Notizen / Notes

Ring-Chain Transformations, IX[1]

Synthesis and Ring-Chain Tautomerism of 2-(ω-Aminoalkyl)-1,3,4-thiadiazoles

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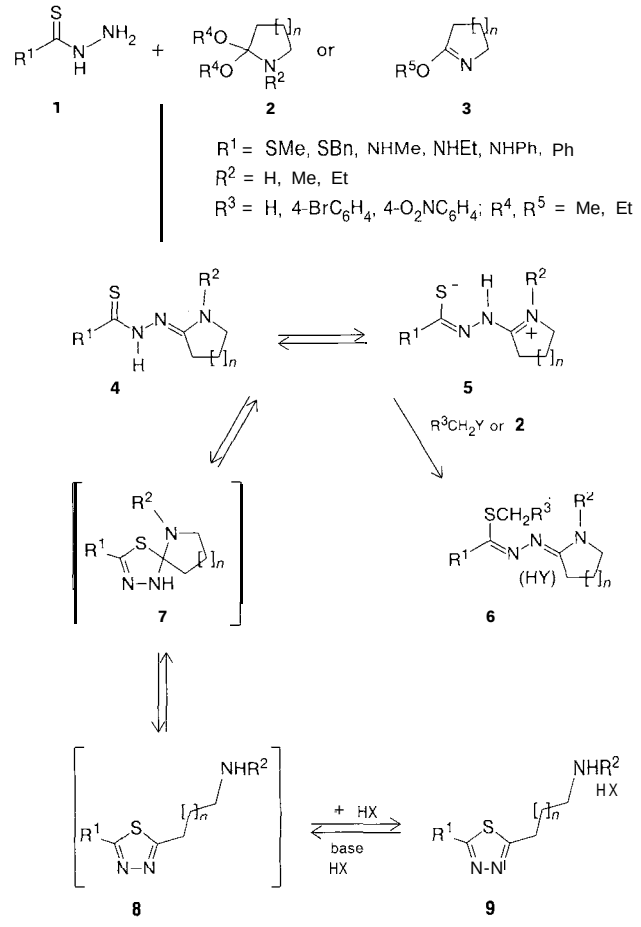
Received November 29, 1991

Key Words: 1,3,4-Thiadiazoles / Ring-chain tautomerism / Zwitterions / Lactam thioacylhydrazones

Thiohydrazide compounds 1 react with lactam acetals 2 or lactim ethers 3 by condensation giving unusual zwitterionic tautomers 5 of lactam thioacylhydrazones 4. These compounds 5 form mixtures of tautomers in neutral solution. In acidic solution, however, most of them undergo a reversible ring-chain transformation to novel 2-(ω-aminoalkyl)-1,3,4-thiadiazole salts 9. Alkylation of zwitterionic thioacylamidrazones 5 gives S-alkylation products 6.

Recently, we reported on the synthesis of (ω-aminoalkyl)thiazoles involving reaction of lactam acetals 2 or lactim ethers 3 with acidic *S*-methylisothioureas[1]. The latter reacted as 1,4-binucleophilic reactant attacking the alkoxy-substituted ring carbon atom of the lactam derivative 2 or 3. This ring is opened, thus affording the ω-aminoalkyl chain, while a new thiazole ring is formed (ring-chain transformation).



4 or 5	6	9	R^1	R^2	X	R^3	Y	n
a	a	a	SCH_3	H	Cl	$4\text{-}O_2NC_6H_4$	Br	1
b	b	–	SCH_3	H	Cl	H	I	2
c	c	–	SCH_3	H	–	$4\text{-}O_2NC_6H_4$	Br	3
d	–	–	SCH_3	H	–	–	–	4
e	e	e	SCH_3	CH_3	Cl	$4\text{-}BrC_6H_4CO$	Br	1
f	f	f	SCH_3	CH_3	ClO_4	$4\text{-}O_2NC_6H_4$	Br	3
g	g	g	SCH_3	CH_2CH_3	Cl	H	I	1
h		h	SCH_3	CH_2CH_3	ClO_4	–		2
i	–	–	$SCH_2C_6H_5$	H	–			2
j		–	$NHCH_3$	CH_3	–			1
k		–	$NHCH_2CH_3$	H	–			3
l	–	–	$NHCH_2CH_3$	CH_3	–	–		1
m	–	–	NHC_6H_5	H	–			3
n	–	–	NHC_6H_5	CH_3	–			1
o	–	–		H	–	–	–	3
P	–	–		CH_3	–			1
q	–	–	C_6H_5	H	–	–	–	1
–	r		SCH_3	CH_3	–	$4\text{-}O_2NC_6H_4$	Br	1

2-(ω-Aminoalkyl)-1,3,4-thiadiazoles prepared from the corresponding 2-(ω-chloroalkyl)-1,3,4-thiadiazoles and amines are of Interest because of their anticonvulsant activity"]. We tried to synthesize new compounds of this series with longer aminoalkyl chains

by means of the above mentioned type of ring transformation, i.e. by using thiohydrazide units as a 1,4-binucleophilic S–C–N–N building block. Thiosemicarbazide **1** ($R^1 = NH_2$)[3,4], 4-pyridinecarbothiohydrazide (**1**; R^1 = 4-pyridyl)[3] and dithiocarbonic acid hydrazides **1** ($R^1 = SCH_3$ or $SCH_2C_6H_5$)[5] are known to react with lactam acetals **2** or lactim ethers **3** by condensation affording semicyclic thioacylamidrazones **4**. However, no experimental details are available for the reactions with lactam acetals **2**[3]. Furthermore, no ring-chain tautomerism was taken into consideration (e.g. **4** ⇌ **8**), which is known to occur with related hydrazones of hydrazinodithioformic acids[6,7]. In the case of the hydrazino dithioates **4** (R^1 = S-alkyl or $NHNHCSOCH_2CH_3$, R^2 = H) further condensation by splitting off the corresponding alkanethiol or hydrosulfide, respectively, was achieved giving partially hydrogenated condensed 1,2,4-triazoles[4,5].

We now report on reactions of thiohydrazide compounds **1** (R^1 = NH-alkyl, NH-aryl, phenyl, and 2-benzimidazolyl) with lactam acetals **2** and lactim ethers **3** as well as of **2** with hydrazinodithioformates **1** (R^1 = S-alkyl). In addition, the reaction of the latter with lactim ethers **3** is reinvestigated.

Generally, the reaction of thiohydrazide derivatives **1** with lactam acetals **2** or lactim ethers **3** gave products where the original lactam ring was maintained. Spectroscopic investigation revealed, that the products cannot be characterized just by structure **4** as reported in the literature[5] for dithioester derivatives **4** (R^1 = S-alkyl) but tautomeric compounds or mixtures of tautomers exist. Furthermore, isomeric structures such as 7 and **8** have to be taken into consideration.

