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N.M.R. STUDIES OF D-RIBOSYLAMINES IN SOLUTION: DERIVATIVES OF HYDROXYLAMINE, HYDRAZINE, THIOSEMICARBAZIDE, AND SECONDARY AMINES*

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ABSTRACT

N.m.r. spectroscopic studies (^1H, ^{13}C) have shown that hydroxylamine and hydrazine react with 2,3-*O*-isopropylidene-D-ribofuranose (**1**) and D-ribose (**2**) to give primarily the acyclic oxime and hydrazone, respectively, whereas thiosemicarbazide affords mainly the cyclic pyranosyl and furanosyl derivatives. Acyclic or cyclic secondary amines, when condensed with either **1** or **2**, furnished only mixtures of the β-pyranosyl and β-furansyl forms, and, in some reactions, Amadori rearrangement products (2–30%).

INTRODUCTION

In continuing our study[1] of the structures of the products obtained from the reaction of 2,3-*O*-isopropylidene-D-ribofuranose (**1**) and D-ribose (**2**) with amines by ^{13}C- and ^1H-n.m.r. spectroscopy, we now report on the reactions of **1** and **2** with hydroxylamine, hydrazine, thiosemicarbazide, and some secondary amines. The first three reagents have been used widely for the characteristion of sugars. The terms αP, βP, αF, and βF connote α-pyranosyl, β-pyranosyl, α-furanosyl, and β-furanosyl structures, respectively, and A connotes Amadori rearrangement products. N.m.r. spectroscopy was conducted on solutions of the products in pyridine-d_5 or Me_2SO-d_6. These solvents are known to influence the equilibrium between the different isomers and their conformers by way of complex formation[2] and suppression of intramolecular hydrogen-bonding[3].

RESULTS AND DISCUSSION

Hydroxylamine (**3**), hydrazine (**4**), methylhydrazine (**5**), thiosemicarbazide (**6**), and 4-phenylthiosemicarbazide (**7**) were reacted severally with 2,3-*O*-iso-

*Part II. For Part I, see ref. 1.

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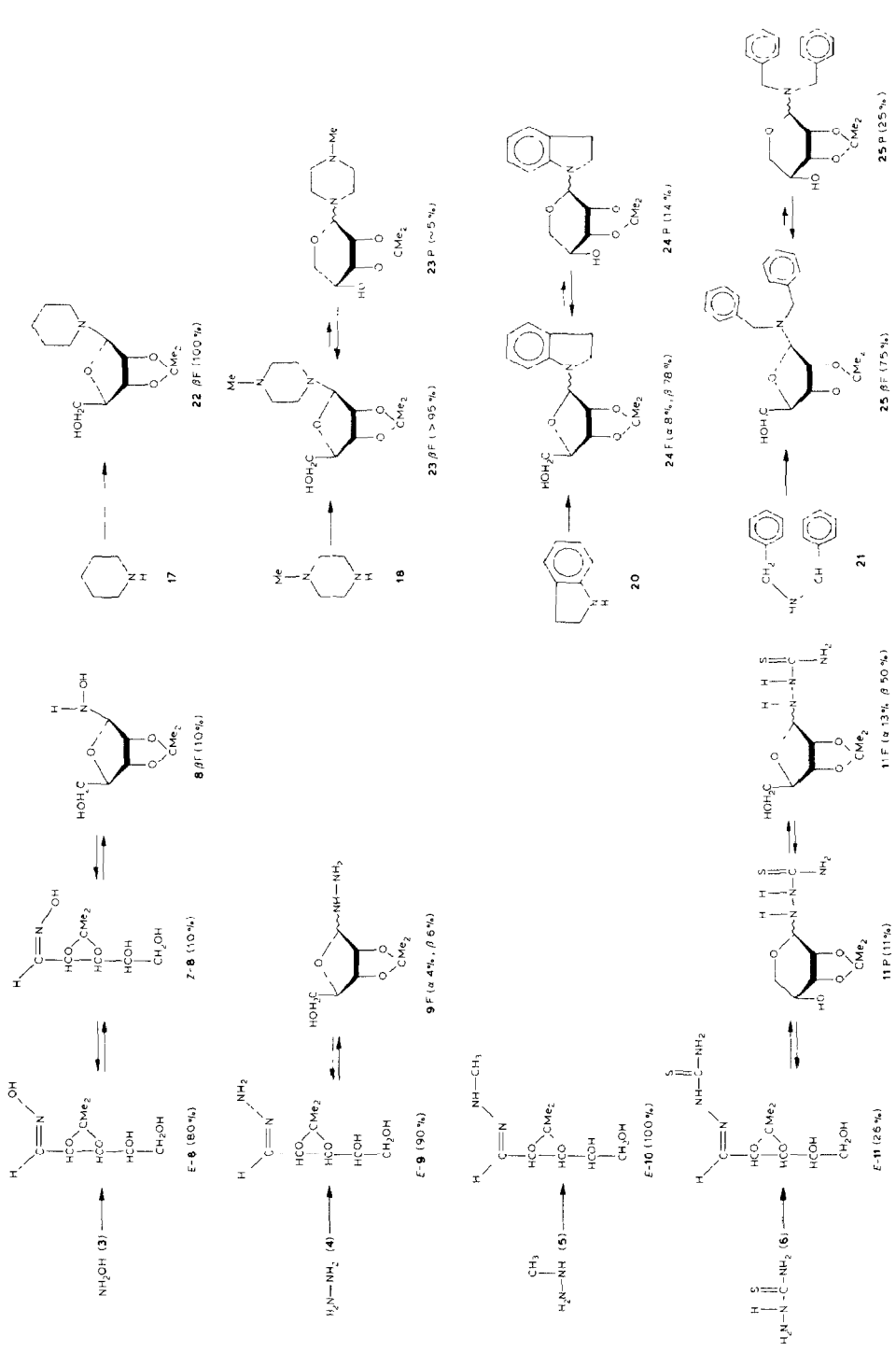


