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SYNTHESIS OF D-*ribo*-*C*-NUCLEOSIDE ANALOGUES BY DEHYDRATION OF NEW D-*allo*-PENTITOL-1-YL HETEROCYCLES

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ABSTRACT

The reaction of 2-amino-2-deoxy-D-*glycero*-D-*altro*-heptose hydrochloride with acyclic and cyclic 1,3-dicarbonyl compounds gives, respectively, (D-*allo*-pentitol-1-yl)-pyrroles and -tetrahydroindoles that can be dehydrated to yield D-*ribo*-*C*-glycosyl heterocycles having furanoid or pyranoid structures, depending on the reaction conditions. Thus, when the reactions were kinetically controlled, α- and β-D-ribofuranosyl heterocycles were obtained, but α- and β-D-ribopyranosyl heterocycles were formed under conditions of thermodynamic control. A criterion is proposed to differentiate between both structures on the basis of the mass spectra of their triacetates.

INTRODUCTION

The reaction of 2-amino-2-deoxyaldoses with 1,3-dicarbonyl compounds yields (alditol-1-yl)pyrroles[1] which can be considered to be acyclic *C*-nucleoside analogues. These compounds can be converted into cyclic *C*-nucleosides by acid-catalysed, intramolecular dehydration of the polyhydroxyalkyl chain[2,3]. We now report on the preparation of some new D-*allo*-pentitol-1-yl heterocycles by reaction of 1,3-dicarbonyl compounds with 2-amino-2-deoxy-D-*glycero*-D-*altro*-heptose[4], and the dehydration of the products to give new D-*ribo*-*C*-nucleoside analogues.

RESULTS AND DISCUSSION

The reaction of 2-amino-2-deoxy-D-*glycero*-D-*altro*-heptose hydrochloride[4] with methyl-3-oxobutanoate or 2,4-pentanedione yielded the 5-(D-*allo*-pentitol-1-yl)pyrroles **1** or **2**, the structures of which were demonstrated by elemental analyses

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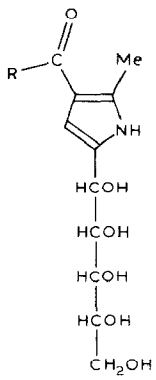
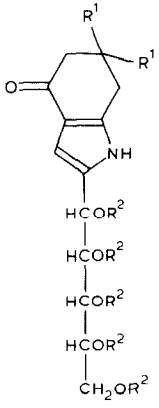
and spectral data (u.v., i.r., and ^{1}H-n.m.r.). The presence of the pentahydroxypentyl chain was proved by periodate oxidation, ~3 mol of formic acid being produced from each compound. In the same way, the reaction of 2-amino-2-deoxy-D-*glycero*-D-*altro*-heptose hydrochloride with cyclohexane-1,3-dione or 5,5-dimethylcyclohexane-1,3-dione gave the 2-(D-*allo*-pentitol-1-yl)-4,5,6,7-tetrahydroindol-4-ones **3** or **5**. The structure of **3** was proved as for **1** and **2**, and the structure assigned to **5** was based on its penta-acetate **6**. Conventional treatment of **3** with acetic anhydride in pyridine gave the penta-acetate **4**. The $J_{1',2'}$ and $J_{2',3'}$ values of **4** and **6** (Table I) reflected a mixture of conformers in which no single conformer prepondered, and with little, if any, contribution of the planar zigzag conformation that would involve two 1,3-interactions of acetoxyl groups (OAc-1′/3′ and OAc-2′/4′)[5].



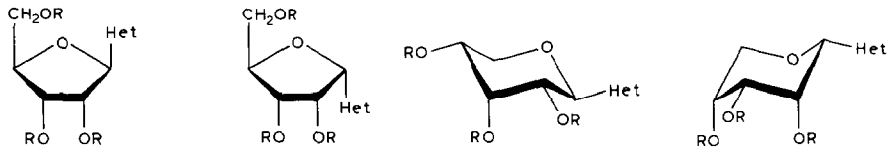
1 R = OMe
2 R = Me



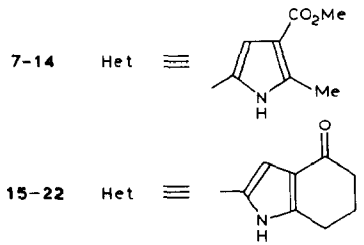
3 R^1 = H, R^2 = H
4 R^1 = H, R^2 = Ac
5 R^1 = Me, R^2 = H
6 R^1 = Me, R^2 = Ac

