On Triazoles. XII [1]. The Carbamoylation and Thiocarbamoylation of 5-Amino-1,2,4-triazoles [2]

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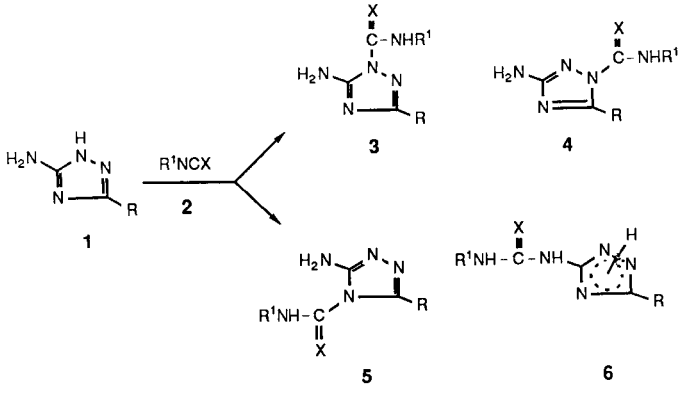
The reaction of 5-amino-3-R-1*H*-1,2,4-triazoles **1** with isocyanates **2** (X = O) and isothiocyanates **2** (X = S) was studied. It was stated that with isocyanates **3a** (X = O) type ring-carbamoylated products were formed which did not rearrange to the corresponding exo-carbamoylated derivatives **6a** (X = O). On the other hand the thiocarbamoylation of derivatives **1** provided at mild conditions lead to derivatives **3a** (X = S) which could be rearranged by heating to derivatives **6a** (X = S). In one case the isomeric **4a** (X = S) type derivative was also isolated. The comparison of the ir, uv, pmr and cmr spectra of the isomers isolated with the corresponding spectra of the carbamoylated and thiocarbamoylated 3,5-diamino-1,2,4-triazole derivatives helped to prove unequivocally the isomeric and tautomeric structure of compounds obtained giving a possibility to correct many confusions in the literature.

J. Heterocyclic Chem., **24**, 1685 (1987).

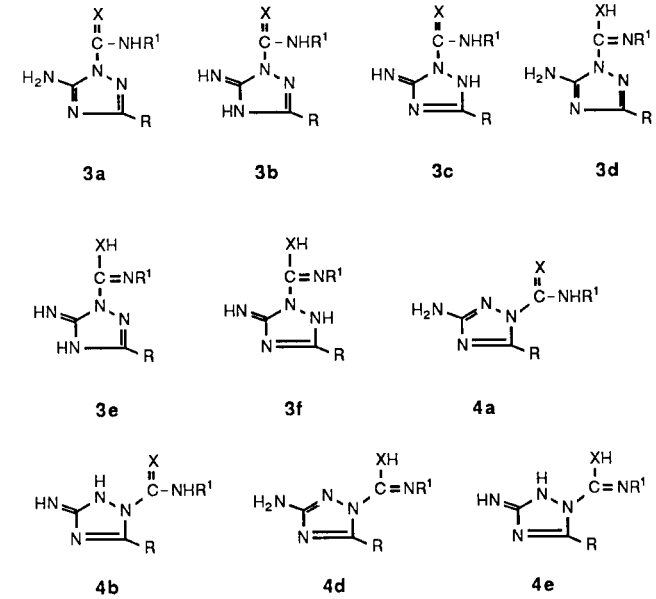
The reaction of 5-amino-3-R-1*H*-1,2,4-triazoles **1** [3,4] with isocyanates **2**, (X = O) or isothiocyanates **2** (X = S) may lead to any of the **3-6** carbamoyl (X = O) or thiocarbamoyl (X = S) derivatives (Scheme 1). Derivatives **3-5** may appear in any of the tautomeric forms **a-f** arising from the tautomerism of the triazole ring and the carbamoyl- or thiocarbamoyl groups (Scheme 2) while derivatives **6** could be characterised by any of the tautomeric forms **a-m** arising from the tautomerism of the triazole ring and the urea- or thiourea-moieties (Scheme 3). Probably this is the reason of the great number of confusions leading to many erroneous structures in the literature.

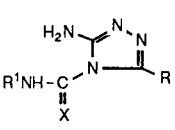
Scheme 1



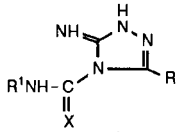
Thus *e.g.* to the product of the carbamoylation of 5-amino-1*H*-1,2,4-triazole (**1**, R = H) was proposed by different authors structure **3a** (R = R¹ = H) [5], **4a** (R = R¹ = H) [6], **6a** (R = R¹ = H) [7], and **6c** (R = R¹ = H) [8], respectively, to the phenylcarbamoyl analogue structure **4a** (R = H, R¹ = Ph) [9] and **6c** (R = H, R¹ = Ph), [10,11], respectively, while to the analogues dimethylcarbamoyl derivative [prepared by the reaction of **1** (R = H) with

Scheme 2

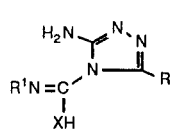




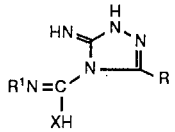
5a



5b

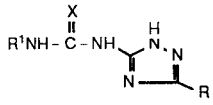


5d

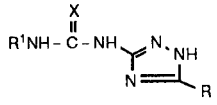


5e

Scheme 3



6a



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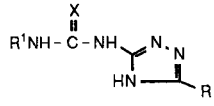

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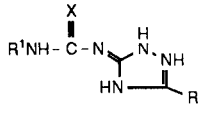

