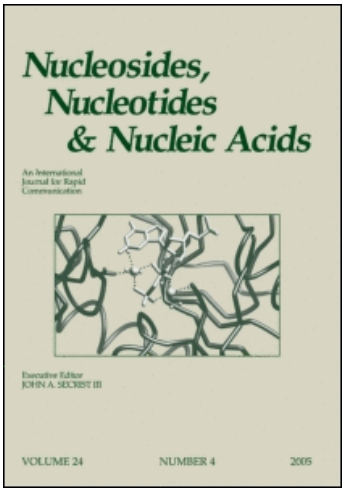

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Studies on the Dehydration of New 2- (Pentitol-1-YL) Pyridines Having D-Gulo, D-IDO, and L-Manno Configurations

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To cite this Article Martínez, M. Bueno , Galán, E. Román and Pérez, J. A. Galbis(1988) 'Studies on the Dehydration of New 2- (Pentitol-1-YL) Pyridines Having D-Gulo, D-IDO, and L-Manno Configurations', Nucleosides, Nucleotides and Nucleic Acids, 7: 2, 227 — 244
To link to this Article: DOI: 10.1080/07328318808070206
URL: http://dx.doi.org/10.1080/07328318808070206

NUCLEOSIDES & NUCLEOTIDES, 7(2), 227-244 (1988)

STUDIES ON THE DEHYDRATION OF NEW 2-(PENTITOL-1-YL)PYRIDINES HAVING D-GULO, D-IDO, AND L-MANNO CONFIGURATIONS

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ABSTRACT

Fusion of 2-trimethylsilylpyridine and tetra-O-acetyl--aldehydo-D-xylose or 2,3:4,5-di-O-isopropylidene-aldehydo-L--arabinose led, after removing of the protecting groups, to 2--(pentitol-1-yl)pyridines of D-gulo and D-ido or L-manno configurations. Dehydration of the sugar-chain with D-gulo and D-ido configurations gave the corresponding 2',5'-anhydro derivatives, whereas 2-(5-O-isopropyl-L-manno-pentitol-1-yl)-pyridine was the only compound formed by dehydration of the sugar-chain with L-manno configuration. Structural proofs are based on ^{1}H and ^{13}C NMR spectra.

INTRODUCTION

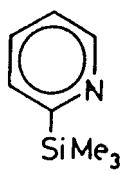
It is well known that the acid-catalyzed dehydrative cyclization of pentahydroxypentyl chains joined to π-excess heterocycles, produces an anomeric mixture of 1',4'- and/or 1',5'-anhydro derivatives, depending on the reaction conditions[1-6]. However in some cases, with the sugar-chain joined to a π-deficient heterocycle, C-1' is not usually involved in the cyclization process, and 2',5'-anhydro derivatives are formed[7].

In a previous publication[8], we described that the direct acid-catalyzed dehydration of 2-(pentitol-1-yl)pyridines with D-allo and D-altro configurations led to 2',5'-anhydro derivatives. Our results contrast with those of Belmans et al[9,10]., who failed in attempting this cyclization, and circumvented the problem by introducing a mesylate group at C-1'.

In this paper, we have extended our study on dehydration reactions to new 2-(pentitol-1-yl)pyridines with D-gulo, D-ido, and L-manno configurations.

RESULTS AND DISCUSSION

The reaction between 2-trimethylsilylpyridine (1) and 2,3,4,5-tetra-O-acetyl-aldehydo-D-xylose (2) led to D-gulo and D-ido compounds (3 and 4, respectively), as a mixture from which only 3 was obtained pure, after column chromatography. Treatment of the impure compound 4 with acetic anhydride-pyridine led to the corresponding mixture of peracetates 5 and 6, yielding pure 6 after crystallization.



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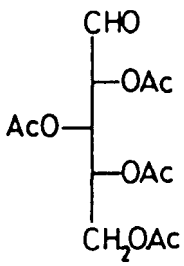

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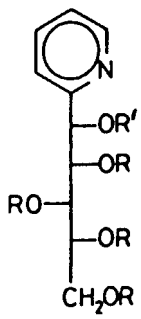
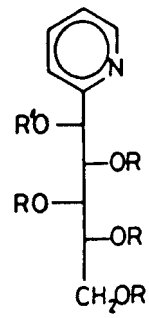


3; R'= H, R= Ac

5; R'= R= Ac

9; R'= R= H

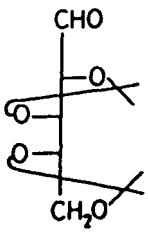


4; R'= H, R= Ac

6; R'= R= Ac

10; R'= R= H

The fusion of 1 and 2,3:4,5-di-O-isopropylidene-aldehydo--L-arabinose (7) was carried out in a similar way; however, in this case, only the L-manno isomer (8) could be isolated. The L-gluco epimer was not detected.



