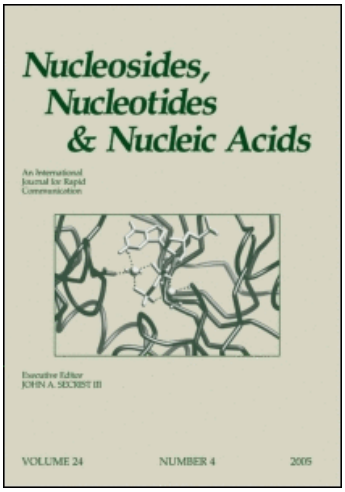

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Reaction of Sugars with 2-Hydrazinopyridine, Precursors for Seco *C*-Nucleosides of 1,2,4-Triazolo[4,3-a]pyridine

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ABSTRACT

Reaction of 2-hydrazinopyridine (**1**) with D-xylose, D-galactose, D-glucose and D-fructose afforded the corresponding hydrazones mainly in the acyclic forms **2**, **3**, **6** and **11** with minor amounts of the cyclic structures. Oxidative cyclization of the hydrazones with bromine in methanol resulted in the formation of the 3-(polyhydroxyalkyl)-1,2,4-triazolo[4,3-a]pyridine derivatives **13**–**15** whose acetylation afforded the acetylated derivatives **16**–**18**. Assignment of 1D and 2D NMR spectral data in addition to ^{15}N NMR experiments led to complete characterization of the products.

Key Words: Seco-nucleoside; 1,2,4-Triazolopyridine; Hydrazinopyridine; Sugar hydrazones; H; C; N NMR.

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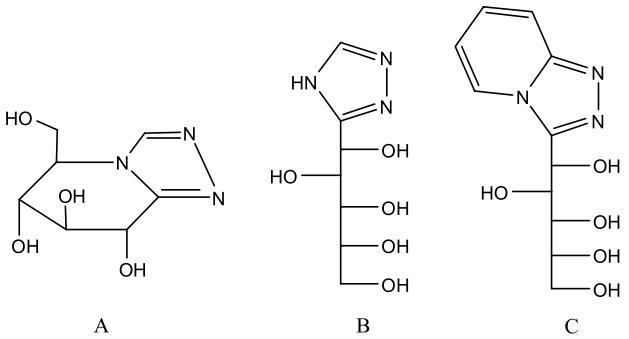
INTRODUCTION

2-Hydrazinopyridines and their derivatives are an interesting class of compounds, which as metal ligands[1–4] have potential applications in nuclear medicine,[5–9] as linkers for metal bioconjugate synthesis,[10] as pharmaceuticals and agrochemicals,[11–14] and for physiochemical studies.[15] They are important precursors for the synthesis of various fused heterocyclic compounds[16–25] such as the 1,2,4-triazolo[4,3-a]pyridines whose aromatic character and physiochemical properties attracted attention[26,27] since their synthesis.[28] The biological activity of compounds incorporating this ring system has been the subject of various reports.[29–33] Trazodone is a triazolopyridine derivative with antidepressant activity.[29] Some triazolopyridine derivatives regulate behavioral disorders and appear to modulate neurodegenerative diseases such as Parkinson's, Alzheimer's and depression,[30] while others exhibit moderate to fairly high anti-HIV and anti-cancer activities.[31] The triazolo[3,4-a]pyridine scaffold provided potent antagonists with favorable pharmacodynamic and pharmacokinetic attributes in drugs.[32,33] A carbocyclic nucleoside of triazolopyridine is a potent active P2T/P2Y12 receptor antagonist.[34] Triazolopyridine *C*-nucleoside analogues have also been synthesized.[35,36]

In spite of the above mentioned significance of 2-pyridylhydrazones, those derived from carbohydrates are not known except that of glucose which was isolated during a study on sequential removal of monosaccharides from the reducing end of oligosaccharides,[37] and a report on the reaction of this hydrazine with glycosuloses.[38] Consequently, we have investigated the reaction of **1** with some sugars to give the respective hydrazones whose subsequent cyclization would give the triazolopyridine analogues as exemplified with **C** which is the benzo analogue of **B** that was formerly prepared[39–41] as an open chain analogue of **A**; a potent glucosidase inhibitor[42–44] that was investigated by Vasella et al.[42] which is an analogue of nojirimycin[43–45] (Figure 1). Moreover, compounds of type **C** are acyclo/seco-nucleoside analogues, a group of nucleosides which became important targets as a consequence of the discovery of potent biological activity of some of their members.[46–48]



A B C

Figure 1. Acyclo/seco-nucleoside analogues.

