On Triazoles. XXV [1]. The Reaction of Methyl (5-Amino-3-Q-1*H*-1,2,4-triazolyl)dithiocarbonates with Amines

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Different "functionalised" triazolylthioamides **3** and -thioureas **4** were synthesised. The ring closure of the ω-hydroxyalkylthioamides **3/2-5** led to the corresponding 2-thiazoline **5/2-4** and 5,6-dihydro-4*H*-1,3-thiazine **5/5** derivatives, respectively. Unexpectedly, the ring closure of the corresponding 2,2-dimethoxyethyl derivative **3/18** led depending on the reaction conditions to a thiazole derivative **6** or to its 1,2,4-triazolo[3,4-*b*]-1,3,5-triazepin-5(9*H*)-thione isomer **7** representing a novel ring system. To corroborate its structure **7** was methylated to the corresponding *S*-methyl derivative **8**. Spectroscopical evidence is given for the structure of derivatives **3-8** obtained.

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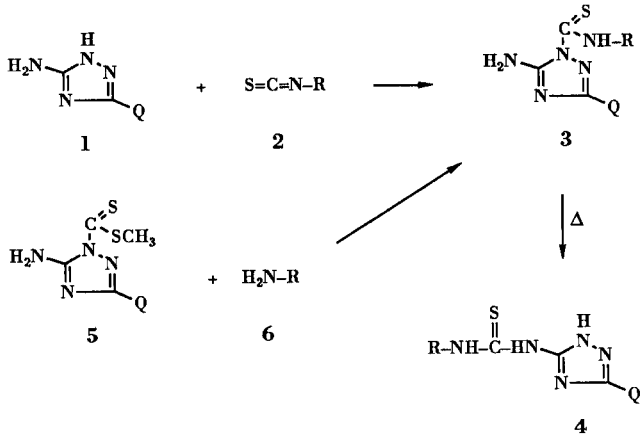
In a previous paper of this series [2] we have described the synthesis and elucidation of structure of different **3** and **4** type triazolylthioamides and -thioureas, respectively, by direct thiocarbamoylation of the corresponding 5-amino-3-Q-1,2,4-triazoles **1** with isothiocyanates **2** (Scheme 1). However, the scope of the above method was limited to those derivatives, where the corresponding isothiocyanates did not contain any group reactive to the isothiocyanate moiety. As our biological structure-activity studies required among others such **3** and **4** type derivatives that contained in place of R alkyl groups substituted with hydroxy, alkoxy, alkoxycarbonyl, *etc.* moieties, we tried to elaborate a more general method for the synthesis of derivatives **3** and **4**. Such a method may serve the reaction of the corresponding methyl (5-amino-3-Q-1*H*-1,2,4-triazol-1-yl)dithiocarbonates **5** described recently [3] with the corresponding amines **6** (Scheme 1). As predicted the above reaction led to the formation of "functionalised" derivatives **3** that could be thermally rearranged to the corresponding derivatives **4**. The spectral data of all derivatives obtained nicely followed the rules elaborated for the structural requirements of both, derivatives **3** and **4**, respectively [2].

Scheme 1



Thus from among the three uv maxima of derivatives **3** taken in ethanol as solvent (unless they were overlapped by another chromophore in the molecule) the middle one appearing at about 250-260 nm proved to be the one with the highest intensity. However, in some cases the lowest peak expected at about 220-240 nm was not developed clearly.

The NH_2 groups of the triazole ring were as a consequence of the electron withdrawing effect of the thiocarbamoyl groups in position 1 of the triazole ring shifted again upfield in the pmr as compared with those of the corresponding 5-aminotriazoles **1**.

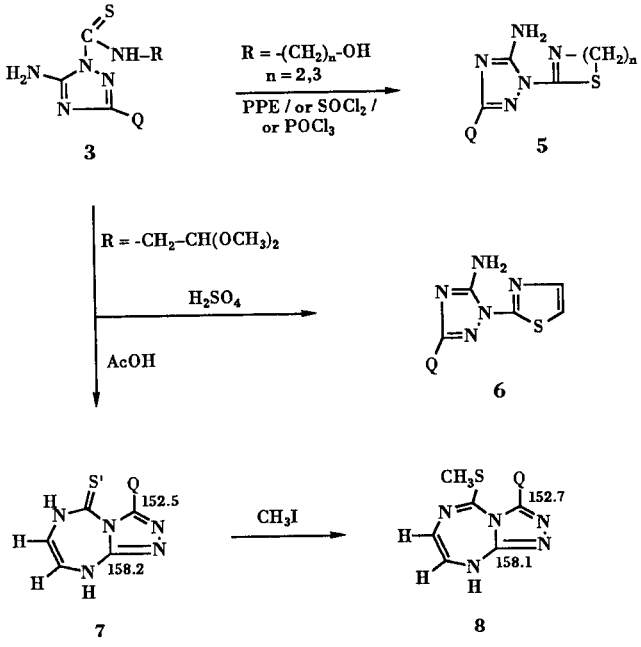
The strongest evidence for the position 1 of the thiocarbamoyl moiety on the triazole ring gave again the cmr spectra where the triazole carbon atoms 3 and 5 appeared at about 160 and 158 ppm, respectively, following the rule [4] that the chemical shift of the triazole carbon atoms was dependent mainly on the "pyrrol-like" or "pyridine-like" character of the neighbouring nitrogen atoms and was little influenced by the quality of its substituents. The chemical shift of the C=S groups (appr. 173 ppm) is also in accordance with the "ring thiocarbamoylated" structure of derivatives **3** [3].

The "exo-thiocarbamoylated" structure **4** of derivative **4/1** is characterised with three NH bands (10.2, 10.7 and 12.4 ppm, respectively) in the pmr and the expected [3] triazole and thiocarbonyl values (154.5, 157.7 and 168.9 ppm, respectively).

The ring-closure reactions of derivatives **3/2-5** provided either with polyphosphoric ester, thionylchloride or phosphoroxychloride led to the corresponding 2-thiazoline **(5/2-4)** and 5,6-dihydro-1,3-thiazine **5/5** derivatives, respectively (Scheme 2). However, even all spectral data of these derivatives were consistent with the structures proposed, the position of the newly built thiazoline or thiazine moiety on the triazole ring had to be proved as the thiocarbamoyl moiety of the triazole ring of derivatives **3/2-5** could be thermally rearranged [2] during the above reac-

tions. An unequivocal proof for the 1-substitution of the triazole ring gave the cmr spectra where the triazole carbon atoms 3 and 5 appeared with the expected [2-4, 6-8] chemical shifts of 161.3-165.2 and 154.8-158.9 ppm, respectively.

