Acyclo *C*-Nucleosides Analogues of Condensed 1,2,4-Triazines

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Z. Naturforsch. **52b,** 873–882 (1997); received February 17, 1997

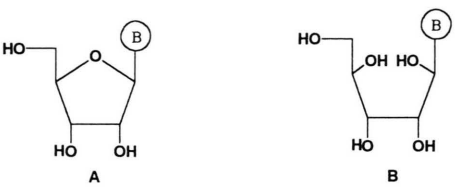
Acyclo *C*-Nucleoside, 1,2,4-Triazine, Indole, Triazinoindole, Triazolotriazinoindole

1-Acyclo *C*-nucleosides of 7-methyl-10*H*-1,2,4-triazolo[3',4':3,4][1,2,4]triazino[5,6-*b*]indoles (**9**) have been prepared by cyclodehydrogenation of the sugar derivatives of 3-hydrazino-8-methyl-5*H*-1,2,4-triazino[5,6-*b*]indole (**1**). The respective linear isomer as **4** has been prepared by a dehydrative cyclization of the amides of **1**. Acetylation of the sugar hydrazones and their cyclized products gave the per-*N*,*O*-acetyl derivatives. The molecular connectivity of the products was established by ^{1}H, ^{13}C, and 2D H,H Cosy spectra.

Various heterocyclic compounds containing a 1,2,4-triazine ring show interesting biological activities including antihypertensive, antiviral and antibacterial properties [1–7], as well as activity against *Staphylococcus aureus* and *Bacillus cereus* and P388 Lymphocytic leukemia [5]. Since the discovery of naturally occurring *C*-nucleosides, a rapid growth in literature on their biological activity as well as their methods of syntheses have been reported [8,9].

Recent interest in the synthesis and biological activity of acyclic nucleosides followed the finding that acyclovir [10] possesses a high antiviral activity that subsequently was followed by a series of highly potent acyclo-nucleosides. These findings led to the conclusion that the furanosyl ring of classical nucleosides (**A**) is not necessary for biological activity. Consequently; a variety of acyclic analogues have been synthesized. Having the above aspects in mind, novel types of acyclo-nucleoside analogues having the furanose ring in an acyclic form as in (**B**) without any loss of carbon or oxygen atoms and the triazolotriazinoindole as the heterocyclic part have been prepared. In the meantime, the regioselectivity for the cyclization of 3-hydrazino-8-methyl-5*H*-1,2,4-triazino[5,6-*b*]indole with one carbon inserting reagents has been investigated.

The fusion of a heterocyclic to the 1,2,4-triazine ring *via* a functional group on position-3 may take place at N-2 or N-4 to give a linear [11–17] or angular [18–21] structure, respectively. In continuation of our study on the regioselective annelation of a triazole to a triazine ring [16,17,22–26] we found that the cyclization of 3-hydrazino-5*H*-1,2,4-triazino[5,6-*b*]indole either *via* the dehydrative cyclization of the respective hydrazide or the dehydrogenative cyclization of the hydrazones gave the linear isomer 10*H*-1,2,4-triazolo[4',3':2,3]-[1,2,4]triazino[5,6-*b*]indole.



Scheme 1.

Surprisingly, the introduction of a methyl group on the benzene ring of the hydrazine as in **1** caused a change in the site of cyclization upon the dehydrogenative cyclization of their hydrazones to give the angular isomer. A model study has been carried out on simple derivatives of **1** in order to assign the site of annelation. Thus, a number of hydrazones **2a-2c** was prepared from **1** by condensation with aldehydes. Cyclodehydrogenation of **2a-2c** was effected by a 2 M solution of iron(III) chloride in ethanol to give products which agreed with either one of the regioisomeric structures **3a-3c** or **4a-4b**. The selection of structure **3a-3c** for the products may be confirmed by an unequivocal synthesis of **4a** by condensing the aminotriazole **6** with 5- methylisatin **5** (Scheme 2). The latter reaction would give only one isomer be-

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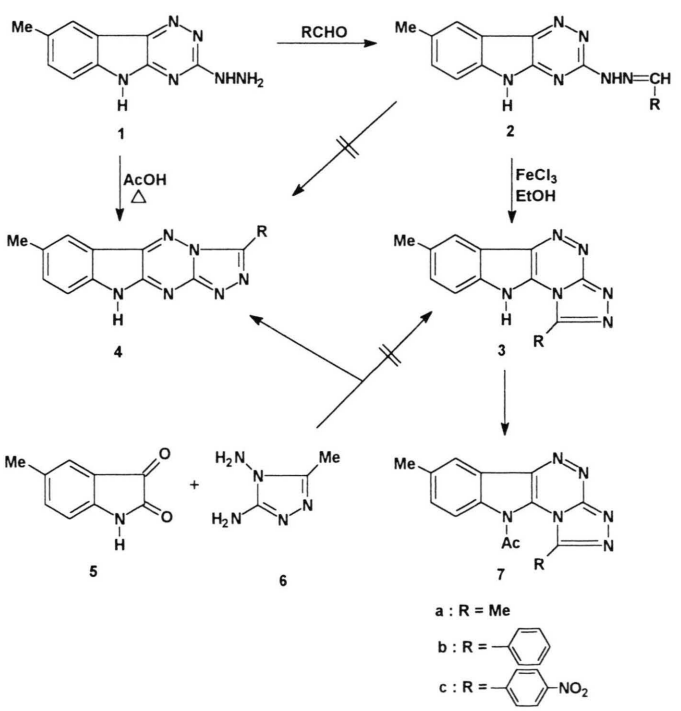
0932–0776/97/0700–0873 $06.00

