Reactions of 2,3-Diamino-4(3*H*)-pyrimidinones. II [1]

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The reaction of 2,3-diamino-4(3*H*)-pyrimidinones with α,β-diketones and orthoesters is described.

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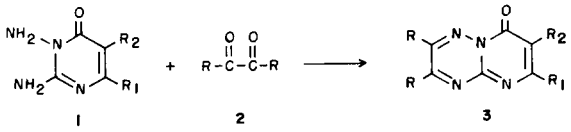
In a recent communication [1] we described a number of new vicinal diaminoheterocycles which were sythesized by the reaction of aminoguanidine with a β-ketoester. We have now extended the study of these diaminopyrimidinones to include their reactions with α,β-diketones and ortho esters with subsequent conversion to some nucleosides.

The reaction of these diaminopyrimidinones **1** with α,β-diketones **2** is of special interest because of the current research attention [2] that has been focused on 1,4-diazines (*i.e.* quinoxaline, phenazine, flavin).



1 2 3

With the proper choice of the α,β-diketone and diaminopyrimidinone, we have synthesized a variety of new bi, tri and tetracyclic 1,4-diazine systems (**5**, **7**, **8**, **9**, **10**, **12**). Chart I gives examples of these novel compounds.

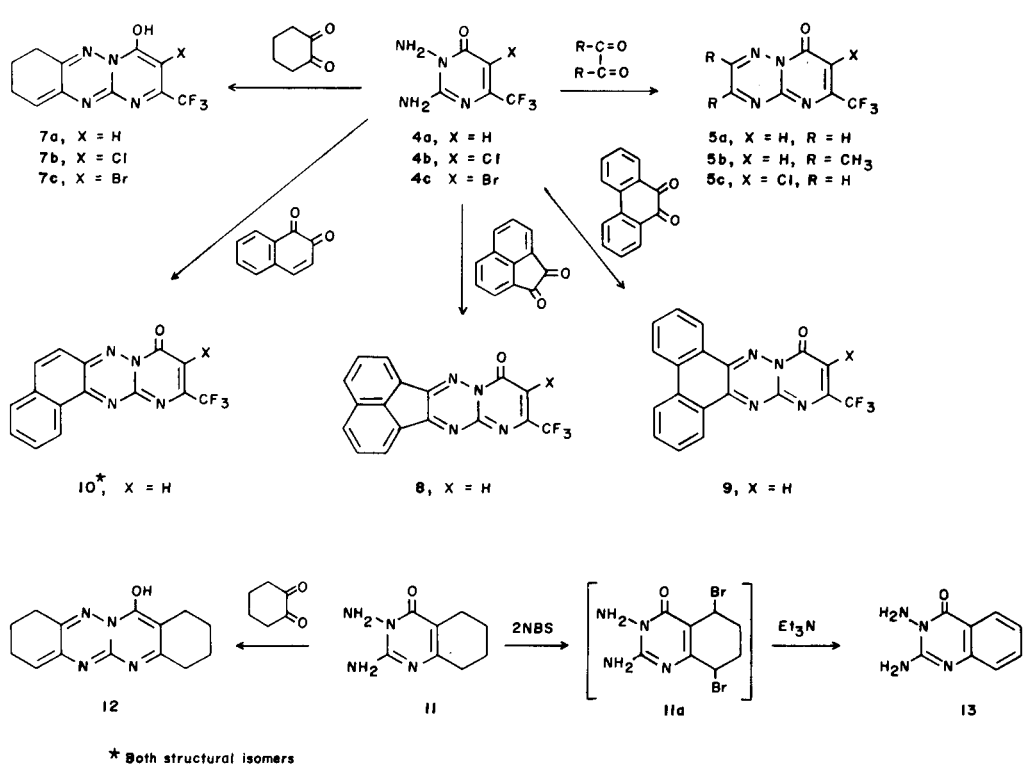
A redox potential on **5a** yielded two values, -1.61 and -1.84 v, suggesting a two electron change as reported for the pteridines [2].

In the case of compounds **7a**, **7b**, **7c** and **12**, ^{1}H nmr spectroscopy exhibited vinyl protons at 5.40 (t, J = 5 Hz) which prompted us to assign the structures in which a double bond has shifted into the cyclohexane ring.

An interesting reaction of the bicyclic pyrimidinone **11** involved reaction of this material with excess of *N*-bromosuccinimide and treating the intermediate dibromo compound **11a**, without purification, with triethylamine to yield **13** [1].

