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SUBSTITUTED GLYCOSYLAMINES CONTAINING THE INDOLE NUCLEUS—II

NMR STUDIES

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Abstract—The synthesis of 33 fully acetylated glycopyranosylamine derivatives (of which 16 are newly reported) is described. The NMR spectra of these compounds are discussed with special reference to the configuration and conformation of the acetylated sugar moieties.

INTRODUCTION

THE general aim of this work was to prepare a series of acetylated glycopyranosylindole derivatives, and to investigate their structures by NMR and mass spectroscopy.[1] The present paper covers the syntheses and NMR spectra of acetylated D-galactopyranosyl-, D-mannopyranosyl-, L-rhamnopyranosyl-, D-xylopyranosyl-, D-lyxopyranosyl-, L-arabinopyranosyl- and D-ribopyranosylamine derivatives; data for previously reported acetylated D-glucopyranosylamines[2,3] are included for comparison. A list of all the compounds discussed here is given in Table 1.

The mass spectra of these compounds are to be discussed separately.

DISCUSSION

The NMR parameters obtained by first-order analyses of the 100 MHz spectra of the acetylated D-glucopyranosyl,[2] D-galactopyranosyl, D-mannopyranosyl, L-rhamnopyranosyl, D-xylopyranosyl, L-arabinopyranosyl and D-ribopyranosyl derivatives prepared are shown in Tables 2–8 respectively. The symbol † indicates that the spectrum was not completely of first-order character, and (m) multiplet.

Parameters were normally obtained by direct measurement of the single-scan spectra. The coupling constants are quoted to $\pm 0{\cdot}3$ Hz. In all cases the assignments as made fully account for the observed spectra (on a first-order basis). For the acetylated β-D-glucopyranosyl compounds I, VIII, XVI and XXIII in $CDCl_3$ and VIII in C_6H_6 the spectra were recorded several times, and the line positions averaged.[2] In these spectra the signals due to the protons on C_5 and C_6 were analysed as ABX patterns using the standard procedures.[4]

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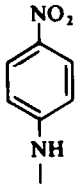
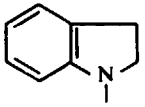
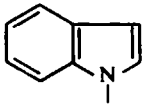
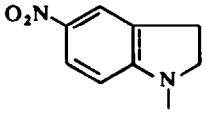
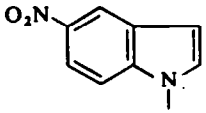
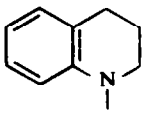
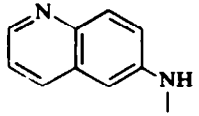
TABLE 1. STRUCTURES OF ACETYLATED GLYCOPYRANOSYL DERIVATIVES

Peracetylated sugar configuration	Aglycone						
							
β-D-Gluco	I	VIII	XVI	XXIII	XXIX	XXXI	XXXIII
β-D-Galacto	II	IX	XVII	XXIV			
D-Manno	III	X		XXV			
L-Rhamno	IV	XI	XVIII	XXVI	XXX		
β-D-Xylo	V	XII	XIX	XXVII		XXXII	
D-Lyxo	VI	XIII	XX				
α-L-Arabino	VII	XIV	XXI	XXVIII			
β-D-Ribo		XV	XXII				

Spectroscopic data are not included for the D-lyxopyranosylamines VI, XIII and XX. Of these, only compound XIII was characterized satisfactorily by elemental analysis. Its NMR spectrum was too complicated to allow reliable first-order assignments.

1. *Acetylated* D-*glucopyranosylamine derivatives* (Table 2). As reported earlier,[2] the coupling constants obtained from the NMR spectra of these compounds indicate that they have the β-D-configuration and in solution exist almost entirely in the Cl conformation (e.g. compound VIII, Fig 1a).

2. *Acetylated* D-*galactopyranosylamine derivatives* (Table 3). The parameters quoted in Table 3 show that the anomeric splitting (J_{12}) is of the order of 9 Hz and that J_{23} is *ca* 10 Hz in each case, indicating that the protons on C_1, C_2 and C_3 are all axially orientated. Where they have been measured, J_{34} and J_{45} lie between 3·4 and 3·9 Hz showing axial-equatorial interaction. Thus the Cl conformation and β-D-configuration must predominate over the other possible forms (e.g. compound IX, Fig 1b). The parameters for IX and XVII are in agreement with those obtained by Preobrazhenskaya *et al.* for the same compounds.[5]

3. *Acetylated* D-*mannopyranosylamine derivatives* (Table 4). The assignments made for the NMR spectra of compounds III and XXV show that J_{34} and J_{45} are *ca* 10 Hz and 9 Hz respectively. These axial–axial splittings prove that these molecules exist almost entirely in the Cl conformation. The spectrum of X in $CDCl_3$, although not of first-order character, showed it to be a mixture of anomers.