The acid-catalysed dehydration of **1** and **3** can lead to anhydro furanoid or pyranoid structures, depending on the reaction conditions. Thus, when **1** was dehydrated at pH <4 and room temperature, the β- and α-furanoid compounds (**7** and **8**) were formed immediately (t.l.c.) and gradually transformed into 3-methoxycarbonyl-2-methyl-5-β-D-ribopyranosylpyrrole (**9**) and a minor product, presumably the α anomer, which could not be isolated by conventional column chromatography or preparative t.l.c. Periodate oxidation of **9** produced 1 mol of formic acid in accord with a pyranoid structure, and the ^{1}H-n.m.r. spectrum (Me_2SO-d_6) contained three doublets for secondary hydroxyl groups. The $J_{1',2'}$ value (10.0 Hz) of **9** reflected a *trans*-diaxial arrangement of H-1′,2′, which is only possible for the β anomer in the $^4C_1$(D) conformation. The same value was also found for $J_{1',2'}$ of the triacetate **13**. When the reaction mixture obtained from **1** was allowed to stabilise (~72 h), acetylation of the products gave **13** as major product. The minor product (**14**) had $J_{1',2'}$ 1.2 Hz, consistent with a *gauche* arrangement of

H-1′,2′ in either the $^4C_1$ or $^1C_4$(D) conformation of the α anomer. The conformation $^1C_4$(D) was assigned on the basis of the coupling constants $J_{4',5'} = J_{4',5''} = 1.2$ and $J_{5',5''}$ 13.3 Hz, which indicated H-4′ to be equatorial[6]. Similar dehydration of **3** and acetylation of the products in the stabilised reaction mixture gave, as the major product, the β-pyranoid derivative **21** ($J_{1',2'}$ 10.0 Hz). The α-pyranoid structure **22** was tentatively assigned to the minor product, on the basis of its mass spectrum (see below).



7,15 R = H **8,16** R = H **9,17** R = H **10,18** R = H
11,19 R = Ac **12,20** R = Ac **13,21** R = Ac **14,22** R = Ac



When **1** was dehydrated in more dilute solutions at 0–5° and pH ~5, and the reaction mixture was neutralised immediately after the starting material had disappeared (t.l.c.), acetylation of the products gave the 2-(tri-*O*-acetyl-α- and -β-D-ribofuranosyl)pyrroles (**12** and **11**). The structures of these compounds were assigned on the basis of the empirical rule[7,8] which states that, in the aldofuranosyl derivatives, H-1′ resonates at lower field when H-1′,2′ are *cis* than when they are *trans*. Thus, the minor product (H-1′, δ 5.20) must be the α anomer (**12**) and the major product (H-1′, δ 4.95) the β anomer (**11**). When **3** was treated under these conditions, the products were 2-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-4,5,6,7-tetrahydroindol-4-one (**19**) and its α anomer (**20**) (H-1′, δ 5.00 and 5.27, respectively).

These results are in good agreement with the mechanism proposed for the dehydration of pentahydroxypentylpyrroles[2], involving an intermediate C-1′ carbocation. The furanosyl compounds, formed first, must be the kinetically controlled products, and the pyranosyl compounds must be the thermodynamically controlled products. Under kinetic control, the β-furanoid compounds are the major products, because the transition state leading to them from the initially formed C-1′ carbocation is more stable than that leading to the α anomers, in which HO-2′ and the bulky C-1′ substituent are *cis*. Under thermodynamic control, the β-pyranoid compounds are the major products because, in their $^4C_1$(D) conformations, there are fewer bulky, axial groups than in any alternative structure.