Scheme 1. Products of reaction of 2,3-*O*-isopropylidene-D-ribose with amino compounds **3–6**, **17**, **18**, **20**, and **21**.

propylidene-D-ribofuranose (**1**) and D-ribose (**2**) in anhydrous methanol. Compounds **5** and **7** were used to ensure that no reaction occurred simultaneously on the two amino terminal groups of hydrazine and thiosemicarbazide[4]. The n.m.r. spectra of the products derived from **1** were of great value in determining the proportions and structures of the products obtained from **2**.

The ^{13}C-n.m.r. spectrum of the condensation products of hydroxylamine with **1** (Table I) revealed three compounds (Scheme 1), namely, the acyclic forms *E*-**8** and *Z*-**8** and the β-furanosyl form **8**βF. The configuration of **8**βF was indicated by the $\Delta\delta CH_3$ value of >1.50 p.p.m. From the ^{1}H-n.m.r. data (Table II), *E*-**8** and *Z*-**8** are easily identified as the *syn* (80%) and *anti* (10%) isomers. Previous studies[5,6] showed that, in aldoximes, the hydrogen atom on the trigonal carbon is more deshielded when it is *syn* to the oxime OH. Thus, H-2 of *Z*-**8** is deshielded by 0.64 p.p.m. compared to H-2 of *E*-**8** because of intramolecular hydrogen-bonding.

Reaction of **1** with hydrazine afforded 90% of *E*-**9**, the acyclic structure of which was based on the chemical shift of the signal for H-2 in comparison with that of *E*-**8** (Table II). Also, 10% of a mixture of the furanosyl derivatives **9**βF and **9**αF was detected, and their configurations were assigned on the basis of the $\Delta\delta CH_3$ rule[1]. The reaction of *N*-methylhydrazine with **1** (Scheme 1) gave only the acyclic derivative *E*-**10**.

It was necessary to condense thiosemicarbazide (**6**) with **1** in hot methanol, because reaction was very slow at room temperature. The ^{13}C-n.m.r. spectrum of

TABLE I

^{13}C-N M.R. DATA[a] FOR THE PRODUCTS OF REACTION OF 2,3-*O*-ISOPROPYLIDENE-D-RIBOSE WITH VARIOUS AMINES

Compound		*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*O* \ *C* / *O*	*C-Me*	*ΔδC-Me*	C_{base}
	Z	147.56	77.70	70.40	68.94	63.24	108.14	25.00, 27.33	2.33	
8	*E*	146.70	76.97	75.06	69.67	63.47	108.37	25.32, 27.70	2.38	
	βF	96.05	86.88	83.27	81.72	62.05	111.42	25.00, 26.74	1.74	
	E	137.77	77.54	77.00	69.54	63.40	107.53	27.75, 25.31	2.45	
9	βF	94.12	84.15	82.10	81.39	62.01	111.56	26.58, 24.92	1.66	
	αF	90.52	81.00	80.66	78.52	64.12	110.77	25.75, 24.65	1.10	
10	*E*	131.31	78.15	77.37	69.86	63.67	107.60	25.44, 27.90	2.46	33.50 CH_3
	E	142.84	77.15	76.86	69.40	63.35	108.51	27.70, 25.26	2.44	177.96 C=S
11	βF	95.73	85.35	82.37	81.05	61.99	111.58	26.68, 24.87	1.81	181.37
	αF	91.00	81.59	81.35	79.10	63.35	110.74	24.48, 25.90	1.42	n.d.[b]
	P	88.90		74.95	73.01	64.82	108.95	27.20, 25.90	1.30	n.d.

[a]Chemical shifts in p.p.m. for solutions in Me_2SO-d_6 (internal Me_4Si). [b]Not determined.

TABLE II

^{1}H-N.M.R. DATA[a] FOR THE PRODUCTS OF REACTION OF 2,3-*O*-ISOPROPYLIDENE-D-RIBOSE WITH VARIOUS AMINES

Compound	*H-1* ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3,H-4,H-5,5'* ($J_{3,4}$)			*Me*	*=N-OH N-Me*
Z-**8**	6.83(d) (6)	5.24(t) (6)			3.10	1.28	11.07(m) ($W_{1/2}$ 10)
E-**8**	7.33(d) (8.5)	4.60(q) (4)	4.08(t) (4)		3.60	1.38	10.13(m) ($W_{1/2}$ 4)
E-**9**	7.03(d) (7.5)	4.50 (6)	4.12		3.23	1.27 1.37	
E-**10**	6.67(d) (7)	4.57(q) (6)	3.97(t) (6)	3.77	3.12	1.27 1.37	CH_3 2.62(d) (*J* 5 Hz)
E-**11**	7.43(d) (7.5)	4.63(q) (6)	4.50		3.22	1.26 1.40	

