SO$] or 3-trimethylsilylpropane-1-sulphonic acid (D_2O).

[a] Total 2H. [b] Total 1H.

and mass spectra. The free glucofuranosyl derivative (XIIa) formed by mild acidic hydrolysis of (Xa) absorbed 2 mol. equiv. of periodate with production of 1 mol. equiv. of formaldehyde. A mixture of (XIIb) and (XIII) was similarly obtained from (Xb) and (XI).

N.m.r. spectra of the *N*-methylglucofuranosyl derivative (Xa) showed a singlet at δ 5·67, confirming the β-configuration. The spectrum of the mixture of anomers (Xb) and (XI) indicated an αβ-ratio of **1 : 1** (Table 3).

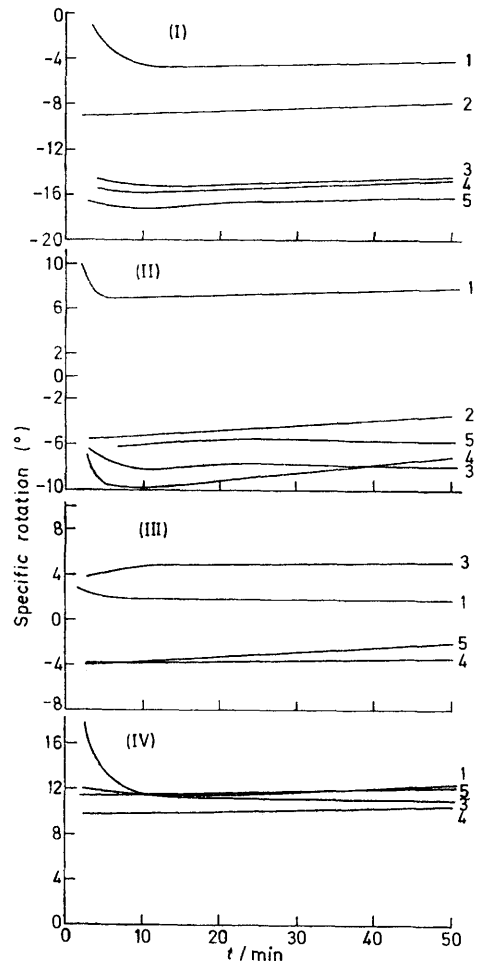
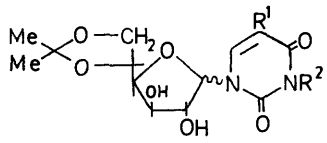
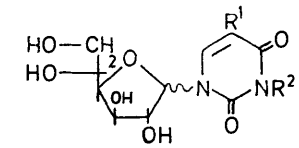


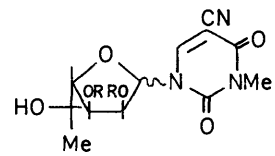
FIGURE 1 Variation of specific rotation with time, in various solvents, of the toluene-*p*-sulphonates of the furanosylamines (I)—(IV); 1 H_2O, 2 EtOH, 3 Me_2SO, 4 Na_2CO_3 aq., 5 NaOMe–MeOH



(X) a ; R^1=CN, R^2=Me, β-anomer
b ; R^1=CN, R^2=H, β-anomer
(XI) R^1=CN, R^2=H, α-anomer



(XII) a ; R^1=CN, R^2=Me, β-anomer
b ; R^1=CN, R^2=H, β-anomer
(XIII) R^1=CN, R^2=H, α-anomer



(XIV) R=Me_2C
(XV) R=H

The n.m.r. spectrum of 5,6-*O*-isopropylidene-D-glucofuranosylamine (II) toluene-*p*-sulphonate in $(CD_3)_2SO$ (Table 2) is obscured in the region δ 4·6—5·6 by a broad OH peak which can be removed by addition of a little D_2O to reveal a doublet at δ 5·03 ($J_{1.2}$ 3 Hz) and a singlet at δ 4·75 (ratio *ca.* 2 : 1; total 1H). Analogy with the data for the xylose derivative indicates an αβ-ratio of 2 : 1. However in contrast to the related xylose derivative the isopropylidene methyl groups give two signals only, both in $(CD_3)_2SO$ and in D_2O. In D_2O a doublet ($J_{1.2}$ 4 Hz) at δ 5·42 and a singlet at δ 5·2 (ratio *ca.* 1 : 1) indicate the presence of the α- and β-anomers in equal

amounts. The specific rotations in various environments (Figure 1) are similar to those of the related xylose derivatives, suggesting that the neighbouring 2-hydroxy-group exerts a similar influence in the glucose derivative also.

Reaction of 2,3-*O*-isopropylidene-L-rhamnofuranosylamine (IV) toluene-*p*-sulphonate with the acrylamide (Vb) gave only one pure anomeric uracil derivative (XIV), identified by elemental analysis, mass spectrum, and hydrolysis to (XV) (which absorbed 1 mol. equiv. of periodate and did not produce formic acid). The n.m.r. spectrum of the nucleoside (XIV) (Table 4) showed a singlet at δ 5·60, two isopropylidene methyl signals at δ 1·42 and 1·32, and a doublet (5 Hz) at δ 1·19. The precise anomeric structure is difficult to assess since the singlet at δ 5·60 could be characteristic of either anomer (see also mannose derivatives). The n.m.r. spectrum of the rhamnosylamine (IV) salt in $(CD_3)_2SO$ (Table 2) shows two peaks in the anomeric region (total 2H), each a singlet with a smaller peak on the high-field sides. Mannofuranosyl derivatives are known to have their anomeric signals superimposed;[4] it appears that L-rhamnose, which is similar in the C(2),C(3) area, exhibits the same behaviour. The isopropylidene methyl signals are complicated by the presence of a doublet due to the C-6 methyl group in the same region. Between δ 1·10 and 1·46 there are eight peaks, attributable to two isopropylidene methyl groups and the C-6 methyl doublet for each anomer. The results indicate that the amine sulphonate forms an anomeric mixture in Me_2SO.

