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Azines and Azoles: CXXVII.* 5-Phenyl-7*H*-[1,2,4]triazolo-[5,1-*b*][1,3]thiazin-7-ones: Synthesis and Structure

N. A. Danilkina[a], L. E. Mikhailov[b], S. I. Selivanov[c], and B. A. Ivin[a]

[a] *St. Petersburg State Chemical and Pharmaceutical Academy, ul. Professora Popova 14, St. Petersburg, 197376 Russia*
e-mail: himi383@mail.ru

[b] *St. Petersburg State Institute of Technology, Moskovskii pr. 26, St. Petersburg, 190013 Russia*

[c] *St. Petersburg State University, Universitetskii pr. 26, St. Petersburg, 198504 Russia*

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Abstract—Reactions of 1-acylthiosemicarbazides with methyl 3-phenylprop-2-ynoate provide a new one-step procedure for the synthesis of 2-substituted 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones. The product structure was determined on the basis of scalar spin–spin coupling constants $^2J(^1H–^{15}N)$ and $^3J(^1H–^{15}N)$ in the ^1H and ^{15}N NMR spectra and was proved by X-ray analysis. Methyl 3-phenylprop-2-ynoate reacted with 1-acetylthiosemicarbazide in ethanol in the presence of H_2SO_4 to give 3-methyl-7-phenyl[1,2,4]triazolo[3,4-*b*]-[1,3]thiazin-5-one as the only product.

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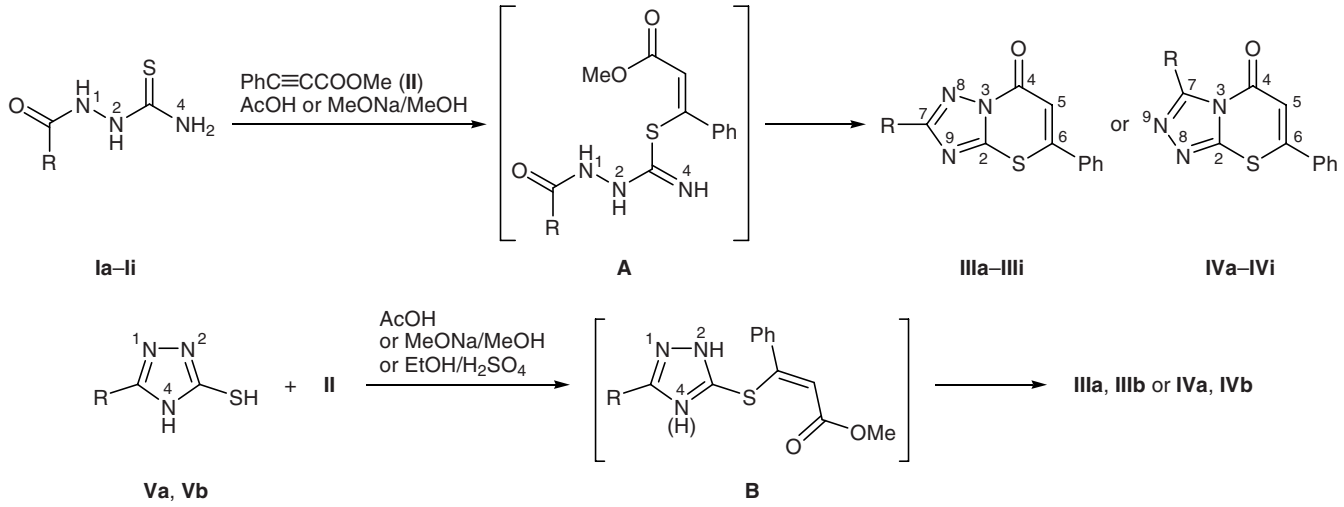
Acetylenic compounds having an activated triple bond are widely used in the synthesis of heterocyclic systems. Condensation of acetylenecarboxylic acid derivatives with thioamides underlies a general method for the preparation of mono- and polycyclic thiazines and thiazolidines [2]. In particular, the condensation of acetylenedicarboxylic acid and its esters with acyclic thioamides usually yields five-membered rings [3–5], while the direction of their reactions with cyclic thioamides depends on the nature of the latter [6, 7]. Acetylene derivatives having only one activating group react with cyclic and acyclic thioamides to give 1,3-thiazines [8]. However, published data on condensations of substituted acetylenemonocarboxylic acids are considerably poorer than the data on reactions with dimethyl acetylenedicarboxylate, while almost no information is available on reactions of thiosemicarbazide derivatives with arylpropynoic acid esters. We previously reported on the formation of mono- and bicyclic thiazine systems in reactions of methyl 3-phenylprop-2-ynoate with unsubstituted thiosemicarbazide [9] and perfluoroacyl-substituted thiosemicarbazides [10]. In the present work we examined reactions of cyclic and acyclic thiosemicarbazide derivatives with methyl 3-phenylprop-2-ynoate.

