On Triazoles. VI [1]. The Acylation of 5-Amino-1,2,4-triazoles

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The isomeric and tautomeric structure of **I** and **II** type monoacylated 5-amino-1,2,4-triazole derivatives was studied with the help of their ir, uv, pmr and cmr spectra as well as model compounds prepared for this purpose. It was stated that the structure of the **I** type ring-acylated derivatives is **2o** and those of their **II** type isomers is **5a**.

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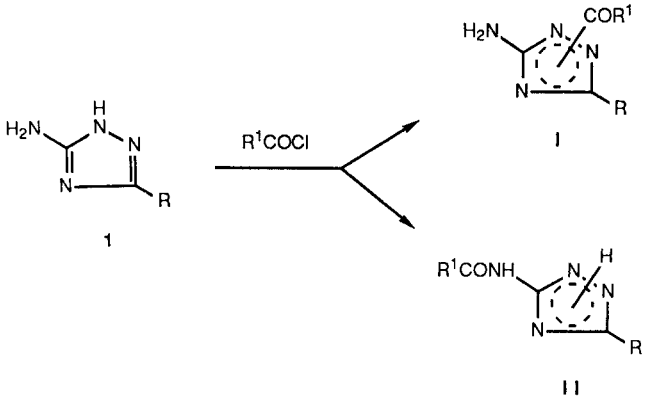
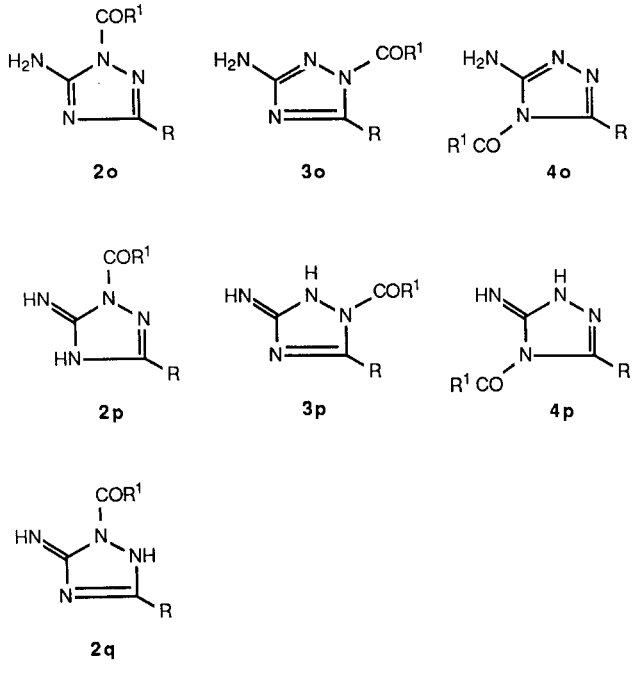
The acylation of 3-*R*-5-amino-1*H*-1,2,4-triazoles **1** to yield either a ring-monoacylated product **I** or its acylamino-isomer **II** (Scheme 1) was studied in the past 40 years by many authors [2-24]. Nevertheless the structure of the compounds obtained - regardless to different corrections and re-studies of the previous results - is in many cases ambiguous. The ring-acylated products **I** can exist in isomeric forms **2, 3** or **4** (Scheme 2) - all having possibility to appear in different tautomeric forms **o, p** or **q** - while the acylamino-isomers **II** can appear in tautomeric forms **a-e** (Scheme 3).

Scheme 1



Scheme 2

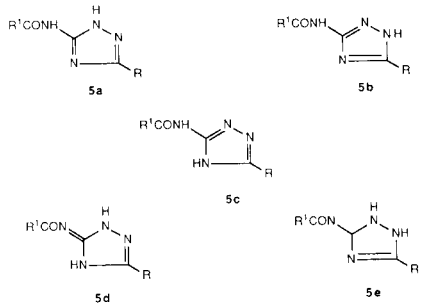


The first spectral evidence to the structure of the **I** and **II** type products obtained by the acetylation of 5-amino-1*H*-1,2,4-triazole (**1**, R = H) gave Staab and Seel [10] who proposed on the basis of the ir carbonyl frequency 2-acetyl-structure **3o** (R = H, $R^1 = CH_3$) to the **I**-type product absorbing at 1732 cm^{-1} and structure **5b** (R = H, $R^1 = CH_3$) to that of **II** absorbing at 1689 cm^{-1}.

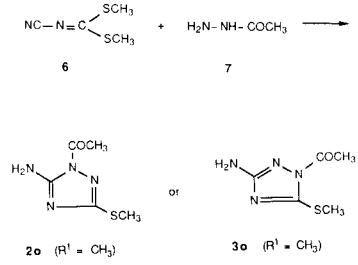
Van den Bos [11] re-investigated the structure of the above products with the help of pmr. He agreed with their structure **I** and **II** proposed by Staab and Seel [10] but was not able to establish the position of the acetyl group on the triazole ring. Thus, for practical reasons he proposed to use the 1-acetyl-structure **2o** (R = H, $R^1 = CH_3$) for the ring-acetylated and **5b** (R = H, $R^1 = CH_3$) for the acetylamino-derivative, respectively. Coburn and co-workers [12], taking into consideration the fact that the acetyl group of the ring acetylated derivative **I** did not cause any change in the chemical shift of the triazole ring proton as compared with that of the non-acetylated **1** (R = H) in the pmr seemed to support the **2o** (R = H, $R^1 = CH_3$) structure of this compound.

Chipen and Grinstein [13] reported in 1962 on the synthesis of 1-acetyl- and 1-benzoyl-5-amino-3-phenyl-1*H*-1,2,4-triazole (**2o**, R = phenyl, R^1 = methyl and phenyl, respectively) giving no evidence for their proposed struc-

Scheme 3



Scheme 4



ture **2o**. Based on ir investigations [14] proposed at the same year the above authors the 4*H*-structure **4o** for these derivatives, but recording their Raman spectra [15] and dipole moment [16] in 1965 and 1966, respectively, they changed their mind proposing again structure **2o**. The 4*H*-structure **4o** of the above monobenzoylated derivative was proposed by Davidson [17], too.

German authors [18] reported in 1975 the synthesis of the 1-(4-methoxybenzyl)-3-methylthio-5-amino-1*H*-1,2,4-triazole without giving any evidence for the proposed **2o**-structure. Based on pmr studies reported in 1981 Sasse and Niedrig [19] on the synthesis of 4-acylated-3-alkylthio-5-amino-4*H*-1,2,4-triazole derivatives (**4o**, R = alkylthio, $R^1 = OCH_3$, OC_2H_5), too, but their structures proved to be later on also erroneous and were corrected in 1983 by Winkler and Kristinson [20] with the help of cmr to be of **2o** (R = alkylthio, $R^1 = OCH_3$, OC_2H_5).

The tautomeric structure of the **II** type acylamino-isomers was not studied in detail. Different authors described them in the **5a** [2, 6-8, 11, 13, 15, 16, 20], **5b** [3, 10, 12, 21, 23, 24], **5c** [14, 17, 19, 22] and **5e** [4, 5] tautomeric forms.

We have synthesized a series of **I** and **II** type derivatives (Table I and III, respectively) and recorded their ir, pmr, cmr and uv spectra (Tables II and IV, respectively). In the ir spectra of the **I** type derivatives the NH_2 signals, regardless on the quality of the R^1 and R^2 appeared as singlets in the region between 3480 and 3380 cm^{-1}, while the corresponding ν NH signals of the **II** type derivatives appeared as broad signals never exceeding the value of 3310 cm^{-1} giving a good possibility to the differentiation between them. The carbonyl frequencies of the above isomeric pairs well followed the rule stated by Staab and Seel [10]. Namely the carbonyl frequency of the **I** type derivative was in all cases higher than that of its **II** type isomeric pair [compare *e.g.* the ν CO bands of **I/1, I/3, I/8, I/12, I/21, I/25, I/28** and **I/41** (Table II) with those of **II/2, II/4, II/7, II/12, II/17, II/20, III/21** and **II/24** (Table IV), respectively]. On the other hand neither the ν NH_2 and ν NH bands, nor the ν CO frequencies gave information about the position of the acyl group on the triazole ring (see isomers **2, 3** or **4**), or on the tautomeric situation of these products. Moreover the range of the carbonyl frequencies of derivatives **I** (ν CO = 1738-1665 cm^{-1}) practically overlaped the range of those of the corresponding derivatives **II** (ν CO = 1718-1654 cm^{-1}) making impossible to formulate any general rule for the differentiation between derivatives **I** and **II** based on the ν CO frequency. In the pmr spectra of derivatives **I** the NH_2 protons appeared as broad singlets between 6.7 and 7.85 ppm. Just to the contrary the two broad, will separated NH signals of derivatives **II** appeared between 9.4 and 11.9 ppm and 10.8 and 13.7 ppm, respectively, making again possible the safe differentiation between derivatives **I** and **II**. The chemical shifts of the amino groups of the 1-acetyl-3,5-diamino-1*H*-1,2,4-triazole[**I/27**, R^1 = amino, R^2 = methyl) (Table II)], where the chemical surrounding of the amino-group (3) is equvalent with that of derivatives **3** and the chemical surrounding of the amino-group (5) is equivalent with that of derivatives **2** and **4**, respectively, appeared to be significantly different [**I/27**: δ NH_2(3) = 5.65 ppm, δ NH_2(5) = 7.4 ppm]. Comparing these data with the NH_2 chemical shifts measured for derivatives **I** (δ NH_2 = 6.7-7.85 ppm) it is clear that derivatives **I** should have either structure **2** or **4**. From among the structures **2** and **4** helped to choose the correct one the reaction of *N*-cyanocarbonimidodithioic acid dimethyl ester (**6**) and acetylhydrazine (**7**) (Scheme 4) in which only derivatives **2** (R^1 = methylthio, R^2 = methyl) and **3** (R^1 = methylthio, R^2 = methyl) could be formed. As the product obtained in this reaction was in all respects identical with that obtained by direct acetylation of **1** (R^1 = methylthio) derivative **I/1,** Table I and II) the structure of the ring-acylated derivatives **I** should be **2**. Moreover the fact that the NH protons of derivatives **I** were equivalent forming in the pmr spectra one NH_2 singlet strongly supported (although it did not prove unambiguously) the idea that these derivatives existed in **2o** tautomeric form. This conclusion is in accordance with the sharp ν NH_2 bands appearing between 3480 and 3380 cm^{-1} (Table II) in the ir. The cmr

