The synthesis of 5*H*-thiazolo[2,3-*c*][1,2,4]triazine derivatives and substituted 3-(2-acylvinylthio)-1,2,4-triazin-5-ones from 6-methyl-3-thioxo-1,2,4-triazin-5-one, 1-acyl-2-bromoacetylenes, and α-acetylenic ketones. X-ray study of 3-benzoyl-6-methyl-5*H*-thiazolo[2,3-*c*][1,2,4]triazin-5-one

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3-Acyl-6-methyl-5*H*-thiazolo[2,3-*c*][1,2,4]triazines were synthesized by reaction of 1-acyl-2-bromoacetylenes with 6-methyl-3-thioxo-1,2,4-triazin-5-one in methanol in the presence of triethylamine at 20 °C. The structure of 3-benzoyl-6-methyl-5*H*-thiazolo[2,3-*c*][1,2,4]triazine was established by X-ray structural analysis. Substituted 3-(2-acetylvinylthio)-1,2,4-triazin-5-ones were obtained by the reaction of α-acetylenic ketones with 6-methyl-3-thioxo-1,2,4-triazin-5-one under the same conditions. The structures of the new compounds were confirmed by IR, ^{1}H, and ^{13}C NMR spectroscopy.

Key words: 1-acyl-2-bromoacetylenes; α-acetylenic ketones; 3-acyl-6-methyl-5*H*-thiazolo[2,3-*c*][1,2,4]triazines; substituted 3-(2-acylvinylthio)-1,2,4-triazin-5-ones; intramolecular cyclization; X-ray structural analysis.

Reactions of α-acetylenic ketones with cyclic thioureas and heterocyclic compounds containing a thiourea moiety have been poorly studied. It is known that imidazolidine-2-thione reacts with benzoylacetylene to give bis(ketovinyl) sulfide in a 50% yield, when heated in MeOH, and 2-benzoylvinylthioimidazoline (yield 78%) in MeCN at 20 °C.[1] 2-(2-Acetylvinylthio)benzimidazoles were obtained in 68—96% yields by the reaction of substituted α-acetylenic ketones and dibenzoylacetylene with benzimidazole-2-thione in MeOH and MeCN.[2] Substituted 3-(2-benzoylvinylthio)-1,2,4-triazoles and substituted 3-(2-benzoylvinylthio)-3-(2-benzoylvinyl)-1,2,4-triazoles were synthesized by heating 1,2,4-triazole-3-thione with benzoylacetylene in EtOH in the presence of Et_3N.[3]

We studied the reaction between equimolar amounts of 6-methyl-3-thioxo-1,2,4-triazin-5-one (**1**) and 1-acyl-2-bromoacetylenes (**2a,b**) in MeOH at 20 °C in the presence of Et_3N (Scheme 1). Apparently, in the first stage intermediate acylethynyl sulfides **3a,b** or **4a,b** form as a result of elimination of HBr, which, under the conditions chosen by us, easily undergo intramolecular cyclization to give substituted thiazolo[2,3-*c*]- (**5a,b**) or thiazolo[3,2-*b*][1,2,4]triazines (**6a,b**). An analysis of the ^{1}H and ^{13}C NMR spectra did not allow us to choose between structures **5a,b** and **6a,b**, but it was established by X-ray structural analysis that the product of the reaction of compound **1** with ketone **2a** has structure **5a**.

The heterocyclic system of the molecule **5a** is planar: the deviations of the atoms from the middle plane do not exceed 0.03 Å. Atoms O(1), C(9), and C(16) deviate from the plane of the heterocyclic system by 0.07, 0.15, and 0.04 Å, respectively.

The angle between the benzoyl group and the heterocyclic system is equal to 95.1°, *i.e.*, there is no conjugation between the π-systems of these fragments of the molecule **5a**. This is also evidenced by lengthening of the C(3)—C(9) bond to 1.524(4) Å (the average statistical length of the C_{sp^2}—C_{sp^2} bonds is 1.465(18) Å) (Fig. 1).[4]

The increase in the C(3)—C(9)—C(10) bond angle to 119.5(3)° (the usual value is 114—115°) is probably due to the shortened intramolecular contact C(3)...H(15) which is equal to 2.57(1) Å (the double geometric mean of the van der Waals radii of carbon and hydrogen atoms is 2.82 Å[5]).