We have found that 1-formyl- and 1-acetylthiosemicarbazides **Ia** and **Ib** react with methyl 3-phenylprop-2-ynoate (**II**) in boiling acetic acid or in methanol in the presence of sodium methoxide to give the same products as those obtained by the condensation of 4*H*-1,2,4-triazole-3-thioles **Va** and **Vb** with ester **II** under analogous conditions or in ethanol in the presence of concentrated sulfuric acid (Scheme 1).** These findings unambiguously indicate that the products contain a triazole ring. The presence of a thiazine ring in their molecules follows from the ^1H and ^{13}C NMR spectra which contain signals from 5-H and C^5 at δ 7.0 and δ_C 114.3 ppm, respectively. These signals are typical of 1,3-thiazin-4-ones having no substituent on C^5. Furthermore, the ^1H NMR spectra of the products lacked signals assignable to NH and SH protons and ester methoxy group. In the mass spectra of the isolated compounds we observed the corresponding molecular ion ($[M]^{+\cdot}$) peaks and peaks from fragment ions $[M - CO]^{+\cdot}$, $[M - CO - RCN]^{+\cdot}$, $[M - CO - RCN - CH_2N{=}N]^{+\cdot}$, $[M - CO - RCN - N_2]^{+\cdot}$, and $[M - CO - RCN - N_2 - CS]^{+\cdot}$. The products displayed in the IR spectra absorption bands corresponding to stretch-

* For communication CXXVI, see [1].

** Hereinafter (except for X-ray diffraction data), the atom numbering in triazolothiazines **III** and **IV** corresponds to that shown in Scheme 1 for the sake of convenience in discussing the NMR spectra (it does not conform to IUPAC rules).

Scheme 1.



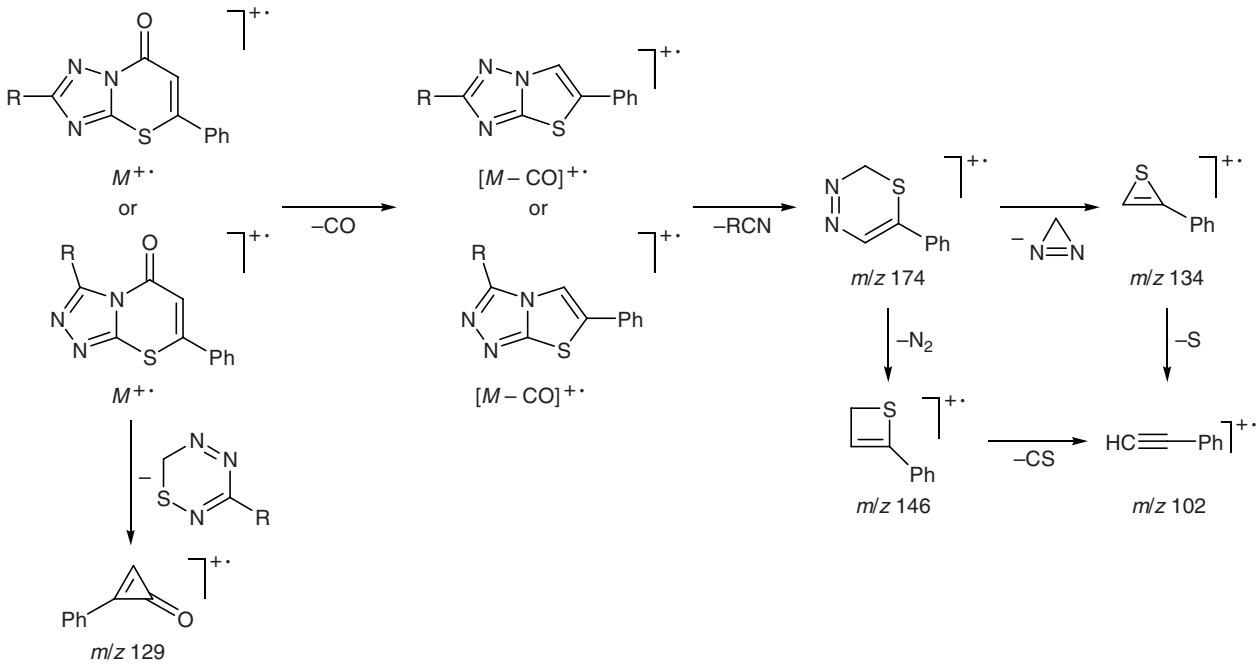
R = H (**a**), Me (**b**), Bzl (**c**), Ph (**d**), 4-MeC_6H_4 (**e**), 4-$MeOC_6H_4$ (**f**), 4-ClC_6H_4 (**g**), 4-$O_2NC_6H_4$ (**h**), pyridin-4-yl (**i**).

