Benzothiazole compounds XXVII. Alkylation and antifungal activity of some 2-R-3-(2-mercaptoethyl)benzothiazolines

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The series of 2-R-3-(2-R'-thioethyl)benzothiazolines and allyl esters of bis[2-(2-R-3-benzothiazolinyl)ethylthio]acetic acid were synthesized by alkylation of 3-(2-mercaptoethyl)-2-benzothiazolinone oxime, 3-(2-mercaptoethyl)-2-benzothiazolinone semicarbazone, and 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone with corresponding reactive compounds. The structures of prepared compounds were confirmed by infrared spectra. The antibacterial activity of compounds is rather low, however the results of the antifungal tests showed more favourable results.

Посредством алкилирования 3-(2-меркаптоэтил)-2-бензотиазолинон-оксима, 3-(2-меркаптоэтил)-2-бензотиазолинонсемикарбазона и 3-(2--меркаптоэтил)-2-бензотиазолинонтиосемикарбазона соответствующими реагентами был синтезирован ряд 2-R-3-(2-R'-тиоэтил)бензотиазолинов и аллиловых эфиров бис[2-(2-R-3-бензотиазолинил)этилтио]уксусной кислоты. Строение полученных соединений было подтверждено их ИК--спектрами. Антибактериальная активность этих соединений довольно низка, однако тесты на противогрибковую активность имели более удовлетворительные результаты.

The present paper represents the continuation of studies of syntheses on the basis of benzothiazole. It is connected with our previous paper [1] in the sense that nucleophilic substitution reactions on 2,3-dihydrothiazolo[2,3-*b*]benzothiazolium chloride [2—4] were used to prepare the starting compounds, *i.e.* 3-(2-mercaptoethyl)-2-benzothiazolinone oxime, 3-(2-mercaptoethyl)-2-benzothiazolinone semicarbazone, and 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone.

The positive charge on the nitrogen atom of benzothiazolium salt causes the increase of polarity of the C=N bond, which creates favourable conditions for nucleophilic substitution reactions. The above-mentioned reactivity of benzothiazolium salts was already discussed [5—8].

Considering the preceding results [9—12] the aim of this work was the alkylation of some benzothiazolinone derivatives substituted in positions 2 and 3. Ethylene

chlorohydrin, esters of chloroformic, chloroacetic, and dichloroacetic acid, chloroacetic acid, acetyl chloride, phenylacetyl chloride, benzoyl chloride, methanesulfonyl chloride, and benzenesulfonyl chloride were used as alkylation agents.

The compounds synthesized were tested for antibacterial and antifungal activity.

The starting compound was prepared by chlorination of 2-(2-hydroxyethylthio)benzothiazole with thionyl chloride and consequent cyclization of the originated 2-(2-chloroethylthio)benzothiazole. Besides of tetrahydrofuran, anhydrous benzene was used as a solvent, too. As nucleophilic agents in the reaction with starting compounds hydroxylamine, semicarbazide, and thiosemicarbazide were employed in the form of chlorides. Using the above-described reactions intermediates were prepared, in which the acidity of the hydrogen atoms of SH, OH, and NH_2 groups in appertaining substituents in positions 2 and 3 on the thiazole ring was utilized. Monosubstituted and disubstituted derivatives or bisderivatives were obtained by alteration of the reaction conditions and the ratio of the quantities of compounds taking place in the reaction. The data of elemental analysis and physical constants of the synthesized compounds are given in Tables 1 and 2.

The most reactive appeared the SH group, on which the substitution reaction passed through in each case. The corresponding disubstituted derivatives of benzothiazolinone were obtained in most cases refluxing the reaction mixture during 2 h.

If the reaction mixture was not cooled sufficiently (in the case of exothermic reaction) bisderivatives were formed simultaneously. Similar mixture of products was isolated in the case of compound *V*. Using column chromatography on silica gel (a mixture of ethanol and benzene (volume ratio = 1 : 8) being the eluent) disubstituted derivative *XII* was isolated from both the first and second fractions, while the third fraction contained monosubstituted derivative *V*.