Scheme 2

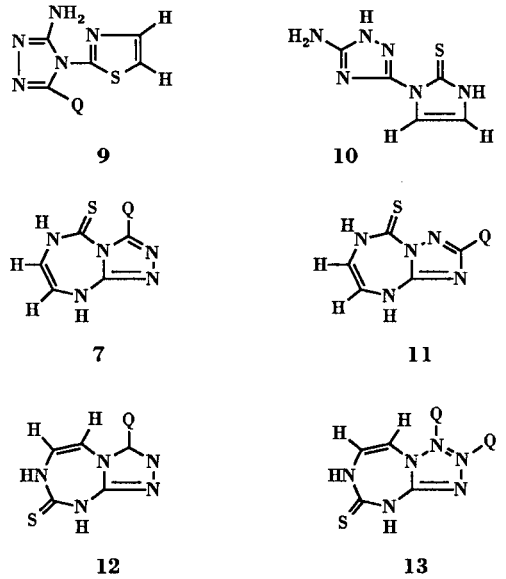


It should be mentioned that the δ NH_2 and δ CH_2 chemical shifts of the newly built 2-thiazoline and 5,6-dihydro-4*H*-thiazine rings in the pmr were in perfect accordance with those described previously [9] for the analogous 2-phenylimino-2-thiazolines and 2-phenylimino-5,6-dihydro-4*H*-1,3-thiazines containing in place of our "quasi-aromatic" triazole moiety a phenyl ring [compare *e.g.* δ NCH_2 of 2-[*N*-(2,6-dimethylphenyl)-*N*-methylamino]thiazoline-2 [9]: 4.15 ppm with δ NCH_2 of **5/2**, **5/3**, and **5/4**: 4.23, 4.22 and 4.24 ppm, respectively, or δ NCH_2 and δ CH_2 (5) of 2-(*N*-(2,6-dimethylphenyl)-*N*-methylamino]-5,6-dihydro-4*H*-1,3-thiazine [9]: 3.70 and 1.78 ppm, respectively, with δ NCH_2 and CH_2 (5) of **5/5**, 3.73 and 1.81 ppm, respectively].

Interestingly, the ring-closure of the corresponding 2,2-dimethoxyethyl derivative **3/18** led depending on the reaction conditions to different products. Thus its reaction in cold sulfuric acid led to **6** which is the corresponding unsaturated analogue of **5/3** while its ring closure in boiling acetic acid provided the mixture of **6** and the isomeric 1,2,4-triazolo[3,4-*b*]-1,3,5-triazepin-5(9*H*)-thione derivative **7** representing a novel ring system (Scheme 2). The structure of **6** was again consistent with its spectral data and its cmr data proved the position 1 of the thiazole moiety on the triazole ring.

However, to prove the structure of the isomeric derivative **7** formed most probably by the rearrangement of the thiocarbonyl moiety from position 1 of triazole ring to position 4 followed by ring-closure to the triazolyl-5-amino group required special spectroscopical measurements. In this case all those structures had to be taken in account that could arise from the ring-closure of the thiocarbamoyl moiety being originally in position 1 as well as the ring closures of the rearranged isomers having this moiety in positions 2 and 4, respectively, of the triazole ring. Moreover the ring closure had to proceed to all possible directions, *i.e.* the corresponding thiazole *e.g.* **6** and **9**, imidazole **10** and triazepine **7**, **11-13** derivatives Scheme 3) had to be taken in account.

Scheme 3



The CH protons appeared in the pmr as two triplets which after irradiation at the chemical shifts of the NH protons (12.4 and 12.8, respectively) simplified to doublets proving the presence of an NH-CH=CH-NH moiety in the molecule. This fact excluded structures **6**, **9**, **10**, **12** and **13** and remained only structures **7** and **11**. The differentiation between these two structures made possible the chemical shifts of the triazole carbon atoms in the cmr. It was predicted [7] that the triazole carbon atoms 3 and 5 of the 4-substituted triazole derivatives such as 4-benzyl-5-amino-3-morpholino-1,2,4-triazole (**14**) (Scheme 4) would posess chemical shifts of approximately 152 and 157 ppm, respectively. Derivative **7** showed the corresponding shifts of 152.5 and 158.2, respectively, being in excellent agreement with that of predicted and differing essentially from those expected for the corresponding 1-substituted isomer **11** (~160 and ~157 ppm, respectively, see *e.g.* cmr data of derivatives **3**, Table III) proving the structure **7** unequivocally.