cause it proceeds by the condensation of the more reactive amino group of **6** with the more reactive carbonyl group of **5**. Acetylation of **3a** and **3b** gave **7a** and **7b**, respectively, indicating the presence of only one NH group. The IR spectra of **3a** and **4a** are different. The difference in their ^{1}H NMR spectra is shown in the chemical shift of the two methyl groups. Their mass spectra showed almost the same molecular ion peaks as base peaks confirming that the molecular formulas of the products from dehydrogenation lack two hydrogens.

Dehydrative cyclization of **1** with acetic acid afforded **4a** and not **3a** which may have taken place by the formation of the hydrazide derivative followed *in situ* by a dehydrative cyclization process. This means that the latter process of cyclization is similar to that of the unsubstituted analogue [27] or its 5-methyl analogue [1]. On the other hand, a reverse situation was found in the case of the cyclization by a dehydrogenative process, *i.e.* the methyl group on the benzene ring directs the site of cyclization towards the angular isomer **3**. This could be attributed to the inductive effect of the methyl group which induces the pair of electrons on N-5 to be more available for contribution in preserving the aromatic ring character, 10π-electrons system, of the indole ring. This would be the case where the intermediate in the dehydrogenation process does not need much space. On the other hand, the dehydration of the respective amide may encounter an intermediate of larger size whereby the angular one is not formed and the linear one prevails.

In order to synthesize the acyclo-*C*-nucleoside analogues of **3**, a series of hydrazones **8a**-**8 g** were prepared by condensation of **1** with the monosaccharides, **D**-galactose, **D**-glucose, **D**-mannose, **D**-arabinose, **L**-arabinose, **D**-ribose and **D**-xylose respectively. Their IR spectra showed bands at 3346- 3388 cm^{-1} (OH) and 3161–3279 cm^{-1} (NH). The ^{1}H NMR spectrum of **8a** showed a singlet at δ 2.41 (Me) and a multiplet at δ 3.40–4.90 (the sugar moiety). The aromatic and methine protons appeared as a multiplet at δ 7.31–7.92 and the NH group as a singlet at δ 11.32.

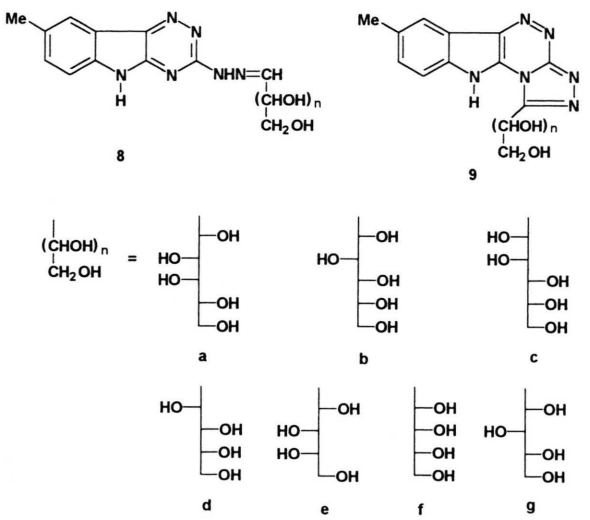
Oxidative cyclization of the sugar hydrazones with iron(III) chloride could be anticipated to give the triazolotriazinoindole derivatives **9** having the angular structure, based on the above model study. The IR spectra of **9** showed bands at 3329–3385 (OH) and 3203–3260 (NH) cm^{-1}. The acetylation of **8** with acetic anhydride in pyridine at room tem-



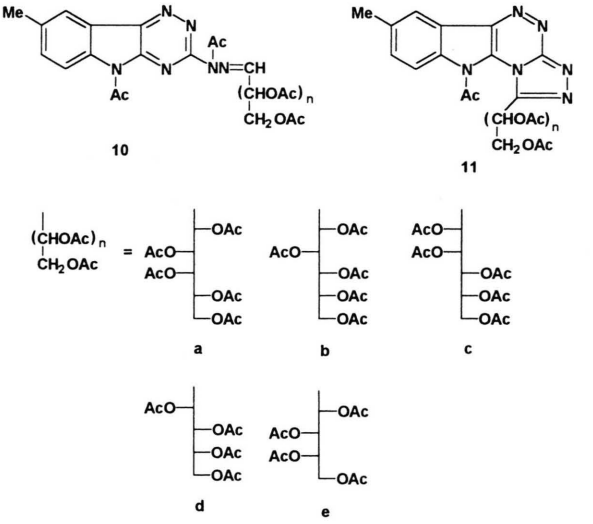
Scheme 2.