ing vibrations of C–H (~3050 cm^{-1}) and C=O bonds (~1700 cm^{-1}), and their electronic absorption spectra were characterized by two maxima at λ 250 and 284 nm. The above data suggests that the condensation products of acylthiosemicarbazides and triazolethiols with methyl 3-phenylprop-2-ynoate have the structure of triazolothiazines **III** or **IV**.

Acetylenic ester **II** reacted in a similar way with other 1-acylthiosemicarbazides **Ic–Ii** in boiling acetic acid to give the corresponding triazolothiazinones **IIIc–IIIi** or **IVc–IVi**. Thus the examined reaction provides a general and universal synthetic route to triazolothiazines via condensation of N^1-acylthiosemicarbazides with propynoic acid esters in acetic acid.

The condensation of thiosemicarbazide derivatives **Ia–Ii**, **Va**, and **Vb** with methyl 3-phenylprop-2-ynoate (**II**) begins with nucleophilic addition of the SH group at the triple bond of ester **II** (this step is believed to be the first in reactions of thioamides with acetylenecarboxylic acid derivatives [2]), and the subsequent intra-

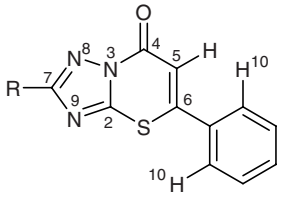
Scheme 2.



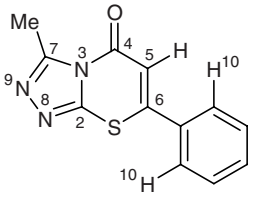
molecular acylation can involve either N^2 or N^4 atom to give triazolothiazinone **III** or **IV**, respectively. However, the ^1H and ^{13}C NMR data (Table 1), including the ^{13}C NMR spectra recorded both with selective decoupling from protons and without broad-band decoupling from protons, did not allow us to distinguish between isomers **III** and **IV**, for the experimental chemical shifts and coupling constants did not contradict both these structures. No useful information can be derived from the mass spectra of the condensation products: the fragmentation pattern is the same for compounds **III** and **IV** (Scheme 2).

One of the main differences in the structures of triazolothiazines **IIIa** and **IVa** is the number of bonds between the 7-H and C^4 atoms. Therefore, we tried to distinguish between isomers **IIIa** and **IVa** by analyzing the scalar coupling constants $^{2-4}J(^1H-^{13}C)$. This approach was successfully applied previously to determine the structure of condensation products formed by dimethyl acetylenedicarboxylate and thioamide derivatives [11–14]. In the ^{13}C NMR spectrum of triazolothiazine **IIIa** (**IVa**), recorded without broad-band decoupling from protons, the multiplicity of the C^4 signal (Fig. 1a) indicates that the C^4 nucleus is involved in two weak scalar interactions. The latter were identified by recording the spectrum with selective decoupling from 7-H (Fig. 1b) and 5-H (Fig. 1c). In such a way we estimated the $^2J(C^4-H^5)$ and $^{(3\text{ or }4)}J(C^4-H^7)$ values at 0.65 and 0.4 Hz, respectively. However, the observed low $J(C^4-H^7)$ value may reflect coupling through both four bonds (as in isomer **IIIa**) and three bonds (as in **IVa**); i.e., the above approach does not allow us to distinguish between possible structures **IIIa** and **IVa**. Therefore, we resorted to ^{15}N NMR spectroscopy and