[a]Chemical shifts in p.p.m., *J* in Hz for solutions in Me_2SO-d_6 (internal Me_4Si).

the product mixture revealed one acyclic derivative (*E*-**11**, 26%) together with three cyclic structures, namely, **11**P, **11**αF, and **11**βF. Compounds **11**αF and **11**βF together were the major products (63%), with the latter preponderating. The product **11**P (11%) showed signals for C-1 and C-5 which were typical of a pyranoid form[1]. In support of this assignment, the signal of the ternary carbon of the CMe_2 group appeared at 108.95 p.p.m., as expected[7,8] since an acetal carbon in a five-membered cyclic acetal fused to a furanoid ring is deshielded more than when the fusion involves a pyranoid ring (*cf.* **11**αF or **11**βF with **11**P in Table I).

Attention was then turned to the reactions of D-ribose (**2**). The products of condensation (Scheme 2) of **2** severally with **3**–**5** were shown by ^{13}C-n.m.r. spectroscopy to be the acyclic structures *Z*-**12**, *E*-**13**, and *E*-**14**, respectively (Table III). The chemical shifts (Table IV) of the signal of the proton on the trigonal carbon of the oximes showed that *Z*-**12** was formed initially and that slow isomerisation to the more stable *E*-**12** occurred. The chemical shifts of the signals for H-2 of *Z*-**12** and *E*-**12** were well differentiated because of the intramolecular hydrogen-bonding in the *Z* isomer. This characteristic allowed the products derived from **1** and hydrazine and *N*-methylhydrazine to be identified as *E*-**13** and *E*-**14**, respectively.

The reaction of **2** with thiosemicarbazide (**6**) is not as straightforward as those of the reagents **3**–**5**. The ^{13}C-n.m.r. spectrum of the product exhibited signals for four distinct structures and was similar to that for the product of reaction of **2** and **7**. The reaction of **6** occurs only at the hydrazine moiety of the molecule. Compari-

son of the chemical shift of the signal for H-2 of *E*-**15** with that of the corresponding protons of *E*-**12**, *E*-**13**, and *E*-**14** allowed the acyclic structure to be assigned to the thiosemicarbazone *E*-**15**. The three other structures are acyclic and exist mainly as a mixture of furanoid (**15**βF) and pyranoid forms (**15**αP and **15**βP), of which **15**βP preponderated. Furthermore, the ^{1}H- and ^{13}C-n.m.r. data revealed the conformation of **15**βP to be $^4C_1$ (δH-1′ 4.86, $J_{1,2}$ 9 Hz) and that of **15**αP to be $^1C_4$ (δH-1′ 4.60, $W_{1/2}$ 4 Hz). The structure of **15**βF was assigned on the basis of analogy of its ^{13}C-n.m.r. spectrum with that of **11**βF.

Unlike those of hydroxylamine and the hydrazides, the reaction of D-ribose with thiosemicarbazide gave a product mixture which contained a large proportion of cyclic structures. One possible explanation for this result may be the difference in the reaction conditions employed. This difference was also observed with **1** (Scheme 1). When a solution of **11** (Me_2SO-d_6) was stored for one month, the equilibrium changed. The new spectrum reflected a large percentage (85%) of acyclic product (*E*-**11**), but no pyranoid (**11**βP) or α-furanoid (**11**αF) forms.