TABLE I

^{1}H-N M R DATA[a] (90 MHz) FOR **1–4, 6, 9, 11–14**, AND **19–21**

Compound	*Carbohydrate moiety*							
	H-1'	*H-2'*	*H-3'*	*H-4'*	*H-5'*	*H-5''*	*OH*	*OAc*
1[c]	3.80–3.10 m						5.15 d (1 H) 4.78–4.47 m (3 H) 4.33 t (1 H)	
2[c]	3.87–3.27 m						5.20 d (1 H) 4 82–4 52 m (3 H) 4.39 t (1 H)	
3[c]	3.90–3.20 m						5.19 d (1 H) 4.78–4.58 m (3 H) 4 32 t (1 H)	
4[d]	5.97 d $J_{1',2'}$ 5.0	5.58 t $J_{2',3'}$ 5.0	5.37 m	$J_{4',5'}$ 2.8 $J_{4',5''}$ 6.5	4 44 dd $J_{5',5''}$ 12.0	4.10 dd		2.09 s (6 H) 2.07 s (3 H) 2.03 s (3 H) 2.01 s (3 H)
6[d]	5.98 d $J_{1',2'}$ 5.0	5.60 t $J_{2',3'}$ 5.0	5.37 m	$J_{4',5'}$ 3.0 $J_{4',5''}$ 6.0	4.44 dd $J_{5',5''}$ 12.0	4.07 dd		2 12 s (9 H) 2.06 s (3 H) 2.04 s (3 H)
9[c]	4.23 d $J_{1',2'}$ 10 0	4.00–3 30 m					4 70 d (1 H) 4.63 d (1 H) 4 46 d (1 H)	
11[d]	4.95 d $J_{1',2'}$ 5.0	5 16 t[e] $J_{2',3'}$ 5.0	5.22 t[e] $J_{3',4'}$ 5 0	4.33 m				2.09 s (6 H) 2 07 s (3 H)
12[d]	5.20 d $J_{1',2'}$ 4.0	5.51 t $J_{2',3'}$ 4.1	5.36 dd $J_{3',4'}$ 6.0	4.45–4.00 m				2.06 s (3 H) 2.03 s (3 H) 1.96 s (3 H)
13[d]	4.62 d $J_{1',2'}$ 10.0	5.07 m $J_{2',3'}$ 2.3	5 71 t $J_{3',4'}$ 2.3	5.07 m	3.98–3.58 m			2.19 s (3 H) 2.03 s (3 H) 1.92 s (3 H)
14[d]	4.64 d $J_{1',2'}$ 1.2	5.20 d	5 46 m	5 20 d $J_{4',5'}$ ~1 $J_{4',5''}$ ~1	4.20 d $J_{5',5''}$ 13.3	3.85 d		2.13 s (3 H) 2.03 s (3 H) 1.99 s (3 H)
19[d]	5.00 m $J_{1',2'}$ 5.0	5.28 m		4.28 m				2.16 s (3 H) 2.09 s (3 H) 2.05 s (3 H)
20[d]	5.27 d $J_{1',2'}$ 3 6	5 47 t $J_{2',3'}$ 3.7	5.36 dd $J_{3',4'}$ 6 0	4.45–4.00 m				2 07 s (3 H) 2.03 s (3 H) 2.00 s (3 H)
21[d]	4.68 d $J_{1',2'}$ 10.0	5.04 m $J_{2',3'}$ 2.4	5 71 t $J_{3',4'}$ 2.4	5.04 m	4.03–3.60 m			2.22 s (3 H) 2.03 s (3 H) 1.91 s (3 H)

[a]Recorded at 35.5°, δ scale (internal Me_4Si), J in Hz, with assignments verified by selective proton-decoupling. [b]Broadening due to ^{14}N-quadrupole relaxation. [c]In $(CD_3)_2SO$. [d]In $CDCl_3$. [e]Values obtained by extrapolation to zero concentration of $Eu(fod)_3$.

Aglycon								
H-1[b]	*H-3*	*H-5,5*	*H-6,6*	*H-7,7*	*Me-6,6*	*Me-5*	*MeO-C(O)*	*Me-C(O)-*
10.73	6.23 d $J_{1,3}$ 2.3					2.39 s	3.66 s	
10.83	6.31 d $J_{1,3}$ ~1					2.43 s		2.26 s
10.87	6.13 d $J_{1,3}$ 1.3	2.90–1.80 m						
9.23	6.54 d $J_{1,3}$ 2.3	2.80 t (3 H); 2.47 t (3 H)						
9.00	6.54 d $J_{1,3}$ 2.2	2.69 s (2 H)		2.37 s (2 H)	1.12 s (6 H)			
10.46	6.25 d $J_{1,3}$ 2.0					2.39 s	3.67 s	
8.90	6.46 d $J_{1,3}$ 2.8					2.51 s	3.78 s	
8.69	6.42 d $J_{1,3}$ 2.9					2.47 s	3.75 s	
8.87	6.45 d $J_{1,3}$ 3.0					2.47 s	3.78 s	
8.74	6.32 d $J_{1,3}$ 2.3					2.48 s	3.76 s	
10.31	6.48 d $J_{1,3}$ 2.5	2.79 t (3 H); 2.45 t (3 H)						
9.70	6.43 d $J_{1,3}$ 2.3	2.78 t (3 H); 2.44 t (3 H)						
9.83	6.44 d $J_{1,3}$ 2.0	2.80 t (3 H); 2.44 t (3 H)						

The signals for the molecular ions (M) in the mass spectra (Table II) of the acetates **11–14** and **19–22** were of low relative intensity (0.3–3.2%). The acetylium ion (*m/z* 43) was the base peak, except in the spectrum of **19**, where its relative intensity was 81%. The presence of a C–C bond between the sugar moiety and the heterocycle (B) is consistent with the reduced intensity of the B, B + H, and B + 2H peaks,and the high intensity of the B + 30 peak[9–11]. Other characteristic peaks of *C*-nucleosides[9], namely, B + 56, B + 55, B + 44, B + 43, B + 42, B + 29, B + 28, and B + 14, were also observed.