Table 1. ^{13}C NMR spectra of compounds **IIIb–IIIe**, **IIIg**, **IIIh**, and **IVb** in $CDCl_3$ and of **IIIf** and **IIIi** in DMSO-d_6[a]



IIIa–IIIi



IVb

Comp. no.	Chemical shifts δ_C, ppm, and $^{13}C-^1H$ coupling constants J, Hz						
	R	Ph	C^2	C^4	C^5	C^6	C^7
IIIa	–	126.8 129.6 132.1 134.0	151.5 d $^3J(C^2-H^7) = 8.7$	155.5 d.d $^2J(C^4-H^5) = 0.65$, $^4J(C^4-H^7) = 0.4$	114.3 d $^1J(C^5-H^5) = 170.8$	151.4 t.d $^2J(C^6-H^5) = 1.9$, $^3J(C^6-H^{10}) = 4.7$	153.2 d $^1J(C^7-H^7) = 212.2$
IIIb	14.1 q $^1J = 129$	126.8 129.6 131.9 134.1	151.5 s	155.4 d $^2J(C^4-H^5) < 1$	114.3 d $^1J(C^5-H^5) = 169.3$	150.6 t.d $^2J(C^6-H^5) = 1.8$, $^3J(C^6-H^{10}) = 5$	163.7 q $^2J(C^7-CH_3) = 6.7$
IIIc	34.9 (CH_2) 127.0 128.7 129.1 136.5	126.8 127.0 129.8 132.1 134.3	152.1	155.8	114.6	151.1	166.0
IIId	127.6 128.7 128.8 130.9	126.9 129.7 132.1 134.1	152.2 s	155.8 d $^2J(C^4-H^5) < 1$	114.5 d $^1J(C^5-H^5)$ 170.4	150.8 t.d $^2J(C^6-H^5) = 1.9$, $^3J(C^6-H^{10}) = 4.3$	163.7 t $^3J(C^7-H^{11}) = 4.8$[b]
IIIe	21.5 (CH_3) 126.0 127.5 129.4 141.2	126.8 129.7 132.0 134.2	152.0	155.8	114.5	150.6	164.0

Table 1. (Contd.)

Comp. no.	Chemical shifts δ_C, ppm, and $^{13}C–^{1}H$ coupling constants J, Hz						
	R	Ph	C^2	C^4	C^5	C^6	C^7
IIIg	127.3 128.9 129.0 137.1	126.9 129.8 132.2 134.1	152.4	155.7	114.6	150.9	163.1
IIIh	134.0 128.5 134.0 134.8	127.0 129.9 132.4 134.0	151.4	155.6	144.6	149.3	162.0
IIIi	127.7 136.0 150.7	127.0 129.8 132.2 133.5	153.1	155.4	114.6	149.5	160.3
IVb	14.24 q (^1J = 131)	126.8 129.7 132.3 134.2	146.7 s	158.4 d $^2J(C^4–H^5)$ = 1.1	113.3 d $^1J(C^5–H^5)$ = 170.6	153.4 t.d $^2J(C^6–H^5)$ = 2.2, $^3J(C^6–H^{10})$ = 4.9	151.0 q $^2J(C^7–CH_3)$ = 7.8

[a] Signals were assigned on the basis of the spectra recorded without broad-band decoupling from protons and with selective decoupling from 5-H and 7-H (**IIIa**), CH_3 and 5-H (**IIIb**, **IVb**), and 11-H and 5-H (**IIId**).

[b] 11-H denotes *ortho*-protons in the phenyl group attached to the triazole ring in compound **IIId**.

analyzed the scalar coupling constants $^{2,3}J(^1H–^{15}N)$. It is known [15] that signals from pyrrole- (N_{pl}) and pyridine-type nitrogen atoms (N_{pn}) in 1,2,4-triazoles can be readily assigned on the basis of the corresponding chemical shifts. The geminal constants $^2J(^1H–^{15}N_{pn})$ usually exceed 10 Hz, while vicinal constants $^3J(^1H–^{15}N_{pn})$ are smaller than 2.5 Hz [16]. Then, to distinguish between structures **IIIa** and **IVa**, it is necessary to determine the scalar coupling constants between the 7-H proton and pyridine-type nitrogen atoms N^8 and N^9.