perature caused acetylation of their polyhydroxyalkylidene residues in addition to the hydrazone residues to give the peracetyl derivatives **10** (Scheme 4). IR spectra of acetates **10** showed the presence of OAc groups (1745–1755 cm^{-1}) and NAc groups (1700–1725 cm^{-1}). The ^1H NMR of **10a** and **10c** showed the presence of 5 OAc groups in addition to 2 NAc groups confirming their structures (Table I). Moreover, the signals in ^{13}C NMR spectra of **10a** and **10c** at δ_c 140.01 and 139.34 respectively, were assigned to the C-1 of the acyclic acetate form. The molecular connectivity was then established by the H,H Cosy spectrum of **10a** (Fig. 1). Drawing horizontal and vertical lines starting at the cross peaks, until the diagonal is intersected, reflected the positions of the signals of the coupling partners.

Acetylation of **9** with acetic anhydride in pyridine at room temperature afforded the polyacetoxyalkyl derivatives **11** whose IR spectra showed



Scheme 3.



Scheme 4.

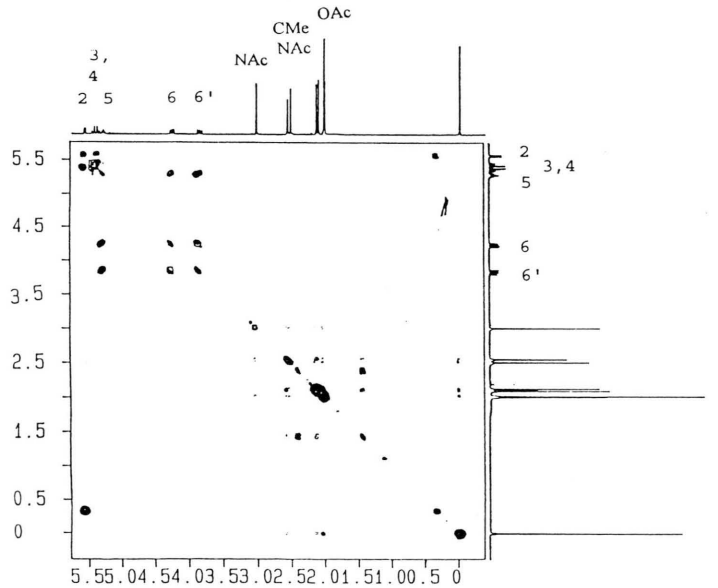


Fig. 1. H,H COSY spectrum of **10a**.

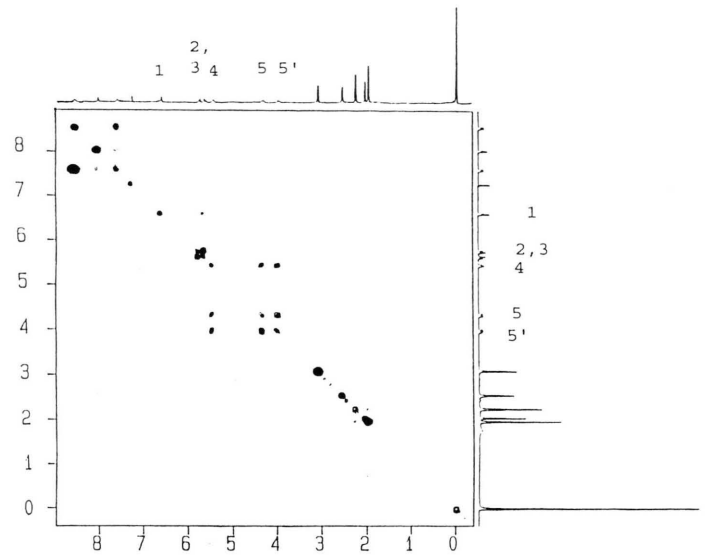
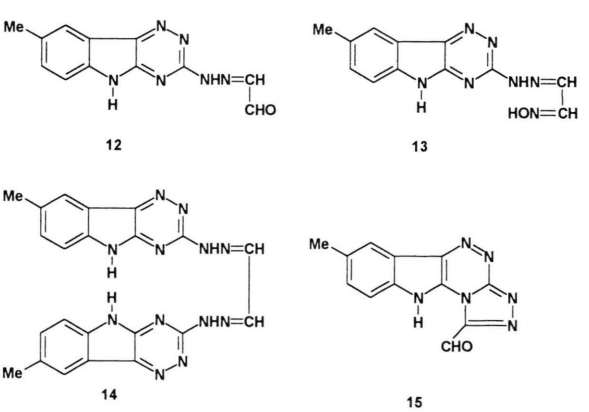


Fig. 2. H,H COSY spectrum of **11a.**

bands at 1747–1757 (OAc and NAc) cm^{-1}. The ^1H NMR spectrum of **11a** confirmed the presence of 5 OAc groups in addition to NAc group, whereas no CH=N signal could be found confirming that the heterocyclization had taken place. The three aromatic protons appeared in a pattern similar to that of **10**. The H,H Cosy of **11a** (Fig. 2) confirmed the assignment.