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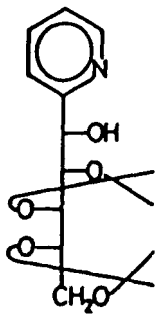

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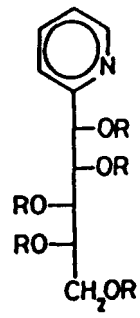


11; R= H

16; R = Ac

Deprotection of 5, 6, and 8 gave the corresponding pentitols 9, 10, and 11. The presence of pentahydroxypentyl side-chains was proved by periodate oxidation; a consumption of 4 mol per mol of substance was shown in each case. Assignments of chain configurations in pentitols are based on the configuration of their respective sugar precursors, and are consistent with the Richtmyer-Hudson rules[11].

As expected, the sugar-chain in compounds 5, 6, 16, and 18 adopt conformations (see Table 1) in agreement with those previously reported for acyclic carbohydrate derivatives[12-15]. ^{1}H and ^{13}C NMR data are indicated in Tables 1 and 2, respectively.

Compounds 9 and 10 could be cyclized by isopropanol-sulfuric acid, to give the anhydro derivatives 12 and 13, together with some minor carbohydrate products. Consumption of 1 mol of periodic

TABLE 1

^{1}H Chemical shifts[a] and coupling constants[b] of compounds 3, 5, 6, 8-16 and 18.

	Comp.	3[c]	5[d,e]	6[d,e]	8[f]	9[f]	10[f]	11[f]
Carbohydrate moiety	H-1'	4.71t	5.90d	6.00d	4.79m	4.65m	4.77m	4.62dd
	H-2'	5.69dd	↑	5.84dd	4.20m	↑	3.85dd	↑
	H-3'	5.33-5.05m	5.82-5.40m	5.42-5.04m	↑	3.95-3.32m	↑	
	H-4'		↓		4.13-3.62m	↓	4.02-3.32m	4.51-3.20m
	H-5'	4.34dd	4.42dd	4.37dd	↓	↓	↓	↓
	H-5"	3.97dd	4.04dd	4.06dd				
	-CH	4.45d			5.69d	5.38d 4.73-4.23m	5.35d 4.68-4.22m	5.38d
Pyridine	H-6	8.54dq	8.58dq	8.60dq	8.50dq	8.50dq	8.50dq	8.50dq
	H-4	7.68dt	7.71dt	7.69dt	7.76dt	7.78dt	7.78dt	7.78dt
	H-3	7.33bd	7.37m	7.28m	7.52bd	7.47bd	7.52bd	7.47bd
	H-5	7.20m	7.23dq	7.22dq	7.23dq	7.26dq	7.25dq	7.25dq
	$J_{1',2'}$	6.3	6.3	6.0	2.2	7.5	3.9	8.0
	$J_{2',3'}$		4.0	4.2			5.4	
	$J_{3',4'}$		6.2	6.3				
	$J_{4',5'}$		4.3	4.0				
	$J_{4',5"}$		6.0	5.5				
	$J_{5',5"}$		-12.3	-12.0				
	$J_{1',OH}$	6.3			5.4	5.8	5.6	6.0
	$J_{3,4}$	8.0	8.0	8.1	8.0	8.0	8.0	8.0
	$J_{3,5}$	1.7	1.7	1.3	1.7	1.7	1.7	1.7
	$J_{3,6}$	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	$J_{4,5}$	8.0	8.0	7.4	8.0	8.0	8.0	8.0
	$J_{4,6}$	2.0	2.0	2.0	2.0	2.0	2.0	2.0
	$J_{5,6}$	4.6	4.6	4.7	4.6	4.6	4.6	4.6
	Sugar-chain Conformation		$_3\underline{C}^*$	$_1\underline{C}^*$, $_3\underline{C}^*$; $_2\underline{C}^-$				

[a] Chemical shifts of acetyl-groups are comprised between 2.14-1.76 ppm. Isopropylidene methyl groups appear between 1.28-1.15 ppm as singlets for 8; in 18, the isopropyl methyl groups appear at 1.06 ppm as a doublet (J 6.0) and the methynic proton at 3.45 ppm as multiplet.
[b] In Hz. [c] $CDCl_3$ at 90 MHz. [d] $CDCl_3$ at 80.13 MHz. [e] J measured in the first-order spectrum observed by adding Eu(fod)$_3$. [f] DMSO-d_6 at 90 MHz. [g] D_2O at 80.13 MHz.

