On the Reaction of Isothiosemicarbazides with Heterocumulenes. Part I

Steffen Ernst and Klaus Schulze*

University of Leipzig, Institute of Organic Chemistry, Talstraße 35, D-04103 Leipzig, Germany

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Isothiosemicarbazides **2** react with acyl isothiocyanates under addition-cyclization to yield 1,3,4-thiadiazoline-2-imines **3** as well as the isomeric 2-amino-substituted 1,3,4-thiadiazolium-5-acylaminides **3'**. In a similar manner the 2-hydrazino-substituted 1,3-thiazoline **4** adds ethoxycarbonyl isothiocyanate to give the thiosemicarbazide **5**, which undergoes a rearrangement to the 1,3,4-thiadiazoline-2-imine **5'**. The [2+2] cycloreversion of **3d** involving ethoxycarbonyl iso(thio)cyanate and the thermal induced Dimroth rearrangement of **3'f** and **h** are also discussed.

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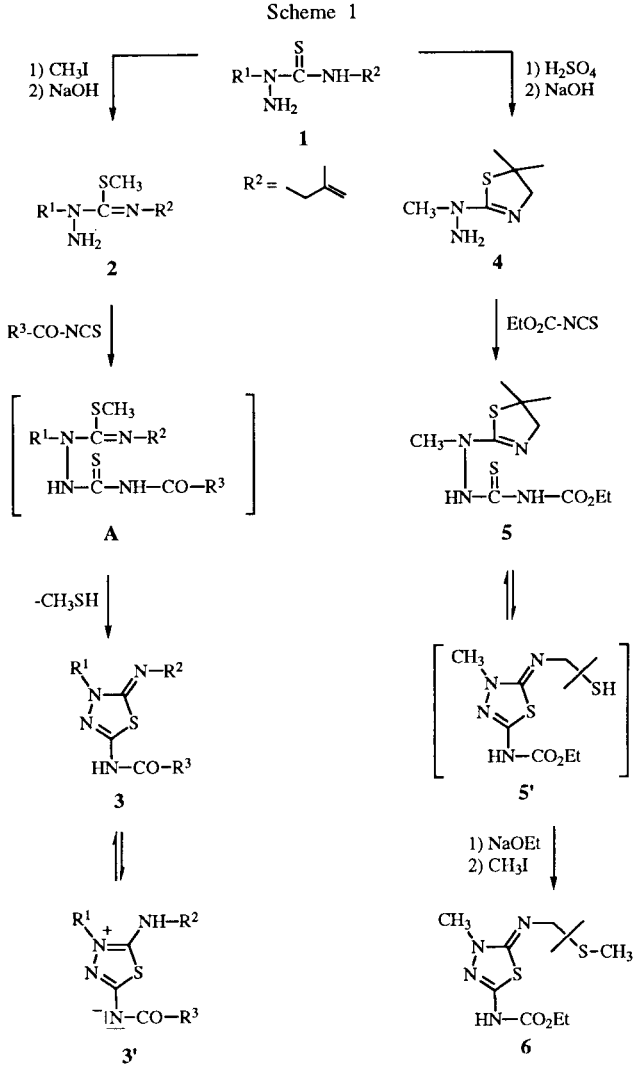
Recently, we reported on the cyclization of bithioureas derived from 2,4-disubstituted thiosemicarbazides and acyl isothiocyanates leading to 1,2,4-triazoline-3-thiones and 1,3,4-thiadiazolin-2-imines [1].

As a continuation of this work, we now describe an alternative synthesis of 1,3,4-thiadiazole derivatives, which is based on the previously unreported reaction of isothiosemicarbazides **2** with acyl isothiocyanates (Scheme 1). Compounds **2** are readily available by *S*-alkylation of the corresponding 2,4-disubstituted thiosemicarbazides **1** with methyl iodide and further treatment with sodium hydroxide. Upon reaction with ethoxycarbonyl as well as benzoyl isothiocyanate in toluene at 0-10°, isothiosemicarbazides **2** underwent addition-cyclization with loss of methyl mercaptane to give the 1,3,4-thiadiazoline-2-imines **3a,c,d,e,g** as well as 1,3,4-thiadiazolium-5-acylaminides **3'b,f** and **h** in 49-86% yield. Compounds **3a,c,d** and **3'b** are identical in all respects with those previously obtained from the corresponding bithioureas and methyl iodide [1]. In both cases *S*-methyl compound **A** is assumed to be involved in the cyclization pathway.