Periodate oxidation of polyols **8a** and **9a** gave the aldehydes **12** and **15** respectively. Condensation of **12** with hydroxylamine hydrochloride gave **13**. Similarly, its reaction with hydrazine **1** afforded the corresponding bishydrazone **14** (Scheme 5).



Scheme 5.

Experimental

Melting points were determined on a Meltemp apparatus and are uncorrected. IR spectra were recorded with a Unicam SP 1025 Spectrometer. ^1H NMR spectra were determined with a Bruker spectrometer at 500 MHz. The ^{13}C NMR spectra were recorded with the Bruker AM-500 spectrometer at 500 MHz. The chemical shifts are expressed in the δ scale using tetramethylsilane as a reference. TLC was performed on Bakerflex silica gel IB-F (2.5–7.5 cm) plates. Microanalyses were performed in the unit of Microanalysis at Cairo University.

3-Hydrazino-8-methyl-5H-1,2,4-triazino[5,6-b]indole (**1**)

It was prepared from 8-methyl-5*H*-1,2,4-triazino[5,6-*b*]indole-3-thione [28,29] (m.p. 250–252 °C).

3-Ethylidenehydrazino-8-methyl-5H-1,2,4-triazino[5,6-b]indole (**2a**)

A solution of **1** (2.14 g, 10.0 mmol) in ethanol (100 ml) was treated with acetaldehyde (0.46 ml, 10.0 mmol) and few drops of acetic acid. The mixture was heated under reflux for 2 h. The product that separated out on cooling, was filtered off, washed with ethanol and dried. It was recrystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (1.64 g, 61% yield), m.p. 272–275 °C.

IR (KBr): 3278 (NH) and 1603 cm^{-1} (C=N).

Table I. ^{1}H NMR spectra of the compounds **10a,c, 11a, b, d, e** in solutions of $CDCl_3$. Chemical shifts are given on (δ) scale and coupling constants in Hz.

Assignment	Compounds		Assignment	Compounds			
	10a	**10c**		**11a**	**11b**	**11d**	**11e**
OAc	1.98(s)	2.03(s)	2OAc	1.98(s)	1.95(s)	2.03(s)	2.08(s)
OAc	2.00(s)	2.04(s)	OAc	2.05(s)	2.00(s)	2.18(s)	2.20(s)
OAc	2.09(s)	2.10(s)	OAc	2.20(s)	2.10(s)	2.22(s)	2.25(s)
OAc	2.11(s)	2.12(s)	OAc	2.23(s)	2.20(s)		
OAc							
NAc	2.48(s)	2.56(s)	CMe	2.55(s)	2.59(s)	2.56(s)	2.58(s)
CMe	2.52(s)	2.59(s)	NAc	3.10(s)	3.14(s)	3.11(s)	3.11(s)
NAc	3.00(s)	3.04(s)					
H-6′	3.85(dd)	4.08(dd)	H-5′	3.99(dd)	4.05(dd)		
($J_{5,6'}$)	(7.6)	(5.2)	($J_{4,5'}$)	(7.6)			
($J_{6,6'}$)	(11.6)	(12.6)	($J_{5,5'}$)	(11.5)			
H-6	4.25(dd)	4.28(dd)	H-5	3.35(dd)	4.19(dd)		
($J_{5,6}$)	(5.1)	(2.7)	($J_{4,5}$)	(4.9)			
H-5	↑	5.12(t)	H-4′			4.28(dd)	4.29(dd)
($J_{4,5}$)	·		($J_{3,4'}$)			(5.1)	(5.1)
	·		($J_{4,4'}$)			(12.5)	(12.5)
H-4	5.49(m)	5.38(d)	H-4	5.45(m)	5.18(m)	4.39(dd)	4.39(dd)
($J_{4,5}$)	·	(2.3)	($J_{3,4}$)			(2.3)	(2.6)
	·						
H-3	↓	5.47(dd)	H-3	5.64(dd)	5.29(dd)	5.53(m)	5.51(m)
($J_{3,4}$)		(2.3)	($J_{3,4}$)	(2.1)			
H-2	5.60(t)	5.51(dd)	H-2	5.78(dd)	6.28(dd)	5.81(dd)	5.78(dd)
($J_{2,3}$)		(5.1)	($J_{2,3}$)	(9.9)		(8.5)	(8.4)
H-1	6.51(d)	6.57(d)	H-1	6.60(d)	6.59(d)	6.74(d)	6.75(d)
($J_{1,2}$)	(3.5)	(5.9)	($J_{1,2}$)	(2.2)		(3.1)	(3.2)
Protons on the heterocyclic ring							
H-6	8.57(d)	8.59(d)		8.58(d)	8.58(d)	8.56(d)	8.59(d)
($J_{6,7}$)	(8.7)	(8.6)		(8.2)	(8.6)	(8.6)	(8.8)
H-7	7.59(d)	7.61(d)		7.60(d)	7.62(d)	7.61(d)	7.62(d)
H-9	8.28(s)	8.30(s)		8.05(s)	8.02(s)	8.05(s)	8.08(s)

Analysis for $C_{12}H_{12}N_6$ (240.3)
Calcd C 60.0 H 5.0 N 35.0%,
Found C 59.9 H 5.1 N 35.2%.