TABLE 1 (Cont.)

12[a]	13[f]	14[d]	15[c]	16[d,e]	18[d]	
4.84m	4.86d	5.88d	6.06d	↑	↑	H-1'
↑	↑	4.76dd	4.83dd	5.77-5.53m	5.80-5.55m	H-2'
4.70-4.00m	4.20-3.20m	5.60dd	5.30-5.00m	↓	↓	H-3'
↓	↓	5.13dq		5.13dq	5.09dq	H-4'
4.09dd	5.40m	4.28dd	4.37dd	4.28dd	3.57dd	H-5'
3.55dd	↓	3.75dd	3.80dd	4.09dd	3.35dd	H-5"
						-OH
8.45dq	8.50dq	8.66dq	8.56dq	8.58dq	8.53dq	H-6
7.85dt	7.83dt	7.70dt	7.67dt	7.68dq	7.53dt	H-4
7.48m	7.55bd	7.42m	7.34bd	7.34m	7.21bd	H-3
7.35dq	7.29dq	7.24dq	7.20m	7.21dq	7.15dq	H-5
8.8	6.8	9.6	7.8	8.6		$J_{1',2'}$
		3.4	4.2	2.0		$J_{2',3'}$
		0.9		9.5	8.4	$J_{3',4'}$
3.7		4.6	4.4	3.2	4.0	$J_{4',5'}$
1.1		1.8	2.2	5.2	5.4	$J_{4',5"}$
-10.0		-10.7	-9.8	-12.6	-10.4	$J_{5',5"}$
						$J_{1',OH}$
7.9	8.0	7.7	8.0	8.1	8.0	$J_{3,4}$
1.4	1.7	1.5		1.2	1.7	$J_{3,5}$
1.0	1.0	0.9	1.0	1.0	1.0	$J_{3,6}$
7.5	8.0	7.7	8.0	7.4	8.0	$J_{4,5}$
1.8	2.0	1.8	2.0	2.0	2.0	$J_{4,6}$
4.9	4.6	4.8	4.8	4.7	4.6	$J_{5,6}$
				P	P	Sugar-chain Conformation

TABLE 2

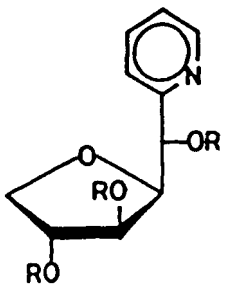
^{13}C NMR Chemical shifts δ (ppm) for compounds 5,6,8,9 and 11-16.

Compound	Carbohydrate moiety					Pyridine						
	C-1'	C-2'	C-3'	C-4'	C-5'	C-2	C-3	C-4	C-5	C-6	$-\underline{C}(CH_3)_2$	$-C(\underline{C}H_3)_2$
5[a]	73.1	71.3	69.6	68.9	61.8	155.3	123.1*	136.3	122.0*	149.1		
6[a]	74.5	71.2	69.5	69.0	61.8	155.2	123.3*	136.4	122.4*	149.5		
8[a]	73.7	82.7	79.0	76.6	66.4	158.8	122.6*	136.2	122.2*	148.2	110.0 109.5	27.3 26.2 25.2
9[b]	74.3	73.7*	73.3*	69.3	62.6	162.4	121.9*	136.1	121.9*	147.7		
11[b]	73.8	72.1	71.2	70.0	63.6	162.7	121.8*	136.0	121.6*	147.7		
12[c]	74.3	83.6	77.5	76.8	72.3	160.3	125.0*	139.4	123.7*	149.7		
13[c]	74.2	84.4	77.8*	77.6*	74.2	159.9	124.8*	139.4	123.2*	149.6		
14[a]	73.4	76.3	71.4	68.5	68.6	152.6	120.0*	132.6	119.6*	145.9		
15[a]	73.6	76.5	72.0	70.4	67.8	152.2	119.3*	132.5	118.6*	145.6		
16[a]	72.5	70.5	68.4*	68.0*	62.0	155.8	123.2*	136.3	122.4*	149.3		

[a] In $CDCl_3$. [b] In DMSO-d_6. [c] In D_2O. *These assignments may have to be interchanged.