Scheme 4

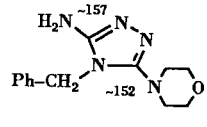


Table 1

Compound No.	Q	R	Method	Conditions of Preparation Reaction Solvent Type/Amount (ml)	Time (hours)	Yield (%)	Mp(°C) (crystallized from)	Molecular formula (MW)	Analysis Calcd./Found C	H	N	S
3/1	Methylthio	2-Hydroxyethyl	A	EtOH 120	12	29	131-132 (CH_3CN)	$C_6H_{11}N_5OS_2$ (233.32)	30.89 30.92	4.75 4.88	30.02 29.93	27.49 27.44
3/2	Dimethylamino	2-Hydroxyethyl	B	EtOH 120	1	65	148-150 (EtOH)	$C_7H_{14}N_6OS$ (230.30)	36.59 36.50	6.13 6.08	36.49 36.55	13.82 13.85
3/3	Morpholino	2-Hydroxyethyl	B	MeOH 250	4	90	144-146 (H_2O)	$C_9H_{16}N_6O_2S$ (272.33)	39.69 39.61	5.92 6.04	30.86 30.92	11.77 11.68
3/4	4-Methylpiperazino	2-Hydroxyethyl	B	EtOH 120	5	87	181-183 (EtOH)	$C_{10}H_{19}N_7OS$ (285.37)	42.09 41.98	6.71 6.68	34.36 34.31	11.24 11.15
3/5	Morpholino	3-Hydroxypropyl	B	MeOH 200	1	66	109-111 (CH_3CN)	$C_{10}H_{18}N_6O_2S$ (286.36)	41.94 42.03	6.34 6.44	29.35 29.30	11.20 11.26
3/6	Morpholino	1-Hydroxybutan-2-yl	A	DMSO 150	10	23 [1]	133-135 (2-PrOH)	$C_{11}H_{20}N_6O_2S$ (300.38)	43.98 44.07	6.71 6.73	27.89 28.02	10.67 10.76
3/7	Methylthio	2-(3,4-dimethoxyphenyl)-ethyl	A	DMSO 100	10	68 [1]	135-137 (EtOH)	$C_{14}H_{19}N_5O_2S_2$ (353.46)	47.57 47.60	5.41 5.45	19.81 20.01	18.14 18.02
3/8	Morpholino	2-(3,4-dimethoxyphenyl)-ethyl	A	DMSO 100	10	72 [1]	142-143 (2-PrOH)	$C_{17}H_{24}N_6O_3S$ (392.48)	52.02 52.11	6.16 6.27	21.41 21.44	8.17 8.15
3/9	Morpholino	Hydroxycarbonylmethyl	[2]			81	191-193 (Dioxane)	$C_9H_{14}N_6O_3S$ (286.32)	37.75 37.70	4.93 5.14	29.35 29.36	11.20 11.11
3/10	Morpholino	Methoxycarbonylmethyl	[2]			34	149-151 (EtOH)	$C_{10}H_{16}N_6O_3S$ (300.34)	39.99 40.13	5.37 5.43	27.98 28.06	10.68 10.76
3/11	Morpholino	Ethoxycarbonylmethyl	[2]			42	135-136 (Benzene)	$C_{11}H_{18}N_6O_3S$ (314.37)	42.03 42.06	5.77 5.82	26.73 26.67	10.20 10.18
3/12	Methylthio	3-[3-(piperidinomethyl)-phenoxy]propyl	A	DMSO 50	5	46 [3]	117-118 (EtOH)	$C_{19}H_{28}N_6OS_2$ (420.60)	54.26 54.30	6.71 6.80	19.98 20.11	15.25 15.21
3/13	Dimethylamino	3-[3-(piperidinomethyl)-phenoxy]propyl	[2]			43	104-106 (2-PrOH)	$C_{20}H_{31}N_7OS$ (417.58)	57.53 57.45	7.48 7.51	23.48 23.56	7.68 7.72
3/14	Diallylamino	3-[3-(piperidinomethyl)-phenoxy]propyl	A	DMSO 50	5	74 [4]	94-96 (2-PrOH)	$C_{24}H_{35}N_7OS$ (469.66)	61.38 61.42	7.51 7.55	20.88 20.92	6.83 6.88
3/15	Piperidino	3-[3-(piperidinomethyl)-phenoxy]propyl	A	DMSO 50	5	60 [3]	110-111 (2-PrOH)	$C_{23}H_{35}N_7OS$ (457.65)	60.36 60.42	7.71 7.77	21.42 21.50	7.01 7.04
3/16	Morpholino	3-[3-(piperidinomethyl)-phenoxy]propyl	[2]				127-129 (CH)	$C_{22}H_{33}N_7O_2S$ (459.62)	57.49 57.55	7.24 7.26	21.33 21.37	6.98 7.04
3/17	4-Methylpiperazino	3-[3-(piperidinomethyl)-phenoxy]propyl	A	DMSO 50	5	52 [5]	90-92 [6]	$C_{23}H_{36}N_8OS$ (472.66)	58.45 58.45	7.68 7.70	23.71 23.65	6.78 6.82
3/18	Morpholino	2,2-Dimethoxyethyl	[2]				134-135 (EtOH)	$C_{11}H_{20}N_6O_3S$ (316.38)	41.76 41.88	6.37 6.43	26.56 26.62	10.13 10.15
4/1	Morpholino	Ethoxycarbonylmethyl	[2]				229-231 (EtOH)	$C_{11}H_{18}N_6O_3S$ (314.37)	42.03 42.11	5.77 5.88	26.73 26.65	10.20 10.21

[1] Crystallized upon addition of 100 ml of water and 50 g of ice to the DMSO solution. [2] See Experimental. [3] Crystallized upon addition of 10 ml of water to the DMSO solution. [4] Crystallized upon addition of 300 ml of *n*-hexane to the DMSO solution. [5] Crystallized upon addition of 10 ml of water and 150 ml of *n*-hexane to the DMSO solution. [6] Purified by stirring with diethyl ether.

Table II
ir and uv Spectral Data

Compound No.	ir [cm^{-1}] ν NH	ν C=N	ν C=S	ν other charecteristic bands	uv λ max [nm] (ε.10^{-3}) EtOH	10% EtOH + 90% 0.1 *N* HCl	% EtOH + 90% 0.1 *N* NaOH
3/1	3330	1664 1641 1527	1288		246 sh (11.3) 261 (12.7) 290 (10.6)	 262 (12.4) 284 (10.4)	247 (8.6)
3/2	3300	1661 1604 1554 1523	1302		257 (12.8) 309 (11.1)	258 (11.7) 305 (10.3)	255 (10.3) 306 (5.2)
3/3	3340	1643 1572 1516	1275	1109	252 (12.9) 296 (10.8)	255 (11.5) 289 (9.3)	228 (9.7) 244 sh (7.8)
3/4	3345	1637 1573 1519	1273		242 sh (10.5) 255 (12.0) 302 (10.9)	236 sh (7.8) 258 (11.5) 294 (9.5)	244 sh (8.3)
3/5	3320	1670 1590 1530	1270	1119	252 (12.8) 296 (10.6)	256 (11.6) 288 (9.1)	240 (10.6)
3/6	3315	1649 1585 1512	1275 1221	1117			
3/7	3320 3290	1655 1526 1489	1269 1240		234 (12.9) 266 (14.2) 282 (13.4)	230 sh (11.5) 266 (12.7) 281 sh (12.6)	246 sh (6.2)
3/8	3290	1672 1568 1522 1506	1275 1236	1117	236 (10.3) 265 (13.1) 307 (10.4)	 263 (11.7) 294 (8.8)	244 (9.7)
3/9	3220	1645 1593 1514	1281 1240	1726 1119	252 (12.0) 304 (9.4)	256 (10.3) 298 (8.6)	256 (10.3) 298 sh (3.1)
3/10	3320	1635 1580 1500	1295 1216	1755 1114	258 (8.8) 298 (10.0)	256 (10.0) 298 (9.6)	256 (9.0) 290 (6.8)
3/11	3337	1643 1582 1510	1306 1213	1751 1115	260 (12.8) 311 (10.5)	256 (10.4) 299 (9.0)	243 (10.4)
3/12	3320	1640 1582 1520	1280 1228		248 (11.6) 263 (14.1) 284 (10.2)	 264 (13.1) 280 (11.6)	248 (7.3)
3/13	3310	1649 1614 1520	1294		222 sh (12.1) 258 (13.2) 308 (10.4)	 262 (10.9) 303 (8.2)	 256 (10.6) 296 (4.2)
3/14	3340 3290	1670 1585 1500	1300		258 (13.4) 308 (11.2)	262 (10.7) 299 (8.7)	
3/15	3310	1655 1585 1520	1259		224 sh (12.6) 256 (13.3) 306 (10.8)	212 (10.3) 262 (11.1) 300 (8.7)	258 (12.8) 302 (5.2)
3/16	3315 3287	1655 1580 1520	1263	1115	220 sh (14.0) 248 (11.6) 302 (9.9)	222 sh (11.5) 262 (11.0) 288 (8.1)	246 (9.8) 302 (4.1)
3/17	3427 3314	1637 1583 1514	1275		258 (11.9) 303 (8.9)	224 (12.8) 260 (14.9) 295 (10.9)	258 (10.1) 302 (4.2)
3/18	3341 3281	1663 1587 1512	1281	1119	228 sh (7.2) 280 (12.1)	228 sh (10.8) 269 (10.8)	
4/1	3344	1593 1558 1495	1223 1265	1736 1119	208 (15.8) 264 (17.3)	210 (15.7) 262 (14.8)	238 (9.7) 266 (9.9)