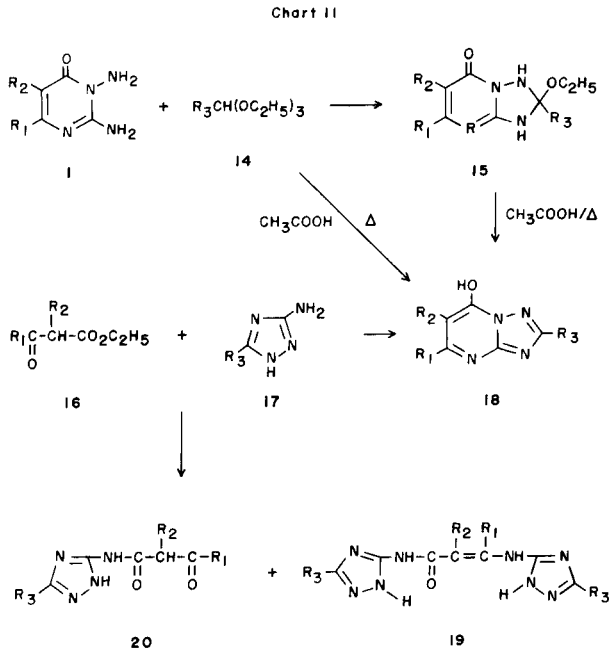
The reaction of ortho esters with these diaminopyrimidinones yielded either **15** or **18** depending on the reaction conditions used. When the ortho ester was reacted neat with the pyrimidinone, the intermediate **15** was obtained which was then converted to the bicyclic derivative **18** by refluxing in acetic acid. If, on the other hand, the pyrimid-

Chart I



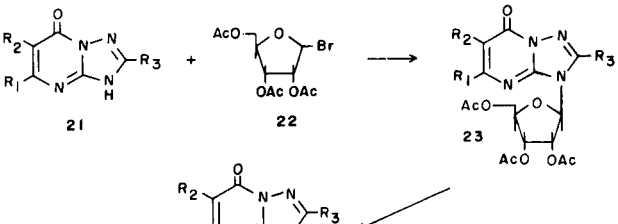
inone and ortho ester are refluxed together in acetic acid the triazolopyrimidinol **18** is obtained directly without isolation of the ethoxy intermediate **15**, see Chart II.

Chart II



In order to confirm these structures, we synthesized a few of these bicyclic derivatives by the alternative route shown in Chart II. This pathway [3], the reaction of a β-ketoester **16** with an aminotriazole **17**, not only confirms the structure of the bicyclic compounds **18** but also confirms the structure of the diaminopyrimidinones **1**. With some β-ketoesters, *i.e.* **16**, R = CF_3, cyclization did not occur when reacted with the aminotriazole and products **19** and **20** were isolated.

A number of these bicyclic pyrimidinones **21**, were converted to the N_3 nucleosides **24** by reaction with the bromosugar **22** followed by deacylation with ammonia.



The exact point of attachment of the sugar was determined by single X-ray spectrometry. A colorless plate crystal of C_{20} H_{24} N_4 O_8 having approximate dimensions of 0.30 × 0.10 × 0.05 mm was grown from ethyl alcohol and mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with CuKα radiation (λ = 1.54184 A) on an Enraf-Nonius CAD4 computer controlled kappa axis diffractometer equipped with a graphite crystal, incident beam monochromator.

Cell constants and an orientation matrix for data collection were obtained from least-squares refinement, using the setting angles of 25 reflections in the range 4 < 0 < 21°C, measured by the computer controlled diagonal slit method of centering. The orthorhombic cell parameters and calculated volume are: a = 14.847(3), b = 16.837(4), c = 8.657 (3) A, V = 2164.0A³. For Z = 4 and f.w. = 448.44 the calculated density is 1.38 g/cm³. As a check on crystal quality, omega scans of several intense reflections were measured; the width at half-height was 0.30° with a take-off angle of 2.8°, indicating fair crystal quality. From the systematic absences of: h00, h = 2n + 1; 0k0, k = 2n + 1; 001, l = 2n + 1, and from subsequent least-squares refinement, the space group was determined to be P2(1)2(1)2(1) (# 19). (This work was performed by the crystallographic staff of Molecular Structure Corporation; College Station, Texas).