With these compounds it is not possible to make a definite assignment of the anomeric configuration on the basis of J_{12}. The fact that J_{12} is *ca* 1 Hz for III, XXV, and for the less abundant anomer of X, suggests that these compounds all have the same anomeric configuration.

The observed coupling constant could nevertheless be consistent with either axial–equatorial coupling (corresponding to Clβ) or diequatorial coupling (Clα). The more abundant anomer in the mixture X, with J_{12} = 2·4 Hz, might be assigned the β-configuration because axial–equatorial coupling constants are normally larger than diequatorial coupling constants. On this basis the other anomer, and compounds III and XXV, would have the Clα configuration (e.g. compound XXV, Fig 1c). While the α-configuration is predicted from instability factors,[6] the $[\alpha]_D$ values for III and XXV indicate, by contrast, the probability that these compounds are β-anomers (cf Ref. 18).

4. *Acetylated* L-*rhamnopyranosylamine derivatives* (Table 5). Although a complete first-order analysis of the NMR spectrum was not possible for any of these compounds, J_{45} could be obtained in every case by analysis of the high field multiplet due to H_5. The value of this coupling constant (9 Hz) shows that H_4 and H_5 are both axial and therefore that these compounds exist in the lC conformation.

As with the mannopyranosylamine derivatives, the values of J_{12} are too small to allow a positive assignment of the anomeric configuration. Both anomers were present in preparation XI (Fig 1d) and the β-configuration has been tentatively assigned to the more abundant component with J_{12} = 2·5 Hz. The less abundant anomer in XI and the other L-rhamnopyranosylamine derivatives might then be assigned the α-configuration because they all have J_{12} *ca* 1 Hz. This, however, is not supported by the optical rotation data or a consideration of the instability factors.[6]

These results for the D-mannopyranosylamine and L-rhamnopyranosylamine

TABLE 2. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED D-GLUCOPYRANOSYLAMINE DERIVATIVES[a]

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	τ_{acetyl}				τ_{N-H}	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	J_{N-1}
I	A	$CDCl_3$	5·14	4·94	4·60	4·93	6·10	5·69	5·91	7·94	7·94	7·94	7·94	4·36	8·9	9·0	9·1	9·7	5·6	2·3	−12·3	7·6
VIII	IH_2	C_6H_6	5·13	4·52	4·63	4·80	6·62	5·76	6·14	8·33	8·33	8·24	8·22		9·0	9·6	9·0	9·8	5·2	2·2	−12·3	
†VIII	IH_2	$CDCl_3$	4·6	——	——	5·1(m)	6·25	5·75	6·00	8·05	8·03	8·00	7·99					9·7	4·8	2·8	−12·3	
†XVI	I	C_6H_6	4·4	——	——	4·8(m)	6·52	5·77	6·06	8·73	8·33	8·28	8·27					9·7	5·0	2·5	−12·4	
†XVI	I	$CDCl_3$	4·3	——	——	4·8(m)	6·02	5·71	5·86	8·36	8·00	7·96	7·95					9·6	5·2	2·2	−12·2	
†XXIII	NIH_2	$CDCl_3$	4·6	——	——	5·0(m)	6·12	5·71	5·91	8·06	7·98	7·98	7·96					9·8	5·0	2·2	−12·4	
†XXIX	NI	$CDCl_3$	4·2	——	——	4·8(m)	~5·95	5·63	5·82	8·33	7·97	7·93	7·93						4·8	2·0	−12·2	
XXXI	Q	$CDCl_3$	4·94	4·86	~4·6	4·92	6·26	5·75	5·92	8·07	7·99	7·96	7·96		9·0	9·5	9·7	9·8	4·8	2·8	−12·0	
XXXIII	AQ	$CDCl_3$	5·12	4·87	4·55	4·89	6·07	5·67	5·90	7·98	7·96	7·96	7·96	4·79	9·0	8·9	9·0	9·6	5·7	2·4	−12·2	8·8

[a] The chemical shifts given here differ slightly, in some cases, from those reported earlier (Refs. 2, 3).