Table I

Compound No.	R^1	R^2	Method	Reaction Time (hours)	Reaction Temperature (°C)	Yield %	MP (°C) (Crystallized from)	Molecular formula (MW) or Reference MP (°C)	Analysis Calcd./Found C	H	N	S	Hal
I/1	Methylthio	Methyl	B	1	-10	75	158-160 (Dioxane)	$C_5H_8N_4OS$ (172.21)	34.87 34.93	4.68 4.74	32.54 32.48	18.62 18.52	
I/2	Methylthio	Ethyl	B	2	-10	58	119-120 (1-BuOH)	$C_6H_{10}N_4OS$ (186.24)	38.69 38.91	5.41 5.29	30.08 29.79	17.22 16.96	
I/3	Methylthio	1-Methylethyl	A	1	-10	65	108-110 (CH)	$C_7H_{12}N_4OS$ (200.27)	41.98 42.09	6.04 6.19	27.98 27.99	16.01 16.29	
I/4	Methylthio	1,1-Dimethylethyl	A	1	10	85	140-142 (EtOH)	$C_8H_{14}N_4OS$ (214.29)	44.84 45.14	6.58 6.64	26.15 26.08	14.96 15.09	
I/5	Methylthio	Heptyl	A	3	-5	71	77-79 (MeOH)	$C_{11}H_{20}N_4OS$ (256.37)	51.53 51.66	7.86 7.99	21.85 21.76	12.51 12.48	
I/6	Methylthio	Prop-1-ene-1-yl	A	0.5	0	52	164-166 (2-PrOH)	$C_7H_{10}N_4OS$ (198.25)	42.41 42.56	5.08 5.21	28.26 28.36	16.17 16.02	
I/7	Methylthio	Dec-1-ene-10-yl	A	5	0	63	84-85 (MeOH)	$C_{14}H_{24}N_4OS$ (296.43)	56.72 56.70	8.16 8.19	18.90 18.93	10.82 10.71	
I/8	Methylthio	Dichloromethyl	C	6	0	62	171-173 (Dioxane)	$C_5H_6Cl_2N_4OS$ (241.10)	24.91 25.20	2.51 2.59	23.24 22.98	13.31 13.04	29.41 29.16
I/9	Methylthio	Ethoxy	E	18	–	70	137-138 (EtOH)	135-136 [19] [a]					
I/10	Methylthio	3-Ketobutyl	A	3	0	87	153-154 (EtOH)	$C_6H_{12}N_4O_2S$ (228.27)	42.09 42.04	5.30 5.44	24.54 24.37	14.05 14.26	
I/11	Methylthio	2-Carbomethoxyethyl	A	2	-5	63	153-155 (Dioxane)	$C_6H_{12}N_4O_3S$ (244.27)	39.33 39.58	4.95 5.24	22.94 22.75	13.13 13.09	
I/12	Methylthio	Phenyl	A	2	10	96	150-152 (Dioxane)	$C_{10}H_{10}N_4OS$ (234.28)	51.26 51.44	4.30 4.52	23.92 24.11	13.69 13.55	
I/13	Methylthio	2-Chlorophenyl	A	2	5	93	164-166 (EtOH)	$C_{10}H_9ClN_4OS$ (268.73)	44.69 44.81	3.38 3.61	20.85 20.62	11.93 11.96	13.19 13.08
I/14	Methylthio	4-Chlorophenyl	A	1.5	10	84	175-177 (EtOH)	$C_{10}H_9ClN_4OS$ (268.73)	44.69 44.96	3.38 3.46	20.85 20.61	11.93 12.10	13.19 13.28
I/15	Methylthio	2-Acetoxyphenyl	A	1	10	70	138-140 (Benzene)	$C_{12}H_{12}N_4O_3S$ (292.32)	49.30 49.22	4.14 4.33	19.17 18.99	10.97 11.04	
I/16	Methylthio	2-Carbomethoxyphenyl	A	1	0	73	208-210 (Dioxane)	$C_{12}H_{12}N_4O_3S$ (292.32)	49.30 49.34	4.14 4.43	19.17 19.34	10.97 11.12	
I/17	Methylthio	3,4-Dimethoxyphenyl	A	1.5	10	77	174-176 (EtOH)	$C_{12}H_{14}N_4O_3S$ (294.33)	48.97 48.80	4.79 5.01	19.04 19.02	10.89 11.04	
I/18	Methylthio	3,4,5-Trimethoxyphenyl	A	4	10	66	154-156 (2-PrOH)	$C_{13}H_{16}N_4O_4S$ (324.36)	48.13 48.31	4.97 5.24	17.27 17.13	9.89 10.01	
II/19	Methylthio	Cyclohexyl	A	2	0	88	160-162 (MeOH)	$C_{10}H_{16}N_4OS$ (240.33)	49.97 50.08	6.71 6.73	23.31 23.14	13.34 13.47	
I/20	Methylthio	2-Phenyleth-1-ene-1-yl	A	1	-5	49	191-193 (Dioxane)	$C_{12}H_{12}N_4OS$ (260.32)	55.36 55.10	4.65 4.61	21.52 21.39	12.32 12.23	
I/21	Methylthio	Phenoxymethyl	A	1	0	63	138-140 (1-BuOH)	$C_{11}H_{12}N_4O_2S$ (264.31)	49.98 50.26	4.58 4.78	21.20 21.02	12.13 12.26	
I/22	Methylthio	2,4-Dichlorophenoxymethyl	A	1	0	63	168-170 (1-BuOH)	$C_{11}H_{10}Cl_2N_4O_2S$ (333.20)	39.65 39.91	3.02 3.15	16.81 16.89	9.62 9.77	21.28 21.55
I/23	Methylthio	2,6-Dichlorophenoxymethyl	A	1	10	53	181-183 (1-BuOH)	$C_{11}H_{10}Cl_2N_4O_2S$ (333.20)	39.65 39.88	3.02 3.22	16.81 16.80	9.62 9.84	21.28 21.46
I/24	Methylthio	3-Phenyl-5-methylisoxazol-4-yl	A	2	5	73	203-205 (EtOH)	$C_{14}H_{13}N_5O_2S$ (315.35)	53.32 53.13	4.15 4.25	22.21 22.02	10.17 10.42	
I/25	4-Chlorobenzylthio	Methyl	A	1	-5	68	142-143 (EtOAc)	$C_{11}H_{11}ClN_4OS$ (282.75)	46.72 46.88	3.92 4.05	19.82 20.12	11.34 11.18	12.54 12.60

Table I (continued)

Compound No.	R^1	R^2	Method	Reaction Time (hours)	Reaction Temperature (°C)	Yield %	MP (°C) (Crystallized from)	Molecular formula (MW) or Reference MP (°C)	Analysis Calcd./Found C	H	N	S	Hal
I/26	4-Chlorobenzylthio	2-Carbomethoxy-ethyl	A	2	0	86	146-148 (Dioxane)	$C_{14}H_{15}ClN_4O_3S$ (354.81)	47.39 47.32	4.26 4.12	15.79 15.63	9.04 9.28	9.99 9.85
I/27	Amino	Methyl	F	1	30	92	228-230 (Dioxane)	≈240 [11] [b]					
I/28	Morpholino	Methyl	A	1	-10	52	185-187 (1-BuOH)	$C_8H_{13}N_5O_2$ (211.22)	45.49 45.39	6.20 6.32	33.16 32.94		
I/29	Morpholino	Ethyl	B	1	0	56	133-135 (EtOH)	$C_9H_{15}N_5O_2$ (225.25)	47.99 48.13	6.71 6.76	31.09 31.12		
I/30	Morpholino	2-Methylethyl	B	1	10	79	130-132 (EtOH)	$C_{10}H_{17}N_5O_2$ (239.28)	50.19 50.24	7.16 7.31	29.27 29.46		
I/31	Morpholino	1,1-Dimethylethyl	A	1	10	56	144-146 (EtOH)	$C_{11}H_{19}N_5O_2$ (253.30)	52.15 52.12	7.56 7.62	27.65 27.69		
I/32	Morpholino	*n*-Heptyl	A	2	-5	65	108-109 (EtOH)	$C_{14}H_{25}N_5O_2$ (295.38)	56.92 56.91	8.53 8.56	23.71 23.87		
I/33	Morpholino	Prop-1-ene-1-yl	B	3.5	0	54	200-202 (Dioxane)	$C_{10}H_{15}N_5O_2$ (237.26)	50.62 50.54	6.37 6.43	29.52 29.40		
I/34	Morpholino	Dec-1-ene-10-yl	A	4	0	57	80-82 (MeOH)	$C_{17}H_{29}N_5O_2$ (335.44)	60.86 61.03	8.71 8.83	20.88 20.72		
I/35	Morpholino	Chloromethyl	C	3	20	63	178-180 (EtOH)	$C_8H_{12}ClN_5O_2$ (245.68)	39.11 39.32	4.92 5.17	28.51 28.32		14.43 14.57
I/36	Morpholino	Ethoxy	E	2	–	65	177-179 (Dioxane)	$C_9H_{15}N_5O_3$ (241.25)	44.80 44.85	6.27 6.38	29.03 28.92		
I/37	Morpholino	Ethoxycarbonyl	A	1	-10	75	145-147 (EtOH)	$C_{10}H_{15}N_5O_4$ (269.26)	44.60 44.42	5.61 5.79	26.01 25.80		
I/38	Morpholino	3-Ketobutyl	B	5	10	68	136-137 (MeOH)	$C_{11}H_{17}N_5O_3$ (267.29)	49.43 49.35	6.41 6.38	26.20 26.07		
I/39	Morpholino	2-Carbomethoxyethyl	B	4	0	53	142-144 (EtOH)	$C_{11}H_{17}N_5O_4$ (283.29)	46.63 46.83	6.05 6.21	24.72 24.69		
I/40	Morpholino	2-Carboxyethyl	D	3	–	94	229-231 (Dioxane)	$C_{10}H_{15}N_5O_4$ (269.26)	44.60 44.86	5.62 5.91	26.01 25.88		
I/41	Morpholino	Phenyl	A	1	10	59	174-175 (Dioxane)	$C_{13}H_{15}N_5O_2$ (273.29)	57.13 57.22	5.53 5.79	25.63 25.62		
I/42	Morpholino	4-Chlorophenyl	A	1	10	59	177-178 (1-BuOH)	$C_{13}H_{14}ClN_5O_2$ (307.74)	50.73 50.99	4.58 4.74	22.76 22.58		
I/43	Morpholino	2-Acetoxyphenyl	B	1	10	88	170-172 (1-BuOH)	$C_{15}H_{17}N_5O_4$ (331.33)	54.37 54.33	5.17 5.47	21.14 20.88		
I/44	Morpholino	3,4-Dimethoxyphenyl	A	1	0	50	189-191 (EtOH)	$C_{15}H_{19}N_5O_4$ (333.34)	54.04 54.34	5.74 5.97	21.01 21.25		
I/45	Morpholino	3,4,5-Trimethoxyphenyl	A	1.5	10	48	202-204 (1-BuOH)	$C_{16}H_{21}N_5O_5$ (363.37)	52.88 53.07	5.83 6.07	19.27 19.22		
I/46	Morpholino	Cyclohexyl	A	2.5	0	63	151-153 (MeOH)	$C_{13}H_{21}N_5O_2$ (279.34)	55.89 55.62	7.58 7.63	25.07 24.85		
I/47	Morpholino	2-Phenyleth-1-ene-1-yl	A	1	5	52	199-201 (Dioxane)	$C_{15}H_{17}N_5O_2$ (299.33)	60.18 60.10	5.73 5.63	23.40 23.25		
I/48	Morpholino	3-Phenyl-5-methylisoxazol-4-yl	A	2	5	72	167-169 (EtOH)	$C_{17}H_{18}N_6O_3$ (354.36)	57.62 57.81	5.12 5.31	23.72 23.54		
I/49	Morpholino	1-(2,6-Dichlorophenyl-4-methyl-pyrazole-3-yl	A	2	4	68	228-230 (MeOH)	$C_{17}H_{17}Cl_2N_7O_2$ (422.28)	48.35 48.58	4.06 4.02	23.22 23.03		16.79 16.96
I/50	Piperidino	3,4,5-Trimethoxyphenyl	A	2	10	59	180-182 (1-BuOH)	$C_{17}H_{23}N_5O_4$ (361.39)	56.50 56.32	6.41 6.35	19.38 19.30		
I/51	Pyridine-3-yl-amino	3,4,5-Trimethoxyphenyl	A	2.5	10	75	212-214 (DMF)	$C_{17}H_{18}N_6O_4$ (370.36)	55.13 54.98	4.90 5.19	22.69 22.48		