As a typical example compound **4e** ($R^1 = SCH_3$, $R^2 = CH_3$, $n = 1$) was investigated in detail. X-ray crystal structure analysis (see Figure 1) revealed, that the rather unusual tautomeric structure **5** exists in the solid state. The proton usually found either at the nitrogen or at the sulfur atom of the thioamide fragment is situated at the amidine fragment. Zwitterionic thiohydrazide structures were also suggested for known *N*-thioformyl-*N'*,*N'*-diethylhydrazine[8] and *N*-benzylidene-*N'*-phenylthioacetylhydrazine[9] in solution. In compound **5e** the thioacylamidrazone fragment is almost planar, thus allowing conjugation. However, it is remarkable that the C–N double bond character is more pronounced at the endocyclic C–N bond as compared with the exocyclic C–N bond. Compound **5e** shows negative solvatochromism of the UV absorption in solution.

Since the absorption curves in different solvents dissect in a narrow region it can be expected[12] that the negative solvatochromism is due to the solvent-dependent position of a tautomeric equilibrium. This fact is also seen in the NMR spectra of **5e**. Two sets of signals are found in the ^{1}H-NMR as well as in the ^{13}C-NMR spectra. The relative intensity of the proton signals changes if measured in different solvents. Since isomeric structures **7** and **8** do not fit to the observed chemical shifts[10], it can be assumed, that a mixture of **5e** and a tautomer **4e** [δ(C=S) = 190.9] exists in solution. The chemical shift of δ = 175.2 (N–C=N$^+$) points to the zwitterionic amidrazonium-thiocarbonyl tautomer **5e** and that of δ = 190.9 (C=S) to the thioacylamidrazone compound **4e**.

Although no further X-ray crystal structure analyses were carried out, it can be assumed, that other products obtained from thiohydrazides **1** and lactam acetals **2** or lactim ethers **3** exist as betaines **5** in the solid state rather than as thiocarbonylamidrazones **4**. This hypothesis is supported by the consistence of IR absorptions. Negative solvatochromism is found in these cases, too (see Table 3). In solution mixtures of two tautomers **4** and **5** are found again. In the ^{13}C-NMR spectrum of compound **5a** additional peaks appear which stem from a third tautomer (e.g. a 2-thioacylhydrazino-1-pyrroline). In contrast, compound **5l** ($R^1 = CH_3CH_2NH$, $R^2 = CH_3$, $n = 1$) shows just one set of ^{13}C-NMR signals with a C=S signal being missed. Obviously, neither tautomer **4** nor **5** is formed but a tautomer with an isothioamide moiety HS–C=N.

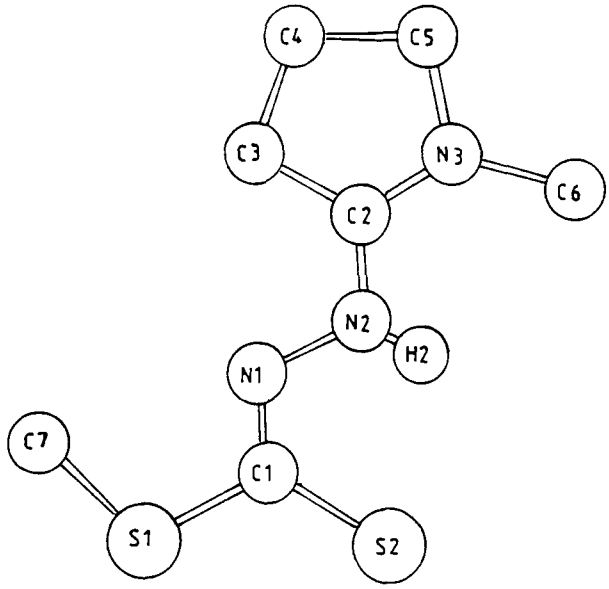


Figure 1. Crystal structure of compound **5e**; selected bond lengths [pm] and bond angles [°]: S1–C1 175.0(4), S2–C1 170.9(4), N1–N2 139.2(5), N1–C1 129.6(5), N2–C2 134.2(6), N2–H2 85(4), N3–C2 128.6(5), N3–C5 145.8(6), N3–C6 145.3(6); N2–N1–C1 113.1(3), N1–N2–H2 119.0(2), C2–N2–H2 122.0(2), C2–N3–C6 126.3(4), S1–C1–N1 115.9(3), S2–C1–N1 128.4(3), N2–C2–N3 124.2(4)

In a number of cases (compounds **5a**, **b**, **c**, **e**, **f**, **g**, **h**, **n**, **p**) ^{1}H-NMR spectra totally change if CF_3CO_2H solutions are investigated. A comparison of these data with the ^{1}H-NMR shifts of (ω-aminoalkyl)heteroaromatics[10] [$\delta(CH_2^{\alpha}) \approx \delta(NCH_2)$] implied that a ring-chain transformation of **4** or **5** must have occurred giving the anticipated 2-(ω-aminoalkyl)-1,3,4-thiadiazoles **8** or their protonated forms **9**. That means, there is a pH-dependent tautomerism where lactam imine derivatives **4** or **5** exist under neutral conditions while 2-(ω-aminoalkyl)-1,3,4-thiadiazoles **8** appear in acidic medium. The ability of compounds **4** or **5** to form 2-(ω-aminoalkyl)-1,3,4-thiadiazole salts **9** does not only depend on the acidic medium but also on the nature of substituents R^1 and R^2. There are also compounds **4** or **5** (**k**, **l**, **m**, **o**) resisting a ring transformation in trifluoroacetic acid. Although we investigated a number of compounds **4** or **5** it is not possible to find reliable rules describing the influence of substituents on the ability of the compound concerned

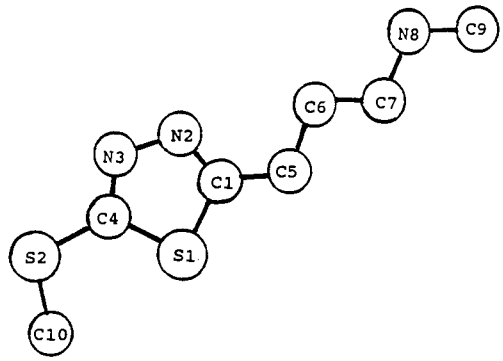


Figure 2. Crystal structure of compound **9e**; selected bond lengths [pm] and bond angles [°]: S1–C1 172.2(7), S1–C4 171.9(6), S2–C4 174.1(7), N2–N3 138.8(8), N2–C1 128.1(9), N3–C4 128.4(9), N8–H81 87(5), N8–H82 82(6), C1–C5 148.5(9); C1–S1–C4 87.1(4), N3–N2–C1 112.4(6), N2–N3–C4 112.7(6), S1–C1–N2 114.0(5), S1–C1–C5 122.3(5), S1–C4–N3 113.8(5)