In addition to the known problems intrinsic to ^{15}N NMR spectroscopy, such as low sensitivity related to the low concentration of the natural ^{15}N isotope (0.365%) and low negative gyromagnetic ratio [17], triazolothiazine **IIIa** (**IVa**) is poorly soluble in most solvents. Therefore, we applied a polarization transfer technique ($^1H–^{15}N$ INEPT). For this purpose, $J(^1H–^{15}N)$ values ($\tau = 1/2J$) were needed; they can be determined from the ^1H NMR spectrum in which satellite peaks at the 7-H signal originate from scalar interactions between 7-H and nitrogen nuclei. At the base of the 7-H signal we observed four doublets with coupling constants J of 6.7, 8.7, 13.6, and 15.9 Hz (Fig. 2), corresponding to interactions of 7-H with C^2, N^3_{pl}, N^8_{pn}, and N^9_{pn}. Comparison with the ^1H NMR

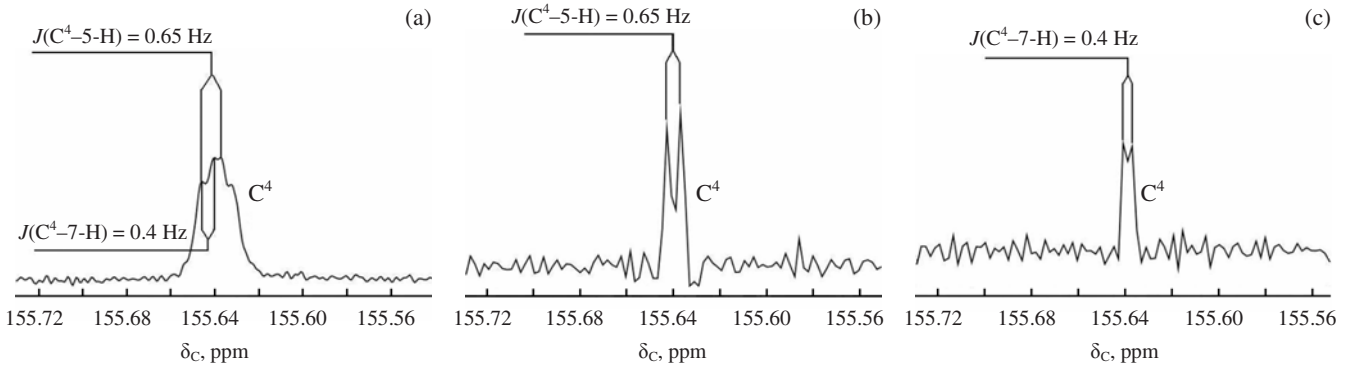


Fig. 1. Fragments of the ^{13}C NMR spectra of triazolothiazine **IIIa** (**IVa**) recorded (a) without broad-band decoupling from protons, (b) with selective decoupling from 7-H, and (c) with selective decoupling from 5-H.

spectrum recorded with selective decoupling from C^2 (Fig. 3a) showed that the coupling constant ^3J = 8.7 Hz belongs to the scalar interaction between 7-H and C^2; this is clearly seen from the difference spectrum*** shown in Fig. 3b. Therefore, the other doublet signals result from scalar interactions between 7-H, on the one hand, and three nitrogen nuclei, on the other. Taking into account the $J(^1H–^{15}N)$ values thus obtained (Fig. 3a), and intermediate value of 10 Hz was selected for $^1H–^{15}N$ INEPT experiment.