3-Benzylidenehydrazino-8-methyl-5H-1,2,4-triazino[5,6-b]indole (**2b**)

To a solution of **1** (2.14 g, 10.0 mmol) in ethanol (100 ml), benzaldehyde (1.0 ml, 10.0 mmol) and two drops of acetic acid were added and the reaction mixture was processed as above. The product was recrystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (1.50 g, 50% yield), m.p. 300 °C. IR (KBr): 3326, 3100 (NH) and 1616 cm^{-1} (C=N and C=C).

Analysis for $C_{17}H_{14}N_6$ (302.3)
Calcd C 67.5 H 4.7 N 27.8%,
Found C 67.3 H 4.8 N 28.0%.

3-(p-Nitrobenzylidenehydrazino)-8-methyl-5H-1,2,4-triazino[5,6-b]indole (**2c**)

A solution of **1** (2.14 g, 10.0 mmol) in ethanol (100 ml) was treated with a solution of *p*-nitrobenzaldehyde (1.5 g,10.0 mmol) in ethanol (25 ml) and few drops of acetic acid. The mixture was processed as above. The product was recrystallized from ethanol/*N,N*-dimethylformamide as orange crystals (1.6 g, 46% yield), m.p. > 350 °C. IR (KBr): 3211 and 3100 (NH) and 1597 cm^{-1} (C=N and C=C).

Analysis for $C_{17}H_{13}N_7O_2$ (347.3)
Calcd C 58.8 H 3.8 N 28.2%,
Found C 58.6 H 3.9 N 28.2%.

Table II. ^{13}C NMR spectral data for the compounds **8a, 10a,c, 11a,c.**

Assignment	Compounds				
	8a	**10a**	**10c**	**11a**	**11c**
Carbon of the sugar part					
C-2	149.42	140.01	139.34	68.52	68.02
C-2	72.84	70.40	70.26	68.38	67.77
C-2	70.64	68.78	68.54	68.21	63.93
C-2	70.14	68.08	61.83	64.21	62.03
C-2	69.45	62.53		62.49	
C-2	63.44				
Carbons of the heterocyclic rings					
C-1				136.57	148.02
C-3	159.9	154.20	157.30		
C-6	112.20	118.08	117.63	123.15	135.45
C-7	120.34	122.73	122.25	123.15	123.34
C-8	119.25	119.35	120.70	123.15	132.63
C-9	120.34	122.73	121.10	118.80	116.01
C-3a				136.57	148.13
C-4a	138.30	149.20	156.40		
C-5a	130.20	135.22	134.70	136.57	141.89
C-5b				118.80	113.29
C-9a	112.20	118.08	118.90	136.57	140.86
C-9b	131.26	136.93	136.40		
C-10a				136.57	144.01
Miscellanous					
XOAc		21.88	20.77	21.23	20.74
		21.09	20.66	21.09	20.68
				20.99	20.63
					20.50
XNAc		28.21	27.64	28.51	21.19
		22.37	21.87		
XCO		177.62	169.76	177.62	170.51
		170.68			170.13
		170.15			170.01
					169.73
C-Me	21.28	21.18	21.37	21.26	21.19

1,7-Dimethyl-10H-1,2,4-triazolo[3',4':3,4]-[1,2,4]triazino[5,6-b]indole (*3a*)

A 2 M solution of iron(III) chloride in ethanol (1.0 ml) was added dropwise to a boiling solution of **2a** (2.4 g, 10.0 mmol) in ethanol (100 ml). Heating was continued for 15 min, and the mixture was kept overnight at room temperature and then concentrated under reduced pressure to about 20 ml. The product that separated out, was filtered, washed repeatedly with water and recrystallized from ethanol/*N,N*-dimethylformamide (1.6 g, 67% yield), m.p. > 340 °C. IR (KBr): 1606 cm^{-1} (C=N); ^1H NMR (DMSO-d_6) δ = 2.45 and 2.74 (2 s, 6 H, 2 Me), 7.33 (d, 1 H, $J_{8,9}$ 8.5 Hz, H-8), 7.53 (d, 1 H, H-9), 7.96 (s, 1 H, H-6) and 11.93 (brs, 1 H, NH), ^{13}C NMR δ_c = 9.6 and 20.5 (2 Me), 112 (C-9 and C-5b), 116.2 (C-7), 122.8 (C-6 and C-8), 127.30 (C-9a), 134.5 (C-5a), 140.3 (C-10a), 143.4 (C-3a) and 144.0 (C-1).