B*	BH		
A	*p*-nitroaniline	NIH_2	5-nitroindoline
I	indole	NI	5-nitroindole
IH_2	indoline	Q	1,2,3,4-tetrahydroquinoline
		AQ	6-aminoquinoline

TABLE 3. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED D-GALACTOPYRANOSYLAMINE DERIVATIVES

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	$\tau_5\tau_6\tau_{6'}$	τ_{acetyl}				τ_{N-H}	J_{12}	J_{23}	J_{34}	J_{45}	J_{N-1}
†II	A	$CDCl_3$	5·19	4·6	——	4·9(m)	4·51	5·87	7·99	7·97	7·84	7·93	4·35	8·5				8·0
†IX	IH_2	$CDCl_3$	5·02	4·52	4·82		4·58	5·96	8·00	8·00	7·82	7·97		9·0	10·2	3·5	3·9	
†XVII	I	$CDCl_3$	4·43	4·25	4·73		4·46	5·82	8·36	8·02	7·78	8·00		8·8	9·9	3·4	3·6	
†XXIV	NIH_2	$CDCl_3$	4·97	4·52	4·81		4·53	5·89	8·06	8·00	7·93	8·00		8·8	10·0	3·4		

B*	BH		
A	*p*-nitroaniline	I	indole
IH_2	indoline	NIH_2	5-nitroindoline

TABLE 4. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED D-MANNOPYRANOSYLAMINE DERIVATIVES

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	τ_{acetyl}			τ_{N-H}	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	J_{N-1}
III	A	$CDCl_3$	4·95	4·46	4·85	4·70	6·15	5·67	5·89	7·73	8·00	7·95	7·95	4·66	~1	~3	10·0	9·2	6·0	2·6	−12·2	8·6
†X[a] β	IH_2	$CDCl_3$	5·22	4·32	———	4·88(m)	6·2	~5·8	~5·8	7·84	7·97	7·97	7·93		2·4							
†X[a] α	IH_2	$CDCl_3$	5·11	4·32	———	4·88(m)	6·2	~5·8	~5·8	7·82	8·03	7·99	7·98		~1							
XXV	NIH_2	$CDCl_3$	4·99	4·36	4·87	4·69	6·15	5·72	5·86	7·86	8·03	7·97	7·97		~1	~3	10·0	9·2	5·8	3·2	−13·4	

[a] Anomeric assignments to the isomers are tentative.

B*	BH	I	indole
A	*p*-nitroaniline	NIH_2	5-nitroindoline
IH_2	indoline		

TABLE 5. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED L-RHAMNOPYRANOSYLAMINE DERIVATIVES

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_{Me}	τ_{acetyl}			τ_{N-H}	J_{12}	J_{23}	J_{34}	J_{45}	$J_{5\text{-}Me}$	J_{N-1}
†IV	A	$CDCl_3$	4·97	4·49	~4·9	~4·9	6·29	8·72	7·76	8·01	7·94	4·57	~1	~3		9·0	6·0	8·6
†XI[a] β	IH_2	$CDCl_3$	5·27	4·45	4·67	4·86	5·90	8·73	7·85	7·98	7·98		2·5	3·1	9·1	8·8	6·4	
†XI[a] α	IH_2	$CDCl_3$	5·10	4·37	~4·9	~4·9	6·27	8·75	7·82	8·02	7·98		0·6	2·9		9·0	6·0	
†XVIII	I	$CDCl_3$	4·21	4·46	~4·76	~4·76	6·24	8·67	8·03	8·01	7·93		1·3	2·7		9·0	6·0	
†XXVI	NIH_2	$CDCl_3$	4·93	4·34	~4·86	~4·86	6·28	8·68	7·84	8·00	7·92		1·2	~2·2		9·0	6·0	
†XXX	NI	$CDCl_3$	4·13	4·43	~4·74	~4·74	6·16	8·61	8·02	8·01	7·90		~1	~2		9·0	6·0	

[a] Anomeric assignments to the isomers are tentative.

B*	BH	I	indole
A	*p*-nitroaniline	NIH_2	5-nitroindoline
IH_2	indoline	NI	5-nitroindole

derivatives emphasize the difficulty in making anomeric assignments by NMR in cases where H_2 is equatorial. Further discussion of this point is to be found in section 8.

5. *Acetylated* D-*xylopyranosylamine derivatives* (Table 6). With the exception of J_{45}, $J_{45'}$ and $J_{55'}$, all the coupling constants for the compounds in Table 6 are *ca* 9 Hz, indicating that these molecules exist almost entirely in the expected Cl conformation with β-D-configuration. Calculation of the dihedral angles involving H_4, H_5 and $H_{5'}$ from the relevant coupling constants, by application of the Karplus relationships,[7] indicates that there is only slight deviation from chair geometry (see compound XII, Fig 1e).

6. *Acetylated* L-*arabinopyranosylamine derivatives* (Table 7). The Cl conformation and α-L-configuration of these compounds (e.g. compound XIV, Fig 1f) follows from the values of J_{12}, J_{23} and J_{34}. The *trans*-diaxial relationship of H_1, H_2 and H_3 is indicated by J_{12} *ca* 9 Hz, and J_{23} *ca* 10 Hz. Likewise, the value of $J_{34} = 3{\cdot}5$ Hz shows that H_4 is equatorial. Application of the Karplus relationship suggests that there is little distortion of the ring.

