1-Amino-1*H*-1,2,4-triazole Derivatives

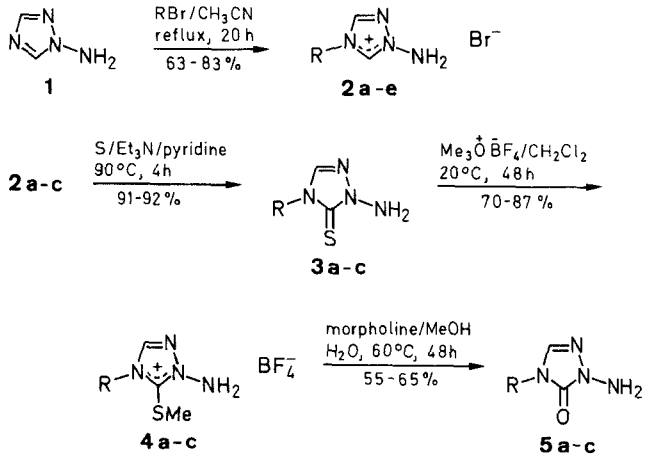
Gerhard Laus, Wilhelm Klötzer*[1]

Institut für Organische und Pharmazeutische Chemie, Universität Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria

Reactions of the title compound and its arylmethylene derivatives include quaternization and subsequent formation of 4-substituted 1-amino-1,2,4-triazoline-5-thiones [1-amino-1*H*-1,2,4-triazole-5(4*H*)-thiones] and 1-amino-1,2,4-triazolin-5-ones[1-amino-1*H*-1,2,4-triazol-5(4*H*)-ones]. Acetylation products and a new class of fused heterocycles, 6-aryl-1-arylalkyl-7*H*-1,2,4-triazolo[3,2-*b*][1,3,4]thiadiazin-1-ium salts, are presented.

In view of the extensive interest of amino-1,2,4-triazoles in applicative areas such as agrochemicals and pharmaceuticals, it is of considerable importance to investigate the almost unexplored field of 1-amino-1*H*-1,2,4-triazole chemistry. An improved synthesis of 1-amino-1*H*-1,2,4-triazole (**1**) has been reported only recently.[2] Now, we present the results of our work on this compound and some of its derivatives.

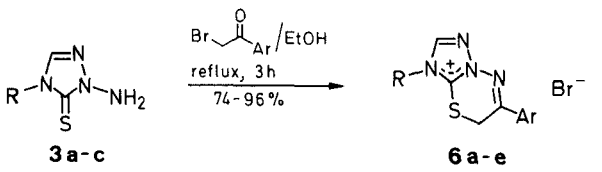
The quaternary salts **2a–e** are obtained by alkylation of 1-amino-1*H*-1,2,4-triazole (**1**) with arylalkyl bromides or aroylmethyl bromides. Like the related 4-amino-1,2,4-triazolium salts,[3] compounds **2a–c** react with sulfur in pyridine in the presence of triethylamine, yielding 1-amino-4-arylalkyl-1,2,4-triazoline-5-thiones **3a–c**. Subsequent methylation with trimethyloxonium tetrafluoroborate affords 1-amino-4-arylalkyl-5-methylthio-1,2,4-triazolium tetrafluoroborates **4a–c** in excellent yields. Treatment of these compounds with morpholine in methanol containing 10% water results in the loss of methanethiol, and **4a–c** are converted to 1-amino-4-arylalkyl-1,2,4-triazolin-5-ones **5a–c**. When the water content is lower, demethylation is observed, and the corresponding thione **3** is recovered again (Scheme **A**, Table 1).



2–5	R	2	R
a	$CH_2C_6H_4NO_2$-4	d	$CH_2COC_6H_4NMe_2$-4
b	$CH_2C_6H_3Cl_2$-2,4	e	$CH_2COC_6H_4Cl$-4
c	$CH_2C_6H_4Br$-4		

Scheme **A**

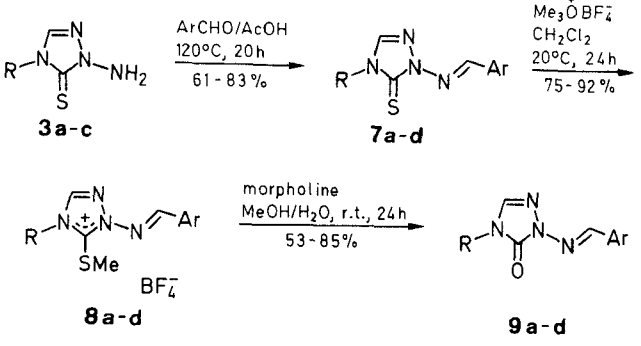
The bifunctional aminothiones **3** can be cyclized with aroylmethyl bromides to give high yields of 6-aryl-1-arylalkyl-7*H*-1,2,4-triazolo[3,2-*b*][1,3,4]thiadiazin-1-ium bromides **6a–e**, examples of a new fused heterocyclic system (Scheme **B**, Table 2).



6	R	Ar
a	$CH_2C_6H_4NO_2$-4	C_6H_4Cl-4
b	$CH_2C_6H_4NO_2$-4	2-naphthyl
c	$CH_2C_6H_3Cl_2$-2,4	C_6H_4Cl-4
d	$CH_2C_6H_3Cl_2$-2,4	$C_6H_4NMe_2$-4
e	$CH_2C_6H_4Br$-4	$C_6H_4NMe_2$-4

Scheme **B**

The arylmethylene derivatives **7a–d** are prepared by condensation of the thiones **5** with aromatic aldehydes in acetic acid. Methylation gives 4-arylalkyl-1-arylmethyleneamino-5-methylthio-1,2,4-triazolium tetrafluoroborates **8a–d**, which can be transformed to 4-arylalkyl-1-arylmethyleneamino-1,2,4-triazolin-5-ones **9a–d** by the same method as the compounds with a free amino group (Scheme **C**, Table 3).