Table 1. Thioacylamidrazones **4** or zwitterionic amidrazones **5**

	Yield [%]/ Solvent Reflux[min]	m.p. [°C]	Empirical formula Elemental analysis Calcd. C H N Found
4/5a	66/Aceton 2	169-171 (iso-C_3H_7OH)	$C_6H_{11}N_3S_2$ (189.3) 38.07 5.86 22.20 38.11 5.70 22.23
4/5b	60/MeOH --	164-166 (iso-C_3H_5OH)	ref. m.p. 159°[5]
4/5c	92/MeOH --	174-176 (CH_3OH)	ref. m.p. 169.5°[5]
4/5d	43/MeOH --	155-157 (C_2H_5OH)	ref. m.p. 154°[5]
4/5e	70/EtOH --	176-177 (CH_3CN)	$C_7H_{13}N_3S_2$ (203.3) 41.35 6.44 20.67 41.43 6.89 20.66
4/5f	45/EtOH --	158-160 (CH_3OH)	$C_9H_{17}N_3S_2$ (231.4) 46.72 7.40 18.16 46.85 7.45 18.40
4/5g	46/EtOH[a] --	166-167 (C_2H_5OH)	$C_8H_{15}N_3S_2$ (217.4) 44.21 6.96 19.33 44.28 6.75 19.32
4/5h	65/EtOH --	142-144 (iso-C_3H_7OH)	$C_9H_{17}N_3S_2$ (231.4) 46.72 7.40 18.16 46.40 7.20 17.92
4/5i	52/MeOH --	154-155 (C_2H_5OH)	ref. mp.154-155°[5]
4/5j	54/EtOH ,60	136-138 (CH_3CN)	$C_7H_{14}N_4S$ (186.3) 45.14 7.57 30.08 44.96 7.38 29.93
4/5k	47/Me_2CHOH 30	125 (CH_3CN)	$C_9H_{18}N_4S$ (214.3) 50.44 8.46 26.14
4/5l	47/EtOH 60	156-158 (iso-C_3H_7OH)	$C_8H_{16}N_4S$ (200.3) 47.97 8.05 27.97 47.54 7.78 27.76
4/5m	88/EtOH 30	166-167 (CH_3CN)	$C_{13}H_{18}N_4S$ (262.4) 59.51 6.91 21.35 59.69 7.21 21.02
4/5n	77/MeCN 60	210-212 (CH_3CN)	$C_{12}H_{16}N_4S$ (248.3) 58.04 6.49 22.56 57.88 6.40 22.60
4/5o	87/Me_2CHOH 2	241-243 (iso-C_3H_7OH)	$C_{14}H_{17}N_5S$ (287.4) 58.51 5.96 24.37 58.17 5.98 24.47
4/5p	73/EtOH --	202-204 (CH_3OH)	$C_{13}H_{15}N_5S$ (273.4) 57.12 5.53 25.62 5.85 25.25
4/5q	59/MeOH --	165-167 (CH_3OH)	$C_{11}H_{13}N_3S$ (219.3) 60.24 5.97 19.16 60.51 6.05 19.25

[a] 0.2 mol of lactam acetal **2** was used.

Table 2. ^{1}H-NMR and MS data of zwitterionic amidrazones **5** or thioacylamidrazones **4**

No.	^{1}H NMR ([D_6]DMSO)	MS (70 eV): m/z (%)
4/5a [a]	1.95 (m, 0.2 H, CH_2), 2.10 (qui, J = 7 Hz, 1.8H , CH_2), 2.28 (s, 0.3 H, SCH_3), 2.34 (s, 2.3 H, SCH_3), 2.42 (m, 0.2 H, SCH_3), 2.94 (t, J = 7 Hz, 1.6 H, CH_2), 3.00 (m, 0.2 H, CH_2), 3.38 (m, 0.1 H, CH_2), 3.55 (m, 1.8 H, CH_2), 8.88 (br, 0.7 H, NH), 11.1 (br, 0.7 H, NH) [b]	189 (M^+, 9), 142 (90), 84 (35), 55 (48), 41 (100), 30 (40)
4/5b	1.75 (m, 4H, $2CH_2$), 2.35 (s, 3 H, SCH_3), 2.69 (m, 2H, CH_2), 3.34 (m, 2H, CH_2), 8.52 (br, 1 H, NH), 10.74 (br, 1H, NH) [c]	203 (M^+, 5), 156 (64), 155 (49), 98 (42), 55 (92), 47 (74), 41 (100) 30 (73)
4/5c	1.92 (m, 6H, $3CH_2$), 2.62 (s, 3H, SCH_3), 3.02 (m, 2 H, CH_2), 3.75 (m, 2 H, CH_2), 8.70 (br, 1 H, NH), 11.18 (s, 1 H, NH)	217 (M^+, 5), 169 (66), 96 (31), 55 (71), 47 (51), 45 (56), 41 (100), 30 (48)
4/5d	1.51 (m, 8 H, $4CH_2$), 2.38 (s, 3 H, SCH_3), 2.77 (m, 2 H, CH_2), 3.50 (m, 2H, CH_2), 8.32 (br, 1 H, NH), 10.92 (s, 1 H, NH)	231 (M^+, 2), 164 (33), 110 (38), 69 (31), 55 (48), 47 (49), 41 (83), 30 (100)
4/5e	1.99 (m, 2 H, CH_2), 2.30 (s, 2 H, SCH_3), 2.39 (s, 1 H, SCH_3), 2.65 (m, 1 H, NCH_3), 3.03 (m, 2H, NCH_3), 3.26 (m, 2 H, CH_2), 3.69 (t, J = 7 Hz, 1 H, CH_2), 11.08 (br, 0.5 H, NH) [d]	203 (M^+, 14), 156 (64), 69 (48), 55 (83), 45 (35), 43 (35), 42 (100), 41 (47)
4/5f [e]	1.79 (m, 6 H, 3 CH_2), 2.44 (s, 3 H, SCH_3), 3.26 (m, 5 H, NCH_3, CH_2), 3.75 (m, 2 H, CH_2), 11.80 (br, 1 H, NH) [f]	231 (M^+, 3), 187 (37), 125 (73), 69 (43), 68 (43), 55 (63), 47 (73), 44 (100), 42 (80), 41 (80), 30 (40)
4/5g [e]	1.36 (m, 3 H, CH_3), 2.23 (m, 2 H, CH_2), 2.42 (s, 2 H, SCH_3), 2.59 (s, 1 H, SCH_3), 2.66 (m, 0.5 H, CH_2), 3.20 (m, 2 H, CH_2), 3.45 (m, 2 H, CH_2), 3.78 (m, 1.5 H, CH_2), 11.60 (br, 1 H, NH)	217 (M^+, 15), 170 (65), 112 (61), 84 (41), 83 (48), 56 (37), 55 (37), 33 (35), 42 (43), 41 (100)
4/5h [e]	1.40 (t, J = 7 Hz, 3 H, CH_3), 1.89 (m, 4 H, $2CH_2$), 2.41 (s, 3 H, SCH_3), 2.98 (m, 2 H, CH_2), 3.50 (m, 4 H, 2 CH_2), 11.80 (br, 1 H, NH) [g]	231 (M^+, 4), 184 (29), 125 (59), 98 (32), 91 (31), 55 (81), 47 (36). 44 (100), 41 (49)
4/5i	1.76 (m, 4 H, 2 CH_2), 2.74 (m, 2 H, CH_2), 3.30 (m, 2 H, CH_2), 4.33 (s, 2 H, SCH_2), 7.28 (m, 5 H, C_6H_5)	123 (24), 91 (34), 55 (73), 41 (100)
4/5j	1.78 (p, J = 7 Hz, 2 H, CH_2), 2.29 (s, 3 H, NCH_3), 2.69 (m, 4H, NCH_2, $=CCH_2$, 3.40 (s, 3H, NCH_3)	186 (M^+, 28), 142 (22), 129 (20), 91 (100), 64 (32), 58 (30), 56 (23), 44 (76), 41 (22)
4/5k	1.31 (t, J = 7 Hz, 3 H, CH_3), 1.93 (m, 6 H, 3 CH_2), 2.85 (m, 2 H, CH_2), 3.70 (m, 4 H, 2 CH_2)	214 (M^+, 30), 181 (44), 113 (57), 96 (100), 69 (41), 60 (56), 54 (60), 44 (49), 41 (76), 30 (97)

