On Triazoles. XXXV [1]. The Reaction of 5-Amino-1,2,4-Triazoles with Di- and Triketones

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Received September 16, 1994

The reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles **1** with aliphatic, aromatic and cyclic 1,3-diketones, 1,4-diketones, and different linear and non linear triketones was studied. It was proved that in case of unsymmetrical aliphatic 1,3-diketones the regiochemical outcome of the reaction was influenced by steric factors. In case of triacetylmethane and 3-(4-chlorobenzyl)-2,4-pentanedione the splitting of one acetyl group from the reactant was observed during the reaction. A liner triketone, namely the 2,4,6-trioxoheptane reacted as a simple 1,3-diketone.

J. Heterocyclic Chem., **32**, 407 (1995).

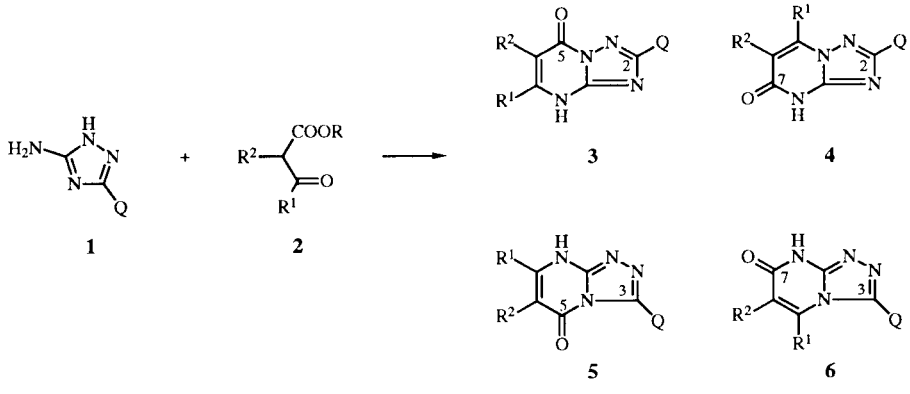
In the previous papers of this series we have discussed the reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles **1** with linear- [2,3], homocyclic- [4,5], and different heterocyclic- [6-9] alkyl 2-oxocarboxylates **2** in acetic acid, to yield the corresponding **3** type 1,2,4-triazolo[1,5-*a*]pyrimidin-5-ones as the main products, besides a small amount of the corresponding isomeric **4** type 1,2,4-triazolo[1,5-*a*]pyrimidin-7-ones (Scheme 1). The structure of products **3** and **4** was proved unambigously [2] with the help of their uv and cmr spectra. Now we will report the reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles **1** with different di- and triketones.

The Reaction with Aliphatic 1,3-Diketones.

The reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles **1** with acetylacetone (**7**, $R^1 = R^3 = CH_3$, $R^2 = H$) to yield 5,7-dimethyl-2-Q-1,2,4-triazolo[1,5-*a*]pyrimidine derivatives **8** ($R^1 = R^3 = CH_3$, $R^2 = H$) (Scheme 2) was known from the literature [10]. It was also reported that in the case of unsymetrically substituted acetylacetones where R^1 is methyl and R^3 is a group different from methyl a mixture of isomers **8** (R^1 = methyl) and **8** (R^3 = methyl) is formed which could be distinquished on the basis of the chemical shifts of the pyrimidine methyl carbons appearing at 24-25 ppm and 16-17 ppm, respectively [11]. We have checked the above rule and found it valid by proton-carbon correlation spectra.

The elucidation of the crude reaction mixtures by pmr showed [12] that the main product of the reactions of **1** (Q = benzylthio) and **7** (R^3 = phenyl, R^2 = H, R^1 = methyl), **7** (R^3 = trifluoromethyl, R^2 = H, R^1 = methyl) and **7** ($R^2 + R^3$ = propylene, R^1 = methyl), respectively, provided in acetic acid is the corresponding derivative **8** (R^1 = methyl) and the ratio of isomers **8** (R^1 = methyl) and **8** (R^3 = methyl) formed is 82:18, 97:3 and 90:10 for **7**