The optical rotation data for the β-D-glucopyranosylamines, β-D-galactopyranosylamines, β-D-xylopyranosylamines and α-L-arabinopyranosylamines discussed in this paper are quite consistent with one another and with the assigned anomeric configurations.

7. *Acetylated* D-*ribopyranosylamine derivatives* (Table 8). The NMR spectra of compounds XV and XXII in $CDCl_3$ have been reported previously by Preobrazhenskaya *et al.*[5] The chemical shifts and splittings found in this study do not differ significantly from their published values. In addition, J_{45} and $J_{45'}$ have been obtained for compound XXII by analysis of the multiplets due to H_5 and $H_{5'}$. The spectrum of XV in $CDCl_3$ is complex, and no splittings could be determined from a first-order analysis. As noted by Preobrazhenskaya *et al.*,[5] the anomeric coupling constant of 9·6 Hz proves that compound XXII is the β-D-anomer and exists predominantly in the Cl conformation (Fig 1g). The calculated dihedral angles involving H_4, H_5 and $H_{5'}$ correspond closely to those predicted for the Cl conformation, while the $[\alpha]_D$ values for both XV and XXII are in conformity with the β-D-configuration.

8. *Anisotropic effects on acetoxy chemical shifts in glycopyranosylindolines and glycopyranosylindoles.* Cushley *et al.*[8] have shown that the resonance of the C_2 acetoxy-group in peracetylated glycopyranosylindoles is shifted strongly downfield upon reduction to the corresponding glycopyranosylindolines in cases where H_1 and H_2 on the sugar ring are *trans*-diaxial. Due to hindered rotation about the $C_{1'}$—N bond, the aglycone exists preferentially in the *anti*-conformation[9] and the anisotropic effect of the indole relative to that of the indoline in these molecules causes the C_2 acetoxy-group signal to be at much higher field than the remaining acetoxy signals. For the peracetylated β-D-glucosyl and β-D-ribosyl indoles (XVI and XXII) and indolines (VIII and XV), in DMSO-d_6, Cushley *et al.*[8] observed a downfield shift of at least 0·29 ppm when the anisotropy of the indole, enhanced by the 2,3 double bond, was removed by reduction to the corresponding indoline derivatives. This phenomenon has also been noted by Preobrazhenskaya *et al.*[5] for peracetylated β-D-glucopyranosylindole and -indoline.

In the compounds studied here, a similar shift is seen (in $CDCl_3$) between the indole and indoline derivatives containing peracetylated β-D-glucosyl (XVI and VIII),

TABLE 6. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED D-XYLOPYRANOSYLAMINE DERIVATIVES

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ_{acetyl}			τ_{N-H}	J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	J_{N-1}
V	A	$CDCl_3$	5·24	4·62	4·99	4·97	5·87	6·55	7·94	7·94	7·94	4·42	8·9	8·9	9·0	5·6	10·4	−11·8	8·0
XII[a]	IH_2	$CDCl_3$	5·08	4·65	4·78	5·00	5·92	6·65	8·02	7·97	7·96		8·9	8·9	9·0	5·7	10·5	−11·6	
†XIX	I	$CDCl_3$	4·4	———	4·6(m)	~4·8	5·73	6·45	8·37	7·98	7·95					5·6	10·4	−11·6	
XXVII	NIH_2	$CDCl_3$	5·02	4·62	4·78	4·98	5·87	6·56	8·08	7·97	7·97		9·0	9·0	8·8	5·5	10·5	−11·4	
†XXXII	Q	$CDCl_3$	4·6	———	———	5·1(m)	5·91	6·65	8·07	7·97	7·97					5·6	10·5	−11·4	

[a] The assignments given for this compound do not account for a singlet at $\tau = 4·71$ (believed to be due to an impurity).

*B**	*BH*		
A	*p*-nitroaniline	I	indole
IH_2	indoline	NIH_2	5-nitroindoline
		Q	1,2,3,4-tetrahydroquinoline

TABLE 7. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED L-ARABINOPYRANOSYLAMINE DERIVATIVES

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ_{acetyl}			τ_{N-H}	J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	J_{N-1}
†VII	A	$CDCl_3$	5·23	4·6	———	4·7(m)	5·94	6·19	7·95	7·94	7·85	4·31	8·6			2·0	1·2	−13·4	8·4
XIV	IH_2	$CDCl_3$	5·14	4·50	4·86	4·71	6·01	6·34	8·03	8·00	7·86		9·0	9·9	3·5	2·0	1·0	−13·4	
XXI	I	$CDCl_3$	4·56	4·24	4·76	4·59	5·87	6·19	8·37	8·01	7·80		9·0	10·0	3·5	2·0	1·1	−13·3	
XXVIII	NIH_2	$CDCl_3$	5·10	4·50	4·84	4·66	5·95	6·24	8·06	7·99	7·83		9·0	9·9	3·5	2·0	1·2	−13·6	