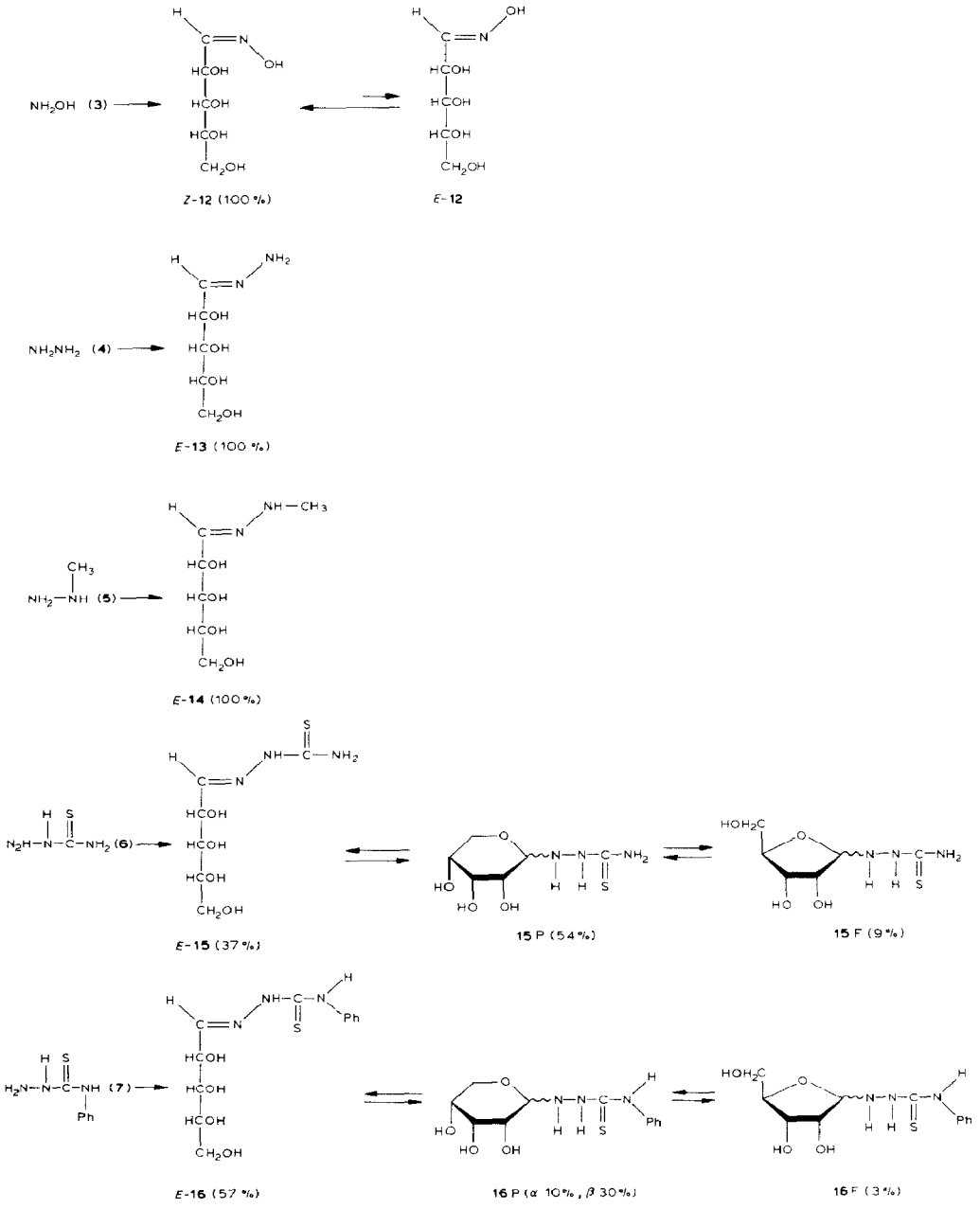
A similar set of reactions was performed with 2,3-*O*-isopropylidene-D-ribofuranose (Scheme 1) and D-ribose (Scheme 2) with piperidine (**17**), *N*-methylpiperazine (**18**), morpholine (**19**), indoline (**20**), and dibenzylamine (**21**). The ^{13}C-n.m.r. spectra (Table V) obtained for the products of the reaction of **1** with these amines show that the β-furanosylamine is always the major component ($\Delta\delta CH_3$ >1.50 p.p.m.) and, for piperidine, it was the only product. For indoline (**20**), a small proportion of the α-furanosylamine (**24**αF) was detected; in addition, for

TABLE III

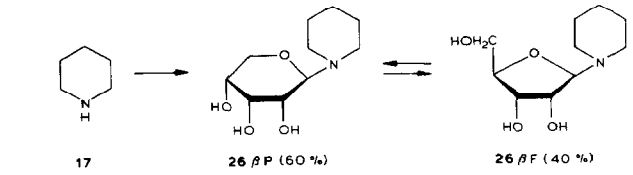
^{13}C-N.M.R DATA[a] FOR THE PRODUCTS OF REACTION OF D-RIBOSE WITH VARIOUS AMINES

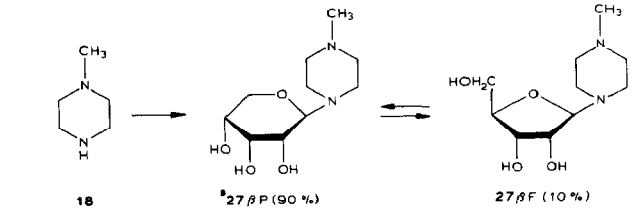
Compound		*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	C_{base}	
12	*Z*	151.81	73.46	71.41	65.52	63.29		
	E	150.48	74.10	71.96	69.90	63.15		
13	*E*	143.10	74.23	72.09	71.73	63.08		
14	*E*	136.27	74.23	72.08	72.08	63.06	CH_3 33.65	
								C=S
15	*E*	146.79	74.18	71.74	71.00	62.96		177.61
	βP	87.10	68.03	66.81	70.03	63.69		181.32
	αP	87.10	68.96	67.50	69.64	62.52		182.84
	βF	93.93	n.d.[b]	n.d.	83.10	61.18		n.d.
16	*E*	147.56	74.52	72.17	71.18	63.20		Ph 176.04
	βP	87.53	68.12	66.93	70.47	64.07		Ph 179.98
	αP	87.20	69.50	67.57	70.20	62.33		Ph 179.65
	βF	94.67	n.d.	n.d.	84.11	61.86		Ph 180.01

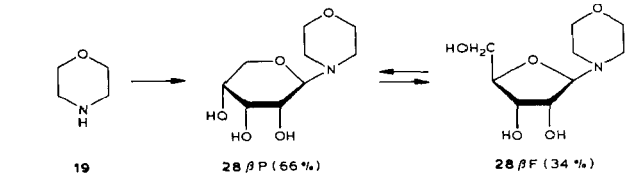
[a]Chemical shifts in p.p.m. for solutions in Me_2SO-d_6 (internal Me_4Si). [b]Not determined.