Scheme 1



Scheme 2

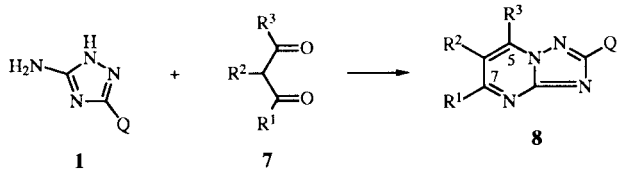


Table 1

Compound	Q	R^1	R^2	R^3	Method	Reaction Time (hours)	Isolated Yield (%)	Mp (°C) (crystallized from)	Molecular Formula (M.W.)	Analysis Calcd./Found C	H	N	S
8/1	Methylthio	Methyl	H	Methyl	A	4	80	154-156	lit [14] mp				
					[1]		58	(2-PrOH)	154-155 (EtOH + H_2O)				
8/2	Benzylthio	Methyl	H	Methyl	A	4	81	133-134	lit [14] mp				
								(2-PrOH)	131-132 (EtOH + H_2O)				
8/3	4-Chlorobenzylthio	Methyl	H	Methyl	[2]		33	144-145	lit [14] mp				
								(EtOAc)	136-137 (EtOH + H_2O)				
8/4	Pyridin-2-yl-methylamino	Methyl	H	Methyl	[3]		42	168-169	$C_{13}H_{14}N_6$	61.40	5.55	33.05	
								(2-PrOH)	(254.30)	61.47	5.88	32.89	
8/5	Pyridin-3-yl-methylamino	Methyl	H	Methyl	[4]		38	179-180	$C_{13}H_{14}N_6$	61.40	5.55	33.05	
								(EtOH)	(254.30)	61.36	5.68	32.98	
8/6	Pyridin-4-yl-methylamino	Methyl	H	Methyl	[5]		70	166-167	$C_{13}H_{14}N_6$	61.40	5.55	33.05	
								(2-PrOH)	(254.30)	61.31	5.57	33.12	
8/7	2-(3,4-di-ethoxyphenyl)-ethylamino	Methyl	H	Methyl	A		67	136-137	$C_{19}H_{25}N_5O_2$	64.21	7.09	19.70	
								(2-PrOH)	(355.45)	64.39	7.19	19.81	
8/8	3,3-Diphenyl-propylamino	Methyl	H	Methyl	A		74	165-166	$C_{22}H_{23}N_5$	73.92	6.49	19.59	
								(EtOH)	(357.47)	74.12	6.65	19.56	
8/9	Morpholino	Methyl	H	Methyl	A	4	58	155-156	$C_{11}H_{15}N_5O$	56.64	6.48	30.02	
								(2-PrOH)	(233.28)	56.89	6.68	29.87	
8/10	Methylthio	Methyl	H	*t*-Butyl	A	4	61	126-128	$C_{11}H_{16}N_4S$	55.90	6.82	23.71	13.57
								(2-PrOH)	(236.34)	56.02	6.99	23.68	13.48
8/11	Methylthio	*t*-Butyl	H	Methyl	[6]		6	93-95	$C_{11}H_{16}N_4S$	55.90	6.82	23.71	13.57
								(PÄ)	(236.34)	55.92	6.97	23.76	13.44
8/12	Morpholino	Methyl	H	*t*-Butyl	A	4	81	105-106	$C_{14}H_{21}N_5O$	61.07	7.69	25.43	
								(CH)	(275.36)	61.21	7.99	25.41	
8/13	Morpholino	*t*-Butyl	H	Methyl	[7]		4	146-148	$C_{14}H_{21}N_5O$	61.07	7.69	25.43	
								(PÄ)	(275.36)	60.98	7.72	25.47	
8/14	H	Methyl	H	Phenyl	A	4	72	148-149	$C_{12}H_{10}N_4$	68.56	4.79	26.65	
								(2-PrOH)	(210.24)	68.61	4.88	26.58	
8/15	H	Phenyl	H	Methyl	[8]		12	161-162	$C_{12}H_{10}N_4$	68.56	4.79	26.65	
								(2-PrOH)	(210.24)	68.48	4.84	26.61	
8/16	Methylthio	Methyl	H	Phenyl	A	4	50	120-122	$C_{13}H_{12}N_4S$	60.92	4.72	21.86	12.51
								(2-PrOH)	(256.34)	60.99	4.81	21.68	12.70
8/17	Methylthio	Phenyl	H	Methyl	[9]		7	161-162	$C_{13}H_{12}N_4S$	60.92	4.72	21.86	12.51
								(2-PrOH)	(256.34)	61.08	4.86	21.75	12.48
8/18	Dimethylamino	Methyl	H	Phenyl	A	4	66	160-162	$C_{14}H_{15}N_5$	66.38	5.97	27.65	
								(2-PrOH)	(253.31)	66.44	6.06	27.68	
8/19	Dimethylamino	Phenyl	H	Methyl	[10]		7	142-143	$C_{14}H_{15}N_5$	66.38	5.97	27.65	
								(2-PrOH)	(253.31)	66.32	5.88	27.77	
8/20	Morpholino	Methyl	H	Phenyl	A	4	66	188-190	$C_{16}H_{17}N_5O$	65.07	5.80	23.71	
								(DMF)	(295.35)	65.11	5.96	23.68	
8/21	Morpholino	Phenyl	H	Methyl	[11]		7	209-211	$C_{16}H_{17}N_5O$	65.07	5.80	23.71	
								(2-PrOH)	(295.25)	65.04	5.77	23.92	
8/22	Methylthio	Phenyl	H	Phenyl	A	8	80	174-176	$C_{18}H_{14}N_4S$	67.90	4.43	17.60	10.07
								(CH_3CN)	(318.41)	68.13	4.59	17.44	10.03
8/23	Morpholino	Phenyl	H	Phenyl	[12]		83	228-230	$C_{21}H_{19}N_5O$	70.57	5.36	19.59	
								(DMF)	(357.43)	70.66	5.36	19.42	
14/1	Methylthio	Methyl	Acetyl	Methyl	[12]		23	115-116	$C_{10}H_{12}N_4OS$	50.83	5.12	23.71	13.57
								(2-PrOH)	(236.30)	51.08	5.30	23.60	13.79
14/2	4-Chlorobenzylthio	Methyl	Acetyl	Methyl	[12]		42	152-153	$C_{16}H_{15}ClN_4OS$	55.41	4.36	16.15	9.25
								(EtOAc)	(346.85)	55.27	4.55	16.30	9.40
14/3	Pyridin-2-yl-methylamino	Methyl	Acetyl	Methyl	[12]		21	141-142	$C_{15}H_{16}N_6O$	60.80	5.44	28.36	
								(EtOAc)	(296.34)	60.72	5.37	28.17	
14/4	Pyridin-3-yl-methylamino	Methyl	Acetyl	Methyl	[12]		41	170-172	$C_{15}H_{16}N_6O$	60.80	5.44	28.36	
								(EtOAc)	(296.34)	60.77	5.64	28.31	
14/5	Pyridin-4-yl-methylamino	Methyl	Acetyl	Methyl	[12]		12	194-197	$C_{15}H_{16}N_6O$	60.80	5.44	28.36	
								(EtOAc)	(296.34)	60.92	5.67	28.35	
16	Morpholino	Methyl	H	4-Chloro-phenyl	[12]		50	208-210	$C_{16}H_{16}ClN_5O$	58.27	4.89	21.24	10.75
								(*n*-BuOH)	(329.80)	58.38	4.84	21.34	11.04
17	Morpholino	4-Chloro-phenyl	H	Methyl	[12]		11	173-175	$C_{16}H_{16}ClN_5O$	58.27	4.89	21.24	10.75
								(EtOH)	(329.80)	58.12	4.81	21.18	10.88

Table 1 (continued)

Compound	Q	R^1	R^2	R^3	Method	Reaction Time (hours)	Isolated Yield (%)	Mp (°C) (crystallized from)	Molecular Formula (M.W.)	Analysis Calcd./Found C	H	N	S
19	Methylthio	H	Acetyl	Methyl	[12]			119-121	$C_9H_{10}N_4OS$	48.64	4.53	25.21	14.43
								(2-PrOH)	(222.27)	48.91	4.70	25.22	14.27
20	Methylthio	Methyl	Acetyl	H	[12]			157-158	$C_9H_{10}N_4OS$	48.64	4.53	25.21	14.43
								(2-PrOH)	(222.27)	48.52	4.45	25.13	14.33
22	Methylthio	Methyl	H	Acetonyl	[12]			130-132	$C_{10}H_{12}N_4OS$	50.83	5.12	23.71	13.57
								(2-PrOH)	(236.30)	51.01	5.22	23.68	13.66
23	Methylthio	Acetonyl	H	Methyl	[12]			102-104	$C_{10}H_{12}N_4OS$	50.83	5.12	23.71	13.57
								(CH)	(236.30)	50.82	5.18	23.66	13.62
24	Benzylthio	Methyl	H	Acetonyl	[12]			137-138	$C_{16}H_{16}N_4OS$	61.52	5.16	17.93	10.26
								(DCIE)	(312.40)	61.48	5.22	18.04	10.21

[1] Obtained as byproduct of **14/1**. [2] Obtained as byproduct of **14/2**. [3] Obtained as byproduct of **14/3**. [4] Obtained as byproduct of **14/4**. [5] Obtained as byproduct of **14/5**. [6] Obtained as byproduct of **8/10**. [7] Obtained as byproduct of **8/12**. [8] Obtained as byproduct of **8/14**. [9] Obtained as byproduct of **8/16**. [10] Obtained as byproduct of **8/18**. [11] Obtained as byproduct of **8/20**. [12] See Experimental.

