Regioisomeric Formation of Acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazines and Their Acyclic C-Nucleoside Analogues

Nagwa RASHED, Mahmoud SHOUKRY, and El Sayed H. EL ASHRY*
Chemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt
(Received March 15, 1993)

The oxidative cyclization of the ethylidene derivative of 3-hydrazinoacenaphtho[1,2-*e*][1,2,4]triazine (**2**) gave regioselectively the angular isomer 1-methylacenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazine (**5**). Its linear isomer 10-methylacenaphtho[1,2-*e*][1,2,4]triazolo[4,3-*b*][1,2,4]triazine (**4**) was synthesized by the condensation of acenaphthenequinone (**6**) with 3,4-diamino-5-methyl-4*H*-1,2,4-triazole. Condensation of **2** with a number of monosaccharides afforded the respective hydrazones **9** whose oxidative cyclization gave the corresponding 1-(polyhydroxyalkyl)acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazine (**10**). Acetylation of **9** and **10** gave 3-[*N*-acetyl-*N'*-(polyacetoxyalkylidene)hydrazino]acenaphtho[1,2-*e*][1,2,4]triazine (**11**) and 1-(polyacetoxyalkyl)-acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazine (**13**) respectively. Periodate oxidation of **9e** gave 3-(2-oxo-ethylidenehydrazino)acenaphtho[1,2-*e*][1,2,4]triazine (**14**).

Among the polyazaindolizine series, the 1,2,4-triazolo[4,3-*b*][1,2,4]triazines and 1,2,4-triazolo[3,4-*c*][1,2,4]triazines are of interest in conjunction with our previous investigations on their fused ring systems with indole.[1,2] These two isomeric triazolotriazines may be formed from the cyclization of 3-hydrazino-1,2,4-triazines via their alkylidene or arylmethylene derivatives, depending on which nuclear nitrogen is involved in the cyclization step[3—17] based on their comparative nucleophilicity. Both isomers have been isolated but, however, from different substrates. The regioselectivity was found to be dependent on the substituent existing on the indole ring in the case of indolotriazine derivatives.[1,2]

The interest in biochemical properties of 1,2,4-triazines is high[18—23] because a number of 3,5-disubstituted 1,2,4-triazines represent aza analogues of pyrimidine bases.

Acenaphthenequinone was shown to be bactericidal and fungicidal to *Pythium ultimum*, *Alternaria solani*, *Sclerotinia americana*, and *Chactomium globosum*.[24] Some substituted acenaphthenequinones showed moderate fungistatic activity against *Trichophyton mentagrophytes*.[25] Acenaphthenequinone hydrogensulfite had a narcotic effect on mice and it inhibited the growth of transplanted tumors.[26] It has no estrogenic effect,[27] on ovariectomized rats.[27] The antihypoxic activity of **1** was studied in rats.[28] Amine derivatives of **1** had fungicidal activity and some were active against *Escherichia coli*.[29] The condensation product of **1** with 2,3-diaminopyrazine was used to provoke ataxia by lowering central nervous system activity.[30]

The goal of the present investigation is the synthesis of compounds compiling the above rings in a fused manner which it could be of potential biological properties. The respective C-nucleoside analogues are target molecules in this study owing to their great value from the biological point of view.[31—33] Moreover, it is interesting to explore the site of fusion in such ring systems.