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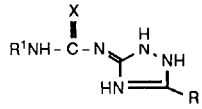

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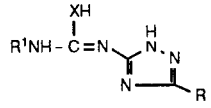

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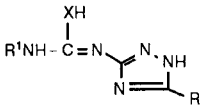

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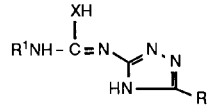

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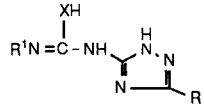

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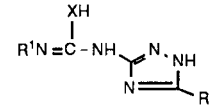

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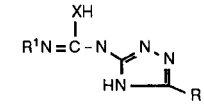
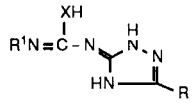
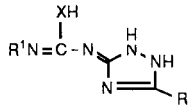


6k

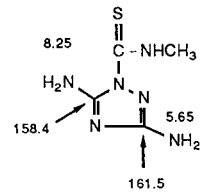


6l

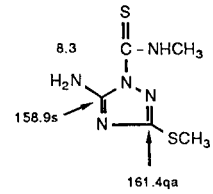


6m

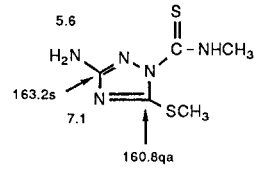
Scheme 4



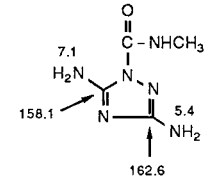
25/3a



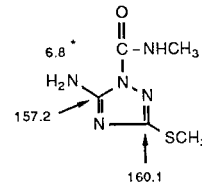
16/3a



17/4a

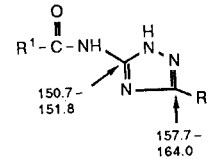


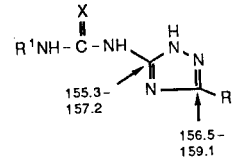
8/3a



2/3a (* $CDCl_3$)

Scheme 5





6a

dimethylcarbamoyl chloride] structure **3a** [12], **4a** [6], **6b** [13] and **6c** [7], respectively, *etc.*

In the case of thiocarbamoyl derivatives the situation is very similar to that of their carbamoyl analogues with the exception that in this case a labile "ring thiocarbamoylated" derivative **3-5** was usually isolated first, which underwent thermal rearrangement to the corresponding "exo"-thiocarbamoylated derivative **6** [6, 14-16]. However the products obtained were described again with different erroneous isomeric and tautomeric structures. Based on the pmr studies Hirata and coworkers [16] proposed the presence of two "ring acylated" thiocarbamoyl derivatives **3a** (R = H, R^1 = CH_3) and **4a** (R = H, R^1 = CH_3), respectively, in the reaction mixture of 5-amino-1*H*-1,2,4-triazole (**1**, R = H) and methyl isothiocyanate but they did not isolate them.

Table I

Carbamoyl Derivatives (X = O)

Compound No. Structure	R	R¹	Conditions of Preparation Reaction: Method	Solvent	Time (hours)	Temperature (°C)	Yield (%)	mp (°C) (Cryst from)	Molecular formula (MW) or Reference mp (°C)	Analysis Calcd./Found: C	H	N	S	Hal
1/3a	Methylthio	H	D	W	2	25	61	175-177 (W)	$C_4H_7N_5OS$ (173.20)	27.74 27.71	4.07 4.15	40.44 40.34	18.51 18.58	
2/3a	Methylthio	Methyl	C	D	12	25	69	128-130 (M)	$C_5H_9N_5OS$ (187.23)	32.08 31.97	4.85 5.03	37.41 37.34	17.13 17.07	
3/3a	Methylthio	Ethyl	C	D	12	25	88	91-93 (M)	$C_6H_{11}N_5OS$ (217.32)	35.81 35.58	5.51 5.53	34.80 34.83	15.93 15.88	
4/3a	Methylthio	*n*-Butyl	A	D	3	25	41	80.5-81.5 (E)	$C_8H_{15}N_5OS$ (229.31)	41.90 41.76	6.59 6.63	30.54 30.59	13.98 13.76	
5/3a	Methylthio	2-Chloroethyl	A	D	2	25	83	144-145 (M)	$C_6H_{10}ClN_5OS$ (235.70)	30.57 30.71	4.28 4.19	29.71 29.51	13.60 13.45	15.04 15.11
6/3a	Methylthio	Cyclohexyl	A	D	2.5	25	62	115-117 (M)	$C_{11}H_{17}N_5OS$ (255.35)	47.04 46.91	6.71 6.54	27.43 27.59	12.56 12.41	
7/3a	Methylthio	1-Naphthyl	B	D	12	80	69	169-171 (B)	$C_{14}H_{13}N_5OS$ (299.35)	56.17 56.33	4.38 4.57	23.39 23.62	10.71 10.52	
8/3a	Amino	Methyl	B	M	5	64	75	158-160 (M)	$C_4H_8N_6O$ (156.15)	30.77 30.92	5.16 5.34	53.82 54.09		
9/3a	Amino	Ethyl	B	M	10	64	71	131-133 (M)	$C_5H_{10}N_6O$ (170.18)	35.29 35.51	5.92 6.11	49.39 49.42		
10/3a	Morpholino	H	D	W	2	25	65	196-198 (W)	$C_7H_{12}N_6O_2$ (212.21)	39.62 39.51	5.70 5.76	39.60 39.47		
11/3a	Morpholino	Ethyl	C	D	12	80	94	168-170 (M)	$C_9H_{16}N_6O_2$ (240.27)	44.99 45.15	6.71 6.81	34.98 35.24		
12/3a	Morpholino	*n*-Butyl	A	D	4.5	25	95	146-148 (M)	$C_{11}H_{20}N_6O_2$ (268.32)	49.24 49.19	7.51 7.51	31.32 31.32		
13/3a	Morpholino	2-Chloroethyl	A	D	12	25	98	172-174 (M)	$C_9H_{15}ClN_6O_2$ (274.72)	39.35 39.52	5.50 5.47	30.59 30.63		
14/3a	Morpholino	Cyclohexyl	A	D	4.5	25	87	207-209 (E)	$C_{13}H_{22}N_6O_2$ (294.36)	53.05 52.89	7.53 7.64	28.55 28.73		
15/3a	Morpholino	1-Naphthyl	B	D	2	80	83	185-187 (*n*-Bu)	$C_{17}H_{18}N_6O_2$ (338.37)	60.34 60.44	5.36 5.59	24.84 24.75		