Table 2

Compound No.	PMR [ppm] (DMSO-d_6) δ Q	δ R^1	δ R^2	δ R^3	CMR [ppm] (DMSO-d_6) δ C-2	δ C-5	δ C-6	δ C-7	δ C-8a	δ R^1	δ R^2	δ R^3	δ Q
8/1	2.65 s	2.56 s	7.01 s	2.70 s	166.9	146.0	110.1	164.0	155.4	24.3		16.4	13.3
8/2	4.51 s (2H)	2.55 s	7.06 s	2.67 s	165.8	146.5	110.1	164.5	155.3	24.4		16.5	34.5
	7.21-7.36 m (3H)												127.5 128.6
	7.49 dd (2H)												129.2 138.1
8/3	4.50 s (2H)	2.55 s	7.06 s	2.68 s	165.5	146.3	110.4	164.3	155.3	24.4		16.4	33.6
	7.35 d (2H)												128.4
	7.52 d (2H)												130.9 132.7 137.3
8/4	4.59 d (2H)	2.44 s	6.83 s	2.56 s	167.1	145.1	108.4	161.6	155.1	24.1		16.6	47.5
	7.25 dt (1H)												121.0
	7.41 dq (1H)												122.1
	7.43 t (NH)												136.8
	7.73 dt (1H)												149.0
	8.51 dq (1H)												160.0
8/5	4.48 d (2H)	2.45 s	6.85 s	2.57 s	166.8	144.9	108.2	161.3	154.9	24.1		16.5	43.5
	7.33 dq (1H)												123.3
	7.46 t (NH)												135.1
	7.76 dt (1H)												135.8
	8.43 dd (1H)												147.4
	8.59 d (1H)												149.0
8/6	4.56 d (2H)	2.45 s	6.80 s	2.56 s	167.0	145.2	108.5	161.7	155.1	24.1		16.6	44.8
	7.39 d (2H)												122.4
	7.60 t (NH)												149.8
	8.52 d (2H)												150.2
8/7	1.31 t (3H)	2.57 s	6.84 s	2.57 s	166.7	144.6	107.9	161.0	154.8	24.0		16.5	14.82
	1.32 t (3H)												14.83
	2.83 t (2H)												35.0
	3.48 qa (2H)												44.1
	3.96 q (2H)												63.7
	3.99 q (2H)												63.9
	6.70-6.82 (3H)												113.6
	6.86 t (NH)												114.3 120.7 144.6 148.2

Table 2 (continued)

Compound No.	PMR [ppm] (DMSO-d_6) δ Q	δ R^1	δ R^2	δ R^3	CMR [ppm] (DMSO-d_6) δ C-2	δ C-5	δ C-6	δ C-7	δ C-8a	δ R^1	δ R^2	δ R^3	δ Q
8/8	2.41 m (2H) 3.23 q (2H) 4.15 t (1H) 6.91 t (NH) 7.14- 7.38 m (10H)	2.44 s	6.74 s	2.54 s	166.7	146.6	107.9	161.0	154.7	24.0		16.5	34.7 40.8 47.9 126.0 127.6 128.3 144.9
8/9	3.49 t 3.72 t	2.48 s	6.89 s	2.60 s	167.1	145.2	108.6	161.8	154.8	24.1		16.4	45.6 65.7
8/10	2.68 s	2.62 s	7.07 s	1.55 s	165.7	156.4	107.2	165.0	155.5	24.7		26.4 35.6	13.3
8/11	2.76 s*	1.48 s	6.92 s	2.73 s* [1]	168.3	145.5	106.0	174.4	155.4	29.4 38.3		17.1	13.8
8/12	3.51 t 3.74 t	2.54 s	6.89 s	1.53 s	166.4	154.8	105.6	162.9	155.9	24.5		26.2 35.0	45.6 65.7
8/13	3.67 t 3.80 t	1.39 s	6.76 qa [2]	2.67 d [1] [2]	167.6	144.8	104.7	172.9	155.2	29.5 37.4		17.2	45.7 66.4
8/14	8.65 s	2.70 s	7.53 s	7.66 m (3H) 8.17 dd (2H)	155.0	146.0	110.0	164.9	155.5	24.4		128.4 129.2 129.5 131.3	
8/15	8.67 s	7.59 m (3H)	7.94 dq [2]	2.85 d [2]	155.9	148.4	107.3	160.0	155.0	127.6 129.1 131.3 136.1		17.0	
8/16	2.61 s* 8.11 dd (2H)	2.60 s*	7.38 s	7.55- 7.62 m (3H)	166.9	145.1	109.5	164.6	156.2	24.5	129.3	128.5 129.5 131.4	13.3
8/17	2.66 s	7.55 dd 8.19 dd	7.81 s	2.75 s	167.5	147.3	106.6	159.4	155.5	127.4 129.0 131.1 136.1		17.0	13.4
8/18	3.05 s	2.55 s	7.21 s	7.61 m 8.21 dd	167.8	143.8	107.1	161.7	155.4	24.1		128.3 128.9 130.2 130.9	37.1
8/19	3.17 s	7.43 dd (3H) 8.12 dd (2H)	7.06 qa [2]	2.68 d [2]	168.3	144.7	104.2	157.7	155.8	127.0 128.4 130.1 136.6		17.2	37.4
8/20	3.48 t 3.71 t	2.57 s	7.28 s	7.60 dd 8.19 dd	167.3	144.4	108.0	162.6	155.9	24.4		128.6 129.3 130.1 131.3	45.6 65.7
8/21	3.54 t 3.73 t	7.54 m 8.19 m	7.70 s	2.71 s	167.4	146.0	105.1	157.5	155.0	126.9 128.9 130.3 136.5		16.7	45.4 65.5
8/22	2.68 s	7.56- 7.66 m (6H) [3] 8.26- 8.37 m (4H) [3]	8.03 s		167.8	146.4	196.1	160.0	156.5	127.7 [3] 128.6 129.0 129.8 130.8 131.3 131.6 136.1			

Table 2 (continued)