In an earlier paper [4] Revankar proposed a structure **23**, R_1 = CH_3, R_2 = R_3 = H, for a compound they prepared by a similar procedure. They reported a mp of 240° dec for the material while our sample melted at 185-186°. The structure of one of our series **23**, R_1 - R_2 = -$CH_2CH_2CH_2CH_2$-, R_3 = H was confirmed by X-ray spectroscopy to be the 3-isomer; therefore, we must consider the Revanker sample to be the 4-isomer.

EXPERIMENTAL

All melting points were taken on a Mel-Temp apparatus. Samples for elemental analysis were dried at 50-60° for 1-24 hours under high vacuum. The ^{1}H nmr measurements were obtained on a Varian Model HA-100 spectrometer, and chemical shift values are reported in δ downfield from tetramethylsilane internal.

A typical procedure for the reaction of α,β-diketones with the pyrimidinones (All the pyrimidinones used are described in ref [1]). is given below. This procedure can be used for compounds given on Chart I, *i.e.*, **5a**, **5b**, **5c**, **7a**, **7b**, **7c**, **8**, **9**, **10** and **12**.

9-(Trifluoromethyl)-11*H*-acetnaphthol[1,2-*e*]pyrimido[1,2-*b*][1,2,4]triazin-11-one (**8**).

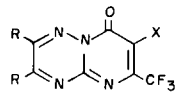
A mixture of 0.585 g (3.02 mmoles) of acetnaphthenequinone and 0.94 g (4.84 mmoles) of 2,3-diamino-6-trifluoromethyl-4(3*H*)-pyrimidinone (**4a**) in 15 ml of glacial acetic acid was heated at reflux for 1½ hours. The mixture was filtered, yield 0.57 g, mp 320° with dec.

Anal. Calcd. for $C_{17}H_7N_4OF_3$: C, 60.01; H, 2.07; N, 16.47. Found: C, 60.17; H, 2.16; N, 16.48.

11-(Trifluoromethyl)-13*H*-phenanthrol[9,10-*e*]pyrimido[1,2-*b*][1,2,4]triazin-13-one (**9**).

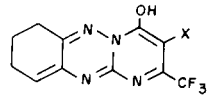
A mixture of 0.585 g (3.02 mmoles) of phenanthranequinone and 728 mg (3.5 mmoles) of 2,3-diamino-6-trifluoromethyl-4(3*H*)-pyrimidinone (**4a**), in 10 ml of glacial acetic acid was heated at reflux for 18 hours. On cooling a solid separated, yield 0.50 g, mp 284-285°.

Anal. Calcd. for $C_{19}H_{19}N_4OF_3 \cdot ½CH_3COOH$: C, 60.6; H, 2.77; N, 14.4. Found: C, 60.93; H, 2.77; N, 14.2.



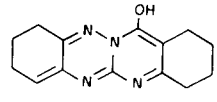
[a]

R	X	mp C	Elemental Analysis Calcd (Found) C	H	N	F	Cl or Br
CH_3	H (**5b**)	152-153°	44.27	2.89	22.95		
			(43.92)	(2.60)	(23.30)		
H	H (**5a**)	137-138°	37.3	2.2	24.8	25.3	
			(36.94)	(1.94)	(24.36)	(24.73)	
H	Cl (**5c**)	193-194°	38.80	2.17	20.11		12.72
			(38.62)	(2.01)	(19.80)		(12.62)



[a]

	H (**7a**)	275-278°	48.89	3.36	20.73	21.09	
			(48.89)	(3.23)	(20.60)	(20.99)	
	Br (**7c**)	230 with dec	37.84	2.31	16.05	16.33	22.89
			(37.60)	(2.22)	(16.25)	(16.47)	(22.90)
	Cl (**7b**)	308 with dec	43.27	2.65	18.39	18.71	11.64
			(42.76)	(2.61)	(17.98)	(18.84)	(11.59)



[a]

	(**12**)	[b] 218-219°	64.20 (63.70)	6.18 (6.15)	20.70 (20.3)		

[a] Prepared by the procedure given for compound **8** given in the Experimental.
[b] Calculated with a ⅓ mole of acetic acid.

11-(Trifluoromethyl)-9*H*-naphtho[1,2*e*]pyrimido[1,2-*b*][1,2,4]triazin-9-one (**10**).