Results and Discussion

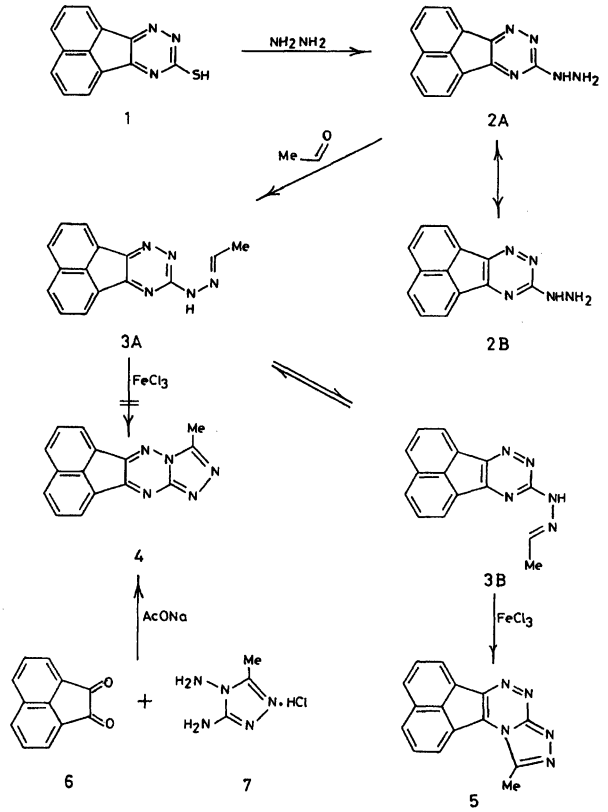
A model study for the cyclization has been done on the ethylidene derivative **3** of 3-hydrazinoacenaphtho-[1,2-*e*][1,2,4]triazine (**2**), which was prepared by condensation of **2** with acetaldehyde. Oxidative cyclization of **3** with iron(III) chloride gave a product whose structure could be assigned as one of the regioisomeric structures **4** or **5**. The selection of structure **5** for that product may be envisioned by an unequivocal synthesis of **4** by condensing the diaminotriazole **7** with acenaphthenequinone **6** (Scheme 1). The latter reaction would give only one isomer due to the symmetric nature of the quinone **6** whatever which amino group in **7** is the reactive one. The infrared spectra of **4** and **5** are different. The difference in their ^{1}H NMR spectra is reflected in the chemical shift of the methyl group.

Condensation of **2** with the monosaccharides D-galactose, D-glucose, D-mannose, D-arabinose, L-arabinose, D-ribose, and D-xylose, gave the hydrazones **9**. Subjection of these hydrazones **9** to the action of iron(III) chloride afforded the corresponding 1,2,4-triazolo[3,4-*c*][1,2,4]triazines (**10**). The selection of the angular structure **10** for these products was based on the above model study (Scheme 2).

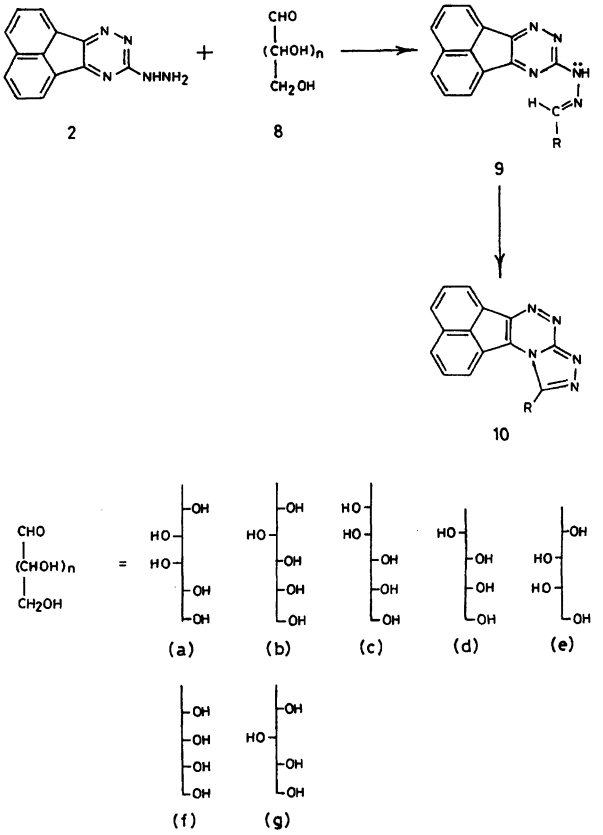
The cyclization may proceed by electrophilic attack[34] of the hard acid iron(III) on the hardest basic site of the hydrazone moiety followed by electrocyclization to cause dehydrogenation and formation of the triazole ring (Scheme 3).

Acetylation of **9** and **10** with acetic anhydride caused acetylation of their polyhydroxyalkylidene residues in addition to the hydrazone residues in case of compounds **9**.

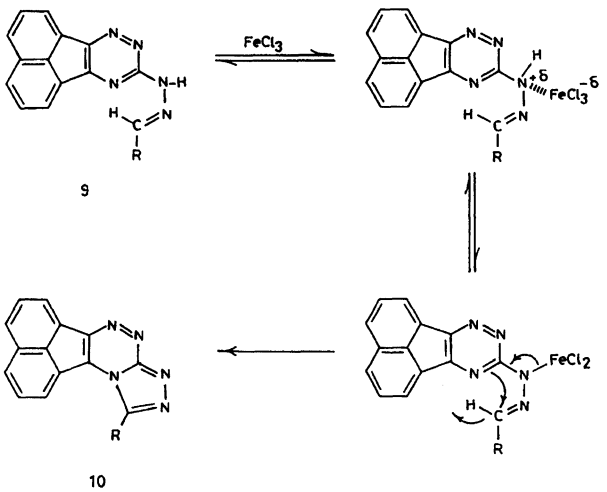
IR spectra of **9** showed absorption bands at 3369—3314 (OH), 3245—3215 (NH), and 1606—1589 cm^{-1} (C=N). The spectra of **10** showed absorption bands at 1617—1611 (C=N) and 3398—3265 cm^{-1} (OH). The acetyl derivatives **11** showed bands at 1700—1684 cm^{-1} (NAc) in addition to bands at 1753—1740 cm^{-1} (OAc),



Scheme 1.