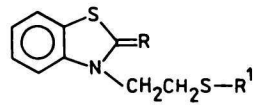
The wavenumbers of characteristic vibrations of the synthesized benzothiazolinones are given in Table 3.

In compounds *II*—*IV* and *VII* the oxime group exhibits a characteristic band of the O—H stretching vibration in the region $\tilde{\nu} = 3360$—$3390\ cm^{-1}$. The presence of the ester group in substituents R^1 can be confirmed by two intensive absorption bands in the region ($\tilde{\nu} = 1676$—$1705\ cm^{-1}$ and 1218—$1285\ cm^{-1}$ belonging to ν(C=O) and ν(C—O) vibrations, respectively. The wavenumbers of the ν(C=O) bands change in harmony with the effect of substituents bonded on the C=O group.

In the spectra of compounds *XII* and *XIII* the absorption in the region of O—H stretching vibrations is absent and the two absorption bands in the region of ν(C=O) at higher and lower values of $\tilde{\nu}$ can be assigned to O—CO—O and

Table 1

2-R-3-(2-R¹-thioethyl)benzothiazolines



Compound	R	R¹	Formula	M_r	w_i(calc.)/% / w_i(found)/%					Yield/%	M.p./°C Mixture of solvents (volume ratio)
					C	H	N	S	Cl		
I	NOH	CH_2CH_2OH	$C_{11}H_{14}ON_2S_2$	254.37	51.94	5.54	11.01	25.21	—	73	98—100
					51.56	5.32	11.10	25.74	—		Acetone—ethanol (2:1)
II	NOH	$CH_2COOC_2H_5$	$C_{13}H_{16}O_3N_2S_2$	312.41	49.98	5.16	8.96	20.52	—	76	109—111
					49.61	5.08	8.87	20.49			Ethanol
III	NOH	$CH_2COOCH_2CH_2Cl$	$C_{13}H_{15}O_3N_2S_2Cl$	346.85	45.01	4.35	8.07	18.48	10.22	59	133—135
					45.37	4.31	7.81	18.60	10.62		Ethanol
IV	NOH	$CH_2COOC_3H_7$	$C_{14}H_{18}O_3N_2S_2$	326.43	51.51	5.55	8.58	19.64	—	85	78—80
					51.90	5.72	8.63	19.94	—		Ethanol
V	NOH	$COOC_2H_5$	$C_{12}H_{14}O_3N_2S_2$	298.38	48.30	4.72	9.38	21.49	—	86	154—156
					48.23	4.74	9.40	21.63			Ethanol
VI	NOH	$COOCH(CH_3)_2$	$C_{13}H_{16}O_3N_2S_2$	312.42	49.97	5.16	8.96	20.52	—	48	149—151
					49.70	4.83	8.50	20.82			Ethanol
VII	NOH	$CH_2COOCH(CH_3)_2$	$C_{14}H_{18}O_3N_2S_2$	326.43	51.51	5.55	8.58	19.64	—	77	88—90
					51.83	5.65	8.84	19.60			Ethanol
VIII	NOH	CH_2COOH	$C_{11}H_{12}O_3N_2S_2$	284.45	46.44	4.25	9.84	22.54	—	53	202—204
					46.07	4.05	10.15	22.19			DMSO[a]—ethanol (5:1)
IX	NOH	SO_2CH_3	$C_{10}H_{12}O_3N_2S_3$	304.41	39.45	3.97	9.20	31.59	—	88	141—142
					39.30	3.82	9.23	31.19			Acetone

a) DMSO — dimethyl sulfoxide.