Comparable results were obtained by the action of ethoxycarbonyl isothiocyanate on the 2-hydrazino-substituted 1,3-thiazoline **4** (Scheme 1). The latter was prepared from 4-methallyl-2-methylthiosemicarbazide by a proton-induced π-cyclization [2]. In contrast to the isothiosemicarbazides which spontaneously reacted with acyl isothiocyanates by addition-cyclization, the 2-hydrazino-substituted 1,3-thiazoline **4** afforded the primary adduct **5** structurally similar to intermediate **A**. Interestingly, the ^{1}H nmr spectrum of the adduct dissolved in deuteriochloroform displayed signals corresponding to a 7:3 mixture of **5** and **5'**. This indicates an intramolecular nucleophilic attack of the thiocarbonyl sulfur on the C-2 atom of the thiazoline ring accompanied by the cleavage of the latter. The conversion **5** → **5'** which occurs to some extent in deuteriochloroform solution may be considered as a rearrangement involving four side-chain atoms. Since all attempts to isolate the 1,3,4-thiadiazoline-2-imine **5'** failed we tried to alkylate the terminal SH-group of **5'**. Indeed, upon treatment

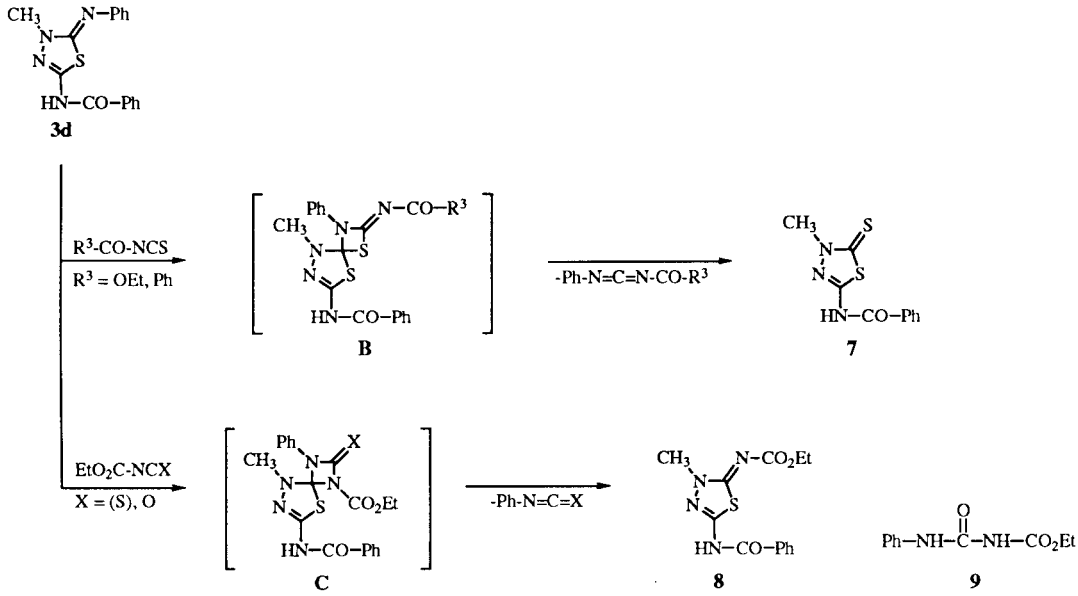
Scheme 1



1,2	R^1	R^2
a	Methyl	Methallyl
b	Methyl	Phenyl
c	Methyl	Benzyl
d	Benzyl	Methyl

3,3'	R^1	R^2	R^3
a	Methyl	Methallyl	Ethoxy
b	Methyl	Methallyl	Phenyl
c	Methyl	Phenyl	Ethoxy
d	Methyl	Phenyl	Phenyl
e	Methyl	Benzyl	Ethoxy
f	Methyl	Benzyl	Phenyl
g	Benzyl	Methyl	Ethoxy
h	Benzyl	Methyl	Phenyl

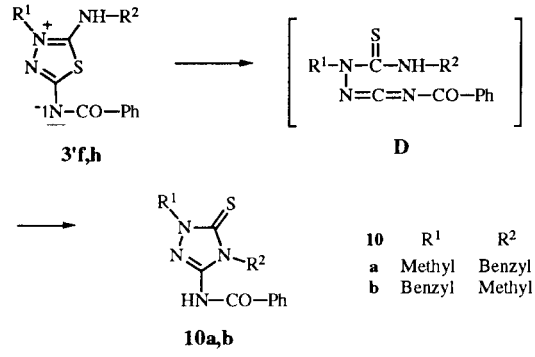
Scheme 2



with methyl iodide in basic medium the thiosemicarbazide **5** enters into the desired rearrangement followed by *S*-methylation to give the 1,3,4-thiadiazoline-2-imine **6** in 71% yield.