Scheme 2.



Scheme 3.

whereas **13** showed only the presence of the latter absorption at 1756—1749 cm^{-1}.

The signals in the ^1H NMR spectrum of **11a** were assigned by decoupling technique. Thus, decoupling of the double doublet signal ($\delta=4.26$) of H-6 caused a change of the triplet ($\delta=5.28$) of H-5 to a doublet and the shape of the double doublet ($\delta=3.86$) of H-6′ was also changed. On the other hand, decoupling at H-5 caused a change of the two double doublets of H-6 and H-6′ to two doublets. Decoupling of the double doublet ($\delta=5.65$) of H-2 changed the doublet ($\delta=6.55$) of H-1 to a singlet and vise versa. However, these assignments did not give any indication whether the acetyl derivative had the tetracyclic structure **11** or the pentacyclic one **12** (Scheme 4). On the other hand, NOE experiments ruled out the pentacyclic structure, since there was no NOE observed between H-1 of D-galactose residue and H-5 of the aromatic system. This ruled out the possibility of the cyclic structure **12**. Moreover, the assignment of the signal of C-1 at $\delta_C=124.90$ was a further indication of the open form.

Assignments (Table 1) of the protons of the triazole **10a** were made by sequential decouplings. The values agreed with the structure. H-1 of the polyacetoxyalkyl part in **13a** appeared at a downfield region as much as H-1 in **11a**. The double doublet of H-1 of **10a** suffered from a downfield shift upon acetylation to **13a** confirming the assigned structure.

The ^{13}C NMR spectra (Table 2) of **10a**, **11a**, and **13a** have been studied. The spectra showed resonances in the high field region corresponding to the sugar carbons. The resonance at $\delta_C=124.90$ in **11a** moved to $\delta_C=149.76$ and 149.86 in **13a** and **10a**, respectively. The resonances of the heterocyclic ring carbons could be differentiated by the intensity and the stronger ones were assigned to carbons carrying a proton.

The acyclic nature of the polyhydroxyalkylidene residues of **9** was also examined by the oxidation of **9e** with sodium periodata to give the oxoethylidenehydrazino derivative **14** (Scheme 5).

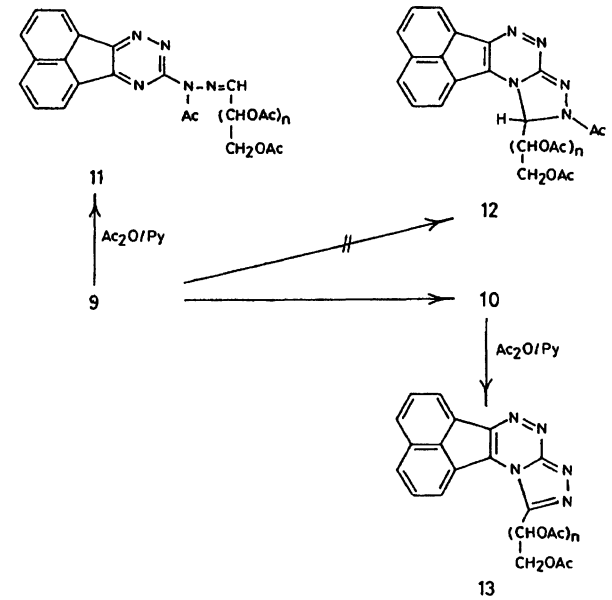
Table 1. ^{1}H NMR Spectra of Several Compounds in $CDCl_3$
Chemical Shifts are Given in δ and Coupling Constants in Hz are Given in Parentheses.