Figure 2 displays the projection of a fragment of the crystal structure of compound **4a** along the *Z* axis. There is a shortened distance N(7)...S(1) equal to 3.055(3) Å between the molecules which are converted with each other by helical axis 2_1 (the double geometric mean of the van der Waals radii of sulfur and nitrogen atoms is

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† Deceased.

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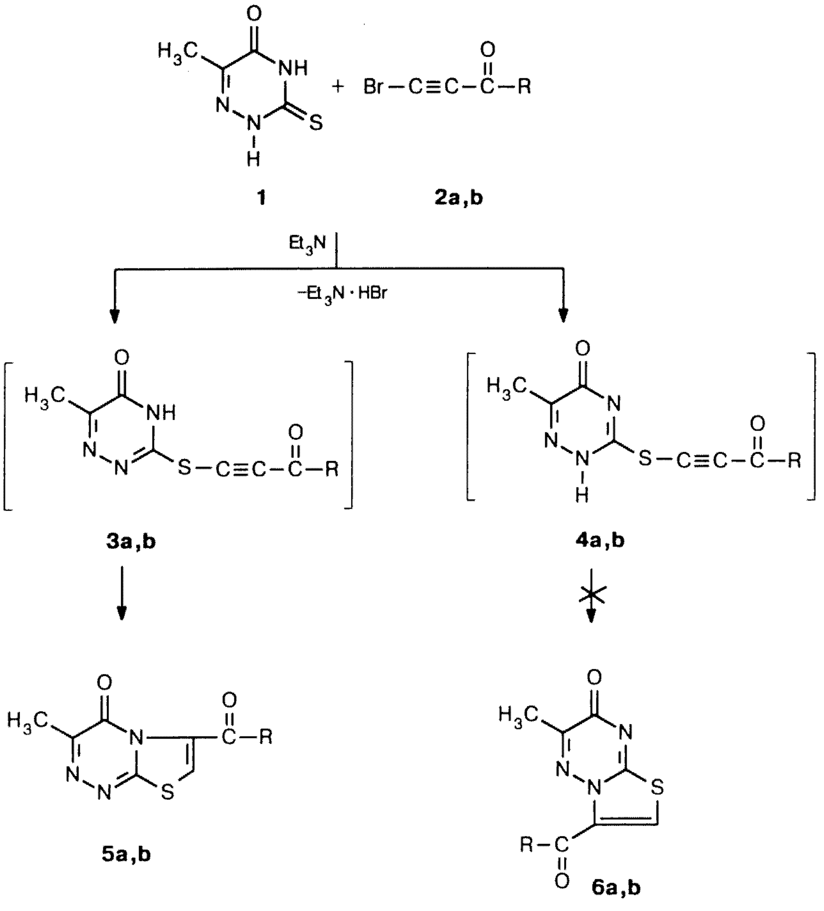
Scheme 1



R = Ph (**a**); 2-thienyl (**b**)

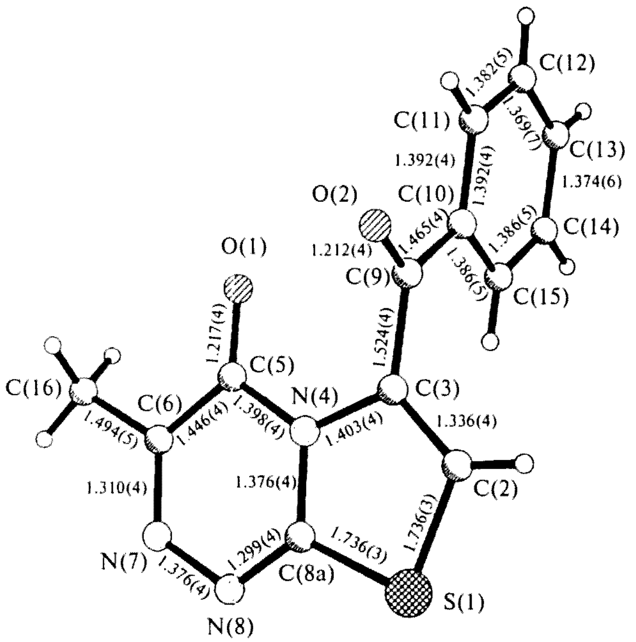


Fig. 1. Perspective views of the molecule **5a** with atomic numbering and bond lengths (Å).