Solvents: D = Dioxane, M = Methanol, B = Benzene, *n*-Bu = 1-Butanol, W = Water, E = Ethanol.

Table II

Thiocarbamoyl Derivatives (X = S)

Compound No. Structure	R	R¹	Conditions of Preparation Reaction: Method	Solvent	Time (hours)	Temperature (°C)	Yield (%)	mp (°C) (Cryst from)	Molecular formula (MW) or Reference mp (°C)	Analysis Calcd./Found: C	H	N	S	Hal
16/3a	Methylthio	Methyl	C	D	8	80	54	184-186 (E)	$C_5H_9N_5S_2$ (203.29)	29.54 29.73	4.46 4.57	34.45 34.61	31.55 31.75	
17/4a	Methylthio	Methyl	E	DMF			12	142-144 (2-P)	$C_5H_9N_5S_2$ (203.29)	29.54 29.58	4.46 4.62	34.45 34.27	31.55 31.57	
18/3a	Methylthio	Ethyl	B	D	5	80	50	155-157 (M)	$C_6H_{11}N_5S_2$ (217.32)	33.16 33.21	5.10 5.28	32.23 32.36	29.51 29.74	
19/3a	Methylthio	Cyclohexyl	A	D	2.5	25	56	169-171 (E)	$C_{10}H_{17}N_5S_2$ (271.41)	44.25 44.51	6.31 6.27	25.80 25.89	23.63 23.57	
20/3a	Methylthio	Phenyl	B	Py	1	110	74	149-151 (E)	$C_{10}H_{11}N_5S_2$ (265.37)	45.26 45.19	4.18 4.08	26.39 26.10	24.17 24.31	
21/3a	Methylthio	4-Chlorophenyl	A	D	12	25	52	140-142 (M)	$C_{10}H_{10}ClN_5S_2$ (299.81)	40.06 40.34	3.36 3.56	23.36 23.16	21.39 21.45	11.83 11.90
22/3a	Methylthio	Benzyl	A	D	72	25	64	155-157 (E)	$C_{11}H_{13}N_5S_2$ (279.39)	47.29 47.51	4.69 4.75	25.07 25.26	22.95 22.89	
23/3a	Methylthio	1-Methylbenzyl	B	D	2	80	61	117-118 (M)	$C_{12}H_{15}N_5S_2$ (293.42)	49.12 49.38	5.15 5.41	23.87 23.80	21.86 21.76	
24/3a	Ethylthio	Methyl	B	M	5	65	90	162-164 (E)	$C_6H_{11}N_5S_2$ (217.32)	33.16 33.30	5.10 5.14	32.23 32.34	29.51 29.63	
25/3a	Amino	Methyl	A	M	12	25	64	174-176 (M)	$C_4H_8N_6S$ (172.22)	27.90 28.02	4.68 4.91	48.80 48.68	18.62 18.75	
26/3a	Dimethylamino	Benzyl	B	D	7	60	65	168-170 (A)	$C_{12}H_{16}N_6S$ (276.36)	52.15 52.25	5.84 5.96	30.41 30.32	11.60 11.53	
27/3a	Piperidino	Benzyl	B	D	6	60	79	146-148 (A)	$C_{15}H_{20}N_6S$ (316.42)	56.93 57.11	6.37 6.45	26.56 26.56	10.13 10.04	
28/3a	Morpholino	Methyl	B	D	5	80	94	193-195 (E)	$C_8H_{14}N_6OS$ (242.31)	39.65 39.72	5.82 5.94	34.69 34.48	13.23 13.40	
29/3a	Morpholino	Cyclohexyl	A	D	3	25	54	136-137 (E)	$C_{13}H_{22}N_6OS$ (310.43)	50.30 50.45	7.14 7.13	27.07 26.89	10.33 10.13	
30/3a	Morpholino	Phenyl	A	D	12	25	45	143-145 (E)	$C_{13}H_{16}N_6OS$ (304.38)	51.30 51.47	5.30 5.55	27.61 27.63	10.53 10.48	

Solvents: A = Acetonitrile, D = Dioxane, DMF = Dimethylformamide, E = Ethanol, M = Methanol, 2-P = 2-Propanol, Py = Pyridine.

