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SYNTHESIS OF N-SUBSTITUTED 3-AMINOTHIAZOLIDIN-4-ONES CONTAINING HETARYL FRAGMENTS

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Condensation of the N-(3,5-dichloropyridyl-2)- and N-(benzothiazolyl-2-thioacetyl)hydrazones of carbonyl compounds with thioglycolic acid gave the 3-(3,5-dichloropyridyl-2)amino- and 3-[N-(benzothiazolyl-2-thioacetyl)amino]-2-R^1-2-R^2-thiazolidin-4-ones. Reaction of 1-(benzothiazolyl-2-thioacetyl)-4-R-thiosemicarbazides with chloroacetic acid in the presence of sodium acetate gave the 2-[N-(benzothiazolyl-2-thioacetyl)hydrazono]-3-R-thiazolidin-4-ones. It was found that the N-(benzothiazolyl-2-thioacetyl)hydrazones, both in the solid state and in solution, exist in the form of an equilibrium mixture of the EZ'- and EE'-isomers as a result of hindered rotation around the amide N–CO bond.

Keywords: N-acylhydrazones, 1-acylthiosemicarbazides, benzothiazole, hydrazones, dichloropyridines, thioglycolic acid, thiazolidin-4-one, condensation.

Hetaryl substituted thiazolidin-4-ones, e.g. those containing Δ^2-imidazoline [1], thiazole[2, 3], benzimidazole [4], acridine [5], quinazolin-4(3H)-one [6], and *sym*-triazine [7] fragments show high antibacterial, antimicrobial, and antitumor activity and also have an effect on the CNS.

In this work we report the preparation of N-substituted 3-aminothiazolidin-4-ones which contain a 3,5-dichloropyridyl or benzothiazole fragment. Derivatives of thiazolidin-4-one with benzothiazolyl substituents have been little studied and there are isolated examples in the literature [8]. Evidence for the synthesis of thiazolidin-4-ones having dichloropyridyl substituents has been absent to the present time.

Compounds with a C=N grouping, e.g. azomethines [1, 3, 4, 6, 7, 9, 10], hydrazones [5, 11], N-acylhydrazones [12], and thiosemicarbazones [13] are convenient synthons for the preparation of thiazolidine derivatives. In this work the starting materials used were the products of the condensation of N-(3,5-dichloropyridyl-2)hydrazine (**1**) and benzothiazolyl-2-thioacetic acid hydrazide (**2**) with different carbonyl compounds giving the N-(3,5-dichloropyridyl-2)hydrazones **3a-g** and the N-(benzothiazolyl-2-thioacetyl)hydrazones **4a-f** (Table 1).

The reaction of hydrazones **3a-g** and N-acylhydrazones **4a-f** with thioglycolic acid gives the corresponding 2-R^1-2-R^2-3-[N-(benzothiazolyl-2-thioacetyl)amino]thiazolidin-4-ones **6a-f**. The best yields of compounds **5a-g** and **6a-f** (Table 2) are achieved by refluxing the reagents in benzene or dioxane for 10-12 h with a molar ratio of hydrazone **3a-g** (or the N-acetylhydrazone **4a-f**) to thioglycolic acid of 1:2 to 1:2.5 in the presence of 3-5 weight % of zinc chloride. It should be noted that when the condensation of the N-acylhydrazones **4a,b,f** with thioglycolic acid is carried out in the absence of the $ZnCl_2$ the yield of the thiazolidin-

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TABLE 1. Parameters for Hydrazine **1**, N-(3,5-Dichloropyridyl-2)hydrazones **3a-g** and N-(Benzothiazolyl-2-thioacetyl)hydrazones **4a-f**