7–9	R	Ar
a	$CH_2C_6H_4NO_2$-4	$C_6H_4NMe_2$-4
b	$CH_2C_6H_3Cl_2$-2,4	$C_6H_4NO_2$-4
c	$CH_2C_6H_3Cl_2$-2,4	$C_6H_4NMe_2$-4
d	$CH_2C_6H_4Br$-4	

Scheme **C**

The hydrochloride of the parent compound **1**, too, is readily condensed with aromatic aldehydes, yielding the substituted 1-benzylideneamino-1*H*-1,2,4-triazoles **10a–e**. Compounds **10a, b** are smoothly reduced to 1-arylalkylamino-1*H*-1,2,4-triazoles **11a, b** by lithium aluminum hydride. Reduction of the phenolic benzyl-

idene derivatives **10c, d**, to **11c, d**, probably being of interest as antioxidants,[4] requires catalytic hydrogenation, since excessive decomposition occurs on contact with the hydride. The nitro group in compound **10e** is tolerated by none of the methods described. Alkylation of the 1-benzylideneamino-1*H*-1,2,4-triazoles **10** gives the quaternary 4-arylalkyl-1-benzylideneamino-1,2,4-triazolium bromides **12a–e** (Scheme **D**, Tables 4 and 5).

Table 1. Compounds **2–5** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)	^{13}C-NMR (DMSO-d_6) δ
2a	63	184	$C_9H_{10}BrN_5O_2$ (300.1)	5.37 (s, 2H), 7.50 (br s, 2H), 7.80 (d, 2H, J = 9), 8.25 (s, 1H), 9.33 (d, 2H, J = 9), 10.37 (s, 1H)	49.5, 123.8, 130.0, 140.1, 140.8, 142.6, 147.7
2b	83	201	$C_9H_9BrCl_2N_4$ (324.0)	5.63 (s, 2H), 7.50 (br s, 2H), 7.52 (dd, 1H, J = 2.8), 7.64 (d, 1H, J = 8), 7.71 (d, 1H, J = 2), 9.23 (s, 1H), 10.28 (s, 1H)	48.1, 128.0, 129.2, 130.0, 132.7, 134.1, 134.8, 140.0, 142.7
2c	70	185	$C_9H_{10}Br_2N_4$ (334.0)	5.54 (s, 2H), 7.50 (br s, 2H), 7.50, 7.62 (AA'BB', 4H), 9.29 (s, 1H), 10.34 (s, 1H)	49.7, 122.3, 130.9, 131.8, 133.0, 139.8, 142.3
2d	72	240	$C_{12}H_{16}BrN_5O$ (326.2)	3.06 (s, 6H), 5.96 (s, 2H), 6.80 (d, 2H, J = 9), 7.50 (br s, 2H), 7.86 (d, 2H, J = 9), 9.07 (s, 1H), 10.06 (s, 1H)	35.0, 110.8, 120.2, 130.2, 140.7, 143.6, 154.1, 186.7
2e	80	225	$C_{10}H_{10}BrClN_4O$ (317.6)	6.16 (s, 2H), 7.65 (br s, 2H), 7.71, 8.07 (AA'BB', 4H), 9.11 (s, 1H), 10.10 (s, 1H)	54.4, 129.2, 130.1, 132.1, 139.5, 140.4, 143.5, 189.5
3a	91	167	$C_9H_9N_5O_2S$ (251.3)	5.33 (s, 2H), 6.17 (br s, 2H), 7.56 (d, 2H, J = 9), 8.21 (d, 2H, J = 9), 8.54 (s, 1H)	47.9, 123.6, 128.8, 137.6, 143.0, 147.0, 162.9
3b	91	141	$C_9H_8Cl_2N_4S$ (275.2)	5.21 (s, 2H), 6.17 (br s, 2H), 7.13 (d, 1H, J = 8), 7.42 (dd, 1H, J = 2.8), 7.65 (d, 1H, J = 2), 8.38 (s, 1H)	46.4, 127.4, 129.0, 130.9, 131.6, 133.1, 133.4, 137.7, 162.9
3c	92	170	$C_9H_9BrN_4S$ (285.2)	5.15 (s, 2H), 6.14 (br s, 2H), 7.30, 7.55 (AA'BB', 4H), 8.48 (s, 1H)	47.9, 121.1, 130.0, 131.4, 135.0, 137.5, 162.7
4a	77	128	$C_{10}H_{12}N_5O_2SBF_4$ (353.1)	2.68 (s, 3H), 5.61 (s, 2H), 7.42 (s, 2H), 7.66, 8.27 (AA'BB', 4H), 9.23 (s, 1H)	16.2, 50.0, 123.9, 129.4, 140.5, 142.9, 147.6, 148.0
4b	87	110	$C_{10}H_{11}Cl_2N_4SBF_4$ (377.0)	2.70 (s, 3H), 5.52 (s, 2H), 7.42 (br s, 2H), 7.46–7.54 (m, 2H), 7.76 (d, 1H, J = 2), 9.14 (s, 1H)	16.2, 48.5, 127.9, 129.4, 129.6, 132.2, 133.8, 134.7, 143.0, 148.2
4c	70	130	$C_{10}H_{12}BrN_4SBF_4$ (387.0)	2.69 (s, 3H), 5.42 (s, 2H), 7.38 (br s, 2H), 7.36, 7.64 (AA'BB', 4H), 9.19 (s, 1H)	16.2, 50.2, 122.2, 130.4, 131.8, 132.6, 142.7, 147.9
5a[b]	55	165	$C_9H_9N_5O_3$ (235.2)	4.93 (s, 2H), 5.59 (s, 2H), 7.52 (d, 2H, J = 9), 7.93 (s, 1H), 8.21 (d, 2H, J = 9)	44.8, 123.7, 128.6, 132.8, 144.1, 147.0, 151.1
5b[b]	65	133	$C_9H_8Cl_2N_4O$ (259.1)	4.83 (s, 2H), 5.54 (s, 2H), 7.22 (d, 1H, J = 8), 7.44 (dd, 1H, J = 2.8), 7.64 (d, 1H, J = 2), 7.80 (s, 1H)	43.1, 127.5, 128.9, 130.9, 132.6, 132.8, 133.1, 133.3, 151.0
5c[b]	60	151	$C_9H_9BrN_4O$ (269.1)	4.73 (s, 2H), 5.51 (s, 2H), 7.23, 7.55 (AA'BB', 4H), 7.85 (s, 1H)	44.7, 120.8, 129.7, 131.4, 132.7, 136.1, 151.1