Table II (continued)

Compound No. Structure	R	R¹	Conditions of Preparation: Method	Solvent	Reaction: Time (hours)	Reaction: Temperature (°C)	Yield (%)	mp (°C) (Cryst from)	Molecular formula (MW) or Reference mp (°C)	Analysis Calcd./Found: C	H	N	S	Hal
31/3a	Morpholino	4-Chlorophenyl	A	D	0.5	25	79	167-169 (D)	$C_{13}H_{15}ClN_6OS$ (338.83)	46.08 46.15	4.46 4.62	24.80 24.68	9.46 9.53	10.46 10.32
32/3a	Morpholino	3-Hydroxy-phenyl	A	D	2	25	89	182-184 (E)	$C_{13}H_{16}N_6O_2S$ (320.38)	48.74 48.57	5.03 4.95	26.23 26.11	10.01 10.15	
33/3a	Morpholino	2,4,6-Trimethyl-phenyl	C	D	10	80	35	170-172 (E)	$C_{16}H_{22}N_6OS$ (346.46)	55.47 55.70	6.40 6.67	24.26 23.98	9.26 9.27	
34/3a	Morpholino	Benzyl	A	D	12	25	64	158-160 (E)	$C_{14}H_{18}N_6OS$ (318.41)	52.81 53.08	5.70 5.77	26.39 26.28	10.07 10.21	
35/3a	Morpholino	1-Methylbenzyl	B	D	2	80	78	127-129 (M)	$C_{15}H_{20}N_6OS$ (332.43)	54.20 54.42	6.06 6.26	25.28 25.11	9.65 9.57	
36/6a	Methylthio	Methyl	E	DMF			11	174-176 (2-P)	$C_5H_9N_5S_2$ (203.29)	29.54 29.67	4.46 4.59	34.45 34.22	31.55 31.80	
37/6a	Methylthio	Phenyl	B	Py	1	110	74	149-151 (A)	$C_{10}H_{11}N_5S_2$ (265.36)	45.26 45.11	4.18 4.26	26.39 26.44	24.17 24.03	
38/6a	Methylthio	4-Chlorophenyl	F	—	0.1	200	53	207-209 (DMF)	$C_{10}H_{10}ClN_5S_2$ (299.81)	40.06 39.61	3.36 3.45	23.36 23.25	21.39 21.17	11.83 11.73
39/6a	Dimethylamino	Benzyl	G	—	6	—	36	209-210 (A)	$C_{12}H_{16}N_6S$ (276.36)	52.15 51.04	5.84 5.88	30.41 30.47	11.60 11.42	
40/6a	Piperidino	Benzyl	G	—	2	—	38	167-169 (A)	$C_{15}H_{20}N_6S$ (316.42)	56.93 57.04	6.37 6.53	26.56 26.43	10.13 10.22	
41/6a	Morpholino	Methyl	F	—	0.1	200	51	236-238 (DMF)	$C_8H_{14}N_6OS$ (242.31)	39.65 39.87	5.82 5.89	34.68 34.78	13.23 13.08	
42/6a	Morpholino	4-Chlorophenyl	F	—	0.1	200	75	240-242 (DMF)	$C_{13}H_{15}ClN_6OS$ (338.83)	46.08 45.83	4.46 4.61	24.80 24.68	9.46 9.35	10.46 10.57
43/6a	Morpholino	Benzyl	G	—	5	—	32	145-147 (2-P)	$C_{14}H_{18}N_6OS$ (318.41)	52.81 52.68	5.70 5.80	26.39 26.41	10.07 10.11	

Solvents: A = Acetonitrile, D = Dioxane, DMF = Dimethylformamide, E = Ethanol, M = Methanol, 2-P = 2-Propanol, Py = Pyridine.

Table III

Spectral Data of Carbamoyl Derivatives (X = O)

Compound No.	IR [cm⁻¹] ν NH	ν C=O	ν C=N	PMR [ppm] (DMSO-d₆) δ SCH₃	δ NH₂	δ NH	CMR [ppm] (DMSO-d₆) δ C₃	δ C₅	δ C=O	UV λ max [nm] (ε 10⁻³) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
1/3a	3470 3380	1740	1635 1600	2.55	7.2	7.5 [b]				206 (11.1) 245 (6.0)	206 (12.8) 244 (6.5)	218 (5.4) 244 (2.7)
2/3a	3410 3280	1694	1640 1620 1550	2.53	6.8 [a]		159.6	156.9 [17]		208 (12.5) 248 (6.7)	206 (13.6) 241 (7.3)	224 (3.9) 245 (2.7)
3/3a	3410 3360	1708	1636	2.55	7.1 [a]					208 (14.4) 248 (7.8)	205 (15.2) 241 (8.4)	223 (3.2) 244 (2.5)
4/3a	3450 3410	1725	1646 1550	2.49	6.9	7.8 [a]				206 (14.8) 246 (8.5)	202 (15.7) 238 (8.9)	218 (4.7) 244 (2.3)
5/3a	3450	1700	1636 1540	2.53	6.4	7.1 [a]				206 (13.3) 249 (8.1)	206 (14.9) 243 (8.1)	220 (4.6) 243 (3.1)
6/3a	3440 3420	1716	1642 1540	2.51		7.8 [a]	161.4	158.8	151.5	206 (13.2) 248 (8.3)	205 sh (14.4) 241 (8.6)	240 (2.8)
7/3a	3450 3290	1732	1655 1580 1565 1550	2.62	6.4	9.1 [a]				221 (6.3) 258 (7.9) 288 (9.5)	220 (6.7) 246 (9.3) 279 (9.0)	288 (5.6)
8/3a	3490 3430 3370	1693	1646 1620 1550		5.4 7.1	7.4	162.6	158.1	153.8	201 (11.6) 247 (6.7)	200 (9.5) 240 (7.3)	245 (7.0)
9/3a	3450 3280	1715	1691		5.4 7.05	7.5	162.3	157.7	152.8			
10/3a	3460 3420	1730	1650 1590		7.15	7.35	161.8	156.5	152.5			
11/3a	3420	1690	1540		6.8 [a]		161.9	156.4	151.3			
12/3a	3430 3330	1700	1652 1580 1548		6.6 [a]					204 (15.5) 255 (8.2)	202 (16.8) 250 (6.5)	254 (7.6)
13/3a	3400 3300	1700	1650 1575 1545		6.35	7.2 [a]						
14/3a	3420 3300	1692	1654 1580 1545		6.45 [a]		161.9	156.4	150.5	203 (14.1) 251 (8.5)	204 sh (17.6) 245 (8.1)	250 (8.1)
15/3a	3430 3380	1692	1648 1575 1545		7.2	9.3	163.5	158.2	151.5	221 (6.8) 290 (12.1)	220 (6.9) 279 (10.7)	288 (6.1)