Compound	Empirical formula	Found, % / Calculated, % C	H	N	S	mp, °C*	R_f*2	^{1}H NMR spectrum, δ, ppm, *J* (Hz)***	Yield, %
1	2	3	4	5	6	7	8	9	10
1	$C_5H_5Cl_2N_3$	33.81 33.73	2.85 2.83	23.57 23.60		180-182	0.32 (c)	6.38 (1H, br. s, NH); 6.58 (2H, br. s, NH_2); 7.38 (1H, d, J_{46} = 2.3, 4-H pyridine); 7.88 (1H, d, J_{46} = 2.3, 6-H pyridine)	90
3a	$C_{12}H_9Cl_2N_3$	54.03 54.13	3.45 3.38	15.84 15.79		171-172	0.52 (a)	7.70-7.74 (5H, m, Ph); 7.78 (1H, d, J_{46} = 2.5, 4-H pyridine); 8.12 (1H, s, CH=N); 8.20 (1H, d, J_{46} = 2.5, 6-H pyridine); 10.37 (1H, br. s, NH)	84
3b	$C_{12}H_9Cl_2N_3O$	51.05 51.09	3.22 3.19	15.02 14.89		162-164	0.44 (a)	6.80-7.02 (2H, m, H arom.); 7.20-7.28 (2H, m, H arom.); 7.76 (1H, d, J_{46} = 2.4, 4-H pyridine); 8.20 (1H, d, J_{46} = 2.4, 6-H pyridine); 8.48 (1H, s, CH=N); 10.37 (1H, br. s, NH); 11.76 (1H, s, HO)	70
3c	$C_{13}H_{11}Cl_2N_3O$	52.61 52.72	3.68 3.74	14.10 14.19		142-143	0.62 (a)	3.82 (3H, s, MeO); 6.90 (2H, d, *J* = 8.0, H arom.); 7.55 (1H, d, J_{46} = 2.4, 4-H pyridine); 7.69 (2H, d, *J* = 8.0, H arom.); 7.98 (1H, s, CH=N); 8.20 (1H, d, J_{46} = 2.4, 6-H pyridine); 8.45 (1H, br. s, NH)	96
3d	$C_{14}H_{94}Cl_2N_4$	54.05 54.37	4.58 4.53	18.10 18.12		160-161	0.81 (b)	3.00 (6H, s, Me_2N); 6.75 (2H, d, *J* = 8.5, H arom.); 7.58 (2H, d, *J* = 8.5, H arom.); 7.73 (1H, d, J_{46} = 2.4, 4-H pyridine); 8.12 (1H, d, J_{46} = 2.4, 6-H pyridine); 8.21 (1H, s, CH=N); 9.48 (1H, br. s, NH)	66
3e	$C_{12}H_8Cl_2N_4O_2$	46.17 46.30	2.44 2.57	18.11 18.00		185-186	0.74 (b)	7.86 (1H, d, J_{46} = 2.4, 4-H pyridine); 7.98 (2H, d, *J* = 8.0, H arom.); 8.23 (1H, d, J_{46} = 2.4, 6-H pyridine); 8.28 (2H, d, *J* = 8.0, H arom.); 8.44 (1H, s, CH=N); 10.23 (1H, br. s, NH)	75
3f	$C_{20}H_{25}Cl_2N_3O$	61.08 60.91	6.22 6.34	10.78 10.66		225-226	0.52 (c)	1.52 (18H, br. s, 2 *t*-Bu); 5.25 (1H, s, OH); 6.77 (1H, s, CH=N); 7.12 (2H, s, H arom.); 7.52 (1H, d, J_{46} = 2.7, 4-H pyridine); 7.88 (1H, d, J_{46} = 2.7, 6-H pyridine); 8.38 (1H, br. s, NH)	75

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10
3g	$C_{16}H_{25}Cl_2N_3$	58.03 58.18	7.65 7.57	12.56 12.73		48-49.5	0.42 (a)	1.14 (6H, t, 2Me); 1.28-1.56 (12H, m, CH_2); 3.22 (4H, t, $2CH_2C$=); 7.80 (1H d, J_{46} = 2.5, 4-H pyridine); 8.10 (1H, d, J_{46} = 2.5, 6-H pyridine); 9.34 (1H, br. s, NH)	83
4a	$C_{13}H_{15}N_3OS_2$	53.37 53.24	5.04 5.12	14.19 14.33	21.62 21.84	142-143	0.37 (a)	0.98 (6H, d, $J_{Me–CH}$ = 5.7, 2Me); 2.22 (1H, m, CH); 4.07 and 4.22 (2H, s, CH_2CO, *EZ'*- and *EE'*-conformers); 6.65 and 6.80 (1H, s, CH=N, *EZ'*- and *EE'*-conformers); 7.84 (4H, m, H arom.); 10.22 and 10.33 (1H, br. s, NH, *EZ'*- and *EE'*-conformers); *EE'*:*EZ'* = 70:30	80
4b	$C_{16}H_{13}N_3OS_2$	58.61 58.72	4.05 3.97	12.96 12.84	19.34 19.57	158-159	0.64 (a)	4.15 and 4.34 (2H, s, CH_2CO, *EZ'*- and *EE'*-conformers), 6.92-7.04 (5H, m, Ph), 7.38 and 7.92 (1H, s, CH=N, *EZ'*- and *EE'*-conformers), 7.70-7.76 (4H, m, H arom.), 10.38 and 10.74 (1H, br. s, NH, *EZ'*- and *EE'*-conformers); *EE'*:*EZ'* = 74:26	74
4c	$C_{24}H_{29}N_3O_2S_2$	63.42 63.30	6.28 6.37	9.09 9.23	13.92 14.06	206-207	0.70 (a)	1.58 (18H, c, 2 *t*-Bu); 4.08 and 4.22 (2H, s, CH_2CO, *EZ'* and *EE'*-conformers); 5.24 (1H, s, OH); 7.10 (2H, c, H arom.); 7.48-7.57 (4H, m, H arom.); 7.74 and 7.84 (1H, s, CH=N, *EZ'*- and *EE'*-conformers); 10.84 and 11.08 (1H, br. s, NH, *EZ'*- and *EE'*-conformers); *EE'*: *EZ'* = 80:20	87
4d	$C_{14}H_{10}N_4O_4S_2$	46.29 46.41	2.87 2.76	15.62 15.47	17.45 17.68	183-184.5 (decomp.)	0.56 (b)	3.92 and 4.32 (2H, s, CH_2CO, *EZ'*- and *EE'*-conformers); 6.70 (1H, d, J_{34} = 3.4, 4-H furan); 7.40 (1H, d, J_{34} = 3.4, 3-H furan); 7.65-7.70 (4H, m, H arom.); 7.90 and 8.04 (1H, s, CH=N, *EZ'*- and *EE'*-conformers); 10.04 and 10.33 (1H, br. s, NH, *EZ'*- and *EE'*-conformers); *EE'*:*EZ'* = 70:30	74
4e	$C_{18}H_{14}N_4OS_2$	58.88 59.01	3.91 3.82	15.21 15.30	17.60 17.48	250-251	0.30 (a)	3.81 and 4.10 (2H, s, CH_2CO, *EZ'*- and *EE'*-conformers); 7.40 (1H, d, *J* = 2.5, 2-H indole); 7.52-7.75 (8H, m, H arom.); 7.94 and 8,08 (1H, s, CH=N, *EE'*- and *EZ'*-conformers); 8.38 (1H, br. s, NH indole); 9.84 and 10.10 (1H, br. s, NH, *EZ'*- and *EE'*-conformers); *EE'*:*EZ'* = 75:25	77
4f	$C_{12}H_{13}N_3OS_2$	51.50 51.61	4.73 4.66	14.92 15.05	23.11 22.94	137-138.5	0.82 (a)	1.78 and 1.83 (6H, s, 2Me, *EZ'*- and *EE'*-conformers); 4.16 and 4.42 (2H, s, CH_2CO, *EZ'*- and *EE'*-conformers); 7.64-7.72 (4H, m, H arom.), 10.04 and 10.12 (1H, br. s, NH, *EZ'*- and *EE'*-conformers); *EE'*:*EZ'* = 63:37	75

