Synthesis of 3,4-Dialkyl-5-(1-oxo-ethyl)-3*H*-thiazole-2-thiones Derivatives and Their Pesticidal Activity

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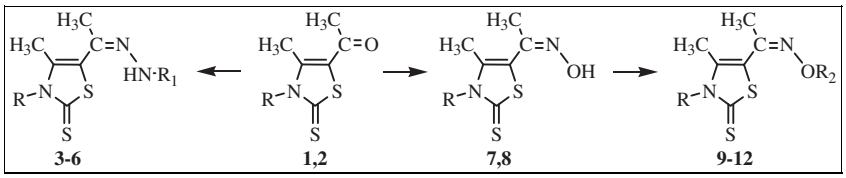

By interaction of N-methyl(ethyl)-dithiocarbamate sodium salt with 3-chloro-pentane-2,4-dion the 1-(3-alkyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanones **1,2** and corresponding oximes **7,8** were synthesized. On the basis of the mentioned compounds hydrazono (**3,4**), ureayl and thioureayl (**5,6**) derivatives, substituted oximes (**9,10**) and azinyl oximes (**11,12**) were obtained. The structures of synthesized compounds were confirmed by proton nuclear magnetic resonance spectroscopy and elemental analysis. The pesticidal activities of synthesized compounds were studied. Some of the synthesized compounds simultaneously have shown growth stimulant and fungicidal activity.

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INTRODUCTION

The chemical means of plants protection, which molecules contain thiazole (thiazoline or thiazolidine) ring, are widely used in agriculture. Among them, there are known herbicides (mefenacet, thiazopir, metabenzthiazuron, fenthiaprop, benazolin, benzthiazuron), fungicides (ethaboxam, thiabendazole, fluthianil, thiadifluor, thifluzamide, metsulfovax, isotianil, octhilinone), insecticides (clothianidin, thiamethoxam, tazimcarb, thiacloprid, imidaclothiz, thiapronil), acaricides (flubenzimine, hexythiazox) and others. At the same time, the search for new pesticides is continuing among the new series of thiazole derivatives [1–9], in particular hydrazones, oximes and their ethers with fungicidal [10,11], herbicidal [12,13] and insecticidal [14] activities. The purpose of the present research was the synthesis of thiazole derivatives on the basis of 1-(3-alkyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanones and study of their pesticidal activity.

RESULTS AND DISCUSSION

The basic 1-(3-alkyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanones **1,2** were synthesized by interaction of N-alkyl-dithiocarbamate sodium salt with 3-chloro-pentane-2,4-dion (Scheme 1). The latter with substituted hidrazines, ureas and thioureas were formed corresponding hydrazones (**3,4**), ureayl-imino and thioureayl-imino derivatives (**5,6**). The interaction of ketones **1,2** with hydroxylamine hydrochloride in alkaline solution lead to 1-(3-alkyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone oximes (**7,8**) formation. When obtained oximes were reacted with dimethyl sulfate, chloro-acetic acid methyl ester, phenyl isocyanate and various azinyl-trimethylammonium chlorides, corresponding O-substituted derivatives (**9–12**) were obtained.

In ^{1}H NMR spectra of oximes (**7,8**) and some of their derivatives (**9,10a**), two groups of absorptions corresponding to *E*-isomers and *Z*-isomers appeared. The *E*/*Z*-isomers ratio depended on steric factor. In unsubstituted oximes (**7,8**), these isomers were in molar ratio of 1:1. When the hydrogen atom was replaced by methyl group (**9,10a**), the amount of *E*-isomer was increased (*Z*/*E* = 1:7). In cases of more steric bulky substituents (**9,10b,c** and **11,12**) in ^{1}H NMR spectra, only signals of *E*-isomers were observed. Probably, the small amounts of *Z*-isomers were lost at purification.