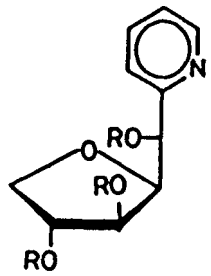
Chemical shifts of acetyl-groups are comprised between 170.2-165.0 ppm for carbonyl carbons and between 20.8-16.3 ppm for methyl carbons.

acid indicated that these structures contain either an 1',4'- or 2',5'-anhydro ring. Their tri-O-acetyl derivatives 14 and 15, clearly showed by ^{1}H and ^{13}C NMR spectra that dehydration proceeded between C-2' and C-5'.



12; R= H

14; R= Ac

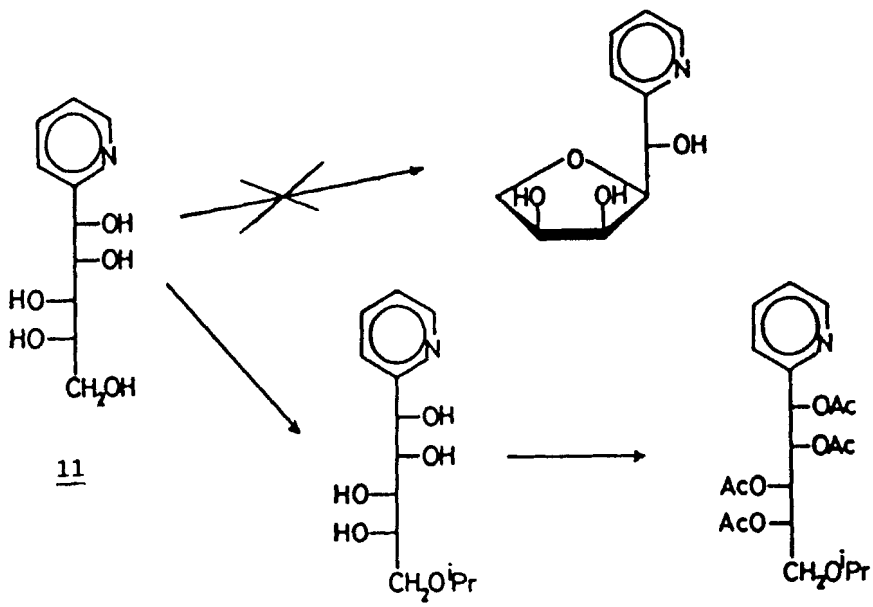


13; R= H

15; R= Ac

The proposed mechanism for the cyclization reaction is similar to that described by Hudson and Barker for the acid-catalyzed dehydration of simple alditols[16,17], which has been suggested to proceed via a S_N2 process. In our case, the protonated C-5' primary hydroxyl group would undergo the displacement induced by C-2' hydroxyl group, leading to 2',5'-anhydro derivatives with β anomeric configuration (retention of configuration). A similar explanation has also been given for the acid-catalyzed cyclization of 6-azauracils[7]. These results contrast with those described for other (pentitol-1-yl)heterocycles, such as pyrrole[1-6] or uracil[18-20] derivatives, in which the ring closure is easier and usually gives an anomeric mixture of 1',4'- and/or 1',5'-anhydro compounds. The qualitative difference in the behaviour of both systems is probably due to the decreased ability of the pyridine (or 6-azauracil) rings to stabilize a carbocation in the α position.

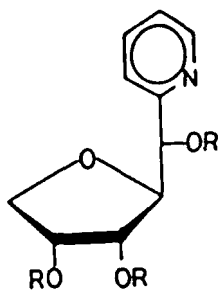
The same conditions applied for the cyclization of compounds 9 and 10 failed in the case of pentahydroxypentylpyridine with L-manno configuration, even after substantially prolonged reaction periods. Also, after refluxing compound 11 in isopropanol--sulfuric acid for 10 days, TLC showed that the starting material was still predominant, and that other minor products had been formed; amongst which the only significant impurity separated by preparative TLC was found to be 2-(5-O-isopropyl-L-manno-pentitol-1-yl)pyridine (17) on the basis of the NMR data of its tetra-O-acetyl derivative (18). Under more drastic conditions decomposition took place with the formation of dark-colored fluorescent by-products. These facts are in agreement with prior studies[16,17,21], indicating a striking influence of configuration on the rate of cyclization of alditols in acid media.



The NMR spectra show that there is no acetoxy group at C-2' indicating that the dehydration took place between C-2' and C-5'. Moreover, the comparison of the triacetates 14 and 15

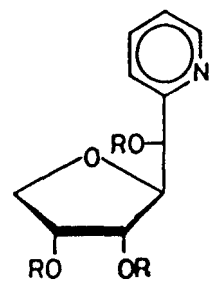
with their precursors 12 and 13, shows that the 1', 3', and 4' protons are typically deshielded by up to 1 ppm, while H-2',5', 5" remain essentially unchanged[7,20].