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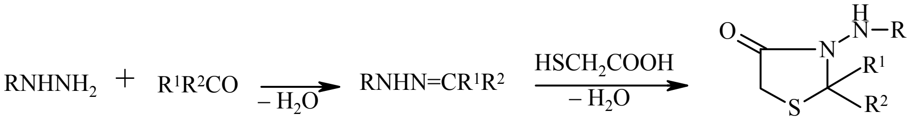
* Compounds were crystallized: **1** from ethanol; **3a,d** from benzene, **3b,c,e** from 1-propanol; **3f,g** from a mixture of hexane and toluene (4:1); **4a** from a mixture of 2-propanol and water (1:1.5); **4b,c** from a mixture of dioxane and water (2:1); **4d** from a mixture of ethanol and water (1:1); **4e** from a mixture of DMF and water (5:1); **4f** from a mixture of benzene and hexane (2:1).

*[2] The solvent system is given in brackets.

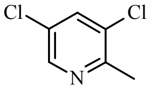
*[3] The spectra of compounds **3a,b,d,e** were recorded in acetone-d_6, compounds **3c,g** in $CDCl_3$, and compounds **3f** and **4a-f** in DMSO-d_6.

4-ones does not exceed 40-45%, even after refluxing for 36-40 h. With a higher boiling solvent (xylene, DMF, *o*-dichlorobenzene), significant tarring of the reaction mixture occurs and as a result the yield of the target compounds is lowered.