However, when isothiosemicarbazide **2b** was allowed to react with benzoyl isothiocyanate in toluene without cooling, the 1,3,4-thiadiazoline-2-thione **7** instead of **3d** was formed. Besides the anticipated addition-cyclization a replacement of the phenylimino by the thiocarbonyl group also occured. This may be interpreted in terms of a [2+2] cycloaddition-cycloreversion process involving a second molecule of benzoyl isothiocyanate *via* thiazetidine **B** as shown in Scheme 2. In order to test this theory we treated **3d** in refluxing toluene with benzoyl as well as ethoxycarbonyl isothiocyanate. In both cases, the 1,3,4-thiadiazoline-2-thione **7** was isolated from the reaction mixture. Using ethoxycarbonyl isothiocyanate the urea **9** and small amounts of a product assigned structure **8** could be separated by column chromatography on silica gel. The formation of urea **9** is explicable by subsequent hydrolysis of the not isolated ethoxycarbonylphenylcarbodiimide providing evidence for the retro [2+2] process. On the other hand, the formation of **8** indicates another exchange reaction with the initial addition of ethoxycarbonylisothiocyanate across its C=N bond. By treating **3d** with ethoxycarbonylisocyanate the imine **8** was obtained as main product. In this case, as expected, the cycloaddition across the C=N double bond is preferred. Our results agree with the studies of Schaumann and co-workers [3,4]. They reported the cycloadditions of persubstituted isothioureas with iso(thio)cyanates and carbon disulfide. A method for the preparation of systems incorporating a C=N group, like amidines and guanidines as well as heterocumulenes, which is based on a [2+2] cycloreversion reaction was already established by Ulrich *et al.* [5].

Scheme 3



The 1,3,4-thiadiazoline-5-acylaminide structure **3'** was established for compounds **b**,**f** and **h** according to their solution ^{13}C nmr spectra. The high melting point and the low solubility of these compounds also support

Table 1

Yields of Compounds **3a**,**c**,**d** and **3'b** [a]

Compound No.	Yield (%)
3a	70
3'b	82
3c	72
3d	71

[a] For physical and spectral data see ref [1]

Table 2
Physical Data of Compounds **2a•HI, 2c•HI, 2d•HI, 3e,g, 3'f,h** and **10a,b**

Compound No.	Yield (%)	Mp (°C) (recrystallization solvent)	MolecularFormula (Molecular Weight)	Analysis (%) Calcd./Found C	H	N
2a•HI	90	108-109	$C_7H_{15}N_3S$•HI	27.91	5.35	13.95
		(ethanol/ether)	(301.19)	28.15	5.21	14.27
2c•HI	92	110-115	$C_{10}H_{15}N_3S$•HI	35.62	4.78	12.46
		(ethanol/ether)	(337.22)	35.78	5.01	12.59
2d•HI	83	104-109	$C_{10}H_{15}N_3S$•HI	35.62	4.78	12.46
		(ethanol/ether)	(337.22)	35.76	5.03	12.59
3e	75	127-128	$C_{13}H_{16}N_4O_2S$	53.41	5.52	19.16
		(ethanol/water)	(292.36)	53.33	5.63	19.16
3'f	86	212-215	$C_{17}H_{16}N_4OS$	62.94	4.97	17.27
		(ethanol/water)	(324.41)	62.84	4.97	17.12
3g	49	119-121	$C_{13}H_{16}N_4O_2S$	53.41	5.52	19.16
		(ethanol/water)	(292.36)	53.05	5.50	19.35
3'h	80	217-222	$C_{17}H_{16}N_4OS$	62.94	4.97	17.27
		(ethanol)	(324.41)	63.05	4.73	17.46
10a	75	140	$C_{17}H_{16}N_4OS$	hrms:	324.1045	
		(toluene)	(324.41)		324.094	
10b	90	149-150	$C_{17}H_{16}N_4OS$	hrms:	324.1045	