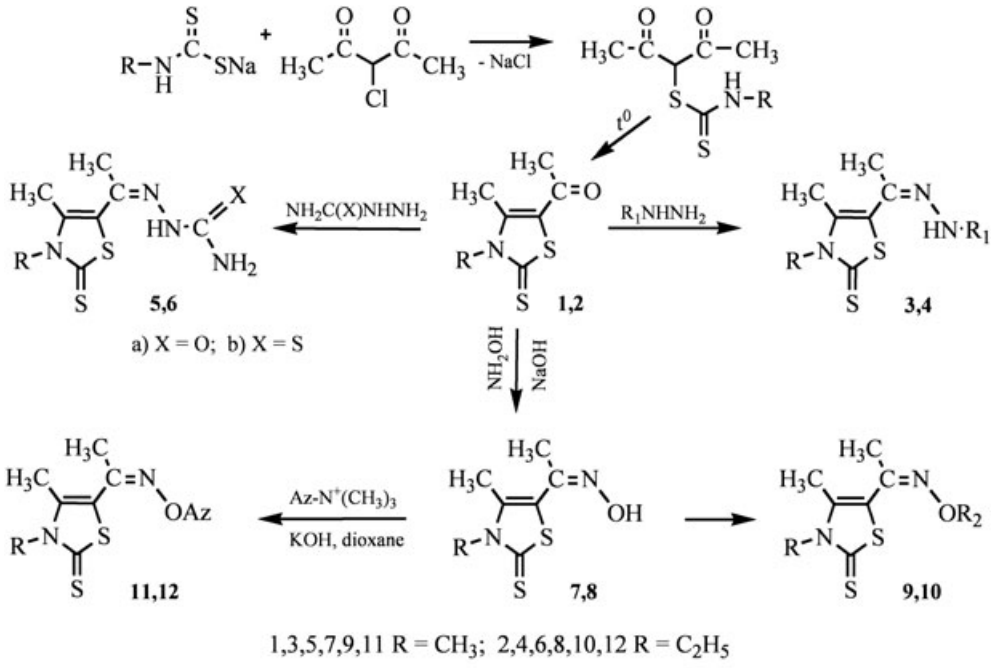
BIOLOGICAL ACTIVITY

In preliminary biological tests, the fungicidal and growth regulatory properties of synthesized compounds were investigated for their aqueous emulsions. As test objects, the monocotyledonous (wheat) and dicotyledonous (French bean) culture plants were taken.

The growth regulatory action of emulsions in concentrations of 25 mg/L and 50 mg/L was investigated on the swelling, germination, growth and survivability of seeds and seedlings of mentioned plants. The activities of these compounds were compared with that of heteroauxin. All investigated substances in varying degrees have shown a growth stimulant activity (Table 1). Some of them surpassed heteroauxin on 10–30%.

The fungicidal activity of emulsions in concentrations of 1000; 100 and 10 mg/L was investigated against the fungi

Scheme 1. Synthesis of 1-(3-4-dialkyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanones and their derivatives.



Tilletia tritici, *Fusarium moniliforme*, *Fusarium oxysporum*, *Helminthosporium sativum*, *Alternaria solani* and *Macrosporium solani*. The most of preparations at concentrations (1000 and 100 mg/L) suppressed *T. tritici* fungi pathogen growth (Table 1). At the lowest concentration (10 mg/L), the inhibitory action, some of them, was in the range of 60–90%. The action of preparations on the other fungi was insignificant.

CONCLUSION

In conclusion, the preliminary screening data indicate that some of the synthesized compounds (**9c**, **11c,e,f,g** and **12e**) have simultaneously high growth stimulant and fungicidal activities. In our opinion, this combination of properties will be useful for pre-sowing seed treatment of grain crops. In addition, the use of preparations with dual action reduces the number of treatments that will have significant economic effect. The aforementioned substances are selected for field trials.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded by Mercury-300MHz spectrometer (Varian, Palo Alto, CA, USA), in the mixture of solvents DMSO-d_6 + CCl_4 (1:3), using tetramethylsilane as internal standard. The reaction course control and individuality of the obtained substances were checked by using the TLC method on UV-254 plates (Silufol, Czech Republic) with the acetone-hexane mixture (2:1) as eluent. Melting points are uncorrected.

General procedure: Synthesis of compounds 1,2. To a solution of methyl(ethyl)-dithiocarbamate sodium salt (0.01 mol) in 10 mL of water, at 0 °C 0.01 mol of 3-chloro-pentane-2, 4-dion was added dropwise with continuous stirring. The reaction mixture was allowed to stand at 20 °C for 24 h, then extracted with benzene and dried over waterless $CaCl_2$. Benzene extract was boiled at reflux for 3 h, benzene was distillated and the residue was processed with hexane and filtered off. Compounds **1,2** were recrystallized from hexane/benzene (2:1).

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone (1). The compound was obtained as yellowish crystals; mp 118–119 °C, yield: 1.5 g (80%). ^{1}H NMR: δ 2.22 (s, 3H, 4-CH_3); 2.30 (s, 3H, C(O)CH_3); 3.65 (s, 3H, 3-CH_3). *Anal*. Calcd for $C_7H_9NOS_2$: C, 44.89; H, 4.84; N, 7.48; S, 34.24. Found: C, 44.69; H, 4.75; N, 7.20; S, 34.02.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone (2). The compound was obtained as yellowish crystals; mp 122–124 °C, yield: 1.33 g (66%). ^{1}H NMR: δ 1.32 (t, J = 7.0, 3H, 3-CH_2CH_3); 2.24 (s, 3H, 4-CH_3); 2.31 (s, 3H, C(O)CH_3); 4.30 (q, J = 7.0, 2H, 3-CH_2CH_3).

General procedure: Synthesis of compounds 3,4. To a suspension of N-substituted hydrazine (0.002 mol) in 5 mL of water, 0.35 mL of 20% HCl was added with continuous stirring. To an obtained solution, 0.002 mol of ketone **1** (or **2**) was added, and reaction mixture was allowed to stand at 20 °C for 24 h. The sediment of hydrazone was filtered off, washed with water and dried in the air. Compounds **3,4** were purified by boiling in benzene.