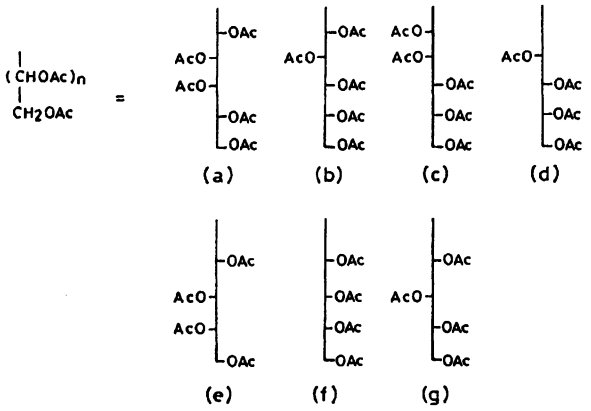
Assignment	Compound No.				Assignment	Compound No.			
	11a	**11d**	**11f**	**11g**		**10a**	**13a**	**13b**	**13c**
H-1	6.55(d)	6.44(d)	6.66(d)	6.62(d)	H-1	5.48(dd)	6.62(d)	6.59(d)	6.60(d)
($J_{1,2}$)	(3.51)	(3.0)	(3.75)	(4.5)	($J_{1,2}$)	(2.46)	(4.5)	(7.5)	(8.1)
H-2	5.65(dd)	5.58(t)		5.63(t)	H-2	4.20(dd)	5.70(dd)	6.19(dd)	6.18(d)
($J_{2,3}$)	(2.1)	(3.0)		(4.0)	($J_{2,3}$)	(2,32)	(9.6)		(9.0)
H-3		5.36(m)	5.48(m)		H-3	3.75(t)	5.82(dd)		5.78(d)
					($J_{3,4}$)	(5.54)	(2.5)		(7.8)
	5.45(m)			5.34(m)				5.25(m)	
H-4		5.16(m)			H-4	3.85(dd)	5.49(m)		5.19(m)
					H-4′				
H-5	5.28(t)	4.13(dd)	4.31(dd)	4.31(dd)	H-5		4.38(dd)		
($J_{4,5}$)	(6.7)	(4.5)	(3.0)	(3.0)	($J_{4,5}$)		(5.1)		
						3.45(m)		4.07(m)	4.18(m)
H-5′		3.93(dd)	3.96(dd)	4.09(dd)	H-5′		4.02(dd)		
($J_{4,5'}$)		(4.5)	(6.0)	(4.5)	($J_{4,5'}$)		(7.3)		
($J_{5,5'}$)		(11.2)	(11.1)	(11.0)	($J_{5,5'}$)		(11.6)		
H-6	4.26(dd)								
($J_{5,6}$)	(5.1)								
H-6′	3.86(dd)								
($J_{5,6'}$)	(7.4)								
($J_{6,6'}$)	(11.7)								
NAc	2.56(s)	2.42(s)	2.57(s)	2.57(s)					
					OH_2	5.57(d)			
					($J_{H_2OH_2}$)	(7.8)			
					OH_3	4.82(d)			
					($J_{H_3OH_3}$)	(6.3)			
					OH_4	4.37(d)			
					($J_{H_4OH_4}$)	(7.8)			
					OH_5	4.33(d)			
					($J_{H_5OH_5}$)	(6.3)			
					OH_6	4.51(t)			
					($J_{H_6OH_6}$)	(5.0)			
OAc	2.01	1.83	1.99	1.82	OAc		2.01	1.89	2.02
	2.03	1.93	2.11	2.00			2.04	2.01	2.05
	2.08			2.06			2.12	2.10	2.21
	2.10			2.10			2.41		
	2.15						2.43		
Aromatic protons									
	7.92(dd)	7.72(t)	7.87(t)	7.79(t)		8.22(m)	7.79(2dd)	7.83(m)	7.88(m)
	8.24(d)	8.13(t)	8.26(t)	8.18(t)		7.82(m)	8.13(d)	8.23(d)	8.19(d)
	(8.2)	8.38(t)	8.48(t)	8.41(t)			(8.3)	8.34(2d)	8.41(2d)
	8.31(d)						8.20(d)		
	(8.2)						(7.0)		
	8.47(d)						8.28(d)		
	(7.1)						(7.0)		
	8.58(d)								
	(7.0)								

Experimental

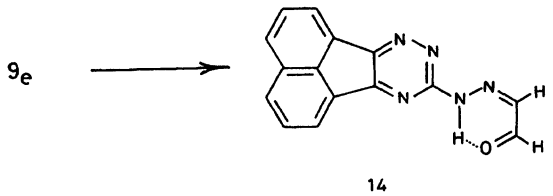
Melting points were determined on a Meltemp apparatus and are uncorrected. IR spectra were recorded with a Unicam SP 1025 spectrometer. ^{1}H NMR spectra were determined with a Varian EM-390 spectrometer at 90 MHz except for compounds **10a**, **11a**, and **13a** which were measured with a Bruker spectrometer 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). Microanalyses were performed in the unit of Microanalysis at the University of Cairo.