TABLE II

SELECTED PEAKS PRESENT IN THE MASS SPECTRA OF COMPOUNDS **11–14** AND **19–22**

	Pyrrole series					*Tetrahydroindole series*				
		Furanoid		*Pyranoid*			*Furanoid*		*Pyranoid*	
		11	**12**	**13**	**14**		**19**	**20**	**21**	**22**
Ion	m/z	*Abundances*[a]				m/z	*Abundances*[a]			
M + 1	398	0.1	0.1	0.4	0.6	394	0.3	0 2	0.2	0.5
M	397	0 7	0 4	1.9	3.2	393	0 9	0.4	0 3	1.3
M − 31	366	1 8	0.3	3.5	2.8					
M − 59	338	0.3			0.3	334	1 1	0 1	0.2	0.4
M − 60	337	1.8	0.1	4.3	1.3	333	5.7	0.2	1.1	1.8
M − 73	324	0.3	0 1	0.5	0.3	320	0.2	0.1		
M − 118	279	1.2	0.1	1.1	0.8	275	1 7	0.2	0.8	0 4
M − 119	278	6.0	0.6	4.2	4.2	274	7.5	1.3	4.2	2 0
M − 120	277	0.2	0 1	4.6	4.6	273	1.2	0.1	6.2	5.0
M − 162	235	0.8	0.1	3.9	3.1	231	2.7	0.3	7.7	4.4
M − 163	234	0 8	0.1	2.2	2.2	230	1.4	0.3	2 8	1.3
M − 178	219	10.4	0.6	4.2	3.3	215	13.8	4.0	5.4	2.4
M − 179	218	84.6	37.0	23.1	18.1	214	100.0	21.9	38 5	14.1
B + 56	194	4.0	0.2	2.9	2.2	190	5.0	2.0	3 6	0 8
B + 55	193			0.3	0.1	189	1.6	0.4	1.0	1.1
B + 44	191	0.4	0.1	3.4	2 5	187	0.9	0 1	4.2	1.2
B + 43	181	5.4	0.3	4.8	5.4	177	5.9	1.8	6.5	1.9
B + 42	180	3.6	0.2	1.6	1.8	176	3 4	1 1	2 6	0.5
B + 30	168	24.6	2.3	47 7	55.4	164	37.5	9.6	61.5	19 6
B + 29	167	3.9	0.3	5.4	6.2	163	3 4	1.5	4.6	1.5
B + 28	166	5.1	0.4	4.2	6 4	162	5.6	1.3	5.4	1.5
B + 14	152	3.7	0 3	4.1	4.6	148	6.3	3.7	8.1	2.6
B + 2H	140	1.8	0.1	3.6	3.2	136	3.4	1 2	4.6	1.1
B + H	139	3.9	0.1	4.0	4.4	135	11 2	4 1	10.8	3.9
B	138	1.2	0.1	0.9	1.1	134	2 1	0 9	2.2	0.8
	136	12.1	0.5	9.9	10.8	132	0.9	0.5	1.0	0.6
	85	12.7	3.1	16.9	1.7	85	10.3	4.6	18.1	12.3
	69	18.5	3.1	42.3	46.2	69	13.8	4.3	30.8	19.2
	57	2.7	16.9	10.0	6.2	57	16.3	50.0	2.4	69.2
Ac	43	100.0	100.0	100.0	100.0	43	81.3	100.0	100.0	100.0

[a]Per cent relative abundance of base peak.

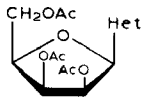
In the pyrrole series (**11–14**), some peaks due to fragmentations of the heterocyclic moiety[12] were found, *e.g.*, M − OMe and B + 30 − MeOH.

The peaks for M − 60, M − 118, M − 119, M − 120, M − 162, M − 163, M − 178, and M − 179 are derived by loss of the acetoxyl groups. Some can be easily assigned, namely, M − 60 (M − AcOH), M − 118 (M − 2 AcO)[13], M − 120 (M − 2 AcOH), and M − 162 (M − 2 AcOH − CH_2CO). The remainder can be explained by the loss of diacetyl peroxide, acetic acid, ketene, acetoxyl, and acetyl radicals, or a hydrogen atom, in various combinations. The intense M − 179 peak can be assigned to M − 2 AcO − H − AcOH or M − 2 AcOH − AcO ions.

The M − 119 peak was more intense than the M − 120 peaks for the compounds having a furanosyl ring (**11, 12, 19, 20**), in contrast to the similar intensities showed by both fragments for the compounds having a pyranosyl ring (**13, 14, 21, 22**). On the other hand, the M − 162 peak was of lower intensity in the mass spectra of the furanoid compounds than in those of the pyranoid isomers. These findings accord with the trend to lose two molecules of acetic acid (M − 120) and then a molecule of ketene (M − 162), previously observed for acetylated glycopyranosyl compounds[14–16]. Furthermore, in the tetrahydroindole series (**19–22**), a weak M − 73 peak appeared in the mass spectra of **19** and **20** only, which is consistent with the loss of the CH_2OAc group in agreement with the furanoid structure of the sugar moiety[9,14]. Nevertheless, the formation of M − 73 fragments from the pyrrole derivatives **11–14** suggested that, for **13** and **14**, it may have originated by loss of ketene from M − OMe whereas, for **11** and **12**, it was due to both breakdown paths M − OMe − CH_2CO and M − CH_2OAc.

