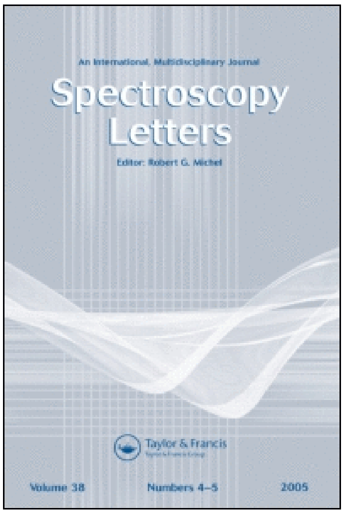

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^{1}H and ^{13}C NMR Spectra of Alditolyl Derivatives of 3-Hydrazino-5-Methyl[1,2,4]triazino[5,6-b]indole and Their Cyclized Products.

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^1H AND ^{13}C NMR SPECTRA OF ALDITOLYL DERIVATIVES OF 3-HYDRAZINO-5-METHYL[1,2,4]TRIAZINO[5,6-b]INDOLE AND THEIR CYCLIZED PRODUCTS.

Key words: Monosaccharides, triazino-indole, hydrazones, triazolo-triazino-indole, ^1H and ^{13}C NMR spectra, 2 D NMR (H,C COSY).

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and El Sayed H. El Ashry

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ABSTRACT

The ^1H and ^{13}C NMR spectra of sugar (5-methyl[1,2,4]-triazino[5,6-b]indol-3-yl)hydrazones (**1**), per-O-acetyl aldehydo sugar 1-acetyl-1-(5-methyl[1,2,4]triazino[5,6-b]-indol-3-yl)hydrazones (**2**), 1-(penta-O-acetyl-pentitol-1-yl)-10-methyl[1,2,4]triazolo[3',4':3,4][1,2,4]triazino[5,6-b]-indoles (**3**) have been investigated. The 2 D NMR (H,C COSY) spectrum of **2a** has been studied.

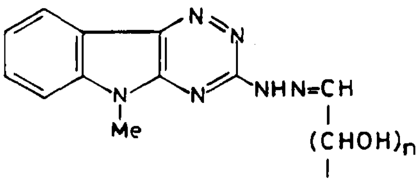
INTRODUCTION

The interesting biological activities of C-nucleosides[1,2] as well as condensed 1,2,4-triazines[3-5] led us to construct novel types of C-nucleoside analogues[6-8]. In the present study, the spectral characteristics of a series of C-nucleosides and their precursors have been investigated.

RESULTS AND DISCUSSION

The studied acyclic C-nucleoside analogues 1-(penta-O-acetyl-pentitol-1-yl)-10-methyl[1,2,4]triazolo[3',4':3,4]-[1,2,4]triazino[5,6-b]indole (**3**) with alditolyl residues having D-galacto-, D-manno-, D-arabino- and L-arabino configurations were prepared by the oxidative cyclization of the respective sugar (5-methyl[1,2,4]triazino[5,6-b]indol-3-yl)hydrazone (**1**) using Ferric chloride as an oxidant followed by acetylation with acetic anhydride in pyridine[9]. Similarly, the acetyl derivatives **2** were prepared[9] from **1**.

The ^{1}H NMR spectra (Table 1) of **2** do not give a confirmation for the structure. However, the problem was solved by studying the 2D NMR (H,C COSY) spectrum (Fig.1) of **2a**. The location of H-1 (δ 6.34) do not give an indication whether it belongs to a $\mathrm{H{-}\overset{|}{C}{=}N}$ or $\mathrm{H{-}C}\langle^{\mathrm{N}}_{\mathrm{N}}$ type of structure. However, its cross peak with C-1 confirmed its identity as $\mathrm{H{-}\overset{|}{C}{=}N}$, since C-1 ($\delta_C$ 138.87) was located at a relatively lower field than that anticipated for the other structure. The resonances of the polyol carbons (Table 2) were also assigned from the corresponding cross peaks with those of hydrogens. Thus, the doublet of doublet of H-2 (δ 5.60) was correlated with C-2 (δ_C 69.95), the double doublet of H-3 (δ 5.41) with C-3 (δ_C 68.18), the double doublet of H-4 (δ 5.44) with C-4 (δ_C 67.89), and the multiplet of H-5



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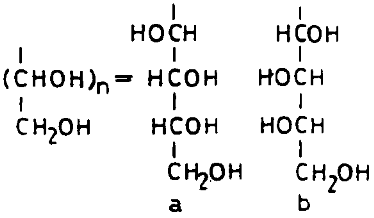