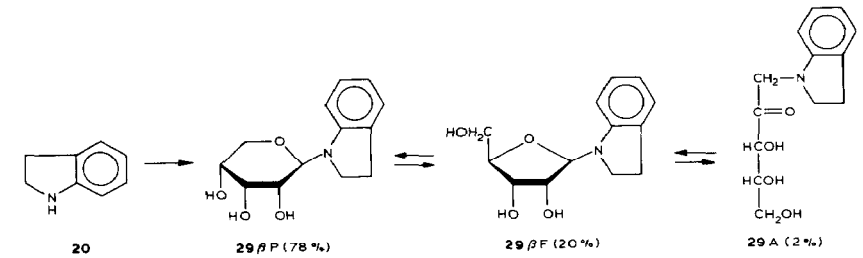


Scheme 2. Reaction of D-ribose with amino compounds **3–7** and **17–21**.


17
26 βP (60 %)
26 βF (40 %)


18
27 βP (90 %)
27 βF (10 %)


19
28 βP (66 %)
28 βF (34 %)


20
29 βP (78 %)
29 βF (20 %)
29 A (2 %)

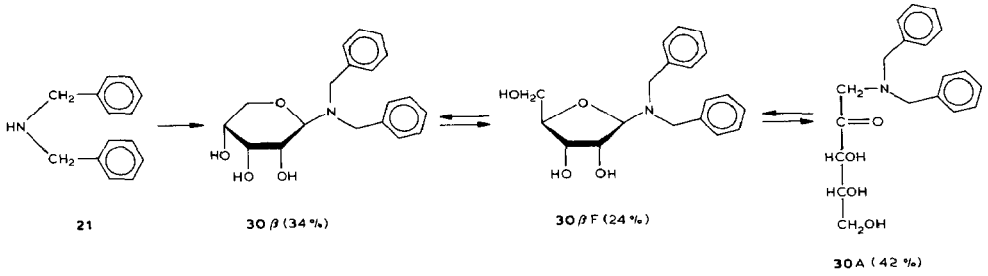

21
30 β (34 %)
30 βF (24 %)
30 A (42 %)

TABLE IV

^{1}H-N M R DATA[a] FOR THE PRODUCTS OF REACTION OF D-RIBOSE WITH VARIOUS AMINES

Compound	*H-1* ($J_{1,2}$)	*H-2* ($J_{2,3}$)	*H-3*	*H-5,5'*	*=N-OH or NHMe*	
12	6.66(d) (6)	4.83(q) (2.5)	3.74	3.20	10.72(m)	
	7.22(d) (7.5)	4.13 (3)	3.67	3.07	10.48(s)	
E-**13**	6.95(d) (6.5)	4.10 (4)	3.77	3.22		
E-**14**	6.68(d) (6)	4.17(q) (4)	3.70	3.10	NH 6.50(q) (*J* 4 Hz)	CH_3 2.62(d) (*J* 4 Hz)
E-**15**	7.43(d) (5)	4 20(q)	4.10	3.10	NH 11.1	

[a]Chemical shifts in p.p.m. and *J* in Hz for solutions in Me_2SO-d_6 (internal Me_4Si).

N-methylpiperazine (**18**), indoline (**20**), and dibenzylamine (**21**), the pyranosyl derivative was formed. The signal of the anomeric proton appeared clearly as a doublet at δ 4.58 ($J_{1,2}$ 10 Hz) only in the spectrum of the products formed from dibenzylamine (**21**), thus establishing the β configuration of these unusual structures. The amount of the β-pyranosyl derivative increased with the bulk of the amine, and the structure was assigned in a manner similar to that for **11P**. Similar products were observed when **1** was treated with pyrrole at reflux temperature[9].

Only two products resulted from the condensations of D-ribose and the amines **17–19**, as indicated by their ^{13}C-n.m.r. spectra (Table VI). Indoline (**20**) and dibenzylamine (**21**), however, produced a third compound (**29**A and **30**A, respectively), which was identified as an acyclic Amadori-rearrangement product. The chemical shifts of the signals for C-2 of these products appeared near 210 p.p.m., indicative[10] of an sp^2 carbon (C=O). The Amadori rearrangement is occasionally accomplished in the absence of an acid catalyst; thus, dibenzylamine reacted with D-glucose to afford, *inter alia*, 1-deoxy-1-dibenzylamino-D-fructose[11,12].

The two structures that are common to all five ribosylamines derived from the amines **17–21** gave signals for anomeric carbons in their ^{13}C-n.m.r. spectra which indicated that they were not anomers. Proof of the β configuration of the pyranoid structure was provided by the chemical shift of the signal for the anomeric carbon and by the $J_{1,2}$ value of 9 Hz (Table VI) which also implies a $^4C_1$ conformation. The furanoid structure was assigned by comparison of the chemical shift of the signal for C-1 with that of the corresponding carbon atom in the isopropylidene derivative. When 5-*O*-trityl-D-ribose was condensed with indoline (**20**), 5'-*O*-trityl-