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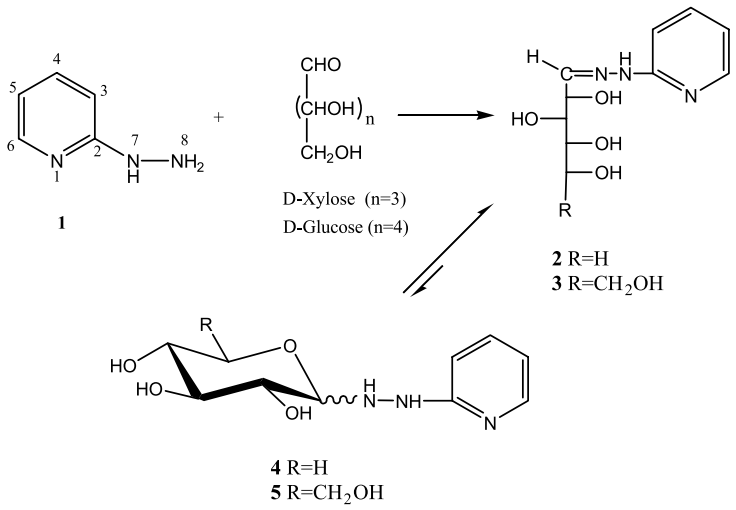
RESULTS AND DISCUSSION

The reaction of D-xylose and D-glucose with 2-pyridylhydrazine (**1**), gave the respective hydrazone derivatives **2** and **3** (Scheme 1). Their ^{1}H NMR spectra were conclusive in assigning their acyclic structures (Tables 1 and 2). The proton assignments were confirmed by H,H correlations. The appearance of H-1′ as a doublet at 7.26 ppm for **2** and at 7.24 ppm for **3** as well as the absence of a signal which would correspond to an anomeric proton of the cyclic structures **4** and **5** led to the conclusion that **2** and **3** are mainly in the acyclic form. However, the solution of **2** showed the appearance of minor signals which may be due to the cyclic structure **4** in a minor amount.

The dd in the spectrum of **3** at 4.15 ppm was assigned to H-2′ which correlated with the d of H-1′ (7.24 ppm) and the dd of H-3′ (3.73 ppm). The assignment of the OH and NH signals was done by addition of D_2O. The NH of the hydrazone residue appeared at 10.40 ppm as a singlet, which also agreed with an acyclic structure. The ^{13}C-NMR and DEPT-135° spectra of the glucose adduct **3** showed the presence of 11 signals (9 methines, 1 methylene and 1 quaternary carbon) (Table 3). The H–C COSY led to the assignment of the sugar carbon signals. The highest field signal at 63.7 ppm was assigned to C-6′, whereas the signal at 73.4 ppm was assigned to C-2′. The resonances at 71.5–71.9 ppm were assigned to the rest of the sugar carbons except that of C-1′ which appeared at 143.5 ppm confirming its nature as C═N and an acyclic structure for **3**.

The D-galactose adduct was obtained as a 7:1 mixture of the acyclic isomer **6** and cyclic isomers **7**–**10** (Scheme 2). The presence of more than one cyclic structure was indicated by the presence of signals that correspond to four anomeric carbons. They appeared at 92.0 and 94.7 ppm (lower intensities) and 92.9 and 97.8 ppm (higher intensities), which could be assigned to the α,β-pyranosyl and α,β-furanosyl isomers,



Scheme 1. Reaction of **1** with D-xylose and D-glucose.

Table 1. ^{1}H NMR chemical shifts for the sugar residue in **2**, **3**, **6**, **11** in DMSO-d_6.