Table 1 (Continued)

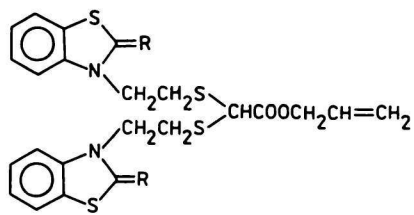
Compound	R	R¹	Formula	M_r	w_i(calc.)/% / w_i(found)/%					Yield/%	M.p./°C Mixture of solvents (volume ratio)
					C	H	N	S	Cl		
X	NOH	COC_6H_5	$C_{16}H_{14}O_2N_2S_2$	330.42	58.16	4.27	8.47	19.40	—	42	152—154
					57.89	4.21	8.40	19.42			Benzene—cyclohexane (5:1)
XI	$NOCOCH_3$	$COCH_3$	$C_{13}H_{14}O_3N_2S_2$	310.39	50.30	4.54	9.02	20.66	—	60	106—107
					50.41	4.68	9.31	20.20			Ethanol
XII	$NOCOOC_2H_5$	$COOC_2H_5$	$C_{15}H_{18}O_5N_2S_2$	370.44	48.63	4.89	7.56	17.31	—	92	137—139
					48.78	4.97	7.58	17.33			Ethanol
XIII	$NOCOOCH(CH_3)_2$	$COOCH(CH_3)_2$	$C_{17}H_{22}O_5N_2S_2$	398.50	51.23	5.56	7.02	16.09	—	39	106—107
					51.33	5.42	6.95	16.16			Ethanol
XIV	$NOCOOCH_2C{\equiv}CH$	$COOCH_2C{\equiv}CH$	$C_{17}H_{14}O_5N_2S_2$	390.43	52.29	3.61	7.17	16.42	—	89	106—108
					52.23	3.49	7.21	16.51			Ethanol
XV	$NOCOC_6H_5$	COC_6H_5	$C_{23}H_{18}O_3N_2S_2$	434.53	63.57	4.17	6.44	14.75	—	27	165—167
					63.80	4.17	6.54	14.84			Benzene—cyclohexane (5:1)
XVI	$NOCOCH_2C_6H_5$	$COCH_2C_6H_5$	$C_{25}H_{22}O_3N_2S_2$	462.59	64.91	4.79	6.05	13.86	—	96	110—112
					64.54	4.78	5.93	13.85			Benzene—cyclohexane (5:1)
XVII	$NOSO_2C_6H_5$	$SO_2C_6H_5$	$C_{21}H_{18}O_5N_2S_4$	506.64	49.78	3.58	5.52	25.31	—	85	111—113
					49.56	3.85	5.31	25.02			Benzene—cyclohexane (5:1)
XVIII	$NNHCONH_2$	$COOC_2H_5$	$C_{13}H_{16}O_3N_4S_2$	340.42	45.86	4.73	16.45	18.83	—	42	239—241
					46.07	4.67	16.60	19.10			Ethanol

Table 1 (Continued)

Compound	R	R¹	Formula	M_r	w_i(calc.)/% / w_i(found)/% C	H	N	S	Cl	Yield/%	M.p./°C Mixture of solvents (volume ratio)
XIX	$NNHCONH_2$	$CH_2COOC_2H_5$	$C_{14}H_{18}O_3N_4S_2$	354.45	47.44	5.11	15.80	18.09	—	56	115—117
					47.76	5.18	15.93	18.15			Ethanol
XX	$NNHCSNH_2$	CH_2CH_2OH	$C_{12}H_{16}ON_4S_3$	328.47	43.88	4.90	17.05	29.28	—	80	174—176
					43.79	4.90	16.93	29.10			Acetone—ethanol (3:1)
XXI	$NNHCSNH_2$	$CH_2COOCH_2CH_2Cl$	$C_{14}H_{17}O_2N_4S_3Cl$	404.96	41.52	4.23	13.83	23.75	8.75	78	176—178
					41.39	4.02	13.56	23.48	8.42		Acetone—ethanol (3:1)
XXII	$NNHCSNHCOOC_2H_5$	$COOC_2H_5$	$C_{16}H_{20}O_4N_4S_3$	428.54	44.84	4.70	13.07	22.44	—	45	162—164
					44.78	4.74	13.30	22.42			Acetone—ethanol (1:1)
XXIII	$NNHCSNHCH_2COOC_2H_5$	$CH_2COOC_2H_5$	$C_{18}H_{24}O_4N_4S_3$	456.61	47.34	5.29	12.27	21.06	—	56	156—158
					47.08	4.95	12.33	21.20			Acetone—ethanol (3:1)
XXIV	$NNHCSNHCH_2COOC_3H_7$	$CH_2COOC_3H_7$	$C_{20}H_{28}O_4N_4S_3$	484.66	49.56	5.82	11.56	19.84	—	70	146—148
					49.41	5.63	11.48	19.52			Ethanol
XXV	$NNHCSNHCH_2COOCH(CH_3)_2$	$CH_2COOCH(CH_3)_2$	$C_{20}H_{28}O_4N_4S_3$	484.66	49.56	5.82	11.56	19.84	—	38	160—161
					49.49	5.73	11.43	19.60			Acetone—ethanol (2:1)