TABLE V

^{13}C-N M.R DATA[a] FOR THE PRODUCTS OF REACTION OF 2,3-*O*-ISOPROPYLIDENE-D-RIBOSE WITH VARIOUS SECONDARY AMINES

Compound		*C-1*	*ΔδC-1*	*C-2*	*C-3*	*C-4*	*C-5*	*O* \ *C* / *O*	*C-Me*	*ΔδC-Me*	C_{base}		
											C-1,C-5	*C-2,C-4*	*C-3*
22	βF	100.68		81.56	80.83	84.20	62.05	112.10	25.03, 26.90	1.87	48.79	25.40	24.12
											CH_3	*C-1,C-5*	*C-2,C-4*
	βF	100.28		81.49	81.04	84.59	61.91	112.11	24.96, 26.83	1.87	47.59	45.63	54.53
23			5.1										
	P	95.16		93.18	75.83	71.62	64.93	108.54	26.19, 28.25	2.06	49.07	47.33	55.01
											C-1	*C-2*	*Ph*
		87.54		81.49	81.15	n.d.[b]	61.60	111.58	25.86, 24.38	1.48	46.36	28.15	118.81, 129.23, 151.18
	αF		3.95										
													108.46, 118.61, 124.41
24	βF	91.59		82.76	80.61	80.13	61.45	113.14	27.21, 25.26	1.95	45.84	27.60	
													126.85, 130.01, 150.06
			7.37										
													107.73, 116.75, 124.07
	P	84.22		n.d.	75.69	72.32	64.71	109.00	28.29, 26.19	2.10	46.96	29.27	
													128.80, 152.45
											C-1	*Ph*	
	βF	95.93		82.47	81.54	80.03	61.79	112.51	27.11, 25.26	1.74	52.18	140.74, 128.02, 126.41	
25			7.6										
	P	88.32		n.d.	75.93	72.57	64.86	108.56	27.50, 26.38	1.12	52.77	139.14, 127.87, 126.75	

[a]Chemical shifts in p.p.m. for solutions in Me_2SO-d_6 (internal Me_4Si). [b]Not determined.

TABLE VI

^{13}C- AND ^{1}H-N M R. DATA[a,b] FOR THE PRODUCTS OF REACTION OF D-RIBOSE WITH SECONDARY AMINES

Compound		*C-1*	*ΔδC-1*	*C-2*	*C-3*	*C-4*	*C-5*	C_{base}		
								C-1,C-5	*C-2,C-4*	*C-3*
	βP	91.35		67.27	66.31	71.09	64.93	48.24	25.90	24.58
26			9.19							
	βF	100.54		70.41	70.27	81.93	62.08	48.47	25.76	24.35
										CH_3
	βP	90.48		67.26	66.39	71.13	64.61	55.07	45.90	46.68
27			9.08							
	βF	99.56		70.50	70.36	82.22	62.10	55.07	47.09	48.59
	βP	90.76		67.30	66.18	71.18	64.45	66.57	47.54	
28			8.94							
	βF	99.70		70.50	70.22	82.36	62.10	66.48	47.91	
								C-1	*C-2*	*Ph*
	A	54.82		207.64	76.68	73.64	63.12			107.34, 107.73, 117.68 117.75, 124.26, 126.80, 129.67, 150.65
29	βP	81.49		67.84	67.11	71.30	64.18	44.92	27.55	
			7.95							
	βF	89.44		70.91	70.32	82.56	61.84			
								C-1	*Ph*	
	A	59.15		211.72	76.52	73.34	61.90	52.04	139.39, 128.22, 122.89	
30	βP	87.18		67.04	67.04	71.39	64.28	52.67	140.30, 128.87, 127.06	
			9.16							
	βF	96.34		70.76	70.20	82.05	61.90	51.41	139.30	

[a]Chemical shifts in p.p.m. for solutions in Me_2SO-d_6 (internal Me_4Si). [b]Chemical shifts for H-1 doublets (δ) and $J_{1,2}$ values (Hz): **26**, P 3.93 (9), F 4.24 (4); **27**, P 3.96 (9), F 4.23 (4); **28**, P 3.96 (9), F 4.24 (4.5); **29**, P 4.90 (9), F 5.27 (5); **30**, P, 3.90 (9), F 4.03 (5).

β-D-ribofuranosylindoline was obtained as the sole product[13]. The chemical shift of the signal for C-1 of this derivative (see Experimental) is in complete agreement with that found for **29F**.

None of the above furanoid structures originated by cyclisation of the Amadori rearrangement product, since the partially decoupled ^{13}C-n.m.r. spectrum of **26P** + **26F**, for example, indicated the absence of quaternary carbon in the sugar moiety.

Glycosylamines continue to receive attention in connection with their synthesis, biological properties, and elucidation of structure[14–17]. Some general comments can now be made on the reaction of ribose with amines, based on the data reported here and in the previous paper[1].

For ribosylamines formed from primary amines, pyranoid derivatives usually preponderate over their furanoid counterparts in solution. Furthermore, the β-pyranosylamines adopt mainly the $^4C_1$ conformation, whereas the α anomers adopt

mainly the $^1C_4$ conformation regardless of the nucleophilic properties of the amino group and the bulk of the substituents attached thereto, and this effect is not restricted to the phenylamino group[18].

In Me_2SO-d_6, D-ribose oxime and hydrazone exist as acyclic structures, and there is no equilibrium involving cyclic derivatives as has been postulated, for example, for the hydrazino derivative[19]. On the other hand, the ribosylthiosemicarbazyl compound appears to be similar to ribosylamine and to the oxime or hydrazone, in that both cyclic and acyclic structures are present, but this conclusion must be taken as tentative because of the experimental conditions necessary to ensure a complete reaction; the relatively high reaction temperature may favour the formation of cyclic structures.