The optical rotation of solutions of the L-rhamnosylamine (IV) toluene-*p*-sulphonate in Me_2SO (Figure 1) is characterised by the large slow change, which suggests mutarotation in this solvent perhaps analogous to that postulated for the isopropylidene-D-ribofuranosylamine derivative.[1] The n.m.r. spectra, which were measured about 15 min after dissolution, confirm mutarotation. The rotation data, however, suggest that the crystalline rhamnosylamine salt may in fact be a pure anomer.

Reaction of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine (III) toluene-*p*-sulphonate with the formimidate (XVIa) [from triethyl orthoformate and ethylamino(cyano)acetate] [5] and base gave a mixture of two aminoimidazole nucleosides (A) and (B), subsequently shown to be (XVIIa) and (XVIIIa), respectively, which were readily separated by fractional crystallisation and produced in roughly equal amounts. A mixture of the same aminoimidazole nucleosides was isolated in similar overall yield and proportion from the reaction of the mannofuranosylamine (III) with ethyl formimidate hydrochloride [to produce an anomeric mixture of mannosylformimidates (XIX) in high yield (≥90%)] and further reaction of these with ethyl amino(cyano)-acetate. The structure (XIX) assigned to the formimidates was confirmed by mass, i.r. (two strong C=N bands at 1700 and 1660 and a CMe_2 doublet at 1380 cm^{-1}), and n.m.r. spectra (low-field HC=N singlet). The structures assigned to the aminoimidazole nucleosides (XVIIa) and (XVIIIa) were confirmed by elemental analysis, mass and u.v. spectra, positive Bratton–Marshall assay [6] and derived visible spectra, and periodate oxidation of the corresponding nucleosides (XXa)

TABLE 3

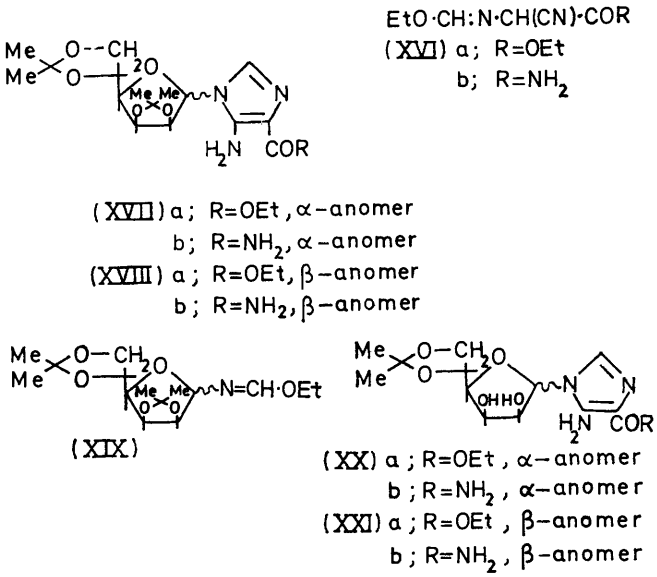
Chemical shifts and coupling constants of some glucofuranosyl nucleosides [δ values; solvent $(CD_3)_2SO$]

	6-H	1′-H	2′- and 3′-OH	5′-OH	6′-OH	2′—6′-H	3-Me	CMe_2
(XIIa)	8·46	5·58	3·85(d, 4 Hz), 5·26(d, 4 Hz)	4·87(d, 4 Hz)	4·57(t)	4·04(m), 3·55(m)	3·19	
(Xa)	8·46	5·67	5·97(d, 4 Hz), 5·63 (d, 4 Hz)			4·62(q), 4·3—3·8(m)	3·19	1·37, 1·33
(XIII)	8·32	5·95(d, 3 Hz)	5·70, 5·30	4·60		4·10(m), 3·50(m)		
(XIIb)	8·44	5·56						
(XI)	8·36	5·97(d, 3 Hz)				4·60—3·70(m)		1·35, 1·31
(Xb)	8·44	5·59	5·60					

TABLE 4

Chemical shifts and coupling constants of some rhamnofuranosyl nucleosides [δ values; solvent $(CD_3)_2SO$]

	6-H	1′-H	5′-OH	2′-, 3′-OH	2′—5′-H	3-Me	CMe_2	5′-Me
(XIV)	8·53	5·60	5·10(d, 5 Hz)		4·91(d, 3 Hz), 4·73, 4·1(m), 3·9(m)	3·18	1·46, 1·32	1·18(d, 5 Hz)
(XV)	8·73	5·74	5·29(d, 6 Hz)	5·06(d, 4 Hz)	4·5(m), 4·0(m)	3·19		1·09(d, 5 Hz)



[4] S. J. Angyal and V. A. Pickles, *Austral. J. Chem.*, 1972, **25**, 1695.

[5] D. H. Robinson and G. Shaw, *J.C.S. Perkin I*, 1972, 1715.

[6] C. Bratton and E. K. Marshall, *J. Biol. Chem.*, 1939, **128**, 537.

and (XXIa) produced by mild acidic hydrolysis of (A) and (B) when in each case a good yield of formaldehyde was produced.[7] In addition, Hudson's rules,[8] which have been shown to apply to other aminoimidazole nucleosides,[1] indicated that compound (A) was the α-anomer (XVIIIa) and compound (B) the β-anomer (XVIIIa). These assignments were further confirmed and incidentally the validity of Hudson's rules in this area extended, by n.m.r. spectra. The α-form (A) (XVIIa) gave a sharp singlet and the β-form (XVIIIa) a broad unresolved band (see Table 5). The c.d. spectra of the two anomers were quite different (Figure 2). During this particular reaction sequence the bismannofuranosylamine (XXII) was isolated and identified by elemental analysis, mass and i.r. spectra (strong CMe_2 doublet at 1380 cm^{-1}), and acidic hydrolysis (mannose was the only sugar detected by t.l.c.).