Table III
PMR and CMR Spectral Data

Compound No.	PMR [ppm] (DMSO-d_6)				CMR [ppm] (DMSO-d_6)				
	δNH_2	δNH	δQ	δR	δC_3	δC_5	$\delta C{=}S$	δQ	δR
3/1	8.36 bs	9.6 t	2.53 s	3.63 b (4H) 4.91 t (OH)	160.1	157.3	173.3	13.4	46.6 (NCH_2) 58.3 (OCH_2)
3/2	8.31 bs	9.16 t	2.94 s	3.76 m (4H) 4.96 t (OH)	161.3	157.0	172.7	37.2	46.0 (NCH_2) 58.6 (OCH_2)
3/3	7.27 bs	8.85 bs	3.40 t 3.74 t	3.88 m (4H) [1]	160.6	157.0	172.9	45.5 65.6	46.1 (NCH_2) 59.5 (OCH_2)
3/4	8.31 bs	9.18 t	2.22 s 2.37 m	3.63 bs (4H) 4.94 t (OH)	160.5	157.0		45.0 54.0	56.1 (NCH_2) 58.3 (OCH_2)
3/5	7.47 bs	8.96 bs	3.39 t 3.75 t	1.91 qi (2H) [1] 3.83 m (4H)					
3/6	7.53 bs	8.61 d	3.39 t 3.74 t	1.01 t (3H) [1] 1.73 m (2H) 3.80 m (2H) 4.45 b (1H)	160.0	157.1	173.7	45.9 66.4	10.4 (CH_3) [1] 23.9 (CCH_2 C) 56.9 (CH) 63.5 (OCH_2)
3/7	7.8 bs	8.75 t	2.45 s	2.93 t (2H) [1] 3.86 s (3H) 3.87 s (3H) 3.89 qa (2H) 6.75-6.81 (3H)	160.4	157.2	173.6	13.4	33.8 ($PhCH_2$) [1] 45.3 (NCH_2) 56.0 (OCH_3) 112.2 112.6 120.8 (Ph) 148.3 149.5
3/8	7.74 bs	8.55 t	3.35 t 3.73 t	2.92 (2H) [1] 3.85 s (3H) 3.86 s (3H) 3.85 qa (2H)	160.2	156.8	173.1	45.5 66.0	33.8 ($PhCH_2$) [1] 44.9 (NCH_2) 55.7 (OCH_3) 55.8 (OCH_3) 111.9 112.4 130.7 (Ph) 148.3 149.5
3/9	8.31 bs	9.49 t	3.35 t 3.66 t	4.22 d (2H) 12.9 b (1H)	160.7	157.1	173.4	45.5 65.6	41.2 ($NHCH_2$) 169.6 (COOH)
3/10	8.30 bs	9.60 t	3.36 t 3.65 t	3.66 s (3H) 4.31 d (2H)	160.6	157.0	173.6	45.3 65.4	45.1 ($NHCH_2$) 51.7 (OCH_3) 168.6 (ester)
3/11	8.30 bs	9.54 t	3.35 t 3.66 t	1.21 t (3H) 4.14 qa (2H) 4.28 d (2H)	160.7	157.2	173.9	45.8 66.3	14.1 (CH_3) [1] 45.6 ($NHCH_2$) 61.8 (OCH_2) 168.4 (ester)
3/12	7.62 bs	9.17 t	2.49 s	1.42 m (2H) [1] 1.57 m (4H) 2.19 qi (2H) 2.44 t (4H) 3.44 s (2H) 3.87 qa (2H) 4.12 t (2H) 6.82-7.28 m (4H)	160.3	158.5	173.7	13.5	24.3 (pip -4) [1] 25.9 (pip -3,5) 27.7 (CCH_2C) 42.6 (NCH_2) 54.4 (pip -2,6) 63.6 ($PhCH_2$) 66.5 (OCH_2) 113.1 115.2 121.9 (Ph) 128.9 140.6 157.3

Table III (continued)