[a] Taken in deuteriochloroform solution. [b] δ NH_2.

We have synthesized a series of carbamoyl- and thiocarbamoyl-derivatives of different 5-amino-3-R-1*H*-1,2,4-triazole derivatives (Tables I and II, respectively) and recorded their ir, uv, pmr and cmr spectra (Tables III and IV).

According to our observation the carbamoylation of all 5-amino-3-R-1*H*-1,2,4-triazoles **1** lead to a sole "ring carbamoylated" derivative **3a** (X = O) (Table I) which could not be rearranged neither by heating nor by reacting it with bases to the corresponding "exo carbamoylated" derivative **6** (X = O). In these reactions only decomposition to the starting 5-amino-3-R-1*H*-1,2,4-triazole derivative **1** was observed.

On the other hand the thiocarbamoylation of the 5-amino-3-R-1*H*-1,2,4-triazoles **1** lead in mild conditions to the formation of "ring thiocarbamoylated" derivatives **3a** (X = S) which were rearranged by heating to the corresponding derivatives **6a** (X = S) (Table II). Providing the thiocarbamoylation of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) with methylisothiocyanate (**2**, R^1 = methyl) in dimethylformamide at 70° *i.e.* using the con-

Table IV

Spectral Data of Thiocarbamoyl Derivatives (X = S)

Compound No.	IR [cm⁻¹] ν NH	ν C=N	ν C=S	PMR [ppm] (DMSO-d₆) δ SCH₃	δ NH₂	δ NH	CMR [ppm] (DMSO-d₆) δ C₃	δ C₅	δ C=S	UV λ max [nm] (ε 10⁻³) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
16/3a	3340 3300	1640 1530 1490	1289	2.57	8.3	9.6	161.4 qa	158.9 s	175.3	245 (10.2) 259 (11.7) 288 (9.9)	210 (11.1) 259 (12.1) 280 (10.6)	223 (12.4) 250 (6.8)
17/4a	3390 3330	1638 1565 1527	1310	3.30	5.6	9.2	160.8 qa	163.2 s	174.3	246 (7.9) 270 (13.7) 305 (6.9)	246 (7.6) 270 (13.3) 300 (6.6)	221 (12.9) 257 (7.0)
18/3a	3350 3300	1644 1520 1500	1300	2.53	7.8	8.6				244 (11.2) 262 (13.2) 289 (11.0)	245 (11.1) 261 (13.4) 285 (11.1)	224 (13.0) 251 (6.9)
19/3a	3340 3300	1650 1550 1525 1500	1293	2.53	8.3		161.0	158.9	173.1	244 (11.8) 263 (14.4) 288 (11.6)	266 (14.3) 284 (11.3)	222 (13.5) 253 (7.0)
20/3a	3320 3210	1645 1590 1530 1450	1270	2.62	8.3 [a]					270 (21.7)	262 (19.9)	261 (14.8)
21/3a	3320 3290	1650 1590 1535 1490	1276	2.60	8.35	10.8						
22/3a	3330	1658 1539 1500	1286	2.56	8.3	10.1	161.5	158.2	175.0	247 (11.7) 263 (13.7) 291 (10.4)	246 (10.7) 262 (13.1) 288 (10.1)	255 (10.3)
23/3a	3300	1650 1618 1490	1300	2.53	7.7	8.9 [a]						
24/3a	3350 3290	1637 1550 1535 1500	1315		8.1	9.1				244 (11.9) 258 (12.8) 286 (10.7)	261 (12.4) 282 (10.7)	252 (9.3)
25/3a	3400 3290	1630 1585 1545 1470	1320		5.65 8.25	8.5	161.5	158.4	175.0	230 (8.1) 255 (11.0) 294 (8.7)	255 (11.3) 284 (8.4)	251 (9.8)
26/3a	3310 3280	1660 1605 1550 1505 1470	1320		8.3	9.8	163.1	159.0	174.7	203 (16.8) 254 (14.0) 298 (11.6)	202 (26.0) 260 (11.9) 290 (9.7)	254 (12.7)
27/3a	3300	1655 1600 1555 1515 1465	1300		8.3	9.8	162.2	158.7	174.6	205 (26.1) 257 (14.2) 310 (12.0)	205 (23.2) 262 (11.8) 301 (9.5)	256 (13.3)
28/3a	3340 3290	1665 1590 1520 1474	1320		8.1	9.1				241 (9.3) 254 (11.2) 300 (9.5)	257 (9.9) 292 (8.0)	252 (10.9)
29/3a	3340 3240	1640 1580 1510 1460	1271		7.5 [a]		162.2	158.8	173.0	238 sh (10.8) 254 (13.4) 298 (11.6)	257 (12.7) 290 (9.7)	252 (11.4)