[a] Described by [19] with erroneous structure **40**. [b] Authors did not prove the position of the acetyl group on the triazole ring.

Table II

Compound No.	IR [cm⁻¹] ν NH	ν CO (acyl)	ν C=N	PMR [ppm] (DMSO-d₆) δ NH₂(5)	δ SCH₃	CMR [ppm] δ C(3)	δ C(5)	uv λ max [nm] (ε .10⁻³) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
I/1	3400 3280 3210	1728	1615 1640 1590	7.55	2.50			233 (11.0) 269 (5.7)	211 (9.0) 231 sh (6.6) 260 (4.0)	241 sh (3.0)
I/2	3450 3300 3200	1727	1646	7.2	2.52 [a]	163.5	159.4	232 (10.0) 269 (5.0)	210 (9.4) 231 sh (6.0) 266 sh (2.4)	238 sh (3.0)
I/3	3430 3294	1712	1644	7.35	2.55 [a]			233 (10.0) 270 (5.4)	211 (9.0) 234 sh (5.2) 261 (3.6)	243 sh (2.7)
I/4	3430 3280	1690	1640	7.4	2.53 [a]	162.5	160.4	234 (10.0) 272 (5.9)	210 (11.0) 251 sh (3.5) 262 sh (3.3)	244 sh (2.7)
I/5	3440 3290 3110	1720	1645 1600	7.3	2.50 [a]			232 (9.4) 269 (4.7)	231 sh (7.2) 263 sh (4.5)	223 sh (4.0) 244 sh (3.3)
I/6	3420 3270 3100	1710	1640 1600	7.3	2.51 [a]					
I/7	3420 3290 3200	1718	1645	7.65	2.52			233 (9.3) 269 (4.5)		244 sh (3.0)
I/8	3440 3320 3180	1727	1695 1590	6.7	2.49			236 (8.3) 267 (4.5)	236 sh (6.5) 262 sh (2.7)	230 sh (4.3) 246 sh (4.1)
I/9	3420 3280 3120	1735	1640 1550	7.1	2.45			221 (10.9) 266 (6.0)	208 (11.2) 222 sh (10.3) 256 (6.6)	240 sh (3.3)
I/10	3440 3190 3100	1705	1650	7.5	2.49					
I/11	3415 3300 3200	1720	1650 1610	7.6	2.52 [a]			233 (8.1) 270 (3.6)	232 (7.8) 267 (3.7)	228 sh (3.5) 242 sh (3.4)
I/12	3420 3110	1690	1594	7.35	2.49 [a]			242 (14.7) 292 (5.5)	239 (13.0) 283 (6.2)	251 sh (2.3)
I/13	3440 3300 3200	1695	1648 1595	7.6	2.42 [a]	164.3	159.5	240 (10.6) 285 (5.5)	241 (9.3) 284 (5.6)	238 sh (4.6) 248 sh (3.2)
I/14	3440 3295 3100	1685	1640 1595	7.85	2.53	164.0	160.3	248 (18.3) 294 sh (5.9)	242 (16.3) 282 sh (7.5)	233 (16.8)
I/15	3400 3300 3120	1700	1648 1608	7.6	2.40 [a]			240 (14.0) 286 (6.2)	236 (10.4) 282 (5.5)	236 sh (11.3) 316 (3.4)
I/16	3420 3280 3130	1715	1648 1600	7.85	2.35			235 (14.0) 284 (5.1)	236 (14.7) 284 (6.2)	269 sh (4.4)
I/17	3470 3350	1670	1628 1600	7.4	2.56 [a]			231 (18.0) 282 sh (9.5) 311 (13.1)	222 (16.0) 282 sh (9.0) 309 (11.4)	250 (12.0) 286 (4.9)
I/18	3480 3440 3255	1675	1590 1510	7.6	2.48 [a]					
I/19	3420 3280 3120	1712	1648	7.4	2.50 [a]			233 (9.3) 271 (5.4)	232 sh (6.3) 262 (4.7)	246 sh (2.6)
I/20	3420 3280 2920	1700	1618 1540	7.6	2.52			223 sh (11.5) 300 (19.2)	224 sh (10.4) 307 (19.8)	269 (15.8)

Table II (continued)

Compound No.	IR [cm⁻¹] ν NH	ν CO (acyl)	ν C=N	PMR [ppm] (DMSO-d_6) δ NH_2(5)	δ SCH_3	CMR [ppm] δ C(3)	δ C(5)	uv λ max [nm] (ε .10⁻³) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
I/21	3430	1735	1680	7.4	2.60					
	3230		1650							
	3100		1590							
I/22	3430	1736	1685	7.6	2.56					
	3280		1660							
	3100		1600							
I/23	3430	1738	1690	7.5	2.60					
	3230		1680							
	3100		1650							
I/24	3400	1700	1640	6.95	2.63			229 (17.6)	230 (18.1)	231 (13.2)
	3280		1610					294 (4.3)	295 (3.7)	
	2980									
I/25	3410	1715	1645	7.6	4.31 [b]					
	3290		1595							
	3200									
I/26	3380	1724	1640	7.6	4.30 [b]			225 (18.6)	223 (16.8)	224 (14.7)
	3280							269 (5.4)	268 sh (3.9)	254 sh (4.0)
	3130									
I/27	3395	1713	1645	5.65 (3)		163.2	158.2			
	3305		1572	7.4 (5)						
	3230		1454							
	3140									
I/28	3440	1708	1647	7.35 [a]				227 (11.5)	209 (12.0)	
	3295		1578					284 (6.5)	276 (4.7)	
	3200									
I/29	3410	1703	1657	7.15 [a]				226 (11.0)	207 (10.0)	243 (11.0)
	3310		1575					283 (6.3)	276 (3.8)	
	3230									
I/30	3380	1704	1650	7.0 [a]				227 (11.5)	205 (13.0)	
	3300		1567					285 (6.5)	278 (4.5)	
	3210									
I/31	3410	1683	1640	7.1 [a]				227 (9.4)	208 (13.0)	
	3280		1570					286 (5.4)	277 (4.0)	
	3200									
I/32	3420	1720	1655	6.9 [a]						
	3300		1540							
	3150									
I/33	3420	1696	1576	7.1 [a]				230 (17.7)	230 (7.1)	
	3300		1540					320 (4.7)	309 (4.9)	
	3150									
I/34	3430	1725	1655	7.0 [a]				228 (9.3)	224 (7.6)	
	3310		1595					285 (5.4)	282 (4.0)	
	3220									
I/35	3420	1732	1650	7.55				216 (8.3)	214 (10.0)	227 (7.2)
	3300		1580					291 (1.4)	284 (1.5)	243 sh (3.6)
	3150									
I/36	3430	1735	1650	7.15						
	3310		1580							
	3240									
I/37	3420	1710	1650	7.45						
	3300		1580							
	3230									
I/38	3400	1710	1654	6.8						
	3310		1570							
	3220									

Table II (continued)

Compound No.	IR [cm⁻¹] ν NH	ν CO (acyl)	ν C=N	PMR [ppm] (DMSO-d₆) δ NH₂(5)	δ SCH₃	CMR [ppm] δ C(3)	δ C(5)	uv λ max [nm] (ε .10⁻³) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
I/39	3410 3310 3200	1720	1574	7.2 [a]				227 (8.8) 284 (5.1)	224 (6.9) 282 (5.2)	222 sh (3.3)
I/40	3410 3300 3230	1720	1640 1585	7.5					217 sh (7.2)	226 (2.3)
I/41	3420	1695	1584	7.15 [a]				239 (15.3) 310 (5.1)	236 (13.8) 312 (5.0)	
I/42	3400 3300 3250	1683	1590 1570	6.86 [a]				247 (17.4) 327 (5.2)	243 (13.6) 307 (4.9)	231 (15.0) 266 (2.6)
I/43	3410 3305 3210	1690	1650 1584	7.05 [a]				235 (13.2) 314 (5.7)	233 (12.0) 307 (5.2)	236 sh (11.4) 298 (3.3)
I/44	3390 3290 3200	1667	1640 1615	7.25 [a]				229 (21.2) 276 (9.7) 313 (12.5)	225 (19.5) 315 (12.2)	250 (10.0) 283 (4.1)
I/45	3405 3290 3200	1690	1585 1510	7.25 [a]				217 sh (20.4) 298 (9.5)	216 sh (24.0) 303 (9.3)	251 (9.4)
I/46	3410 3290 3140	1705	1645 1567	6.75 [a]				227 (9.2) 285 (5.2)	278 (5.7)	
I/47	3400 3290 3050	1690	1645 1620	6.85 [a]				222 (13.1) 295 (21.2) 340 sh (6.3)	224 (6.3) 307 (10.4)	267 (18.8)
I/48	3405 3300 3210	1685	1640 1580	7.05 [a]				228 (19.7) 314 (5.8)	228 (18.4) 314 (4.7)	226 (13.6) 269 sh (1.2)
I/49	3420	1677	1600	7.1 [a]				250 (11.0) 328 (5.1)	248 (9.5) 330 (4.7)	244 sh (7.8)
I/50	3420 3290 3130	1675	1580 1505	7.2 [a]				215 sh (21.9) 284 (9.4)	217 sh (25.0) 300 (9.8)	250 (9.1)
I/51	3420 3360 3130	1680	1600 1550	7.25 [a]				217 sh (22.8) 258 (19.2) 292 (13.3)	260 (20.4) 305 (12.5)	256 (17.6)

[a] Taken in deuteriochloroform solution. [b] SCH_2.