	Chemical shift (ppm), multiplicity/coupling constants (Hz)			
	Compound no.			
	2	3	6	11
Assigned data after addition of D_2O				
H-1′	7.26 d	7.24 d	7.35 d	4.34 d
$J_{1',2'}$	6.0	6.5	5.4	
$J_{1'a\text{-}1'b}$				8.7
H-2′	4.16 t	4.15 t	4.37 dd	
$J_{2',1'}$	6.0	6.5	5.4	
$J_{2',3'}$	5.6	6.7	2.2	
H-3′	3.53 bdd	3.73 dd	3.58 bdd	4.38 bd
$J_{3',2'}$	5.6	6.7	2.2	
$J_{3',4'}$		1.4	3.5	2.3
H-4′	3.53 bm	3.33–3.39 m	3.58 bd	3.50–3.39 m
$J_{4',3'}$	5.7		3.5	
H-5′a	3.50–3.44 m	3.47–3.48 m	3.74 t	3.50–3.39 m
$J_{5',6'}$			6.7	
H-5′b	3.42–3.36 m			
H-6′a		3.58 dd	3.47 dd	3.59 dd
$J_{6'a,6'b}$		11.0	13.5	10.8
$J_{6a',5'}$		3.2	6.8	2.7
H-6′b		3.33–3.39 m		3.50–3.39 m
Assigned data before addition of D_2O				
OH-1′				5.54 t
$J_{OH\text{-}1'}$				5.0
OH-2′	5.04 d	5.07 d	4.82 d	
$J_{OH\text{-}2'}$	4.9	4.5	6.0	
OH-3′	4.40 d	4.42 d	4.45 bd	4.71 d
$J_{OH\text{-}3'}$	5.4	6.3	6.5	6.3
OH-4′	4.45 d	4.24 d	4.20–4.27 bd	4.44 d
$J_{OH\text{-}4'}$	6.1	7.1	4.9	6.9
OH-5′	4.52 t	4.52 d	4.20–4.27 bd	4.53 d
$J_{OH\text{-}5'}$	5.4	5.5	4.9	5.3
OH-6′		4.33 t	4.45 bd	4.37–4.29 m
$J_{OH\text{-}6'}$		5.6	6.5	

respectively. Moreover the presence of minor signals in the region 60.0–80.0 ppm agreed also with the presence of cyclic isomers, but their values could not be measured due to their overlapping with each other and with signals of the acyclic isomers.

The fructose adduct **11** was obtained as a mixture of two acyclic isomers, probably the *syn*- and *anti*-isomers in an ~ 10:1 ratio (Scheme 3), and a minor percentage of cyclic isomers **12**. Recrystallizing the mixture from ethanol led only to an increase in the percentage of the minor component. Alternatively, a sample of the reaction mixture was washed repeatedly with cold absolute ethanol until the major component was obtained in a pure form, on which full spectral analysis was carried out.

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Table 2. ^{1}H NMR chemical shifts for the pyridylhydrazine in **1**–**3**, **6**, **11** in DMSO-d_6.

	Chemical shift (ppm), multiplicity/coupling constants (Hz)				
	Compound no.				
	1	2	3	6	11
Assigned data before addition of D_2O					
NH_2	7.40				
NH	6.70	10.40	10.40	10.38	9.97
Assigned data after addition of D_2O					
H-3	6.71 d	7.03 d	7.03 d	7.04 d	7.12 d
$J_{3,4}$	8.4	8.4	8.4	8.4	8.4
H-4	7.46 ddd	7.55 ddd	7.55 ddd	7.55 ddd	7.60 ddd
$J_{4,3}$	8.4	8.4	8.4	8.4	8.4
$J_{4,5}$	7.0	7.2	7.2	6.9	7.2
$J_{4,6}$	1.8	1.8	1.9	1.7	1.7
H-5	6.58 dd	6.68 dd	6.68 ddd	6.68 dd	6.74 ddd
$J_{5,4}$	7.0	7.2	7.2	6.9	7.2
$J_{5,6}$	6.1	4.9	4.9	4.8	4.9
$J_{5,3}$			0.9		0.6
H-6	7.92 dd	8.11 dd	8.04 dd	8.06 dd	8.05 dd
$J_{6,5}$	6.1	4.9	4.8	4.8	4.9
$J_{6,4}$	1.8	1.8	1.7	1.7	1.8