Table IV (continued)

Compound No.	IR [cm^{-1}] ν NH	ν C=N	ν C=S	δ SCH_3	PMR [ppm] (DMSO-d_6) δ NH_2	δ NH	CMR [ppm] (DMSO-d_6) δ C_3	δ C_5	δ C=S	UV λ max [nm] (ε 10^{-3}) EtOH	10% EtOH + 90% 0.1 *N* HCl	10% EtOH + 90% 0.1 *N* NaOH
30/3a	3320	1672 1650 1600 1470	1330		7.9	9.6 [a]						
31/3a	3350	1660 1590 1510 1470	1320		8.3	10.8 [a]				222 (25.9) 270 (15.6) 289 (15.8)	220 (27.9) 266 (15.4) 286 (15.0)	254 (14.6)
32/3a	3400 3280	1640 1600 1510 1467	1310		8.4	9.4				229 sh (16.2) 258 (12.9) 304 (10.3)	261 (8.5) 297 (9.5)	256 (12.5)
33/3a	3310	1650 1580 1555 1465	1305		8.35		162.4	158.9	174.8	228 sh (17.0) 256 (13.4) 304 (11.8)	258 (12.4) 297 (10.8)	254 (14.6)
34/3a	3330	1648 1600 1520 1468	1310		8.3	9.9	162.2	158.9	174.8	205 (21.6) 258 (14.3) 304 (11.6)	204 (25.9) 260 (12.6) 296 (9.9)	254 (12.6)
35/3a	3320	1648 1590 1505	1310		7.6	8.8 [a]				244 (10.3) 258 (13.0) 306 (10.5)	257 (12.3) 303 (9.8)	256 (11.9)
36/6a	3260	1575 1555 1500 1450	1305	2.60	9.80 [b] 10.6 [b]	11.9	155.9	157.9	180.7	211 (13.7) 260 (21.4)	212 (14.0) 255 (20.5)	238 (10.9) 259 (14.6)
37/6a	3210	1600 1585 1570 1500 1470	1340		9.9 [b] 11.2 [b]	11.5	155.3	156.5	178.7	206 (23.2) 270 (22.8)	206 (23.1) 262 (21.1)	260 (15.7)
38/6a	3250	1610 1570 1495 1450	1340	2.68	10.2 [b] 10.5 [b]	11.6				207 (19.1) 224 (14.6) 273 (14.4)	221 (21.5) 274 (15.1)	262 (17.5)
39/6a	3190	1640 1580 1490 1450	1345		10.3 [b] 10.5 [b]	12.1				208 (24.5) 244 sh (12.6) 262 (17.7)	206 (25.8) 245 sh (13.8) 258 (15.1)	238 (13.9) 258 (10.7)
40/6a	3180	1610 1560 1490 1420	1335		10.3 [b] 10.5 [b]	12.2	157.2	158.9	180.2	209 (23.4) 246 sh (13.3) 262 (17.6)	207 (25.0) 244 sh (14.7) 258 (15.2)	238 (13.4) 266 (10.3)
41/6a	3240	1610 1570 1505 1460	1310		9.8 [b] 10.4 [b]	11.1				203 (15.3) 254 (16.6)	206 (15.4) 249 (13.7)	229 (10.3) 257 (9.8)
42/6a	3280	1645 1570 1495 1450	1345		10.1 [b] 11.1 [b]	11.7				207 (20.6) 227 (16.8) 278 (18.8)	208 (28.7) 267 (15.2)	222 (14.0) 268 (12.8)
43/6a	3230	1660 1575 1530 1445	1346		10.3 [b] 10.5 [b]	12.2	156.4	159.1	180.1	208 (20.9) 263 (16.6)	206 (22.1) 244 sh (13.3) 258 (14.4)	239 (11.6) 266 (10.0)

[a] Taken in deuteriochloroform solution. [b] δ NH.

ditions described by Hirata and coworkers [16] for the analogues reaction of 5-amino-1*H*-1,2,4-triazole (**1**, R = H) we were able to isolate both "ring thiocarbamoylated" derivatives **17/3a** (R = methylthio, R^1 = methyl) and **18/4a** (R = methylthio, R^1 = methyl), respectively, from the reaction mixture besides the "exo thiocarbamoylated" analogue **36/6a** (R = methylthio, R^1 = methyl).

The ir spectra of the carbamoyl derivatives **3a** (X = O) were characterised by the ν NH_2 bands appearing between 3450 and 3400 cm^{-1} and ν C=O frequencies appearing between 1732 and 1690 cm^{-1} (Table III). These data were in good agreement with the proposed "ring carbamoylated" structures **3-5** (X = O) but gave no information which one of them is correct. The same was the situation with the thiocarbamoyl derivatives **3a** (X = S) where the ν NH_2 bands appeared between 3400 and 3320 cm^{-1}, the ν C=N frequencies between 1672 and 1630 cm^{-1} and those of the ν C=S between 1330 and 1270 cm^{-1} (Table IV) which gave again no answer which one of the corresponding "ring acylated" derivatives **3-5** (X = S) was present. Moreover the corresponding 2-thiocarbamoylated derivative **18/4a** absorbed at 3390, 1638 and 1310 cm^{-1}, respectively (Table IV), *i.e.* in regions exactly the same as those observed for derivatives **3a** (X = S) giving a further evidence that the above frequencies are not characteristic for any of the structures **3-5** (X = S).