*B**	*BH*		
A	*p*-nitroaniline	I	indole
IH_2	indoline	NIH_2	5-nitroindoline

TABLE 8. PARAMETERS OBTAINED FROM 100 MHz SPECTRA OF ACETYLATED D-RIBOPYRANOSYLAMINE DERIVATIVES[a]

Compound	B*	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ_{acetyl}			J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$
†XV	IH_2	$CDCl_3$	4·80	4·80	4·30	4·99	6·17		8·00	7·77	7·97					
XXII	I	$CDCl_3$	4·19	4·55	4·20	4·81	~6·0	~6·0	8·34	7·78	8·00	9·6	2·9	2·9	6·8	9·9

[a] See also Ref. 5.

*B** *BH*

IH_2 indoline

I indole

β-D-galactosyl (XVII and IX), β-D-xylosyl (XIX and XII), α-L-arabinosyl (XXI and XIV) and β-D-ribosyl (XXII and XV) moieties. In all cases the high-field C_2 acetoxy-group signal of the indole compound occurs between τ 8·34 and 8·37, and there is a minimum downfield shift of between 0·31 and 0·36 ppm upon reduction of the indole 2,3 double bond. Only a minimum value for the downfield shift can be given because unambiguous assignment of the acetoxy-group resonances other than for the C_2 acetoxy-group of the indole derivative is not possible without undertaking deuteration studies. The finding of this anisotropic shift in the above compounds correlates perfectly with the conformations and configurations advanced for them on the basis of the coupling constants of the sugar ring protons (see Fig 1). In each case H_1 and H_2 on the sugar are *trans*-diaxial, although the relative orientations of the other sugar ring hydrogens may be different. These results, in addition to confirming and extending the findings of Cushley *et al.*[8] and Preobrazhenskaya *et al.*,[5] underline the use of this method in assigning sugar conformation and configuration in suitable glycopyranosylindole derivatives.

A similar anisotropic shift is not observed when the spectrum of peracetylated rhamnopyranosyl indole (XVIII) is compared with that of either of the anomers in mixture XI. This is to be expected because the evidence from coupling constants shows these compounds have the 1C conformation with H_2 equatorial.

EXPERIMENTAL

All m.ps were determined on a Fisher-Johns m.p. apparatus and are uncorrected. Optical rotations (quoted throughout to the nearest 1°) were determined for chloroform solns. NMR spectra were recorded for dilute solns in benzene and $CDCl_3$ on a Varian HA-100 spectrometer, with TMS as internal standard.

TLC was carried out on silica-gel plates with the following solvent systems (all v/v):

A. $CHCl_3$–EtOAc (5:2); B. Benzene–EtOAc (19:1); C. Benzene–EtOAc (4:1); D. Benzene–$CHCl_3$ (1:3).

Components were made visible by spraying with *p*-dimethylaminobenzaldehyde in HCl soln (Ehrlich reagent) or by charring with 2N H_2SO_4.

The 33 compounds described in this paper were prepared utilizing a total of 11 different methods,[2,10–14] of which only the last two are newly reported. Physical properties and analytical data for compounds I–XXXII are recorded in Tables 9 to 14. The preparation (Method 2) and properties of XXXIII can be found in reference 3.

Method 1. Aldose (10·0 mmole) and *p*-nitroaniline (13·0 mmole) were heated under reflux in a solvent mixture of MeOH–H_2O (8:1 v/v, 4 ml) and glacial HOAc (2 ml).[10] The products were dried and then acetylated to give the products listed in Table 9.

Method 2. Aldose and amine (in slight molar excess) were heated under reflux in MeOH containing a trace of HCl.[11] The products from these reactions were dried and acetylated to give the relevant compounds in Tables 9, 10, 12 and 14.

Method 3. Penta-O-acetyl-β-D-glucopyranose (5 mmole), indoline (17 mmole) and HOAc (2 ml) in EtOH (40 ml) were stored at room temp overnight[13] and the crystalline product was filtered off and recrystallized (Table 10).

Method 4. Glucose (10 mmole) and indoline (10 mmole) in water (0·2 ml) were stirred on a boiling water bath until soln was complete.[13] The solvent was removed *in vacuo*, and the product was acetylated to give compound VIII (Table 10).

Method 5. Compound VIII (Table 10) was prepared by the reaction of 3,4,6-tri-O-acetyl-α-D-glucopyranose 1,2-(ethyl orthoacetate) (0·4 mmole) with indoline (0·4 mmole) in EtOH (2 ml).[2]

Method 6. Peracetylated aldopyranose (5 mmole) in hot EtOH (36 ml) was treated with indoline (10 mmole) and HOAc (1·8 ml).[14] The mixture was stirred until reaction was complete, and the product was isolated by crystallization after reducing the solvent volume (Table 10).