Thus, it is proposed that, for the acetylated *C*-nucleosides derived from aldopentoses, the relative abundances of the M − 73, M − 119, M − 120, and M − 162 peaks can be used to distinguish between the furanoid and pyranoid structures. However, there were no significant differences between the mass spectra of α and β anomers.

Comparison of the mass-spectral data for a D-*lyxo*-*C*-nucleoside[10] and the furanoid structure **23** shows that, for the former, the M − 120 peak (40%) is more intense than the M − 119 peak (8%), and there is no M − 73 peak, suggesting the pyranoid structure (**24**) as proposed[2] for its 3,7-anhydroheptulose phenylosazone precursor on the basis of ^{1}H-n.m.r. and periodate oxidation data. The α-pyranoid structures proposed for these compounds are also in good agreement with the chiroptical results obtained by Sallam[10] and not with the β-furanoid structures suggested. Likewise, the mass spectrum of a D-*ribo*-*C*-nucleoside analogue described[11] as **25** shows a greater abundance of the M − 120 (26%) over the M − 119 (5%) peak, and a high intensity (30%) for the M − 162 peak; the formation of a M − 73 peak was not reported. These data and the $J_{1',2'}$ values reported[11] for **25** and its non-acetylated precursor (9.1 and 9.8 Hz, respectively) are consistent with the β-pyranoid structure in the $^4C_1$(D) conformation (**26**).



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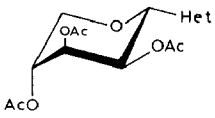

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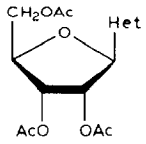

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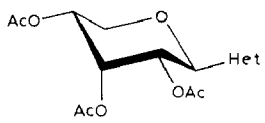

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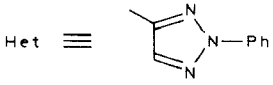

EXPERIMENTAL

General methods. — Solutions were concentrated *in vacuo* at <50°. Melting points were determined with a Gallenkamp apparatus and are uncorrected. Optical rotations were measured at 25 ±5° with a Perkin–Elmer 141 polarimeter (10-cm, 1-mL cell). T.l.c. was performed on Silica Gel GF_{254} (Merck) with detection by u.v. light or iodine vapour. Column chromatography was performed in the "flash" mode[17], using an ethyl acetate–ethanol gradient. Preparative t.l.c. was performed on Silica Gel PF_{254} (Merck). I.r. spectra (KBr discs or solutions in chloroform) were recorded with a Perkin–Elmer 399 spectrometer, and u.v. spectra with a Beckman 25 instrument. ^{1}H-N.m.r. (90 MHz, internal Me_4Si or sodium 4,4-dimethyl-4-silapentane-1-sulphonate) were recorded with a Perkin–Elmer R-32 spectrometer, and coupling constants were measured directly from spectra recorded at 300-Hz sweep-width (probe temperature, 35.5°). Assignments were confirmed by double resonance experiments, and overlapping signals were separated by incremental additions of $Eu(fod)_3$. E.i. mass spectra (70 eV) were obtained using an AEI MS-30 mass spectrometer, operated at a resolution of 1.000, with the direct insertion probe at 50° for syrups and 30° below the m.p. for solids.

Formic acid produced in the periodate oxidation was determined as previously described[18,19].

*3-Methoxycarbonyl-2-methyl-5-(*D-allo-*pentitol-1-yl)pyrrole* (**1**). — A solution of 2-deoxy-2-(phenylamino)-D-*glycero*-D-*altro*-heptononitrile[4] (6.7 g, 23.7 mmol) in M hydrochloric acid (55 mL) was hydrogenated at atmospheric pressure and room temperature in the presence of 10% $Pd/BaSO_4$ (2.8 g) for 7 days, then filtered, and concentrated until crystals of ammonium chloride appeared. These were removed, the filtrate was concentrated, and ethanol and benzene were repeatedly evaporated from the syrupy residue to yield almost pure, amorphous 2-amino-2-deoxy-D-*glycero*-D-*altro*-heptose (4.9 g, 84%) that was used in the next step without purification.