On the other hand the ν NH frequencies of the "exo thiocarbamoylated" derivatives **6a** (X = S) appeared between 3280-3250 cm^{-1} (Table IV) *i.e.* at completely different values than those of derivaties **3-5** (X = S) giving a possibility of differentiation between them. The ν C=S bands appearing around 1300 cm^{-1} seemed to support the idea that they exist in the thio-keto form, *i.e.* in one of the tautomeric structures **6a-6e**.

The structure of the "ring-carbamoylated" and "ring-thiocarbamoylated" 5-amino-3-R-1*H*-1,2,4-triazoles **3-5** (X = O or S, respectively) can be easily deduced from the pmr spectra of the 3,5-diamino-1-methylcarbamoyl-1*H*-1,2,4-triazole (**8/3a**) and 3,5-diamino-1-methylthiocarbamoyl-1*H*-1,2,4-triazole (**25/3a**) taken in DMSO-d_6 solutions (Scheme 4). Namely, the chemical surrounding of the amino group 5 of **8a** is exactly the same as that of the amino group of 1-methylcarbamoyl-3-methylthio-1*H*-1,2,4-triazole (**2/3a**), the chemical surrounding of the amino group of **25/3a** adjacent to the triazole carbon atom 5 is exactly the same as that of the amino group of 5-amino-3-methylthio-1-methylthiocarbamoyl-1*H*-1,2,4-triazole (**16/3a**) and the chemical surrounding of the amino group adjacent to the triazole carbon atom 3 of **25/3a** is exactly the same as that of the 5-amino-3-methylthio-2-methylthiocarbamoyl-2*H*-1,2,4-triazole (**17/4a**), respectively (Scheme 4). Consequently they are expected to appear with approximately the same chemical shifts, respectively.

As shown from Table III the 5-amino groups of all carbamoyl derivatives were characterised with the chemical shifts of 6.35-7.2 ppm giving proof for their **3a** type structure. These data are in good agreement with those of the 3,5-diamino-1-dimethylcarbamoyl-1*H*-1,2,4-triazole [δ $NH_2(C_5)$ = 6.96 pm, δ $NH_2(C_3)$ = 5.25 ppm], 5-amino-1-dimethylcarbamoyl-3-methylthio-1*H*-1,2,4-triazole (δ NH_2 = 6.85 ppm) and 5-amino-3-dimethylamino-1-dimethylcarbamoyl-1*H*-1,2,4-triazole (δ NH_2 = 7.25 ppm) reported recently [17].

The situation was the same with the chemical shifts of the 5-amino-groups of the corresponding methylthiocarbamoyl derivaties (Table IV) appearing between 7.5 and 8.4 ppm giving again a clear evidence to the **3a** structure of derivatives **16** and all those of **18-35**. On the other hand the chemical shift of 5.6 ppm (Table IV) observed for the 5-amino-group of derivative **17** nicely supported its **4a** structure.

The "exo-thiocarbamoylated" derivatives **36-43/6a** were characterised with three different NH signals appearing above 9.8 ppm giving an unequivocal proof to their structure **6** but again giving no information about the tautomeric situation.

The uv spectra of the "ring-carbamoylated" derivatives **1/3a-15/3a** - unless they did not contain another chromophore overlapping the original chromophore system (see *e.g.* **7/3a** and **15/3a**) - consisted of two well developed bands the higher one of which underwent a slight hypsochromic shift in acidic and alkaline media.

The uv spectra of the **3a** type "ring-thiocarbamoylated" derivatives **16** and **18-35** - again unless they were not overlapped by another chromophore system - were characterised with three bands of the approximately same intensity one of which appeared above 286 nm. They suffered a slight hypsochromic shift in acidic media, while the highest absorption band had disappeared in alkaline media.

The uv spectrum of the **4a** type isomer **17** was very similar to those of derivatives **3a** characterised again with three peaks the middle one being of double intensity giving a possibility of its differentation. This spectrum also suffered a slight hypsochromic shift in acidic media and was simplified by dissappearing the highest band in alkaline media.

The uv spectra of derivatives **6** were usually again characterised with three absorption bands suffering a hypsochromic shift in acidic media and simplifying in alkaline media but were strongly influenced by the R^1-groups. However the fact that the highest maximum usually appeared at about 260 nm, (but at least below 278 nm) helped in case of isomeric pairs to their safe ordering to structure **6** but gave again no information as to which one of structures **6a-6e** they corresponded.

In the cmr spectra of the "ring-carbamoylated" and "ring-thiocarbamoylated" derivatives **1-15** and **16-35**, respectively, the C=O and C=S bands appeared at about 151 and 175 ppm, respectively, (Tables III and IV) finally excluding the tautomeric forms **3d-3f**, **4d-4e** and **5d-5e**, arising from the keto-enol and thioketo-thioenol tautomerism, respectively. The triazole carbon atoms 3 of the diamino-derivatives **8/3a** and **25/a** (Scheme 4) chosen as models appeared with the chemical shifts of 162.6 and 161.5, while those of carbon atoms 5 with the chemical shifts of 158.1 and 158.4 ppm, respectively. Taking into account the same chemical surrounding of the above carbon atoms with the carbon atoms 5 of derivatives **4a** and **3a**, respectively, and comparing them with the chemicals shifts of all other derivatives (Tables III and IV) we found an unequivocal proof for the isomeric and the dominant tautomeric structure of all carbamoyl- (Table III) and thiocarbamoyl- (Table IV) derivatives. Our data are again in accordance with the data published recently [17] for the 5-amino-1-dimethylcarbamoyl- and 5-amino-1-methylcarbamoyl-3-methylthio-1*H*-1,2,4-triazole (159.0 and 156.9 ppm, respectively), for 5-amino-3-dimethylamino-1-dimethylcarbamoyl-1*H*-1,2,4-triazole (158.7 ppm) and for 5-amino-3-methylthio-1-phenylcarbamoyl-1*H*-1,2,4-triazole (157.2 ppm).