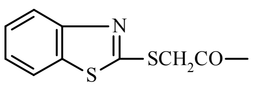


1, **2** **3a–g**, **4a–f** **5a–g**, **6a–f**

1, **3**, **5** R =

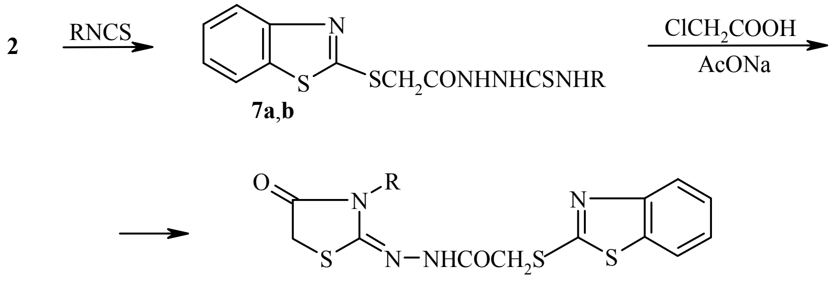


; **2**, **4**, **6** R =



3, **5** **a–f** $R^2 = H$, **g** $R^2 = C_5H_{11}$; **a** $R^1 = Ph$, **b** $R^1 = 2\text{-}HOC_6H_4$, **c** $R^1 = 4\text{-}MeOC_6H_4$,
d $R^1 = 4\text{-}Me_2NC_6H_4$, **e** $R^1 = 4\text{-}O_2NC_6H_4$, **f** $R^1 = 4\text{-}HO\text{-}3,5\text{-}(t\text{-}Bu)_2C_6H_2$, **g** $R^1 = C_5H_{11}$;
4, **6** **a–e** $R^2 = H$, **f** $R^2 = Me$; **a** $R^1 = i\text{-}Pr$, **b** $R^1 = Ph$, **c** $R^1 = 4\text{-}HO\text{-}3,5\text{-}(t\text{-}Bu)_2C_6H_2$,
d R^1 = 5-nitrofuryl-2, **e** R^1 = indolyl-3, **f** $R^1 = Me$

Reaction of the hydrazine **2** with isothiocyanates gives the 1-(benzothiazolyl-2-thioacetyl)-4-R-thiosemicarbazides **7a,b** and refluxing of these with chloroacetic acid and sodium acetate (molar ratio 1:1:3) in absolute ethanol gives the 2-[N-(benzothiazolyl-2-thioacetyl)hydrazino]-3-R-thiazolidin-4-ones **8a,b** in 64-68% yields.



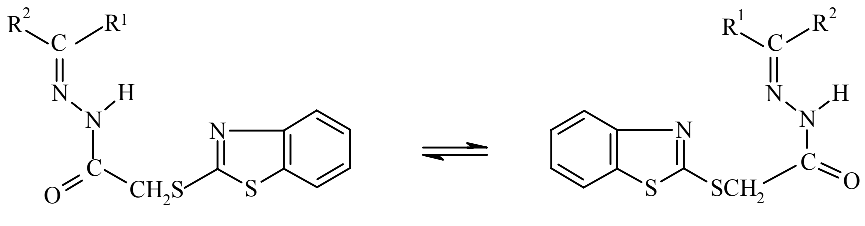
7a,**b** **8a**,**b**

7, **8** **a** $R = CH_2{=}CHCH_2$, **b** R = Ph

The IR spectra of compounds **3a-g** show strong absorption bands in the region 1625-1615 cm^{-1} which are typical for the C=N stretching vibrations of hydrazones [14]. In the spectra of the N-acylhydrazones **4a-f** the absorption bands of these groups are shifted to higher frequency and appear at 1650-1630 cm^{-1} [15].

It is known [11, 15-17] that N-acylhydrazones can exist in four stereoisomeric forms due to geometrical isomerism about the C=N bond (*E*- and *Z*-isomers) and rotational (conformational) isomerism due to hindered amide rotation around the C–N bond of the acyl fragment (*E'*- and *Z'*-isomers).

It was found that the N-(benzothiazolyl-2-thioacetyl)hydrazones **4a-f** exist in the solid state and in solution as an equilibrium mixture of the two conformational forms of the more stable *E*-isomer (the *EZ'*-isomers (A) and *EE'*-isomers (B)) due to the hindered rotation around the amide N–CO bond.



EZ'-**4a–f** (A) ⇌ *EE'*-**4a–f** (B)

In the IR spectra of the N-acylhydrazones **4a-f** (solid phase and solutions) the stretching vibrations of the C=O group appear as doublet absorption bands in the region 1695-1655 cm^{-1} (Table 3). Associates with an intermolecular hydrogen bond of the type C=O···H–N are absent in solution since the appearance of the spectrum is not changed with dilution. The doublet for the $\nu_{C=O}$ in the solid state (vaseline oil) and the same difference in frequencies for its components in $CHBr_3$, CH_2Cl_2, and dioxane point to the fact that association with solvent is not responsible for the splitting of this band. Hence the doublet for the $\nu_{C=O}$ band is due to the presence of the two *EZ'*- and *EE'*-rotational isomers. This is also indicated by the presence of two absorption bands in the region for NH stretching vibrations, e.g. for compound **4a** at 3350 and 3325 ($CHBr_3$), 3362 and 3320 (CH_2Cl_2), for compound **4b** 3365 and 3320 ($CHBr_3$), and for compound **4f** 3355 and 3315 cm^{-1} (CH_2Cl_2).

The temperature dependence (20-120°C) of the strength of the components of the $\nu_{C=O}$ doublet is small but sufficient to assign the low frequency component to the associated C=O group. The increased intensity of the high frequency component of the $\nu_{C=O}$ in more polar solvent ($CHBr_3 \rightarrow CH_2Cl_2 \rightarrow$ dioxane $\rightarrow$ MeCN) allows one to assign the absorption in the spectrum of the N-acylhydrazone **4b** at 1690 cm^{-1} to the C=O group of the more polar *EZ'*-isomer and that at 1675 cm^{-1} to the C=O group of the less polar *EE'*-isomer [18, 19].