Oxidative cyclization of the hydrazone residues of D-xylose, D-glucose, D-galactose and D-fructose **2**, **3**, **6** and **11** was carried out in methanol using bromine as an oxidizing agent in the presence of three equivalents of sodium acetate. The cyclization reaction was successful with the xylo, gluco and galacto adducts to afford the 1,2,4-triazolo[4,3-a]pyridine derivatives **13**–**15**, respectively (Scheme 4). The

Table 3. ^{13}C NMR spectral data **1**–**3**, **6**, **11** in DMSO-d_6.

	Chemical shifts (ppm)				
	Compound no.				
	1	2	3	6	11
C-1′	–	143.7	143.5	145.2	58.2
C-2′	–	72.2	73.4	70.6	150.9
C-3′	–	72.6	71.6	72.7	72.3
C-4′	–	71.8	71.5	69.5	71.5
C-5′	–	62.9	71.9	70.2	73.5
C-6′	–	–	63.7	63.4	63.7
C-2	160.4	157.7	157.6	157.7	157.5
C-3	104.8	106.4	106.4	106.3	107.2
C-4	135.3	138.0	138.0	138.0	137.9
C-5	110.9	114.7	114.7	114.6	115.3
C-6	145.8	147.9	148.0	149.2	147.9

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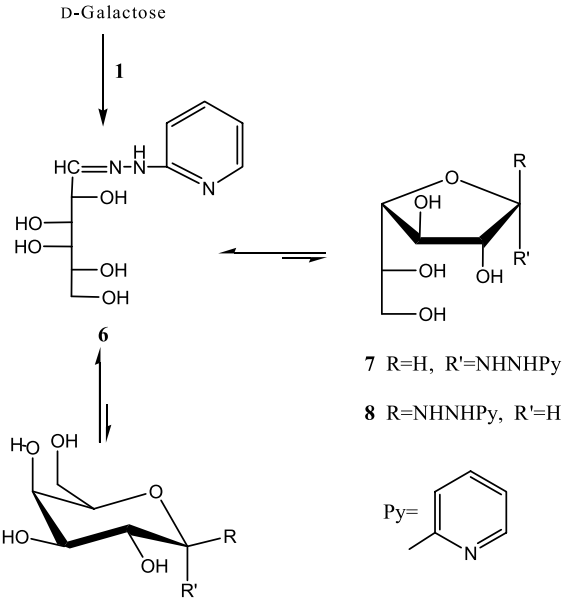
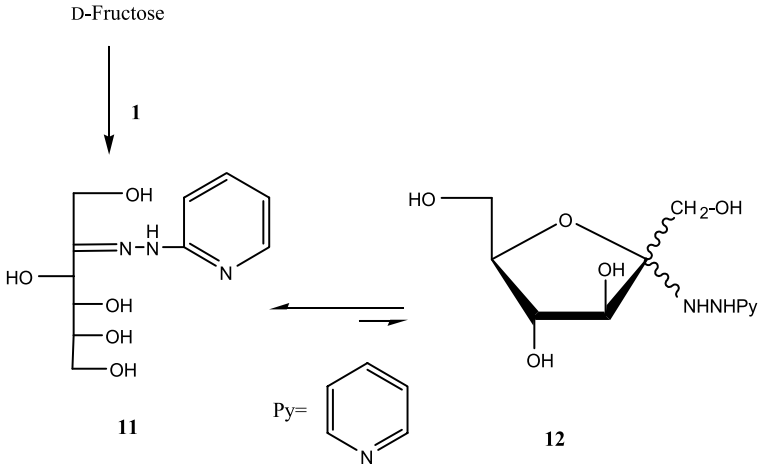


Scheme 2. Reaction of **1** with D-galactose.



Scheme 3. Reaction of **1** with D-fructose.