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.20, N ±0.35.
[b] IR (KBr): ν(cm^{-1}) = 1695 **(5a)**, 1705 **(5b)**, 1700 **(5c)**.

Table 2. Compounds **6a–e** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ
6a	92	242	$C_{17}H_{13}BrClN_5O_2S$ (466.8)	4.66 (s, 2H), 5.71 (s, 2H), 7.72 (d, 2H, J = 9), 7.81 (d, 2H, J = 9), 8.07 (d, 2H, J = 9), 8.30 (d, 2H, J = 9), 9.43 (s, 1H)
6b	74	248	$C_{21}H_{16}BrN_5O_2S$ (482.4)	4.82 (s, 2H), 5.73 (s, 2H), 7.70 (m, 2H), 7.83 (d, 2H, J = 9), 8.04–8.18 (m, 4H), 8.32 (d, 2H, J = 9), 8.72 (s, 1H), 9.45 (s, 1H)
6c	96	216	$C_{17}H_{12}BrCl_3N_4S$ (490.6)	4.67 (s, 2H), 5.62 (s, 2H), 7.56 (dd, 1H, J = 2.8), 7.71, 8.07 (AA'BB', 4H), 7.74 (d, 1H, J = 8), 7.80 (d, 1H, J = 2), 9.44 (s, 1H)
6d	78	194	$C_{19}H_{18}BrCl_2N_5S$ (499.3)	3.06 (s, 6H), 4.58 (s, 2H), 5.60 (s, 2H), 6.85 (d, 2H, J = 9), 7.56, 7.72 (AB, 2H), 7.80 (s, 1H), 7.91 (d, 2H, J = 9), 9.36 (s, 1H)
6e	84	203	$C_{19}H_{19}Br_2N_5S$ (509.3)	3.06 (s, 6H), 4.58 (s, 2H), 5.50 (s, 2H), 6.84 (d, 2H, J = 9), 7.48, 7.65 (AA'BB', 4H), 7.91 (d, 2H, J = 9), 9.36 (s, 1H)

[a] Satisfactory microanalyses obtained: C ±0.25, H ±0.28, N ±0.22.

Table 3. Compounds **7**, **8**, **9** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)
7a	81	260	$C_{18}H_{18}N_6O_2S$ (382.5)	3.01 (s, 6H), 5.41 (s, 2H), 6.79 (d, 2H, J = 9), 7.60 (d, 2H, J = 9), 7.72 (d, 2H, J = 9), 8.22 (d, 2H, J = 9), 8.82 (s, 1H), 8.84 (s, 1H)
7b	83	190	$C_{16}H_{11}Cl_2N_5O_2S$ (408.3)	5.30 (s, 2H), 7.26 (d, 1H, J = 8), 7.43 (dd, 1H, J = 2.8), 7.69 (d, 1H, J = 2), 8.18, 8.35 (AA'BB', 4H), 8.80 (s, 1H), 9.13 (s, 1H)
7c	61	210	$C_{18}H_{17}Cl_2N_5S$ (406.3)	3.01 (s, 6H), 5.29 (s, 2H), 6.79 (d, 2H, J = 9), 7.20 (d, 1H, J = 8), 7.42 (dd, 1H, J = 2.8), 7.70 (d, 1H, J = 2), 7.73 (d, 2H, J = 9), 8.68 (s, 1H), 8.85 (s, 1H)
7d	76	239	$C_{14}H_{10}BrN_5O_3S$ (408.2)	5.23 (s, 2H), 7.35, 7.57 (AA'BB', 4H), 7.48 (d, 1H, J = 4), 7.80 (d, 1H, J = 4), 8.90 (s, 1H), 8.92 (s, 1H)
8a	92	206	$C_{19}H_{21}N_6O_2SBF_4$ (484.3)	2.84 (s, 3H), 3.07 (s, 6H), 5.68 (s, 2H), 6.85 (d, 2H, J = 9), 7.73 (d, 2H, J = 9), 7.88 (d, 2H, J = 9), 8.28 (d, 2H, J = 9), 9.12 (s, 1H), 9.43 (s, 1H)
8b	75	184	$C_{17}H_{14}Cl_2N_5O_2SBF_4$ (510.1)	2.96 (s, 3H), 5.61 (s, 2H), 7.54–7.62 (AB, 2H), 7.82 (s, 1H), 8.35–8.44 (AA'BB', 4H), 9.50 (s, 1H), 9.59 (s, 1H)
8c	91	190	$C_{19}H_{20}Cl_2N_5SBF_4$ (508.2)	2.84 (s, 3H), 3.07 (s, 6H), 5.57 (s, 2H), 6.84 (d, 1H, J = 9), 7.49–7.57 (m, 2H), 7.78 (d, 1H, J = 2), 7.87 (d, 2H, J = 9), 9.11 (s, 1H), 9.36 (s, 1H)
8d	80	190	$C_{15}H_{13}BrN_5O_3SBF_4$ (510.1)	2.90 (s, 3H), 5.51 (s, 2H), 7.45, 7.67 (AA'BB', 4H), 7.78, 7.88 (AB, 2H), 9.34 (s, 1H), 9.49 (s, 1H)
9a	83	275	$C_{18}H_{18}N_6O_3$ (366.4)	2.98 (s, 6H), 5.03 (s, 2H), 6.76 (d, 2H, J = 9), 7.59 (d, 2H, J = 9), 7.63 (d, 2H, J = 9), 8.23 (d, 2H, J = 9), 8.29 (s, 1H), 8.59 (s, 1H)
9b	85	220	$C_{16}H_{11}Cl_2N_5O_3$ (392.2)	4.96 (s, 2H), 7.38, 7.47, 7.71 (ABC, 3H), 8.10, 8.32 (AA'BB', 4H), 8.35 (s, 1H), 8.82 (s, 1H)
9c	53	237	$C_{18}H_{17}Cl_2N_5O$ (390.3)	2.98 (s, 6H), 4.93 (s, 2H), 6.76 (d, 2H, J = 9), 7.32, 7.46, 7.70 (ABC, 3H), 7.63 (d, 2H, J = 9), 8.20 (s, 1H), 8.58 (s, 1H)
9d	75	214	$C_{14}H_{10}BrN_5O_4$ (392.2)	4.86 (s, 2H), 7.31, 7.59 (AA'BB', 4H), 7.36 (d, 1H, J = 4), 7.79 (d, 1H, J = 4), 8.43 (s, 1H), 8.60 (s, 1H)