Table 2

Allyl ester of bis[2-(2-R-3-benzothiazolinyl)ethylthio]acetic acid



Compound	R	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield/%	M.p./°C Mixture of solvents (volume ratio)
				C	H	N	S		
XXVI	NOH	$C_{23}H_{24}O_4N_4S_4$	548.72	50.34	4.40	10.21	23.37	36	118—120
				50.12	4.37	10.21	23.28		Acetone—water (3:1)
XXVII	$NHNCSNH_2$	$C_{25}H_{28}O_2N_8S_6$	664.93	45.15	4.24	16.85	28.93	38	108—110
				45.45	4.35	16.56	28.54		Acetone—water (3:1)

Table 3

Wavenumbers of the characteristic vibrations of 2-R-3-(2-R¹-thioethyl)benzothiazolines

Compound	$\tilde{\nu}$/cm^{-1}									
	ν(C=O)		ν(C=N)	ν(BT-ring)	Other vibrations					
II	1690 s		1615 vs	1574 m	ν(OH)	3390 vs,	ν(C—O)	1285 vs		
III	1705 s		1598 s	—	ν(OH)	3370 s,	ν(C—O)	1277 vs		
IV	1686 s		1613 vs	1573 m	ν(OH)	3382 vs,	ν(C—O)	1283 vs		
VII	1676 s		1608 vs	1573 m	ν(OH)	3363 s,	ν(C—O)	1285 vs		
IX	—		1650 w	1640 vs	ν(OH)	3410 s,	$\nu_{as}(SO_2)$	1325 vs,	$\nu_s(SO_2)$	1165 vs
XII	1760 vs,	1680 s	–[a]	1565 s	ν(C—O)	1163 vs,	1218 vs			
XIII	1765 s,	1685 s	1650 sh	1575 s	ν(C—O)	1164 vs,	1222 vs			
XV	1723 s,	1710 sh	1650 m	1553 vs	ν(C—O)	1250 vs				
XVII	—		1650 w	1650 vs	$\nu_{as}(SO_2)$	1350 vs,	$\nu_s(SO_2)$	1143 m		
XVIII	1687 s,	1646 vs	—[a]	1565 vs[b]	$\nu(NH_2)$	3400 s,	ν(NH)	3158 s		
XIX	1698 sh,	1655 vs	1610 m	1550 vs[b]	$\nu(NH_2)$	3420 s,	ν(NH)	3140 s		
XX	—		1595 m	1525 vs[c]	ν(OH)	3380 m,	ν(NH)	3200 m		
XXIII	1710 m,	1685 s	1610 s	1648 vs[b]	ν(NH)	3100 m				
XXIV	1715 m,	1685 s	1601 s	1670 vs[b]	ν(NH)	3100 m				
XXV	1700 sh,	1685 s	1608 s	1670 vs[b]	ν(NH)	3110 m				

BT — benzothiazole, vs — very strong, s — strong, m — medium, w — weak.
a) Overlapped with the ν(C=O) band; *b*) overlapped with δ(NH) and $\delta(NH_2)$ bands; *c*) overlapped with δ(NH) and δ(OH) bands.