Table 2 *(Continued)*

No.	^{1}H NMR ([D$_6$]DMSO)	MS (70 eV): m/z (%)
4/5l [h]	1.15 (m, 3 H, CH_3), 1.82 (m, 2 H, CH_2), 2.33 (s, 3 H, NCH_3), 2.70 (m, 2 H, CH_2), 3.40 (q, J = 7 Hz, 2 H, NCH_2), 3.95 (q, 2 H, J = 7 Hz, NCH_2), 4.67 (m, 2 H, NCH_2)	200 (M^+, 4), 156 (22), 115 (28), 58 (53), 44 (100)
4/5m [h]	1.76 (m, 6 H, 3 CH_2), 2.70 (m, 2 H, CH_2), 3.55 (m, 2 H, CH_2), 7.25 (m, 6 H, C_6H_5, NH), 8.73 (m, 1 H, NH)	262 (M^+, 4), 169 (67), 98 (30), 93 (100), 82 (33), 66 (78), 55 (52), 51 (41), 44 (70), 39 (90), 28 (74)
4/5n	1.62 (m, 2 H, CH_2), 2.18 (s, 3 H, NCH_3), 2.91 (m, 2 H, CH_2), 3.31 (m, 2 H, CH_2), 7.51 (m, 5 H, C_6H_5), 9.20 (br, 1 H, NH)	248 (M^+, 4), 77 (13), 58 (26), 51 (11), 44 (100), 39 (11), 30 (14)
4/5o [h]	1.82 (m, 6 H, 3 CH_2), 2.88 (m, 2 H, CH_2), 3.62 (m, 2 H, CH_2), 7.62 (m, 5 H, C_6H_4, NH, 8.90 (s, 1 H, NH)	253 (54), 185 (46), 144 (100), 34 (36)
4/5p [h]	2.42 (m, 2 H, CH_2), 2.92 (m, 3 H, NCH_3), 3.45 (m, 4 H, 2 CH_2), 6.30 (m, 2 H, NH), 7.78 (m, 4 H, C_6H_5)	273 (M^+, 30), 216 (77), 212 (33), 144 (53), 118 (35), 84 (54), 69 (38), 55 (100), 44 (83), 42 (78), 41 (39)
4/5q [a]	2.10 (qui, J = 7.6 Hz, 2 H, CH_2), 3.00 (t, J = 8 Hz, CH_2), 3.60 (t, J = 7 Hz, CH_2),7.29 (m, 3 H, C_6H_5), 8.20 (m, 2 H,C_6H_5)	219 (M^+, 22), 189 (40), 176 (100), 121 (53), 116 (37), 104 (65), 83 (61), 77 (66), 56 (32), 55 (64), 51 (37), 41 (86), 30 (70)

[a] Recorded on a 300-MHz Bruker spectrometer. – [b] ^{1}H NMR (CF_3CO_2H): δ = 2.59 (m, 2H, CH_2), 3.02 (s, 3H, SCH_3), 3.69 (m, 4H, 2 CH_2). – [c] ^{1}H NMR (CF_3CO_2H): δ = 2.08 (m, 4H, 2 CH_2), 2.98 (s, 3H, SCH_3), 3.38 (m, 4H, 2 CH_2), 7.00 (m, 1H, NH). – [d] ^{1}H NMR (CF_3CO_2H): δ = 2.31 (m, 2H, CH_2), 2.91 (s, 6H, SCH_3, NCH_3), 3.35 (m, 4H, 2 CH_2), 7.35 (m, 1H, NH). – [e] In $CDCl_3$. – [f] ^{1}H NMR (CF_3CO_2H): δ = 1.90 (m, 6H, 3 CH_2), 2.97 (s, 6H, SCH_3, NCH_3), 3.26 (m, 4H, 2 CH_2). – [g] ^{1}H NMR (CF_3CO_2H): δ = 1.46 (t, *J* = 7 Hz, 3H, CH_3), 2.06 (s, 4H, 2 CH_2), 2.99 (s, 3H, SCH_3), 3.35 (m, 6H, 3 CH_2). – [h] In CF_3CO_2H.

to undergo ring transformations to **9**. Methylthio-substituted compounds **4** or **5** unterwent ring transformation in all cases regardless of the nature of substituents R^2. Some of the ring-transformed 2-(ω-aminoalkyl)-1,3,4-thiadiazoles were isolated as salts **9** (X = Cl, ClO_4) on a preparative scale by the addition of hydrochloric or perchloric acid. The final structural proof was furnished by an X-ray crystal structure analysis of compound **9e** (see Figure 2). Protonation is found at the exocyclic amino group. Interestingly, all non-H atoms of **9e** are found almost in one plane in the crystal lattice regardless of the hybridization state. Mass spectra show typical fragment peaks (R^2NHCH_2, $R^2NHCH_2CH_2$)[10] of (ω-aminoalkyl)heteroaromatics. Unlike in CD_3OD solution the ^{13}C-NMR spectrum of compound **9a** in [D$_6$]DMSO exhibits additional signals of low intensity probably caused by protonated thioacylhydrazone starting material **4** or **5**. Deprotonation of the (ω-aminoalkyl)thiadiazole salts **9** to the corresponding free bases **8** failed, because the ring-transformed **5** or **4** were obtained again. For example, treatment of aqueous solution of the thiadiazole salt **9e** as hydroperchlorate with concd. NaOH affords the hydrazinodithiocarbonic ester **4e** after extraction with trichloromethane. This demonstrated that 2-(ω-aminoalkyl)-1,3,4-thiadiazoles **8** exist only in form of their salts **9**. This behavior remarkably differs from that of

Table 3. ^{13}C-NMR and UV data of zwitterionic amidrazones **5** or thioacylamidrazones **4**