Compound No.	PMR [ppm] (DMSO-d_6) δ Q	δ R^1	δ R^2	δ R^3	CMR [ppm] (DMSO-d_6) δ C-2	δ C-5	δ C-6	δ C-7	δ C-8a	δ R^1	δ R^2	δ R^3	δ Q
8/23	3.57 t 3.75 t	7.53- 7.64 m (6H) [3] 8.31 m (4H) [3]	7.84 s		168.0	145.5	104.6	158.5	156.4	127.5 [3] 128.6 128.9 129.6 130.5 130.8 131.4 136.7			45.5 65.8
14/1	2.65 s	2.51 s	2.66 s	2.68 s	167.6	142.9	123.7	159.3	153.7	23.1	32.0 201.0	14.5	13.1
14/2	4.51 s 7.35 d 7.52 d	2.52 s	2.64 s	2.68 s	166.5	143.3	124.3	159.8	154.0	23.1	32.0 201.5	14.6	33.6 128.3 130.8 131.9 137.1
14/3	4.59 d (2H) 7.25 dt (1H) 7.38 dq (1H) 7.63 t (NH) 7.73 dt (1H) 8.51 dq (1H)	2.44 s	2.56 s	2.59 s	167.6	142.4	122.8	159.7	154.0	23.3	32.5 202.4	15.0	47.5 121.0 122.2 136.9 149.1 157.3
14/4	4.51 d (2H) 7.34 dq (1H) 7.38 d (1H) 7.66 t (NH) 8.44 dd (1H) 8.60 s (1H)	2.44 s	2.58 s	2.59 s	167.4	142.5	122.7	157.3	153.9	23.4	32.5 202.0	15.1	43.6 123.7 135.3 135.7 148.2 149.1
14/5	4.52 d (2H) 7.35 dd (2H) 7.72 t (NH) 8.49 dd (2H)	2.44 s	2.56 s	2.59 s	167.5	142.5	122.4	157.4	153.9	23.3	32.5 202.4	15.0	44.7 122.4 122.8 149.6 149.8
16	3.49 t 3.71 t	2.57 s	7.30 s	7.67 d 8.24 d	167.5	143.4	108.2	162.9	156.1	24.4		128.9 129.1 131.4 136.3	45.6 65.8
17	3.54 t 3.73 t	7.60 d 8.19 d	7.69 s	2.70 s	167.9	146.6	105.4	156.5	155.3	129.0 129.2 135.5 135.8		17.0	45.6 65.8
19	2.68 s	9.22 s	2.97 s	2.72 s	169.2	149.8	119.4	155.2	155.0		30.0 196.8	15.5	13.4
20	2.69 s	2.65 s	2.73 s	9.88 s	169.7	139.0	120.1	164.7	154.6	25.7	29.1 196.4		13.4
22	2.63 s	2.59 s	7.12 s	2.33 s 4.39 s	166.9	143.5	111.7	164.7	155.4	24.5		30.3 44.3 202.1	13.3
23	2.66 s	2.33 s 4.07 s	7.11 s	2.72 s	167.0	146.7	111.0	161.0	155.2	30.3 52.1 204.2		16.8	13.4
24	4.47 s 7.24- 7.34 m (3H) 7.46 dd (2H)	2.59 s	7.12 s	2.31 s 4.39 s	165.8	143.6	111.9	164.8	155.3	24.5	44.4 202.0	30.2 127.5 128.6	34.4 129.2 138.1

[1] Taken in deuteriochloroform. [2] J = 0.8 Hz. [3] Together with δ R^3.

(R^3 = phenyl), **7** (R^3 = trifluoromethyl) and **7** (R^2 + R^3 = propylene), respectively.

However, in all cases discussed above the R^3 group of the unsymmetrically substituted acetylacetone derivative

Table 3

Q	7 (R^3)	Method	Product Ratio (%) 8 (R^1 = methyl)	8 (R^3 = methyl)
H	Phenyl	[1]	76.7	23.3
Methylthio	Phenyl	[1]	77.6	22.4
Benzylthio	Phenyl	[2]	82.0	18.0
Morpholino	Phenyl	[1]	86.2	13.8
Dimethylamino	Phenyl	[1]	87.2	12.8
Methylthio	*t*-Butyl	[1]	97.5	2.5
Morpholino	*t*-Butyl	[1]	98.0	2.0
Methylthio	CH_2COCH_3	[1]	94.3	5.7 [3]
Benzylthio	$-(CH_2)_3-$ [4]	[2]	90.0	10.0
Benzylthio	Trifluoromethyl	[2]	97.0	3.0

[1] hplc. [2] ^{1}H-nmr, lit. [12]. [3] Isolated as **24b**. [4] $R^2 + R^3$.

7 was a strong electron withdrawing one and thus remained the question whether the regiochemical outcome of the above reactions was influenced by electrochemical or by steric factors.

To study this problem different 5-amino-3-Q-1*H*-1,2,4-triazoles **1** were reacted with different type **7** unsymmetrically substituted acetylacetone derivatives having in place of R^3 bulky electron withdrawing (*e.g.* phenyl) and electron attracting (*e.g. tert*-butyl) groups. The isomers formed were isolated, distinquished on the basis of the chemical shifts of the pyrimidine methyl carbon atoms and compared their ratio in the crude reaction mixtures by hplc. For isomers **8** obtained see Table 1, for their nmr data Table 2 and for the ratio of their formation Table 3.

It can be concluded from the data of Table 3 (containing also literary data) that the main product of the above reactions provided in acetic acid as solvent is always isomer **8** (R^1 = methyl). The ratio of products **8** (R^1 = methyl) and **8** (R^3 = methyl) is influenced much more by the inductive ("I") effect of the substituent Q of derivatives **1** than by that of R^3 of derivatives **7**. On the other hand, the more bulky R^3 gave a higher ratio of isomers **8** (R^1 = methyl) leading us to the conclusion that steric factors had the dominant influence in the regiochemical outcome of these reactions.

The Reaction with Aromatic 1,3-Diketones.

Dibenzoylmethane (**7**, $R^1 = R^3$ = phenyl, R^2 = H) also reacted readily in acetic acid with the 1 type 5-amino-1,2,4-triazoles to give the expected type **8** 5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidine derivatives (Scheme 2, Tables 1 and 2).

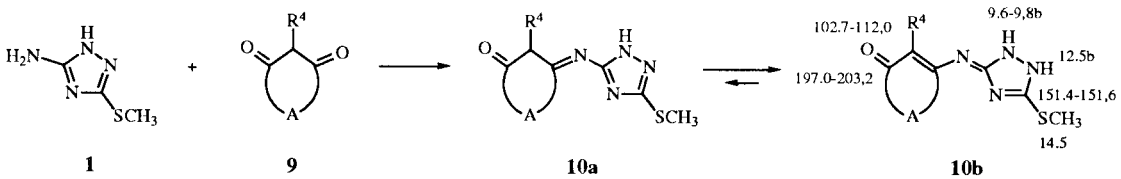
The Reaction with Cyclic 1,3-Diketones.

The reaction of **1** (Q = SCH_3) with type **9** cyclic diketones [**9/1** (R^4 = methyl, A = CH_2CH_2), **9/2** (R^4 = H, A = $CH_2C(CH_3)_2CH_2$)] yielded type **10** Schiff bases [**10/1** (R^4 = methyl, A = CH_2CH_2), **10/2** (R^4 = H, A = $CH_2C(CH_3)_2CH_2$)] (Scheme 3) appearing according to their pmr and cmr spectra in DMSO-d_6 solution in **b** dominant tautomeric forms. The dominant tautomeric form **b** is in agreement with the two broad triazole NH signals at 9.6-9.8 and 12.5 ppm, respectively, as well as with the chemical shifts of the triazole carbon atoms 3 at 151.4 and 151.6 ppm, respectively, (compare with the chemical shifts of the triazole carbon atoms 3 of different 2-substituted 5-amino-2*H*-1,2,4-triazole derivatives appearing between 149.6 and 153.1 ppm [13]). The cyclopentanone and cyclohexanone carbon atoms 2 appeared at 112.0 and 102.7 ppm, respectively, definitely excluding the tautomeric forms **a** in which the above carbon atoms have simple sp^3 character.

The Reaction with 1,4-Diketones.

Acetonylacetone (**11**) reacted with **1** (Q = methylthio and morpholino) to yield 1,2,4-triazol-5-yl-pyrrole derivatives **12** (Q = methylthio and morpholino) (Scheme 4) appearing in DMSO-d_6 solution in **12b** tautomeric forms.