Similar reactions in methanol or water of the mannofuranosylamine sulphonate with the amide imidate (XVIb) [from ethyl amino(cyano)acetamide and triethyl orthoformate] gave a mixture (t.l.c.) of anomeric aminoimidazolecarboxamide nucleosides (XVIIb) and (XVIIIb), but only one form (the β-anomer) (XVIIIb) was isolated in crystalline form. The structure assigned was confirmed by elemental analysis, mass and u.v. spectra, the Bratton–Marshall assay and derived visible spectra, and a c.d. spectrum very similar to that of the related aminoimidazole β-ester derivative (XVIIIa) (Figure 2). The relationship between the esters and amides in this series was finally confirmed by reaction of the α- and β-ester derivatives (XVIIa) and (XVIIIa) with aqueous ammonia to produce the corresponding amides (XVIIb) and (XVIIIb), which were readily distinguishable by t.l.c.

TABLE 5
Physical data for some aminoimidazole nucleosides

Nucleoside	$[\alpha]_D^{20}$ (c) *	$\lambda_{max.}$/nm (ε) †	$\lambda_{max.}$/nm of dyestuff formed in Bratton–Marshall assay	$\delta_{H-1'}$	R_F (A)	R_F (B)
(XVIIIa)	+43° (0·2%)	266 (12,700)	508	5·61br	0·65	0·64
(XVIIa)	+95° (0·2%)	267 (13,000)	520	5·97(s)	0·76	0·69
(XVIIIb)	+61° (0·35%)	265 (11,900)	522		0·39	0·62
(XVIIb)					0·45	0·62

* In Me_2SO. † In MeOH.

TABLE 6
Chemical shifts and coupling constants of some mannofuranosyl nucleosides [δ values; solvent $(CD_3)_2SO$]

	6-H	1'-H	2'-,3'-,5'-,6'-OH	2'—6'-H	CMe_2
(XXIII)	8·64	5·63		5·18(d, 5 Hz), 4·9(m), 4·3(m), 3·95(m)	1·44, 1·34, 1·29
(XXIV)	8·73	5·77(d, 7 Hz)	5·10br	4·3(m), 3·7(m), 3·45(m)	

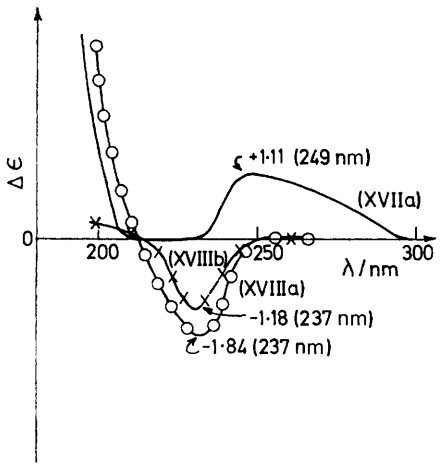
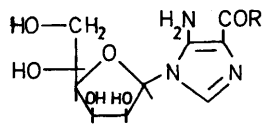
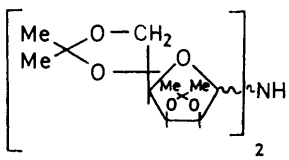


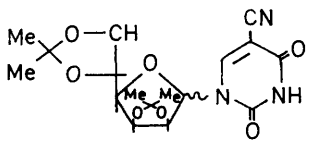
FIGURE 2 C.d. spectra of some imidazole D-mannofuranosides



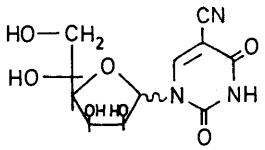
(XXIa; R = OEt
b; R = NH_2)



(XXII)



(XXIII)



(XXIV)

The mannofuranosylamine also reacted with (Vc) to produce the corresponding nucleoside (XXIII), which was readily hydrolysed to (XXIV) (n.m.r. data in Table 6). Periodate titration of this compound gave a characteristic variable, pH-dependent over- (non-Malapradian) oxidation with consumption of *ca.* 4 mol. equiv. of periodate and formation of formic acid from the intermediate hydroxymalonaldehyde.[9]

The n.m.r. spectrum of 2,3:5,6-di-*O*-isopropylidenemannofuranosylamine (III) toluene-*p*-sulphonate in

[7] R. E. Reeves, *J. Amer. Chem. Soc.*, 1941, **64**, 1476.
[8] C. S. Hudson, *J. Amer. Chem. Soc.*, 1909, **31**. 66.
[9] A. B. Zanlungo, J. O. Defferrari, and R. A. Cadenas, *Carbohydrate Res.*, 1970, **14**, 245; B. G. Hudson and R. Barker, *J. Org. Chem.*, 1967, **32**, 2101; P. Szabo and L. Szabo, *Carbohydrate Res.*, 1967, **4**, 206.

$(CD_3)_2SO$ showed two singlets in the anomeric region, the down-field signal integrated for one proton and the other for two (Table 2). Thus it could be supposed to be the spectrum of a single anomer; however the mannofuranoses and the 5-methoxy-derivatives are known to have their anomeric signals superimposed.[4] The isopropylidene methyl signals are complex in that, although only the expected four signals are seen, they vary greatly in intensity; this suggests a mixture of anomers. In D_2O the anomeric region shows four small singlets on the side of the HOD peak; the isopropylidene methyl signals split into six peaks of varying size and a substantial acetone methyl signal is observed, indicating that some hydrolysis occurs.

The optical rotation of the amine (III) toluene-*p*-sulphonate shows little variation in various systems (Figure 1), suggesting that the fully protected sugar is not readily subject to mutarotation or hydrolysis, although the n.m.r. evidence suggests some hydrolysis in D_2O.