In the $^1H–^{15}N$ INEPT spectrum we identified signals from N^3_{pl} (δ_N −135.7 ppm), N^8_{pn} (δ_N −123.3 ppm), and N^9_{pn} (δ_N −88.0 ppm), which appeared as characteristic antiphase doublets with coupling constants of ~12, ~13.5, and ~16 Hz, respectively. The doublet structure of the N^8_{pn} and N^9_{pn} signals is likely to originate from their scalar interactions with 7-H since the coupling constants observed in the $^1H–^{15}N$ INEPT spectrum (~13.5 and ~16 Hz) almost coincide with those found using the 7-H satellites in the ^1H NMR spectrum (Fig. 3a). Triplet signals in INEPT spectra are known [18] to appear as antiphase doublets with a doubled ^nJ(S–I) constant as a result of visual disappearance of the central component. Therefore, the presence of a doublet signal from N^3_{pl} (δ_N 135.7 ppm) with a large coupling constant (~12 Hz; cf. 6.7 Hz in Fig. 3a) may be rationalized in terms of the existence of two similar scalar couplings (~6 Hz) of N^3_{pl} with 7-H and 5-H. Obviously, reliable identification of scalar interactions between N^8_{pn} and N^3_{pl} and 7-H and 5-H is crucial for the choice of isomer **IIIa** or **IVa**. Insofar as the difference in the doublet splitting between the N^8_{pn} and N^3_{pl} nuclei is not large (~2.5 Hz), we recorded the ^1H NMR spectra of triazolothiazine **IIIa** (**IVa**) with selective decoupling from N^8_{pn} (Fig. 4a) and N^9_{pn} (Fig. 4c) with a view to confirm the occurrence of strong scalar interactions (J >10 Hz) between 7-H and pyridine-type nitrogens. Comparison of these spectra with that measured without decoupling from nitrogen nuclei (Fig. 2) showed that the coupling constant J = 13.6 Hz characterizes scalar interaction between 7-H and N^8 (δ_N −123.3 ppm) and that the constant J = 15.9 Hz belongs to the interaction with N^9 (δ_N −88.0 ppm). These scalar interactions are clearly seen in the difference spectra (Figs. 4b, 4d). The large values of $^2J(7\text{-H–N}^8)$ and $^2J(7\text{-H–N}^9)$ (13.6 and 15.9 Hz, respectively) indicate that the 7-H proton is separated by two bonds from each of the pyridine-type nitrogen atoms N^8_{pn} and N^9_{pn}. Therefore, the condensation product of 1-formylthiosemicarbazide (**Ia**) with methyl 3-phenylprop-2-ynoate (**II**) has the structure of triazolothiazinone **IIIa** rather than **IVa**.

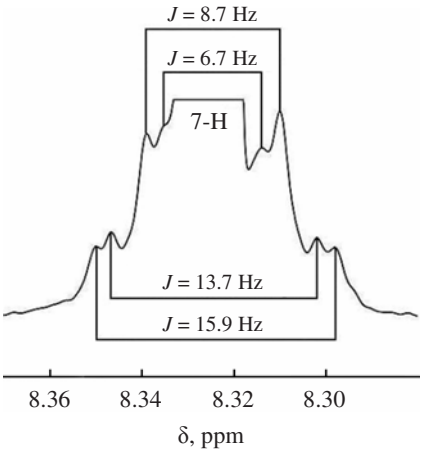


Fig. 2. Fragment of the ^1H NMR spectrum of triazolothiazine **IIIa** (**IVa**).

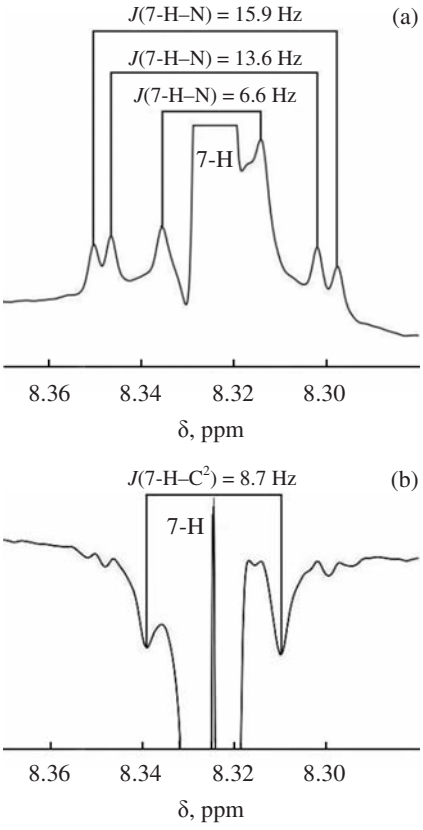


Fig. 3. Fragments of (a) conventional and (b) difference ^1H NMR spectra of triazolothiazine **IIIa** (**IVa**) recorded with selective decoupling from C^2.