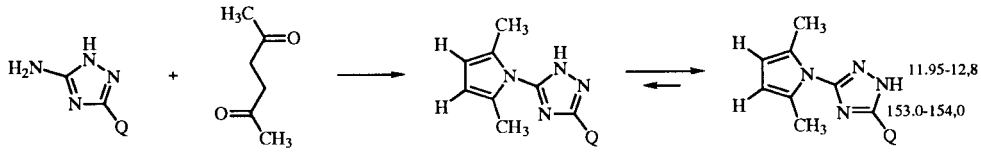
Scheme 3



1 **9** **10a** **10b**

9/1, 10/1: A = CH_2CH_2, R^4 = CH_3
9/2, 10/2: A = $CH_2C(CH_3)_2CH_2$, R^4 = H

Scheme 4



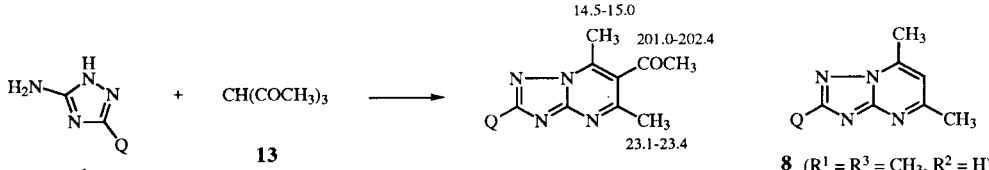
1 11 12a 12b

This is again in agreement with the chemical shifts of the triazole carbon atoms **3** appearing at 153.0 and 154.0 ppm, respectively, see [13].

The Reaction with Triketones.

Triacetylmethane (**13**) reacted with different type **1** 5-amino-3-Q-1*H*-1,2,4-triazoles to yield the corresponding 6-acetyl-1,2,4-triazolo[1,5-*a*]pyrimidine derivatives **14** together with the corresponding deacetylated derivatives **8** (R^1 = R^3 = methyl, R^2 = H) formed most probably by splitting an acetyl group from the reactant **13** (Scheme 5).

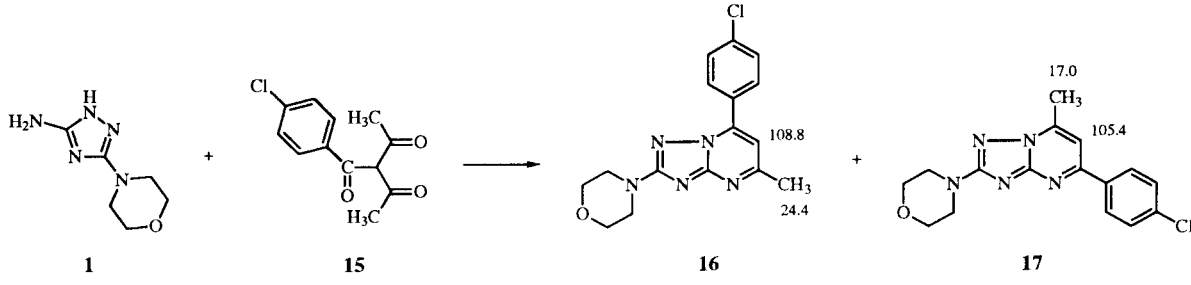
Scheme 5



1 13 14 8 ($R^1 = R^3 = CH_3$, $R^2 = H$)

In an analogues reaction 3-(4-chlorobenzoyl)acetylacetone (**15**) gave with **1** (Q = morpholino) the mixture of the 5-methyl, **17** and 7-methyl, **16** 1,2,4-triazolo[1,5-*a*]-pyrimidine isomers again by splitting an acetyl group from **15** (Scheme 6).

Scheme 6

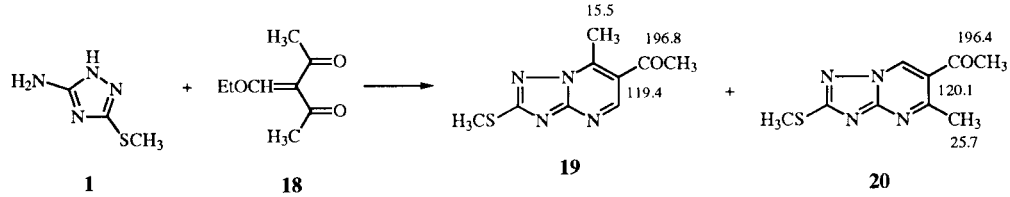


1 15 16 17

Ethoxymethyleneacetylacetone (**18**) as a formyl acetylacetone equivalent afforded with **1** (Q = methylthio) a mixture of 5-methyl, **19** and 7-methyl, **20** 6-acetyl-1,2,4-triazolo[1,5-*a*]pyrimidine isomers (Scheme 7).

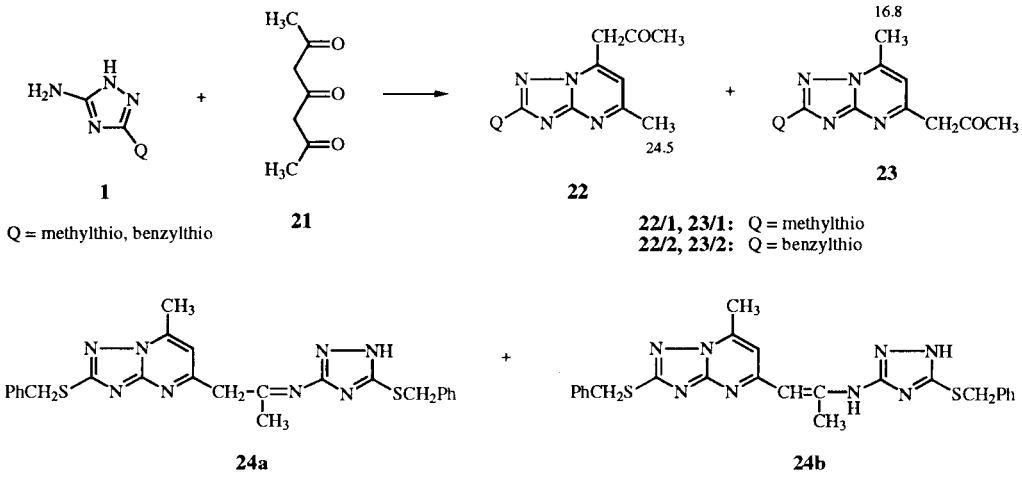
A linear triketone, the 2,4,6-trioxoheptane (**21**) used in the form of its disodium salt reacted with **1** (Q = methylthio) in acetic acid as a simple 1,3-diketone to yield isomers **22/1** and **23/1** (Q = methylthio) (Scheme 8) the 7-methyl isomer **22/1** (Q = methylthio) being the main product of the reaction in nice agreement with the conclusions mentioned above for the reaction of asymmetric

Scheme 7



1 18 19 20

Scheme 8



diketones.