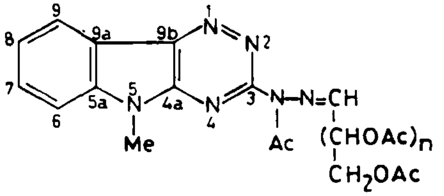

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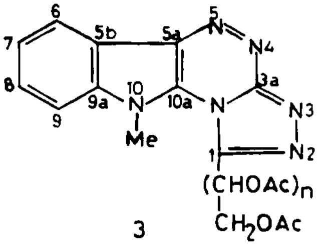

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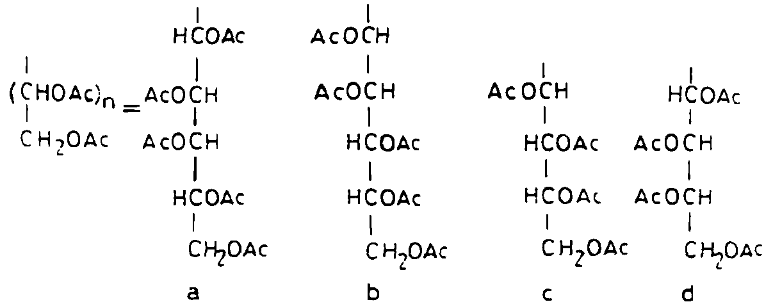

(δ 5.28) with C-5 (δ_C 67.61). The two double doublets of H-6,6' at δ 4.25 and 3.86 were correlated to the same carbon C-6 (δ_C 61.95).

The assignment of the resonances of the heterocyclic ring in the spectrum of **2a** was followed by taking into consideration the reported carbon chemical shifts for the

Table 1.

^{1}H NMR Spectral Data of Compounds 1-3*. Chemical Shifts are Given in (δ) Scale and Coupling Constants in Hz.

Assignment	Compound						
	1a	**1b**	**2a**	**2c**	**2d**	**3a**	**3b**
H-1 $J_{1,2}$	5.05(d)	5.02(d)	6.34(d) (3.66)	6.37(d) (3.5)	6.45(d) (3.0)	6.66(d) (1.5)	6.55(d) (8.0)
H-2 $J_{2,3}$	4.43(m)	4.62(m)	5.60(dd) (2.29)	5.63(t)	5.50(t)	5.73(m)	6.19(dd) (3.0)
H-3			5.41(dd)	5.45(m)	5.36(m)		5.15(m)
H-4 $J_{3,4}$			5.44(dd) (9.77)	5.2(m)	5.14(m)	5.45(m)	
H-5 $J_{4,5}$			5.28(m) (1.67)			4.32(dd) (3.0)	
	4.65(m)	4.41(m)		4.16(m)	4.16(m)		4.09(m)
H-5' $J_{4,5'}$						4.00(dd) (6.0)	
H-6 $J_{5,6}$ $J_{6,6'}$			4.25(dd) (5.19) (11.75)				
H-6' $J_{5,6'}$			3.86(dd) (9.46)				
N-Me	3.74(s)	3.78(s)	3.84(s)	3.83(s)	3.86(s)	3.80(s)	3.77(s)
N-H	11.45(s)						
N-Ac			2.54(s)	2.52(s)	2.44(s)		
X-OAc			2.01(s) 2.02(s) 2.05(s) 2.11(s) 2.12(s)	2.00(s) 2.03(s) 2.10(s)	1.96(s) 2.02(s) 2.06(s) 2.08(s)	1.93(s) 1.95(s) 2.04(s) 2.24(s)	1.90(s) 2.00(s) 2.02(s) 2.08(s)
Heterocyclic ring protons							
	7.41(m) 7.66(m) 8.19(d)	7.25(m) 7.58(m) 8.11(d)	7.46(dd) 7.49(ddd) 7.74(ddd) 8.41(dd)	7.50(m) 7.77(t) 8.47(d) (8.0)	7.44(m) 7.68(m) 8.32(d) (9.0)	7.50(m) 7.75(m) 8.26(d) (6.0)	7.35(m) 7.73(m) 8.18(d) (8.0)

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* DMSO-d_6 was used as a solvent for 1 and CDCl$_3$ as a solvent for 2 and 3.