EXPERIMENTAL

Evaporations were carried out with a Büchi rotary evaporator, under water-pump vacuum with a flask temperature $\leqslant 40°$, 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 JNM-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; c.d. spectra were provided by Professor W. Klyne and Dr. P. M. Scopes, Westfield college, University of London, whom we thank. Silica gel (0·05—0·20 mm; 325—370 mesh; Machery Nagel and Co.) was used for column chromatography, and silica gel $60F_{254}$ 025 mm precoated glass plates (Merck) were used for t.l.c. with (A) chloroform–methanol (9 : 1) and (B) n-butanol–acetic acid–water (12 : 3 : 5) as development systems.

D-*Xylopyranosylamine*.—D-Xylose (750 g) was stirred until dissolved in ammonia-saturated methanol (2 l) at 0° as ammonia was bubbled through the solution. The clear solution was transferred to a thick-walled plastic bag, which was sealed and kept at room temperature. Crystals separated after 2 days and were collected after 1 week, washed with methanol, and dried, to give the xylosylamine (700 g, 94%), m.p. 135—136° (decomp.) (lit.,[10] 130°; lit.,[11] 142—143°).

D-*Glucopyranosylamine*.—D-Glucose (200 g) was dissolved, in portions, with stirring, in ice-cold ammonia-saturated methanol (250 ml) with ammonia gas bubbling through. The solution was transferred to a plastic bag, sealed, and kept at room temperature for 4 weeks; crystallisation occurred after 1 week. The D-glucopyranosylamine, filtered off and washed with methanol (112 g, 57%), had m.p. 125° (decomp.). Dissolution in ammonia (*d* 0·88)–water (1 : 10) and precipitation with methanol (2 vol.) then ethanol (2 vol.) (*cf.* ref. 12) gave material of m.p. 127—128° (lit.,[13] 127—128°).

L-*Rhamnopyranosylamine*.—L-Rhamnose monohydrate (25 g) dissolved rapidly in ice-cold ammonia-saturated methanol (50 ml) with ammonia gas bubbling through. The solution was kept at 4° for 2 weeks; crystallisation occurred after 1 week; L-rhamnopyranosylamine (19 g, 77%) was filtered off, washed with methanol, and recrystallised from dry methanol; m.p. 114—116° (lit.,[10] 116°).

D-*Mannopyranosylamine Monohydrate*.—D-Mannose (100 g) and ammonium chloride (0·5 g) were dissolved with stirring in ice-cold ammonia-saturated methanol (100 ml) with ammonia gas bubbling through. The solution was kept at 4° for 1 day, then seeded to give crystals of D-mannopyranosylamine monohydrate which were filtered off, washed with methanol, and dried. The product (110 g, 99%) had m.p. 92—93° (lit.,[12] 93—94°).

3,5-O-*Isopropylidene*-D-*xylofuranosylamine* (I) *Toluene*-p-*sulphonate*.—Dry, finely powdered D-xylopyranosylamine (100 g, 0·67 mol) was stirred into a solution of dry toluene-*p*-sulphonic acid monohydrate (200 g, 0·95 mol) in dry acetone (600 ml, 7·5 mol), and 2,2-dimethoxypropane (600 ml, 4·9 mol) in a stoppered flask, to exclude moisture. After stirring for 5—10 min the last of the xylopyranosylamine just dissolved as a white precipitate formed. This was collected within 5 min, before it began to redissolve, washed three times with dry acetone, then twice with dry ether, and dried *in vacuo* to give the *furanosylamine salt* (130 g, 54%) as rectangular plates, m.p. 120—122° (decomp.) (darkens at 115°) (Found: C, 49·85; H, 6·6; N, 3·95. $C_{15}H_{23}NO_7S$ requires C, 49·85; H, 6·4; N, 3·9%).

5,6-O-*Isopropylidene*-D-*glucofuranosylamine* (II) *Toluene*-p-*sulphonate*.—Dry, finely powdered, D-glucopyranosylamine (100 g, 0·56 mol) was stirred into a solution of dry toluene-*p*-sulphonic acid monohydrate (160 g, 0·84 mol) in dry acetone (500 ml, 6·8 mol) and 2,2-dimethoxypropane (500 ml, 4·1 mol) in a stoppered flask. After 35 min the precipitate (60 g, 41%) was collected, washed three times with dry acetone and twice with dry ether, and dried *in vacuo* to give *needles*, m.p. 122—123° (decomp.) (Found: C, 49·3; H, 6·15; N, 3·55. $C_{16}H_{25}NO_9S$ requires C, 49·1; H, 6·45; N, 3·6%). If the precipitated product was not removed from the reaction it redissolved in about 1 h.

2,3-O-*Isopropylidene*-L-*rhamnofuranosylamine* (IV) *Toluene*-p-*sulphonate*.—L-Rhamnopyranosylamine (20 g, 0·12 mol) was added to a stirred solution of dry toluene-*p*-sulphonic acid monohydrate (32 g, 0·17 mol) in dry acetone (100 ml) and 2,2-dimethoxypropane (100 ml, 0·82 mol) to give, immediately, a clear solution. Dry ether was added to incipient turbidity and the solution was stored at 0° overnight. A thick oil separated which rapidly crystallised when stirred vigorously with the supernatant for 4—5 h. The product was collected, washed with dry acetone then dry ether, and dried *in vacuo* to give the *furanosylamine salt* (14·5 g, 31%), m.p. 143° (decomp.) (Found: C, 51·3; H, 6·35; N, 3·9. $C_{16}H_{25}NO_7S$ requires C, 51·2; H, 6·7; N, 3·75%).