Analysis for $C_{12}H_{10}N_6$ (238.3)
Calcd C 60.5 H 4.2 N 35.3%,
Found C 60.3 H 4.2 N 35.0%.

7-Methyl-1-phenyl-10H-1,2,4-triazolo-[3',4':3,4][1,2,4]triazino[5,6-b]indole (**3b**)

A 2 M solution of iron(III) chloride in ethanol (1.0 ml) was added dropwise to a boiling solution of **2b** (3.0 g, 10.0 mmol) in ethanol (100 ml). The reaction mixture was processed as before. The product was crystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (2.20 g, 74% yield), m.p. > 300 °C. IR (KBr): 1619 cm^{-1} (C=N).

Analysis for $C_{17}H_{12}N_6$ (300.3)
Calcd C 68.0 H 4.0 N 28.0%,
Found C 67.8 H 3.9 N 28.0%.

3,7-Dimethyl-10H-1,2,4-triazolo-[4',3':2,3][1,2,4]triazino[5,6-b]indole (**4a**)

(a) A solution of **1** (0.2 g, 1.0 mmol) in glacial acetic acid (20 ml) was boiled under reflux for 8 h. The yellow product that separated out on cooling, was filtered, washed with ethanol and recrystallized from ethanol/*N,N*-dimethylformamide (0.16 g, 73% yield), m.p. 320–321 °C. IR (KBr): 3044 (NH) and 1612 cm^{-1} (C=N). ^1H NMR (DMSO-d_6) δ = 2.46 and 2.48 (2 s, 6 H, 2 Me), 7.25 (d, 1 H, $J_{8,9}$ 8.3 Hz, H-8), 7.48 (d, 1 H, H-9), 7.94 (s, 1 H, H-6) and 11.67 (brs, 1 H, NH); ^{13}C NMR δ_c = 9.55 and 20.45 (2 Me), 112.22 (C-9 and C-5b), 116.33 (C-7), 122.69 (C-6,8), 131.48 (C-8a), 134.38 (C-5a), 140.0 (C-10a), 143.80 (C-11a) and 144.09 (C-3).

Analysis for $C_{12}H_{10}N_6$ (238.3)
Calcd C 60.1 H 4.2 N 35.3%,
Found C 60.1 H 4.2 N 35.1%.

(b) A solution of 5-methylisatin (**5**) (0.16 g, 1.0 mmol), 4,5-diamino-3- methyl-1,2,4-triazole hydrochloride (**6**) (0.15 g, 1.0 mmol) and sodium acetate (0.08 g, 1.0 mmol) in a mixture of ethanol (20 ml) and water (5 ml) was heated under reflux for 1 h. Acetic acid (0.2 ml) was added, and the reflux was continued for 2 h. The product that separated out on cooling, was filtered, washed with ethanol and recrystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (0.18 g, 75%), m.p. 320–322 °C. It was found to be identical with the product obtained from method (a).

10-Acetyl-1,7-dimethyl-1,2,4-triazolo-[3',4':3,4][1,2,4]triazino[5,6-b]indole (**7a**)

A cold solution of **3a** (0.5 g, 2.1 mmol) in dry pyridine (5 ml) was treated with acetic anhydride (5 ml) and the mixture was then kept overnight at room temperature with occasional shaking. It was poured onto crushed ice and the product that separated was filtered off, washed repeatedly with water and dried. It was recrystallized from ethanol as yellow needles (0.45 g, 77% yield), m.p. 270–272 °C. IR (KBr): 1724 (NCO) and 1610 cm^{-1} (C=N and C=C).

Analysis for $C_{14}H_{12}N_6O$ (280.3)
Calcd C 60.0 H 4.3 N 30.0%,
Found C 59.9 H 4.1 N 29.9%.

10-Acetyl-7-methyl-1-phenyl-1,2,4-triazolo-[3',4':3,4][1,2,4]triazino[5,6-b]-indole (**7b**)

A cold solution of **3b** (0.5 g, 1.7 mmol) in dry pyridine (5 ml) was treated with acetic anhydride (5 ml) and the reaction mixture was processed as above. The product was crystallized from ethanol as yellow needles (0.3 g, 62% yield), m.p. 288–290 °C. IR (KBr): 1717 (NCO) and 1611 cm^{-1} (C=N and C=C).

Analysis for $C_{19}H_{14}N_6O$ (342.4)
Calcd C 66.7 H 4.1 N 24.6%,
Found C 66.8 H 4.3 N 24.2%.

8-Methyl-3-polyhydroxyalkylidenehydrazino-5H-1,2,4-triazino[5,6-b]indole (**8a-8 g**)

To a solution of **1** (2.14 g, 10.0 mmol) in ethanol (100 ml) was added the solution of the respective sugar (10.0 mmol) in water (5 ml) and few drops of acetic acid. The mixture was heated under reflux for 2 h. The product that separated out on cooling, was collected by filteration, washed with ethanol and dried. The yellow product was recrystallized from ethanol/*N,N*-dimethylformamide (Table III).