*** Hereinafter, by difference spectra we mean those obtained by subtraction of ^1H NMR spectrum recorded without decoupling from carbon nuclei or protons (Fig. 2) from the spectra recorded with selective decoupling from the corresponding nuclei.

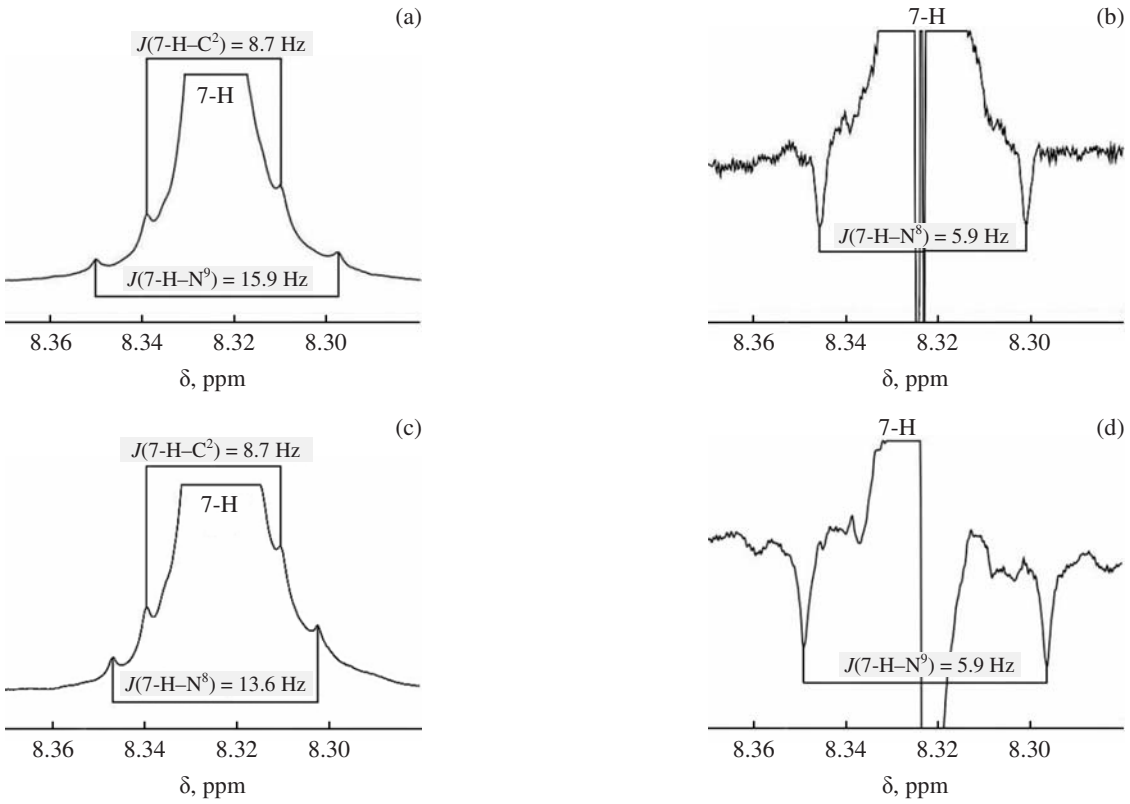


Fig. 4. Fragments of (a, c) conventional and (b, d) difference ^{1}H NMR spectra of triazolothiazine **IIIa** (**IVa**), recorded with selective decoupling from (a, b) N^{8}_{pn} and (c, d) N^{9}_{pn}.

The structure of 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*]-[1,3]thiazin-7-one (**IIIa**) in solution, determined on the basis of the scalar coupling constants $^{2}J(^{1}H–^{15}N)$ and $^{3}J(^{1}H–^{15}N)$, was proved by the X-ray diffraction data (Fig. 5, Tables 2–4). The bicyclic triazolothiazine skeleton is nearly planar: the dihedral angle between the triazole and thiazine ring planes is 1.7°. The benzene ring lies almost in the thiazine ring plane: the corresponding dihedral angle is equal to 5.52°.