The proposal that the N-acylhydrazones **4a-f** exist in solution as a mixture of two stereoisomers is also supported by the doubling of the signals for the NH and CH_2CO group protons in the ^1H NMR spectra of all of the compounds (Table 1) and the CH=N group proton in the spectra of the aldehyde N-acylhydrazones **4a-e** (which undergo coalescence when the spectra are recorded in DMSO-d_6 solution heated to 120°C).

According to data in [16, 20] the chemical shift of NH and CH_2CO group protons signals lie to higher field and the CH=N group proton to lower field for the *EZ'*-isomers when compared with the analogous signals for the *EE'*-isomers. A quantitative reckoning of the conformational isomers was carried out by a comparison of the integral intensities of the signals for the protons of the CH=N and CH_2CO groups. The data obtained indicates that an increase in the solvent polarity leads to an increase in the proportion of the more polar *EZ'*-conformer, e.g. for the N-acylhydrazone **4a** in chloroform the *EZ'*:*EE'* ratio is 63:37 and in DMSO 70:30 and for the N-acylhydrazone **4f** it is 54:46 and 65:35 respectively.

In the IR spectra of the thiazolidin-4-ones **5a-g**, **6a-f**, and **8a,b** there are observed absorption bands of varying intensity corresponding to vibrations of the thiazolidine ring [21, 22]: 1470-1450, 1445-1425 (CH_2 scissoring vibrations) 1290-1280, 1085-1070 (ν_{ring}), 1180-1165, and 1010-995 cm^{-1}. The strong absorption maxima in the region 1755-1735 cm^{-1} are typical of a carbonyl group stretching vibration in thiazolidinones [10, 12, 21, 22] and in the region 1670-1655 cm^{-1} in the spectra of compounds **6a-f** to the "amide I" type vibration of an N-acetyl group [14]. The thiazolidin-4-ones **8a,b** also show strong absorption bands at 1630-1625 cm^{-1} which are assigned to the stretching vibrations of the C=N group of the hydrazone fragment [14].

The ^1H NMR spectra of the thiazolidin-4-ones **5a-g**, **6a-f**, and **8a,b** (Table 2) show methylene proton signals at position 5, typical of an AB-spin system, as two unsymmetrical doublets at 3.92-4.12 and 4.24-4.48 ppm with J_{AB} = 16.5-18.5 Hz [14]. In the case of the 2-substituted thiazolidin-4-ones **5a-f** and **6a-e** (R^2 = H) the 2-H proton appears as a singlet signal at 3.32-3.58 ppm. In the spectrum of compound **6f** the proton signals for the methyl groups are seen as two singlets at 1.25 and 1.34 ppm and this is typical of *gem*-dimethyl groups in cyclic systems [14, 21, 23].

TABLE 2. Parameters for the Synthesized Thiazolidin-4-ones **5a-g**, **6a-f**, and **8a,b**