In an analogues reaction described by O'Brien [14] claimed to yield **22/2** (Q = benzylthio) but giving no mp for the product just its ir, uv, and pmr data, 2,4,6-trioxoheptane (**21**) reacted with **1** (Q = benzylthio) in acetic acid to give the expected **22/2** (Q = benzylthio) besides **24** formed by the further reaction of **23/2** (Q = benzylthio) with a molecule of the starting material **1** (Q = benzylthio). In spite of the slight differences between the ir, uv and pmr data described for **22/2** (Q = benzylthio) [14] and our data measured (see Experimental) structure **22/2** (Q = benzylthio) of the product obtained by O'Brien seems to be correct. Derivative **24** may exist in tautomeric forms **24a** and **24b**. The dominant tautomeric structure **24b** of this material in DMSO-d_6 solution is in agreement with the absence of the 7-CH_2 moiety which is replaced by a CH-group appearing at 5.40 and 96.9 ppm in the pmr and cmr, respectively.

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrophotometer. The ultraviolet spectra were obtained by a Pye Unicam SP 8-150 instrument. The pmr and the cmr measurements were performed using Bruker WM-250 instrument. The hplc measurements were performed using a Knauer instrument with a Knauer UV-1 detector and C-8 colunm. The ms spectra were recorded on a Kratos MS25RFA instrument using a direct inlet probe in EI or CI mode. All tlc determinations were performed on DC-Alufolien Kieselgel 60 F_{254} (Merck) plates. The spots were detected by uv light.

General Method for the Reaction of 5-Amino-3-Q-1*H*-1,2,4-triazoles **1** with Acetylacetone (**7**, $R^1 = R^3$ = methyl, R^2 = H) (Method A).

A mixture of 0.02 mole of the appropriate 5-amino-3-Q-1*H*-1,2,4-triazole (**1**) [15,16], 2.05 ml (2.00 g, 0.02 mole) of acetylacetone (**7**, $R^1 = R^3$ = methyl, R^2 = H) (Fluka) and 10 ml of acetic acid was refluxed with stirring for the time given in Table 1. After cooling diethyl ether was added to the reaction mixture while stirring. The crystals that precipitated were collected and recrystallized from an appropriate solvent. For their physical and spectral data see Tables 1 and 2.

2-Morpholino-5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/23**).

A mixture of 6.09 g (0.036 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, Q = morpholino) [16], 7.85 g (0.035 mole) of dibenzoylmethane (**7**, $R^1 = R^3$ = phenyl, R^2 = H) (Aldrich) and 50 ml of acetic acid was refluxed for 18 hours. The reaction mixture was evaporated *in vacuo* to dryness, the residue was partitioned between 100 ml of chlorofom and 100 ml of water, the water layer was extracted with 100 ml of chloroform, the combined chloroform layers were extracted twice with 100 ml portions of water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 10.4 g (83%) of the title product that after recrystallization from dimethylformamide melted at 228-230°. For its physical and spectral data see Tables 1 and 2.

1-Methyl-2-(3-methylthio-1*H*-1,2,4-triazol-1-yl)amino-Δ^1-cyclopentene-5-one (**10/1b**, A = CH_2CH_2, $R^4 = CH_3$).

A mixture of 2.60 g (0.02 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [15], 2.24 g (0.02 mole) of 2-methylcyclopentane-1,3-dione (**9/1**, A = CH_2CH_2, $R^4 = CH_3$) (Fluka) and 10 ml of acetic acid was refluxed with stirring for 1 hour. After cooling the crystals that precipitated were collected and washed with acetonitrile to yield 3.03 g (68%) of 1-methyl-2-(3-methylthio-1*H*-1,2,4-triazol-1-yl)amino-Δ^1-cyclopenten-5-one (**10/1b**, A = CH_2CH_2, $R^4 = CH_3$) that after recrystallization from a 1:1 mixture of dimethylformamide and acetonitrile melted at 261-264°; ir: ν C=O = 1589 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.62 (s, 3H, CCH_3), 2.24 (m, 2H, CH_2-3), 2.60 (s, 3H, SCH_3), 2.93 (m, 2H, CH_2-4), 8.0 (b, 1H, NH-2), 12.5 (b, 1H, triazole NH); cmr (DMSO-d_6): δ ppm 6.9 (CCH_3), 14.3 (SCH_3), 26.9 (C-3), 33.1 (C-4), 112.0 (C-1), 151.6 (triazole C-3), 158.9 (triazole C-5), 167.7 (C-2), 203.2 (C=O).

Anal. Calcd. for $C_9H_{12}N_4OS$ (MW 224.29): C, 48.20; H, 5.39; N, 24.98; S, 14.30. Found: C, 48.04; H, 5.54; N, 25.11; S, 14.56.

4,4-Dimethyl-2-(3-methylthio-1*H*-1,2,4-triazol-1-yl)amino-Δ^1-cyclohexen-6-one (**10/2b**, A = $CH_2C(CH_3)_2CH_2$, R^4 = H).

A mixture of 2.60 g (0.02 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [15], 2.80 g (0.02 mole) of 5,5-dimethylcyclohexane-1,3-dione (**9/2**, A = $CH_2C(CH_3)_2CH_2$, R^4 = H) (Dimedone, Reanal) and 10 ml of acetic acid was refluxed with stirring for 1 hour. After cooling the crystals that precipitated were collected and washed with acetonitrile to yield 4.25 g (82%) of 4,4-dimethyl-2-(3-methylthio-1*H*-1,2,4-triazol-1-yl)amino-Δ^1-cyclohexen-6-one (**10/2b**, A = $CH_2C(CH_3)_2CH_2$, R^4 = H) that after recrystallization from a 1:2 mixture of dimethylformamide and acetonitrile melted at 238-240°; ir: ν C=O = 1564 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.01 (s, 6H, CCH_3), 2.07 (s, 2H, CH_2-3), 2.39 (s, 3H, SCH_3), 2.62 (s, 2H, CH_2-5), 6.41 (s, 1H, CH), 9.6 (bs, 1H, NH-2), 12.5 (b, 1H, triazole NH); cmr (DMSO-d_6): δ ppm 14.5 (SCH_3), 28.0 (CH_3), 32.4 (CH_2-3), 41.5 (C-4), 50.2 (CH_2-5), 102.7 (C-1), 151.4 (triazole C-3), 156.3 (C-2), 158.9 (triazole C-5), 197.0 (C=O).

Anal. Calcd. for $C_{11}H_{16}N_4OS$ (MW 252.34): C, 52.36; H, 6.39; N, 22.20; S, 12.71. Found: C, 52.44; H, 6.62; N, 22.11; S, 12.80.

5-(2,5-Dimethylpyrrol-1-yl)-3-methylthio-1*H*-1,2,4-triazole (**12b**, Q = methylthio).