Method 7. β-D-Glucopyranosylindoline was dehydrogenated by heating under reflux with chloranil in *m*-xylene[2,12] to give compound XVI (Table 11).

TABLE 9. PHYSICAL PROPERTIES OF ACETYLATED N-*p*-NITROPHENYLGLYCOPYRANOSYLAMINES

Compound	Method of prep.	Yield %	m.p.	$[\alpha]_D$($CHCl_3$)	Crystals	Found % C	H	N	Calculated % C	H	N	Formula
I	1	55	156–157°*	−94° (*c*2·2)*	pale yellow needles	51·2	5·1	5·8	51·3	5·3	6·0	$C_{20}H_{24}N_2O_{11}$
	2	47										
β-D-gluco	(lit) 10		182–183°	−101°								
	11		180°									
	15		155°	−101°								
II	1	46	98–100°	−68° (*c*1·1)*	yellow amorphous powder	51·1	5·1	5·8	51·3	5·3	6·0	$C_{20}H_{24}N_2O_{11}$
	2	39										
β-D-galacto	(lit) 10		98°	−72° (*c*1·0)								
	15			−73°								
III	1	38	189–190°*	−150° (*c*2·0)*	pale yellow needles	51·1	5·1	5·9	51·3	5·3	6·0	$C_{20}H_{24}N_2O_{11}$
	2	42										
D-manno	(lit) 10		210–211°	−153°								
	15		184°	−150°								

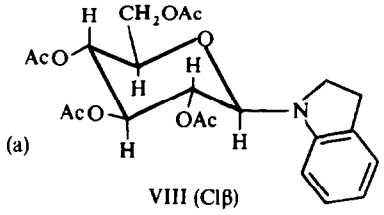
TABLE 9—*Continued*

IV	2	32	211–212°	+149° (*c*1·1)[a]	bright yellow needles	52·4	5·3	6·8	52·7	5·4	6·8	$C_{18}H_{22}N_2O_9$
L-rhamno	(lit) 15		209°	+123°								
V	1 2 10	46 36 41	214–215°[a]	−31° (*c*2·0)	pale yellow needles	51·3	5·1	7·1	51·5	5·1	7·1	$C_{17}H_{20}N_2O_9$
β-D-xylo	(lit) 10		212–213°	−40°								
VI D-lyxo	2	12	209–210°	−126° (*c*1·5)[a]	yellow amorphous powder							
VII	1 2	23 34	178–179°	+9° (*c*3·0)[a]	yellow platelets	51·8	5·1	7·2	51·5	5·1	7·1	$C_{17}H_{20}N_2O_9$
α-L-arabino	(lit) 10		177–178°	+5°								

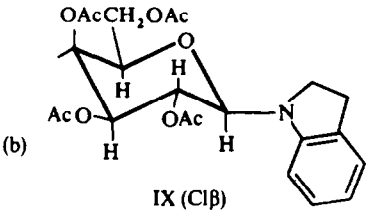
[a] Measured after 3 min.

TLC: solvent system A.

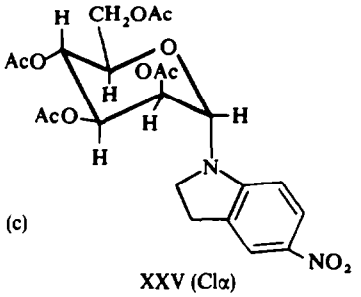
[b] M.p.'s not depressed by samples generously provided by Dr. R. D. Guthrie, X-ray diffraction patterns of each pair were similar, but not identical.



(a) VIII (Clβ)

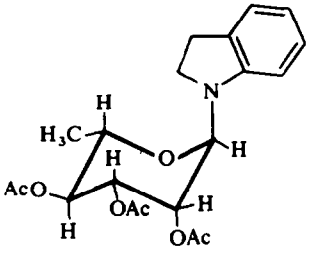


(b) IX (Clβ)



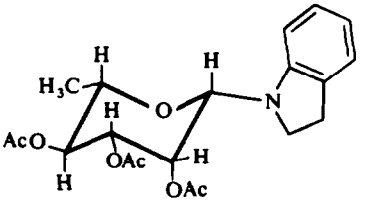
(c) XXV (Clα)

7

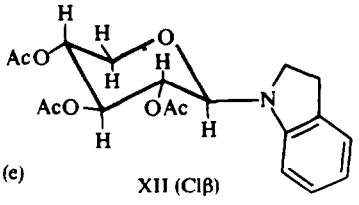


XI (ICα)