Com-pound	Empirical formula	Found, % Calculated, %				mp, °C*	R_f*2	^{1}H NMR spectrum, δ, ppm, *J* (Hz)*3				Yield, %
		C	H	N	S			2-H (1H, s)	5-CH_2, d	NH (1H, br. s.)	Other protons	
1	2	3	4	5	6	7	8	9	10	11	12	13
5a	$C_{14}H_{11}Cl_2N_2OS$	51.38 51.53	3.44 3.37	8.71 8.59	9.94 9.82	127-128	0.67 (b)	3.38	3.95, 4.34 (J_{AB} = 17.0)	8.52	7.28-7.36 (5H, m, Ph); 7.64 (1H, d, J_{46} = 2.5, 4-H pyridine); 8.08 (1H, d, J_{46} = 2.5, 6-H pyridine)	64
5b	$C_{14}H_{11}Cl_2N_2O_2S$	49.03 49.12	3.31 3.22	8.05 8.19	9.50 9.36	153-154.5	0.56 (a)	3.46	4.05, 4.40 (J_{AB} = 18.5)	8.84	6.94-7.18 (4H, m, H arom.); 7.72 (1H, d, J_{46} = 2.4, 4-H pyridine); 8.01 (1H, d, J_{46} = 2.4, 6-H pyridine); 8.36 (1H, s, OH)	68
5c	$C_{15}H_{13}Cl_2N_2O_2S$	50.34 50.56	3.52 3.65	7.98 7.86	9.15 8.99	165-166	0.60 (c)	3.34	3.92, 4.28 (J_{AB} = 16.5)	8.74	3.66 (3H, s, MeO); 6.97 (2H, d, *J* = 7.6, H arom.); 7.46 (2H, d, *J* = 7.6, H arom.); 7.80 (1H, d, J_{46} = 2.3, 4-H pyridine); 8.14 (1H, d, J_{46} = 2.3, 6-H pyridine)	73
5d	$C_{16}H_{16}Cl_2N_3OS$	51.94 52.03	4.27 4.34	11.54 11.38	8.81 8.67	123-124	0.55 (b)	3.50	4.02, 4.36 (J_{AB} = 17.5)	8.80	3.25 (6H, s, Me_2N); 6.78 (2H, d, *J* = 8.2, H arom.); 7.28 (2H, s, *J* = 8.2, H arom.); 7.69 (1H, d, J_{46} = 2.6, 4-H pyridine); 8.21 (1H, d, J_{46} = 2.6, 6-H pyridine)	75
5e	$C_{14}H_{10}Cl_2N_3O_3S$	45.16 45.28	2.60 2.69	11.18 11.32	8.81 8.63	169-170	0.56 (a)	3.60	3.92, 4.42 (J_{AB} = 18.0)	8.87	7.38 (2H, d, *J* = 6.7, H arom.); 7.67 (1H, d, J_{46} = 2.5, 4-H pyridine); 7.80 (2H, d, *J* = 6.7, H arom.); 8.10 (1H, d, J_{46} = 2.5, 6-H pyridine)	60
5f	$C_{22}H_{27}Cl_2N_2O_2S$	58.28 58.15	6.05 6.14	6.29 6.17	7.17 7.05	185-186	0.70 (c)	3.42	4.10, 4.35 (J_{AB} = 16.7)	8.94	1.58 (18H, s, 2 *t*-Bu); 5.18 (1H, s, HO); 7.08 (2H, s, H arom.); 7.60 (1H, d, J_{46} = 2.7, 4-H pyridine); 7.88 (1H, d, J_{46} = 2.7, 6-H pyridine)	58
5g	$C_{18}H_{27}Cl_2N_2OS$	55.25 55.38	7.07 6.92	7.34 7.18	8.06 8.20	88-90	0.61 (b)	—	3.98, 4.37 (J_{AB} = 17.4)	8.85	1.18 (6H, t, 2Me); 1.33-1.52 (12H, m, CH_2); 3.40 (4H, t, 2CH_2); 7.67 (1H d, J_{46} = 2.6, 4-H pyridine); 7.92 (1H, d, J_{46} = 2.6, 6-H pyridine)	51
6a	$C_{15}H_{17}N_3O_2S_3$	48.87 49.05	4.72 4.63	11.27 11.44	26.27 26.15	108-109.5	0.72 (a)	3.32	3.92, 4.30 (J_{AB} = 17.2)	9.82	1.12 (6H, d, *J* = 8.6, Me_2CH); 2.14 (1H, m, Me_2CH); 3.70 (2H, s, CH_2CO); 7.72-7.90 (4H, m, H arom.)	64

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11	12	13
6b	$C_{18}H_{15}N_3O_2S_3$	$\frac{53.72}{53.86}$	$\frac{3.62}{3.74}$	$\frac{10.70}{10.47}$	$\frac{24.11}{23.94}$	137-138.5	0.60 (a)	3.42	4.08, 4.24 (J_{AB} = 18.5)	10.34	3.88 (2H, s, CH_2CO); 6.82-7.05 (5H, m, Ph), 7.58-7.70 (4H, m, H arom.)	60
6c	$C_{26}H_{31}N_3O_3S_3$	$\frac{59.14}{58.98}$	$\frac{5.72}{5.86}$	$\frac{8.17}{7.94}$	$\frac{18.04}{18.15}$	161-162.5	0.67 (a)	3.54	4.05, 4.48 (J_{AB} = 18.0)	10.10	1.44 (18H, s, 2 *t*-Bu); 3.90 (2H, s, CH_2CO); 5.24 (1H, s, OH); 7.24 (2H, s, H arom.); 7.80-7.88 (4H, m, H arom.)	68
6d	$C_{16}H_{12}N_4O_5S_3$	$\frac{43.88}{44.04}$	$\frac{2.64}{2.75}$	$\frac{12.97}{12.84}$	$\frac{22.18}{22.02}$	188-189.5	0.51 (b)	3.38	3.97, 4.28 (J_{AB} = 16.7)	10.62	3.85 (2H, s, CH_2CO); 6.54 (1H, d, J_{34} = 3.8, 3-H furan); 7.32 (1H, d, J_{34} = 3.8, 4-H furan); 7.88-7.96 (4H, m, H arom.)	70
6e	$C_{20}H_{16}N_4O_2S_3$	$\frac{54.71}{54.54}$	$\frac{3.52}{3.64}$	$\frac{12.90}{12.73}$	$\frac{21.64}{21.82}$	175-177	0.33 (c)	3.50	4.05, 4.30 (J_{AB} = 17.3)	10.18	3.76 (2H, s, CH_2CO); 7.18-7.24 (2H, m, H arom.); 7.32 (1H, d, J = 4.0, 2-H indole); 7.46-7.52 (4H, m, H arom.); 7.67-7.72 (4H, m, H arom.); 8.36 (1H, br. s., NH indole)	62
6f	$C_{14}H_{15}N_3O_2S_3$	$\frac{47.67}{47.59}$	$\frac{4.17}{4.25}$	$\frac{12.07}{11.90}$	$\frac{27.33}{27.20}$	98-99	0.85 (a)	—	3.96, 4.28 (J_{AB} = 16.5)	10.50	1.25 (3H, s, 2-Me); 1.34 (3H, s, 2-Me); 3.74 (2H, s, CH_2CO); 7.56-7.62 (4H, m, H arom.)	58
8a	$C_{15}H_{14}N_4O_2S_3$	$\frac{47.51}{47.62}$	$\frac{3.77}{3.70}$	$\frac{14.95}{14.81}$	$\frac{25.26}{25.40}$	164-165 (with decomp.)	0.52 (c)	—	3.92, 4.32 (J_{AB} = 17.2)	10.28	3.74 (2H, s, CH_2CO); 4.08 (2H, d, CH_2N); 5.06 (1H, d, J = 3.5, CH_2=C); 5.20 (1H, d, J = 3.5, CH_2=C); 5.56 (1H, m, =CH–); 7.66-7.72 (4H, m, H arom.)	64
8b	$C_{18}H_{14}N_4O_2S_3$	$\frac{52.24}{52.17}$	$\frac{3.44}{3.38}$	$\frac{13.36}{13.53}$	$\frac{23.31}{23.19}$	185-186	0.44 (c)	—	3.96, 4.26 (J_{AB} = 16.5)	10.22	3.82 (2H, s, CH_2CO); 6.88-6.95 (5H, m, Ph); 7.58-7.67 (4H, m, H arom.)	68