A mixture of 2.60 g (0.02 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [15], 2.35 ml (2.28 g, 0.02 mole) of acetonylacetone (**11**) (Aldrich) and 10 ml of acetic acid was refluxed with stirring for 4 hours. After cooling 35 ml of water was added to the reaction mixture and extracted twice with 30 ml portions of chloroform. The combined chloroform layers were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness. The residue (3.8 g) was dry-column flash chromatographed [17] on a silica gel layer. The washings obtained with a 20:1 mixture of benzene and ethyl acetate were collected and evaporated *in vacuo* to dryness to yield 2.60 g (62%) of 5-(2,5-dimethyl-pyrrol-1-yl)-3-methylthio-1*H*-1,2,4-triazole (**12b**, Q = methylthio) that after recrystallization from cyclohexane melted at 100-102°; pmr (DMSO-d_6): δ ppm 2.12 (s, 6H, CCH_3), 2.64 (s, 3H, SCH_3), 5.80 (s, 2H, CH), 11.95 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 13.0 (CCH_3), 14.3 (SCH_3), 107.1 (C-2' + 5'), 128.7 (C-3' + 4'), 153.0 (C-3), 156.6 (C-5).

Anal. Calcd. for $C_9H_{12}N_4S$ (MW 208.29): C, 51.90; H, 5.81; N, 26.90; S, 15.39. Found: C, 51.97; H, 5.86; N, 26.83; S, 15.40.

5-(2,5-Dimethylpyrrol-1-yl)-3-morpholino-1*H*-1,2,4-triazole (**12b**, Q = morpholino).

A mixture of 3.38 g (0.02 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, Q = morpholino) [16], 2.35 ml (2.28 g, 0.02 mole) of acetonylacetone (**11**) (Aldrich) and 10 ml of acetic acid was refluxed with stirring for 4 hours. After cooling 35 ml of water was added to the reaction mixture and extracted twice with 30 ml portions of chloroform. The combined chloroform layers were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 3.8 g (72%) of 5-(2,5-dimethylpyrrol-1-yl)-3-morpholino-1*H*-1,2,4-triazole (**12b**, Q = morpholino) that after recrystallization first from ethyl actate then from acetonitrile melted at 219-221°; pmr (DMSO-d_6): δ ppm 2.10 (s, 6H, CH_3), 3.30 (t, 4H, NCH_2), 3.69 (t, 4H, OCH_2), 5.74 (s, 2H, CH), 12.8 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.0 (CH_3), 46.1 (NCH_2), 65.4 (OCH_2), 106.6 (C-2' + 5'), 128.4 (C-3' + 4'), 154.0 (C-3), 158.0 (C-5).

Anal. Calcd. for $C_{12}H_{17}N_5O$ (MW 247.30): C, 58.28; H, 6.93; N, 28.32. Found: C, 58.35; H, 6.98; N, 28.29.

6-Acetyl-5,7-dimethyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/1**) and 5,7-Dimethyl-2-methylthio-1,2,4-triazolo-[1,5-*a*]pyrimidine (**8/1**).

A solution of 5.2 g (0.04 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [15], 5.68 g (0.04 mole) of triacetylmethane (**7**, R^1 = R^3 = methyl, R^2 = acetyl) [18], 10 ml of acetic acid and 30 ml of dimethylformamide was refluxed with stirring for 20 minutes. After cooling the crystals that precipitated were collected to yield 4.5 g (58%) of 5,7-dimethyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/1**) that after recrystallization from 2-propanol melted at 154-156°.

To the mother liquor 50 ml of water was added and extracted twice with 100 ml portions of chloroform. The combined chloroform layers were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness. The residue (3.05 g) was chromatographed on a silica gel column (eluent a 1:2 mixture of benzene and ethyl acetate) to yield 2.2 g (23%) of 6-acetyl-5,7-dimethyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/1**) that after recrystallization from 2-propanol melted at 115-116°. For physical and spectral data of both products see Tables 1 and 2.

6-Acetyl-2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo-[1,5-*a*]pyrimidine (**14/2**) and 2-(4-Chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/3**).

A mixture of 5.9 g (0.0245 mole) of 5-amino-3-(4-chlorobenzylthio)-1*H*-1,2,4-triazole (**1**, Q = 4-chlorobenzylthio) [15], 3.48 g (0.0245 mole) of triacetylmethane (**7**, R^1 = R^3 = methyl, R^2 = acetyl) [18] and 50 ml of acetic acid was stirred at room temperature for 3 days. The solution thus obtained was poured into 200 g of cracked ice, extracted two times with 100 ml portions of chlorofom, the combined chloroform layers were extracted with a saturated solution of sodium hydrogencarbonate and water, dried over anhydrous sodium sulfate, and evaporated *in vacuo* to dryness to yield 12.5 g of an oily product that partly crystallized upon standing. This was chromatographed on a silica gel colunm (eluent a 1:2 mixture of benzene and ethyl acetate) to yield 3.55 g (42%) of 6-acetyl-2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/2**) that after recrystallization from ethyl acetate melted at 152-153°.

Continuing the chromatography 2.5 g (33%) of 2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/3**) was obtained after recrystallization from ethyl acetate melted at 144-145° (lit [14] mp 136-137°). For physical and spectral data of both products see Tables 1 and 2.

6-Acetyl-2-(pyridin-2-ylmethylamino)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/3**) and 2-(Pyridin-2-ylmethylamino)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/4**).

These compounds were prepared as those of 6-acetyl-2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/2**) and 2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo-[1,5-*a*]pyrimidine (**8/3**) starting from 2.95 g (0.0142 mole) of 5-amino-3-(pyridin-2-ylmethylamino)-1*H*-1,2,4-triazole (**1**, Q = pyridin-2-ylmethylamino) [16] and 2.02 g (0.0142 mole) of tri-

acetylmethane (**7**, $R^1 = R^3$ = methyl, R^2 = acetyl) [18] with the exception that ethyl acetate was used as eluent during their chromatography. For their physical and spectral data see Tables 1 and 2.

6-Acetyl-2-(pyridin-3-ylmethylamino)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/4**) and 2-(Pyridin-3-ylmethylamino)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/5**).

These compounds were prepared as those of 6-acetyl-2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/2**) and 2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo-[1,5-*a*]pyrimidine (**8/3**) starting from 8.3 g (0.0436 mole) of 5-amino-3-(pyridine-3-ylmethylamino)-1*H*-1,2,4-triazole (**1**, Q = pyridin-3-ylmethylamino) [16] and 6.40 g (0.045 mole) of triacetylmethane (**7**, $R^1 = R^3$ = methyl, R^2 = acetyl) [18] with the exception that ethyl acetate was used as eluent during their chromatography. For their physical and spectral data see Tables 1 and 2.

6-Acetyl-2-(pyridin-4-ylmethylamino)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/5**) and 2-(Pyridin-4-ylmethylamino)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/6**).

These compounds were prepared as those of 6-acetyl-2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**14/2**) and 2-(4-chlorobenzylthio)-5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**8/3**) starting from 11.63 g (0.06 mole) of 5-amino-3-(pyridine-4-ylmethylamino)-1*H*-1,2,4-triazole (**1**, Q = pyridin-4-ylmethylamino) [16] and 7.53 g (0.06 mole) of triacetylmethane (**7**, $R^1 = R^3$ = methyl, R^2 = acetyl) [18] with the exception that ethyl acetate was used as eluent during their chromatography. For their physical and spectral data see Tables 1 and 2.