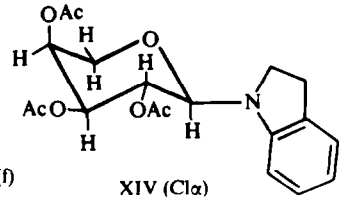
(d)



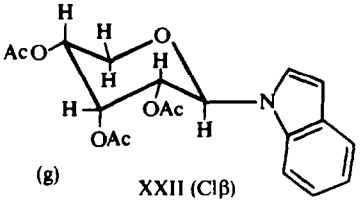
XI (ICβ)



(e) XII (Clβ)



(f) XIV (Clα)



(g) XXII (Clβ)

FIG 1. Conformations and anomeric configurations of acetylated glycopyranosylamine derivatives in solution

TABLE 10. PHYSICAL PROPERTIES OF ACETYLATED GLYCOPYRANOSYLINDOLINES

Compound	Method of prep.	Yield %	m.p.	$[\alpha]_D$($CHCl_3$)	Crystals	Found % C	H	N	Calculated % C	H	N	Formula
VIII	3 4 5 (Ref. 2)	74 27 7	119–120°	+8° (*c*2·1)	white needles	58·8	6·2	3·2	58·8	6·1	3·1	$C_{22}H_{27}NO_9$
β-D-gluco	(lit) 13		117·8–118·5°	+11° (*c*6)								
IX	6 2	58 11	109–110°	+27° (*c*7·6)	white needles	57·3	6·2	2·9	58·8	6·1	3·1	$C_{22}H_{27}NO_9$
β-D-galacto	(lit) 16		108·5–109·5°	+20° (*c*5)								
X[a] D-manno	6	26	130–131°	−58° (*c*2·4)	white plates	58·4	5·9	3·2	58·8	6·1	3·1	$C_{22}H_{27}NO_9$
XI[a] L-rhamno	6	33	164–165°	−34° (*c*8·0)	white plates	61·1	6·4	3·6	61·4	6·4	3·6	$C_{20}H_{25}NO_7$
XII β-D-xylo	10 11	25 38	108–109°	+47° (*c*4·2)	white needles	60·4	6·0	3·9	60·5	6·2	3·8	$C_{19}H_{23}NO_7$
XIII D-lyxo	10	41	147–148°	−104° (*c*4·0)	white needles	60·4	5·9	3·9	60·5	6·2	3·8	$C_{19}H_{23}NO_7$
XIV α-L-arabino	6	42	121–122°	+112° (*c*5·8)	white needles	60·5	6·1	3·5	60·5	6·2	3·8	$C_{19}H_{23}NO_7$
XV	6	59	150–151°	+76° (*c*4·5)	white needles	60·2	6·3	3·5	60·5	6·2	3·8	$C_{19}H_{23}NO_7$
β-D-ribo	(lit) 14 17		151–153° 147–148°	+76° (*c*1) +69° (*c*5)								

[a] obtained as a mixture of anomers.
TLC: solvent systems A, B and C.

TABLE 11. PHYSICAL PROPERTIES OF ACETYLATED GLYCOPYRANOSYLINDOLES

Compound	Method of prep.	Yield %	m.p	$[\alpha]_D$($CHCl_3$)	Crystals	Found % C	H	N	Calculated % C	H	N	Formula
XVI	7, 8 (Ref. 2)	25, 78	134–135°	+2° (*c*2·2)	white needles	58·8	5·7	3·2	59·1	5·6	3·1	$C_{22}H_{25}NO_9$
β-D-gluco	(lit) 13		148·5–149°	+2° (*c*5·5)								
XVII	8	48	128–129°	+9° (*c*3·9)	white needles	59·2	5·7	3·1	59·1	5·6	3·1	$C_{22}H_{25}NO_9$
β-D-galacto	(lit) 16		123–125°	+12° (*c*4)								
XVIII L-rhamno	8	32	117–118°	+45° (*c*1·8)	white plates	61·8	6·0	3·5	61·7	6·0	3·6	$C_{20}H_{23}NO_7$
XIX β-D-xylo	8	70	152·0–152·5°	+15° (*c*3·9)	white needles	60·7	5·8	3·7	60·8	5·6	3·7	$C_{19}H_{21}NO_7$
XX D-lyxo	8		syrup									
XXI α-L-arabino	8	40	136·5–137·0°	+54° (*c*3·9)	white platelets	60·6	5·7	3·8	60·8	5·6	3·7	$C_{19}H_{21}NO_7$
XXII	8	42	173–174°	+41° (*c*4·6)	white plates	59·8	5·5	3·6	60·8	5·6	3·7	$C_{19}H_{21}NO_7$
β-D-ribo	(lit) 14 17		169–171° 165–166°	+40° (*c*1) +37° (*c*3·5)								

TLC: solvent systems A and C.