the zwitterionic structure **3'** in the solid state. This structure results from the protonation of the imino-nitrogen atom by the strong acidic NH-proton in structure **3**. All other compounds **a,c-e,g**, where the acidity of the NH-group and/or basicity of the imino-nitrogen atom are lower, were formulated as 1,3,4-thiadiazolin-2-imines **3**. In view of a possible proton-transfer reaction in solution we performed a temperature-dependent ^{13}C nmr study of compound **3e**. Indeed, the results reported in Table 5 are consistent with a fast equilibrium between the imine and the zwitterionic structure **3e** ⇌ **3'e**. The carbons C-2, C-5, the carbonyl-carbon and the carbon atom attached to the exocyclic nitrogen-atom have previously been shown to be sensitive to the protonation [1]. The ^{13}C nmr values at 50° are typical for the 1,3,4-thiadiazoline-2-imine **3** whereas those at -50° are consistent with the zwitterionic structure **3'**. It follows that the protonation is favored on

Table 3
^1H-NMR and Mass Spectral Data of Compounds **2a•HI, 2c•HI, 2d•HI, 3e,g, 3'f,h** and **10a,b**

Compound No.	^1H-NMR, δ (ppm) [a] R^1	R^2	R^3/other signals	MS, m/z
2a•HI	3.97 (s, 3H, CH_3)	1.80 (s, 3H, CCH_3) 4.22 (s, 2H, $=NCH_2$) 4.97 (s, 2H, $=CH_2$)	2.67 (s, 3H, SCH_3)	159 (9, M^+-CH_3I), 142 (91, CH_3I^+), 55 (100, $C_4H_7^+$)
2c•HI	3.87 (s, 3H, CH_3)	4.85 (s, 2H, $=NCH_2$) 7.24-7.38 (m, 5H, C_6H_5)	2.52 (s, 3H, SCH_3)	209 (1, M^+-HI), 195 (24, M^+-CH_3I), 142 (44, CH_3I^+), 91 (100, $C_7H_7^+$)
2d•HI	5.39 (s, 2H, CH_2) 7.34 (s, 5H, C_6H_5)	3.34 (s, 3H, $=NCH_3$)	2.68 (s, 3H, SCH_3)	195 (20, M^+-CH_3I), 142 (97, CH_3I^+), 91 (100, $C_7H_7^+$)
3e	3.59 (s, 3H, CH_3)	4.44 (s, 2H, CH_2) 7.21-7.39 (m, 5H, C_6H_5)	1.24 (t, 7.1 Hz, 3H, CH_2CH_3) 4.17 (q, 7.1 Hz, 2H, CH_2CH_3)	292 (63, M^+), 91 (100, $C_7H_7^+$)
3'f	3.69 (s, 3H, CH_3)	4.55 (s, 2H, CH_2) 7.3- 8.1 (m, 10H, C_6H_5)		324 (31, M^+), 105 (100, $C_6H_5CO^+$), 77 (51, $C_6H_5^+$)
3g	5.03 (s, 2H, CH_2) 7.14-7.21 (m, 5H, C_6H_5)	3.01 (s, 3H, CH_3)	1.24 (t, 7.0 Hz, 3H, CH_2CH_3) 4.15 (q, 7.1 Hz, 2H, CH_2CH_3)	292 (20, M^+), 91 (61, $C_7H_7^+$), 75 (100)
3'h	5.19 (s, 2H, CH_2) 7.3-8.0 (m, 10H, C_6H_5)	3.02 (s, 3H, CH_3)	7.3-8.0 (m, 10H, C_6H_5)	324 (16, M^+), 105 (100, $C_6H_5CO^+$), 91 (36, $C_7H_7^+$), 77 (50, $C_6H_5^+$)
10a	3.75 (s, 3H, CH_3)	5.20 (s, 2H, CH_2) 7.2-7.8 (m, 10H, C_6H_5) 11.07 (s, 1H, NH)		324 (12, M^+), 112 (88), 105 (26, $C_6H_5CO^+$), 77 (100, $C_6H_5^+$)
10b	5.29 (s, 2H, CH_2) 7.2-7.8 (m, 10H, C_6H_5)	3.32 (s, 3H, CH_3)	7.2-7.8 (m, 10H, C_6H_5) 8.81 (s, 1H, NH)	324 (38, M^+), 105 (100, $C_6H_5CO^+$), 91 (53, $C_7H_7^+$), 77 (36, $C_6H_5^+$)

[a] The spectra were taken in deuteriochloroform (**2a•HI, 2c•HI, 2d•HI, 3e,g, 10b**), dimethyl sulfoxide-d_6 (**10a**) and dimethylformamide-d_7 (**3'f,h**).