2,3:5,6-*Di*-O-*isopropylidene*-D-*mannofuranosylamine* (III) *Toluene*-p-*sulphonate*.—A solution of dry toluene-*p*-sulphonic acid monohydrate (21 g, 0·11 mol) in 2,2-dimethoxypropane (45 ml, 0·35 mol) and acetone (200 ml) was stirred at room temperature for 15 min. Finely powdered D-mannosylamine monohydrate (11 g, 0·056 mol) was added and the mixture was stirred until dissolution was complete (*ca.* 2 h). The solution was than evaporated to *ca.* 100 ml, dry ether (*ca.* 20 ml) was added to incipient turbidity, and

[10] C. A. Lobry de Bruyn and F. H. van Leent, *Rec. Trav. chim.*, 1895, **14**, 134.
[11] K. Onodera and S. Kitaoka, *J. Org. Chem.*, 1960, **25**, 1322.
[12] H. S. Isbell and H. L. Frush, *J. Org. Chem.*, 1958, **23**, 1309.
[13] C. A. Lobry de Bruyn, *Rec. Trav. chim.*, 1895, **14**, 98.

the mixture was set aside at 4°. After 24 h the solid was collected, washed with ether, and dried to give *needles* (16 g, 66%), m.p. 133—134° (decomp.) (Found: C, 52·65; H, 6·7; N, 3·3. $C_{19}H_{29}NO_8S$ requires C, 52·9; H, 6·75; N, 3·25%).

5-Acetyl-1-(3,5-O-isopropylidene-α- and β-D-xylofuranosyl)uracils [(VIa) *and* (VIIa)].—To a suspension of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (3·6 g, 10 mmol) and α-acetyl-β-ethoxy-*N*-ethoxycarbonylacrylamide [14] (2·3 g, 10 mmol) in methanol (90 ml), was added M-sodium methoxide in methanol (10 ml) and the mixture was boiled. The resulting solution was evaporated to dryness and the solid residue extracted with 4% methanolic dichloromethane (5 × 20 ml). The undissolved sodium toluene-*p*-sulphonate was filtered off and the filtrate was evaporated to dryness. T.l.c. of the crude nucleoside showed two spots. The foam was crystallised from water to give, first, the *α-nucleoside* (VIIa), which crystallised from ethanol as long needles (0·8 g, 26%), m.p. 205°, R_F 0·5 (A) (Found: C, 51·35; H, 5·65; N, 8·4%; M^+, 326. $C_{14}H_{18}N_2O_7$ requires C, 51·55; H, 5·5; N, 8·6%; *M*, 326). The aqueous mother liquor was cooled to 0° and after 3 days *β-anomer* (VIa) crystallised as rhomboids (0·4 g, 13%), m.p. 243° (from ethanol), R_F 0·4 (A) (Found: C, 51·55; H, 5·6; N, 8·4%; M^+, 326).

5-Acetyl-1-α- and β-D-xylofuranosyluracil [(IXa) *and* (VIII)].—A solution of 5-acetyl-1-(3,5-*O*-isopropylidene-β-D-xylofuranosyl)uracil (0·5 g) in 30% aqueous acetic acid, was heated at 100° for 1 h then cooled to give 5-acetyl-1-β-D-xylofuranosyluracil (VIII) (0·22 g) as rod-like crystals, m.p. 220°, *m/e* 286 (M^+). The α-anomer was obtained by heating a solution of 5-acetyl-1-(3,5-*O*-isopropylidene-α-D-xylofuranosyl)uracil (0·22 g) in 30% aqueous acetic acid at 100° for 1 h; evaporation gave a foam which crystallised from aqueous ethanol as platelets (0·15 g), m.p. 205°, *m/e* 286 (M^+).

5-Cyano-1-(3,5-O-isopropylidene-α-D-xylofuranosyl)-3-methyluracil (VIIb).—2·85M-Sodium methoxide in methanol (4 ml) was added to a mixture of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (3·61 g, 10 mmol) and α-cyano-β-ethoxy-*N*-ethoxycarbonyl-*N*-methylacrylamide [15] (2·26 g, 10 mmol) wetted with methanol (8 ml), to give a yellow suspension from which heat was evolved. The suspension was kept at room temperature for 2 h, and evaporated to a dry foam. This was extracted with 4% methanolic dichloromethane (10 ml) and filtered, and the residual solid was washed with methanolic dichloromethane. The extract was evaporated to a dry foam which crystallised from methanol to give the *cyanonucleoside* (VIIb) (1·25 g, 39%) as needles, m.p. 221° (Found: C, 52·0; H, 5·3; N, 12·75%; M^+, 323. $C_{14}H_{17}N_3O_6$ requires C, 52·0; H, 5·3; N, 13·0%; *M*, 323).

5-Cyano-3-methyl-1-α-D-xylofuranosyluracil (IXb).—A solution of the 3,5-*O*-isopropylidene derivative (VIIb) (0·323 g, 10 mmol) in 30% aqueous acetic acid (6 ml) was heated at 100° for 2 h, then evaporated to an oil; this was evaporated with water (2 × 5 ml), then with toluene (2 × 5 ml), and with ethanol (5 ml) to give a white foam which crystallised from ethanol as needles (0·17 g, 60%), m.p. 212°, *m/e* 283 (M^+). In 24 h at 20° the substance consumed 1·15 mol. equiv. of sodium periodate and liberated no formic acid.

5-Cyano-1-(5,6-O-isopropylidene-β-D-glucofuranosyl)-3-methyluracil (Xa).—Sodium methoxide (63 mmol) in methanol (72·5 ml) was added to a mixture of α-cyano-β-ethoxy-*N*-ethoxycarbonyl-*N*-methylacrylamide (14·25 g, 65 mmol) and 5,6-*O*-isopropylideneglucofuranosylamine toluene-*p*-sulphonate (25·47 g, 63 mmol) wetted with methanol (15 ml), to give a green solution, which was boiled, for *ca.* 10 min, until crystals appeared in the (then orange) solution. The solution was evaporated to dryness; the residue was swirled with 4% methanolic dichloromethane (60 ml), filtered off, and washed with 4% methanolic dichloromethane (3 × 30 ml) until all the orange colour had been extracted. The filtrate was evaporated to dryness and the product crystallised from water (20 ml) to give rectangular *platelets* (6·5 g, 28%), m.p. 233—234° (Found: C, 48·55; H, 5·65; N, 11·0%; M^+, 353. $C_{15}H_{19}N_3O_7,H_2O$ requires C, 48·5; H, 5·70; N, 11·3%; *M*, 353), $\lambda_{max.}$ 277 nm (ε 11,790) (in EtOH).