A mixture of 388 mg (2 mmoles) of 2,3-diamino-6-trifluoromethyl-4(3*H*)-pyridinone (**4a**), and 474 mg (3 mmoles) of 1,2-naphthoquinone in 8 ml of glacial acetic acid was heated at reflux for 2½ hours. On cooling, a solid crystallized, yield 100 mg, mp 178-180°.

Anal. Calcd. for $C_{15}H_7N_4OF_3 \cdot CH_3COOH$: C, 54.26; H, 2.95; N, 14.89; F, 15.15. Found: C, 54.40; H, 2.65; N, 14.70; F, 15.00.

2,3-Diamino-4(3*H*)-quinazolinone (**13**) [1].

To a solution of 3.0 g (0.0165 mole), of 2,3-diamino-5,6,7,8-tetrahydro-1,3-benzatriazin-4(3*H*)-one (**11**), in 25 ml of glacial acetic acid was added 7.25 g (0.041 mole) of *N*-bromosuccinimide. The solution was stirred at room temperature overnight and then evaporated *in vacuo*. The residue was triturated with 40 ml of water and the solid that remained was dried *in vacuo*. To this was added 200 ml of tetrahydrofuran and 20 ml of collidine and the mixture was heated at reflux for 1 hour. The residue was triturated with 100 ml of ether followed by 100 ml of water. The residue was identified by nmr and mp to the material prepared in reference [1].

5-Ethyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ol (**18**) ($R_1 = C_2H_5$, $R_2 = H$, $R_3 = H$).

Procedure A. Typical Example for Substituted 1,2,4-Triazolo[1,5-*a*]pyrimidin-7-ol.

A solution of 1.5 g of 2,3-diamino-4(3*H*)-pyrimidinone [1] 1 ($R = C_2H_5$, $R_2 = H$) in 10 ml of glacial acetic acid and 10 ml of triethyl orthoformate was refluxed for 2 hours and then cooled to room temperature. The crystalline precipitate was collected, washed with water and dried to give 0.616 g (39%) of **18** ($R_1 = C_2H_5$, $R_2 = H$, $R = H$) as pale yellow crystals.

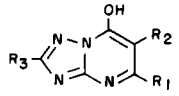
2-Ethoxy-2,3-dihydro-2-methyl-5-(trifluoromethyl)-1,2,4-triazolo-[1,5-*a*]pyrimidin-7(1*H*)-one (**15**) ($R_1 = CF_3$, $R_2 = H$, $R_3 = CH_3$). Typical Example of 2-Ethoxy-2,3-dihydro-5-substituted-1,2,4-triazolo[1,5-*a*]pyrimidin-7(1*H*)-one.

A solution of 970.6 mg (5 mmoles) of 2,3-diamino-6-(trifluoromethyl)-4(3*H*)-pyrimidinone (**1**) ($R_1 = CF_3$, $R_2 = H$) [1] in 5 ml of triethyl orthoacetate was prepared by heating at 110-115° for one hour. Solution was cooled to room temperature and crystalline precipitate was collected, washed with ether and dried to give 180 mg (59%) of white crystals.

2-Methyl-5-(trifluoromethyl)-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ol (**18**) ($R_1 = CF_3$, $R_2 = H$, $R_3 = CH_3$).

A solution of 2.09 g of 2-ethoxy-2,3-dihydro-2-methyl-5-(trifluoromethyl)-1,2,4-triazolo[1,5-*a*]pyrimidin-7(1*H*)-one (**15**) ($R_1 = CF_3$, $R_2 = H$, $R_3 = CH_3$) in 20 ml of glacial acetic acid was refluxed overnight and cooled to room temperature. The crystalline precipitate was collected, washed with ether and dried to give 965 mg (56%) of white crystals.

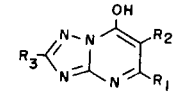
5-(4-Fluorophenyl)-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ol (**18**) ($R_1 = p\text{-}C_6H_4F$, $R_2 = R_3 = H$). Procedure B. Typical Example from 3-Amino-1,2,4-triazole and α,β-Keto-ester.