Nr.	^{13}C NMR ([D$_6$]DMSO) (75 MHz)	UV λ_{max} [nm](lg ε)
4/5a	15.0 (SCH_3), 15.5 (SCH_3), 16.8 (SCH_3), 20.1 (CH_2), 21.0 (CH_2), 21.8 (CH_2), 28.6 ($\underline{C}H_2$-C=), 29.4 ($\underline{C}H_2C$=), 29.5 ($\underline{C}H_2$-C=), 45.6 (CH_2N), 46.7 (CH_2N), 47.0 (CH_2N), 160.6, 165.4, 174.5, 177.8, 209.7 (C=S)	(CH_3OH): 261 (4.04), 293 (4.23) ($CHCl_3$): 270 (4.04), 314 (4.18) (C_6H_6): 321
4/5c		(CH_3OH): 266 (4.11), 303 (4.27) ($CHCl_3$): 276 (4.12), 317 (4.20) (C_6H_6): 333 (4.21)
4/5e	14.5 (SCH_3), 16.5 (SCH_3), 18.8 (CH_2), 19.2 (CH_2), 27.2 ($\underline{C}H_2$-C=), 30.3 ($\underline{C}H_2$-C=), 31.2 (NCH_3), 32.0 (NCH_3), 51.5 (CH_2N), 55.0 (CH_2N), 161.7, 163.4, 175.2, 190.9 (C=S)[a]	(CH_3OH): 257 (4.08), 295 (4.20) ($CHCl_3$): 267 (4.12), 316 (4.17) ($CH_3COOC_2H_5$): 263 (4.02), 318 (4.23) (C_6H_6): 325 (4.20) (CCl_4): 327
4/5f	14.6 (SCH_3), 16.7 (SCH_3), 22.8 (CH_2), 24.5 (CH_2), 25.8 (CH_2), 26.4 (CH_2), 27.0 (CH_2), 27.6 (CH_2),28.8 ($\underline{C}H_2$-C=C), 29.0 ($\underline{C}H_2$-C=), 37.7 (NCH_3), 38.8 (NCH_3), 52.3 (CH_2N), 55.0 (CH_2N), 162.2, 165.0, 176.6, 191.9 (C=S)	(CH_3OH): 260 (4.10), 302 (4.21) ($CHCl_3$): 268 (4.14), 319 (4.17) (C_6H_6): 329
4/5g	10.7 (CH_3), 11.4 (CH_3), 14.6 (SCH_3), 16.6 (SCH_3), 18.8 (CH_2), 19.3 (CH_2), 27.6 (CH_2), 30.8 (CH_2), 31.7 (CH_2), 38.8 (CH_2), 40.6 (CH_2), 49.0 (NCH_2), 52.7 (NCH_2), 163.2[b]	
4/5h [c]	12.1 (CH_3), 19.4 (CH_2), 27.2 (CH_2), 30.8 (CH_2), 46.6 (NCH_2), 49.7 (NCH_2), 175.3, 182.0	(CH_3OH): 260 (4.08), 304 (4.28) ($CHCl_3$): 268 (4.14), 320 (4.16) (C_6H_6): 332 (4.10)
4/5l	13.1 (CH_3), 22.2 (CH_2), 35.7 (NCH_3), 37.8 (NCH_2), 50.1 (NCH_2), 152.9, 165.9	
4/5n	23.4 (CH_2), 25.2 (CH_2), 35.7 (NCH_3), 50.2 (NCH_2), 128,4 (C_6H_5), 129.4 (C_6H_5), 129.5 (C_6H_5), 152.3 (ipso-C_6H_5), 167.8 (C=N),	(CH_3OH): 269 (4.20), 290 sh (4.13) ($CHCl_3$): 350 (4.23)
4/5q	20.7 (CH_2), 28.6 (CH_2), 46.7 (NCH_2), 127.0 (CH), 127.6 (CH), 128.4 (CH), 141.7 (ipso-C_6H_5), 161.9 (NCN), 176.9 (CS)	

[a] After addition of a small amount of TFA: δ = 16.4 (SCH_3), 25.0 (CH_2), 26.3 (CH_2), 32.4 (NCH_3), 47.3 (NCH_2), 166.8, 168.4. – ^{13}C NMR (TFA): δ = 19.6 (SCH_3), 25.7 (CH_2), 28.5 (CH_2), 35.6 (NCH_3), 50.9 (NCH_2), 171.4, 184.0. – IR (KBr): $\tilde{\nu}$ = 3300 cm^{-1} m, 3100 m, 1680 s, 1450 s. – [b] ^{13}C NMR ($CDCl_3$): δ = 11.2 (CH_3), 11.6 (CH_3), 14.1 (SCH_3), 15.2 (SCH_3), 17.4 (SCH_3), 19.0 (CH_2), 19.6 (CH_2), 20.0 (CH_2), 27.3 (CH_2), 30.8 (CH_2), 32.0 (CH_2), 39.3 (NCH_2), 40.9 (NCH_2), 44.1 (NCH_2), 49.2 (NCH_2), 52.6 (NCH_2), 55.1 (NCH_2), 160.4, 161.5, 178.4, 193.8 (C=S). – [c] In CF_3CO_2H.

isomeric 3-(ω-aminoalkyl)-1,2,4-thiadiazole salts, which can be transformed to the corresponding free bases by deprotonation[11]. It seems to be essential for the ring-chain tautomerism found with compounds **9** that the ω-aminoalkyl chain is at the ring carbon atom of the thiadiazole skeleton which is adjacent to the sulfur atom.

Table 4. Semicyclic isothioacylamidrazones **6**

	Yield [%]/ Method Solvent/ time	m.p. [°C]	Empirical formula Elemental analysis Calcd. C H N Found
6a	91/B MeOH/60'	166-167 (iso-PropOH)	$C_{13}H_{17}BrN_4O_2S_2$ (405.3) 38.52 4.23 13.82 38.46 4.36 13.60
6b	99/A MeOH/60'	135-136 (iso-PropOH)	$C_8H_{16}IN_3S_2$ (345.3) 27.83 4.67 12.17 27.55 4.55 11.89
6c	62/B MeOH/20'	145-147 (MeCN)	$C_{15}H_{20}N_4O_2S_2$ (352.5) 51.12 5.72 15.90 51.31 5.65 15.47
6e	99/B MeOH/60'	92-93 (MeCN)	$C_{15}H_{19}Br_2N_3OS_2$ (441.3) [a]
6f[b]	85/B EtOH/60'	144-146 (iso-PropOH)	$C_{16}H_{22}N_4O_2S_2$ (366.5) 52.43 6.05 15.29 52.53 6.01 15.01
6g	58/B Me_2CHOH/ 20'	114-116 (iso-PropOH)	$C_{10}H_{20}IN_3S_2$ 373.3 32.17 5.40 11.26 32.05 5.23 11.12
6r[c]	86/B MeOH/20'	154-156 (iso-PropOH)	$C_{14}H_{19}BrN_4O_2S_2$ 419.4 40.10 4.57 13.36 40.27 4.60 13.55

[a] Not analytically pure; corresponding free base prepared by treatment of the hydrobromide with triethylamine: m.p. 122–123°C; $C_{15}H_{18}BrN_3OS_2$ (399.4) Calcd. C 45.11 H 4.29 N 10.52, Found C 45.38 H 4.63 N 10.49. – [b] Free base. – [c] Corresponding free base prepared in 96% yield according to method B, 10 ml of triethylamine is added after heating for 20 min at reflux temp. in methanol; m.p. 153–155°C.