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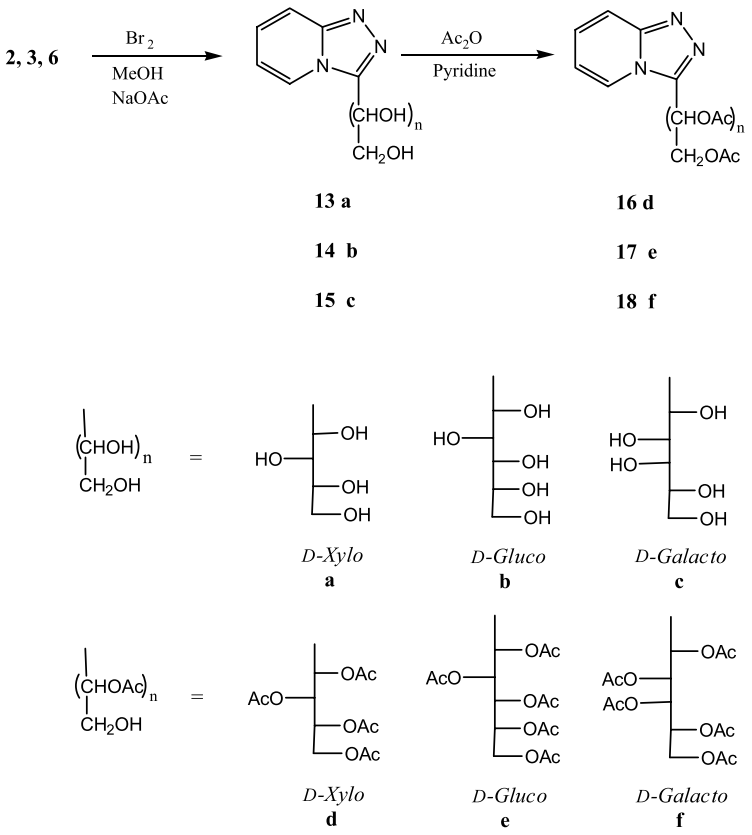

Scheme 4. Synthesis of triazolo[4,3-a]pyridines.

reaction occurred through the involvement of the pyridine nitrogen and C-1′ of the sugar hydrazone carbon generating a fused bicyclic system.

The triazolopyridine products **13**–**15** were highly hygroscopic, and this resulted in the presence of a water signal in their ^{1}H NMR spectra (Table 4). Their spectra (DMSO-d_6 + D_2O) showed the disappearance of the sugar H-1′ doublet (7.42–7.28 ppm) of adducts **2**, **3** and **6** with the appearance of a doublet in the 5.50–5.27 ppm region due to the H-1′ of the alditolyl residue in **13**–**15**, which confirms the involvement of C-1′ and H-1′ of the hydrazones in the cyclization process. The downfield shift of H-1′ of **13**–**15** compared with the corresponding H-2′ in **2**, **3** and **6** is due to its attachment to the carbon bearing the1,2,4-triazole ring.

The ^{13}C and DEPT-135° NMR spectra of **13**–**15** also confirmed the formation of the triazolopyridine rings (Table 5). The loss of the sugar methine proton H-1′ in **2**, **3** and **6** was accompanied by the formation of a new quaternary carbon in the 142–148 ppm region which was assigned to C-3 of the triazole ring. The assignment of the two quaternary carbons 3 and 7a to the two carbon peaks in the 142–151 ppm region was achieved by carrying out a long range C–H correlation HMBC NMR experiment.

Table 4. ^{1}H NMR chemical shifts for **13–15** in DMSO-d_6 and **16–18** in $CDCl_3$.