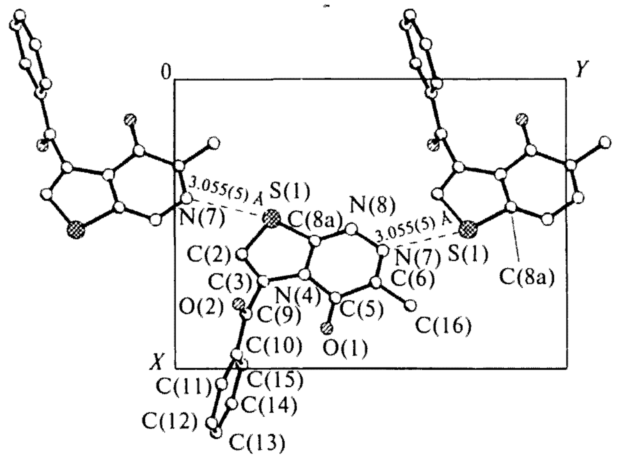
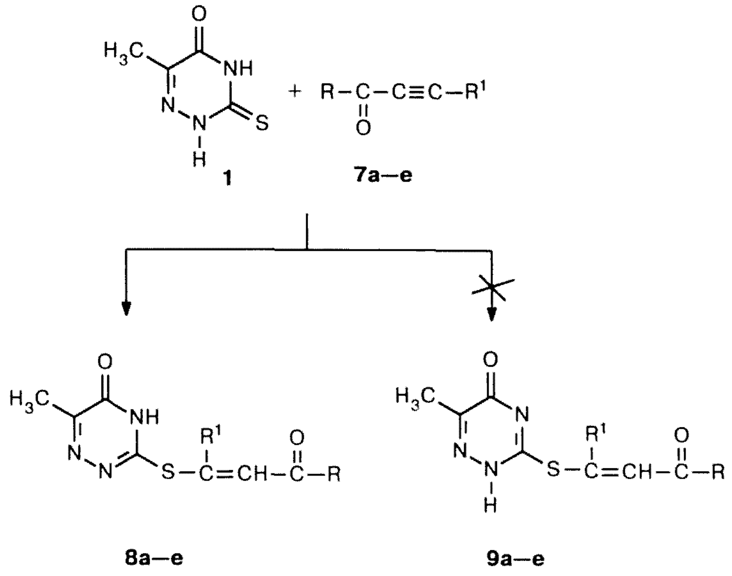


Fig. 2. Projection of the fragment of the crystal structure of compound **5a** along the *Z* axis (the dotted lines indicate shortened S...N distances).

3.32 Å[5]). It should be noted that the sulfur atom of one molecule is localized in the plane C(6)—N(7)—N(8) of another molecule, and the angles N(8)—N(7)...S(1) and C(6)—N(7)...S(1) are equal to 115.7 and 122.5°, respec-

Scheme 2



R = C_6H_5, R^1 = H (**a**); R = CH_3, R^1 = C_6H_5 (**b**);

R = R^1 = C_6H_5 (**c**); R = C_4H_3S, R^1 = C_6H_5 (**d**);

R = C_4H_3O, R^1 = C_6H_5 (**e**)

tively, and angle N(7)...S(1)—C(8a) is equal to 166.7°. Such a mutual arrangement of the sulfur and nitrogen atoms of two neighboring molecules implies the possible existence of a donor-acceptor interaction between them, which probably causes shortening of the S...N intermolecular distance in the crystal structure of compound **5a**.

The reaction between equimolar amounts of α-acetylenic ketones (**7a—e**) and thione **1** in MeOH at 20 °C or on slight heating (30—35 °C) in the presence of Et_3N was studied (Scheme 2). 3-Acylvinylthio-1,2,4-triazin-5-ones (**8a—e**) were isolated as the sole reaction products.