Table III

Compound No.	R¹	R²	Method	Reaction Time (hours)	Reaction Temperature (°C)	Yield %	MP (°C) (Crystallized from)	Molecular formula (MW) or Reference MP (°C)	Analysis Calcd./Found C	H	N	S	Hal
II/1	Methylthio	Hydrogen					210-211 (BuOH)	210-212 [27]					
II/2	Methylthio	Methyl	B	0.2	185	72	250-252 (Dioxane)	$C_5H_8N_4OS$ (172.21)	34.87 34.82	4.68 4.51	32.54 32.45	18.62 18.53	
II/3	Methylthio	Ethyl	C	5		71	238-240 (Dioxane)	$C_6H_{10}N_4OS$ (186.24)	38.69 38.64	5.41 5.37	30.08 29.90	17.22 17.24	

Table III (continued)

Compound No.	R^1	R^2	Method	Reaction Time (hours)	Reaction Temperature (°C)	Yield %	MP (°C) (Crystallized from)	Molecular formula (MW) or Reference MP (°C)	Analysis Calcd./Found C	H	N	S	Hal
II/4	Methylthio	1-Methylethyl	A	2		52	200-202 (MeOH)	$C_7H_{12}N_4OS$ (200.27)	41.98 41.75	6.04 6.19	27.98 27.81	16.01 16.20	
II/5	Methylthio	Prop-1-ene-1-yl	A	2		61	198-200 (EtOH)	$C_7H_{10}N_4OS$ (198.25)	42.41 42.53	5.08 5.25	28.26 28.11	16.17 16.30	
II/6	Methylthio	Chloromethyl	A	1		90	225-226 (Dioxane)	$C_5H_7ClN_4OS$ (206.66)	29.05 29.30	3.41 3.69	27.11 26.98	15.52 15.62	17.15 17.37
II/7	Methylthio	Dichloromethyl	A	1		55	221-223 (Dioxane)	$C_5H_6Cl_2N_4OS$ (241.10)	24.91 25.08	2.51 2.64	23.24 23.51	13.30 13.15	29.41 29.32
II/8	Methylthio	Methoxy	B	0.5	230	65	222-224 (Dioxane)	$C_5H_8N_4O_2S$ (188.20)	31.91 31.97	4.30 4.45	29.77 19.75	17.03 17.01	
II/9	Methylthio	Ethoxy	B	0.5	230	73	213-215 (Dioxane)	210 [19]					
II/10	Methylthio	Ethoxycarbonyl	A	1		57	181-183 (Dioxane)	$C_7H_{10}N_4O_3S$ (230.25)	36.51 36.71	4.38 4.63	24.33 24.18	13.92 13.81	
II/11	Methylthio	Carboethoxymethyl	A	1		67	149-150 (MeOH)	$C_8H_{12}N_4O_3S$ (244.28)	39.33 39.31	4.95 4.82	22.94 22.91	13.13 12.98	
II/12	Methylthio	Phenyl	B	0.2	225	77	228-229 (Dioxane)	$C_{10}H_{10}N_4OS$ (234.28)	51.26 51.31	4.30 4.35	23.92 23.85	13.69 13.67	
II/13	Methylthio	2-Chlorophenyl	B	2	230	90	214-216 (Dioxane)	$C_{10}H_9ClN_4OS$ (268.73)	44.69 44.77	3.37 3.23	20.85 20.78	11.93 11.77	13.19 13.26
II/14	Methylthio	4-Chlorophenyl	B	0.5	230	88	266-268 (Dioxane)	$C_{10}H_9ClN_4OS$ (268.73)	44.69 44.71	3.37 3.56	20.85 20.63	11.93 11.85	13.19 13.15
II/15	Methylthio	2-Carboxyphenyl	E			75	195-197 (EtOH)	$C_{11}H_{10}N_4O_3S$ (278.28)	47.47 47.37	3.62 3.44	20.13 19.91	11.52 11.34	
II/16	Methylthio	3,4-Dimethoxyphenyl	B	0.5	230	50	219-221 (Dioxane)	$C_{12}H_{14}N_4O_3S$ (294.33)	48.97 49.15	4.79 4.68	19.04 19.36	10.89 11.04	
I/17	Methylthio	Phenoxymethyl	A	1		50	172-174 (EtOH)	$C_{11}H_{12}N_4O_2S$ (264.30)	49.98 50.28	4.57 4.85	21.19 21.23	12.13 12.37	
II/18	Methylthio	2,4-Dichlorophenoxy	C	4		54	206-208 (Dioxane)	$C_{11}H_{10}Cl_2N_4O_2S$ (333.20)	39.65 39.87	3.02 2.98	16.81 16.54	9.62 9.61	21.28 21.37
II/19	Methylthio	2,6-Dichlorophenoxy	A	1		72	206-208 (MeOH)	$C_{11}H_{10}Cl_2N_4O_2S$ (333.20)	39.65 39.47	3.02 2.92	16.81 16.60	9.62 9.85	21.28 21.11
II/20	4-Chlorobenzylthio	Methyl	A	2		48	250-252 (DMF)	$C_{11}H_{11}ClN_4OS$ (282.75)	46.72 46.88	3.92 4.02	19.82 19.88	11.34 11.47	12.54 12.42
II/21	Morpholino	Methyl	D	2		50	207-209 (DMF)	$C_8H_{13}N_5O_2$ (211.22)	45.49 45.38	6.20 6.27	33.16 33.10		
II/22	Morpholino	Trichloromethyl	A	1		81	219-221 (EtOH)	$C_8H_{10}Cl_3N_5O_2$ (314.57)	30.54 30.62	3.20 3.29	22.26 22.14		33.81 33.72
II/23	Morpholino	Carboethoxymethyl	A	1		51	233-235 (Dioxane)	$C_{11}H_{17}N_5O_4$ (283.29)	46.63 46.55	6.05 5.92	24.72 24.63		
II/24	Morpho lino	Phenyl	B	6.0	240	77	232-233 (DMF)	$C_{13}H_{15}N_5O_2$ (273.29)	57.13 57.18	5.53 5.59	25.63 25.58		
II/25	Morpholino	4-Chlorophenyl	B	0.5	240	82	296-298 (DMF)	$C_{13}H_{14}ClN_5O_2$ (307.76)	50.73 50.45	4.58 4.41	22.75 22.57		11.52 11.65
II/26	Morpholino	2-Carboxyphenyl	E			94	191-193 (Dioxane)	$C_{14}H_{15}N_5O_4$ (317.30)	53.00 52.84	4.76 5.01	22.07 21.86		
II/27	Benzylamino	Methyl	A	2		46	304-306 (Dioxane)	$C_{11}H_{13}N_5O$ (231.25)	57.13 57.22	5.67 5.72	30.29 30.23		

spectra of the *I*-type ring-acylated derivatives were also in accordance with the proposed **2o** structure. Namely it was known from our previous work [29] that the change of the quality of the *N*-alkyl-, aralkyl- or aryl- substituents of the 5-amino-1,2,4-triazole isomers did not cause any significant change of the chemical shift of the triazole carbon atoms. It was also known from the chemistry of tetrazole and its monomethylated isomers [25] that the change of the NH hydrogen to the (*N*)-methyl group caused negligible change on the chemical shift of the alfa carbon atom but caused a big change of the chemical shift of the beta carbon atom. Consequently it was expected that the chem-

Table IV

Compound No.	IR [cm^{-1}] ν NH	ν CO (acyl)	ν C=N	PMR [ppm] (DMSO-d_6) δ NH(exo)	δ NH(1)	δ SCH_3	CMR [ppm] δ C(3)	δ C(5)	uv λ max [nm] (ε .10^{-3}) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
II/1	3280	1690	1600	13.5	11.6	2.60			208 (16.4)	209 (14.3)	244 (8.0)
	3200		1555		11.2	2.69 [a]			233 sh (9.0)	236 sh (7.4)	
	3070										
II/2	3280	1684	1580	11.5	9.7	2.50	158.5	151.8	208 (18.6)	208 (18.0)	208 (17.9)
	3180		1530						232 (6.5)	236 sh (7.4)	236 sh (7.4)
	3160										
II/3	3290	1687	1608		10.0	2.50	158.2	151.0	208 (20.0)	208 (15.8)	238 (6.1)
	3110		1551						232 (7.2)	231 (8.4)	
II/4	3160	1695	1570	12.0	10.1	2.52			208 (19.5)	208 (16.0)	238 sh (6.0)
	3050		1550						233 sh (6.8)	231 sh (8.6)	
	2980										
II/5	3190	1685	1600	11.8	10.0	2.50			216 (20.5)	219 (17.9)	244 sh (6.5)
	3120		1540						260 sh (7.8)	257 sh (8.3)	256 sh (5.4)
II/6	3260	1695	1605	13.6	11.7	2.51			208 (14.0)	208 (14.2)	244 (4.9)
	3120		1550						237 sh (6.0)	234 sh (7.5)	
II/7	3250	1698	1610	13.7	11.9	2.52			212 (13.0)	213 (11.8)	243 sh (4.3)
	3120		1550						238 sh (6.9)	235 sh (7.9)	
II/8	3280	1680	1595	12.0	10.2	2.50			205 (18.5)	202 (17.4)	240 sh (4.4)
	3160		1530						223 sh (5.7)	237 (4.8)	
	3050								240 sh (2.4)		
II/9	3290	1685	1600	12.1	10.2	2.52			202 (18.6)	203 (16.5)	241 (4.2)
	3160		1550						223 sh (6.1)	237 (4.9)	
	3000								241 sh (2.6)		
II/10	3270	1695	1595		11.3	2.63			212 (8.7)	212 (8.2)	243 (4.7)
	3150		1535						238 (6.5)	232 (7.2)	
	3000								273 sh (4.0)	264 sh (4.1)	
II/11	3290	1678	1600		11.6	2.49	158.4	151.6	234 (8.3)	234 (9.0)	262 (4.3)
	3130		1595						296 (1.3)	285 sh (0.9)	
	3000										
II/12	3300	1654	1587	12.5	10.7	2.57	159.3	151.7	231 (5.2)	234 (5.4)	244 sh (4.8)
	2900		1550						261 (2.9)	259 sh (3.2)	265 sh (2.0)
II/13	3260	1675	1582	12.1	10.6	2.57			232 (5.9)	234 sh (3.7)	243 sh (2.4)
	3100		1549						253 sh (2.4)		
	2940										
II/14	3290	1658	1595		10.9	2.60	158.8	151.6	242 (6.4)	244 (6.3)	245 (5.5)
	3100		1550								
	2940										
II/15	3220	1700	1590	11.8	10.5	2.51			227 sh (16.1)	226 sh (17.8)	226 (10.5)
	3100								270 sh (5.5)	272 sh (4.2)	268 sh (4.7)
II/16	3275	1660	1590	11.6	10.1	2.53			219 (13.5)	218 (12.4)	259 (6.1)
	3120		1551						271 (7.3)	270 (7.0)	289 (5.3)
	2920		1519						295 (6.6)	291 (5.9)	
II/17	3240	1682	1590		10.3	2.57			209 (25.4)	209 (22.6)	237 sh (6.9)
	3090		1565						234 sh (7.5)	234 sh (8.5)	
			1540								
II/18	3240	1680	1590	11.8	9.9	2.57					
	3080		1540								
	2930										
II/19	3250	1682	1590	11.6	10.1	2.58			241 sh (6.7)	238 sh (7.7)	243 sh (7.1)
	3090		1565								
	2930		1540								
II/20	3300	1700	1595	13.5	11.5	4.23 [c]	157.1	151.3			
	3210		1545								
	3080		1490								
II/21	3300	1700	1610	10.8	9.4		164.0	150.7	208 (17.4)	206 (18.6)	245 (3.7)
	3200		1580						238 (5.5)	249 (2.9)	
	2800		1515								
II/22	3270	1718	1590	12.7	11.1				217 (10.0)	214 (14.2)	274 sh (3.1)
	3200		1575						276 (4.8)	274 sh (2.2)	
	2970										