It should be mentioned that these results are also in full accordance with those obtained for the simple 1-acylated-5-amino-3-R-1*H*-1,2,4-triazoles [18].

In the cmr spectra of the "exo-thiocarbamoylated" derivatives **6** the C=S carbon atoms appeared with the chemical shift of about 180 ppm again at once excluding all those tautomeric forms arising from the thioketo-thioenol tautomerism (structures **6f-6m**, Scheme 3). From among the remaining tautomeric structures **6a-6e** helped to choose the dominant tautomeric structure **6a** the close analogy of the chemical shifts of the triazole carbon atoms 3 with those of the analogues 5-acylamino-3-R-1*H*-1,2,4-triazoles (Scheme 5) of previously proved structure [18].

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 pmr and the cmr measurements were performed using Varian XL-100, Bruker WM-250 and Bruker WP-80 SY instruments.

General Methods for the Preparation of Carbamoyl and Thiocarbamoyl Derivatives.

Method A.

To a solution of 0.01 mole of the corresponding 3-R-5-amino-1*H*-1,2,4-triazole derivative **1** in 100 ml of an appropriate solvent (Tables I and II) 0.105 mole of the appropriate isocyanate or isothiocyanate was added by dropping it through a dropping funnel at room temperature. The reaction was completed by stirring at room temperature for the time given in Tables I and II. The product crystallised upon dropping water to the reaction mixture was filtered off and re-crystallised from an appropriate solvent (Tables I and II).

Method B.

A solution of 0.01 mole of the corresponding 3-R-5-amino-1*H*-1,2,4-triazole derivatives **1** and 0.105 mole of the appropriate isocyanate of isothiocyanate in 100 ml of an appropriate solvent (Tables I and II) was refluxed for the time given in Tables I and II. After cooling the reaction mixture was evaporated *in vacuo* to dryness and the residue was recrystallized from an appropriate solvent (Tables I and II).

Method C.

The Method was in all respects identical with that of Method A with the exception that after completing the reaction the reaction mixture was evaporated *in vacuo* to dryness and the residue was recrystallised from an appropriate solvent (Tables I and II).

Method D.

To a solution of 0.04 mole of the corresponding 3-R-5-amino-1*H*-1,2,4-triazole (**1**) in 50 ml of an appropriate solvent (Table I) 3.65 g (0.045 mole) of potassium cyanate was added while stirring in small portions at room temperature. After the cyanate was dissolved 3.8 ml of concentrated hydrochloric acid was dropped slowly to the reaction mixture and stirred for further two hours. The crystals precipitated were filtered off and recrystallised from water (Table I).

Method E.

To a solution of 8.9 g (0.0864 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) in 35 ml of dimethylformamide 5.0 g (0.0683 mole) of methylisothiocyanate was added and stirred at 70° for 15 hours. After cooling 40 ml of water was dropped to the reaction mixture, the crystals precipitated were filtered off and purified twice by dissolving them at room temperature in 50 ml of dimethylformamide and adding 70 ml of water to yield 8.6 g (62%) of pure 5-amino-3-methylthio-1-methylthiocarbamoyl-1*H*-1,2,4-triazole (**17/3a**), mp 184-186° [tlc (Kieselgel HF, Merck), R_f = 0.76 (benzene:ethyl acetate = 1.2)]. The three dimethylformamide containing mother liquors obtained above were collected, diluted with 200 ml of water and extraced twice with 100 ml portions of chloroform. The chloroform layers were collected, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 5.3 g of crystalline product which was chromatographed on a silica-gel column using a 1:2 mixture of benzene and ethyl acetate as eluent.

A further crop of **17/3a** was obtained first [1.2 g (9%), mp 184-186°], then 1.7 g (12%) of 5-amino-3-methylthio-2-methylthiocarbamoyl-2*H*-1,2,4-triazole (**18/4a**), mp 142-144° (2-propanol), [tlc (Kieselgel HF, Merck), R_f = 0.33 (benzene:ethyl acetate = 1:2)] and 1.5 g (11%) of *N*-(3-methylthio-1*H*-1,2,4-triazole-5-yl)-*N*-methylthiourea (**36/6a**), mp 174-176° (2-propanol), [tlc (Kieselgel HF, Merck), R_f = 0.28 (benzene: ethyl acetate = 1:2)].

Method F.

One-hundreth mole of the corresponding 1-carbamoyl-, or 1-thiocarbamoyl-5-amino-3-R-1*H*-1,2,4-triazole derivative **3a** was heated neat on an oil bath at the temperature and time given in Tables I and II. After cooling the melt obtained was recrystallised from an appropriate solvent (Tables I and II).

Method G.

A solution of 0.01 mole of the corresponding 1-(R'-thiocarbamoyl)-5-amino-3-R-1*H*-1,2,4-triazole (**3a**) in 5 ml of dimethylformamide was refluxed for the time given in Table II. The solution obtained was evaporated *in vacuo* to dryness and the residue was chromatographed on a silica-gel column (eluent the 1:2 mixture of benzene and ethyl acetate). The product obtained was recrystallised from an appropriate solvent (Table II).

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