Compound No.	PMR [ppm] (DMSO-d_6)				CMR [ppm] (DMSO-d_6)				
	δ NH_2	δ NH	δ Q	δ R	δC_3	C_5	C=S	δ Q	δ R
3/13	7.60 bs	8.91 t	2.95 s (6H)	1.43 m (2H) [1] 1.57 m (4H) 2.18 qi (2H) 2.36 m (4H) 2.95 s (6H) 3.43 s (2H) 3.87 qa (2H) 4.10 t (2H) 6.80-7.26 m (4H)	160.8	158.5	173.1	37.5	24.2 (pip -4) [1] 25.4 (pip -3,5) 27.9 (CCH_2C) 41.8 (NCH_2) 54.3 (pip -2,6) 63.5 ($PhCH_2$) 66.1 (OCH_2) 112.9 115.1 121.7 (Ph) 128.7 140.3 157.0
3/14	7.68 bs	8.85 t		1.45 m (2H) [1] 1.59 m (4H) 2.18 qi (2H) 2.41 m (4H) 3.46 s (2H) 3.86 qa (2H) 3.94 d (4H) 4.10 t (2H) 5.15 dd (4H) 5.82 m (2H) 6.83-7.39 m (4H)	159.9	158.7	173.4	49.5 116.6 133.7	24.3 (pip -4) [1] 25.8 (pip -3,5) 28.1 (CCH_2C) 41.6 (NCH_2) 54.4 (pip -2,6) 63.5 ($PhCH_2$) 66.2 (OCH_2) 113.3 115.1 121.7 (Ph) 128.8 140.5 157.0
3/15	7.60 bs	8.90 t	1.59 bs*	1.43 m (2H) [1] 1.59 m (10H)* 2.18 qi (2H) 2.39 m (4H) 3.37 bs (4H) 3.46 s (2H) 3.86 qa (2H) 4.10 t (2H) 6.82-7.26 m (4H)	160.6	158.7	173.5	25.1 [2] 46.3	24.3 (pip -4) [1] 25.9 (pip -3,6) 28.1 (CCH_2C) 41.8 (NCH_2) 54.4 (pip -2,6) 63.6 ($PhCH_2$) 66.4 (OCH_2) 113.1 115.2 121.8 (Ph) 128.9 140.5 156.9
3/16	7.52 bs	8.98 t	3.37 t 3.72 t	1.43 m (2H) [1] 1.57 m (4H) 2.18 qi (2H) 2.36 m (4H) 3.43 s (2H) 3.87 qa (2H) 4.11 t (2H) 6.82-7.30 m (4H)	160.3	158.5	173.5	45.6 66.1	24.2 (pip -4 [1] 25.8 (pip -3,5) 27.8 (CCH_2C) 41.9 (NCH_2) 54.3 (pip -2,6) 63.5 ($PhCH_2$) 66.4 (OCH_2) 113.3 115.1 121.8 (Ph) 128.7 140.5 156.9

Table III (continued)

Compound No.	PMR [ppm] (DMSO-d_6)						CMR [ppm] (DMSO-d_6)		
	δNH_2	δNH	δQ	δR	δC_3	C_5	C=S	δQ	δR
3/17	7.52 bs	8.96 t	2.32 s 2.31 m* 3.43 m	1.44 m (2H) [1] 1.58 m (4H) 2.18 qi (2H) 2.13 m (8H)* 3.48 s (2H) 3.86 qa (2H) 4.11 t (2H) 6.83-7.30 m (4H)	160.4	158.7	173.5	45.3 46.1 54.4	24.3 (pip -4) [1] 25.8 [pip -3,5] 28.0 (CCH_2C) 41.9 (NCH_2) 54.3 (pip -2,6) 63.5 ($PhCH_2$) 66.4 (OCH_2) 113.5 115.1 121.8 (Ph) 128.8 140.4 156.9
3/18	7.55 bs	8.67 t	3.41 t 3.75 t	3.44 s (6H) [1] 3.80 qa 4.58 t	160.4	156.9	173.8	45.6 66.1	45.4 (NCH_2) 54.4 (OCH_2) 101.7 (CH)
4/1	10.7 bs [3] 12.4 bs [4]	10.2 bs	3.33 t 3.70 t	1.21 t (3H) [1] 4.14 qa (2H) 4.39 d (2H)	154.5	157.7	178.8	46.1 65.2	13.9 (CH_3) 46.5 ($NHCH_2$) 60.6 (OCH_2) 168.9 (ester)

[1] Taken in deuteriochloroform solution. [2] Piperazine-3,4,5. [3] δ NH (exo). [4] δ NH (triazole).

As expected, derivative **7** could be methylated with methyl iodide in ethanol to yield the corresponding methylthio derivative **8** the spectra of which were again fully consistent with its structure (compare *e.g.* its pmr and cmr data with the corresponding data of **7**, see Experimental).

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrophotometer. The electron impact mass spectra were determined with a Varian MAS SM-1 spectrometer. The ultraviolet spectra were obtained by a Pye Unicam SP 8-150. The pmr and the cmr measurements were performed on a Varian EM-390 and Bruker WM-250 instruments at 90 and 250 MHz, respectively in the CW or FT mode at ambient temperature using broad band and proton decoupling, internal standard was tetramethylsilane.

General Methods for the Synthesis of Derivatives **3**.

Method A.

The mixture of 0.1 mole of the appropriate dithioester **1**, 0.12 mole of the appropriate amine **2** and appropriate amount of a solvent given in Table I was stirred at room temperature for the time given in Table I. The solution obtained was evaporated to dryness and the residue crystallised from a solvent given in Table I.

Method B.

The mixture of 0.1 mole of the appropriate dithioester **1**, 0.12 mole of the appropriate amine **2** and an appropriate amount of a solvent given in Table I was refluxed for the time given in Table I. After cooling the crystals precipitated were filtered off and the residue crystallised from a solvent given in Table I.

(3-Morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetic Acid (**3/9**).

To the solution of 4.2 g (0.105 mole) of sodium hydroxide in 400 ml of water 25.2 g (0.08 mole) of ethyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetate (**3/11**) was added and the mixture was stirred at room temperature for 75 minutes. The solution obtained was acidified with 88 ml of 1 *N* hydrochloric acid to *p*H = 5-5.5. The crystals which precipitated were filtered off and recrystallised from dioxane to yield 19.5 g (81%) of (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetic acid (**3/9**), mp 191-193°. For the analytical and spectral data see Tables I, II and III.

Methyl (3-Morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetate (**3/10**).

To the solution of 0.23 g (0.01 mole) of sodium in 150 ml of methanol 1.39 g (0.01 mole) of methyl aminoacetate hydrochloride and 2.59 g (0.01 mole) of methyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)dithiocarbonate [3] was added and refluxed for 16 hours. After cooling the crystals precipitated were filtered off and recrystallised from ethanol to yield 0.92 g (34%) of methyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetate (**3/10**), mp 166-168°. For the analytical and spectral data see Tables I, II and III.

Ethyl (3-Morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetate (**3/11**) and N^1-(3-Morpholino-1*H*-1,2,4-triazol-5-yl)-N^2-ethoxycarbonylmethylthiourea (**4/1**).