Table 1

The growth stimulant and fungicidal activity of compounds **5–12**.

	Growth stimulant activity		Fungicidal activity			Growth stimulant activity		Fungicidal activity	
No.	Concen-tration (mg/L)	Activity (%)	Concen-tration (mg/L)	*Tilletia tritici* pathogen growth suppression (%)	No.	Concen-tration (mg/L)	Activity (%)	Concen-tration (mg/L)	*Tilletia tritici* pathogen growth suppression (%)
Hetero-auxin	50	100			**11b**	50	121	1000	100
	25	100				25	110	100	40
								10	8
5a	50	100	1000	100	**11c**	50	121	1000	100
	25	100	100	60		25	90	100	100
			10	5				10	80
5b	50	80	1000	100	**11d**	50	57	1000	100
	25	80	100	60		25	48	100	100
			10	10				10	10
6a	50	10			**11e**	50	110	100	100
	25	0				25	86	100	100
								10	60
6b	50	60			**11f**	50	108	1000	100
	25	20				25	131	100	100
								10	40
7	50	88	1000	100	**11g**	50	80	1000	100
	25	87	100	100		25	82	100	100
			10	40				10	90
9a	50	110			**11h**	50	78	1000	100
	25	81				25	84	100	60
								10	25
9b									
	50	37	1000	100	**12b**	50	90	1000	100
	25	115	100	100		25	90	100	90
			10	10				10	6
9c	50	80	1000	100	**12c**	50	49	1000	100
	25	100	100	100		25	74	100	100
			10	80				10	40
10c	50	100			**12e**	50	123	1000	100
	25	90				25	81	100	100
								10	70
11a	50	90			**12f**	50	126	1000	100
	25	65				25	44	100	70
								10	5

3,4-Dimethyl-5-[1-(benzene-sulfonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (3a). The compound was obtained as yellow crystals; mp 222–224 °C (with decomposition), yield: 0.6 g (88%). ^{1}H NMR: δ 2.11 (3H, s, 4-CH_3); 2.45 (s, 3H, N=C–CH_3); 3.61 (s, 3H, 3-CH_3); 7.40–7.85 (m, 4H, C_6H_5); 10.45 (s, 1H, NH). *Anal*. Calcd for $C_{13}H_{15}N_3O_2S_3$: C, 45.73; H, 4.43; N, 12.31; S, 28.17. Found: C, 45.61; H, 4.49; N, 12.03; S, 28.39.

3,4-Dimethyl-5-[1-(p-tolyl-sulfonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (3b). The compound was obtained as yellow crystals; mp 216–218 °C (with decomposition), yield: 0.6 g (84.5%). ^{1}H NMR: δ 2.11 (3H, s, 4-CH_3); 2.34 (s, 3H, CH_3-tolyl); 2.44 (s, 3H, N=C–CH_3); 3.60 (s, 3H, 3-CH_3); 7.33 and 7.76 (d,d, 4H, C_6H_4); 10.47 (s, 1H, NH). *Anal*. Calcd for $C_{14}H_{17}N_3O_2S_3$: C, 47.30; H, 4.82; N, 11.82; S, 27.06. Found: C, 47.18; H, 4.70; N, 11.58; S, 27.24.

3,4-Dimethyl-5-[1-(2-benzene-sulfonamido-4-methyl-thiazol-5-yl-carbonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (3c). The compound was obtained as yellow crystals; mp 236–238 °C (with decomposition), yield: 0.8 g (83%). ^{1}H NMR: δ 2.27 (s, 3H, 4-CH_3); 2.48 (s, 3H, N=C–CH_3); 2.55 (s, 3H, 4′-CH_3); 3.71 (s, 3H, 3-CH_3); 7.30–7.80 (m, 4H, C_6H_5); 10.92 (s, 1H, NH); 12.75 (b.s, 1H, NH). *Anal*. Calcd for $C_{18}H_{19}N_5O_3S_4$: C, 44.89; H, 3.98; N, 14.54; S, 26.63. Found: C, 44.97; H, 4.00; N, 14.72; S, 26.51.

3,4-Dimethyl-5-[1-(2-p-tolyl-sulfonamido-4-methyl-thiazol-5-yl-carbonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (3d). The compound was obtained as yellow crystals; mp 260–261 °C (with decomposition), yield: 0.8 g (81%). ^{1}H NMR: δ 2.25 (s, 3H, 4-CH_3); 2.41 (s, 3H, CH_3-tolyl); 2.50 (s, 3H, N=C–CH_3); 2.57 (s, 3H, 4′-CH_3); 3.73 (s, 3H, 3-CH_3); 7.28 and 7.65 (d,d, 4H, C_6H_4); 10.88 (s, 1H, NH); 12.89 (b.s, 1H, NH). *Anal*. Calcd for $C_{19}H_{21}N_5O_3S_4$: C, 46.04; H, 4.27; N, 14.13; S, 25.88. Found: C, 46.21; H, 4.20; N, 14.33; S, 25.63.