Table 4

^{13}C-NMR Data of Compounds **3e,g, 3'f,h** and **10a,b**

Compound No.	^{13}C-NMR, δ (ppm) [a] R^1	ring carbons	R^2	R^3/other signals
3e [c]	35.3	157.4 (C-2) 142.5 (C-5)	59.3 (CH_2) 126.9 (*para*), 127.6, 128.4, 139.9 (ipso) (C_6H_5)	14.4 (CH_3), 62.6 (CH_2) 153.9 (CO)
3'f	36.4	161.2 (C-2) 155.0 (C-5)	52.2 (CH_2) (127.7), 127.7 (*para*) (128.4), 137.0 (ipso) (C_6H_5)	(128.1), (128.7), 131.0 (*para*) 137.4 (ipso) (C_6H_5) [b] 171.3 (CO)
3g [c]	51.1 (CH_2) 127.4 (*para*), 127.8 128.3, 136.7 (ipso) (C_6H_5)	158.3 (C-2) 143.2 (C-5)	41.2 (CH_3)	14.3 (CH_3), 62.3 (CH_2) 154.4 (CO)
3'h	52.2 (CH_2) (128.0), 128.3 (*para*), (128.4), 135.0 (ipso) (C_6H_5)	162.6 (C-2) 156.1 (C-5)	34.7 (CH_3)	(128.2), (128.9), 131.2 (*para*), 137.0 (ipso) (C_6H_5) 172.1 (CO)
10a	36.5 (CH_3)	167.3 (C-3) 143.7 (C-5)	47.8 (CH_2) (128.2), (128.9), 132.1 (ipso), 135.4 (*para*) (C_6H_5)	(127.6), (128.8), 130.5 (ipso), 133.2 (*para*) (C_6H_5) 166.8 (CO)
10b	52.9 (CH_2) 128.8 (*para*), (129.2), (129.5), 135.4 (ipso) (C_6H_5)	167.7 (C-3) 144.3 (C-5)	32.6 (CH_3)	(128.3), (128.9), 131.5 (ipso), 134.0 (*para*) (C_6H_5) 167.4 (CO)

[a] The spectra were taken in deuteriochloroform (**3e,g,10b**), dimethyl sulfoxide-d_6 (**10a**) and dimethylformamide-d_7 (**3'f,h**),
[b] The values in the bracket could not be exactly assigned to one of the phenyl groups of the substituents,
[c] Spectra were recorded at 50°.

cooling. This may be explained from the thermodynamic point of view presuming a loss of entropy ($\Delta_R S < 0$) in going from the imine to the charged structure. In application of the Gibbs-Helmholtz equation the free energy $\Delta_R G$ decreases upon lowering the temperature. As a result the equilibrium will be shifted towards the zwitterionic structure. Finally, more detailed studies estimating the influence of solvents on the equilibrium are necessary.

We found that upon melting the 1,3,4-thiadiazolium-5-benzoylaminides **3'f** and **h**, both underwent a Dimroth rearrangement yielding the isomeric 1,2,4-triazoline-3-thiones **10a** and **b**, respectively. This conversion involves a ring cleavage and recyclization probably *via* carbodiimide **D** as shown in Scheme 3. Regarding our examples the rearrangement proceeds only when the starting heterocycle exists as a zwitterion. In fact, the 1,3,4-thiadiazoline-2-imines **3** did not rearrange thermally.

Table 5

Selected ^{13}C NMR Data of Compound **3e** at Different Temperatures

Temperature (°)	δ (ppm) NCH_3	NCH_2	ring carbons (C-2, C-5)	CO
50	35.3	59.3	157.4, 142.5	153.9
26	36.4	55.0	160.4, 151.5	159.1
20	36.6	53.9	161.1, 153.9	160.3
0	37.1	51.8	162.2, 157.7	162.5
-50	37.3	50.4	162.4, 159.2	163.6

EXPERIMENTAL

Melting points were determined on a Boëtius melting point apparatus. The nmr spectra were recorded on the Varian Gemini 200 (^{1}H nmr: 200 MHz, ^{13}C nmr: 50 MHz) and Unity-400 (^{1}H nmr: 400 MHz, ^{13}C nmr: 100 MHz) spectrometer. The chemical shifts given in ppm are referenced to the deuterated solvent. Mass spectra were measured with the V6 12-250 mass spectrometer of Analytical Instruments Manchester. The elemental analyses were performed using a CHN-Rapid Heraeus Elemental Analyzer.