To the suspension of 25.93 g (0.1 mole) of methyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)dithiocarbonate [3] in 100 ml of dimethyl sulfoxide 3.3 g (0.11 mole) of sodium hydride (80% solution in paraffin oil) was added at room temperature. To the red suspension obtained the solution of 13.96 g (0.1 mole) ethyl aminoacetate hydrochloride in 35 ml of dimethylsulfoxide was added

dropwise at room temperature with stirring. The stirring of the yellow mixture obained was continued at laboratory temperature for further 12 hours. The mixture was decomposed with 500 ml of water and 50 g of crushed ice. The crystals precipitated were filtered off washed with water and a small amount of ether to yield 18.1 g (58%) of a product which was the mixture of ethyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetate (**3/11**) and *N*¹-(3-morpholino-1*H*-1,2,4-triazol-5-yl)-*N*²-ethoxycarbonylmethylthiourea (**4/1**). This was recrystallised from benzene to yield 13.1 g (42%) of ethyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)thiocarbonylaminoacetate (**3/11**), mp 135-136°. The crystals insoluble in benzene were recyrstallised from ethanol to yield 0.3 g (1%) of *N*¹-(3-morpholino-1*H*-1,2,4-triazol-5-yl)-*N*²-ethoxycarbonylmethylthiourea (**4/1**), mp 229-231°. For the analytical and spectral data see Tables I, II and III.

*N*¹-(3-Morpholino-1*H*-1,2,4-triazol-5-yl)-*N*²-ethoxycarbonylmethylthiourea (**4/1**).

To the suspension of 2.59 g (0.01 mole) of methyl (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)dithiocarbonate [3] in 50 ml of dioxane 0.33 g (0.011 mole) of sodium hydride (80% solution in paraffin oil) was added at room temperature. To the red suspension obtained the solution of 1.40 g (0.01 mole) of ethyl aminoacetate hydrochloride was added dropwise at room temperature and the mixture obtained was refluxed for 12 hours. After cooling the inorganic salts which precipitated (0.66 g) were filtered off, the filtrate was poured into 200 ml of water, and extracted 4 times with 50 ml portions of chloroform. The combined chloroform layers were extracted with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 1.17 g (37%) of *N*¹-(3-morpholino-1*H*-1,2,4-triazol-5-yl)-*N*²-ethoxycarbonylmethylthiourea (**4/1**) that after recrystallisation from ethanol melted at 228-230°. The product is identical with that of **4/1** obtained above.

(3-Dimethylamino-5-amino-1,2,4-triazol-1-yl)-*N*-[3-(piperidinomethylphenoxy)propyl]thioamide (**3/13**).

To the solution of 24.8 g (0.1 mole) of 3-(3-piperidinomethylphenoxy)propylamine [5] in 50 ml of dimethyl sulfoxide 21.7 g (0.1 mole) of methyl (3-dimethylamino-5-amino-1*H*-1,2,4-triazole-1-yl)dithiocarbonate [3] was added at room temperature and the mixture was stirred for 12 hours. The solution obtained was poured into 600 ml of water and 100 g of crushed ice, the oily product precipitated was extracted twice with 150 ml portions of chloroform, the combined chloroform layers were washed with water dried over sodium sulfate and evaporated *in vacuo* to dryness. The residue was trituated with 60 ml of ethanol, the crystals precipitated were filtered off and recrystallised from 2-propanol to yield 18.0 g (43%) of (3-dimethylamino-5-amino-1,2,4-triazol-1-yl)-*N*-[3-(piperidinomethylphenoxy)propyl]thioamide (**3/13**), mp 104-106°. For the analytical and spectral data see Tables I, II and III.

(3-Morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)-*N*-3-[3-(piperidinomethylphenoxy)propyl]thioamide (**3/16**).

To the solution of 25.9 g (0.1 mole) of methyl (3-morpholino-5-amino-1*H*-1,2,4-triazole-1-yl)dithiocarbonate [3] in 50 ml of dimethylsulfoxide 24.8 g (0.1 mole) of 3-(3-piperidinomethylphenoxy)propylamine [5] was added below 20° and the mixture obtained was stirred at room temperature for 12 hours. The solution obtained was poured into 700 ml of water, the oily product was extracted twice with 150 ml portions of chloroform, the combined chloroform layers were washed with water dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 57.65 g of an oily residue, which after addition of 120 ml of 2-propanol crystallised. The crystals precipitated were filtered off and recrystallised from cyclohexane to yield 17.5 g (38%) of (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)-*N*-3-[3-(piperidinomethylphenoxy)propyl]thioamide (**3/16**), mp 127-129°. For the analytical and spectral data see Tables I, II and III.

(3-Morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)-*N*-(2,2-dimethoxyethyl)thioamide (**3/18**).

To the solution of 2.59 g (0.01 mole) of methyl (3-morpholino-5-amino-1*H*-1,2,4-triazole-1-yl)dithiocarbonate [3] in 140 ml of methanol 1.1 ml (1.05 g = 0.01 mole) of aminoacetaldehyde dimethylacetal (Fluka) was added and the mixture was refluxed for 1 hour. The solution obtained was evaporated *in vacuo* to dryness and the crystalline residue was recrystallised from ethanol to yield 2.14 g (68%) of (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)-*N*-(2,2-dimethoxyethyl)thioamide (**3/18**), mp 134-135°. For the analytical and spectral data see Tables I, II and III.

2-(5-Amino-3-dimethylamino-1*H*-1,2,4-triazol-1-yl)-2-thiazoline (**5/2**, Q = dimethylamino, n = 2).

The mixture of 2.30 g (0.01 mole) of 1-(5-amino-3-dimethylamino-1*H*-1,2,4-triazol-1-yl)-*N*-(2-hydroxyethyl)thioamide (**3/2**), 40 ml of chloroform and 12 g of polyphosphoric ester was refluxed with stirring for 2 hours. After cooling the organic phase was washed several times with water, evaporated to dryness and the residue was recrystallised from 2-propanol to yield 1.42 g (71%) of 2-(5-amino-3-dimethylamino-1*H*-1,2,4-triazol-1-yl)-2-thiazoline (**5/2**, Q = dimethylamino, n = 2), mp 180-182°; ir: ν C=N= 1658 and 1590 cm^{-1}, ν NH_2 = 3345 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.85 (s, 6H, NCH_3), 3.41 (t, 2H, SCH_2), 4.23 (t, 2H, NCH_2), 7.43 (s, 2H, NH_2); cmr (DMSO-d_6): δ ppm 34.5 (SCH_2), 39.2 (NCH_3), 61.4 (NCH_2), 157.1 (thiazoline), 158.3 (triazole-C_5), 165.2 (triazole-C_3); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 219 (9.2), 280 (6.1).

Anal. Calcd. for $C_7H_{12}N_6S$ (MW 212.28): C, 39.61; H, 5.70; N, 39.59; S, 15.10. Found: C, 39.73; H, 5.88; N, 39.47; S, 15.22.