Table IV (continued)

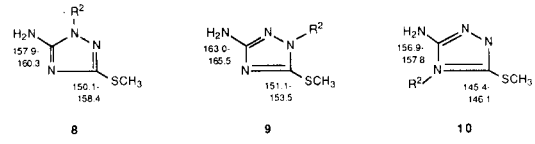
Compound No.	IR [cm^{-1}] ν NH	ν CO (acyl)	ν C=N	PMR [ppm] (DMSO-d_6) δ NH(exo)	δ NH(1)	δ SCH_3	CMR [ppm] δ C(3)	δ C(5)	EtOH	uv λ max [nm] (ε .10^{-3}) 10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
II/23	3270	1685	1600		11.0						
	3160		1520								
	2995										
II/24	3300	1680	1585	11.6	10.0		163.9	150.7	228 (9.0)	227 (8.8)	225 (6.6)
	2800		1534						272 (2.9)	266 (3.6)	278 (3.3)
II/25	3310	1667	1590		10.7				238 (9.6)	245 (8.8)	236 (7.0)
	3100		1532						282 sh (3.0)	279 sh (3.6)	292 (4.0)
II/26	3300	1685	1590	11.7							
	3280		1535								
	2960										
II/27	3280	1686	1591	11.2	9.8	4.34 d [d]	164.0	150.7	205 (20.8)		243 sh (11.5)
	3260		1555						249 (3.2)		
	3030										

[a] 1:1 mixture of *syn* and *anti* isomers. [b] Taken in deuteriochloroform. [c] δ SCH_2. [d] δ NCH_2.

ical shift of the triazole carbon atom (5) of the acylated derivatives **I** would not change significantly as compared with that of the 1-alkylated derivatives (**8**) (Scheme 5), while the chemical shift of the "en-amino" triazole carbon atom (3) would undergo as a consequence of the -I effect of the CO group a significant downfield shift. The observed chemical shifts of the triazole carbon atoms 3 and 5 of the **I** type ring-acylated derivatives (Table II) were in full agreement with those expected for the **2o** structure appearing between 162.8-164.9 ppm (*i.e.* shifted downfield by about 7-8 ppm as compared with those in derivates **8**) and 157.8-160.4 ppm (*i.e.* with the exact same values as those in derivatives **8**), respectively. It is interesting to emphase that even such a big change of the quality of the alfa triazole substituents as the change of the alkyl substituents to acyl ones did not cause any change of their chemical shifts. Our data were in accordance with those of measured by Winkler and Kristinson [20] for 5-amino-1-carbomethoxy-3-methylthio-, 3-dimethylamino-, and 3-amino-1*H*-1,2,4-triazole (**I**, R = SCH_3, $N(CH_3)_2$ and NH_2, respectively, R^1 = OCH_3). They obtained for the carbon atoms (3) 163.0, 163.4 and 161.8 ppm, and for the carbon atoms (5) 158.2, 157.4, and 157.1 ppm, respectively.

The uv spectra of the **I** type ring-acylated derivatives recorded in ethanolic solution (Table II) were characterized - unless having a further chromophore-, or a conjugated double bond system in the molecule - by two well developed, clear maxima appearing between 220-248 nm and 266-292 nm, respectively. [See *e.g.* the spectra of 1-acetyl-3-methythio-5-amino-1*H*-1,2,4-triazole (**I**, R = SCH_3, R^1 = CH_3), or 1-phenyl-3-methylthio-5-amino-1*H*-1,2,4-triazole (**I**, R = SCH_3, R^1 = Phenyl) (Figure 1)]. These maxima suffered a slight hypsochromic shift in acidic media, while in alkaline media the spectrum completely changed to a

Scheme 5



8 9 10

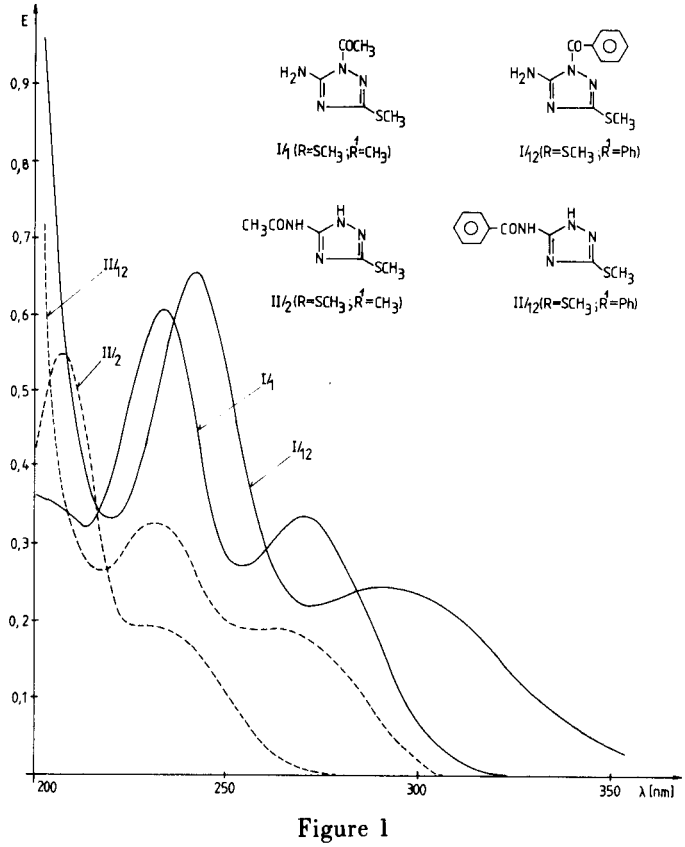


Figure 1

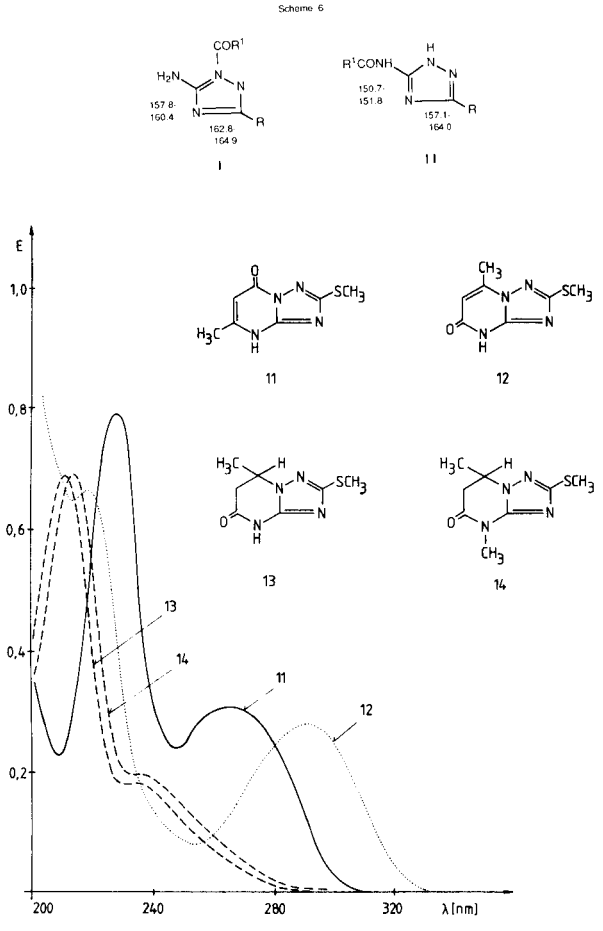
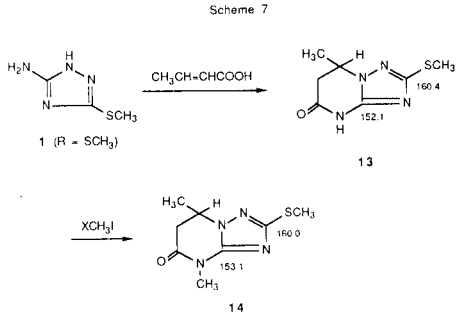