	Chemical shift (ppm), multiplicity/coupling constants (Hz)					
	Compound no.					
	13	14	15	16	17	18
Data for sugar residue						
H-1′	5.28 d	5.37 d	5.50 d	6.39 d	6.25 d	6.55 d
$J_{1',2'}$	5.8	5.7	1.6	8.7	9.3	3.3
H-2′	3.95 dd	4.18 m	3.74 m	6.17 dd	6.41 dd	5.67 dd
$J_{2',3'}$	2.7	1.9		2.9	1.6	9.7
H-3′	3.47 m	3.24 dd	3.74 m	5.03 ddd	5.11 m	5.52 dd
$J_{3'-2'}$				2.9		9.7
$J_{3'-4'a}$				5.2		2.0
$J_{3'-4'b}$				6.7		
H-4′a	3.50 m	3.55 m	3.74 m	4.25 dd	5.11 m	5.26 m
$J_{4'a-4'b}$				11.7		
$J_{4',5'}$						5.1
$J_{4',5'b}$						7.4
H-4′b				4.08 dd		
H-5′a		3.52 m	3.47 m		4.2 dd	4.25 dd
$J_{4'-5'a}$					2.3	5.1
$J_{5'a-5'b}$					12.7	12.6
H-5′b		3.34 m			4.06 dd	3.84 dd
$J_{4-'5'b}$					4.1	7.3
OAc				2.09, 2.02, 1.96, 1.95	2.12, 2.07, 2.04, 2.03, 1.93	2.08, 2.05, 1.99, 1.98, 1.87
Data for heterocyclic rings						
H-7	7.71 bd	7.70 dd	7.65 d	7.78 d	7.83 d	7.75 d
$J_{7,6}$	9.3	9.3	9.3	9.4	9.3	9.1
$J_{7,5}$		0.9				
H-6	7.38 ddd	7.39 ddd	7.36 ddd	7.30 dd	7.34 dd	7.24 dd
$J_{6,7}$	9.3	9.3	9.3	9.4	9.0	8.9
$J_{6,5}$	6.6	6.5	6.5	6.7	6.7	6.8
$J_{6,4}$	1.0	1.0	1.0			
H-5	6.96 dt	6.96 dt	6.82dt	6.9 d	6.94 t	6.89 t
$J_{5,4}/J_{5,6}$	7.1	6.9	6.7	6.7	6.8	6.8
$J_{5,7}$	0.9	1.0	1.0			
H-4	8.59 bd	8.56 d	8.72 d	8.29 d	8.29 d	8.30 d
$J_{4,5}$	7.1	7.1	7.1	7.1	7.0	7.0

Acetylation of **13–15** in pyridine resulted in the full acetylation of the sugar residues. These were purified by preparative TLC and identified as **16–18** (Scheme 4). Full NMR 1D and 2D spectral analysis (Tables 4 and 5), and mass spectrometric studies for products **16–18** confirmed the assigned structures.

NMR spectral data, including ^{1}H, ^{13}C, DEPT-135°, H,H-COSY, HMQC and ^{15}N NMR experiments for 2-hydrazinopyridine (**1**), made possible the assignments of chemical shifts, splitting patterns and coupling constants for the newly synthesized compounds. Thus the ^{1}H-NMR spectrum of **1** (Table 2) showed broad absorptions at

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Table 5. ^{13}C NMR chemical shifts for **13**–**15** in DMSO-d_6 and **16**–**18** in $CDCl_3$.

	Chemical shifts (ppm)					
	Compound no.					
	13	14	15	16	17	18
C-1′	67.6	67.7	67.2	64.89	64.4	65.2
C-2′	73.1	71.4	74.3	69.9	69.5	69.6
C-3′	72.1	70.8	69.9	69.3	68.4	68.3
C-4′	62.7	68.8	69.1	62.2	68.7	67.9
C-5′	–	61.3	61.3	–	61.9	62.3
Ac CH_3				21.2, 20.9 20.9, 20.8	21.3, 21.0 20.9, 20.9	21.7, 21.02 20.9, 20.89, 20.86
Ac C=O				170.7, 170.6 170.2, 169.8	171.4, 170.9 170.4, 170.2	171.3, 171.1, 170.7, 170.6, 169.9
C-7a	148.6	147.8	149.3	150.0	151.0	151.0
C-7	115.3	113.1	114.6	116.8	117.4	117.7
C-6	128.0	127.0	127.2	128.4	128.9	128.6
C-5	113.0	111.8	111.7	114.9	115.6	115.3
C-4	126.3	123.5	126.7	123.5	123.9	124.1
C-3	146.8	145.7	148.7	142.1	142.5	143.0

7.40 (2H) and 6.70 (1H) ppm which underwent exchange with D_2O and were assigned to the NH_2 and NH protons, respectively, of the hydrazine group. The 2D-COSY and HMQC experiments led to the assignment of the ring protons and carbon signals (Tables 2 and 3). Decoupling of the doublet of doublets of H-6 located at 7.92 ppm caused a change of the doublet of doublets at 6.58 ppm to a doublet, confirming its assignment to H-5, and allowed the measure of the long range coupling of H-5 with H-3 ($J_{3,5}$ = 0.7 Hz).