2-(5-Amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-2-thiazoline (**5/3**, Q = morpholino, n = 2).

Method A.

With Polyphosphoric Ester.

The mixture of 2.72 g (0.01 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N*-(2-hydroxyethyl)thioamide (**3/3**), 80 ml of chloroform and 20 g of polyphosphoric ester was refluxed with stirring for 16 hours. After cooling the organic phase was washed several times with water, evaporated to dryness and the residue was recrystallised from 2-propanol to yield 2.06 g (81%) of 2-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-2-thiazoline (**5/3**, Q = morpholino, n = 2), mp 169-170°; ir: ν C=N = 1663, 1622 and 1578 cm^{-1}, ν NH_2 = 3346 cm^{-1}; pmr (DMSO-d_6): δ ppm 3.22 (t, 4H, morpholine-NCH_2), 3.40 (t, 2H, SCH_2), 3.63 (t, 4H, OCH_2), 4.22 (t, 2H, thiazoline-NCH_2), 7.46 (s, 2H, NH_2); cmr (deuteriochloroform): δ ppm 33.6 (SCH_2), 46.2 (NCH_2), 61.4 (thiazoline-NCH_2), 66.4 (OCH_2), 155.3 (thiazoline), 158.3 (triazole-C_5), 163.1 (triazole-C_3); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 218 (12.3), 274 (7.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 252 (7.7), 322 (2.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 273 (7.3).

Anal. Calcd. for $C_9H_{14}N_6OS$ (MW. 254.32): C, 42.51; H, 5.55; N,

33.05; S, 12.61. Found: C, 42.46; H, 5.70; N, 33.12; S, 12.60.

Method B.

With Thionyl Chloride.

A mixture of 2.72 g (0.01 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N*-(2-hydroxyethyl)thioamide (**3/3**), 20 ml of benzene and 7.2 ml of thionyl chloride was refluxed with stirring for 30 minutes. After cooling the crystals which precipitated were filtered off and recrystallised from 2-propanol to yield 1.85 g (73%) of 2-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-2-thiazoline (**5/3**, Q = morpholino, n = 2), mp 169-170°.

Method C.

With Phosphorus Oxychloride.

A mixture of 2.72 g (0.01 mole) of 1-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-*N*-(2-hydroxyethyl)thioamide (**3/3**), 9.4 ml of phosphorus oxychloride and 0.8 ml of pyridine was stirred at 90° for 30 minutes. After cooling the mixture was poured into water, the crystals which precipitated were filtered off and recyrstallised from 2-propanol to yield 1.75 g (69%) of 2-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)-2-thiazoline (**5/3**, Q = morpholino, n = 2), mp 169-170°.

2-[5-Amino-3-(4-methylpiperazin-1-yl)-1*H*-1,2,4-triazol-1-yl]-2-thiazoline (**5/4**, Q = 4-methylpiperazin-1-yl, n = 2).

The mixture of 2.85 g (0.01 mole) of 1-[5-amino-3-(4-methylpiperazin-1-yl)-1*H*-1,2,4-triazol-1-yl]-*N*-(2-hydroxyethyl)thioamide (**3/4**), 40 ml of chloroform and 12 g of polyphosphoric ester was refluxed with stirring for 2 hours. After cooling the organic phase was washed several times with water, evaporated to dryness and the residue was recrystallised from acetonitrile to yield 1.74 g (65%) of 2-[(5-amino-3-(4-methylpiperazin-1-yl)-1*H*-1,2,4-triazol-1-yl]-2-thiazoline (**5/4**, Q = 4-methylpiperazin-1-yl, n = 2), mp 170-171°, ir: ν C=N = 1647, 1621 and 1568 cm^{-1}, ν NH_2 = 3390 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.21 (s, 3H, CH_3), 2.36 (t, 4H, piperazine-NCH_2), 3.28 (t, 4H, piperazine-NCH_2), 3.42 (t, 2H, SCH_2), 4.24 (t, 2H, thiazoline-NCH_2), 7.47 (s, 2H, NH_2); cmr (DMSO-d_6): δ ppm 34.7 (SCH_2), 47.1 (piperazine-NCH_2), 47.7 (NCH_3), 55.7 (NCH_2), 63.0 (thiazoline-NCH_2), 157.1 (thiazoline), 158.9 (triazole-C_5), 164.6 (triazole-C_3); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 217 (12.6), 275 (7.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 250 (8.5), 310 (3.1); uv (10% ethanol + 90% sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 254 (6.5), 271 (7.6).

Anal. Calcd. for $C_{10}H_{17}N_7S$ (MW. 267.36): C, 44.92; H, 6.41; N, 36.67; S, 11.99. Found: C, 45.04; H, 6.59; N, 36.70; S, 12.03.

2-[5-Amino-3-morpholino-1*H*-1,2,4-triazol-1-yl]-4*H*-5,6-dihydro-1,3-thiazine (**5/5**, Q = morpholino, n = 3).

The mixture of 2.95 g (0.01 mole) of 1-[5-amino-3-(4-methylpiperazin-1-yl)-1*H*-1,2,4-triazol-1-yl]-*N*-(2-hydroxypropyl)thioamide (**3/5**), 90 ml of chloroform and 25 g of polyphosphoric ester was refluxed with stirring for 4 hours. After cooling the organic phase was washed several times with water, evaporated to dryness and the residue was recrystallised from ethanol to yield 1.97 g (71%) of 2-[5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl]-4*H*-5,6-dihydro-1,3-thiazine (**5/5**, Q = morpholino, n = 3), mp 162-163°; ir: ν NH_2 = 3320 cm^{-1}, ν C=N = 1638 and 1554 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.81 (qi, 2H, CCH_2C), 3.10 (t, 2H, SCH_2), 3.32 (t, 4H, morpholine-NCH_2), 3.65 (t, 4H, OCH_2), 3.73 (t, 2H, thiazine-NCH_2), 7.49 (bs, 2H, NH_2); cmr (DMSO-d_6): δ ppm 19.2 (thiazine C-5), 25.8 (thiazine C-6), 45.0 (thiazine C-4), 46.0 (morpholine-NCH_2), 65.6 (morpholine-OCH_2), 147.7 (thiazine C-2), 154.8 (triazole C-5), 161.6 (triazole C-3); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 216 (12.3), 273 (6.6); uv (10% ethanol + 90% hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 247 (8.9), 324 (4.9); uv (10% ethanol + 90% sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 270 (6.7).