In this reaction one could also expect the formation of isomeric 3-(2-acylvinylthio)-1,2,4-triazin-5-ones (**9a—e**). But it was previously established by X-ray structural analysis that thione **1** reacts with 1-benzoyl-2-bromoacetylene (**2a**) to form compound **5a**.

In contrast to intermediates **3a**,**b**, 3-(2-acylvinylthio)-1,2,4-triazin-5-ones (**8a—e**) obtained are stable compounds and do not undergo intramolecular cyclization under the experimental conditions.

The IR spectra of compounds **8a—e** exhibit the absorption bands of the C=C bond and the C=O group in the side chain at 1630—1640 cm^{-1}, of the ring C=O group at 1670—1685 cm^{-1}, of the C=N bond at 1560—1590 cm^{-1}, and of the NH group at 3440—3460 cm^{-1}. The absorption band of the stretching vibrations of the CH= group at 945 cm^{-1} indicates that compound **8a** is a *trans*-isomer.

Experimental

The ^1H NMR spectra of solutions in DMSO-d_6, $CDCl_3$, and CD_3OD were obtained on a DS-487 spectrometer (80 MHz, ethanol—HMDS), and the ^{13}C NMR spectra were obtained on an FX-90Q (22.49 MHz, $CDCl_3$), with HMDS as the internal standard.

3-Benzoyl-6-methyl-*5H*-thiazolo[2,3-*c*][1,2,4]triazin-5-one (5a). Three drops of Et_3N and then a solution of 1-benzoyl-2-bromoacetylene **2a** in 20 mL of MeOH was slowly added with stirring to a solution of triazine **1** (1.43 g, 0.01 mol) in 30 mL of MeOH. The mixture was stirred at 20 °C for 3 h and cooled to 0 °C. The precipitate that formed was filtered off and recrystallized from EtOH. The yield of compound **5a** was 1.0 g (38%), m.p. 226—228 °C. Found (%): C, 57.4; H, 3.2; N, 15.3; S, 11.7. $C_{13}H_9N_3O_2S$. Calculated (%): C, 57.6; H, 3.3; N, 15.5; S, 11.8. ^1H NMR (DMSO-d_6), δ: 2.35 (s, 3 H, CH_3); 7.99 (s, 1 H, S—CH=); 7.57—8.04 (m, 5 H arom.). ^{13}C NMR (DMSO-d_6), δ: 16.63 (CH_3); 117.93 (C-2); 134.18 (C-6); 128.58, 129.53, 132.12, 135.98 (C_6H_5); 149.73 (C-3); 150.44 (C-8a); 160.08 (C-5); 183.70 (CO—Ph).

6-Methyl-3-(2-thenoyl)-*5H*-thiazolo[2,3-*c*][1,2,4]triazin-5-one (5a) was obtained from triazine **1** and 2-bromo-1-thienoylacetylene (**2b**) analogously to compound **5a**. The yield of compound **5b** was 32%, m.p. 203—206 °C (from EtOH). Found (%): C, 47.4; H, 2.7; N, 15.2; S, 23.4. $C_{11}H_7N_3O_2S_2$. Calculated (%): C, 47.7; H, 2.5; N, 15.2; S, 23.1. ^1H NMR (DMSO-d_6), δ: 2.41 (s, 3 H, CH_3); 8.12 (s, 1 H, S—CH=); 7.32—8.25 (m, 3 H, C_4H_3S).

3-(2-Benzoylvinyl)thio-6-methyl-1,2,4-triazin-5-one (8a). Three drops of Et_3N and a solution of benzoylacetylene (**7a**)

Table 1. Coordinates of non-hydrogen atoms ($\times 10^4$) and their equivalent isotropic temperature factors for compound **5a**