The assigned β configuration at C-2' is supported by the mechanism for the acid-catalyzed cyclization and by chemical shift measurements; thus, Nishimura and Shimizu[22] noted that the anomeric protons in trans-aldofuranosyl derivatives resonate at higher field than in the corresponding cis compounds. We observe that in 14 and 15 (H-2',3', cis) the signals of H-2' are at lower field (4.76 and 4.83 ppm) than in 2',5'-anhydro of D-allo[8] (21) and D-altro[8] (22) configurations (4.54 and 4.52 ppm) (H-2',3', trans). This effect may result from the diamagnetic shielding of the OAc-3' on H-2', when they both are cis[23].



19; R= H

21; R= Ac



20; R= H

22; R= Ac

Assignments of ^{13}C NMR chemical shifts in 2',5'-anhydro derivatives are similar to those reported for model compounds[13]. When the spectra of compounds 12 and 13 were compared with their corresponding tri-O-acetyl derivatives 14 and 15, the signals of C-2' (which has two acetoxy groups in the β-positions and none in the α) are the furthest shifted upfield, while the signals of C-1' (which has only one acetoxy group in the α-position) suffer the furthest downfield shift. On the other hand, for an 1',4'-anhydro structure, carrying a primary hydroxyl group[24,25]

at C-5', the signals of C-5' should appear at higher field (60--64 ppm) than actually found (71.7-72.3 ppm). Chemical shifts for C-2' are at lower field than for the other glycosyl carbons, thus corroborating the proposed structures, since it is known[13] that the anomeric carbon atoms in pyranoses and furanoses, and in their derivatives, resonates at lowest field. The δ values for C-2' also support the β configuration, because for furanoses possessing trans-oriented substituents at C-1' and C-2', the signals of the anomeric carbons are always found at lower field than in the case of the corresponding cis isomers[26,27]. Thus, in the case of 2-(2,5-anhydro-D-allo and D-altro-pentitol-1-yl)-pyridines[8] (19 and 20) with H-2' and H-3' in trans-position, the signals of these carbons appear at 86.8 and 84.9 ppm, whereas in 2-(2,5-anhydro-D-gulo and D-ido-pentitol-1-yl)pyridines (12 and 13), with H-2' and H-3' in cis, these signals are at 83.6 and 84.4 ppm. This same conclusion can be deduced by comparison of the δ values of C-2' of their tri-O-acetyl derivatives.

EXPERIMENTAL

Melting points were determined with a Gallenkamp apparatus, and are uncorrected. Optical rotations were measured at 22± 5° with a Perkin-Elmer 141 polarimeter (10-cm cell). TLC was performed on silica gel GF_{254} (Merck) with detection by UV light or iodine vapour. Preparative layer chromatography was performed on 20x20 cm glass plates coated with 2 mm layer of silica gel PF_{254} (Merck). Column chromatography was performed in the "flash" mode[28]. IR Spectra (KBr discs or chloroform solutions) were recorded with a Perkin-Elmer 399 spectrometer, and UV spectra with a Pye-Unicam SP8-250 instrument. The ^{1}H NMR spectra were recorded at 90 MHz on a Perkin-Elmer R-32 spectrometer and at 80.13 MHz on a Bruker WP-80-SY spectrometer, using Me_4Si as internal standard. ^{13}C NMR Spectra were recorded at 20.15 MHz on a Bruker SP--80-SY instrument.

2-(2,3,4,5-Tetra-O-acetyl-D-gulo and D-ido-pentitol-1-yl)-pyridines (3 and 4). A mixture of 2-trimethylsilylpyridine (1, 7.1 g, 47.0 mmol) and tetra-O-acetyl-aldehydo-D-xylose (2, 11.0 g, 34.5 mmol) was kept for 24 h at room temperature and then was heated at 55° for 2½ h. After cooling, the mixture was stirred until dissolution with 50% ethanol (120 mL) and a catalytic amount of pyridinium trifluoroacetate (10 mg). Then, the solution was refluxed gently for 2 h, evaporated under vacuum to dryness and co-evaporated several times with ethanol, giving a residue that was chromatographed on a silica gel column, using ether as the eluant. Evaporation of the fractions containing 3 (R_F 0.29, ether) led to a syrup that was crystallized from ethanol (2.2 g, 15%); m.p. 92-94°, $[\alpha]_D$ -10°, $[\alpha]_{578}$ -11°, $[\alpha]_{546}$ -13°, $[\alpha]_{436}$ -30°, $[\alpha]_{365}$ -69° (c 0.5, chloroform); λ_{max}^{EtOH} 255, 260 and 266 nm (ε_{mM} 2.5, 2.8 and 2.0); ν_{max} 3440 (OH), 1740 (C=O), 1585, 1565 and 1470 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{18}H_{23}NO_9$: C, 54.40; H, 5.83; N, 3.52. Found: C, 54.33; H, 6.00; N, 3.59.