A solution of the heptosamine hydrochloride (5 g, 20 mmol) in water (20 mL) was treated with methyl 3-oxobutanoate (2.1 mL, 20 mmol) in ethanol (5 mL), and sodium carbonate (1.1 g, 10.2 mmol) was added. The mixture was kept for 6

days at room temperature and the ethanol was then evaporated under diminished pressure. The resulting solution was washed with ether (6 × 25 mL) and extracted with 10:1 ethyl acetate–ethanol (8 × 40 mL), the combined extracts were concentrated to dryness, and the residue was subjected to flash chromatography (ethyl acetate–ethanol, 3:1). The fraction containing the product of R_F 0.64 was concentrated to give a white solid (2.3 g, 39%), which was recrystallised from ethyl acetate–ethanol to yield **1**, m.p. 154–155°, $[\alpha]_D$ +4°, $[\alpha]_{578}$ +5°, $[\alpha]_{546}$ +5°, $[\alpha]_{436}$ +9°, $[\alpha]_{365}$ +20° (*c* 0.5, pyridine): λ_{max}^{EtOH} 259 and 210 nm (ε 6.3 and 12.6); ν_{max} 3380–3100 (OH, NH), 1672 (C=O), 1597 and 1523 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I. Periodate oxidation gave 2.8 mol of formic acid.

Anal. Calc. for $C_{12}H_{19}NO_7$: C, 49.82; H, 6.62; N, 4.84. Found: C, 49.84; H, 6.90; N, 4.64.

*3-Acetyl-2-methyl-5-(*D-allo-*pentitol-1-yl)pyrrole* (**2**). — A solution of the above heptosamine hydrochloride (3.0 g, 12.2 mmol) in water (8 mL) was treated with 2,4-pentanedione (1.3 mL, 12.2 mmol) in ethanol (5 mL) and sodium carbonate (0.65 g, 6.1 mmol). The mixture was kept for 5 days at room temperature and then the ethanol was evaporated under diminished pressure. The resulting solution was washed with ether (6 × 25 mL), the aqueous layer was concentrated, and the residue was dried by azeotropic distillation of ethanol therefrom. The resulting amorphous solid was subjected to column chromatography (ethyl acetate–ethanol, 3:1). The fraction with R_F 0.42 was crystallised from ethanol to yield **2** (0.4 g, 11%), m.p. 134–135°, $[\alpha]_D$ −3°, $[\alpha]_{578}$ −2°, $[\alpha]_{546}$ −2°, $[\alpha]_{436}$ −1° (*c* 0.5, pyridine): λ_{max}^{EtOH} 287, 246, and 213 nm (ε 2.9, 3.9, and 10.0); ν_{max} 3450, 3350–3140 (OH, NH), 1600 (C=O), 1510 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I. Periodate oxidation gave 3.1 mol of formic acid.

Anal. Calc. for $C_{12}H_{19}NO_6$: C, 52.74; H, 7.01; N, 5.13. Found: C, 52.84; H, 7.07; N, 5.38.

*2-(*D-allo-*Pentitol-1-yl)-4,5,6,7-tetrahydroindol-4-one* (**3**). — A solution of the above heptosamine hydrochloride (10 g, 40.7 mmol) in water (25 mL) was treated with 1,3-cyclohexanedione (4.6 g, 40.7 mmol) in water (25 mL) and sodium carbonate (2.2 g, 20.4 mmol). The mixture was kept for 9 days at room temperature, and then concentrated under diminished pressure to a thin syrup that was extracted with acetone (10 × 25 mL). The combined extracts were concentrated, and the residue was dried by azeotropic distillation with ethanol and then subjected to column chromatography (ethyl acetate–ethanol 3:1). The fraction (1.1 g, 9%) with R_F 0.31 was recrystallised from ethanol to yield **3**, m.p. 139–140°, $[\alpha]_D$ +5°, $[\alpha]_{578}$ +4°, $[\alpha]_{546}$ +5°, $[\alpha]_{436}$ +13°, $[\alpha]_{365}$ +24° (*c* 0.5, pyridine): λ_{max}^{EtOH} 279, 243, and 217 nm (ε 2.6, 3.1, and 3.7); ν_{max} 3420–3000 (OH, NH), 1605 (C=O), 1480 and 1400 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I. Periodate oxidation gave 3.1 mol of formic acid.

Anal. Calc. for $C_{13}H_{19}NO_6$: C, 54.73; H, 6.71; N, 4.91. Found: C, 54.42; H, 7.01; N, 4.96.

*2-(Penta-*O*-acetyl-*D*-allo-pentitol-1-yl)-4,5,6,7-tetrahydroindol-4-one* (**4**). —

Conventional treatment of **3** (0.1 g, 0.35 mmol) with pyridine (0.5 mL) and acetic anhydride (0.5 mL), with recrystallisation of the crude product (0.13 g, 73%) from ether, gave **4**, m.p. 129°, $[\alpha]_D$ +82°, $[\alpha]_{578}$ +86°, $[\alpha]_{546}$ +98°, $[\alpha]_{436}$ +183°, $[\alpha]_{365}$ +319° (*c* 0.5, chloroform): ν_{max} 3250–3080 (NH), 1735 (C=O acetate), 1615 (C=O ketone), 1480, and 1368 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{23}H_{29}NO_{11}$: C, 55.75; H, 5.90; N, 2.83. Found: C, 56.06; H, 6.09; N, 2.86.