1-(Polyhydroxyalkyl)-7-methyl-10H-1,2,4-triazolo-[3',4':3,4][1,2,4]triazino[5,6-b]indole (**9a-9e**)

A 2 M solution of iron(III) chloride in ethanol (1.0 ml) was added dropwise to a boiling solution of **8** (2.5 mmol) in ethanol (100 ml). The reaction mixture was processed as before. The product was recrystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (Table IV).

5-Acetyl-3-[N-acetyl-N'-(polyacetoxyalkylidene)-hydrazino-8-methyl-1,2,4-triazino[5,6-b]indole (**10a-10e**)

A cold solution of **8** (1.5 mmol) in dry pyridine (5 ml) was treated with acetic anhydride (5 ml) and the mixture was kept 3 days at room temperature with occasional shaking. It was poured onto crushed ice and the product was filtered, washed

Table III. Elemental analysis and IR spectral data of the compounds **8a–g.**

Compound	Yield [%]	M.p. [°C]	Molcular formula		Analysis [%] C	H	N	IR (KBr [cm^{-1}]) OH & NH	C=N/C=C
8a	75	190–192	$C_{16}H_{20}N_6O_5$	Calcd	51.1	5.4	22.3	3346,3205	1612
				Found	51.4	5.6	22.0		
8b	65	228–230	$C_{16}H_{20}N_6O_5$	Calcd	51.1	5.4	22.3	3373,3216,3161	1615
				Found	51.2	5.0	22.1		
8c	62	241–243	$C_{16}H_{20}N_6O_5$	Calcd	51.1	5.4	22.3	3358,3279,3203	1609
				Found	51.0	5.8	22.3		
8d	64	193–195	$C_{15}H_{18}N_6O_4$	Calcd	52.0	5.2	24.3	3388,3225	1612
				Found	52.3	5.7	24.0		
8e	63	187–189	$C_{15}H_{18}N_6O_4$	Calcd	52.0	5.2	24.3	3364,3220	1612
				Found	52.3	5.1	24.2		
8f	58	173–175	$C_{15}H_{18}N_6O_4$	Calcd	52.0	5.2	24.3	3361,3221	1615
				Found	52.5	5.5	24.3		
8g	60	183–186	$C_{15}H_{18}N_6O_4$	Calcd	52.0	5.2	24.3	3382,3207	1611
				Found	52.3	4.9	24.4		

Table IV. Elemental analysis and IR spectral data of the compounds **9a–e.**

Compound	Yield [%]	M.p. [°C]	Molcular formula		Analysis [%] C	H	N	IR (KBr [cm^{-1}]) OH & NH	C=N/C=C
9a	56	264–266	$C_{16}H_{18}N_6O_5$	Calcd	51.3	4.9	22.5	3375,3260	1621
				Found	51.6	4.4	22.0		
9b	54	243–245	$C_{16}H_{18}N_6O_5$	Calcd	51.3	4.9	22.5	3385,3255	1621
				Found	51.1	5.0	22.4		
9c	52	268–270	$C_{16}H_{18}N_6O_5$	Calcd	51.3	4.9	22.5	3360,3203	1617
				Found	51.0	5.1	22.4		
9d	45	276–278	$C_{15}H_{16}N_6O_4$	Calcd	52.3	4.7	24.4	3336,3205	1622
				Found	52.6	5.1	24.2		
9e	48	244–246	$C_{15}H_{16}N_6O_4$	Calcd	52.3	4.7	24.4	3329,3207	1622
				Found	52.2	4.6	24.4		

with water, dried and recrystallized from ethanol as colourless needles (Table V).

10-Acetyl-7-methyl-1-(polyacetoxyalkyl)-1,2,4-triazolo[3',4':3,4][1,2,4]triazino[5,6-b]indole (**11a-11e**)

A cold solution of **9** (1.3 mmol) in dry pyridine (5 ml) was treated with acetic anhydride (5 ml) and the mixture was processed as before. It was recrystallized from ethanol as yellow needles (Table VI).

3-(2-Oxoethylidenehydrazino)-8-methyl-5H-1,2,4-triazino[5,6-b]indole (**12**)

A suspension of **8a** (3.76 g, 10.0 mmol) in water (150 ml) was treated with a solution of sodium metaperiodate (8.6 g, 40.0 mmol) in water (100 ml). The mixture was stirred for 5 h, and kept overnight at room temperature. The product was filtered, washed with water, sodium thiosulphate and dried. It was recrystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (1.60 g, 63% yield), m.p. 257–259 °C. IR (KBr): 3213 and 3128 (NH), 1689 (CHO) and 1614 cm^{-1} (C=N and C=C).

Analysis for $C_{12}H_{10}N_6O$ (254.3)
Calcd C 56.7 H 4.0 N 33.1%,
Found C 56.7 H 3.7 N 33.0%.