Figure 2

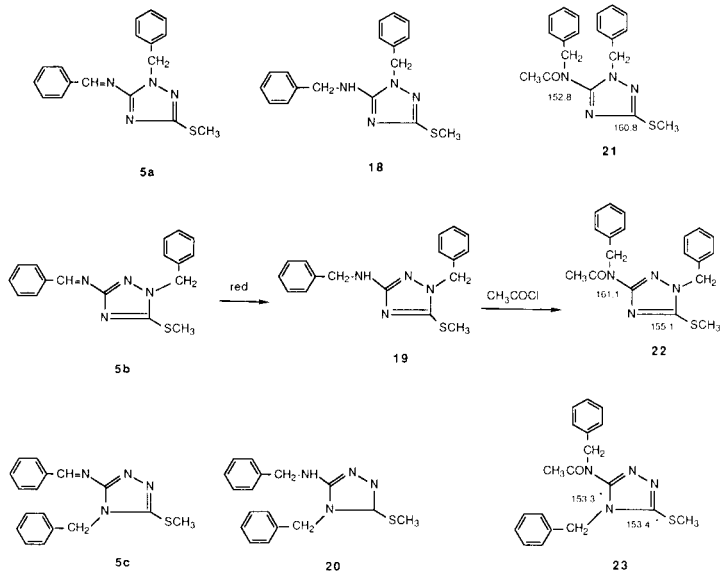
simpler one characterized by a sole shoulder or maximum at about 250 nm. These spectra will corresponded to that of the spectrum of 7-methyl-2-methylthio-1,2,4-triazolo-[1,5-*a*]pyrimidin-5(8*H*)-one (**11**) [26] (Figure 2) of proved isomeric and tautomeric structure giving a further evidence for the **2o** structure of derivatives **I**. The uv spectra of derivatives **II** recorded in ethanolic solution - again unless being conjugated with other double bonds or having in the molecule an other chromophore system - were characterized with a mximum between 202-217 nm and a good visible shoulder usually developing into a maximum between 232-241 nm, respectively (Table IV). These maxima were extremely sensitive to the conjugation effects which caused their strong batochromic shift. The acidic media caused similarily to the case of derivative **I** only a slight hypsochromic shift of the shoulder while the alkaline media changed the spectrum to a similar one as observed in case of derivatives **I**. The shape of curves obtained for derivatives **I** and **II** in the ethanolic media was significantly different (Figure 1) giving a good possibility for their differentiation. On the other hand the uv spectra of derivatives **II** recorded in ethanolic solution did not correspond to the spectrum of 5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine-7(8*H*)-one (**12**) (Figure 2) of previously proved structure [26]. The difference is caused by the conjugated (C_5) double bond present in **12** as proved by the uv spectrum of the corresponding dihydro analogue, the 5,6-dihydro-5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine-7(8*H*)-one (**13**) and its *N*-methyl derivative the 5,6-dihydro-5,8-dimethyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidin-7(8*H*)-one (**14**) (Figure 2) prepared as model compounds (Scheme 7). It should be mentioned that the position of the *N*-methyl group in **14** was proved unambiguously with the help of the multiplicity of the quaternary carbon atoms in the proton coupled cmr.



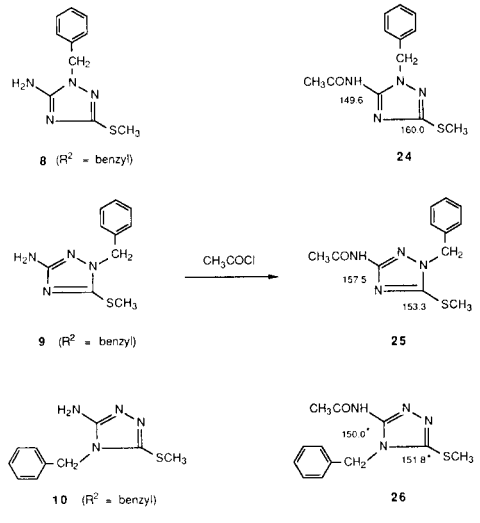
In the cmr spectra of derivatives **II** the triazole carbon atoms appeared between 150.7-151.8 and 157.1-164.0 ppm, respectively. Unfortunately the recording of the proton coupled cmr spectra failed as a consequence of their extreme insolubility in the nmr solvents causing big problems with the unambiguous ordering of these data to the triazole carbon atoms (3) and (5). Thus *e.g.* the figures 150.7-151.8 ppm measured for one of the triazole carbon atoms of derivatives **II** were practically identical with those of measured for the carbon atom (3) of the 5-amino-2-alkylated-3-methylthio-2*H*-1,2,4-triazoles **9** (Scheme 5) [27, 28, 29]. This fact seemed to predict the idea [4,5] that the chemical surrounding of the triazole carbon atom (3) of derivatives **II** is analogues to that of the carbon atom (3) of derivatives **9**, *i.e.* tautomers **5b** and **5e** have to be taken in account. As the uv spectrum of derivatives **II** was analogues to that of **13** (Figures 1 and 2) which can be understood as a 1-exo-dialkylated-5-amino-1,2,4-triazole derivative the tautomeric structure **5e** seemed to be the most probable. Nevertheless the ir ν CO bands appearing between 1718 and 1654 cm^{-1} indicated the presence of the amide structure, *i.e.* one of the tautomeric forms **5a**, **5b** or **5c** which was just in contrary to the tautomeric structure **5e**.

To solve the above contradiction further model compounds representing the tautomeric structures **5a**, **5b** and **5c** in "fixed" forms were required. Such model compounds might be the acetylated dibenzyl isomers **21**, **22**

Scheme 8



Scheme 9



and **23** as well as their monobenzyl analogues **24, 25** and **26**, which were synthesized according to the reaction Schemes 8 and 9, respectively. The ir carbonyl bands of these derivatives appeared between 1709 and 1676 cm^{-1} indicating that the acetylation really occured on the exocyclic nitrogen atom.

The uv spectra of the isomeric pairs **21-24, 22-25** and **23-26**, respectively, were completely analogues (Figures 3 and 4) indicating that the NH proton of derivatives **24, 25** and **26** replaced the exocyclic *N*-benzyl group of derivatives **21, 22** and **23**, respectively, or in other words that the tautomeric structure shown on Scheme 9 for these derivatives was correct. The uv spectra of the isomeric pairs **21-24, 22-25** and **23-26**, respectively, differed from each other (Figure 3 and 4), making possible the safe differentiantion among them. Nevertheless the safe and unambiguous differentiation among structures **5a, 5b** and **5c** represented by the above model compounds **21-24**,

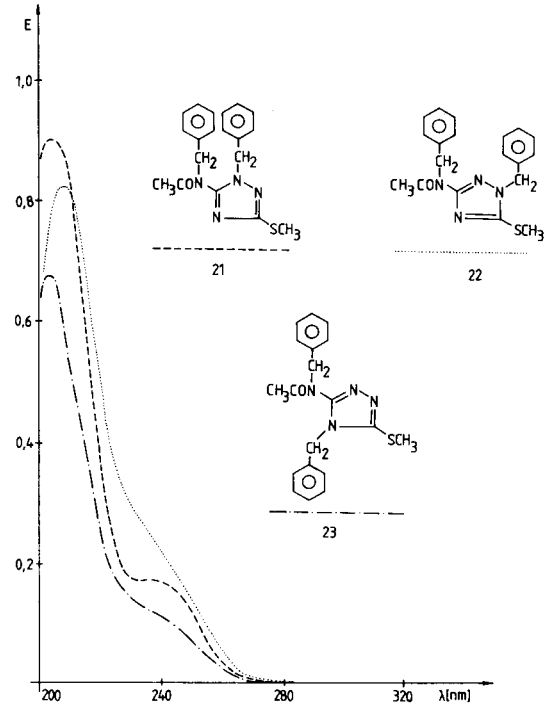


Figure 3

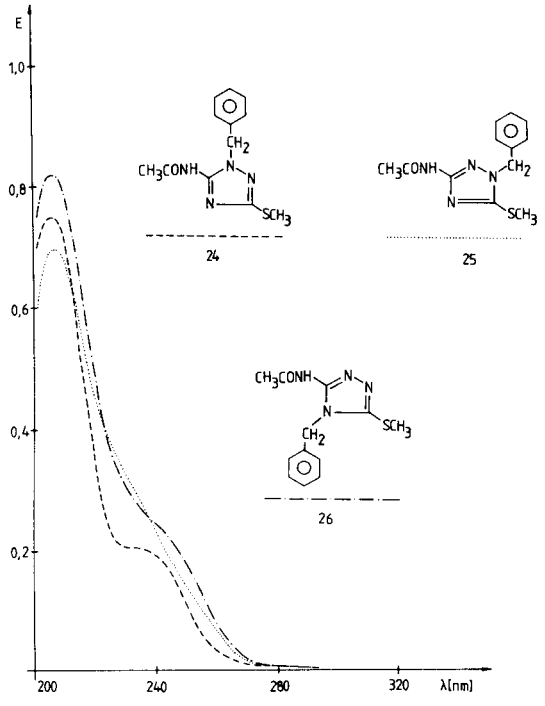


Figure 4

22-25 and **23-26**. respectively, made posible only the cmr spectra where the carbon atoms (3) and (5) appeared with the significantly different chemical shifts (See Schemes 8 and 9). These data were inagreement with those obtained for **13** and **14**, respectively, and -as they were not sensitive to the change of quality of the substituents R and R^1 -proved unambiguously the isomeric and tautomeric structure **5a** of all **II** type derivatives (Table IV).

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using Perkin-Elmer 577 spectrophotometer. The ultraviolet spectra were obtained by a Varian Cary 118 and a Pye Unicam SP 8-150 instrument. The ^{1}H-nmr and the ^{13}C-nmr measurements were performed using Varian XL-100, Brucker WM-250 and Brucker WP-80 SY instruments.

General Methods for the Preparation of **I** type 1-Acyl-5-amino-3-*R*-1,2,4-triazole Derivatives. Method A.

To the solution of 0.05 mole of appropriate 5-amino-3-*R*-1*H*-1,2,4-triazole derivative **1** in 50 ml of the appropriate solvent (Table I) 0.052 mole of the appropriate acid chloride was added through a dropping funnel while cooling and stirring the reaction mixture. After the addition the reaction was completed by stirring for 90 minutes at the temperature given in Table I. After completing the reaction 100 ml of water was added to the reaction mixture, the crystals precipitated were filtered off and recrystallized from an appropriate solvent (Table I).

Method B.

The same procedure was used as in Method A with the exception that after the addition of water to the reaction mixture the product was extracted three times with 30 ml of chloroform, the combined chloroform layers were dried over anhydrous sodium sulfate, evaporated *in vacuo* to dryness, and the product thus obtained was recrystallized from an appropriate solvent (Table I).

Method C.