5-Cyano-1-β-D-glucofuranosyl-3-methyluracil (XIIa).—A solution of the 5,6-*O*-isopropylidene derivative (Xa) (0·43 g, 1·2 mmol) in 30% aqueous acetic acid (15 ml) was heated at 100° for 30 min; t.l.c. then showed complete reaction. Evaporation gave a white solid which crystallised from aqueous ethanol to afford cubic *crystals* (0·23 g, 61%), m.p. 207—208° [mixed m.p. with 5-cyano-1-D-glucopyranosyl-3-methyluracil (m.p. 204°, sinters at 135°) 180—185°][15] (Found: C, 45·95; H, 4·85; N, 13·35%; M^+, 313. $C_{12}H_{15}N_3O_7$ requires C, 46·0; H, 4·85; N, 13·35%; *M*, 313), $\lambda_{max.}$ 278 nm (ε 12,350) (in EtOH) [pyranosyl derivative has $\lambda_{max.}$ 273 nm (ε 7800)]. In 24 h at 20° the substance consumed 2·25 mol. equiv. of sodium periodate and liberated formaldehyde, characterised as the dimedone derivative,[7] m.p. and mixed m.p. 190°.

5-Cyano-1-(5,6-O-isopropylidene-α- and β-D-glucofuranosyl)uracils [(XI) *and* (Xb)].—To a mixture of 5,6-*O*-isopropylideneglucofuranosylamine toluene-*p*-sulphonate (9·75 g, 25 mmol) and α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide [16] (5·3 g, 25 mmol), wetted with methanol (10 ml), was added sodium methoxide (25 mmol) in methanol (29 ml). The solution was boiled for 10 min, cooled, and evaporated to a foam. This was swirled with 4% methanolic dichloromethane (8 ml); the solution was filtered and the solid residue was washed with 4% methanolic dichloromethane until all the colour had been extracted. The filtrate was evaporated to a foam and crystallised (over 2 days) from a mixture of water (18 ml) and ethanol (2 ml) to give the mixture of anomers (3 g, 36%), which crystallised from water as needles, m.p. 233—234° (Found: C, 47·65; H, 5·2; N, 11·45%; M^+, 339. Calc. for $C_{14}H_{17}N_3O_7,H_2O$: C, 47·05; H, 5·35; N, 11·75%; *M*, 339).

5-Cyano-1-α- and β-D-glucofuranosyluracils [(XIII) *and* (XIIb)]. The 5,6-*O*-isopropylidene derivatives (1 g, 3 mmol) were heated at 100° for 30 min with aqueous acetic acid; t.l.c. then indicated reaction to be complete. The solution was evaporated to a syrup which afforded crystals (0·6 g, 89%), m.p. 208° (from absolute ethanol), of the mixture of anomers, *m/e* 242 ($M - CH_2OH - CN$), 213 ($M - CH_2OH{\cdot}CHOH - CN + 1$), and 137 (base residue +1).

5-Cyano-1-(2,3-O-isopropylidene-L-rhamnofuranosyl)-3-methyluracil (XIV).—A solution of 2,3-*O*-isopropylidene-L-rhamnofuranosylamine toluene-*p*-sulphonate (10 g, 27 mmol) and α-cyano-β-ethoxy-*N*-ethoxycarbonyl-*N*-methylacrylamide (6 g, 27 mmol) in methanolic sodium methoxide (31 ml containing 27 mmol) and methanol (40 ml) was kept at room temperature for 1 h; more sodium methoxide

[14] J. H. Dewar and G. Shaw, *J. Chem. Soc.*, 1961, 3254.
[15] R. K. Ralph and G. Shaw, *J. Chem. Soc.*, 1956, 1877.
[16] G. Shaw, *J. Chem. Soc.*, 1955, 1834.

solution (31 ml) was added and the solution was kept at room temperature for 2 days. The *nucleoside* (XIV) crystallised after cooling as needles (3·2 g, 35%), m.p. 272° (from ethanol) (Found: C, 53·35; H, 5·7; N, 12·65. $C_{15}H_{19}N_3O_6$ requires C, 53·4; H, 5·8; N, 12·45), *m/e* 322 ($M - CH_3$), 292 ($M - CH_3 - CHOH$), 187 (M − base), and 152 (base + 2) (characteristic of isopropylidene nucleosides [17]).

*5-Cyano-3-methyl-1-*L*-rhamnofuranosyluracil* (XV).—A solution of the 2,3-*O*-isopropylidene derivative (2 g, 6 mmol) in hot water was boiled and stirred with Amberlite resin (IR 120; H^+ form) (50 ml) for 3 h, filtered, and cooled. The *nucleoside* (XV) (1·4 g, 80%) crystallised as needles, m.p. 242° (Found: C, 48·3; H, 5·05; N, 14·1%; M^+, 297. $C_{12}H_{15}N_3O_6$ requires C, 48·9; H, 5·1; N, 14·15%, M, 297). In 24 h at 20° the substance consumed 0·95 mol. equiv. of sodium periodate and liberated no formic acid.