3-Ethyl-4-methyl-5-[1-(benzene-sulfonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (4a). The compound was obtained as yellow crystals; mp 180–182 °C (toluene), yield: 0.53 g (75%).

^{1}H NMR: δ 1.32 (t, J = 7.1, 3H, 3-CH_2CH_3); 2.13 (s, 3H, 4-CH_3); 2.43 (s, 3H, N=C–CH_3); 4.28 (q, J = 7.1, 2H, 3-CH_2CH_3); 7.40–7.82 (m, 4H, C_6H_5); 10.37 (s, 1H, NH). *Anal*. Calcd for $C_{14}H_{17}N_3O_2S_3$: C, 47.30; H, 4.82; N, 11.82; S, 27.06. Found: C, 47.12; H, 4.73; N, 11.64; S, 26.81.

3-Ethyl-4-methyl-5-[1-(p-tolyl-sulfonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (4b). The compound was obtained as yellow crystals; mp 190–192 °C (toluene), yield: 0.0.60 g (81%). ^{1}H NMR: δ 1.33 (t, J = 7.1, 3H, 3-CH_2CH_3); 2.10 (s, 3H, 4-CH_3); 2.35 (s, 3H, CH_3-tolyl); 2.46 (s, 3H, N=C–CH_3); 4.30 (q, J = 7.1, 2H, 3-CH_2CH_3); 7.30 and 7.75 (d,d, 4H, C_6H_4); 10.52 (s, 1H, NH). *Anal*. Calcd for $C_{15}H_{19}N_3O_2S_3$: C, 48.75; H, 5.18; N, 11.37; S, 26.03. Found: C, 48.89; H, 5.28; N, 11.16; S, 26.20.

3-Ethyl-4-methyl-5-[1-(2-p-tolyl-sulfonamido-4-methyl-thiazol-5-yl-carbonyl-hydrazono)-ethyl]-3H-thiazole-2-thione (4d). The compound was obtained as yellow crystals; mp 244–246 °C (toluene), yield: 0.75 g (74%). ^{1}H NMR: δ 1.33 (t, J = 7.1, 3H, 3-CH_2CH_3); 2.23 (s, 3H, 4-CH_3); 2.40 (s, 3H, CH_3-tolyl); 2.53 (s, 3H, N=C–CH_3); 2.56 (s, 3H, 4′-CH_3); 4.28 (q, J = 7.1, 2H, 3-CH_2CH_3); 7.30 and 7.68 (d,d, 4H, C_6H_4); 10.75 (s, 1H, NH); 12.75 (b.s, 1H, NH). *Anal*. Calcd for $C_{20}H_{23}N_5O_3S_4$: C, 47.13; H, 4.55; N, 13.74; S, 25.16. Found: C, 47.02; H, 4.41; N, 13.45; S, 25.28.

General procedure: Synthesis of compounds 5,6. A suspension of semicarbazide (or thiosemicarbazide) hydrochloride (0.005 mol) and ketone **1** (or **2**) (0.005 mol) in 10 mL of water was boiled with reflux for 4–5 h. The mixture was cooled and filtered off, and the residue was washed with water and dried in the air. Compounds **5,6** were purified by boiling in benzene.

3,4-Dimethyl-5-[1-(urea-1-yl-imino)-ethyl]-3H-thiazole-2-thione (5a). The compound was obtained as white crystals; mp 285–287 °C, yield: 0.8 g (66%). ^{1}H NMR: δ 2.16 (s, 3H, 4-CH_3); 2.44 (s, 3H, N=C–CH_3); 3.62 (s, 3H, 3-CH_3); 6.26 (b.s, 2H, NH_2); 9.52 (s, 1H, NH). *Anal*. Calcd for $C_8H_{12}N_4OS_2$: C, 39.33; H, 4.95; N, 22.93; S, 26.25. Found: C, 39.19; H, 4.81; N, 22.68; S, 26.09.

3,4-Dimethyl-5-[1-(thiourea-1-yl-imino)-ethyl]-3H-thiazole-2-thione (5b). The compound was obtained as white crystals; mp 240–242 °C, yield: 1.15 g (88.5%). ^{1}H NMR: δ 2.17 (s, 3H, 4-CH_3); 2.45 (s, 3H, N=C–CH_3); 3.60 (s, 3H, 3-CH_3); 5.12 (b.s, 2H, NH_2); 8.63 (s, 1H, NH). *Anal*. Calcd for $C_8H_{12}N_4S_3$: C, 36.90; H, 4.64; N, 21.52; S, 36.94. Found: C, 36.71; H, 4.54; N, 21.29; S, 36.73.

3-Ethyl-4-methyl-5-[1-(urea-1-yl-imino)-ethyl]-3H-thiazole-2-thione (6a). The compound was obtained as white crystals; mp 258–260 °C, yield: 1.04 g (80%). ^{1}H NMR: δ 1.30 (t, J = 7.1, 3H, 3-CH_2CH_3); 2.16 (s, 3H, 4-CH_3); 2.44 (s, 3H, N=C–CH_3); 4.30 (q, J = 7.1, 2H, 3-CH_2CH_3); 6.28 (b.s, 2H, NH_2); 9.62 (s, 1H, NH). *Anal*. Calcd for $C_9H_{14}N_4OS_2$: C, 41.84; H, 5.46; N, 21.69; S, 24.82. Found: C, 41.61; H, 5.32; N, 21.30; S, 24.49.