It can be assumed that generally an equilibrium of the two tautomeric structures **5** or **4** and **8** exists, which is either almost completely on the side of **5** and **4** or on the side of **8**. In order to obtain evidence for this assumption we tried to trap 2-(ω-aminoalkyl)-1,3,4-thiadiazoles **8** by subsequent reactions. By reaction of lactam hydrazone derivatives **5** or **4** with alkylating agents, however, *S*-alkylation products **6** were obtained. Hence, not the aminoalkyl-1,3,4-thiadiazole **8** is trapped but the lactam hydrazone structure **5**. It is worth mentioning that *S*-methylation products **6** are also formed, if thiohydrazides **1** are treated with excess lactam acetal **2** ($R^2 = CH_3$) (method C).

The reaction of the zwitterionic compound **5a** or thioacylamidrazone **4a** with phenyl isocyanate occurs at a nitrogen atom to afford a phenylurea (^{13}C NMR: δ = 150.3) But a signal of a thiocarbonyl carbon atom is still found in ^{13}C-NMR spectra of the product at δ = 195, indicating that no ring-transformed thiadiazole **8** is trapped but again the lactam hydrazone structure.

Experimental

M.p.: Heating block, Boetius. – IR: IR-Specord 71, Carl-Zeiss-Jena. – UV: UV/Vis spectrometer Specord, Carl-Zeiss-Jena. – ^1H NMR: BS 487/c (80 MHz), Tesla Brno; WP 200 (200 MHz), Bruker. – ^{13}C NMR: WP 200 (50 MHz), WP 300 (75 MHz), Bruker. – MS (70 eV): HP 5995 A, Hewlett-Packard. – Elemental analyses: Elementaranalysator 240, Perkin-Elmer.

Zwitterionic Amidrazonium Compounds **5** *or Lactam Thioacylhydrazones* **4** (see Tables 1, 2, 3): A mixture of 0.05 mol of thiohydrazide **1**, 0.10 mol of lactam acetal **2** or *O*-methyllactim ether **3** and 50 ml of acetone, 25 ml of methanol, or 50 ml of ethanol is kept at

Table 5. Spectroscopic data of semicyclic isothioacylamidrazones **6**

	^1H NMR ([D$_6$]DMSO)	MS (70 eV): m/z (%)
6a	[a] 2.15 (m, 2 H, CH_2), 2.51 (s, 3 H, SCH_3), 2.98 (t, J = 8 Hz, 2 H, CH_2), 3.62 (t, J = 8 Hz, 2 H, CH_2), 4.60 (s, 2 H, SCH_2), 7.67 (d, J = 8 Hz, 2 H, C_6H_4), 8.20 (d, J = 8 Hz, 2 H, C_6H_4), 9.86 (s, 1 H, NH)[b]	324 (M^+, 6), 84 (100), 55 (50), 45 (31), 30 (60)
6b	[c] 1.91 (m, 4 H, 2 CH_2), 2.44 (s, 1.5 H, SCH_3), 2.61 (s, 3 H, SCH_3), 2.70 (s, 1.5 H, SCH_3), 3.00 (m, 2 H, CH_2), 3.69 (m, 2 H, CH_2)	217 (M^+, 19), 170 (23), 142 (48), 128 (29), 127 (37), 98 (25), 97 (23), 55 (100), 47 855), 45 (52), 30 (30)
6c	[d] 1.96 (m, 6 H, 3 CH_2), 2.56 (s, 1.5 H, SCH_3), 2.70 (s, 1.5 H, SCH_3), 2.88 (m, 2 H, CH_2), 3.70 (m, 2 H, CH_2), 4.49 (s, 2 H, SCH_2), 7.64 (d, J = 7.5 Hz, 2 H, C_6H_4), 8.29 (d, J = 7.5 Hz, 2 H, C_6H_4)	352 (M^+, 4), 112 (86), 96 (32), 69 (42), 55 (41), 41 (57), 30 (100)
6e	[c] 2.29 (m, 2 H, CH_2), 2.41 (s, 3 H, SCH_3), 2.68 (m, 2 H, CH_2), 3.55 (s, 3 H, NCH_3), 4.12 (t, 2 H, CH_2), 4.81 (s, 2 H, SCH_2), 7.64 (d, J = 8 Hz, 2 H, C_6H_4), 7.92 (d, J = 8 Hz, 2 H, C_6H_4)	170 (98), 69 (100), 55 (58), 44 (39), 42 (59), 41 (34)
6f	1.64 (m, 6 H, 3 CH_2), 2.52 (s, 3 H, SCH_3), 2.61 (s, 3 H, NCH_3), 2.87 m, 2 H, CH_2), 3.68 (m, 2 H, CH_2), 4.56 (s, 2 H, SCH_2), 7.73 (s, J = 8 Hz, 2 H, C_6H_4), 8.23 (d, J = 8 Hz, 2 H, C_6H_4)	366 (M^+, 13), 126 (100), 81 (25), 80 (48), 69 (35), 68 (33), 55 (32), 45 (47), 44 (31), 42 (35), 41 (37)
6g	[d] 1.51 (t, J = 7 Hz, 3 H, CH_3), 2.08 (m, 4 H, 2 CH_2), 3.04 (m, 5 H, SCH_3, CH_2), 3.83 (m, 4 H, 2 CH_2)	245 (M^+, 12), 128 (37), 125 (59), 83 (100), 55 (90)
6r	2.10 (m, 2 H, CH_2), 2.50 (m, 3 H, SCH_3), 2.89 (m, 5 H, CH_2, NCH_3), 3.79 (m, 2 H, CH_2), 4.59 (s, 2 H, SCH_2), 7.73 (d, J = 9 Hz, 2 H, C_6H_4), 8.23 (d, J = 9 Hz, 2H, C_6H_4)	[e] 338 (M^+, 2), 98 (100), 69 854), 55 (66), 42 (40), 30 (39)

[a] 250 MHz. – [b] ^{13}C NMR ([D$_6$]DMSO) (63 MHz): δ = 15.5 (SCH_3), 20.4 (CH_2), 29.2 ($CH_2CH=$), 38.7 (SCH_3), 47.3 (NCH_2), 123.6 (CH), 130.3 (CH), 144.1, 146.6, 159.1, 165.0. – [c] In $CDCl_3$. – [d] In CF_3CO_2H. – [e] Of the corresponding free base.