Table 4

Biological activity of 2-R-3-(R'-thioethyl)benzothiazolines and allyl esters of bis[2-(2-R-3-benzothiazolinyl)ethylthio]acetic acids

Compound	Fungicidal $\varrho/(\mu g\ cm^{-3})$/fungistatical $\varrho/(\mu g\ cm^{-3})$	
	Microsporum gypseum	*Trichophyton rubrum*
I	400/>200	400/200
IV	200/50	200/50
VI	>400/400	400/100
VIII	400/200	400/200
IX	200/50	200/50
X	200/50	200/50
XI	200/50	200/50
XII	>400/400	400/100
XIII	>400/400	>400/400
XIV	>400/400	400/200
XV	400/200	200/>30
XVI	400/400	400/200
XVII	400/200	200/>50
XVIII	400/400	400/100
XIX	>400/400	400/100
XXI	400/>100	400/>100
XXII	>400/400	400/100
XXIII	400/400	400/100
XXIV	400/>100	400/>100
XXV	>400/400	400/100
XXVI	>400/400	400/100
XXVII	>400/400	400/>100

S—CO—O groups, respectively. It follows from the above data that the structures of compounds *XII* and *XIII* correspond to disubstituted derivatives.

Similarly, compound *XV* exhibits a structure of disubstituted derivative, which follows from a doubled band of ν(C=O), whereby the maximum at higher wavenumbers corresponds to the O—CO group and the shoulder at lower wavenumbers can be assigned to the S—CO grouping.

The spectra of compounds *XVIII* and *XIX* can be described in analogous way. The wavenumbers of ν(C=O) in the NH—CO—NH_2 group are observed at lower values than those in the CO—O group. The structure of the above-discussed compounds can be proved also in the region $\tilde{\nu} = 3140$—$3420\ cm^{-1}$ by the absorption bands corresponding to stretching vibrations of NH and NH_2 groups, respectively.

In the case of compounds *XXIII*—*XXV* the occurrence of a doublet in the

wavenumber region of the ν(C=O) vibrations and the absence of absorption in the range of NH_2 stretching vibrations demonstrates again the structure of disubstituted derivatives.

The structure of compounds *IX* and *XVII* can be confirmed by two strong absorption bands in the region $\tilde{\nu} = 1325—1350\ cm^{-1}$ and $1143—1165\ cm^{-1}$ belonging to $\nu_{as}(SO_2)$ and $\nu_s(SO_2)$ vibrations, respectively.

In the case of compound *XX* because of the presence of NH_2 and OH groups it is rather complicated to interpret the spectra in the region $\tilde{\nu} = 3200—3400\ cm^{-1}$. It can be supposed, however, that the band at higher wavenumbers corresponds to the stretching vibration of OH group, while that at the lower values can be assigned to the stretching vibration of the NH_2 group.

The presence of the C=N group in all compounds investigated can be proved by the absorption bands of ν(C=N) at $\tilde{\nu} \approx 1600\ cm^{-1}$.

The antibacterial tests (carried out by both the plate-diffusion and dilution methods [13]) showed rather a slight activity of the compounds prepared. On the other hand, most of the compounds investigated possess a satisfactory antifungal activity when tested against *Microsporum gypseum* and *Trichophyton rubrum* using a dilution method (Table 4).

Experimental

Infrared spectra were measured on a 75 IR Specord (Zeiss, Jena) spectrophotometer in the region $\tilde{\nu} = 700—4000\ cm^{-1}$ in paraffin oil suspensions using cells of 0.02 mm thickness. The wavenumber scale of the instrument was calibrated according to standard spectra of polystyrene. The wavenumber values were determined with the accuracy of $\pm 2\ cm^{-1}$.

2,3-Dihydrothiazolo[2,3-*b*]benzothiazolium chloride, 3-(2-mercaptoethyl)-2-benzothiazolinone oxime, 3-(2-mercaptoethyl)-2-benzothiazolinone semicarbazone, and 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone were prepared according to the method described in [1].

3-[2-(Ethoxycarbonylmethylthio)ethyl]-2-benzothiazolinone oxime (II)

3-(2-Mercaptoethyl)-2-benzothiazolinone oxime (22.6 g; 0.10 mol) was dissolved in anhydrous acetone (150 cm^3) under heating and triethylamine (13.0 g; 0.12 mol) was added. Afterwards ethyl ester of monochloroacetic acid (12.2 g; 0.10 mol) was added dropwise under simultaneous stirring. Then the reaction mixture was refluxed for 1 h on a water bath, allowed to stand for 24 h at the room temperature and poured on crushed ice. The crude product was purified with activated carbon and recrystallization.