The ^{15}N NMR spectra (Table 6) showed a clear change in the chemical shifts of the nitrogen resonance frequencies of the sugar hydrazones **2**, **3**, **6**, **11** compared to that observed for the 2-hydrazinopyridine (**1**). The signal at 56.9 ppm which was assigned to the sp^3 hybridized nitrogen in hydrazine **1** disappeared and a new absorption in the series of hydrazones in the 312–322 ppm region appeared. This signal was assigned to the sp^2 hybridized nitrogen N-8 of the hydrazone group, thus confirming the formation of the carbon–nitrogen double bond and consequently favoring the acyclic isomers. The pyridine nitrogen N-1 had only a slight downfield shift from 255.2 to 266–287 ppm, while N-7 showed an appreciable downfield shift from 97.9 ppm to 140–150 ppm. On the other hand the ^{15}N NMR study of 1,2,4-triazolo[4,3-a]pyridines **13**, **14**, **15** (Table 6) showed signals in the 309–319 and 282–287 ppm regions which were assigned, respectively, to nitrogens N-1 and N-2 of the triazolo ring. These signals were consistent with their nature as two neighboring sp^2 nitrogens in the ring. The signal at 192 ppm was assigned to the bridge ring nitrogen N-3a. Its upfield shift relative to the respective nitrogen in the precursors **2**, **3**, **6**, **11** (265–287 ppm) may be due to the change of its status, where it became the bridge atom of the triazolopyridine bicyclic system, instead of being part of the C=N double bond of a pridine ring.

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Table 6. ^{15}N NMR spectral data for **1**–**3**, **6**, **11**, **13**–**15** in DMSO-d_6.

	Assignments/chemical shifts (ppm)		
Compound no.	N-1	N-7	N-8
1	255.2	97.9	56.9
2	266.0	150.4	322.2
3	265.9	150.6	322.8
6	287.1	139.3	330.1
11	267.4	142.7	312.2
	N-3a	N-1	N-2
13	192.7	315.3	282.7
14	192.8	319.9	287.6
15	192.0	309.6	278.0

EXPERIMENTAL

General Procedures. Melting points were determined on a Griffin Melting point apparatus and are uncorrected. NMR spectra were determined on a Bruker Avance 300 spectrometer. The chemical shifts are expressed in ppm using tetramethylsilane as reference for ^1H and ^{13}C experiments and formamide as reference (11.6 ppm) for ^{15}N experiments. Mass spectra was obtained on a Shimadzu E.I. Mass Spectrometer GC-MS QP5050A. Microanalysis were performed on a EuroVector EA Instrument, at the Central Laboratory at Beirut Arab University.

Sugar 2-Pyridylhydrazones

General Procedure. Equimolar amounts (0.01 mole) of the sugar and 2-hydrazino-pyridine in ethanol (40 ml) were heated under reflux in a hot water bath for 12–15 hours (reaction progress was monitored by TLC). The mixture was then allowed to cool for overnight. The product was then collected by filtration, washed with ethanol, dried and crystallized from ethanol.

D-Xylose 2-pyridylhydrazone (2). 83% yield, light yellow solid, m.p. 152–154°C. Anal. Calcd. for $C_{10}H_{15}O_4N_3$: C, 49.80; H, 6.22; N, 17.40. Found: C, 49.79; H, 6.19; N, 17.36.

D-Glucose 2-pyridylhydrazone (3). 93% yield, white solid, m.p. 179–181°C. Anal. Calcd. for $C_{11}H_{17}O_5N_3$: C, 48.71; H, 6.27; N, 15.49. Found: C, 48.87; H, 6.24; N, 15.46.

D-Galactose 2-pyridylhydrazone (6). 79% yield, yellowish solid, m.p. 151–153°C. Anal. Calcd. for $C_{11}H_{17}O_5N_3$: C, 48.71; H, 6.27; N, 15.49. Found: C, 48.76; H, 6.27; N, 15.34.