[a] Satisfactory microanalyses obtained: C ±0.32, H ±0.35, N ±0.30.

Table 4. Compounds **10**, **11** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)
10a	80	148 (CH_2Cl_2/hexane)	$C_{11}H_{13}N_5$ (215.3)	3.00 (s, 6H), 6.78 (d, 2H, J = 9), 7.73 (d, 2H, J = 9), 8.07 (s, 1H), 8.77 (s, 1H), 9.02 (s, 1H)
10b	75	128 (hexane)	$C_{10}H_{10}N_4$ (186.2)	2.37 (s, 3H), 7.33 (d, 2H, J = 8), 7.83 (d, 2H, J = 8), 8.15 (s, 1H), 8.89 (s, 1H), 9.17 (s, 1H)
10c	87	197 (CH_3CN)	$C_{17}H_{24}N_4O$ (300.4)	1.41 (s, 18H), 7.72 (s, 2H), 8.11 (s, 1H), 8.89 (s, 1H), 9.13 (s, 1H)
10d	77	214 (CH_2Cl_2/hexane)	$C_{11}H_{12}N_4O_3$ (248.2)	3.82 (s, 6H), 7.24 (s, 2H), 8.13 (s, 1H), 8.88 (s, 1H), 9.09 (s, 1H), 9.36 (br s, 1H)
10e	74	202 (CH_3CN)	$C_9H_7N_5O_2$ (217.2)	8.19, 8.35 (AA'BB', 4H), 8.24 (s, 1H), 9.02 (s, 1H), 9.35 (s, 1H)
11a	95	133 (EtOAc/hexane)	$C_{11}H_{15}N_5$ (217.3)	2.84 (s, 6H), 4.09 (d, 2H, J = 4), 6.62, 7.02 (AA'BB', 4H), 7.18 (t, 1H, J = 4), 7.87 (s, 1H), 8.06 (s, 1H)
11b	85	77 (hexane)	$C_{10}H_{12}N_4$ (188.2)	2.25 (s, 3H), 4.17 (d, 2H, J = 4), 7.06–7.13 (AA'BB', 4H), 7.31 (t, 1H, J = 4), 7.89 (s, 1H), 8.11 (s, 1H)
11c	75	173 (CH_3CN)	$C_{17}H_{26}N_4O$ (302.4)	1.32 (s, 18H), 4.08 (d, 2H, J = 4), 6.87 (s, 1H), 6.89 (s, 2H), 7.23 (t, 1H, J = 4), 7.91 (s, 1H), 8.10 (s, 1H)
11d	75	171 (CH_3CN)	$C_{11}H_{14}N_4O_3$ (250.3)	3.69 (s, 6H), 4.10 (d, 2H, J = 4), 6.46 (s, 2H), 7.27 (t, 1H, J = 4), 7.89 (s, 1H), 8.15 (s, 1H), 8.19 (br s, 1H)

[a] Satisfactory microanalyses obtained: C ±0.20, H ±0.15, N ±0.25.