TABLE 12. PHYSICAL PROPERTIES OF ACETYLATED GLYCOPYRANOSYL-5-NITROINDOLINES

Compound	Method of prep.	Yield %	m.p.	$[\alpha]_D(CHCl_3)$	Crystals	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Formula
XXIII β-D-gluco	9 (Ref. 2) 2	38 43	162–163° (*d*)	+30° (*c*0·4)	yellow needles	52·6	5·2	4·9	53·4	5·3	5·7	$C_{22}H_{26}N_2O_{11}$
XXIV β-D-galacto	2	78	162·5–163·5°	+67° (*c*4·3)	yellow plates	53·3	5·3	5·6	53·4	5·3	5·7	$C_{22}H_{26}N_2O_{11}$
XXV D-manno	2	23	219–220°	−56° (*c*2·3)	yellow needles	53·5	5·4	5·8	53·4	5·3	5·7	$C_{22}H_{26}N_2O_{11}$
XXVI L-rhamno	9	34	145–147°	+29° (*c*4·3)	yellow plates	54·5	5·3	6·8	55·0	5·5	6·4	$C_{20}H_{24}N_2O_9$
XXVII β-D-xylo	2	39	188–189°	+126° (*c*2·0)	yellow rods	54·0	5·1	6·4	54·0	5·3	6·6	$C_{19}H_{22}N_2O_9$
XXVIII α-L-arabino	2	50	152–154°	+150° (*c*2·0)	yellow needles	53·9	5·2	6·5	54·0	5·3	6·6	$C_{19}H_{22}N_2O_9$

d decomposition point.
TLC: solvent systems A and B.

TABLE 13. PHYSICAL PROPERTIES OF ACETYLATED GLYCOPYRANOSYL-5-NITROINDOLES

Compound	Method of prep.	Yield %	m.p.	$[\alpha]_D(CHCl_3)$	Crystals	Found % C	H	N	Calculated % C	H	N	Formula
XXIX β-D-gluco	8 (Ref. 3)	8	195–197°	+7° (c2·0)	yellow needles	53·9	4·9	5·5	53·7	4·9	5·7	$C_{22}H_{24}N_2O_{11}$
XXX L-rhamno	8	24	194–195°	−13° (c2·8)	yellow plates	55·3	5·2	6·6	55·3	5·1	6·5	$C_{20}H_{22}N_2O_9$

TLC: solvent systems A and B.

TABLE 14. PHYSICAL PROPERTIES OF ACETYLATED GLYCOPYRANOSYL-1,2,3,4-TETRAHYDROQUINOLINES

Compound	Method of prep.	Yield %	m.p.	$[\alpha]_D(CHCl_3)$	Crystals	Found % C	H	N	Calculated % C	H	N	Formula
XXXI β-D-gluco	2 (Ref. 3)	43	133–135°	+70° (c4·4)	white needles	59·7	6·5	3·0	59·7	6·3	3·0	$C_{23}H_{29}NO_9$
XXXII β-D-xylo	2	41	121–122°	+102° (c3·2)	white needles	60·6	6·4	3·5	61·4	6·4	3·6	$C_{20}H_{25}NO_7$

TLC: solvent systems B and D.

Method 8. The peracetylated glycopyranosylindoline derivatives (5 mmole) were heated under reflux with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (5 mmole) in *m*-xylene.[2,14] The peracetylated glycopyranosylindole derivatives were isolated when the solvent volume was reduced, and recrystallized from EtOH (Tables 11, 13).

Method 9. Aldose (15 mmole) and 5-nitroindoline (15 mmole) in water (1 ml) was stirred at 100° for 1 hr after soln was complete.[2] The products were isolated, dried, and then acetylated to give the compounds listed in Table 12.

Method 10. Peracetylated pentose (1·3 mmole) and amine (4·2 mmole) were dissolved in a mixture of abs EtOH and HOAc (*ca* 20:1 v/v) with slight warming. The mixture was left at room temp overnight, and the product obtained on removal of solvent was recrystallized from EtOH (Tables 9, 10).

Method 11. Tetra-O-acetyl-β-D-xylopyranose (5·03 g, 15·7 mmole) was dissolved in EtOH (88 ml) and treated with freshly distilled indoline (3·52 g, 29·6 mmole) and HOAc (4·5 ml). The soln was stirred at room temp for 2 days and then concentrated *in vacuo* to 10 ml. A seed crystal of XII was introduced and the product that separated was recrystallized from EtOH (Table 10).

The synthesis of 1-(2,3,4,6-tetra-O-acetyl-D-mannopyranosyl)-indole could not be achieved. Dehydrogenation of the peracetylated glycopyranosyl-5-nitroindoline derivatives to the corresponding peracetylated glycopyranosyl-5-nitroindole derivatives proceeded with difficulty; only the D-glucosyl and L-rhamnosyl derivatives were isolated.

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