Further elution yielded 4 (R_F 0.23, ether) which on evaporation gave a syrup that was found, by TLC, to be always contaminated with its D-gulo isomer. Overall yield: 60%.

2-(Penta-O-acetyl-D-gulo-pentitol-1-yl)pyridine (5). A solution of 3 (0.2 g, 0.45 mmol) in pyridine (0.2 mL) and acetic anhydride (0.2 mL) was stirred at room temperature for 24 h. After pouring into ice-water (20 mL), the mixture was extracted into chloroform, washed with a solution of sodium hydrogen carbonate, water, and evaporated to give a syrup that was co-distilled several times with water until 5 solidified (0.19 g, 86%). M.p. 101-103° (from ethanol), $[\alpha]_D$ +15°, $[\alpha]_{578}$ +16°, $[\alpha]_{546}$ +19°, $[\alpha]_{436}$ +39°, $[\alpha]_{365}$ +77° (c 0.5, chloroform); λ_{max}^{EtOH} 256, 261 and 266 nm (ε_{mM} 3.0, 3.4 and 2.4); ν_{max} 1735 (C=O), 1585, 1565 and 1470 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{20}H_{25}NO_{10}$: C, 54.67; H, 5.74; N, 3.19. Found: C, 54.91; H, 5.90; N, 2.99.

2-(Penta-O-acetyl-D-ido-pentitol-1-yl)pyridíne (6). Compound 4 (0.09 g, 0.23 mmol; slightly contaminated with its isomer 3) was acetylated as described for 5, yielding pure 6 after fractional crystalization from ethanol (0.06 g, 60%); m.p. 100-102°, $[\alpha]_D$ -46°, $[\alpha]_{578}$ -47°, $[\alpha]_{546}$ -56°, $[\alpha]_{436}$ -105°, $[\alpha]_{365}$ -182° (c 0.5, chloroform), λ_{max}^{EtOH} 256, 261 and 267 nm (ϵ_{mM} 3.0, 3.4 and 2.4); ν_{max} 1740 (C=O), 1590, 1570 and 1470 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{20}H_{25}NO_{10}$: C, 54.67; H, 5.74; N, 3.19. Found: C, 54.93; H, 5.71; N, 3.07.

2-(D-gulo-Pentitol-1-yl)pyridine (9). To a solution of 5 (1.20 g, 2.73 mmol) in dry methanol (75 mL) was added a catalytic amount of sodium methoxide. After 24 h at room temperature, the solution was neutralized with two drops of dilute acetic acid and evaporated to a syrup that was crystallized from ethanol (0.67 g, 97%); m.p. 113-115°, $[\alpha]_D$ +23°, $[\alpha]_{578}$ +22°, $[\alpha]_{546}$ +25°, $[\alpha]_{436}$ +40°, $[\alpha]_{365}$ +61° (c 0.5, water); λ_{max}^{EtOH} 254, 259 and 265 nm (ϵ_{mM} 3.1, 3.4 and 2.5); ν_{max} 3400, 3300 and 3220 (OH), 1585, 1565 and 1475 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{10}H_{15}NO_5$: C, 52.42; H, 6.59; N, 6.11. Found: C, 52.69; H, 6.75; N, 5.92. Periodate consumption: 4.00 mol/mol

2-(D-ido-Pentitol-1-yl)pyridine (10). Deacetylation of 6 (1.26 g, 2.86 mmol) as described for 9 led, after neutralization and evaporation, to compound 10 as a syrup that crystallized from ethanol containing a few drops of ethyl acetate. Yield: 0.52 g (78%); m.p. 84-86°, $[\alpha]_D$ -29°, $[\alpha]_{578}$ -32°, $[\alpha]_{546}$ -36°, $[\alpha]_{436}$ -65°, $[\alpha]_{365}$ -110° (c 0.5, water); λ_{max}^{EtOH} 254, 259 and 265 nm (ϵ_{mM} 3.1, 3.4 and 2.5); ν_{max} 3420 (OH), 1595, 1570 and 1480 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{10}H_{15}NO_5$: C, 52.42; H, 6.59; N, 6.11. Found: C, 52.38; H, 6.70; N, 5.95. Periodate consumption: 3.93 mol/mol