3-(Ethylidenehydrazino)acenaphtho[1,2-*e*][1,2,4]-triazine (3). A solution of **2** (1.0 g, 4.26 mmol) in ethanol (160 ml) was treated with acetaldehyde (0.5 ml, 8.94 mmol) and the mixture was heated under reflux for 2 h. The product that separated out was recrystallized from ethanol to give **3** as yellow crystals (0.9 g, 85%), mp 218—220 °C;





Scheme 4.



Scheme 5.

ν_{max} (KBr) 3215 (NH) and 1604 cm^{-1} (C=N).

Found: C, 68.7; H, 4.3; N, 26.6%. Calcd for $C_{15}H_{11}N_5$: C, 69.0; H, 4.2; N, 26.8%.

1-Methylacenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazine (5). A solution of **3** (1.0 g, 3.83 mmol) in ethanol (50 ml) was heated till boiling, and then a 2 M solution (1 M=1 mol dm^{-3}) of iron(III) chloride in ethanol (1.0 ml) was added. The mixture was boiled for 10 min, and the resulting solution was left overnight at room temperature. The product that separated out was recrystallized from ethanol to give pale yellow crystals (0.6 g, 50%), mp 198 °C; ν_{max} (KBr) 1597 cm^{-1} (C=N).

Found: C, 69.7; H, 3.7; N, 26.8%. Calcd for $C_{15}H_9N_5$: C, 69.5; H, 3.5; N, 27.0%.

10-Methylacenaphtho[1,2-*e*][1,2,4]triazolo[4,3-*b*][1,2,4]triazine (4). A mixture of solutions of 3,4-diamino-5-methyl-4*H*-1,2,4-triazole hydrochloride (**7**) (0.21 g, 1.36 mmol) in ethanol (5 ml), sodium acetate (0.11 g, 1.36 mmol) in water (2 ml), acenaphthenequinone (0.25 g, 1.36 mmol) in ethanol (30 ml), and two drops of acetic acid was heated under reflux for 1.5 h. The product was recrystallized from a mixture of ethanol and *N*,*N*-dimethylformamide to give yellowish brown crystals (0.8 g, 71%), mp 236—238 °C; ν_{max} (KBr) 1602 cm^{-1} (C=N).

Found: C, 69.8; H, 3.7; N, 27.0%. Calcd for $C_{15}H_9N_5$: C, 69.5; H, 3.5; N, 27.0%.

(Acenaphtho[1,2-*e*][1,2,4]triazin-3-yl)hydrazones of Aldoses (9). To a solution of **2** (1.5 g, 6.38 mmol) in ethanol (100 ml) was added a solution of the respective aldoses **8** (6.38 mmol) and few drops of acetic acid. The mixture was heated under reflux for 1.5 h. The solid, which separated out on cooling, was filtered, washed with water and ethanol and dried. The yellow product was crystal-

Table 2. ^{13}C NMR Spectral Data of Compounds **10a**, **11a**, and **13a**
Chemical Shifts are Given in δ Scale.

Assignment	Compound No.		
	10a	**11a**	**13a**
Carbons of the sugar part			
C-1		124.90	
C-2	71.29	70.00	67.83
C-3	69.88	68.20	67.83
C-4	65.15	67.57	67.64
C-5	69.31	67.57	63.62
C-6	62.96	61.95	63.82
Carbons of the heterocyclic rings			
Carbons with protons			
	129.57	139.16	129.92
	128.38	131.18	128.35
	122.96	126.40	123.16
	122.08	129.04	122.37
	129.01	129.22	128.70
	130.33	133.31	130.74
Carbons without protons			
	149.86	160.00	149.76
	155.09	156.24	155.86
	147.35	127.94	143.72
	131.19	134.81	138.88
	129.21	129.90	129.18
	126.35	128.51	126.16
	137.98	156.12	131.37
	149.02		147.95
Miscellaneous			
XOAc		20.51	20.33
		20.51	20.33
		20.58	20.45
		20.58	20.52
		20.63	20.57
NAc		21.78	
XCO		169.38	169.49
		169.54	169.65
		169.63	169.78
		170.10	170.07
		170.34	170.27
		172.84	

Table 3. Elemental Analysis and IR Spectral Data of (Acenaphtho[1,2-*e*][1,2,4]triazin-3-yl)hydrazones of Aldoses (**9**)