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* Compounds were crystallized: **5a** from a mixture of ethanol and water (2:1), **5b, 6f** from a mixture of benzene and hexane (1:1), **5c** from a mixture of methyl cellusolve and water (2:1), **5d,g** from a mixture of benzene and hexane (1:3), **5e** from a mixture of chloroform and hexane (3:1), **5f** from a mixture of benzene and hexane (1:1.5), **6a,c** from a mixture of benzene and hexane (5:1), **6b** from a mixture of ethanol and water (1:1), and **6d,e, 8a,b** from a mixture of DMF and water (2:1).

*[2] The solvent system is given in brackets.

*[3] The spectra of compounds **5a-f, 6a-e** and **8a,b** were recorded in DMSO-d_6 and compounds **5g, 6f** in $CDCl_3$.

TABLE 3. IR Spectra of N-(Benzothiazolyl-2-thioacetyl)hydrazones **4a-f**

Compound	$\nu_{C=O}$*, cm^{-1}			
	in vaseline oil	in $CHBr_3$	in CH_2Cl_2	in dioxan
4a	1652, 1664	1668, 1688	1678, 1695	1679, 1700
4b	1645,1660	1665, 1668	1675, 1695	1678, 1695
4c	1642, 1652	1658, 1680	1670, 1690	1672, 1692
4d	1640, 1655	1665, 1682	1675, 1692	1678, 1702
4e	1650, 1664	1665, 1685	1678, 1697	1684, 1705
4f	1645, 1657	1662, 1681	1674, 1694	1682, 1702

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* Solution concentration 5 mmol/l.

In the spectra of the hydrazones **3a-g** and the thiazoldin-4-ones **5a-g** the signals for the protons of the 3,5-dichloropyridyl fragment are seen as doublets at 7.52-7.86 (4-H) and 7.88-8.23 ppm (6-H) with J_{46} = 2.4-2.7 Hz. The protons of the benzothiazole fragment in the spectra of compounds **4a-f**, **6a-f**, and **8a,b** appear as multiplet signals at 7.44-7.84 ppm.

EXPERIMENTAL

IR spectra were obtained on a Bruker IFS-48 instrument for KBr tablets, as a suspension in vaseline oil, and in solvents (CH_2Cl_2, $CHBr_3$, dioxane). ^{1}H NMR spectra were recorded on a Bruker WP-250 spectrometer (250 MHz) for 10-15% solutions with TMS internal standard. Monitoring of the reaction course and the purity of the compounds obtained was carried out using TLC on Merck LU-074 alumina bonded layer plates with the solvent systems chloroform–methanol, 30:1 (a), chloroform–methanol, 40:1 (b), and benzene–methanol, 20:1 (c) and were visualized using iodine vapor.

The starting benzothiazolyl-2-thioacetic acid hydrazide (**2**) was prepared by a known method [24].