3-[2-(2-Hydroxyethylthio)ethyl]-2-benzothiazolinone oxime (*I*), 3-[2-(2-chloroethyloxycarbonylmethylthio)ethyl]-2-benzothiazolinone oxime (*III*), 3-[2-(propyloxycarbonylmethylthio)ethyl]-2-benzothiazolinone oxime (*IV*), 3-[2-(isopropyloxycarbonylmethylthio)ethyl]-2-benzothiazolinone oxime (*VII*), and 3-[2-(carboxymethylthio)ethyl]-2-benzothiazolinone oxime (*VIII*) were prepared in the same way.

3-[2-(Methylsulfonylthio)ethyl]-2-benzothiazolinone oxime (IX)

3-(2-Mercaptoethyl)-2-benzothiazolinone oxime (11.3 g; 0.05 mol) was dissolved in anhydrous acetone (150 cm^3) at the room temperature and triethylamine (8.0 g; 0.07 mol) was added. Then a solution of methanesulfonyl chloride (5.7 g; 0.05 mol) in anhydrous acetone (3 cm^3) was added dropwise under stirring. The course of the reaction is exothermic and therefore it is necessary to cool the reaction mixture with glacial water. A precipitate of triethylammonium chloride was formed as a secondary product during the addition of the second reaction component. The reaction mixture was allowed to stand for 1 h and poured on crushed ice. The crude product was isolated, purified with activated carbon and recrystallized.

3-[2-(Ethoxycarbonylthio)ethyl]-2-benzothiazolinone oxime (*V*), 3-[2-(isopropyloxycarbonylthio)ethyl]-2-benzothiazolinone oxime (*VI*), and 3-[2-(benzoylthio)ethyl]-2-benzothiazolinone oxime (*X*) were synthesized in the similar way.

2-Acetyloxyimino-3-[2-(acetylthio)ethyl]benzothiazoline (XI)

3-(2-Mercaptoethyl)-2-benzothiazolinone oxime (11.3 g; 0.05 mol) was dissolved in anhydrous acetone (100 cm^3) under heating. The excess of triethylamine (20.0 g; 0.19 mol) and afterwards a solution of the double quantity excess of acetyl chloride (10.0 g; 0.12 mol) in anhydrous acetone (10 cm^3) was added dropwise to the reaction mixture at the temperature 30—40 °C under simultaneous stirring. Then the reaction mixture was refluxed for 2 h on a water bath, allowed to stand for 24 h and poured on crushed ice. The isolated crude product was purified using activated carbon and crystallization.

The same procedure was used to prepare 2-ethoxycarbonyloxyimino-3-[2-(ethoxycarbonylthio)ethyl]benzothiazoline (*XII*), 2-isopropyloxycarbonyloxyimino-3-[2-(isopropyloxycarbonylthio)ethyl]benzothiazoline (*XIII*), 2-propargyloxycarbonyloxyimino-3-[2--(propargyloxycarbonylthio)ethyl]benzothiazoline (*XIV*), 2-benzoyloxyimino-3-[2-(benzoylthio)ethyl]benzothiazoline (*XV*), 2-benzylcarbonyloxyimino-3-[2-(benzylcarbonylthio)ethyl]benzothiazoline (*XVI*), and 2-phenylsulfonyloxyimino-3-[2-(phenylsulfonylthio)ethyl]benzothiazoline (*XVII*).

2-Semicarbazono-3-[2-(ethoxycarbonylthio)ethyl]benzothiazoline (XVIII)

3-(2-Mercaptoethyl)-2-benzothiazolinone semicarbazone (13.4 g; 0.05 mol) was dissolved in minimal quantity of dimethyl sulfoxide at the room temperature, then anhydrous acetone (80 cm^3) and a slight excess of triethylamine (7.0 g; 0.07 mol) was added. Afterwards ethyl ester of chloroformic acid (5.4 g; 0.05 mol) in anhydrous acetone (3 cm^3) was added dropwise under stirring. A precipitate of triethylammonium chloride originated gradually. The reaction mixture was allowed to stand for 2 h and poured on crushed ice. The isolated crude product was purified with activated carbon and recrystallization.