*Ethyl 5-Amino-1-(2,3:5,6-di-O-isopropylidene-α- and β-*D*-mannofuranosyl)imidazole-4-carboxylates* [(XVIIa) *and* (XVIIIa)].—(*a*) A mixture of ethyl amino(cyano)acetate (2·96 g, 20 mmol) and triethyl orthoformate (3·7 ml, 22 mmol) was boiled under reflux in acetonitrile (50 ml) for 45 min, cooled, and added to a mixture of (2,3:5,6-di-*O*-isopropylidene)-D-mannofuranosylamine toluene-*p*-sulphonate (6·9 g, 16 mmol) and ethanolic sodium ethoxide (50 ml containing 16 mmol). The resulting mixture was set aside at room temperature overnight. T.l.c. [system (A)] showed two major Bratton–Marshall-active products at R_F 0·76 and 0·65, respectively. The mixture was filtered and the filtrate evaporated to a foam which was dissolved in chloroform (100 ml); the solution was washed with 2N-sodium hydroxide (2 × 15 ml) and water (15 ml), dried (Na_2SO_4), and evaporated to a pale yellow gum. This was dissolved in ethyl acetate; the solution was rendered slightly turbid with light petroleum (b.p. 40—60°) and soon yielded a crystalline mixture of α- and β-nucleosides (3·5 g, 54%), which was collected and washed with 1 : 1 ethyl acetate–light petroleum (b.p. 40—60°). Recrystallisation from 1 : 1 ethanol–water gave, after 2 days, the pure *α-anomer* (XVIIa), R_F 0·76 (A) as spars (1·4 g, 22%), m.p. 225—226°, $[\alpha]_D^{20}$ +95° (*c* 0·2 in Me_2SO) (Found: C, 54·25; H, 6·95; N, 10·15%; M^+, 397. $C_{18}H_{27}N_3O_7$ requires C, 54·4; H, 6·85; N, 10·55%; M, 397). The mother liquors, after a further 7 days produced the *β-anomer* (XVIIIa), R_F 0·65 (A), as needles (1·5 g, 23%), m.p. 190—192° $[\alpha]_D^{20}$ +43° (*c* 0·2 in Me_2SO) (Found: C, 54·2; H, 6·65; N, 10·4%; M^+, 397).

A similar reaction in acetonitrile with triethylamine again gave the α- and β-nucleosides. The crude mother liquors from the foregoing reaction after 2 weeks at 4° produced a further crop of colourless crystals (150 mg), which gave prisms, m.p. 157—159° (from ethyl acetate), $[\alpha]_D^{20}$ +86° (*c* 0·8 in Me_2SO). The solid had no u.v. absorption and gave a negative Bratton–Marshall test, and its i.r. spectrum showed strong bands at 1308 cm^{-1} (CMe_2). A small amount of the solid (5 mg) in 0·1N-hydrochloric acid (2 ml) was heated at 100° for 1 h. T.l.c. [system (B)] followed by development with the anisaldehyde spray reagent showed a single discrete blue-green spot which corresponded to mannose. The solid was identified as *bis-(2,3:5,6-di-O-isopropylidene-*D*-mannofuranosyl)amine* (Found: C, 57·3; H, 7·95; N, 2·85%; M^+, 501. $C_{24}H_{39}NO_{10}$ requires C, 57·5; H, 7·8; N, 2·8%; M, 501), also prepared as follows. A solution of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine toluene-*p*-sulphonate (2·1 g) in ethanolic sodium ethoxide (20 ml, containing 5 mmol) was set aside at room temperature overnight. Evolution of ammonia was detected. The mixture was filtered, refluxed for 1 h, and evaporated to a gum. A solution of the residue in chloroform (20 ml) was washed with water (2 × 10 ml), dried (Na_2SO_4), and evaporated. A solution of the residual gum in ethyl acetate (2 ml) was stored at 4° for 4 weeks. The resulting crystals (320 mg) had m.p. and mixed m.p. (with the dimannosylamine) 157—159°.

(*b*) *Preparation* via *ethyl* N-(2,3:5,6-*Di*-O-*isopropylidene-α- and* β-D-*mannofuranosyl)formimidates* (XIX). A suspension of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine toluene-*p*-sulphonate (4·3 g, 10 mmol) and ethyl formimidate hydrochloride (1·2 g, 11 mmol) in triethylamine (1·4 ml, 10 mmol) and acetonitrile (60 ml) was shaken at room temperature for 20 min. The solution was filtered and evaporated. A solution of the residue in chloroform (50 ml) was washed with water (2 × 20 ml), dried (Na_2SO_4), and evaporated to give the mixture of formimidates (2·9 g, 92%) as a gum, $[\alpha]_D^{20}$ +50° (*c* 4·2 in Me_2SO) (Found: M^+, 315. Calc. for $C_{15}H_{25}NO_6$: M, 315), $\nu_{max.}$ 1700s and 1660s (C=N) and 1380 cm^{-1} (CMe_2 doublet).

A solution of the foregoing gum (2·8 g, 8·9 mmol) and ethyl amino(cyano)acetate (1·3 g, 10 mmol) in acetonitrile (30 ml) was refluxed for 0·5 h. T.l.c. [system (A)] showed the presence of two major Bratton–Marshall active spots at R_F 0·76 and 0·65. The solution was evaporated. A solution of the residue in chloroform (30 ml) was washed with 2N-sodium hydroxide solution (20 ml), dried, and evaporated to a yellow gum. This gum when triturated with ethyl acetate gave crystals. The α-mannofuranosylimidazole (1·0 g, 28%) crystallised from aqueous ethanol as spars, m.p. and mixed m.p. with the product from (*a*) 225—226°. Seeding the combined mother liquors with the β-mannofuranosylimidazole soon yielded a further precipitate. (0·95 g, 27%), which crystallised from aqueous ethanol as needles, m.p. and mixed m.p. with the β-nucleoside from (*a*) 190—192°.

Action of Sodium Periodate on the Hydrolysis Products of the Nucleosides (XVIIa) *and* (XVIIIa).—A suspension of each isopropylidenemannosylimidazole (40·0 mg) in 10% aqueous acetic acid (5 ml) was heated at 100° for 3·5 h, cooled, and evaporated to a gum, which was re-evaporated with water (3 × 5 ml) to remove the last traces of acid. A solution of the gum in water (2 ml) was treated with N-sodium hydrogen carbonate (2 ml) and 0·1N-sodium periodate (6 ml). The mixture was set aside at room temperature for 4 h. N-Hydrochloric acid (3 ml) and 1·2N-sodium arsenite (2 ml) were added and the mixture was stirred vigorously until the precipitate and yellow colouration had disappeared. M-Sodium acetate (2 ml) and ethanolic dimedone (1 ml containing 80 mg) were added. The mixture was then heated at 100° for 10 min and allowed to cool to room temperature during 2 h. The cream formaldehyde dimedone derivative [7] was collected on a tared sinter, washed well with water, dried for 0·5 h at 90° and weighed; m.p. and mixed m.p. 189—190°. The α-anomer produced 0·88 mol. equiv. of formaldehyde, and the β-anomer 0·66 mol. equiv.