Compound	Yield	Mp	Molecular		Analysis/%			ν_{max}(KBr)/cm^{-1}		
	%	°C	formula		C	H	N	OH	NH	C=N
9a	80	179—181	$C_{19}H_{19}N_5O_5$	Calcd	57.4	4.8	17.6	3347	3217	1600
				Found	57.2	4.7	17.5			
9b	75	185—187	$C_{19}H_{19}N_5O_5$	Calcd	57.4	4.8	17.6	3314	3239	1589
				Found	57.6	4.6	17.3			
9c	80	193—195	$C_{19}H_{19}N_5O_5$	Calcd	57.4	4.8	17.6	3361	3215	1606
				Found	57.3	4.9	17.4			
9d	70	180—182	$C_{18}H_{17}N_5O_4$	Calcd	58.9	4.7	19.1	3355	3225	1603
				Found	59.0	4.5	19.0			
9e	75	172—174	$C_{18}H_{17}N_5O_4$	Calcd	58.9	4.7	19.1	3348	3239	1605
				Found	58.5	4.4	19.5			
9f	80	168—170	$C_{18}H_{17}N_5O_4$	Calcd	58.9	4.6	19.1	3341	3227	1602
				Found	59.3	4.7	18.7			
9g	70	212—213	$C_{18}H_{17}N_5O_4$	Calcd	58.9	4.7	19.1	3369	3245	1600
				Found	59.2	4.6	19.3			

Table 4. Elemental Analysis and IR Spectral Data of 1-(Polyhydroxyalkyl)acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazines (**10**)

Compound	Yield	Mp	Molecular		Analysis/%			ν_{max}(KBr)/cm^{-1}	
	%	°C	formula		C	H	N	OH	C=N
10a	75	229—233	$C_{19}H_{17}N_5O_5$	Calcd	57.7	4.3	17.7	3328	1614
				Found	57.5	4.0	17.5		
10b	50	240—241	$C_{19}H_{17}N_5O_5$	Calcd	57.7	4.3	17.7	3304	1616
				Found	57.5	4.0	17.5		
10c	65	263—265	$C_{19}H_{17}N_5O_5$	Calcd	57.7	4.3	17.7	3347	1617
				Found	57.5	4.6	17.3		
10d	70	223—225	$C_{18}H_{15}N_5O_4$	Calcd	59.2	4.1	19.2	3350	1613
				Found	59.6	4.3	19.2		
10e	70	189—191	$C_{18}H_{15}N_5O_4$	Calcd	59.2	4.1	19.2	3374	1611
				Found	59.5	4.4	19.4		
10f	60	239—240	$C_{18}H_{15}N_5O_4$	Calcd	59.2	4.1	19.2	3398	1612
				Found	59.0	3.8	19.5		
10g	50	225—227	$C_{18}H_{15}N_5O_4$	Calcd	59.2	4.1	19.2	3265	1611
				Found	59.5	3.7	19.0		

Table 5. Elemental Analysis and IR Spectral Data of 3-[*N*-Acetyl-*N'*-(polyacetoxyalkylidene)hydrazino]acenaphtho[1,2-*e*][1,2,4]triazines (**11**)

Compound	Yield	Mp	Molecular		Analysis/%			ν_{max}(KBr)/cm^{-1}		
	%	°C	formula		C	H	N	OCO	NCO	C=N
11a	70	199—200	$C_{31}H_{31}N_5O_{11}$	Calcd	57.3	4.8	10.8	1749	1697	1616
				Found	57.4	4.7	10.6			
11b	55	110—112	$C_{31}H_{31}N_5O_{11}$	Calcd	57.3	4.8	10.8	1753	1699	1616
				Found	57.1	4.8	10.5			
11c	50	116—118	$C_{31}H_{31}N_5O_{11}$	Calcd	57.3	4.8	10.8	1749	1700	1616
				Found	57.0	4.8	10.9			
11d	75	210—212	$C_{28}H_{27}N_5O_9$	Calcd	58.2	4.7	12.1	1749	1695	1614
				Found	58.3	4.7	11.7			
11e	75	206—208	$C_{28}H_{27}N_5O_9$	Calcd	58.2	4.7	12.1	1740	1698	1613
				Found	57.9	4.6	12.0			
11f	70	169—170	$C_{28}H_{27}N_5O_9$	Calcd	58.2	4.7	12.1	1746	1693	1614
				Found	58.4	4.4	11.8			
11g	50	108—109	$C_{28}H_{27}N_5O_9$	Calcd	58.2	4.7	12.1	1745	1684	1614
				Found	58.0	4.5	12.0			