Table 6. 2-(ω-Aminoalkyl)-1,3,4-thiadiazole salts **9**

	Yield [%]	m.p. [°C]	Empirical formula Elemental analysis Calcd. C H N Found
9a	46	142-144 (iso-C_3H_7OH)	$C_6H_{12}ClN_3S_2$ (225.8) 31.92 5.36 18.61 32.04 5.31 18.76
9e[a]	83	108-109 (iso-C_3H_7OH)	$C_7H_{14}ClN_3S_2$ (239.8) 35.06 5.88 17.52 35.24 5.68 17.68
9f	58	93-95 (iso-C_3H_7OH)	$C_9H_{18}ClN_3O_4S_2$ (331.8) 32.58 5.47 12.66 32.26 5.47 12.57
9g	88	122-124 (iso-C_3H_7OH)	$C_8H_{16}ClN_3S_2$ 37.86 6.35 16.56 37.79 6.52
9h	61	76-77 (iso-C_3H_7OH)	$C_9H_{18}ClN_3O_4S_2$ (331.8) 32.58 5.47 12.66 5.30 12.96

[a] Corresponding perchlorate (X = ClO_4): m. p. 112–114 °C; yield 71%; $C_7H_{14}ClN_3O_4S_2$ (303.8) Calcd. C 27.68 H 4.64 N 13.83 Found C 27.70 H 4.56 N 14.06.

Table 7. Spectroscopic data of 2-(ω-aminoalkyl)-1,3,4-thiadiazole salts **9**

	^{1}H NMR ([D$_6$]DMSO)	MS (70 eV): m/z (%)
9a [a]	[b]2.06 (m, 2 H. CH_2), 2.75 (s, 3 H, SCH_3), 3.03 (m, 2 H, CH_2), 3.20 (t, J = 7.5 Hz, 2 H, NCH_2), 8.32 (br. 2 H, NH)	189 (M^+-Cl, 2), 159 (27), 146 (59), 36 (100), 30 (54)
9e[c]	2.04 (p, J = 7.3 Hz, 2 H, CH_2), 2.50 (s, 3 H, SCH_3), 2.75 (s, 3 H, NCH_3), 2.91 (t, J = 7.3 Hz, 2 H, CH_2), 3.17 (t, J = 7.3 Hz, 2 H, CH_2), 8.92 (br, 2 H, NH)	204 (M^+-Cl, 1), 146 (28), 58 (78), 44 (100)
9f	1.50 (m, 6 H, 3 CH_2), 2.51 (s, 3 H, SCH_3), 2.73 (s, 3 H, NCH_3), 3.00 (m, 4 H, 2 CH_2), 8.28 (br, 1 H, NH)	231 (M^+-ClO_4, 0.4), 159 (27), 125 (34), 44 (100)
9g[d]	1.22 (t, J = 7 Hz, 3 H, CH_3), 2.10 (m, 2H, CH_2), 2.74 (s, 3 H, SCH_3), 3.00 (m, 4 H, 2 CH_2), 3.15 (q, J = 7 Hz, 2 H, NCH_2)	217 (M^+-Cl, 0.2), 146 (54), 72 (100), 58 (69), 56 (20), 44 (21), 41 (24), 30 (80)
9h	[b]1.42 (t, J = 7 Hz, CH_3), 1.93 (m, 4 H, 2 CH_2), 2.76 (s, 3 H, SCH_3), 3.30 (m, 6 H, 3 CH_2), 7.41 (br, 2 H, NH)	231 (M^+-ClO_4, 2), 146 (28), 125 (26), 84 (21), 58 (100), 56 (20), 45 (30), 44 (28), 36 (32), 30 (70)

[a] ^{13}C NMR (CD_3OD) (75 MHz): δ = 16.95 (SCH_3), 27.7 (CH_2), 27.8 (CH_2), 39.8 (NCH_2), 170.2 (C=N), 170.3 (C=N). – ^{13}C NMR ([D$_6$]DMSO) (75 MHz): δ = *16.6* (SCH_3), 18.1 (SCH_3), 20.6, *26.6*, *26.8*, 30.1, *39.2*, 41.7, *166.7* (C=N), *168.7* (C=N) (high-intensity signals are printed in *italics*). – [b] In $CDCl_3$. – [c] ^{13}C NMR ([D]$_6$DMSO) (75 MHz): δ = 16.4 (SCH_3), 25.0 (CH_2), 26.4 (CH_2), 32.1 (NCH_3), 47.1(NCH_2), 166.6 (C=N), 168.3 (C=N). – UV of corresponding perchlorate (X = ClO_4) (CH_3OH): λ_{max} (lg ε) = 270 nm (3.91); (C_2H_5OH): λ_{max} (lg ε) = 270 (3.90); ($CHCl_3$): λ_{max} (lg ε) = 273 (3.93). – [d] ^{13}C NMR ($CDCl_3$) (75 MHz): δ = 11.2 (CH_3), 16.5 (SCH_3), 25.1 (CH_2), 27.3 (CH_2), 43.1 (NCH_2), 46.3 (NCH_2), 167.3 (C=N), 167.7 (C=N).

Table 8. X-ray structural analysis of **5e** and **9e**[a]

5e: $C_7H_{13}N_3S_2$ (203.3); colorless prismatic crystal (0.2 × 0.2 × 0.4 mm); space group $P2_1/n$; a = 787.9(4), b = 1137.9(4), c = 1144.6(2) pm; β = 99.71(3)°; V = 1011.5 × 10^6 pm^3; Z = 4; $d_{calcd.}$ = 1.335 gcm^{-3}; μ_A = 4.8 cm^{-1}; λ = 71.073 pm; Enraf-Nonius CAD4; graphite crystal incident beam monochromator; Mo-K_α radiation (Θ = 50°); ω scan: 1760 reflections collected, 1064 unique, 1063 used [$I > 3\sigma(I)$]; 162 variable parameters; no absorption correction. Structure was solved by direct methods. H atoms were located in Δρ (x,y,z). Refinement performed by full-matrix least squares anisotropically (H atoms isotropically) with unit weights to R_1 = 0.042; R_w = 0.041; residual electron density < 0.53.

9e: $C_7H_{14}ClN_3O_4S_2$ (303.8); colorless prismatic crystal (0.3 × 0.3 × 0.3 mm); space group $P1$; a = 690.6(2), b = 748.4(2), c = 1314.4(4) pm; α = 96.86(7), β = 91.99(2), γ = 93.91(2)°; V = 672.3 × 10^6 pm^3; Z = 2; $d_{calcd.}$ = 1.50 gcm^{-3}; μ_A = 5.9 cm^{-1}; λ = 71.073 pm; Enraf-Nonius CAD4; graphite crystal incident beam monochromator; Mo-K_α radiation ($2\Theta_{max}$ = 56°); Θ-ω scan; 2772 reflections measured, 1216 unique, 1215 used [$I > 3\sigma(I)$]; 210 variables. H atoms located in final difference map. Refinement performed by fullmatrix least squares anisotropically (H atoms isotropically) with $w = 4F_0^2/\sigma^2(F_0^2)$ to R_1 = 0.051 and R_w = 0.052; residual electron density < 0.35.