Table 5. Compounds **12a–e** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)
12a	50	231	$C_{18}H_{19}BrN_6O_2$ (431.3)	3.06 (s, 6H), 5.74 (s, 2H), 6.83 (d, 2H, J = 9), 7.82 (d, 4H, J = 9), 8.28 (d, 2H, J = 9), 9.12 (s, 1H), 9.46 (s, 1H), 10.68 (s, 1H)
12b	61	204	$C_{18}H_{19}Br_2N_5$ (465.2)	3.05 (s, 6H), 5.58 (s, 2H), 6.81 (d, 2H, J = 9), 7.54, 7.65 (AA'BB', 4H), 7.81 (d, 2H, J = 9), 9.10 (s, 1H), 9.49 (s, 1H), 10.73 (s, 1H)
12c	68	208	$C_{16}H_{13}BrN_6O_4$ (433.2)	5.82 (s, 2H), 7.87, 8.29 (AA'BB', 4H), 8.31, 8.41 (AA'BB', 4H), 9.60 (s, 1H), 9.64 (s, 1H), 11.07 (s, 1H)
12d	55	176	$C_{16}H_{12}BrCl_2N_5O_2$ (457.1)	5.81 (s, 2H), 7.54–7.67 (m, 3H), 8.29, 8.43 (AA'BB', 4H), 9.55 (s, 1H), 9.57 (s, 1H), 10.94 (s, 1H)
12e	74	155	$C_{27}H_{36}BrN_5O_2$ (542.5)	1.42 (s, 18H), 3.06 (s, 6H), 6.06 (s, 2H), 6.81 (d, 2H, J = 9), 7.86 (s, 2H), 7.90 (d, 2H, J = 9), 8.12 (s, 1H), 9.36 (s, 2H), 10.63 (s, 1H)[b]

[a] Satisfactory microanalyses obtained: C ±0.15, H ±0.08, N ±0.18.
[b] When a drop of D_2O is added to the sample, the peak at 9.36 is split to give two signals at δ = 9.30 (s, 1H) and 9.34 (s, 1H), revealing that there are actually two different protons isochronic by chance. In addition, the peak at δ = 8.12 (OH) disappears.

Table 6. Compounds **13**, **14** Prepared

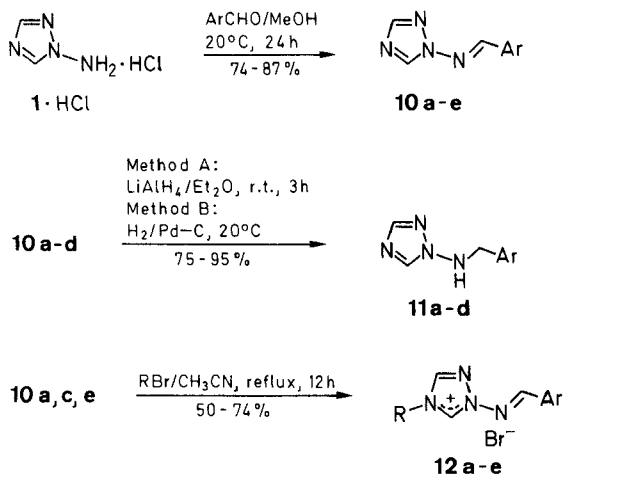
Product	Yield	mp (°C) (solvent)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)	IR (KBr) $\nu_{C=O}$ (cm^{-1})
13	80	134 (dioxane)	$C_4H_6N_4O$ (126.1)	2.03 (s, 3H), ~6 (br s, 1H), 7.95 (s, 1H), 8.50 (s, 1H)	1700
14	77	97 (Et_2O/hexane)	$C_6H_8N_4O_2$ (168.2)	2.23 (s, 6H), 8.20 (s, 1H), 8.75 (s, 1H)	1730

[a] Satisfactory microanalyses obtained: C ±0.10, H ±0.05, N ±0.08.

Table 7. Compounds **16–19** Prepared

Product	Yield (%)	mp (°C)	Molecular Formula[a]	^{1}H-NMR (DMSO-d_6/TMS) δ, J(Hz)	^{13}C-NMR (DMSO-d_6) δ
16[b]	87	182	$C_{20}H_{24}ClN_7$ (397.9)	3.05 (s, 12H), 6.83 (d, 2H, J = 9), 6.84 (d, 2H, J = 9), 7.73 (d, 2H, J = 9), 7.82 (d, 2H, J = 9), 9.15 (s, 1H), 9.19 (s, 1H), 9.96 (s, 1H), 11.26 (s, 1H)	39.5, 111.6, 116.7, 116.8, 131.2, 131.6, 134.1 (C-5), 138.3 (C-3), 153.7, 153.8, 159.1 (CH=N^1), 163.7 (CH=N^4)
17	85	250	$C_{20}H_{23}N_7S$ (393.5)	3.02 (s, 6H), 3.03 (s, 6H), 6.80 (d, 2H, J = 9), 6.82 (d, 2H, J = 9), 7.70 (d, 2H, J = 9), 7.74 (d, 2H, J = 9), 8.87 (s, 1H), 9.01 (s, 1H), 9.13 (s, 1H)	39.5, 39.6, 111.5, 111.6, 116.5, 119.4, 130.1, 130.4, 135.9 (C-3), 151.9 (CH=N^1), 152.5, 153.1, 158.3 (C-5), 162.9 (CH=N^4)
18	93	230	$C_{21}H_{26}N_7SBF_4$ (495.4)	3.00 (s, 3H), 3.05 (s, 6H), 3.07 (s, 6H), 6.84 (d, 2H, J = 9), 6.86 (d, 2H, J = 9), 7.75 (d, 2H, J = 9), 7.85 (d, 2H, J = 9), 8.87 (s, 1H), 9.08 (s, 1H), 9.82 (s, 1H)	16.2, 39.7, 111.9, 117.1, 117.3, 131.5, 131.8, 136.5 (C-3), 144.1 (C-5), 153.9, 154.0, 157.6 (CH=N^1), 163.8 (CH=N^4)
19[c]	79	242	$C_{20}H_{23}N_7O$ (377.5)	2.99 (s, 6H), 3.01 (s, 6H), 6.77 (d, 2H, J = 9), 6.79 (d, 2H, J = 9), 7.64 (d, 2H, J = 9), 7.66 (d, 2H, J = 9), 8.59 (s, 1H), 8.63 (s, 1H), 9.13 (s, 1H)	39.6, 39.7, 111.6, 111.7, 119.4, 120.2, 129.2, 129.6, 133.2 (C-3), 145.0 (C-5), 147.3 (CH=N^1), 152.0, 152.6, 156.7 (CH=N^4)