Secondary amines react with D-ribose to give a mixture of β-pyranosyl and β-furanosyl derivatives, with the former preponderating. No explanation can be given at present to account either for the absence of any α anomer or for the presence of the Amadori-rearrangement product in the special cases of dibenzylamine[12] (42%) and indoline (2%).

The condensations between secondary amines (except for piperidine) and 2,3-*O*-isopropylidene-D-ribofuranose, conducted at reflux temperature in order to accelerate the reaction, gave partly the β-D-ribopyranosylamine derivatives. These compounds, although they are usually unexpected because of ring strain[20], seem to be thermodynamically favoured.

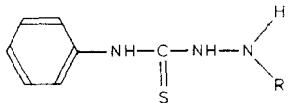
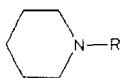
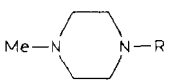
EXPERIMENTAL

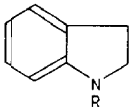
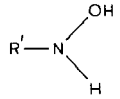
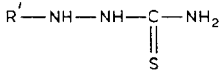
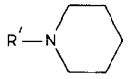
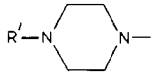
General methods. — Melting points were determined with a Gallenkamp apparatus and are uncorrected. T.l.c. was performed on silica gel F-254 (Merck) with detection by u.v. light and charring with sulphuric acid. Column chromatography was performed with silica gel (70–230 mesh, ASTM Merck). Optical rotations were determined with a Perkin–Elmer 241 M.C. polarimeter, and u.v. spectra with an Optica Model 10 spectrometer. ^{1}H-N.m.r. spectra were recorded with a Varian HA-100 spectrometer, and ^{13}C-n.m.r. spectra with a Bruker WP-80 or Jeol PS-100 spectrometer for solutions in Me_2SO-d_6 or pyridine-d_5 (internal Me_4Si). Chemical shifts are expressed on the δ scale. Selective decoupling was accomplished by the use of monochromatic irradiation at the resonance of the anomeric proton; the frequency was determined from ^{1}H-n.m.r. spectra obtained for the same sample as used for ^{13}C-n.m.r. spectra. Accurate mass measurements were recorded with a Jeol JMS D-100 spectrometer by the direct-insertion procedure. Analyses were performed by the Service Central de Micro-Analyse du C.N.R.S.

Synthesis of D-*ribosylamines.* — *Process A.* To a solution of dry 2,3-*O*-isopropylidene-D-ribofuranose[21] (**1**; 2 g, 10 mmol) or D-ribose (**2**; 2 g, 13 mmol) in the minimum amount of anhydrous methanol was added a stoichiometric amount of freshly purified amine. The mixture was stirred at room temperature for the time

TABLE VII

PHYSICAL DATA[a] FOR **14–16**, **26**, **28**, AND **29**

Compound		*Method*	*Yield (%)*	*M p (degrees)*	R_f *(t l c)*	*Crystallisation solvent*	$[\alpha]_D^{20}$ *(degrees)*	*Formula*	*Anal (%)*						λ_{max}^{EtOH} *(nm)* *(ε)*
									Calc			*Found*			
									C	*H*	*N*	*C*	*H*	*N*	
MeNH—NHR	(**14**)	A (1 h)	91	108–109	0 52 $CHCl_3$–MeOH (5 5)	MeOH	+1 (Me_2SO)	$C_6H_{14}N_2O_6$	40 44	7 92	15 72	40 25	7 81	15 88	
	(**15**)	B (4 h)	91	Foam	0.46 $CHCl_3$–MeOH (5 5)		−5 5 (MeOH)	$C_6H_{13}N_3O_4S$ 0 5H_2O	31 03	6 08	18 09	31 04	6.25	17 74	270(11200) 243(9080)
	(**16**)	B (11 h)	90	Foam	0 50 AcOEt–MeOH (6 4)		−56 (MeOH)	$C_{12}H_{17}N_3O_4S$ 0 5H_2O	46 75	5 56	13 63	46 82	5 50	13.50	
	(**26**)	A (32 h)	80	82–85	0 42 $CHCl_3$–MeOH (5 5)	MeOH	−25 (MeOH)	$C_{10}H_{19}NO_4$	55 28	8 81	6 44	55 20	8 79	6.48	
	(**28**)	A (24 h)	87	74–76	0 40 $CHCl_3$–MeOH (5:5)	MeOH	−52 (MeOH)	$C_{10}H_{20}N_2O_4$	51 71	8 68	12 06	51 63	8.55	12 20	

	(29)	A (24 h)	75	107–110	0 57 $CHCl_3$–MeOH (8·2)	MeOH	+26 (MeOH)	$C_{13}H_{17}NO_4$ 0 5CH_3OH	60.87	7.11	5.24 60.83	6.84	5 42 291(3265) 244(6695) [EtOH 95°]
	(8)	B (24 h)	69	oil	0 45 $CHCl_3$–MeOH (8:2)			$C_8H_{15}NO_5$	46 82	7 37	6 22 46 75	7.41	6.18
	(11)	B (48 h)	45	oil	0 54 $CHCl_3$–MeOH (8 2)			$C_9H_{17}N_3O_4S$	41 06	6 51	15 96 41 15	6 45 15 80	241(13800) 270(10112) [EtOH 95°]
	(22)	A (48 h)	74	oil	0.57 $CHCl_3$–MeOH (9.5 0 5)		−17 6 (MeOH)	$C_{13}H_{23}NO_4$	60.68	9.01	5.44 60.49	8.97	5.42
	(23)	B (60 h)	65	oil	0 37 CH_2Cl_2–MeOH (9 5:0.5)		−25 0 (MeOH)	$C_{13}H_{24}N_2O_5$	54 15	8.39	9.72 54.00	8.35	9.70

[a] R = D-ribosyl, R′ = 2,3-*O*-isopropylidene-D-ribofuranosyl

noted in Table VII and then subjected to short-column chromatography on silica gel, or the product was crystallised.