2-Semicarbazono-3-[2-(ethoxycarbonylmethylthio)ethyl]benzothiazoline (XIX)

The conditions of the synthesis were the same as in the case of compound *XVIII*, with differences that ethyl ester of chloroacetic acid (6.1 g; 0.05 mol) was used as the reaction component and the reaction mixture was refluxed for 1 h.

2-Thiosemicarbazono-3-[2-(2-hydroxyethylthio)ethyl]benzothiazoline (XX)

The preparation was analogous to that of compound *XVIII*, with differences that 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (14.2 g; 0.05 mol) and ethylene chlorohydrin (4.0 g; 0.05 mol) were used as the reaction components. The reaction mixture was refluxed for 1 h on a water bath.

2-Thiosemicarbazono-3-[2-(2-chloroethoxycarbonylmethylthio)-ethyl]benzothiazoline (XXI)

The synthesis was similar to that of compound *XVIII*, however 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (7.8 g; 0.05 mol) and chloroethyl ester of chloroacetic acid were used as the reaction components. The reaction mixture was heated to 50—60 °C for 2 h on a water bath.

2-Ethoxycarbonylthiosemicarbazono-3-[2-(ethoxycarbonylthio)-ethyl]benzothiazoline (XXII)

The procedure of the synthesis was analogous as in the case of compound *XVIII*, with differences that 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (14.2 g; 0.05 mol), triethylamine (14.0 g; 0.13 mol), and ethyl ester of chloroformic acid (10.8 g; 0.10 mol) in a double quantity were used as reaction components.

2-Ethoxycarbonylmethylthiosemicarbazono-3-[2-(ethoxycarbonyl-methylthio)ethyl]benzothiazoline (XXIII)

The synthesis was the same as in the case of compound *XVIII* with differences that 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (14.2 g; 0.05 mol) and a double quantity of triethylamine (14.0 g; 0.13 mol) and ethyl ester of chloroacetic acid (12.2 g; 0.10 mol) were used in the reaction. The reaction mixture was heated for 1 h on a water bath under reflux.

2-Propyloxycarbonylmethylthiosemicarbazono-3-[2-(propyloxy-carbonylmethylthio)ethyl]benzothiazoline (XXIV)

The compound was prepared in the same way as the compound *XVIII*, with a difference that 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (14.2 g; 0.05 mol) and

a double quantity of triethylamine (14.0 g; 0.13 mol) and propyl ester of chloroacetic acid (13.6 g; 0.10 mol) were used. The reaction mixture was heated for 1 h on a water bath under reflux.

2-Isopropyloxycarbonylmethylthiosemicarbazono-3-[2-(isopropyl-oxycarbonylmethylthio)ethyl]benzothiazoline (XXV)

The procedure was the same as in the case of compound *XVIII*, but 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (14.2 g; 0.05 mol) and a double quantity of triethylamine (14.0 g; 0.13 mol) and isopropyl ester of chloroacetic acid (13.6 g; 0.10 mol) were used as the reactive components. The reaction mixture was heated for 1 h to 50—60 °C on a water bath.

Allyl ester of bis[2-(2-thiosemicarbazono-3-benzothiazolinyl)-ethylthio]acetic acid (XXVII)

The preparation was the same as in the case of compound *XVIII*, but 3-(2-mercaptoethyl)-2-benzothiazolinone thiosemicarbazone (14.2 g; 0.05 mol), allyl ester of dichloroacetic acid (8.4 g; 0.05 mol), and a double quantity of triethylamine (14.0 g; 0.13 mol) were used. The reaction mixture was allowed to stand for 1 h.

The compound *XXVI* was synthesized analogously, however 3-(2-mercaptoethyl)-2--benzothiazolinone oxime (11.3 g; 0.05 mol) was used.

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