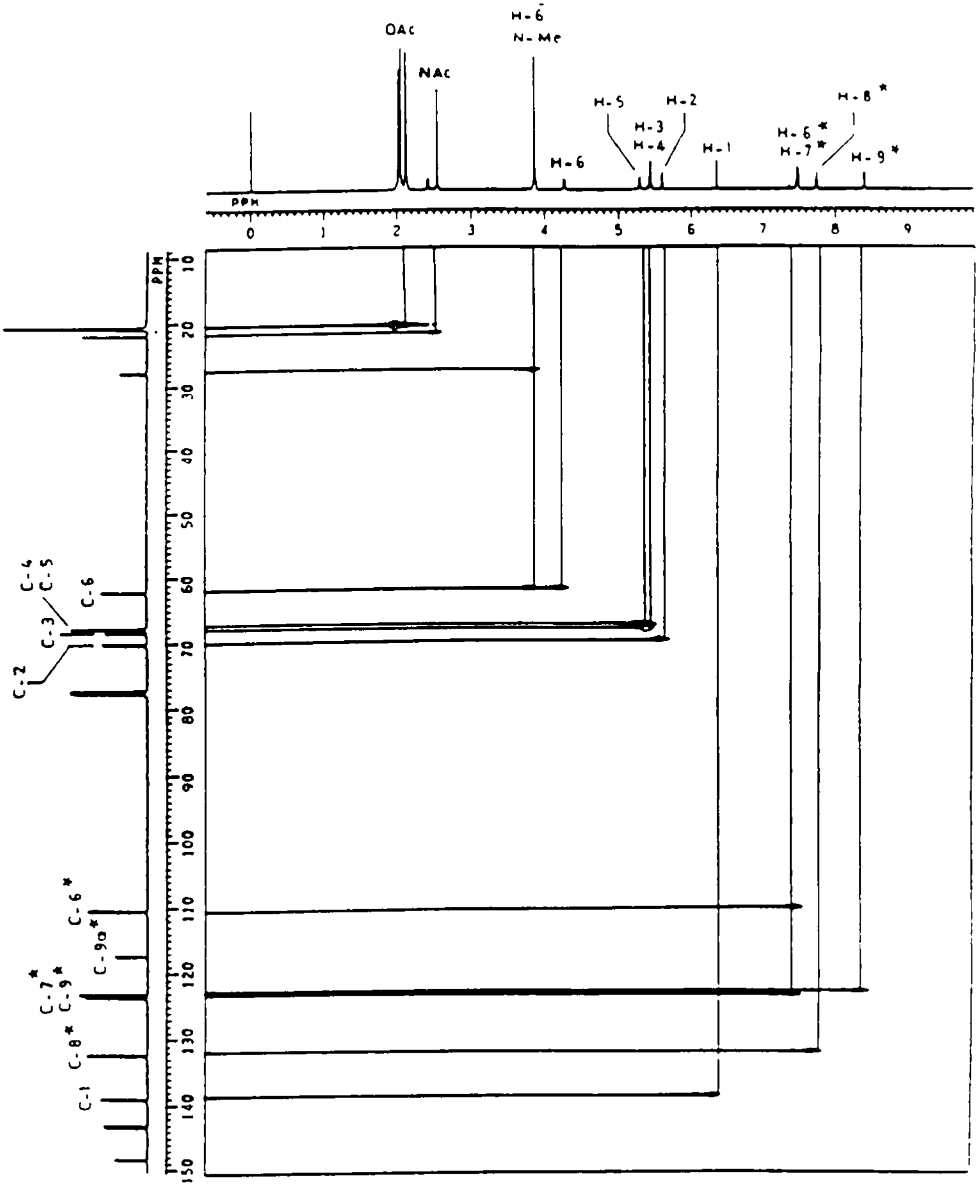

Fig. 1 2D NMR (H,C COSY) Spectrum of 2a.

* Indicates heterocyclic ring protons and carbons.

Table 2.

^{13}C **NMR Spectral Data of Compounds 1-3. Chemical Shifts are Given in (δ) Scale.**