Process B. The reaction mixture, as in process A, was boiled under reflux.

The physical constants of the following compounds are recorded in Table VII.

2,3-*O*-Isopropylidene-D-ribose hydrazone (**9**) was obtained, as an oil, by following the literature procedure[19].

2,3-*O*-Isopropylidene-D-ribose *N*-methylhydrazone (**10**) was obtained as an oil by boiling a solution of 2,3-*O*-isopropylidene-D-ribofuranose (3.62 g, 19 mmol) and *N*-methylhydrazine (0.88 g, 19 mmol) in anhydrous methanol (30 mL) under reflux for 1.5 h, followed by concentration under diminished pressure and treatment of the residue with anhydrous ether. Mass spectrum: *m/z* 218.12649 (M^+) (Calc. for $C_9H_{18}N_2O_4$, 218.12665).

2,3-*O*-Isopropylidene-D-ribose thiosemicarbazone (**11**) was prepared by process B (48 h). The solvent was removed under diminished pressure and the oily residue was purified by column chromatography (chloroform–methanol, 9.3:0.7).

D-Ribose oxime (*Z*-**12**) was prepared by treating a solution of hydroxylamine hydrochloride (1.32 g, 12 mmol) in anhydrous methanol (10 mL) with methanolic 1.7M sodium methoxide (10 mL). The sodium chloride was collected and washed with anhydrous methanol (10 mL), D-ribose (1.5 g, 10 mmol) was added to the filtrate, and the mixture was stirred at room temperature for 3 h and then kept for 12 h at 0°. The product (quantitative yield), after drying over phosphorus pentaoxide, had m.p. 138–140°, $[\alpha]_D^{20}$ +41.5° (*c* 1, water), R_F 0.48 (ether–methanol, 3:2); lit.[22] m.p. 140°.

D-Ribose hydrazone (*E*-**13**), obtained by the literature[23] procedure, had m.p. 127–129°.

N-(2,3-*O*-Isopropylidene-β-D-ribosyl)-*N'*-methylpiperazine (**23**) was synthesised as an oil (0.493 g, 65%) by process B (60-h reaction). The solution was concentrated under diminished pressure and the oily residue was chromatographed on silica gel (25 g/g of product).

N-(2,3-*O*-Isopropylidene-β-D-ribosyl)indoline (**24**) was obtained using process B (2-h reaction). The solvent was removed under vacuum and the oily residue was purified by column chromatography. It had R_F 0.41 (chloroform–methanol, 95:5). Mass spectrum: *m/z* 291.14666 (M^+) (Calc. for $C_{16}H_{21}NO_4$, 291.14705).

Di-*N*-benzyl-2,3-*O*-isopropylidene-β-D-ribosylamine (**25**) was synthesised using process A (3-day reaction). After removal of the solvent, attempted purification of the resulting oil by chromatography failed because of rapid degradation.

N-D-Ribosylmorpholine (**28**) was prepared by process A (54-h reaction). The resulting yellow oil could not be crystallised or chromatographed without rapid degradation. It had R_F 0.58 (dichloromethane–methanol, 3:2). Mass spectrum: *m/z* 219.11028 (M^+) (Calc. for $C_9H_{17}NO_5$, 219.11067).

Di-*N*-benzyl-D-ribosylamine (**30**) was synthesised by process A (9-day reac-

tion). The reaction solution was concentrated under diminished pressure, but the oily residue rapidly decomposed on attempted purification, thus precluding the usual analyses. It had R_F 0.53 (chloroform–methanol, 8.5:1.5). Mass spectrum: *m/z* 329.05376 (M^+) (Calc. for $C_{19}H_{23}NO_4$, 329.05343).

N-(5-*O*-Trityl-β-D-ribofuranosyl)indoline was prepared by keeping a solution of 5-*O*-trityl-D-ribofuranose[24] (1.176 g, 3 mmol) and indoline (0.35 mL, 3 mmol) in anhydrous methanol (5 mL) at room temperature for 3 h. The solvent was then removed under diminished pressure, and the oily residue was crystallised from anhydrous ethanol to give the desired compound (1.1 g, 74%), m.p. 134–136°; lit.[13] m.p. 132–135°. ^{13}C-N.m.r. data (Me_2SO-d_6): δ 90.48 (C-1β), 71.40 (C-2β), 70.50 (C-3β), 80.76 (C-4β), 64.27 (C-5β), 45.49 (N-CH_2) 27.65 (CH_2), 108.09, 128.31, 124.52, 127.03, 127.85, 128.40, 129.86, 143.82, 150.57, (Ph), and 86.05 (Ph_3-CO).

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