Table 6. Elemental Analysis and IR Spectral Data of 1-(Polyacetoxyalkyl)acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazines (**13**)

Compound	Yield	Mp	Molecular		Analysis/%			ν_{max}(KBr)/cm^{-1}	
	%	°C	formula		C	H	N	OCO	C=N
13a	75	202—203	$C_{29}H_{27}N_5O_{10}$	Calcd	57.5	4.5	11.6	1753	1617
				Found	57.8	4.5	12.0		
13b	75	190—191	$C_{29}H_{27}N_5O_{10}$	Calcd	57.5	4.5	11.6	1754	1616
				Found	57.2	4.6	11.3		
13c	70	197—199	$C_{29}H_{27}N_5O_{10}$	Calcd	57.5	4.5	11.6	1756	1615
				Found	57.6	4.7	12.0		
13d	75	208—210	$C_{26}H_{23}N_5O_8$	Calcd	58.5	4.4	13.1	1749	1614
				Found	58.7	4.5	13.3		
13e	70	175—177	$C_{26}H_{23}N_5O_8$	Calcd	58.5	4.4	13.1	1751	1616
				Found	58.7	4.3	13.5		
13f	75	120—122	$C_{26}H_{23}N_5O_8$	Calcd	58.5	4.4	13.1	1750	1615
				Found	58.9	4.2	12.9		

lized from a mixture of ethanol and *N,N*-dimethylformamide (Table 3).

1-(Polyhydroxyalkyl)acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazine (10). A 2 M solution of iron(III) chloride in ethanol (1.0 ml) was added dropwise to a boiling solution of **9** (1.0 g) in ethanol (150 ml). Heating was continued for 10 min, and the mixture was then kept overnight at room temperature. The pale yellow precipitates were filtered and then washed with water and recrystallized from a mixture of ethanol and *N,N*-dimethylformamide (Table 4).

3-[*N*-Acetyl-*N'*-(polyacetoxyalkylidene)hydrazino]acenaphtho[1,2-*e*][1,2,4]triazine (11). A cold solution of **9** (0.5 g) in dry pyridine (5.0 ml) was treated with acetic anhydride (5.0 ml). The mixture was kept for 24 h, at room temperature with occasional shaking. It was poured onto crushed ice and the product that separated out was filtered, washed repeatedly with water, dried and recrystallized from the suitable solvent as colorless crystals (Table 5).

1-(Polyacetoxyalkyl)acenaphtho[1,2-*e*][1,2,4]triazolo[3,4-*c*][1,2,4]triazine (13). A cold solution of **10** (0.5 g) in dry pyridine (5.0 ml) was treated with acetic anhydride (5.0 ml) and the mixture was kept overnight at room temperature and then processed as above. The products were recrystallized from ethanol as pale yellow crystals (Table 6).

3-(2-Oxoethylidenehydrazino)acenaphtho[1,2-*e*][1,2,4]triazine (14). A suspension of **9e** (1.7 g, 4.62 mmol) in distilled water (100 ml) was treated with a solution of sodium periodate (3.0 g, 13.86 mmol) in distilled water (40 ml). The mixture was stirred for 1 h, and then left in the dark at room temperature for 4 d with occassional shaking. The product was filtered off and recrystallized from a mixture of ethanol and *N,N*-dimethylformamide (0.97 g, 76%), mp 228—230 °C; ν_{max} (KBr) 3215 (NH), 1693 (CHO), and 1606 cm^{-1} (C=N).

Found: C, 65.8; H, 3.5; N, 25.5%. Calcd for $C_{15}H_9N_5O$: C, 65.5; H, 3.3; N, 25.4%.

The authors thank Professor J. Krepinsky, University of Toronto for spectral measurements and valuable discussions.