3-Ethyl-4-methyl-5-[1-(thiourea-1-yl-imino)-ethyl]-3H-thiazole-2-thione (6b). The compound was obtained as white crystals; mp 218–220 °C, yield: 1.1 g (80%). ^{1}H NMR: δ 1.29 (t, J = 7.0, 3H, 3-CH_2CH_3); 2.17 (s, 3H, 4-CH_3); 2.45 (s, 3H, N=C–CH_3); 4.30 (q, J = 7.0, 3H, 3-CH_2CH_3); 5.20 (b.s, 2H, NH_2); 8.59 (s, 1H, NH).). *Anal*. Calcd for $C_9H_{14}N_4S_3$: C, 39.39; H, 5.14; N, 20.42; S, 35.05. Found: C, 39.18; H, 5.06; N, 20.21; S, 34.79.

General procedure: Synthesis of compounds 7,8. To a solution of NaOH (0.014 mol) in 5 mL of water, at 0 °C 0.014 mol of hydroxylamine hydrochloride was added by portions with continuous stirring and then 0.01 mol of ketone **1** (or **2**). The reaction mixture was homogenized with 10 mL of ethanol and allowed to stand at 20 °C for 24 h. The mixture was heated at $32#50–60 °C for 3 h, cooled, processed with 15 mL of water and filtered off. Compounds **7,8** were purified by boiling in heptane.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone oxime (7). The compound was obtained as white crystals; mp 208–210 °C, yield: 1.62 g (80%). ^{1}H NMR: δ 2.12 and 2.15 (s,s, 3H, 4-CH_3, 1:1); 2.28 and 2.46 (s,s, 3H, N=C–CH_3, 1:1); 3.64 (s, 3H, 3-CH_3); 11.15 and 11.29 (s,s, 1H, N-OH, 1:1). *Anal*. Calcd for $C_7H_{10}N_2OS_2$: C, 41.56; H, 4.98; N, 13.85; S, 31.70. Found: C, 41.65; H, 4.88; N, 13.66; S, 31.58.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone oxime (8). The compound was obtained as white crystals; mp 170–172 °C, yield: 1.6 g (74%). ^{1}H NMR: δ 1.28 (t, J = 7.0, 3H, 3-CH_2CH_3); 2.14 and 2.17 (s,s, 3H, 4-CH_3, 1:1); 2.28 and 2.45 (s,s, 3H, N=C–CH_3, 1:1); 4.35 (q, J = 7.0, 3H, 3-CH_2CH_3); 11.05 and 11.18 (s,s, 1H, N-OH, 1:1). *Anal.* Calcd for $C_8H_{12}N_2OS_2$: C, 44.42; H, 5.59; N, 12.95; S, 29.65. Found: C, 44.22; H, 5.41; N, 12.72; S, 29.51.

General procedure: Synthesis of compounds 9a,10a. To a solution of KOH (0.01 mol) in 7 mL of water, at 0–5 °C 0.01 mol of oxime **7** (or **8**) was added by portions with continuous stirring, then 0.01 mol of dimethyl sulfate. The mixture was stirred at 20 °C for 3–4 h and allowed to stand at 20 °C for 24 h. The residue was filtered off, washed with water and dried in the air.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-methyl-oxime (9a). The compound was obtained as white crystals; mp 102–104 °C (toluene), yield: 1.77 g (82%). ^{1}H NMR: δ 2.12 and 2.13 (s,s, 3H, 4-CH_3, 1:7); 2.25 and 2.47 (s,s, 3H, N=C–CH_3, 1:7); 3.65 (s, 3H, 3-CH_3); 3.85 and 3.91 (s,s, 3H, OCH_3, 1:7). *Anal*. Calcd for $C_8H_{12}N_2OS_2$: C, 44.42; H, 5.59; N, 12.95; S, 29.65. Found: C, 44.59; H, 5.68; N, 12.75; S, 29.31.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-methyl-oxime (10a). The compound was obtained as white crystals; mp 82–84 °C (toluene), yield: 1.77 g (77%). ^{1}H NMR: δ 1.30 (t, J = 7.0, 3H, 3-CH_2CH_3); 2.12 and 2.13 (s,s, 3H, 4-CH_3, 1:7); 2.25 and 2.47 (s,s, 3H, N=C–CH_3, 1:7); 3.85 and 3.91 (s,s, 3H, OCH_3, 1:7); 4.31 (q, J = 7.0, 3H, 3-CH_2CH_3). *Anal.* Calcd for $C_9H_{14}N_2OS_2$: C, 46.93; H, 6.13; N, 12.16; S, 27.84. Found: C, 47.14; H, 6.06; N, 12.38; S, 27.56.