General Procedure for the Preparation of Isothiosemicarbazide Hydriodides **2a•HI, 2c•HI, 2d•HI**.

A solution of the appropriate 2,4-disubstituted thiosemicarbazide **1** (0.1 mole) in ethanol (200 ml), treated with methyl iodide (17 g, 0.12 mole), was refluxed for 2 hours. After removal of the solvent *in vacuo*, the resulting oily residue crystallized on triturating with ether as well as *n*-pentane. The crude hydriodides were crystallized from ethanol/ether. Physical and spectral data are given in Tables 2 and 3.

General Procedure for the Reaction of Isothiosemicarbazides with Acyl Isothiocyanates.

To a solution of the isothiosemicarbazide hydriodide **2•HI** (0.01 mole) in water (50 ml), 2*M* sodium hydroxide (5 ml, 0.01 mole) was added. The isothiosemicarbazide **2** deposited as an oil was extracted with ether (3 x 20 ml) and the organic phase was dried with sodium sulfate. The solvent was removed under reduced pressure and the oily residue was dissolved in toluene (35 ml). After cooling in an ice-water bath, ethoxycarbonyl or benzoyl isothiocyanate (0.01 mole) was added dropwise and with stirring, maintaining a temperature between 0 and 10° (evolution of methyl mercaptane). The resulting precipitate

was filtered off, dried and crystallized from the solvents given in Table 2.

2,*S*-Dimethyl-4-phenylisothiosemicarbazide (**2b**) was prepared from thiosemicarbazide **1b** (0.01 mole) according to the procedure in ref [6].

Physical and spectral data of the resulting 1,3,4-thiadiazoline-2-imines **3** as well as 2-amino-substituted 1,3,4-thiadiazolium-5-acylaminides **3'** are listed in Tables 1, 2, 3 and 4.

5-Benzoylamino-1,3,4-thiadiazoline-2-thione (**7**) by [2+2] Cycloreversion of **3d**.

5-Benzoylamino-2-phenylimino-1,3,4-thiadiazoline (**3d**) (1.55 g, 5 mmoles) in toluene (50 ml) was heated to reflux. Ethoxycarbonyl isothiocyanate (0.66 g, 5 mmoles) was then added and the reaction mixture was refluxed for further 30 minutes under stirring. After cooling the flaky precipitate was filtered off, washed with toluene and crystallized from glacial acetic acid to yield 0.51 g (41%) of **7** as colorless needles, mp 192°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.89 (s, 3H, NCH_3), 7.65 (t, 7.7 Hz, 2H, C_6H_5), 7.77 (t, 7.3 Hz, 1H, C_6H_5), 8.14 (d, 7.3 Hz, 2H, C_6H_5), 13.06 (bs, 1H, NH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 38.3 (NCH_3), 128.4, 128.8, 130.8 (ipso), 133.4 (para) (C_6H_5), 150.3 (C-5), 166.0 (CO), 180.7 (C-2); ms: (70 eV) m/z 251 (24, M^+), 105 (100, $C_6H_5CO^+$), 77 (69, $C_6H_5^+$).

Anal. Calcd. for $C_{10}H_9N_3OS_2$ (251.33): C, 47.79; H, 3.61; N, 16.72. Found: C, 47.73; H, 3.61; N, 16.70.