Assignment	Compound					
	1a	1b	2a	2c	2d	3a
Carbons of the sugar part						
C-1	141.08	140.85	138.87	139.01	140.53	68.21
C-2	73.61	73.51	69.95	70.37	70.26	68.04
C-3*	71.07	71.08	68.18	69.34	69.13	67.77
C-4*	70.24	70.26	67.89	68.37	68.10	64.03
C-5	63.42	63.38	67.61	61.76	61.49	62.03
C-6			61.95			
Carbons of the heterocyclic rings						
C-1						146.98
C-3	158.74	158.35	153.57	153.64	153.42	
C-6	110.60	110.35	110.28	110.19	111.11	123.68
C-7*	120.06	119.83	123.46	123.57	123.19	128.83
C-8*	128.95	128.72	132.19	132.13	132.02	122.98
C-9*	122.35	122.11	122.95	123.19	122.22	110.35
C-3a						146.98
C-4a	148.77	148.38	148.26	148.44	148.28	
C-5a	137.90	137.66	142.87	143.02	142.97	134.08
C-5b						115.99
C-9a	118.52	118.32	117.16	117.45	116.75	130.89
C-9b	148.77	147.84	143.24	143.40	143.13	
C-10a						134.08
Miscellaneous						
XOAc			20.50 20.55 20.63	20.59 20.69	19.99 20.37	20.63 20.76 20.84
NAc			21.73	21.78	21.34	
XCO			169.42 169.56 169.66 170.10 170.36 172.82	169.46 169.57 169.67 170.49 172.87	169.08 169.84 171.62	169.67 169.78 169.95 170.16 178.56
N-Me	27.47	27.03	27.74	27.74	27.63	27.90

* Assignments may be interchanged in the same vertical column.

N-methyl derivatives of indolotriazine[10], indole[11-14] and isatin[15,16] as well as those of triazines[17-21] and triazolotriazines[15]. Moreover, the resonances of the non protonated carbons were always of considerably lower intensity than the resonances of protonated carbons. The resonance at the lowest field at δ_C 153.57 was assigned to C-3 due to the high deshielding nature around it. The two carbons of the junction of the indolotriazine system were expected to resonate at different chemical shifts in accordance with their relatively deshielded nature. Thus, C-4a resonated at δ_C 148.26 compared to that of C-9b which appeared at δ_C 143.24. This relative deshielding is a consequence of the presence of two nitrogens linked to C-4a. The two fused carbons C-5a and C-9a of the indole system resonated at δ_C 142.87 and 117.16 respectively where the former is more deshielded as a result of its direct attachment to the nitrogen of the indole ring. The resonances at δ_C 110.28 and 122.95 were assigned to C-6 and C-9 respectively, as they showed cross peaks with the two double doublets at δ 7.46 and 8.41 which may be assigned to H-6 and H-9 respectively. This assignment was based on those assignments in the indole system[5], however, they may be interchanged. Similarly, the resonances at δ_C 123.46 and 132.19 were assigned to C-7 and C-8, based on their cross peaks with the doublet of doublet of doublets at δ 7.49 and 7.74 due to H-7 and H-8 respectively. Similarly the ^{13}C NMR spectra of **2c** and **2d** were interpreted.

The spectra of **1a** and **1b** showed almost similar patterns to those of the acetates. The C-1 resonance of the sugar part of **1a** appears at a slightly higher value (δ_C 141.08) than that of the acetyl derivative. The C-2 resonance is shifted downfield by 3.24 ppm whereas the other carbons are also shifted downfield by ca. 2.0 ppm when compared with the corresponding acetyl derivative. This could be considered as a summation of the acetyl group effects. Some of the carbon of the heterocyclic ring are also affected by acetylation. The most pronounced effect is the downfield shift of C-3 and C-9b and the upfield shifts of C-5a, C-7 and C-8.

The spectrum of the triazole **3a** was based on the interpretation of the above triazines and their fused rings with a triazole. The intensity of the signal at δ_C 146.98 indicated that it belongs to two carbons and assigned to C-1 and C-3a. That of C-1 appears at a lower field than the respective carbon in **2** confirming the cyclization. The C-3a is more shielded than those of the respective carbons of **1** and **2** as a consequence of its presence as a junction of the triazole and triazine ring. The signal of C-5b of **3** appears at almost the same region of those of C-9a of **1** and **2**. Similarly, the aromatic ring carbons are almost the same as those of **1** and **2**.

EXPERIMENTAL

General methods.— ^{1}H NMR spectra were determined with a Varian EM-390 spectrometer except for **2a**. ^{13}C NMR spectra were determined with JEOL FX-900 spectrometer. 2 D NMR was measured with a JOEL GX-500 MHz speectrometer. The chemical shifts are expressed in the δ scale using tetramethylsilane as a reference.

Arabinose (5-methyl[1,2,4]triazino[5,6-b]indol-3-yl)-hydrazone (**1**), per-O-acetylaldehydosugar-1-acetyl-1-(5-methyl-[1,2,4]triazino[5,6-b]indol-3-yl)hydrazone (**2a,c,d**), and 1-(penta-O-acetyl-pentitol-1-yl)-10-methyl[1,2,4]triazolo-[3',4':3,4][1,2,4]triazino[5,6-b]indole (**3a,b**), were prepared as reported earlier[9].

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