[1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethylid-eneaminooxy]-acetic acid methyl ester (9b). To a suspension of KOH (0.56 g, 0.01 mol) in 7 mL of dimethylformamide at 0–5 °C, 2.02 g (0.01 mol) of oxime (**7**) was added by portions with continuous stirring. After the salt formation, 0.9 mL (ρ=1.23 g/mL, 0.01 mol) of chloro-acetic acid methyl ester was added dropwise, and the mixture allowed to stand at 20 °C for 24 h. The suspension was steamed; the residue was washed with water and filtered off. The compound was obtained as white crystals; mp 96–98 °C (processed with ethanol), yield: 1.97 g (72%). ^{1}H NMR: δ 2.21 (s, 3H, 4-CH_3); 2.46 (s, 3H, N=C–CH_3); 3.65 (s, 3H, 3-CH_3); 3.72 (s, 3H, OCH_3); 4.65 (s, 2H, OCH_2). *Anal*. Calcd for $C_{10}H_{14}N_2O_3S_2$: C, 43.78; H, 5.14; N, 10.21; S, 23.37. Found: C, 43.61; H, 5.05; N, 10.39; S, 23.11.

General procedure: Synthesis of compounds 9c,10c. The mixture of oxime **7** (or **8**) (0.01 mol), and phenyl isocyanate (0.01 mol) in 10 mL of absolute toluene in the presence of catalytic amounts of pyridine was boiled for 3 h. After cooling, the mixture was filtered off, and the residue was recrystallized from 50% ethanol.

3,4-Dimethyl-5-[1-(N-phenyl-formamide-1-yl-oxime)-ethyl]-3H-thiazole-2-thione (9c). The compound was obtained as yellow crystals; mp 188–189 °C (with decomposition), yield: 2.4 g (75%). ^{1}H NMR: δ 2.34 (s, 3H, 4-CH_3); 2.60 (s, 3H, N=C–CH_3); 3.69 (s, 3H, 3-CH_3); 6.90–7.55 (m, 5H, C_6H_5); 9.48 (s, 1H, NH). *Anal*. Calcd for $C_{14}H_{15}N_3O_2S_2$: C, 52.32; H, 4.70; N, 13.07; S, 19.95. Found: C, 52.12; H, 4.57; N, 13.21; S, 19.69.

3-Ethyl-4-methyl-5-[1-(N-phenyl-formamide-1-yl-oxime)-ethyl]-3H-thiazole-2-thione (10c). The compound was obtained as white crystals; mp 130–132 °C (with decomposition), yield: 2.5 g (75%). ^{1}H NMR: δ 1.28 (t, J = 7.0, 3H, 3-CH_2CH_3); 2.35 (s, 3H, 4-CH_3); 2.62 (s, 3H, N=C–CH_3); 4.31 (q, J = 7.0, 3H, 3-CH_2CH_3); 6.92–7.56 (m, 5H, C_6H_5); 9.39 (s, 1H, NH). *Anal*. Calcd for $C_{15}H_{17}N_3O_2S_2$: C, 53.71; H, 5.11; N, 12.53; S, 19.12. Found: C, 53.62; H, 5.03; N, 12.31; S, 18.81.