[a] Further crystal structure data have been deposited at the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, F.R.G., inquiries should be accompanied by the depository number CSD-55947, the names of the authors, and the journal citation.

Table 9. Positional and thermal parameters of compound **5e** (numbers in parentheses are estimated standard deviations of the last significant digit); starred atom was refined isotropically; anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as (4/3) × [a^2 × $B(1,1)$ + b^2 × $B(2,2)$ + c^2 × $B(3,3)$ + $ab(\cos\gamma)$ × $B(1,2)$ + $ac(\cos\beta)$ × $B(1,3)$ + $bc(\cos\alpha)$ × $B(2,3)$]

Atom	x	y	z	B_i(Å^2)
S1	0.0398(2)	0.2529(1)	0.3135(1)	4.16(2)
S2	0.2164(2)	0.4807(1)	0.2202(1)	4.77(3)
N1	0.1909(5)	0.4210(3)	0.4496(3)	3.80(8)
N2	0.2852(5)	0.5348(3)	0.4652(3)	4.21(8)
N3	0.4028(5)	0.6754(3)	0.6028(3)	4.20(8)
C1	0.1584(5)	0.3947(4)	0.3407(4)	3.43(9)
C2	0.3163(5)	0.5730(4)	0.5754(4)	3.61(9)
C3	0.2522(6)	0.4998(4)	0.6783(4)	4.4(1)
C4	0.3185(7)	0.5792(5)	0.7810(4)	5.6(1)
C5	0.4201(6)	0.6929(4)	0.7287(4)	4.8(1)
C6	0.4853(7)	0.7658(4)	0.5219(5)	5.4(1)
C7	-0.0051(7)	0.1934(4)	0.4581(4)	5.0(1)
H2*	0.335(4)	0.572(3)	0.407(3)	0.6(8)

room temp. for 1 h or heated under reflux. The product either precipitates from the reaction mixture or is separated by evaporating the solvent. It is filtered by suction and recrystallized.

Semicyclic Isothiohydrazides **6** (see Table 4). – *Method A:* A mixture of 0.05 mol of thioacylamidrazone derivative **4** or **5** and 25 ml of iodomethane is heated under reflux for 40 min. Excess iodomethane is evaporated. As far as the residue resists crystallization some

diethyl ether is added. The product is filtered by suction and recrystallized.

Method B: A mixture of 0.03 mol of thioacylamidrazone derivative **4** or **5**, 0.03 mol of alkylating agent and methanol, ethanol, or 2-propanol is heated under reflux (for reaction time and solvent used see Table 4) and worked up as described above.

Table 10. Positional and thermal parameters of compound **9e**; starred atoms were refined isotropically; anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as $(4/3) \times [a^2 \times B(1,1) + b^2 \times B(2,2) + c^2 \times B(3,3) + ab(\cos\gamma) \times B(1,2) + ac(\cos\beta) \times B(1,3) + bc(\cos\alpha) \times B(2,3)]$

Atom	x	y	z	$B_i(A^2)$
Cl	0.1243(3)	0.2391(2)	0.9082(1)	4.36(4)
S1	0.3011(3)	0.2463(3)	0.5573(1)	4.41(4)
S2	0.7352(3)	0.2414(3)	0.6190(2)	5.02(4)
O1	0.2819(8)	0.1280(8)	0.8948(5)	7.2(2)
O2	0.1634(8)	0.3601(8)	1.0004(4)	6.8(2)
O3	-0.0501(8)	0.1269(8)	0.9172(4)	6.2(1)
O4	0.1028(9)	0.3355(8)	0.8235(5)	8.4(2)
N2	0.4070(8)	0.2646(9)	0.3763(4)	5.0(1)
N3	0.5760(8)	0.2606(9)	0.4360(4)	5.1(1)
N8	-0.1932(8)	0.2646(8)	0.1226(4)	3.9(1)
C1	0.2543(9)	0.258(1)	0.4288(5)	3.9(1)
C4	0.5432(9)	0.2505(9)	0.5307(5)	3.7(1)
C5	0.0541(9)	0.261(1)	0.3843(5)	4.7(2)
C6	0.0359(9)	0.265(1)	0.2713(5)	4.1(2)
C7	-0.1722(9)	0.268(1)	0.2350(5)	4.0(2)
C9	-0.394(1)	0.274(1)	0.0840(6)	5.7(2)
C10	0.614(1)	0.226(2)	0.7317(7)	9.3(3)
H81	-0.145(8)	0.172(8)	0.089(4)	1(1)*
H82	-0.110(9)	0.340(8)	0.108(5)	1(1)*

Method C: 0.02 mol of lactam acetal **2** is prepared as described before[13]. Without isolating **2** 0.01 mol of thiohydrazide **1** is added to the resulting ethanolic solution. After stirring at ambient temp. for 1 h, the product is precipitated by the addition of some water. The precipitate is filtered by suction and recrystallized.

2-(ω-Aminoalkyl)-1,3,4-thiadiazole Salts **9**: 5 ml of 15% aqueous HCl or $HClO_4$ is added with stirring to a suspension of 0.02 mol of thioacylamidrazone derivative **4** or **5**. If no solution is obtained the mixture is shortly brought to the boil. After 30 min, the solvent is evaporated in vacuo. When crystallization fails, some diethyl ether is added. The product is filtered by suction and recrystallized.

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CAS Registry Numbers

1a: 5397-03-5 / **1i**: 13331-31-2 / **1j**: 6610-29-3 / **1k**: 13431-34-0 / **1m**: 5351-69-9 / **1o**: 127627-22-9 / **1q**: 20605-40-7 / **4a**: 140439-90-3 / **4b**: 18595-90-9 / **4c**: 18596-83-3 / **4d**: 18595-91-0 / **4e**: 140439-91-4 / **4f**: 140439-92-5 / **4g**: 140439-93-6 / **4h**: 140439-94-7 / **4i**: 18596-84-4 / **4j**: 140439-95-8 / **4k**: 140439-96-9 / **4l**: 140439-97-0 / **4m**: 140439-98-1 / **4n**: 140439-99-2 / **4o**: 140440-00-2 / **4p**: 140440-01-3 / **4q**: 140440-02-4 / **6a**: 140440-03-5 / **6b**: 140440-04-6 / **6c**: 140440-05-7 / **6e**: 140440-06-8 / **6e** (free base): 140440-17-1 / **6f**: 140440-07-9 / **6g**: 140440-08-0 / **6r**: 140440-09-1 / **6r** (free base): 140440-18-2 / **9a**: 140440-10-4 / **9e**: 140440-11-5 / **9e** ($HClO_4$ salt): 140440-20-6 / **9f**: 140440-13-7 / **9g**: 140440-14-8 / **9h**: 140440-16-0

Correction (May 20, 1992): Compound **6g** does not contain a five-membered ring ($n = 1$), as indicated on p. 1389, but a six-membered ring ($n = 2$).