Anal. Calcd. for $C_{10}H_{16}N_6OS$ (MW. 268.35): C, 44.76; H, 6.01; N, 31.32; S, 11.95. Found: C, 44.80; H, 6.20; N, 31.35; S, 12.10.

2-(5-Amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)thiadiazole (**6**).

To 30 ml of cooled concentrated sulfuric acid 3.16 g (0.01 mole) of (3-morpholino-5-amino-1*H*-1,2,4-triazol-1-yl)-*N*-(2,2-dimethoxyethyl)thioamide (**3/18**) was added with stirring in small portions keeping the temperature of the reaction mixture below 10°. The mixture was stirred at this temperature for 2 hours, then it was poured into 150 g of crushed ice and its *p*H was adjusted with 20% sodium hydroxide to 5. The crystals which precipitated were filtered off, washed with water and triturated with hot methanol. The methanol solution obtained was evaporated *in vacuo* to dryness and the honey-like residue was triturated with a small amount of ether to yield crystals that were filtered off and recrystallised from a 1:1 mixture water and dimethylformamide, 0.63 g (25%) of 2-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)thiadiazole **6** was thus obtained, mp 164-166°; ir: ν NH_2 = 3390 cm^{-1}, ν C=N = 1663 and 1570 cm^{-1}; pmr (deuteriochloroform): δ ppm 3.34 (t, 4H, NCH_2), 3.70 (t, 4H, OCH_2), 6.88 [d(J = 2.5 Hz), 1H, CH-5], 7.00 (bs, 2H, NH_2), 7.36 [d(J = 2.5 Hz), 1H, CH-4); cmr (deuteriochloroform): δ ppm 45.4 (NCH_2), 65.3 (OCH_2), 112.4 (thiazole C-5), 138.5 (thiazole C-4), 153.1 (thiazole C-2), 159.4 (triazole C-5), 162.5 (triazole C-3); ms: M^+ = 252.

Anal. Calcd. for $C_9H_{12}N_6OS$ (MW. 252.30): C, 42.85; H, 4.79; N, 33.31; S, 12.71. Found: C, 42.98; H, 4.96; N, 33.40; S, 12.56.

2-(5-Amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)thiadiazole (**6**) and 5,6-Dihydro-3-morpholino-1,2,4-triazolo[3,4-*b*]-1,3,5-triazepin-5(9*H*)-thione (**7**).

The mixture of 12.64 g (0.04 mole) of (3-morpholino-5-amino-1*H*-1,2,4-triazole-1-yl)-*N*-(2,2-dimethoxylethyl)thioamide (**3/18**) and 20 ml of acetic acid was refluxed for 2 hours. The solution obtained crystallised upon cooling to yield after filtration 1.6 g (16%) of 5,6-dihydro-3-morpholino-1,2,4-triazolo[3,4-*b*]-1,3,5-triazepin-5(9*H*)-thione (**7**), which after recrystallisation from a 1:2 mixture of water and acetonitrile melted at 295-298°; ir: ν NH = 3100-3000, ν C=N = 1592, 1539 and 1502, ν C=S = 1261 cm^{-1}; pmr (DMSO-d_6): δ ppm 3.33 (t, 4H, NCH_2); 3.71 (t, 4H, OCH_2), 7.01 (t, 1H, CH-8), 7.16 (t, 1H, CH-7), 12.4 (bs, 1H, NH-7), 12.8 (bs, 1H, NH-9); cmr (DMSO-d_6): δ ppm 46.0 (NCH_2), 65.3 (OCH_2), 115.5 (C-7), 119.0 (C-8), 152.5 (C-3), 158.2 (C-9a), 163.1 (C-5); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 206 (23.1), 272 (12.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 206 (22.8), 264 (13.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 248 (13.6); ms: M^+ = 252.

Anal. Calcd. for $C_9H_{12}N_6OS$ (MW. 252.30): C, 42.85; H, 4.79; N, 33.31, S, 12.71. Found: C, 42.80; H, 4.85; N, 33.27; S, 12.66.

The mother liquor was evaporated to dryness and the residue was triturated with ether to yield 2.0 g (20%) of 2-(5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)thiadiazole (**6**) that after recrystallisation from a 1:1 mixture of water and dimethylformamide melted at 163-166°. The product was identical (ir, mixed mp) with that of **6** obtained above.

5-Methylthio-3-morpholino-9*H*-1,2,4-triazolo[3,4-*b*]-1,3,5-triazepine (**8**).

The mixture of 1.51 g (0.006 mole) of 5,6-dihydro-3-morpholino-1,2,4-triazolo[3,4-*b*]-1,3,5-triazepin-5(9*H*)-thione (**7**), 2.13 g (0.015 mole) of methyl iodide and 9 ml of ethanol was refluxed with stirring for 4 hours. After cooling the crystals precipitated were filtered off to yield 2.30 g (97%) of crude 5-methylthio-3-morpholino-9*H*-1,2,4-triazolo[3,4-*b*]-1,3,5-triazepine hydroiodide (**8.HI**), mp 181-204°. This was dissolved in 8 ml of water, treated with charcoal, filtered and the filtrate was made alkaline (*p*H = 8) with 5 *N* sodium hydroxide. The crystals which precipitated were filtered off and washed with water to yield 1.26 g (79%) of 5-methylthio-3-morpholino-9*H*-1,2,4-triazolo[3,4-*b*]-1,3,5-triazepine (**8**), which after recrystallistion from 2-propanol melted at 95-97°; ir: ν NH_2 = 3450, 3340 cm^{-1}, ν C=N = 1605, 1560 and 1520 cm^{-1}, ν C-O-C = 1108 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.54 (s, 3H, SCH_3), 3.39 (t, 4H, NCH_2), 3.71 (t, 4H, OCH_2), 7.03 [d (J = 1.5 Hz), 1H, CH-8], 7.56 [d (J = 1.5 Hz), 1H, CH-7), 12.9 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 14.8 (SCH_3), 46.1 (NCH_2), 65.3 (OCH_2), 119.7 (C-8), 128.8 (C-7), 143.3 (C-5), 152.7 (C-3), 158.1 (C-9a); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 212 sh (15.8), 250 (7.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 212 sh (13.0), 253 (7.7); uv (10% ethanol + 90% sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 244 sh (10.8).

Anal. Calcd. for $C_{10}H_{14}N_6OS$ (MW. 266.33): C, 45.10; H, 5.30; N, 31.56; S, 12.04. Found: C, 45.22; H, 5.35; N, 31.53; S, 12.13.

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