General procedure: Synthesis of compounds 11,12. To a suspension of KOH (0.01 mol) in 10 mL of dioxane, 0.01 mol of oxime **7** (or **8**) was added with continuous stirring. When salt formation was completed, 0.01 mol of corresponding azinyl-trimethylammonium chloride was added by portions. The reaction mixture was stirred at 20 °C, then at 50–60 °C for 3 h for trimethylamine moving off. The suspension was steamed, processed with water, and the sediment of compounds **11,12** was filtered off.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4,6-bis-dimethyl-amino-[1,3,5]triazin-2-yl)-oxime (11a). The compound was obtained as white crystals; mp 213–215 °C (processed with ether), yield: 2.4 g (66%). ^{1}H NMR: δ 2.34 (s, 3H, 4-CH_3); 2.67 (s, 3H, N=C–CH_3); 3.14 [s, 12H, N(CH_3)$_4$]; 3.68 (s, 3H, 3-CH_3). *Anal*. Calcd for $C_{14}H_{21}N_7OS_2$: C, 45.76; H, 5.76; N, 26.68; S, 17.45. Found: C, 45.49; H, 5.61; N, 26.42; S, 17.21.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-dimethyl-amino-6-pyrrolidin-1-yl-[1,3,5]triazin-2-yl)-oxime (11b). The compound was obtained as white crystals; mp 195–196 °C (toluene), yield: 2.95 g (75%). ^{1}H NMR: δ 1.90 (b.m., 4H, CH_2CH_2-pyrrol.); 2.33 (s, 3H, 4-CH_3); 2.67 (s, 3H, N=C–CH_3); 3.13 [s, 6H, N(CH_3)$_2$]; 3.53 [b.m, 4H, N(CH_2)$_2$-pyrrol.]; 3.68 (s, 3H, 3-CH_3). *Anal*. Calcd for $C_{16}H_{23}N_7OS_2$: C, 48.83; H, 5.89; N, 24.91; S, 16.30. Found: C, 48.98; H, 5.97; N, 24.71; S, 16.12.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-ethyl-amino-6-pyrrolidin-1-yl-[1,3,5]triazin-2-yl)-oxime (11c). The compound was obtained as white crystals; mp 170–172 °C (processed with ether), yield: 3.14 g (80%). ^{1}H NMR: δ 1.16 (t, J_1 = 7.1, 3H, CH_3CH_2N); 1.94 (b.m., 4H, CH_2CH_2-pyrrol.); 2.32 (s, 3H, 4-CH_3); 2.62 (s, 3H, N=C–CH_3); 3.34 (m, J_1 = 7.1, J_2 = 5.2, 2H, NCH_2CH_3); 3.52 [b.m, 4H, N(CH_2)$_2$-pyrrol.]; 3.69 (s, 3H, 3-CH_3); 6.73 and 6.90 (t,t, J_2 = 5.2, 1H, NH). *Anal*. Calcd for $C_{16}H_{23}N_7OS_2$: C, 48.83; H, 5.89; N, 24.91; S, 16.30. Found: C, 48.70; H, 5.71; N, 24.61; S, 16.08.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-ethyl-amino-6-piperidin-1-yl-[1,3,5]triazin-2-yl)-oxime (11d). The compound was obtained as white crystals; mp 158–160 °C (processed with ether), yield: 3.3 g (81%). ^{1}H NMR: δ 1.18 (t, J_1 = 7.1, 3H, CH_3CH_2N); 1.89 [b.m., 6H, (CH_2)$_3$-piper.]; 2.32 (s, 3H, 4-CH_3); 2.65 (s,s, 3H, N=C–CH_3); 3.36 (m, J_1 = 7.1, J_2 = 5.2, 2H, NCH_2CH_3); 3.52 [b.m, 4H, N(CH_2)$_2$-piper.]; 3.69 (s, 3H, 3-CH_3); 6.70 and 6.85 (t, J_2 = 5.2, 1H, NH). *Anal*. Calcd for $C_{17}H_{25}N_7OS_2$: C, 50.10; H, 6.18; N, 24.06; S, 15.74. Found: C, 50.21; H, 6.03; N, 23.79; S, 15.61.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-amino-6-diisobutyl-amino-1-yl-[1,3,5]triazin-2-yl)-oxime (11e). The compound was obtained as white crystals; mp 176–178 °C (hexane/benzene, 1:1), yield: 2.11 g (50%). ^{1}H NMR: δ 1.02 [m, 12H, (CH_3)$_4$-isobut.]; 2.09 [m, 2H, (CH)$_2$-isobut.]; 2.30 (s, 3H, 4-CH_3); 2.62 (s, 3H, N=C–CH_3); 3.42 [m, 4H, (NCH_2)$_2$]; 3.70 (s, 3H, 3-CH_3); 6.12 (s, 2H, NH_2). *Anal*. Calcd for $C_{18}H_{29}N_7OS_2$: C, 51.04; H, 6.90; N, 23.15; S, 15.14. Found: C, 51.18; H, 6.74; N, 22.85; S, 14.87.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(2-amino-6-methyl-pyrimidin-4-yl)-oxime (11f). The compound was obtained as yellow crystals; mp 203–204 °C (processed with ethanol), yield: 2.3 g (74%). ^{1}H NMR: δ 2.26 (s, 3H, CH_3-pyrim.); 2.40 (s, 3H, 4-CH_3); 2.58 (s, 3H, N=C–CH_3); 3.69 (s, 3H, 3-CH_3); 6.06 (s, 2H, NH_2); 6.32 (s, 1H, CH-pyrim.). *Anal*. Calcd for $C_{12}H_{15}N_5OS_2$: C, 46.58; H, 4.89; N, 22.63; S, 20.73. Found: C, 46.70; H, 4.99; N, 22.47; S, 20.51.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-methoxy-6-methyl-pyrimidin-2-yl)-oxime (11g). The compound was obtained as white crystals; mp 170–172 °C (processed with ethanol), yield: 1.94 g (60%). ^{1}H NMR: δ 2.37 (s, 3H, CH_3-pyrim.); 2.38 (s, 3H, 4-CH_3); 2.66 (s, 3H, N=C–CH_3); 3.69 (s, 3H, 3-CH_3); 3.95 (s, 3H, OCH_3); 6.35 (s, 1H, CH-pyrim.). *Anal*. Calcd for $C_{13}H_{16}N_4O_2S_2$: C, 48.13; H, 4.97; N, 17.27; S, 19.77. Found: C, 48.01; H, 4.85; N, 17.00; S, 19.51.