5-Benzoylamino-2-ethoxycarbonylimino-3-methyl-1,3,4-thiadiazoline (**8**).

a) After separation of **7** (see above) the filtrate was evaporated *in vacuo* and the residue was treated with toluene/ethyl acetate (1:1.5, v/v). The precipitate was filtered off to give 80 mg (5%) of crude **8**.

b) The preparation of **8** as main product was achieved by refluxing **3d** (1.55 g, 5 mmoles) in toluene (50 ml) with ethoxycarbonyl isocyanate (0.58 g, 5 mmoles) for 1 hour. After cooling the precipitate was filtered off, washed with toluene and crystallized from acetonitrile to give 0.3 g (20%) of **8** as pale yellow prisms, mp 220-232°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.25 (t, 7.1 Hz, 3H, CH_2CH_3), 3.74 (s, 3H, NCH_3), 4.14 (q, 7.2 Hz, 2H, CH_2CH_3), 7.58 (t, 2H, C_6H_5), 7.69 (t, 1H, C_6H_5), 8.08 (d, 2H, C_6H_5), 12.67 (s, 1H, NH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 14.8 (CH_3), 37.0 (NCH_3), 61.2 (CH_2), 128.6, 128.9, 131.6 (ipso), 133.3 (*para*) (C_6H_5), 150.5, 162.7, 165.1, 166.0; ms: (70 eV) m/z 306 (14, M^+), 261 (10, M^+-C_2H_5O), 105 (100, $C_6H_5CO^+$), 77 (37, $C_6H_5^+$).

Anal. Calcd. for $C_{13}H_{14}N_4O_3S$ (306.34): C, 50.97; H, 4.61; N, 18.29. Found: C, 50.90; H, 4.47; N, 17.94.

N-Ethoxycarbonyl-*N'*-phenylurea **9**.

This compound was obtained after separation of **8** prepared by the reaction of **3d** and ethoxycarbonyl isothiocyanate as follows: the solvent was removed under reduced pressure and the residue was chromatographed on 60 g silica gel using toluene/ethyl acetate (5:1, v/v) as eluent. The crude urea **9** was crystallized twice from cyclohexane to give colorless leaflets with mp 103-105°, lit [7] 100-103°; ^{1}H nmr (deuteriochloroform): δ 1.32 (t, 7.2 Hz, 3H, CH_2CH_3), 4.25 (q, 7.1 Hz, 2H, CH_2CH_3), 7.10 (t, 7.4 Hz, 1H, C_6H_5), 7.31 (t, 7.8 Hz, 2H, C_6H_5), 7.53 (d, 7.6 Hz, 2H, C_6H_5), 8.69 (s, 1H, NH), 9.97 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 14.0 (CH_3), 62.4 (CH_2), 120.0, 124.0 (*para*), 128.8, 137.1 (ipso) (C_6H_5), 151.1 (CO), 154.5 (CO).

N-Methyl-*N*-(5,5-dimethyl-1,3-thiazolin-2-yl)hydrazine (**4**).

4-Methallyl-2-methylthiosemicarbazide (**1a**) (19.2 g, 0.12 mole) was added in portions under stirring to concentrated sulfuric acid (60 ml), keeping the temperature below 50°. The clear solution was gradually added to 400 g of crushed ice and the resulting mixture treated with a 33% sodium hydroxide solution (193 ml). After extraction with chloroform (3 x 50 ml), drying the organic phase with sodium sulfate and removing the solvent *in vacuo*, the hydrazine was obtained as an oil. It was treated with *tert*-butyl methyl ether and allowed to crystallize at -20°. The crude material was recrystallized from *n*-hexane to yield 10.6 g (55%) of **4** as colorless crystals, mp 63-69°; ^{1}H nmr (deuteriochloroform): δ 1.41 (s, 6H, $C(CH_3)_2$), 3.05 (s, 3H, NCH_3), 3.65 (s, 2H, $=NCH_2$), 4.02 (bs, 2H, NH_2); ^{13}C nmr (deuteriochloroform): δ 29.4 ($C(CH_3)_2$), 42.6 (NCH_3), 60.0 ($C(CH_3)_2$), 74.4 ($=NCH_2$), 167.5 (N=C-S); ms: (70 eV) m/z 159 (66, M^+), 69 (100).

Anal. Calcd. for $C_6H_{13}N_3S$ (159.26): C, 45.25; H, 8.23; N, 26.39. Found: C, 45.28; H, 8.01; N, 26.56.

4-Ethoxycarbonyl-1-methyl-1-(5,5-dimethyl-1,3-thiazolin-2-yl)thiosemicarbazide (**5**).