Glyoxal-1-(8-methyl-5H-1,2,4-triazino[5,6-b]indol-3-yl)hydrazone-2-oxime (**13**)

A solution of **12** (0.25 g, 1.0 mmol), hydroxylamine hydrochloride (0.07 g, 1.0 mmol) and sodium acetate (0.08 g, 1.0 mmol) in a mixture of ethanol (25 ml) and water (5 ml) was heated under reflux for 1 h. The product that separated out on cooling, was filtered, washed with ethanol and dried. It was recrystallized from ethanol/*N,N*-di-

Table V. Elemental analysis and IR spectral data of the compounds **10a–e.**

Compound	Yield [%]	M.p. [°C]	Molcular formula		Analysis [%] C	H	N	IR (KBr [cm^{-1}]) OCO	NCO	C=N/C=C
10a	80	196–198	$C_{30}H_{34}N_6O_{12}$	Calcd	53.7	5.1	12.5	1753	1702	1635,1603
				Found	54.0	5.2	12.5			
10b	74	204–206	$C_{30}H_{34}N_6O_{12}$	Calcd	53.7	5.1	12.5	1755	1725(sh)	1628,1600
				Found	53.9	5.2	12.4			
10c	72	176–178	$C_{30}H_{34}N_6O_{12}$	Calcd	53.7	5.1	12.5	1752	1700(sh)	1628,1602
				Found	53.4	4.7	12.6			
10d	68	160–162	$C_{27}H_{30}N_6O_{10}$	Calcd	54.2	5.1	14.0	1751	1705(sh)	1627
				Found	53.7	4.8	13.7			
10e	70	164–166	$C_{27}H_{30}N_6O_{10}$	Calcd	54.2	5.1	14.0	1745	1715(sh)	1630,1600
				Found	53.9	5.0	13.7			

Table VI. Elemental analysis and IR spectral data of the compounds **11a–e.**

Compound	Yield [%]	M.p. [°C]	Molcular formula		Analysis [%] C	H	N	IR (KBr [cm^{-1}]) OCO & NCO	C=N/C=C
11a	82	210–212	$C_{28}H_{30}N_6O_{11}$	Calcd	53.7	4.8	13.4	1753	1612
				Found	53.9	5.0	13.5		
11b	78	202–204	$C_{28}H_{30}N_6O_{11}$	Calcd	53.7	4.8	13.4	1747	1614
				Found	53.6	4.9	13.1		
11c	84	218–220	$C_{28}H_{30}N_6O_{11}$	Calcd	53.7	4.8	13.4	1747	1614
				Found	53.3	4.9	13.5		
11d	72	207–209	$C_{25}H_{26}N_6O_9$	Calcd	54.2	4.7	15.2	1756	1611
				Found	53.9	4.8	15.3		
11e	65	222–224	$C_{25}H_{26}N_6O_9$	Calcd	54.2	4.7	15.2	1757	1612
				Found	54.1	4.7	15.4		

methylformamide as yellow crystals (0.17 g, 64% yield), m.p. 294–296 °C. IR (KBr): 3338 (OH), 3210, 3114 (NH) and 1619 cm^{-1} (C=N and C=C).

Analysis for $C_{12}H_{11}N_7O$ (269.3)
Calcd C 53.5 H 4.1 N 36.4%,
Found C 53.4 H 4.3 N 36.3%.

Glyoxal bis(8-methyl-5H-1,2,4-triazino[5,6-b]-indol-3-yl)hydrazone (**14**)

To a solution of **12** (0.25 g, 1.0 mmol) in ethanol (50 ml), a solution of **1** (0.2 g, 1.0 mmol) in ethanol (20 ml) and few drops of acetic acid were added. The mixture was heated under reflux for 1 h. The product that separated out on cooling, was filtered, washed with ethanol and dried. It was recrystallized from ethanol/ *N,N*-dimethylformamide as yellow crystals (0.16 g, 64% yield), m.p. 282–284 °C. IR (KBr): 3275, 3215, 3160, 3110 (NH), and 1604 cm^{-1} (C=N and C=C).

Analysis for $C_{22}H_{18}N_{12}$ (450.5)
Calcd C 58.7 H 4.0 N 37.3%,
Found C 58.5 H 3.6 N 37.2%.

7-Methyl-10H-1,2,4-triazolo[3',4':3,4]-[1,2,4]triazino[5,6-b]indole-1-carbaldehyde (**15**)

A suspension of **9a** (1.9 g, 5.0 mmol) in water (100 ml) was treated with a solution of sodium metaperiodate (4.3 g, 20.0 mmol) in water (50 ml). The mixture was then processed as above and the product was recrystallized from ethanol/*N,N*-dimethylformamide as yellow crystals (0.95 g, 50% yield), m.p. > 300 °C. IR (KBr): 3325 (NH), 1694 (CHO) and 1620 cm^{-1} (C=N and C=C).

Analysis for $C_{12}H_8N_6O$ (252.2)
Calcd C 57.1 H 3.2 N 33.3%,
Found C 57.2 H 3.3 N 33.2%.

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Satz und Druck: Allgäuer Zeitungsverlag GmbH, Kempten