1-(3,4-Dimethyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-methyl-6-pirrolidin-1-yl-pyrimidin-2-yl)-oxime (11h). The compound was obtained as white crystals; mp 176–178 °C (processed with ethanol), yield: 2.8 g (77%). ^{1}H NMR: δ 2.01 (b.m, 4H, CH_2CH_2-pyrrol.); 2.26 (s, 3H, CH_3-pyrim.); 2.34 (s, 3H, 4-CH_3); 2.66 (s, 3H, N=C–CH_3); 3.45 [b.m, 4H, N(CH_2)$_2$-pyrrol.]; 3.69 (s, 3H, 3-CH_3); 5.94 (s, 1H, CH-pyrim.). *Anal*. Calcd for $C_{16}H_{21}N_5OS_2$: C, 52.87; H, 5.82; N, 19.27; S, 17.64. Found: C, 52.87; H, 5.82; N, 19.27; S, 17.64.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-dimethyl-amino-6-pyrrolidin-1-yl-[1,3,5]triazin-2-yl)-oxime (12b). The compound was obtained as white crystals; mp 150–152 °C (processed with ethanol), yield: 3.3 g (82%). ^{1}H NMR: δ 1.35 (t, J = 7.0, 3H, 3-CH_2CH_3); 1.97 (b.m., 4H, CH_2CH_2-pyrrol.); 2.34 (s, 3H, 4-CH_3); 2.66 (s, 3H, N=C–CH_3); 3.13 [s, 6H, N(CH_3)$_2$]; 3.55 [b.m, 4H, N(CH_2)$_2$-pyrrol.]; 4.33 (q, J = 7.0, 3-CH_2CH_3). *Anal*. Calcd for $C_{17}H_{25}N_7OS_2$: C, 50.10; H, 6.18; N, 24.06; S, 15.74. Found: C, 50.22; H, 6.27; N, 24.31; S, 15.98.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-ethyl-amino-6-pyrrolidin-1-yl-[1,3,5]triazin-2-yl)-oxime 3-ethyl-4-methyl-5-[1-(4-ethylamino-6-pyrrolidin-1-yl-[1,3,5]triazin-2-yl-oxime)-ethyl]-3H-thiazole-2-thione (12c). The compound was obtained as white crystals; mp 188–189 °C (processed with ethanol), yield: 2.9 g (71%). ^{1}H NMR: δ 1.16 (t, J_1 = 7.1, 3H, CH_3CH_2NH); 1.34 (t, J = 7.0, 3H, 3-CH_2CH_3); 1.95 (b.m., 4H, CH_2CH_2-pyrrol.); 2.32 (s, 3H, 4-CH_3); 2.65 (s, 3H, N=C–CH_3); 3.34 (m, J_1 = 7.1, J_2 = 5.1, 2H, HNCH_2CH_3); 3.51 (b.m, 4H, N(CH_2)$_2$-pyrrol.); 4.31 (m, J = 7.0, 2H, 3-CH_2CH_3); 6.73 and 6.88 (t,t, J_2 = 5.1, 1H, NH). *Anal*. Calcd for $C_{17}H_{25}N_7OS_2$: C, 50.10; H, 6.18; N, 24.06; S, 15.74. Found: C, 49.95; H, 6.06; N, 24.24; S, 15.92.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(4-amino-6-diisobutyl-amino-1-yl-[1,3,5]triazin-2-yl)-oxime (12e). The compound was obtained as white crystals; mp 165–166 °C (benzene), yield: 2.97 g (68%). ^{1}H NMR: δ 1.04 [m, 12H, (CH_3)$_4$-isobut.]; 1.34 (t, J = 7.0, 3H, 3-CH_2CH_3);

2.10 [m, 2H, $(CH)_2$-isobut.]; 2.28 (s, 3H, 4-CH_3); 2.66 (s, 3H, N=C–CH_3); 3.42 [m, 4H, $(NCH_2)_2$-isobut.]; 4.30 (q, $J = 7.0$, 3-CH_2CH_3); 6.05 (s, 2H, NH_2). *Anal*. Calcd for $C_{19}H_{31}N_7OS_2$: C, 52.15; H, 7.14; N, 22.40; S, 14.65. Found: C, 52.01; H, 7.08; N, 22.22; S, 14.36.

1-(3-Ethyl-4-methyl-2-thioxo-2,3-dihydro-thiazol-5-yl)-ethanone O-(2-amino-6-methyl-pyrimidin-4-yl)-oxime (12f). The compound was obtained as yellow crystals; mp 174–176 °C (benzene), yield: 2.0 g (61%). ^{1}H NMR: δ 1.32 (t, $J = 7.0$, 3H, 3-CH_2CH_3); 2.28 (s, 3H, 4-CH_3); 2.42 (s, 3H, CH_3-pyrim.); 2.60 (s, 3H, N=C–CH_3); 4.30 (q, $J = 7.0$, 3-CH_2CH_3); 6.15 (s, 2H, NH_2); 6.35 (s, 1H, CH-pyrim.). *Anal*. Calcd for $C_{13}H_{17}N_5OS_2$: C, 48.27; H, 5.30; N, 21.65; S, 19.83. Found: C, 48.11; H, 5.25; N, 21.39; S, 19.60.

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