To the solution of 0.0077 mole of the appropriate 5-amino-3-*R*-1*H*-1,2,4-triazole **1** and 1.6 g (0.0077 mole) of dicyclohexylcarbodiimide in 25 ml of tetrahydrofurane 1.0 g (0.0077 mole) of dichloroacetic acid was added through a dropping funnel keeping the temperature at 0°. The reaction was completed by stirring the rection mixture at room temperature for 24 hours. The dicyclohexycarbamide crystallized from the reaction mixture was filtered off, the mother liquor was evaporated *in vacuo* to dryness and the residue recrystallized from an appropriate solvent (Table I).

Method D.

The solution of 1.0 g (0.0059 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole **1**, (R = morpholino) and 0.6 g (0.0059 mole) of succinic acid anhydride in 30 ml of acetonitrile was refluxed for three hours. After cooling the product crystallized was filtered off and recrystallized from dioxane (Table I).

Method E.

The solution of 0.05 mole of the appropriate 5-amino-3-*R*-1*H*-1,2,4-triazole **1** in 100 ml of acetonitrile, 13.7 ml = 10.0 g (0.01 mole) of triethylamine and 5.7 ml = 6.98 g (0.06 mole) of ethyl chloroformiate was added and refluxed for 18 hours. After cooling the reaction mixture was evaporated *in vacuo* to dryness, the residue partitioned between water and chloroform, the chloroform layer was dried over anhydrous sodium sulfate and again evaporated *in vacuo* to dryness. The product thus obtained was recrystallized from 2-propanol (Table I).

Method F.

Five g (0.05 mole) of finely powdered 3,5-diamino-1*H*-1,2,4-triazole **1** (R = NH_2) [30] was poured at room temperature into 30 ml of stirred acetic acid anhydride. The reaction started immediately and the temperature of the reaction mixture arose to 45°. The solid added was still only partly dissolved when the product began to crystallize. The reaction was completed by stirring at room temperature for 1 hour, the product crystallized was filtered off and recrystallized from dioxane (Table I).

General Methods for the Preparation of **II** type 5-Acylamino-3-*R*-1,2,4-triazole Derivatives. Method A.

To the solution of 0.05 mole of the appropriate 5-amino-3-*R*-1*H*-1,2,4-triazole derivative **1** in 50 ml of the appropriate solvent (Table III) 0.05 mole of the appropriate acid chloride was added through a dropping funnel while stirring at room temperature. After the addition of the acid chloride the reaction mixture was boiled while stirring for the time given in Table III. After the completion of the reaction 100 ml of water was added to the reaction mixture, the product precipitated was filtered off and recrystallized from an appropriate solvent (Table III).

Method B.

The appropriate 1-acyl-5-amino-3-*R*-1,2,4-triazole derivative **1** (0.05 mole) was heated at the temperature and the time given in Table (III). After cooling the product obtained was recrystallized from the solvent given in Table III.

Method C.

The solution of 0.05 mole of the appropriate 1-acyl-5-amino-3-*R*-1,2,4-triazole derivative **1** in the solvent given in Table III was refluxed for the time given in Table III. After cooling the crystals precipitated were filtered off and recrystallized from a solvent given in Table III.

Method D.

The solution of 10.66 g (0.05 mole) of 1-acetyl-5-amino-3-morpholino-1*H*-1,2,4-triazole (**I/29**) in 50 ml of acetic acid anhydride was refluxed for 2 hours. After cooling 8.8 g (70%) of 2-acetyl-3-morpholino-5-acetylamino-2*H*-1,2,4-triazole was precipitated, which was filtered off mp 142-144°; ir: ν CO = 1690 and 1715 cm^{-1}; pmr (deuteriochloroform): δ ppm 2.46 (s, CH_3, 3H), 2.57 (s, CH_3, 3H), 3.40 (t, NCH_2, 2H), 3.75 (t, OCH_2, 2H), 9.4 (bs, NH, 1H); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) = 230 (13.2), 300 (4.7); uv (10% ethanol + 90% 0.1*N* hydrochloric acid):λ max nm ($\epsilon.10^{-3}$) = 228 (12.8), 301 (4.7). The product obtained above was taken into 40 ml of distilled water, refluxed for 5 minutes, filtered off and recrystallized from dimethylformamide (Table III).

Method E.

a) The mixture of 0.05 mole of 5-amino-3-methyltio-, or 3-morpholino-1*H*-1,2,4-triazole **1** (R = SCH_3 and morpholino, respectively) [28,30] and 0.05 mole of phtalic acid anhydride was heated at 200° for 1 hour or 230° for 1.5 hours, respectively. After cooling the solid obtained was recrystallized from dimethyl formamide and 1-butanol, respectively, yield 12.3 g (82%) of 3-methylthio-5-phtalimido-1*H*-1,2,4-triazole, mp 264-266°; ir: ν CO = 1795 and 1745 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.70 (s, SCH_3, 3H), 8.02 (s, ArH, 4H), 11 (b, NH, 1H) and 9.1 g (61%) of 3-morpholino-5-phtalimido-1*H*-1,2,4-triazole, mp 249-250°; ir: ν CO = 1795 and 1740 cm^{-1}; pmr (DMSO-d_6): δ ppm 3.40 (t, NCH_2, 4H), 3.80 (t, OCH_2, 4H), 8.00 (s, ArH, 4H), 11 (b, NH, 1H), respectively.

b) The solution of 0.25 mole of the corresponding 5-phtalimido-3-*R*-1*H*-1,2,4-triazole in 5 ml of 25% potassium hydroxyde was stirred at room temperature for 1 hour. The solution thus obtained was acidified with 10% hydrochloric acid to *p*H = 4. The crystals precipitated were filtered off, washed with 15 ml of distilled water and recrystallized from an appropriate solvent (Table I).

1-Benzyl-5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**18**).

To the solution of 3.08 g (0.01 mole) or 5-benzalimino-1-benzyl-3-methylthio-1*H*-1,2,4-triazole (**5a**) [28] in 60 ml of absolute tetrahydrofuran 0.77 g (0.02 mole) of lithium aluminium hydride was added in small portions while stirring at room temperature. During the addition the temperature of the reaction mixture erose to 45°. The mixture was stirred further for 3 hours at room temperature then decomposed with a few drops of water and the product precipitated filtered off, yield 1.94 g (63%), mp 74-76° (2-propanol); ir: ν C=N 1601, 1582 and 1514 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.43 (s, SCH_3, 3H), 4.53 (d, $NHCH_2$, 2H), 5.22 (s, NCH_2, 2H), $\approx$7.3 (m, NH + ArH, 11H); cmr (DMSO-d_6): δ ppm 158.3 (triazole C_3), 158.3 (triazole C_5), 15.3 (SCH_3), 48.5 ($NHCH_2$), 50.9 (NCH_2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 206 (31.2), 228 sh (9.3), 247 sh (4.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 219 (17.5), 242 sh (8.2); uv (10 % ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 202 (23.2), 242 sh (5.7).

Anal. Calcd. for $C_{17}H_{18}N_4S$ (MW 310.41): C, 65.77; H, 5.85; N, 18.05; S, 10.33. Found: C, 65.72; H, 5.98; N, 17.99; S, 10.45.

2-Benzyl-5-benzylamino-3-methylthio-2*H*-1,2,4-triazole (**19**).

The same procedure was used as in the preparation of **18** starting from 5-benzalimino-2-benzyl-3-methylthio-2*H*-1,2,4-triazole (**5b**) [28], yield 2.95 g (95%), mp 81-82° (2-propanol); ir: ν C=N = 1547 and 1504 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.57 (s, SCH_3, 3H), 4.28 (d, $NHCH_2$, 2H), 5.06 (s, NCH_2, 2H), 6.58 (t, NH, 1H), 7.15-7.40 (m, ArH, 10H); cmr (DMSO-d_6): δ ppm 152.1 (triazole C_3), 165.7 (triazole C_5), 17.1 (SCH_3), 48.2 ($NHCH_2$); 52.6 (NCH_2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 203 (27.7), 236 sh (6.5), 254 sh (4.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 219 (18.7), 251 sh (9.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 204 (27.0), 263 (5.6).

Anal. Calcd. for $C_{17}H_{18}N_4S$ (MW 310.41): C, 65.77; H, 5.85; N, 18.05; S, 10.33. Found: C, 65.89; H, 6.04; N, 18.22, S, 10.28.

4-Benzyl-5-benzylamino-3-methylthio-4*H*-1,2,4-triazole (**20**).

To the solution of 9.87 g (0.032 mole) of 5-benzalimino-4-benzyl-3-methylthio-4*H*-1,2,4-triazole (**5c**) [27] in 60 ml of methanol the solution of 2.5 g (0.065 mole) of sodium borohydride in 10 ml of water was added while stirring through a dropping funnel at 50°. The mixture was kept at 50° for a further hour, decomposed with 30 ml of 1% hydrochloric acid, (*p*H = 3) made alkaline (*p*H = 9) with sodium hydrocarbonate and extracted twice with 150 ml portions of chloroform. The combined chloroform layers were dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness, yield 9.2 g (93%), mp 133-134° (2-propanol); ir: ν C=N = 1599, 1580 and 1526 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.39 (s, SCH_3, 3H), 4.45 (d, $NHCH_2$, 2H), 5.10 (s, NCH_2, 2H), 6.91 (t, NH, 1H), 7.1-7.4 (m, ArH, 10H); cmr (DMSO-d_6): δ ppm 146.7 (triazole C_3), 157.9 (triazole C_5), 17.7 (SCH_3), 46.7$^+$ ($NHCH_2$); 47.9$^+$ (NCH_2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 205 (30.1), 228 sh (10.9), 251 sh (8.4); uv (10% ethanol + 90% 0.1 *N* sodium hdroxide): λ max nm ($\epsilon.10^{-3}$) 218 (16.4), 227 sh (12.7), 250 (10.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 214 sh (15.6), 242 sh (7.3).

Anal. Calcd. for $C_{17}H_{18}N_4S$ (MW 310.41): C, 65.77; H, 5.85; N, 18.05; S, 10.33. Found: C, 65.53; H, 5.76; N, 18.11; S, 10.23.

5-(*N*-Acetyl-*N*-benzylamino)-1-benzyl-3-methylthio-1*H*-1,2,4-triazole (**21**).