Atom	x	y	z	$U \cdot 10^3/\text{Å}^2$
S(1)	4812(1)	2487(1)	2459(1)	37(1)
O(1)	8605(3)	3881(2)	5659(3)	50(1)
O(2)	7757(3)	1630(2)	6456(3)	51(1)
N(4)	6730(2)	3324(2)	4175(2)	27(1)
N(7)	5914(3)	5316(2)	3621(3)	37(1)
N(8)	5169(3)	4522(2)	2937(3)	38(1)
C(2)	6051(4)	1719(3)	3433(4)	38(1)
C(3)	6980(3)	2257(2)	4284(3)	32(1)
C(5)	7557(3)	4099(3)	4869(3)	31(1)
C(6)	7027(3)	5123(2)	4511(3)	32(1)
C(8a)	5589(3)	3585(2)	3237(3)	30(1)
C(9)	8111(3)	1818(2)	5360(3)	30(1)
C(10)	9527(3)	1566(2)	5007(3)	29(1)
C(11)	10548(4)	1173(3)	6006(4)	38(1)
C(12)	11884(4)	914(3)	5696(5)	46(1)
C(13)	12206(4)	1027(3)	4408(5)	51(2)
C(14)	11210(4)	1429(3)	3420(4)	52(1)
C(15)	9868(4)	1706(3)	3713(4)	39(1)
C(16)	7812(5)	6016(3)	5206(5)	45(1)

(0.94 g, 7 mmol) in 15 mL of MeOH were slowly added with stirring to a solution of triazine **1** (1 g, 7 mmol) in 15 mL of MeOH, and the reaction mixture was stirred at 20 °C for 4 h. Then the MeOH was partially evaporated, and the mixture was cooled to 0 °C. The precipitate that formed was filtered off and recrystallized from MeCN. The yield of triazine **8a** was 0.8 g (88%), m.p. 195—196 °C (from EtOH). Found (%): C, 56.8; H, 4.6; N, 15.6; S, 11.9. $C_{13}H_{11}N_3O_2S$. Calculated (%): C, 56.9; H, 4.4; N, 15.3; S, 11.7. ^{1}H NMR (DMSO-d_6), δ: 2.37 (s, 3 H, CH_3); 8.00 (d, 1 H, CO—CH=, J^3 = 16.6 Hz); 8.64 (d, 1 H, S—CH=, J^3 = 16.6 Hz); 7.29—7.82 (m, 5 H arom.).

6-Methyl-5-oxo-3-(4-oxopent-2-enyl)thio-1,2,4-triazine (8b) was obtained from triazine **1** and 1-acetyl-2-phenylacetylene (**7b**) analogously to compound **8a**. The yield of compound **8b** was 48%, m.p. 178—180 °C (from EtOH). Found (%): C, 58.8; H, 4.5; N, 14.7; S, 11.3. $C_{14}H_{13}N_3O_2S$. Calculated (%): C, 58.5; H, 4.5; N, 14.6; S, 11.1.

6-Methyl-5-oxo-3-(3-oxo-1,3-diphenylprop-1-enyl)thio-1,2,4-triazine (8c) was obtained from triazine **1** and 1-benzoyl-2-phenylacetylene (**7c**) analogously to compound **8a**. The yield of compound **8c** was 51%, m.p. 174—175 °C. Found (%): C, 65.3; H, 4.7; N, 12.2; S, 9.1. $C_{19}H_{15}N_3O_2S$. Calculated (%): C, 65.1; H, 4.6; N, 12.1; S, 9.1. ^{1}H NMR (DMSO-d_6), δ: 2.20 (s, 3 H, CH_3); 7.42 (s, 1 H, CH=); 7.25—8.05 (m, 10 H arom.).

6-Methyl-5-oxo-3-[3-oxo-3-(2-thienyl)-1-phenylprop-1-enyl]thio-1,2,4-triazine (8d) was obtained from triazine **1** and 1-(2-thenoyl)-2-phenylacetylene (**7d**) analogously to compound **8a**. The yield was 53%, m.p. 171—173 °C (from EtOH). Found (%): C, 57.8; H, 3.8; N, 11.8; S, 18.2. $C_{17}H_{13}N_3O_2S_2$. Calculated (%): C, 57.5; H, 3.7; N, 11.8; S, 18.0. ^{1}H NMR (CD_3OD), δ: 2.15 (s, 3 H, CH_3); 7.25 (s, 1 H, CH=); 7.25—7.82 (m, 8 H arom., 2-thienyl). ^{13}C NMR (CD_3OD), δ: 17.39 (CH_3); 128.99, 130.29, 135.80, 137.12 (C_6H_5); 129.40, 130.87, 132.24, 136.50 (C_4H_3S); 134.22 (C-6); 144.97 (CH); 145.68 (C—Ph); 152.93 (C-3); 162.25 (C-5); 184.03 (CO—C_4H_3S).