References

1) A. Mousaad, H. Abdel Hamid, A. El Nemr, and E. S. H. El Ashry, *Bull. Chem. Soc. Jpn.*, **65**, 546 (1992).
2) N. Rashed, A. Mousaad, E. Ramadan, and E. S. H. El Ashry, *J. Prakt. Chem.*, submitted for publication.
3) S. Rossi and R. Trave, *Chem. Ind. (Milan)*, **40**, 827 (1958); *Chem. Abstr.*, **53**, 7194 (1959).
4) T. Mukaiyama and K. Sato, *Bull. Chem. Soc. Jpn.*, **36**, 99 (1963).
5) T. Sasaki, K. Minamoto, and S. Fukuda, *Chem. Ber.*, **101**, 2747 (1968).
6) J. Daunis and M. Follet, *Bull. Soc. Chim. Fr.*, **1975**, 857.
7) M. M. Goodman, J. L. Atwood, R. Carlin, W. Hunter, and W. W. Paudler, *J. Org. Chem.*, **41**, 2860 (1976).
8) E. J. Gray and M. F. G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 1492.
9) J. Daunis, H. Lopes, and G. Maury, *J. Org. Chem.*, **42**, 1018 (1977).
10) A. Messmer, G. Hajos, J. Tamas, and A. Neszmelyi, *J. Org. Chem.*, **44**, 1823 (1979).
11) F. M. Lovell and N. A. Perkinson, *J. Heterocycl. Chem.*, **16**, 1393 (1979).
12) A. Monge Vega, I. Aldama, M. M. Robbani, and E. Frenandez-Alvarez, *J. Heterocycl. Chem.*, **17**, 77 (1980).
13) K. C. Joshi and P. Chand, *J. Heterocycl. Chem.*, **17**, 1783 (1980).
14) S. Castillon, E. Melendez, and J. Vilarrasa, *J. Heterocycl. Chem.*, **19**, 61 (1982).
15) M. I. Younes, A. M. Abdel-Alim, H. H. Abbas, and S. A. Metwally, *Arch. Pharm. (Weinheim, Ger.)*, **320**, 1196 (1987).
16) M. I. Younes, H. H. Abbas, and S. A. Metwally, *Arch. Pharm. (Weinheim, Ger.)*, **320**, 1191 (1987).
17) F. F. Abdel-Latif, R. M. Shaker, S. A. Mahgoub, and M. Z. A. Badr, *J. Heterocycl. Chem.*, **26**, 769 (1989).
18) J. M. Gwaltncy, *Proc. Soc. Exp. Biol. Med.*, **133**, 1148 (1970).
19) J. M. Z. Gladych, R. Hornby, J. Hunt, D. Jack, J. J. Boyle, R. J. Ferlauto, R. Haff, C. Kormendy, F. Stanfield, and R. Stewart, *J. Med. Chem.*, **15**, 277 (1972).

20) R. Haff, J. J. Boyle, R. Stewart, R. J. Ferlauto, J. M. Z. Gladych, J. Hunt, and D. Jack, *Nature*, **221**, 286 (1969).
21) Allen and Hanburys Ltd., Netherlands Patent 6410823 (1965); *Chem. Abstr.*, **63**, 13295 (1965).
22) Allen and Hanburys Ltd., Netherlands Patent 6410715 (1965); *Chem. Abstr.*, **63**, 13294 (1965).
23) D. Kaminsky, U. S. Patent 3752891 (1971); *Chem. Abstr.*, **79**, 149326 (1973).
24) E. C. Ladd, U. S. Patent 2435501 (1948); *Chem. Abstr.*, **42**, 2724 (1948).
25) J. E. McDavid and T. C. Daniels, *J. Am. Pharm. Assoc.*, **40**, 325 (1951); *Chem. Abstr.*, **45**, 8594 (1951).
26) A. E. G. Pearson and A. K. Powell, *Br. J. Cancer*, **9**, 204 (1955); *Chem. Abstr.*, **49**, 11898 (1955).
27) R. M. Kunz, *Helv. Chim. Acta*, **22**, 939 (1939).
28) A. B. Tomchin, A. E. Aleksandrova, and V. M. Vinogradov, *Farmakol. Toksikol. (Moscow)*, **41**, 482 (1978); *Chem. Abstr.*, **89**, 157164 (1978).
29) M. N. Rotmistrov, G. V. Kulik, T. V. Gorbonos, A. N. Bredikhina, and E. M. Skrynik, *Visn. Kiiv. Univ., Ser. Biol.*, **14**, 90 (1972); *Chem. Abstr.*, **79**, 38890 (1973).
30) C. K. Cain, Fr. Patent 6196 (1968); *Chem. Abstr.*, **72**, 12767 (1970).
31) R. J. Suhadolnik, "C-Nucleoside Antibiotics," Wiley Interscince, New York (1970).
32) S. Hanessian and A. G. Pernet, *Adv. Carbohydr. Chem. Biochem.*, **33**, 111 (1976).
33) E. S. H. El Ashry, N. Rashed, and A. Mousaad, *J. Carbohydr. Chem.*, **6**, 599 (1987).
34) R. Noto, F. Buccheri, G. Cusmano, M. Gruttadauria, and G. Werber, *J. Heterocycl. Chem.*, **28**, 1421 (1991).