1-Benzyl-5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**18**) (0.465 g, 0.0015 mole) was refluxed with 2 ml of acetic acid anhydride for 1 hour. After cooling 10 ml of water and 10 ml of chloroform was added to the reaction mixture, the layers were separated, the chloroform layer was washed with 10 ml of water, dried over anhydrous sodium sulfate and evaporated to dryness. The honey-like residue thus obtained (0.45 g) was chromatographed on a short silica-gel column using the 2:1 mixture of benzene and ethyl acetate as eluent, yield 0.31 g (59%), mp 85-86° (2-propanol); ir: ν CO = 1680 cm^{-1}; pmr (DMSO-d_6) δ ppm 1.60 (s, $COCH_3$, 3H), 2.47 (s, SCH_3, 3H), 4.78 (s, $CONCH_2$, 2H), 5.12 (s, NCH_2, 2H), 7.1-7.35 (m, ArH, 5H); cmr (DMSO-d_6): δ ppm 160.8 (triazole C_3), 152.8 (triazole C_5), 15.3 (SCH_3), 23.2 ($COCH_3$), 53.0$^+$ ($CONCH_2$), 52.7$^+$ (NCH_2), 171.5 (CO); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 204 (32.7), 240 sh (6.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 219 (18.1), 241 sh (8.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 240 sh (5.5).

Anal. Calcd. for $C_{19}H_{20}N_4OS$ (MW 352.45): C, 64.74; H, 5.72; N, 15.90; S, 9.10. Found: C, 64.56; H, 5.70; N, 15.67; S, 9.25.

5-(*N*-Acetyl-*N*-benzylamino)-2-benzyl-3-methylthio-2*H*-1,2,4-triazole (**22**).

The same procedure was used as in the preparation of **21**, starting from 2-benzyl-5-benzylamino-3-methylthio-2*H*-1,2,4-triazole (**19**), yield 0.42 g (79%), honey-like product; ir: ν CO = 1676 cm^{-1}; pmr (deuteriochloroform): δ ppm 2.25 (s, $COCH_3$, 3H), 2.60 (s, SCH_3, 3H), 5.04 (s, NCH_2, 2H), 5.11 (s, $CONCH_2$, 2H), 7.15-7.35 (m, ArH, 10H); cmr (deuteriochloroform): δ ppm 155.1 (triazole C_3), 161.1 (triazole C_5), 17.1 (SCH_3), 24.9 ($COCH_3$), 51.2$^+$ ($COCH_2$), 53.6$^+$ (NCH_2), 171.8 (CO); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 208 (30.0), 237 sh (9.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 240 sh (5.9); uv (10% ethanol + 90% hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 240 sh (5.4).

Anal. Calcd. for $C_{19}H_{20}N_4OS$ (MW 352.45): C, 64.74; H, 5.72; N, 15.90; S, 9.10. Found: C, 64.85; H, 5.90; N, 15.77; S, 9.24.

5-(*N*-Acetyl-*N*-benzylamino)-4-benzyl-3-methylthio-4*H*-1,2,4-triazole (**23**).

The same procedure was used as in the preparation of **21**, starting from 4-benzyl-5-benzylamino-3-methylthio-4*H*-1,2,4-triazole (**20**), yield 0.39 g (74%), mp 124-126° (2-propanol); ir: ν CO = 1692 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.46 (s, $COCH_3$, 3H), 2.68 (s, SCH_3, 3H), 5.04 (s, NCH_2 + $CONCH_2$, 4H), 7.15-7.4 (m, ArH, 10H); cmr (DMSO-d_6): δ ppm 153.3$^+$ (triazole C_3), 153.4$^+$ (triazole C_5), 16.3 (SCH_3), 22.9 ($COCH_3$), 48.5 (NCH_2), 53.3 ($CONCH_2$), 171.7 (CO); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 205 (27.6), 239 sh (6.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 244 sh (7.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 205 (27.2), 232 sh (6.5).

Anal. Calcd. for $C_{19}H_{20}N_4OS$ (MW 352.45): C, 64.74; H, 5.72; N, 15.90; S, 9.10. Found: C, 64.76; H, 5.88; N, 15.98; S, 9.21.

5-Acetylamino-1-benzyl-3-methylthio-1*H*-1,2,4-triazole (**24**).

To the solution of 2.2 g (0.01 mole) of 5-amino-1-benzyl-3-methylthio-1*H*-1,2,4-triazole (**8**) [28] in 10 ml of pyridine 1.42 ml (0.02 mole) of acetylchloride was added while stirring at room temperature. The stirring was continued for a further hour, then 30 ml of water was added, the product extracted twice with 50 ml portions of benzene, the combined benzene layers were washed with water (50 ml), dried over anhydrous sodium sulfate and evaporated to dryness, yield 2.33 g (89%), mp 130-132° (2-propanol); ir: ν C=O = 1707 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.06 (s, $COCH_3$, 3H), 2.46 (s, SCH_3, 3H), 5.17 (s, NCH_2, 2H), 7.2-7.4 (m, ArH, 5H), 10.6 (bs, NH, 1H); cmr (DMSO-d_6): δ ppm 160.0 (triazole C_3), 149.6 (triazole C_5), 15.3 (SCH_3), 24.2 ($COCH_3$), 53.1 (NCH_2), 171.3 (CO); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 206 (25.0), 236 sh (6.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide):λ max nm ($\epsilon \cdot 10^{-3}$) 238 sh (10.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 238 sh (8.4).

Anal. Calcd. for $C_{12}H_{13}N_4OS$ (MW 261.32): C, 55.15; H, 5.01; N, 21.44; S, 12.27. Found: C, 55.05; H, 4.89; N, 21.38; S, 12.36.

5-Acetylamino-2-benzyl-3-methylthio-2*H*-1,2,4-triazole (**25**).

The same procedure was used as in the preparation of **24** starting from 5-amino-2-benzyl-3-methylthio-2*H*-1,2,4-triazole (**9**) [28], yield 2.10 g (80%), mp 112-114° (2-propanol); ir: ν C=O = 1676 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.02 (s, $COCH_3$, 3H), 2.61 (s, SCH_3, 3H), 5.20 (s, NCH_2, 2H), 7.2-7.4 (m, ArH, 5H), 10.4 (bs, NH, 1H); cmr (DMSO-d_6): δ ppm 153.3 (triazole C_3), 157.5 (triazole C_5), 17.0 (SCH_3), 24.7 ($COCH_3$), 53.2 (NCH_2), 169.8 (CO); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 207 (23.2), 222 sh (11.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 239 sh (8.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 207 (22.8), 231 sh (9.8).

Anal. Calcd. for $C_{12}H_{13}N_4OS$ (MW 261.32): C, 55.15; H, 5.01; N, 21.44; S, 12.27. Found: C, 55.23; H, 5.30; N, 21.48; S, 12.18.

5-Acetylamino-4-benzyl-3-methylthio-4*H*-1,2,4-triazole (**26**).

The same procedure was used as in the preparation of **24** starting from 5-amino-4-benzyl-3-methylthio-4*H*-1,2,4-triazole (**10**) [27], yield 2.3 g (88%), mp 163-165° (2-propanol); ir: ν C=O = 1709 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.03 (s, $COCH_3$, 3H), 2.54 (s, SCH_3, 3H), 4.98 (s, NCH_2, 2H), $\approx$7.3 (m, ArH, 5H), 10.4 (bs, NH, 1H); cmr (DMSO-d_6): δ ppm 151.8* (triazole C_3), 150.0* (triazole C_5), 16.5 (SCH_3), 24.0 ($COCH_3$), 48.4 (NCH_2), 172.1 (CO); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 206 (23.0), 225 sh (11.6), 242 sh (7.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 242 sh (10.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 205 (25.8), 240 (13.4).

Anal. Calcd. for $C_{12}H_{13}N_4OS$ (MW 261.32): C, 55.15; H, 5.01; N, 21.44; S, 12.27. Found: C, 55.22; H, 5.18; N, 21.66; S, 12.13.

5,6-Dihydro-5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidin-7(8*H*)-one (**13**).

The mixture of 20.8 g (0.16 mole) of powdered 5-amino-3-methylthio-1*H*-1,2,4-triazole **1** (R = SCH_3) [28] and 34.4 g (0.04 mole) of powdered crotonic acid was heated at 160° for 1 hour. The water libetarted during the reaction was continuously distilled off. To the still warm melt 100 ml of warm water was added, kept to boil for 5 minutes and the crystals obtained filtered while hot off, yield 18.7 g (59%), mp 200-201° (dimethylformamide); ir: ν CO = 1700 cm^{-1}; pmr (DMSO-d_6) δ ppm 1.40 (d, CH_3, 3H), 2.49 (s, SCH_3, 3H), 2.80 (dqa, CH_2, 2H), 4.4 (m, CH, 1H), 11.5 (b, NH, 1H); cmr (DMSO-d_6): δ ppm 160.4 (qa, triazolopyrimidine C_2), 169.5 (dqa, triazolopyrimidine C_7), 152.1 (d, triazolopyrimidine C_{8a}); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 212 (21.4), 236 (7.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 220 (14.6), 242 sh (8.7), 262 sh (7.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 212 (19.1), 236 sh (6.5).

Anal. Calcd. for $C_7H_{10}N_4OS$ (MW 198.25): C, 42.41; H, 5.08; N, 28.26; S, 16.17. Found: C, 42.49; H, 5.14; N, 28.12; S, 16.25.

5,6-Dihydro-5,8-dimethyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidin-7(8*H*)-one (**14**).

To the solution of 4.0 g (0.02 mole) of 5,6-dihydro-5-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidin-7(8*H*)-one (**13**) in 50 ml of absolute dimethylformamide 0.72 g (0.03 mole) of sodium hydride was added while stirring in small portions at room temperature. Keeping the reaction temperature at 20° (cooling with water) 1.87 ml = 4.25 g (0.03 mole) of methyl iodide was added through a dropping funnel. The reaction was completed by further stirring at room temperature for 1 hour. The mixture thus obtained was decomposed with 250 ml of water and the product obtained extracted with 3 X 100 ml portions of chloroform. The combined chloroform layers were washed with water (100 ml), dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness, yield 4.05 g (95%), mp 70-72° (2-propanol); ir: ν CO = 1705 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.43 (d, CH_3, 3H), 2.53 (s, SCH_3, 3H), 2.95 (dqa, CH_2, 2H), 3.25 (s, NCH_3, 3H), 4.50 (m, CH, 1H); cmr (DMSO-d_6): δ ppm 160.0 (qa, triazolopyrimidine C_2), 167.4 (m, triazolopyrimidine, C_7), 153.1 (dqa, triazolopyrimidine C_{8a}); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 214 (20.8), 237 sh (5.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 221 (14.0), 241 sh (10.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 215 (18.8), 239 sh (6.9).

Anal. Calcd. for $C_8H_{12}N_4OS$ (MW 212.27): C, 45.26; H, 5.70; N, 26.40; S, 15.11. Found: C, 45.40; H, 5.84; N, 26.22; S, 15.08.

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