18 [a]

R1	R2	R3	mp °C	Elemental Analysis Calcd. (Found) C	H	N	X (Cl, Br, I)	F
H	I	H	260-262	22.92	1.15	21.38	I = 48.43	
				(22.55)	(1.17)	(21.33)	(48.66)	
H	Br	H	307-308	27.92	1.41	26.05	Br = 37.16	
				(27.75)	(1.32)	(26.26)	(36.82)	
CH3	Br	H	275-276 dec	31.46	2.20	24.46	Br = 34.89	
				(31.47)	(2.10)	(24.47)	(34.66)	
CH3	I	H	200 dec	26.11	1.83	20.30	I = 45.97	
				(26.04)	(1.74)	(20.39)	(45.76)	
CH3 [b]	Br	-SMe	>320	30.56	2.56	20.36	Br = 29.04	
				(30.61)	(2.51)	(20.44)	(28.71)	
CH3 [b]	I	-SMe	dec at 235	26.10	2.19	17.39	I = 39.40	
				(26.33)	(2.12)	(17.60)	(39.01)	
CH3 [b]	Br	$-C_6H_5$	—	47.24	2.97	18.36	Br = 26.19	
				(46.95)	(2.81)	(18.25)	(26.19)	
CH3 [b]	I	$-C_6H_5$	dec 300	40.93	2.58	15.91	I = 36.04	
				(40.63)	(2.41)	(15.80)	(35.98)	
CH3	$-CH_2C_6H_5$	H	224-226	64.99	5.03	23.32		
				(64.66)	(5.04)	(23.58)		

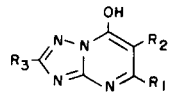
[a] Prepared by Procedure A given in the Experimental. [b] Prepared by both Procedure A and Procedure B given in the Experimental.



18 [a]

R1	R2	R3	mp °C	Elemental Analysis Calcd. (Found) C	H	N	X (Cl, Br, I)	F
Et	H	H	210-212	51.21	4.91	34.13		
				(51.29)	(4.94)	(34.51)		
CH3	Pr	H	220-222	56.24	6.29	29.15		
				(56.09)	(6.11)	(29.29)		
CF3	H	H	262	35.31	1.48	27.45		27.92
				(35.11)	(1.49)	(27.84)		(28.10)
CF3	Br	H	348-350 dec	25.46	0.71	19.80	Br = 28.24	20.14
				(25.11)	(0.61)	(19.88)	(28.27)	(20.20)
CF3	I	H	318-320 dec	21.84	0.61	16.98	I = 38.45	17.27
				(21.44)	(0.48)	(17.01)	(38.32)	(17.18)
CF3	H	CH3	346-348	38.54	2.31	25.68		26.13
				(38.23)	(2.29)	(25.60)		(26.08)
CF3	Br	CH3	344-345 dec	28.31	1.36	18.86	Br = 26.90	19.19
				(28.37)	(1.32)	(19.03)	(26.67)	(18.96)
CF3	I	CH3	295 dec	24.44	1.17	16.29	I = 36.89	16.57
				(24.22)	(1.15)	(16.45)	(36.97)	(16.84)
CF3	H	Et	301-304	41.39	3.04	24.13		24.55
				(40.99)	(2.81)	(24.19)		(24.20)

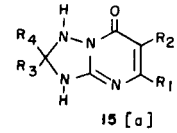
[a] Prepared by Procedure A given in the Experimental.



18 [a]

R_1	R_2	R_3	m.p. °C.	Elemental Analysis Calcd. (Found) C	H	N	X (Cl, Br, I)	F
CF_3	Br	Et	296-299	30.89	1.94	18.01	Br = 25.69	18.32
				(30.57)	(1.67)	(17.84)	(25.39)	(18.80)
t-Bu	H	H	274-276	56.24	6.29	29.15		
				(56.36)	(6.33)	(29.36)		
$-C_6H_5$	I	H	260 dec	39.08	2.09	16.57	I = 37.53	
				(39.05)	(1.89)	(16.51)	(37.57)	
$-C_6H_4$-F (*p*) [b]	H	H	>310	57.39	3.07	24.34		8.25
				(56.99)	(3.08)	(24.36)		(8.30)
$-C_6H_4$-F (*p*)	H	Et	308-310	60.46	4.29	21.69		7.36
				(60.32)	(4.38)	(21.55)		(7.33)
$-C_6H_4$-Cl (*p*) [b]	H	H		53.57	2.86	22.71	Cl = 14.37	
				(53.70)	(2.76)	(22.60)	(13.99)	
$-C_6H_4-CH_3$ (*p*)	H	H	310-312	63.71	4.46	24.76		
				(63.64)	(4.44)	(25.01)		
$-C_6H_4$-OMe (*p*)	H	H	287-290	59.50	4.16	23.13		
				(59.25)	(4.28)	(23.05)		
$-C_6H_2(OMe)_3$(3,4,5)- [b]	H	H	295-299	55.80	4.68	18.59		
				(55.73)	(4.70)	(18.83)		
$-CH_2CH_2CH_2-CH_2$ [c]		H	274-277	56.83	5.30	29.46		
				(56.53)	(5.26)	(29.54)		

[a] Prepared by Procedure A given in the Experimental. [b] Prepared by Procedure A and/or B given in the Experimental. [c] R_1 and R_2 connected.