To a solution of *N*-methyl-*N*-(5,5-dimethyl-1,3-thiazolin-2-yl)hydrazine (**4**) (6.4 g, 0.04 mole) in toluene (40 ml) ethoxycarbonyl isothiocyanate (5.2 g, 0.04 mole) was added, while maintaining the temperature between 0 and 10°. The precipitate was filtered off and crystallized from toluene below 60°, giving 3.9 g (34%) of **5** as colorless crystals, mp 96-97°; ^{1}H nmr (deuteriochloroform): δ 1.29 (t, 7.2 Hz, 3H, CH_2CH_3), 1.53 (s, 6H, $C(CH_3)_2$), 3.34 (s, 3H, CH_3), 3.76 (s, 2H, $=NCH_2$), 4.21 (q, 7.1 Hz, 2H, CH_2CH_3); ^{13}C nmr (deuteriochloroform): δ 14.7 (CH_3), 29.0 ($C(CH_3)_2$), 39.4 (NCH_3), 61.1 ($C(CH_3)_2$), 63.4 (CH_2), 71.1 ($=NCH_2$), 152.8 (CO), 165.1 (N=C-S), 181.6 (CS); ms: (70 eV) m/z 290 (5, M^+), 215 (100, M^+-C_3H_7S).

Anal. Calcd. for $C_{10}H_{18}N_4S_2O_2$ (290.41): C, 41.36; H, 6.25; N, 19.29. Found: C, 41.31; H, 5.96; N, 19.07.

5-Ethoxycarbonylamino-2-(2-mercapto-2-methyl-propylimino)-3-methyl-1,3,4-thiadiazoline (**5'**).

This compound was not isolated but detected in deuteriochloroform solution of **5** by nmr spectroscopy; ^{1}H nmr (deuteriochloroform): δ 1.29 (t, 7.2 Hz, 3H, CH_2CH_3), 1.39 (s, 6H, $C(CH_3)_2$), 3.11 (s, 2H, $=NCH_2$), 3.43 (s, 3H, CH_3), 4.23 (q, 7.2 Hz, 2H, CH_2CH_3); ^{13}C nmr (deuteriochloroform): 14.9 (CH_3), 30.6 ($C(CH_3)_2$), 35.3 (NCH_3), 46.3 ($C(CH_3)_2$), 63.1 (CH_2), 71.8 ($=NCH_2$), 141.3 (C-5), 153.6 (CO), 156.2 (C-2).

5-Ethoxycarbonylamino-2-(2-methylmercapto-2-methylpropylimino)-3-methyl-1,3,4-thiadiazoline (**6**).

To a stirred solution of 4-ethoxycarbonyl-1-methyl-1-(5,5-dimethyl-1,3-thiazolin-2-yl)thiosemicarbazide (**5**) (1.45 g, 5 mmoles) in ethanol (30 ml), was sequentially added 1*M* sodium ethanolate in ethanol (10 ml, 10 mmoles) and methyl iodide (0.71 g, 5 mmoles). After 15 minutes the reaction mixture was neutralized with diluted hydrochloric acid and then the ethanol was removed *in vacuo*. The residue upon crystallizing from *n*-hexane yields 1.08 g (71%) of **6** as colorless needles, mp 113-115°; ^{1}H nmr (deuteriochloroform): δ 1.29 (t, 7.1 Hz, 3H, CH_2CH_3), 1.30 (s, 6H, $C(CH_3)_2$), 2.06 (s, 3H, SCH_3), 3.15 (s, 2H, $=NCH_2$), 3.42 (s, 3H, NCH_3), 4.23 (q, 7.1 Hz, 2H,

CH_2CH_3), 8.13 (bs, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 11.8 (SCH_3), 14.8 (CH_3), 26.6 ($C(CH_3)_2$), 35.4 (NCH_3), 45.9 ($C(CH_3)_2$), 63.2 (CH_2), 67.8 (=NCH_2), 142.0 (C-5), 153.7 (CO), 156.0 (C-2); ms: (70 eV) m/z 304 (5, M^+), 215 (100, M^+-C_4H_9S).

Anal. Calcd. for $C_{11}H_{20}N_4S_2O_2$ (304.44): C, 43.40; H, 6.62; N, 18.40. Found: C, 43.57; H, 6.57; N, 18.23.

General Procedure for the Preparation of the 1,2,4-Triazoline-3-thiones **10a** and **b** by Dimroth Rearrangement.

The corresponding 2-amino-substituted 1,3,4-thiadiazolium-5-benzoylaminide (**3'**) (2.5 mmoles) was heated to 245° for 10 minutes. After cooling the yellow colored solid residue was crystallized first from *tert*-butyl methyl ether and then from toluene. Physical and spectral data are listed in Tables 2, 3 and 4.

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