[a] Satisfactory microanalyses obtained: C ±0.20, H ±0.12, N ±0.30.
[b] UV (MeOH): λ_{max} = 410 nm, log ε = 5.04.
[c] IR (KBr): ν = 1710 cm^{-1}.

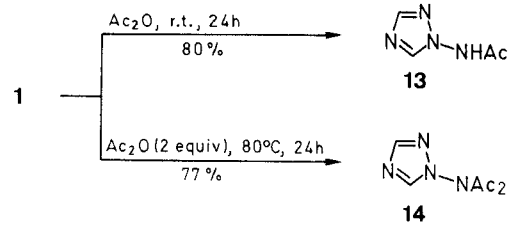


10,11	Ar	10,11	Ar
a	$C_6H_4NMe_2$-4	d	$C_6H_2(OMe)_2$-3,5,OH-4
b	$C_6H_4CH_3$-4	e	$C_6H_4NO_2$-4
c	$C_6H_2(Bu\text{-}t)_2$-3,5,OH-4		

12	R	Ar
a	$CH_2C_6H_4NO_2$-4	$C_6H_4NMe_2$-4
b	$CH_2C_6H_4Br$-4	$C_6H_4NMe_2$-4
c	$CH_2C_6H_4NO_2$-4	$C_6H_4NO_2$-4
d	$CH_2C_6H_3Cl_2$-2,6	$C_6H_4NO_2$-4
e	$CH_2COC_6H_4NMe_2$-4	$C_6H_2(Bu\text{-}t)_2$-3,5,OH-4

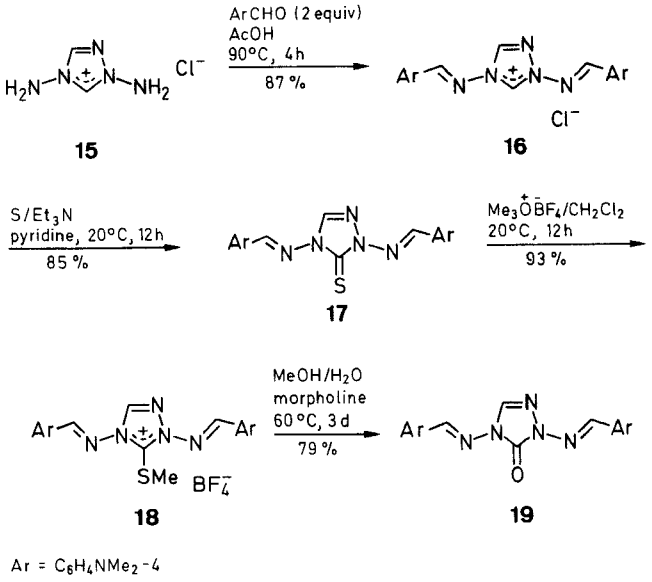
Scheme **D**

Acylation of 1-amino-1*H*-1,2,4-triazole (**1**) with acetic anhydride yields, depending on the conditions applied, 1-acetylamino-1*H*-1,2,4-triazole (**13**) or 1-diacetylamino-1*H*-1,2,4-triazole (**14**), respectively, in good yields (Scheme **E**, Table 6).



Scheme **E**

1,4-Bis(4-dimethylaminobenzylideneamino)-1,2,4-triazolium chloride (**16**) is prepared by condensation of 1,4-diamino-1,2,4-triazolium chloride (**15**)[2] with 4-dimethylaminobenzaldehyde in acetic acid. This compound may be of interest because of its close relationship to some imidazole derivatives which have been patented as filaricides.[5] Again, the quaternary salt **16** is converted to the corresponding triazoline-5-thione **17**, methylated to give 1,4-bis(4-dimethylaminobenzylideneamino)-5-methylthio-1,2,4-triazolium tetrafluoroborate (**18**) and, finally, transformed to the triazolin-5-one **19** using the methods previously described (Scheme **F**, Table 7).



Scheme **F**

While in the ^{13}C-NMR spectra of 1-amino-1*H*-1,2,4-triazoles, their benzylidene derivatives, and 4-substituted 1-amino-1,2,4-triazolium salts **2**, the signal for C-3 is shifted downfield compared to C-5,[2] this trend is reversed, of course, when C-5 bears a methylthio substituent or is part of a thiocarbonyl or carbonyl group.

In summary, general procedures for the preparation of 1-amino-1*H*-1,2,4-triazole derivatives have been developed. All products are novel and further work is in progress.

The following instruments were used for recording the spectra. IR: Beckmann Acculab 4 spectrophotometer, UV: Gilford 250 spectrophotometer, NMR: Bruker AM 300 spectrometer.

4-Substituted 1-Amino-1,2,4-triazolium Bromides 2a–e; General Procedure:

To a solution of 1-amino-1*H*-1,2,4-triazole (**1**; 0.84 g, 10.0 mmol) in CH_3CN (25 mL), the appropriate alkyl bromide (10.5 mmol) is added. The mixture is refluxed for 20 h and then cooled to 0 °C. The precipitate is filtered, washed with cold CH_3CN, Et_2O, and dried at 40 °C/0.01 mbar (Table 1).