15 [a]

R_1	R_2	R_3	R_4	mp °C	Elemental Analysis Calcd. (Found) C	H	N	F
CF_3	H	-OEt	CH_3	158-160	40.91	4.20	21.21	21.57
					(40.60)	(3.97)	(21.11)	(21.63)
CF_3	H	-OEt	Et	—	43.17	4.71	20.14	20.48
					(43.13)	(4.69)	(20.40)	(20.23)
CF_3	H	-OEt	H	dec	38.41	3.63	22.39	22.78
					(38.05)	(3.57)	(22.34)	(22.84)

[a] Prepared by Procedure given for compound **15** in the Experimental.

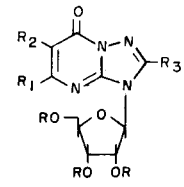
A solution of 8.4 g (0.1 mole) of 3-amino-1,2,4-triazole and 19.6 g (0.1 mole) of ethyl 4-fluorobenzoyl acetate in 30 ml of glacial acetic acid was refluxed for two hours. The crystalline suspension was cooled at room temperature and the product was collected, washed with ether and dried to give 2.4 g of white crystals.

6-Iodo-5-methyl-1,2,4-triazolo[1,5-α]pyrimidin-7-ol(**18**)(R_1 = CH_3, R_2 = I, R_3 = H). Typical example of 6-Halo-2 and/or 5-substituted-1,2,4-triazolo[1,5-α]-pyrimidin-7-ol.

A suspension of 3.0 g (0.02 mole) of 5-methyl[1,2,4]triazolo[1,5-*a*]pyrimidin-7-ol and 4.5 g (0.02 mole) of *N*-hydrosuccinimide in 20 ml of glacial acetic acid was refluxed for one and one half hours and then cooled to room temperature. The crystalline precipitate was collected, washed with acetic acid, ether and dried to give 5.1 g (93%) or white crystals.

5-(Trifluoromethyl)-3-[2,3,5-tris(acetyloxy)-β-D-ribofuranosyl]-1,2,4-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one (**23**) (R_1 = CF_3, R_2 = R_3 = H) Typical Example of a Nucleoside.

To tetra-*O*-acetyl-D-ribofuranose (3.44 g, 0.0108 mole) in dry dichloromethane (15 ml) at -20° was added a solution of dry dichloromethane (15 ml) which had been saturated at -20° with dry hydrogen bromide gas. The mixture was protected from moisture and allowed to warm to room



23, R = CH_3C(=O) [a]

24, R = H [b]

R_1	R_2	R_3	R	mp °C	Elemental Analysis Calcd. (Found) C	H	N	F
CH_3	H	H	Ac	185-186	50.00	4.94	13.72	
					(49.98)	(4.99)	(13.53)	
CH_3	H	H	H	150-155	46.81	5.00	19.85	
					(46.85)	(5.08)	(19.48)	
CF_3	H	H	Ac	198-200	44.16	3.71	12.12	12.33
					(43.81)	(3.68)	(11.88)	(12.09)
CF_3	H	H	H	50-55	39.30	3.30	16.66	16.95
					(39.03)	(3.20)	(16.90)	(16.62)
$-C_6H_4-F$ (*p*)	H	H	Ac	135-137	54.10	4.33	11.47	3.98
					(53.92)	(4.50)	(11.40)	(3.78)
$-C_6H_4-F$ (*p*)	H	H	H	192-193	53.04	4.17	15.46	5.24
					(52.89)	(4.20)	(15.12)	(5.02)
$-C_6H_5-$	H	H	Ac	137-138	56.17	4.71	11.91	
					(55.80)	(4.50)	(11.85)	
$-C_6H_5-$	H	H	H	dec	55.81	4.68	16.27	
					(55.70)	(4.66)	(15.93)	
$CH_2CH_2CH_2CH_2$ [c]		H	Ac	170-172	53.57	5.39	12.49	
					(53.32)	(5.39)	(12.35)	
$-CH_2CH_2CH_2CH_2$ [c]		H	H	dec at 85°	52.17	5.63	17.38	
					(52.23)	(5.41)	(17.25)	