N-(3,5-Dichloropyridyl-2)hydrazine (1). A mixture of 2,3,5-trichloropyridine (2.45 g, 13.4 mmol), $N_2H_4.H_2O$ (30%, 2.6 ml, 46.9 mmol), and propanol (1 ml) was refluxed with stirring for 4 h, cooled to 20°C, and a solution of NaOH (0.53 g, 13.4 mmol) in water (10 ml) was added with stirring. The reaction mixture was stirred for 30 min at 20°C, and the precipitate formed was filtered off, washed on the filter with water, and dried at 80°C (Table 1).

N-(3,5-Dichloropyridyl-2)hydrazones of the Carbonyl Compounds (3a-g). A mixture of the pyridylhydrazine **1** (0.89 g, 5.0 mmol) and the corresponding aldehyde or ketone (5.25 mmol) in propanol (10 ml) was refluxed with stirring until the starting hydrazine had disappeared (monitored using TLC; 30-45 min for the preparation of hydrazones **3a-e**, 3-3.5 h for hydrazones **3f,g**) and then cooled to 20°C. The precipitated solid was filtered off, dried, and crystallized from the appropriate solvent (Table 1).

N-(Benzothiazolyl-2-thioacetyl)hydrazones of the Carbonyl Compounds (4a-f). A mixture of the hydrazide **2** (2.39 g, 10 mmol), the corresponding aldehyde or ketone (10 mmol) and acetic acid (0.5 ml) in dioxane (40 ml) was refluxed with stirring for 3.5 h, cooled to 20°C, poured into iced water (150 ml), and held for 3 h at 5°C. The precipitate formed was filtered off, dried, and crystallized from the appropriate solvent (Table 2).

2-R^1-2-R^2-3-(3,5-Dichloropyridyl-2-amino)- (5a-g) and 2-R^1-2-R^2-3-[N-(benzothiazolyl-2-thioacetyl)amino]thiazolidin-4-ones (6a-f). A mixture of the hydrazone **3a-g** or **4a-f** (8 mmol), freshly distilled thioglycolic acid (1.47 g, 16 mmol), and anhydrous $ZnCl_2$ (0.2 g) in 40 ml of anhydrous benzene (for the preparation of the thiazolidin-4-ones **5a-g**) or anhydrous dioxane (for the preparation of the thiazolidin-4-

ones **6a-f**) were refluxed with stirring for 10-12 h. The solvent was removed at reduced pressure and the residue was washed with 3% sodium bicarbonate solution (3 × 20 ml), water (2 × 20 ml), dried, and crystallized from the appropriate solvent (Table 2).

1-(Benzothiazolyl-2-thioacetyl)-4-allylthiosemicarbazide (7a). A mixture of the hydrazine **2** (4.78 g, 20 mmol) and freshly distilled allyl isothiocyanate (1.9 g, 20 mmol) in 2-propanol (50 ml) was refluxed with stirring for 5 h and evaporated to dryness at reduced pressure. The oil remaining was carefully triturated with cold petroleum ether (4 × 25 ml) and held for 24 h at 0°C. The precipitate formed was filtered off and crystallized from benzene to give the thiosemicarbazide **7a** (6.1 g, 90%); mp 117-119.5°C and R_f 0.44 (a). ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm, J (Hz): 3.92 (2H, s, CH_2S); 4.08 (2H, t, CH_2N); 4.88 (1H, d, J_{AB} = 3.8, CH_AH_B); 5.02 (1H, d, J_{AB} = 3.8, CH_AH_B); 5.25 (1H, m, CH=); 6.84 (1H, br. s, NH). Found, %: C 46.02; H 4.05; N 16.83; S 28.22. $C_{13}H_{14}N_4OS_3$. Calculated, %: C 46.15; H 4.14; N 16.57; S 28.40.

1-(Benzothiazolyl-2-thioacetyl)-4-phenylthiosemicarbazide (7b) was synthesized similarly from the hydrazide **2** and phenylisothiocyanate in 85% yield; mp 160-162°C (ethanol) (according to data in [25]: mp 157°C) and R_f 0.54 (b). ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm, J (Hz): 4.14 (2H, s, CH_2S): 6.79 (1H, br. s, NH); 6.96-7.04 (5H, m, Ph); 7.50-7.58 (4H, m, H_{arom}); 8.50 (2H, br. s, NH).

2-[N-(Benzothiazolyl-2-thioacetyl)hydrazino]-3-R-thiazolidin-4-ones (8a,b). A mixture of the thiosemicarbazide **7a,b** (10 mmol), chloroacetic acid (0.95 g, 10 mmol) and anhydrous sodium acetate (2.46 g, 30 mmol) in absolute ethanol (50 ml) was refluxed with stirring for 8 h, cooled to 20°C, poured into iced water (120 ml), and held for 12 h at 5°C. The precipitate formed was filtered off, washed on the filter with water, dried, and crystallized from a mixture of DMF and water (2:1).

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