*6,6-Dimethyl-2-(penta-*O*-acetyl-*D*-allo-pentitol-1-yl)-4,5,6,7-tetrahydroindol-4-one* (**6**). — A solution of the above heptosamine hydrochloride (5.5 g, 22.4 mmol) in water (30 mL) was treated with 5,5-dimethylcyclohexane-1,3-dione (3.1 g, 22.4 mmol) in 2:1 acetone–water (30 mL) and sodium carbonate (1.2 g, 11.2 mmol). The mixture was kept for 10 days at room temperature, the acetone was then evaporated under diminished pressure, and the resulting solution was washed with chloroform (5 × 25 mL) and then concentrated to a thin syrup that was extracted with acetone (10 × 25 mL). The combined extracts were concentrated, and the residue was dried by azeotropic distillation with ethanol and then subjected to column chromatography (ethyl acetate–ethanol,3:1). The fractions containing the component of R_F 0.33 were concentrated to give **5** as a yellow gel (0.65 g, 9%).

Conventional treatment of **5** (0.1 g, 0.32 mmol) with pyridine (0.5 mL) and acetic anhydride (0.5 mL), with recrystallisation of the crude product (0.13 g, 78%) from ethanol, gave **6**, m.p. 142–143°, $[\alpha]_{578}$ +79°, $[\alpha]_{546}$ +92°, $[\alpha]_{436}$ +170°, $[\alpha]_{365}$ +269° (*c* 0.3, chloroform); ν_{max} 3250–3080 (NH), 1740 (C=O ester), 1625 (C=O ketone), 1480, and 1368 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{25}H_{33}NO_{11}$: C, 57.35; H, 6.35; N, 2.67. Found: C, 57.06; H, 6.60; N, 2.82.

*3-Methoxycarbonyl-2-methyl-5-β-*D*-ribopyranosylpyrrole* (**9**). — A solution of **1** (0.3 g, 1.0 mmol) in water (7 mL) was treated with trifluoroacetic acid (0.1 mL) for 72 h at room temperature, then neutralised with Amberlite IR-45 (HO^-) resin, and concentrated to dryness. Acetone was repeatedly evaporated from the residue, and the resulting white powder was purified by preparative t.l.c. (acetone–light petroleum–chloroform–benzene–methanol, 1:1:1:1:1, two developments). Crystallisation from acetone then gave **9** (0.16 g, 57%), m.p. 180–181°, $[\alpha]_D$ −73°, $[\alpha]_{578}$ −76°, $[\alpha]_{546}$ −87°, $[\alpha]_{436}$ −155°, $[\alpha]_{365}$ −260°, (*c* 0.5, pyridine); λ_{max}^{EtOH} 258 and 213 nm (ε 5.9 and 7.7); ν_{max} 3531, 3380–3170 (OH, NH), 1670 (C=O), 1593, 1525, and 1481 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I. Periodate oxidation gave 1.0 mol of formic acid.

Anal. Calc. for $C_{12}H_{17}NO_6$: C, 53.13; H, 6.32; N, 5.16. Found: C, 52.99; H, 6.60; N, 4.87.

*3-Methoxycarbonyl-2-methyl-5-(2,3,4-tri-*O*-acetyl-β-*D*-ribopyranosyl)pyrrole* (**13**). — Conventional treatment of **9** (0.08 g, 0.29 mmol) with pyridine (0.8 mL) and acetic anhydride (0.8 mL, 8.47 mmol) gave **13** as an amorphous solid (67 mg, 56%), m.p. 70–72°, $[\alpha]_D$ −4°, $[\alpha]_{578}$ −2°, $[\alpha]_{546}$ −4°, $[\alpha]_{436}$ −4°, $[\alpha]_{365}$ −2° (*c* 0.5,

chloroform): ν_{max} 3380–3240 (NH), 1760–1660 (C=O), 1590 and 1520 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I, and the m.s. data in Table II.

Anal. Calc. for $C_{18}H_{23}NO_9 \cdot 0.5\ H_2O$: C, 53.20; H, 5.95; N, 3.45. Found: C, 52.99; H, 6.10; N, 3.63.

3-Methoxycarbonyl-2-methyl-5-(2,3,4-tri-O-acetyl-β- and -α-D-ribopyranosyl)pyrrole (**13** *and* **14**). — A solution of **1** (0.2 g, 0.74 mmol) in water (5 mL) was treated with trifluoroacetic acid (0.1 mL) as described above, and the resulting white powder was treated conventionally with pyridine (2 mL) and acetic anhydride (2 mL, 21.2 mmol). Preparative t.l.c. (chloroform–light petroleum–acetone, 8:1:1, two developments) of the product gave **13** (0.12 g, 40%), R_F 0.32, and **14** (40 mg, 14%), R_F 0.20, as a syrup, $[\alpha]_D$ +16°, $[\alpha]_{578}$ +17°, $[\alpha]_{546}$ +20° (*c* 1.5, chloroform); ν_{max} 3340–3210 (NH), 1760–1660 (C=O), 1590, and 1520 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I and the m.s. data in Table II.