2-Morpholino-5-(4-chlorophenyl)-7-methyl-1,2,4-triazolo-[1,5-*a*]pyrimidine (**16**) and 2 Morpholino-7-(4-chlorophenyl)-5-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**17**).

A solution of 7.61 g (0.045 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, Q = morpholino) [16], 9.55 g (0.04 mole) of 3-(4-chlorobenzoyl)-2,4-petanedione (**15**) [19] and 40 ml of acetic acid was stirred at room temperature for 3 days. The solution thus obtained was poured into 300 g of cracked ice, the crystals that precipitated were collected and chromatographed on a silica gel column (eluent a 1:2 mixture of benzene and ethyl acetate) to yield 1.4 g (11%) of 2-morpholino-7-(4-chlorophenyl)-5-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**17**) that after recrystallization from ethanol melted at 173-175°.

Continuing the chromatography 6.6 g (50%) of 2-morpholino-5-(4-chlorophenyl)-7-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**16**) was obtained that after recrystallization from butanol melted at 208-210°. For physical and spectral data of both products see Tables 1 and 2.

6-Acetyl-5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**19**) and 6-Acetyl-7-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]-pyrimidine (**20**).

A mixture of 1.3 g (0.01 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [15], 1.87 g (0.012 mole) of ethoxymethyleneacetylacetone (**18**) [20] and 20 ml of acetonitrile was refluxed with stirring for 4 hours. The reaction mixture was evaporated *in vacuo* to dryness and the crystalline residue (2.35 g) was recrystallized twice from 2-propanol to yield 1.2 g (50%) of 6-acetyl-5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]-pyrimidine (**19**), mp 119-121°.

The combined mother liquors were evaporated *in vacuo* to dryness and the residue chromatographed on a silica gel column (eluent a 1:1 mixture of *n*-hexane and ethyl acetate) to yield 0.5 g (23%) of 6-acetyl-7-methyl-2-methylthio-1,2,4-triazolo-[1,5-*a*]pyrimidine (**20**) that after recrystallization from 2-propanol melted at 157-158°. For physical and spectral data of both compounds see Tables 1 and 2.

5-Acetonyl-7-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**22/1**, Q = methylthio) and 7-Acetonyl-5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**23/1**, Q = methylthio).

A mixture of 2.60 g (0.02 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [15], 3.36 g (0.02 mole) of heptane-2,4,6-trione disodium salt (**21**) [21] and 10 ml of acetic acid was refluxed with stirring for 3 hours. Twenty ml of water was added to the reaction mixture, it was extracted twice with 20 ml portions of chloroform, the combined chloroform layers were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 3.25 g of crystalline product that after two recrystallizations from 2-propanol afforded 2.7 g (57%) of 5-acetonyl-7-methyl-2-methylthio-1,2,4-triazolo-[1,5-*a*]pyrimidine (**22/1**, Q = methylthio), mp 130-132°.

The combined mother liquors were evaporated *in vacuo* to dryness and the residue chromatographed on a silica gel column (eluent a 9:1 mixture of chloroform and acetic acid) to yield 0.2 g (4%) of 7-acetonyl-5-methyl-2-methylthio-1,2,4-triazolo-[1,5-*a*]pyrimidine (**23/1**, Q = methylthio) that after recrystallization from cyclohexane melted at 102-104°. For physical and spectral data of both compounds see Tables 1 and 2.

5-Acetonyl-2-benzylthio-7-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**22/2**, Q = benzylthio) and 2-Benzylthio-7-[2-(5-benzylthio-1*H*-1,2,4-triazol-3-ylamino)propenyl]-5-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**24b**).

A mixture of 4.12 g (0.02 mole) of 5-amino-3-benzylthio-1*H*-1,2,4-triazole (**1**, Q = benzylthio) [22], 3.36 g (0.02 mole) of heptane-2,4,6-trione disodium salt (**21**) [21] and 10 ml of acetic acid was refluxed with stirring for 4 hours. Thirty ml of water was added to the reaction mixture, it was extracted three times with 20 ml portions of chloroform, the combined chloroform layers were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 6.2 g of crystalline product that after two recrystallizations from dichloroethane afforded 4.41 g (71%) of 5-acetonyl-2-benzylthio-7-methyl-1,2,4-triazolo[1,5-*a*]pyrimidine (**22/2**, Q = benzylthio), mp 137-138°; ir: ν C=O = 1721 cm^{-1}; uv (methanol): λ max nm (log ε) 229 (4.32), 304 (3.90), 379 (3.48); for its physical and nmr data see Tables 1 and 2. The product is most probably identical with that described by O'Brien [14] for which the mp was not given only the following spectral data: ir: ν C=O = 1730 cm^{-1}; uv (methanol): λ max nm (log ε) 230 (3.67), 305 (3.23); pmr (DMSO-d_6): δ ppm 2.35 (s, 3H), 2.60 (s, 3H), 4.4 (s, 2H), 4.5 (s, 2H), 7.15 (s, 1H), 7.35 (m, 5H).

The combined mother liquors were evaporated *in vacuo* to dryness and the residue chromatographed on a silica gel column (eluent a 9:1 mixture of chloroform and methanol) to yield 0.2 g (4%) of 2-benzylthio-7-[2-(5-benzylthio-1*H*-1,2,4-triazol-3-ylamino)propenyl]-5-methyl-1,2,4-triazolo[1,5-α]pyrimidine (**24b**) that after recrystallization from acetonitrile melted at 149-150.5°; uv (methanol): λ max nm (log ε) 265 (3.93), 387 (4.30);

pmr (DMSO-d_6): δ ppm 2.42 [s, 3H, C=N(CH_3)], 2.62 (s, 3H, CCH_3), 4.41 (s, 2H, SCH_2), 4.51 (s, 2H, SCH_2), 5.40 (bs, 1H, C*H*=C(CH_3)), 6.76 (s, 1H, Het-H), 7.25-7.49 (m, 11H, ArH + NH), 12.2 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 16.6 (Het-CH_3), 22.1 (CCH_3), 34.6 and 36.1 (2 x SCH_2), 96.9 (CH), 108.8 (C-6), 127.3, 127.4, 128.5 (two peaks), 128.9, 129.0, 137.2 and 137.7 (PhC), 145.2 (C-5), 151.5 (triazole-5'), 154.4 (C-8a), 158.3 (triazole-3'), 160.6 (C-7), 164.6 (C-2); ms: (EI) M^+ = 500, (CI) M^+ = 501.

Anal. Calcd. for $C_{25}H_{24}N_8S_2$ (MW 500.66): C, 59.98; H, 4.83; N, 22.38; S, 12.81. Found: C, 60.05; H, 5.07; N, 22.34; S, 12.90.

Acknowledgement.

The authors wish to express their thanks to Miss Zsófia Kárpáti for recording the uv spectra, to Mrs. Sándorné Sólyom for recording the ir spectra, to Mr. Attila Fürjes for recording the nmr spectra, to Mr. Kálmán Ujszászy for recording the ms spectra and helpful discussions, to Mrs. Lászlóné Zalavári for performing the elemental analyses and to Mrs. Lászlóné Nyikos for technical help.

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