1-Amino-4-arylalkyl-1,2,4-triazoline-5-thiones (1-Amino-4-arylalkyl-1*H*-1,2,4-triazole-5-(4*H*)-thiones) 3a–c; General Procedure:

A solution of the appropriate 1-amino-4-arylalkyl-1,2,4-triazolium bromide **2a–c** (5.0 mmol), sulfur (160 mg) and Et_3N (0.5 g, 5.0 mmol) in pyridine (50 mL) is heated at 90 °C for 4 h. The the mixture is poured into H_2O (100 mL) and set aside at 0 °C for 12 h. The crystals are filtered, washed with H_2O (20 mL), EtOH (20 mL) and dried. Recrystallization from hot EtOH gives the pure product (Table 1).

1-Amino-4-arylalkyl-5-methylthio-1,2,4-triazolium Tetrafluoroborates 4a–c; General Procedure:

The appropriate 1-amino-4-arylalkyl-1,2,4-triazoline-5-thione **3a–c** (1.0 mmol) is dissolved or suspended in dry CH_2Cl_2 (10 mL) and Me_3OBF_4 (150 mg, 1.0 mmol) is added. The mixture is stirred at 20 °C for 48 h. In the case of compound **4a**, the product is obtained by filtration, in the cases of **4b** and **4c**, the solvent is evaporated and the residue is crystallized by treatment with dry Et_2O (5 mL) (Table 1).

1-Amino-4-arylalkyl-1,2,4-triazolin-5-ones (1-Amino-4-arylalkyl-1*H*-1,2,4-triazol-5(4*H*)-ones) 5a–c; General Procedure:

A solution of the appropriate 1-amino-4-arylalkyl-5-methylthio-1,2,4-triazolium tetrafluoroborate **4a–c** (0.5 mmol) and morpho-

line (50 mg) in MeOH/H_2O (9:1, 10 mL) is stirred at 60 °C for 48 h, while the MeSH evolved is led to a hood. Then the solvent is removed and the residue treated with EtOH (1 mL). The crystalline product is filtered and dried at 40 °C/0.01 mbar (Table 1).

6-Aryl-1-arylalkyl-7*H*-1,2,4-triazolo[3,2-*b*][1,3,4]thiadiazin-1-ium-Bromides 6a–e; General Procedure:

A solution of an 1-amino-4-arylalkyl-1,2,4-triazoline-5-thione **3a–c** (0.35 mmol) and an aroylmethyl bromide (0.35 mmol) in EtOH (10 mL) is refluxed for 3 h. Then the solution is concentrated, and Et_2O (5 mL) is added. The precipitate is filtered, washed with Et_2O and dried at 40 °C/0.01 mbar (Table 2).

4-Substituted 1-Arylmethyleneamino-1,2,4-triazoline-5-thiones (4-Substituted 1-Arylmethyleneamino-1*H*-1,2,4-triazol-5(4*H*)-thiones) 7a–d; General Procedure:

A mixture of the appropriate 4-substituted 1-amino-1,2,4-triazoline-5-thione **3a–c** (1.0 mmol) and an aromatic aldehyde (1.05 mmol) in glacial AcOH (10 mL) is stirred at 120 °C (bath temperature) for 20 h. In the cases of **7a** and **7d** the product is isolated by suction, whereas in the case of **7b** the solvent is reduced to half prior to filtration. For compound **7c**, a seed crystal is prepared by treating a few drops of the solution with H_2O and used for crystallization. All products are dried at 50 °C/0.01 mbar (Table 3).

4-Substituted 1-Arylmethyleneamino-5-methylthio-1,2,4-triazolium Tetrafluoroborates 8a–d; General Procedure:

The appropriate triazoline-5-thione **7a–d** (1.0 mmol) is dissolved or suspended in anhydrous CH_2Cl_2 (20 mL), and Me_3OBF_4 (150 g, 1 mmol) is added. The mixture is stirred under N_2 at 20 °C for 24 h. After removal of the solvent, the residue is treated with Et_2O, and the product is filtered, washed with Et_2O and dried (Table 3).

4-Substituted 1-Arylmethyleneamino-1,2,4-triazolin-5-ones (4-Substituted 1-Arylmethyleneamino-1*H*-1,2,4-triazol-5(4*H*)-ones) 9a–d; General Procedure:

A mixture of the 5-methylthio-1,2,4-triazolium salt **8a–d** (1.0 mmol) and morpholine (100 mg) in MeOH/H_2O (98:2, 20 mL) is stirred at r.t. for 24 h, while the MeSH evolved is passed to a hood. The precipitate is filtered, washed with MeOH and dried (Table 3).

1-Benzylideneamino-1*H*-1,2,4-triazoles 10a–e; General Procedure:

To a solution of 1-amino-1*H*-1,2,4-triazole hydrochloride (240 mg, 2.0 mmol) in MeOH (5 mL) the appropriate aromatic aldehyde (2.1 mmol) is added. The mixture is stirred at 20 °C for 24 h. Then, the solvent is evaporated, H_2O (20 mL) is added, and pH 7 is adjusted by the addition of sat. aq. $NaHCO_3$. The mixture is extracted with CH_2Cl_2 (2 × 40 mL), the organic layer dried ($MgSO_4$) and evaporated to dryness. The product is purified by recrystallization and dried (Table 4).