[a] Prepared by Procedure for compound **23** given in the Experimental.
[b] Prepared by Procedure for compound **24** given in the Experimental.
[c] R_1 and R_2 are connected.

temperature. The solution was evaporated to near dryness and the resulting syrup was co-evaporated with 2-15 ml portions of toluene. The residual syrup was dissolved in dry acetonitrile (15 ml) and was added to the trimethylsilyl derivative [prepared from 2.04 g (0.01 mole) of 5-trifluoromethyl-1,2,4-triazolo[1,5-*a*]pyrimidin-7-ol, 10 ml of 1,1,1,3,3,3,-hexamethyldisilazane and 0.5 ml of *N,N*-dimethylformamide by heating at 155° for 16 hours and evaporating the mixture to dryness] in acetonitrile (15 ml). After 48 hours at room temperature the reaction mixture evaporated to a syrup. Sodium bicarbonate (1.6 g, 9.47 mmoles), ethanol (20 ml) and water (10 ml) were added. The mixture was evaporated to dryness. Co-evaporation with absolute ethanol several times afforded dry residue which was extracted with chloroform (3 × 30 ml). The combined extracts were washed with cold saturated aqueous sodium bicarbonate solution (2 × 30 ml) followed by water (3 × 30 ml). The chloroform phase was dried over anhydrous magnesium sulfate and then evaporated to dryness. Product was crystallized from ethanol to give 1.9 g of light yellow crystals.

3-β-D-Ribofuranosyl-5-(trifluoromethyl)-1,2,4-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one (**24**) (R_1 = CF_3, R_2 = R_3 = H).

5-(Trifluoromethyl)-3-[2,3,5-tris(acetyloxy)-β-D-ribofuranosyl]-1,2,4-triazolo[1,5-*a*]pyrimidin-7(3*H*)-one (1.3 g) was dissolved in methanolic ammonia (50 ml methanol saturated with ammonia at 0°). The container was sealed and left at room temperature overnight. Solution evaporated to dryness. It was purified by dissolving it in water and passing the solution slowly through a column packed with amberlite XAD-2 column (non ionic polymeric absorbent). Column was first washed with water (100 ml) and then with methanol (100 ml). The organic wash was collected and evaporated to dryness to give 193 mg of analytically pure product.

4,4,4-Trifluoro-*N*-(5-methyl-1*H*-1,2,4-triazol-3-yl)-3-oxobutanamide (**20**) (R_1 = CF_3, R_2 = H, R_3 = CH_3).

A solution of 294.3 mg (0.003 mole) of 2-methyl-5-amino-1,3,4-triazole and 2 ml of ethyl 4,4,4-trifluoroacetoacetate was stirred at room temperature for one hour. The cloudy solution was filtered and the filtrate was heated for 10 minutes at 90°, the thick suspension was cooled to room temperature and crystalline product filtered, washed with ether and air dried to give 528 mg (22%) of **20** as white crystals, mp 300-305°.

Anal. Calcd. for $C_7H_7N_4O_2F_3$: C, 35.60; H, 2.99; N, 23.72; F, 24.13. Found: C, 35.67; H, 2.93; N, 23.87; F, 23.85.

4,4,4-Trifluoro-*N*-(5-methyl-4*H*-1,2,4-triazol-3-yl)-3-[(5-methyl-4*H*-1,2,-4-triazol-3-yl)amino]-2-butenamide (**19**) (R_1 = CF_3, R_2 = H, R_3 = CH_3).

A solution of 294.3 mg (0.003 mole) of 2-amino-5-methyl-1,3,4-triazole and 1.3 g (0.007 mole) of ethyl 4,4,4-trifluoroacetoacetate in 10 ml of 1-butanol was refluxed for 5 hours. Heat was removed and suspension cooled to room temperature. The crystalline product was filtered, washed with 1-butanol, water and dried to give 434 mg (13%) of white crystals, mp 305-308°.

Anal. Calcd. for $C_{10}H_{11}N_8OF_3$: C, 37.97; H, 3.5; N, 35.65; F, 18.02. Found: C, 37.73; H, 3.36; N, 35.65; F, 17.81.

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