2-(2,5-Anhydro-D-gulo-pentitol-1-yl)pyridine (12). A solution of 9 (0.6 g, 2.6 mmol) in 1% isopropanol-sulfuric acid (120 mL) was refluxed for 10 days. After neutralization with sodium hydrogen carbonate, the solution was evaporated under diminished pressure, and the residue was treated with ethanol. The precipitate obtained was filtered off and the filtrate evaporated again. This procedure of adding ethanol, filtering the salts formed (mainly sodium isopropyl sulfate) and evaporating, was repeated until a homogeneous syrup was obtained. This syrup was crystallized from ethanol, yielding 12 (0.24 g, 44%); m.p. 180-182°, $[\alpha]_D$ +21°, $[\alpha]_{578}$ +21°, $[\alpha]_{546}$ +24°, $[\alpha]_{436}$ +42°, $[\alpha]_{365}$ +62° (c 0.5, water); λ_{max}^{EtOH} 255, 261 and 267 nm (ε_{mM} 2.8, 3.2 and 2.3); ν_{max} 3380 (OH), 1595, 1570 and 1480 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.97; H, 6.33; N, 6.51. Periodate consumption: 1.02 mol/mol

2-(1,3,4-Tri-O-acetyl-2,5-anhydro-D-gulo-pentitol-1-yl)pyridine (14). Conventional treatment of 12 (0.11 g, 0.53 mmol) with pyridine (1 mL) and acetic anhydride (1 mL) gave the triacetate 14 as a syrup that was crystallized from ethanol (0.1 g, 56%); m.p. 73-75°, $[\alpha]_D$ -27°, $[\alpha]_{578}$ -29°, $[\alpha]_{546}$ -33°, $[\alpha]_{436}$ -54°, $[\alpha]_{365}$ -81° (c 2.0, chloroform); λ_{max}^{EtOH} 256, 261 and 266 nm (ε_{mM} 3.1, 3.3 and 2.4); ν_{max} 1735 (C=O), 1585, 1570 and 1475 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 56.87; H, 5.80; N, 4.24.

2-(2,5-Anhydro-D-ido-pentitol-1-yl)pyridine (13). Compound 13 was prepared from 10 (0.54 g, 2.35 mmol) as described for 12. The resulting syrup was subjected to preparative layer chromatography with 5:1:1 chloroform-methanol-acetone as eluant, yielding 13 (R_F 0.42) as a syrup (0.17 g, 35%); $[\alpha]_D$ -19°, $[\alpha]_{578}$ -22°, $[\alpha]_{546}$ -25°, $[\alpha]_{436}$ -71° (c 0.26, water); λ_{max}^{EtOH} 257, 261 and 266 nm (ε_{mM} 2.8, 3.0 and 2.2); ν_{max} 3340 (OH), 1595 and 1570 cm^{-1} (C=C, C=N aromatic) (nujol).

Anal. Calc. for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.52; H, 6.47; N, 6.50.

2-(1,3,4-Tri-O-acetyl-2,5-anhydro-D-ido-pentitol-1-yl)pyridine (15). Acetylation of 13 (0.045 g, 0.21 mmol) as described for 12 gave the triacetate 15 as a syrup (0.034 g, 74%); $[\alpha]_D$ -86°, $[\alpha]_{578}$ -89°, $[\alpha]_{546}$ -103°, $[\alpha]_{436}$ -176°, $[\alpha]_{365}$ -280° (c 0.3, chloroform); λ_{max}^{EtOH} 257, 261 and 267 nm (ε_{mM} 2.8, 3.0 and 2.2); ν_{max} 1740 (C=O), 1590, 1570 and 1470 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{16}H_{19}NO_7$: C, 56.97; H, 5.68; N, 4.15. Found: C, 56.69; H, 5.46; N, 3.87.