D-Fructose 2-pyridylhydrazone (11). 92% yield, white solid, m.p. 169–171°C. Anal. Calcd. for $C_{11}H_{17}O_5N_3$: C, 48.71; H, 6.27; N, 15.49. Found: C, 48.70; H, 6.29; N, 15.29.

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3-(Polyhydroxyalkyl)-1,2,4-triazolo[4,3-a]pyridines 13–15

General Procedure. To a solution of the sugar pyridylhydrazone (0.005 mol) and three molar equivalents of sodium acetate in 50 ml of pure methanol, a molar equivalent of bromine in 20 ml of methanol was added dropwise (10 min). The mixture was stirred for 24 hours. The methanol was then removed on a rotary evaporator until about 3–5 ml of the methanol remained in the flask and then dry acetone (20 ml) was added. The precipitated material was removed by filtration and the solvent was removed in vacuo using a rotary evaporator to obtain 3-(D-*xylo*-tertritol)-1,2,4-triazolo[4,3-a]pyridine (**13**), 3-(D-*gluco*-pentitol)-1,2,4-triazolo[4,3-a]pyridine (**14**) and 3-(D-*galacto*-pentitol)-1,2,4-triazolo[4,3-a]pyridine (**15**), which were highly hygroscopic, and subsequently used in the next step without further purification.

3-(Polyacetoxyalkyl)-1,2,4-triazolo[4,3-a]pyridine 16–18

General Procedure. A mixture of **13**–**15**, pyridine (5 ml) and acetic anhydride (5 ml) was stirred for 24 hours. The mixture was then placed on a rotary evaporator to remove the pyridine and acetic anhydride. Water (25 ml) was added and the reaction mixture was neutralized. The aqueous solution was then extracted with ethyl acetate that was then removed in vacuo to obtain the crude products which were purified by Preparative TLC using a 1:1 hexane:EtOAc mixture for elution.

3-(1,2,3,4-Tetra-*O*-acetyl-D-*xylo*-tetritol)-1,2,4-triazolo[4,3-a]pyridine (16). Solid (crystallized from methanol), m.p. 114–116°C. Anal. Calcd. for $C_{18}H_{21}O_8N_3$: C, 53.07; H, 5.16; N, 10.32. Found: C, 52.59; H, 5.11; N, 10.00. m/z = 407 ($M^{+\cdot}$); 348 (M-OAc)$^{+\cdot}$, 288 (M-C_6HN_3)$^{+\cdot}$, 262 [M-(CHOAc–CH_2OAc)]$^{+\cdot}$, 202 [M-(HOAc–CHOAc–CH_2OAc)]$^{+\cdot}$, 190 [M-CHOAc–CHOAc–CH_2OAc)]$^{+\cdot}$.

3-(1,2,3,4,5-Penta-*O*-acetyl-D-*gluco*-pentitol)-1,2,4-triazolo[4,3-a]pyridine (17). Thick liquid, $C_{21}H_{25}O_{10}N_3$, m/z = 479 ($M^{+\cdot}$); 420 (M-OAc)$^{+\cdot}$, 360 (M-C_6HN_3)$^{+\cdot}$, 334 [M-(CHOAc–CH_2OAc)]$^{+\cdot}$, 274 [M-(OAc–CHOAc–CH_2OAc)]$^{+\cdot}$, 190 [M-CHOAc–CHOAc–CHOAc–CH_2OAc)]$^{+\cdot}$.

3-(1,2,3,4,5-Penta-*O*-acetyl-D-*galacto*-pentitol)-1,2,4-triazolo[4,3-a]pyridine (18). Thick liquid $C_{21}H_{25}O_{10}N_3$, $M^{+\cdot}$ m/z = 479 ($M^{+\cdot}$); 420 (M-OAc)$^{+\cdot}$, 360 (M-C_6HN_3)$^{+\cdot}$, 334 [M-(CHOAc–CH_2OAc)]$^{+\cdot}$, 274 [M-(OAc–CHOAc–CH_2OAc)]$^{+\cdot}$, 190 [M-CHOAc–CHOAc–CHOAc–CH_2OAc)]$^{+\cdot}$.

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