3-Methoxycarbonyl-2-methyl-5-(2,3,5-tri-O-acetyl-β- and -α-D-ribofuranosyl)pyrrole (**11** *and* **12**). — A solution of **1** (0.2 g, 0.74 mmol) in water (25 mL) was treated with aqueous 10% trifluoroacetic acid (0.05 mL) at ~5° until t.l.c. (acetone–light petroleum–chloroform–benzene–methanol, 1:1:1:1:1) showed that **1** had almost disappeared. The reaction mixture was then processed as described for **13** and **14** to yield **11**, R_F 0.43, as a syrup (0.1 g, 38%), $[\alpha]_D$ −2°, $[\alpha]_{578}$ −2°, $[\alpha]_{546}$ −2°, $[\alpha]_{436}$ −4°, $[\alpha]_{365}$ −6° (*c* 0.5, chloroform); ν_{max} 3460–3170 (NH), 1770–1650 (C=O), 1595, and 1525 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I and the m.s. data in Table II.

Anal. Calc. for $C_{18}H_{23}NO_9$: C, 54.41; H, 5.83; N, 3.53. Found: C, 54.63; H, 5.91; N, 3.80.

Crystallisation from acetone of the product with R_F 0.26 gave **12** (50 mg, 17%), m.p. 125–127°, $[\alpha]_D$ +34°, $[\alpha]_{578}$ +36°, $[\alpha]_{546}$ +42°, $[\alpha]_{436}$ +74°, $[\alpha]_{365}$ +111° (*c* 0.3, chloroform); ν_{max} 3350 (NH), 1770–1685 (C=O), 1595, and 1530 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I and the m.s. data in Table II.

Anal. Found: C, 54.20; H, 5.94; N, 3.53.

2-(2,3,5-Tri-O-acetyl-β- and -α-D-ribofuranosyl)-4,5,6,7-tetrahydroindol-4-one (**19** *and* **20**). — A solution of **3** (220 mg, 0.77 mmol) was dehydrated and acetylated as described for the preparation of **11** and **12**. The product mixture was subjected to preparative t.l.c. (acetone–light petroleum–ether–benzene, 2:2:1:1, two developments).

The band of R_F 0.31 contained **19**, isolated as a syrup (160 mg, 53%), $[\alpha]_D$ −3°, $[\alpha]_{578}$ −3°, $[\alpha]_{546}$ −3°, $[\alpha]_{436}$ −1°, $[\alpha]_{365}$ −12° (*c* 1.4, chloroform); ν_{max} 3400–3100 (NH), 1740 (C=O ester), 1630 (C=O ketone), 1585, 1485, and 1373 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I and the m.s. data in Table II.

Anal. Calc. for $C_{19}H_{23}NO_8$: C, 58.01; H, 5.89; N, 3.56. Found: C, 57.64; H, 6.12; N, 3.44.

The band of R_F 0.22 contained **20**, isolated as a syrup (80 mg, 26%), $[\alpha]_D$ +38°, $[\alpha]_{578}$ +40°, $[\alpha]_{546}$ +44°, $[\alpha]_{436}$ +69°, $[\alpha]_{365}$ +94° (*c* 1.2, chloroform); ν_{max}

3400–3100 (NH), 1740 (C=O ester), 1630 (C=O ketone), 1380, 1485, and 1373 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I and the m.s. data in Table II.

Anal. Found: C, 57.79; H, 6.12; N, 3.31.

2-(2,3,4-Tri-O-acetyl-β- and -α-D-ribopyranosyl)-4,5,6,7-tetrahydroindol-4-one (**21** *and* **22**). — These compounds were prepared from **3** as described for **15** and **16**. The product mixture was subjected to preparative t.l.c. (acetone–light petroleum–ether–benzene, 2:2:1:1, two developments).

The band of R_F 0.29 gave **21** (95 mg, 46%), m.p. 190–193° (from acetone–ether), $[\alpha]_D$ +11°, $[\alpha]_{578}$ +11°, $[\alpha]_{546}$ +13°, $[\alpha]_{436}$ +29°, $[\alpha]_{365}$ +58° (*c* 0.3, chloroform); ν_{max} 3290–3120 (NH), 1740 (C=O ester), 1625 (C=O ketone), 1590, 1485, and 1370 cm^{-1} (C=C pyrrole). The ^{1}H-n.m.r. data are given in Table I and the m.s. data in Table II.

Anal. Calc. for $C_{19}H_{23}NO_8$: C, 58.01; H, 5.89; N, 3.56. Found: C, 57.87; H, 5.92; N, 3.84.

A second substance (20 mg, 10%) of R_F 0.16 was tentatively identified as **22** on the basis of its mass spectrum (Table II).

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