6-Methyl-5-oxo-3-[3-oxo-1-phenyl-3-(2-furyl)prop-1-enyl]thio-1,2,4-triazine (8e) was obtained from triazine **1** and 1-phenyl-2-(2-furoyl)acetylene (**7e**) analogously to compound **8a**. The yield was 42%, m.p. 190—192 °C (from EtOH). Found (%): C, 60.3; H, 3.8; N, 12.5; S, 9.6. $C_{17}H_{13}N_3O_2S$. Calculated (%): C, 60.2; H, 3.8; N, 12.4; S, 9.4. ^{1}H NMR ($CDCl_3$), δ: 2.13 (s, 3 H, CH_3); 7.23 (s, 1 H, CH); 6.58—7.61 (m, 8 H arom., C_4H_3O).

Table 2. Bond angles (ω) in molecule **5a**

Angle	ω/deg	Angle	ω/deg
C(2)—S(1)—C(8a)	90.1(2)	C(5)—C(6)—C(16)	117.3(3)
C(3)—N(4)—C(5)	126.1(2)	S(1)—C(8a)—N(4)	110.7(2)
C(3)—N(4)—C(8a)	113.8(2)	S(1)—C(8a)—N(8)	124.1(2)
C(5)—N(4)—C(8a)	120.0(3)	N(4)—C(8a)—N(8)	125.1(3)
N(8)—N(7)—C(6)	120.7(3)	O(2)—C(9)—C(3)	117.4(3)
N(7)—N(8)—C(8a)	117.4(2)	O(2)—C(9)—C(10)	122.9(3)
S(1)—C(2)—C(3)	113.5(3)	C(3)—C(9)—C(10)	119.5(3)
N(4)—C(3)—C(2)	111.9(3)	C(9)—C(10)—C(11)	118.6(3)
N(4)—C(3)—C(9)	121.1(2)	C(9)—C(10)—C(11)	121.9(3)
C(2)—C(3)—C(9)	126.7(3)	C(11)—C(10)—C(15)	119.5(3)
O(1)—C(5)—N(4)	120.8(3)	C(10)—C(11)—C(12)	119.8(3)
O(1)—C(5)—C(6)	126.9(3)	C(11)—C(12)—C(13)	120.5(3)
N(4)—C(5)—C(6)	112.4(2)	C(12)—C(13)—C(14)	120.0(4)
N(7)—C(6)—C(5)	124.4(3)	C(13)—C(14)—C(15)	120.4(4)
N(7)—C(6)—C(16)	118.4(3)	C(10)—C(15)—C(14)	119.7(3)

X-ray structural analysis of compound 5a. The crystals of compound **5a** are monoclinic, at 20 °C a = 9.459(2), b = 12.937(3), c = 9.999(2) Å, β = 97.52(2)°, V = 1213(1) Å^3, Z = 4, d_{calc} = 1.49 g cm^{-3}, space group $P2_1/c$. The parameters of the unit cell and intensities of 1553 reflections with $I > 3\sigma(I)$ were measured on an automatic Enraf-Nonius CAD-4 diffractometer (Mo-Kα radiation, θ/2θ-scanning, θ < 26°). The structure was solved by the Paterson method. The hydrogen atoms were localized from the electronic density difference map. The refinement of the structure in the anisotropic (isotropic for the hydrogen atoms) approximation was repeated to R = 0.046, R_w = 0.046, GOF = 1.08. The coordinates of the non-hydrogen atoms of the molecule **5a** and their equivalent isotropic temperature factors are given in Table 1. A perspective view of the molecule **5a** with numbering of the atoms and bond lengths are displayed in Fig. 1. The bond angles are given in Table 2.

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