2-(2,3:4,5-Di-O-isopropylidene-L-manno-pentitol-1-yl)pyridine (8). 2-Trimethylsilylpyridine (1, 9.1 g, 59.9 mmol) was added to 2,3:4,5-di-O-isopropylidene-aldehydo-L-arabinose (7, 10.4 g, 45.1 mmol) with external cooling. When the exothermic reaction ceased the mixture was kept at room temperature for 17 h, and then heated at 65° for 9 h. After cooling, the mixture was stirred with 50% ethanol (162 mL) and a catalytic amount of pyridinium trifluoroacetate, and the solution was refluxed gently for 1 h, evaporated under vacuum to dryness, dissolved in water, and extracted into chloroform. The extracts were combined, dried, and evaporated again to a syrup that was dissolved in 1:1 ethyl acetate-n-hexane, yielding crystalline 8 (6.2 g,

45%); m.p. 72-74°, $[\alpha]_D$ -14°, $[\alpha]_{578}$ -14°, $[\alpha]_{546}$ -17°, $[\alpha]_{436}$ -37°, $[\alpha]_{365}$ -85° (c 0.56, chloroform); λ_{max}^{EtOH} 257, 261 and 267 nm (ϵ_{mM} 3.2, 3.4 and 2.5); ν_{max} 3220 (OH), 1595, 1570 and 1475 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.52. Found: C, 62.20; H, 7.66; N, 4.38.

2-(L-manno-Pentitol-1-yl)pyridine (11). A solution of 8 (5.3 g, 17.13 mmol) in 25% acetic acid (180 mL) was heated at 100° for 8 h. The solvent was eliminated and the residue dissolved in ethanol and kept at room temperature, yielding 11 (3.04 g, 78%); m.p. 159-161°, $[\alpha]_D$ +21°, $[\alpha]_{578}$ +22°, $[\alpha]_{546}$ +25°, $[\alpha]_{436}$ +42°, $[\alpha]_{365}$ +65° (c 0.5, water); λ_{max}^{EtOH} 258, 261 and 266 nm (ϵ_{mM} 3.7, 3.8 and 3.1); ν_{max} 3400, 3300 and 3240 (OH), 1595, 1570 and 1480 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{10}H_{15}NO_5$: C, 52.42; H, 6.59; N, 6.11. Found: C, 52.12; H, 6.49; N, 5.94. Periodate consumption: 4.02 mol/mol

2-(Penta-O-acetyl-L-manno-pentitol-1-yl)pyridine (16). Acetylation of 11 (0.3 g, 1.31 mmol) as described for 5 gave the pentaacetate 16 as a syrup that crystallized on scratching (0.5 g, 89%). M.p. 136-138° (from ethanol), $[\alpha]_D$ -31°, $[\alpha]_{578}$ -33°, $[\alpha]_{546}$ -37°, $[\alpha]_{436}$ -59°, $[\alpha]_{365}$ -86° (c 0.55, chloroform); λ_{max}^{EtOH} 255, 259 and 266 nm (ϵ_{mM} 2.7, 2.9 and 2.1); ν_{max} 1740 (C=O), 1595, 1575 and 1480 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{20}H_{25}NO_{10}$: C, 54.67; H, 5.73; N, 3.19. Found: C, 54.60; H, 5.83; N, 3.18.

2-(5-O-Isopropyl-L-manno-pentitol-1-yl)pyridine (17) and its tetra-O-acetyl derivative (18). A solution of 11 (0.6 g, 2.62 mmol) in 5% isopropanol-sulfuric acid (120 mL) was refluxed for 10 days. After neutralization with barium hydroxide, the

solution was processed as described for 12. The resulting syrup was subjected to preparative layer chromatography, using 3:1 ethyl acetate-ethanol as eluant, yielding 17 (R_F 0.19) as a syrup (0.09 g, 13%). Acetylation of the foregoing product by a conventional procedure led to a syrup from which compound 18 was isolated by preparative layer chromatography (4:1, ether--light petroleum) as a syrup that crystallized on standing (0.03 g); m.p. 77-79°, $[\alpha]_D$ -28°, $[\alpha]_{578}$ -29°, $[\alpha]_{546}$ -33°, $[\alpha]_{436}$ -56°, $[\alpha]_{365}$ -78° (c 0.38, chloroform); λ_{max}^{EtOH} 254, 259 and 266 nm (ε_{mM} 2.7, 2.9 and 2.1); ν_{max} 1740 (C=O), 1590, 1570 and 1470 cm^{-1} (C=C, C=N aromatic).

Anal. Calc. for $C_{21}H_{29}NO_9$: C, 57.39; H, 6.65; N, 3.18. Found: C, 57.05; H, 6.67; N, 3.13.

ACKNOWLEDGMENTS

One of us (M.B.M.) thanks the Ministry of Education and Science of Spain for the award of a scholarship.

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Received April 27, 1987