*5-Amino-1-(2,3:5,6-di-O-isopropylidene-β-*D*-mannofuranosyl)imidazole-4-carboxamide* (XVIIIb).—(a) *Methanol solvent.* A solution of ethyl *N*-[carbamoyl(cyano)methyl]-formimidate [5] (3·1 g, 20 mmol) in a mixture of 2,3:5,6-di-*O*-

[17] 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.

isopropylidene-D-mannofuranosylamine toluene-*p*-sulphonate (8·64 g, 20 mmol) and ethanolic sodium ethoxide (100 ml containing 20 mmol) was set aside overnight. T.l.c. [system (A)] showed two major Bratton–Marshall active products, R_F 0·45 and 0·39. The solution was filtered and evaporated to a red gum which was dissolved in chloroform (80 ml) and washed with 2N-sodium hydroxide (20 ml). The organic phase was dried and evaporated to a gum which readily crystallised from ethyl acetate. The β-*mannofuranosylimidazole*, R_F 0·39 (A) crystallised from methanol as laths (2·6 g, 35%), m.p. 218—220°, $[\alpha]_D^{20}$ +61° (*c* 0·35 in Me_2SO) (Found: C, 52·25; H, 6·65; N, 15·15%; M^+, 365. $C_{16}H_{24}N_4O_6$ requires C, 52·15; H, 6·55; N, 15·2%; *M*, 365). The α-D-mannofuranosylimidazole, R_F 0·45 (A), did not crystallise. When the reaction was carried out in acetonitrile the β-imidazole was obtained in 38% yield; some α-anomer was again detected in the mother liquors.

(b) *Water solvent.* N-Sodium hydroxide (10 ml, 10 mmol) was added to a solution of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine toluene-*p*-sulphonate and ethyl *N*-[carbamoyl(cyano)methyl]formimidate in water (30 ml) and the mixture was set aside overnight at room temperature. T.l.c. [system (A)] showed the presence of the α- and β-imidazoles and an intensely u.v.-absorbing spot that corresponded to the aglycone. The aqueous solution was extracted with chloroform (3 × 50 ml) and the organic layer was dried (Na_2SO_4) and evaporated to a clear gum. This was dissolved in ethyl acetate (2 ml) to give the β-mannofuranosylimidazole as laths (660 mg, 22%), m.p. and mixed m.p. 218—220°.

Action of Aqueous Ammonia on the Nucleoside Esters (XVIIa) *and* (XVIIIa).—(a) α-*Anomer* (XVIIa). A solution of the α-nucleoside (5 mg) in aqueous ammonia (0·5 ml; *d* 0·880) and ethanol (0·5 ml) was heated in a sealed tube at 100° for 48 h. T.l.c. [system (A)] showed the absence of starting material and the presence of a new discrete u.v.-absorbing spot at R_F 0·45, which corresponded to the isopropylidene-α-D-mannofuranosylimidazolecarboxamide (R_F 0·45) already described. The product gave a deep purple colour with the Bratton–Marshall reagent, whereas the corresponding imidazole ester produced a bright red spot.

(b) β-*Anomer* (XVIIIa). The β-nucleoside was treated with aqueous ammonia as in (a). T.l.c. showed the absence of starting material and the presence of a new discrete u.v.-absorbing spot at R_F 0·39 which corresponded to the amide (XVIIIb).

5-*Cyano*-1-(2,3:5,6-*di*-O-*isopropylidene*-D-*mannofuranosyl*)*uracil* (XXIII).—α-Cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide (10·6 g, 50 mmol) soon dissolved when added to a solution of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranosylamine toluene-*p*-sulphonate (21·6 g, 50 mmol) in methanolic sodium methoxide (250 ml containing 100 mmol of sodium). The mixture was kept at room temperature overnight, refluxed for 1 h, and evaporated to half volume, to give a precipitate of sodium toluene-*p*-sulphonate. The mixture was then filtered and the filtrate evaporated to a foam. This, in water (200 ml), was cooled to 0° and acidified to pH 6 with acetic acid to give a precipitate which was collected. The solid was dissolved in ethanol and the solution was evaporated to a foam. This procedure was repeated, then the foam was dissolved in methanol and treated with decolorising charcoal. The solution was evaporated to a foam, which was dissolved in dry benzene (100 ml), and the product was precipitated with cyclohexane (300 ml), collected, and washed with cyclohexane then light petroleum to give the nucleoside (XXIII) (14 g, 70%) as a powder, m.p. 80—85° (decomp.) with retained methanol (Found: C, 52·9; H, 5·9; N, 9·9. $C_{17}H_{21}N_3O_7$,-CH_3OH requires C, 52·55; H, 6·1; N, 10·2%).

5-*Cyano*-1-D-*mannofuranosyluracil* (XXIV).—A solution of 5-cyano-1-(2,3:5,6-di-*O*-isopropylidene-D-mannofuranosyl)uracil (7·62 g, 20 mmol) in acetic acid (15 ml) was diluted to 60 ml with boiling water and kept at 100° for 4 h. (t.l.c. showed two u.v.-absorbing spots, one of which corresponded to the title material). The solution was treated with decolorising charcoal, filtered, and evaporated to a partially crystalline gum, which crystallised from boiling ethanol to give 5-*cyano*-1-D-*mannofuranosyluracil* (1·8 g, 30%). Crystallisation from water gave needles, m.p. 218—220° (Found: C, 44·15; H, 4·35; N, 14·15. $C_{11}H_{13}N_3O_7$ requires C, 44·2; H, 4·5; N, 14·05%).

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