1-Arylmethylamino-1*H*-1,2,4-triazoles 11a–d; General Procedure:

Method A (*for* **11a,b**): To a solution of the 1-arylmethyleneamino-1*H*-1,2,4-triazole **10a,b** (2 mmol) in dry Et_2O (30 mL), $LiAlH_4$ (200 mg) is added at 0 °C. The mixture is stirred under Ar at r.t. for 3 h and is then cooled to 0 °C again. H_2O (10 mL) is added cautiously, and the mixture is extracted with CH_2Cl_2 (2 × 40 mL). The combined extracts are dried ($MgSO_4$), and evaporated. The residue is recrystallized (Table 4).

Method B (*for* **11c,d**): The arylmethyleneamino-1*H*-1,2,4-triazole **10c,d** (1 mmol) is dissolved in MeOH (50 mL), Pd-C (10%, 100 mg) is added, and the solution is hydrogenated at 20 °C/1 bar until no more H_2 is consumed. The catalyst is filtered off and the solvent removed *in vacuo*. The residue is recrystallized and dried (Table 4).

4-Arylalkyl-1-arylmethyleneamino-1,2,4-triazolium Bromides 12a–e; General Procedure:

A solution of 1-arylmethyleneamino-1*H*-1,2,4-triazole **10** (1 mmol) and arylalkyl bromide (1 mmol) in CH_3CN (4 mL) is refluxed for 12 h. The mixture is concentrated, cooled to 0 °C and the product collected by filtration. In the case of **12e** addition of Et_2O is necessary to precipitate the product. The salts are washed with Et_2O and dried (Table 5).

1-Acetylamino-1*H*-1,2,4-triazole (13):

1-Amino-1*H*-1,2,4-triazole (**1**; 420 mg, 5 mmol) and acetic anhydride (510 mg, 5 mmol) are mixed with gentle warming, and the viscous mixture is allowed to stand for 24 h at 20 °C. Then, Et_2O is added to precipitate the product, which is recrystallized from dioxane, and dried at 40 °C/0.01 mbar.

1-Diacetylamino-1*H*-1,2,4-triazole (14):

A mixture of 1-amino-1*H*-1,2,4-triazole (**1**; 84 mg 1 mmol) and acetic anhydride (205 mg, 2 mmol) is heated at 80 °C for 24 h. After cooling Et_2O/hexane (1:1, 10 mL) is added, and the solution is set aside at r.t. After 2–3 d large crystals of the diacetyl derivative **14** can be collected (Table 6).

1,4-Bis(4-dimethylaminobenzylideneamino)-1,2,4-triazolium Chloride (16):

A solution of 1,4-diamino-1,2,4-triazolium chloride (**15**; 1.35 g, 10 mmol) and 4-dimethylaminobenzaldehyde (3.73 g, 25 mmol) in AcOH (50 mL) is heated at 90 °C for 4 h. The solvent is distilled off under reduced pressure and the residue is chromatographed on silica gel, eluting with CH_2Cl_2/MeOH (97:3) to give **16** (Table 7).

1,4-Bis(4-dimethylaminobenzylideneamino)-1,2,4-triazoline-5-thione (1,4-Bis(4-dimethylaminobenzylidene amino)-1*H*-1,2,4-triazol-5(4*H*)-thione, 17):

A mixture of quaternary salt **16** (3.2 g, 8 mmol), Et_3N (0.8 g, 8 mmol), and sulfur (0.26 g) in pyridine (120 mL) is stirred at 20 °C for 12 h. The mixture is then poured into cold H_2O (600 mL). The crude product is filtered, washed well with H_2O, slurried with hot EtOH, filtered, and dried. Further purification is accomplished by filtration through a column of silica gel, eluting with CH_2Cl_2/MeOH (9:1).

1,4-Bis(4-dimethylaminobenzylideneamino)-5-methylthio-1,2,4-triazolium Tetrafluoroborate (18):

To a solution of thione **17** (2.4 g, 6.1 mmol) in dry CH_2Cl_2 (90 mL) Me_3OBF_4 (0.91 g, 6.1 mmol) is added, and the mixture is stirred at 20 °C for 12 h. Then, the yellow product is filtered, washed with CH_2Cl_2 (3 × 25 mL), Et_2O (50 mL), and dried at 50 °C/0.01 mbar.

1,4-Bis(4-dimethylaminobenzylideneamino)-1,2,4-triazolin-5-one (1,4-Bis(4-dimethylaminobenzylideneamino)-1*H*-1,2,4-triazol-5(4*H*)-one, 19):

To a suspension of salt **18** (0.5 g, 1 mmol) in MeOH (30 mL) containing 1% H_2O morpholine (0.2 g, 2.3 mmol) is added. The mixture is stirred at 60 °C for 3 d, while the MeSH evolved is allowed to escape through a hood. Then, the precipitate is filtered and washed with MeOH (30 mL). The crude product is chromatographed on silica gel using CH_2Cl_2/MeOH (95:5) as eluent to give compound **19**, which may be recrystallized from CH_3CN.

Received: 12 December 1989

(1) Deceased. Please address correspondence to the Institut für Organische und Pharmazeutische Chemie, Universität Innsbruck.

(2) Laus, G.; Klötzer, W. *Synthesis* **1989**, 269.
(3) Becker, H.G.O.; Nagel, D.; Timpe, H.J. *J. Prakt. Chem.* **1973**, *315*, 97.
(4) Sies, H. *Angew. Chem.* **1986**, *98*, 1061; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1058.
(5) Karpitschka, E.M.; Klötzer, W.; Link, H.; Montavon, M.; Müssner, R. *Eur. Patent* EP 200947 (1986), Hoffmann-La Roche and Co. A.G.; *C.A.* **1987**, *107*, 198319.