Taking into account that the main IR absorption bands, UV maxima, and chemical shifts of protons and carbon nuclei in the NMR spectra (Table 1) of 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (**IIIa**) and its substituted analogs are fairly similar, the condensation products of 1-acylthiosemicarbazides **Ib**–**Ii** with ester **II** were also assigned structures **IIIb**–**IIIi** rather than **IVb**–**IVi**. It should be noted that we previously [9] assigned structure **IVb** to the product obtained by condensation of 1-acetylthiosemicarbazide with methyl 3-phenylprop-2-ynoate.

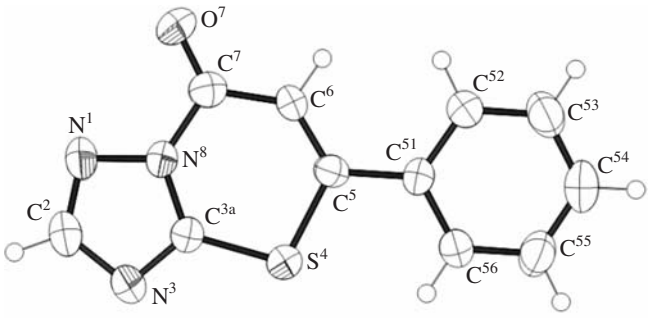


Fig. 5. Structure of the molecule of 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (**IIIa**) according to the X-ray diffraction data.

When the condensation of ester **II** with 1-acetylthiosemicarbazide (**Ib**) was carried out in ethanol in the presence of a small amount of concentrated sulfuric acid, the conversion of **Ib** being ~10%, we isolated ~7% of a compound which (according to the TLC data) was formed as the only product. Its elemental composition was identical to that of triazolothiazine **IIIb**. The product melted at a higher temperature (by 20°C) than compound **IIIb**. It could have the structure of 3-methyl-7-phenyl[1,2,4]triazolo[3,4-*b*][1,3]thiazin-5-one (**IVb**), for its fragmentation pattern under electron impact was identical to that of **IIIb**. However, their spectral parameters differed considerably.

In the UV spectrum of the isolated compound, both absorption maxima were displaced to the short-wave

region by about 30 nm relative to the corresponding maxima of isomer **IIIb**. The positions of signals from the methyl protons, olefinic proton, and protons in the benzene ring in the ^{1}H NMR spectra of these compounds differed by no more than 0.5 ppm, whereas the differences in the chemical shifts of the C^2 and C^7 atoms were ~5 and 13 ppm, respectively (Table 1). Clearly, the product is not triazolothiazine **IIIb**. The cyclization of 1-acetylthiosemicarbazide in acid medium could also give rise to 5-methyl-1,3,4-thiadiazol-2-amine [19]; therefore, the product could also have the structure of thiadiazolopyrimidine **VI** or **VII**. The latter were synthesized previously [20, 21] from 5-methyl-1,3,4-thiadiazol-2-amine and ethyl benzoylacetate (Scheme 3).

The main difference in the IR spectra of the isolated compound and thiadiazolopyrimidines **VI** and **VII** is the position of the carbonyl band: 1696, 1685 [20], and 1640 cm^{-1} [20], respectively. In the ^{1}H NMR spectra of solutions of **VI** and **VII** in $CDCl_3$ [20], signals from the methyl protons were displaced, respectively, by 0.2 (δ 2.75 ppm) and 0.3 ppm upfield (δ 2.63 ppm) relative to the corresponding signal in the spectrum of the isolated product (δ 2.93 ppm); the olefinic proton in the latter resonated at δ 6.73 ppm against δ 6.87 and 6.42 ppm for **VI** and **VII**, respectively. On the basis of the above spectral data, the product of condensation of thiosemicarbazide **Ib** with ester **II** in ethanol in the presence of sulfuric acid was assigned the structure of triazolothiazine **IVb**.

Thus we can conclude that methyl 3-phenylprop-2-ynoate (**II**) reacts with 1-acylthiosemicarbazides **Ia**–**Ii** and 1,2,4-triazole-3-thiols **Va** and **Vb** to give mainly the corresponding 2-substituted 5-phenyl-7*H*-[1,2,4]-triazolo[5,1-*b*][1,3]thiazin-7-ones **IIIa**–**IIIi**. An exception is 1-acetylthiosemicarbazide (**Ib**) whose condensation with ester **II** in ethanol in the presence of sulfuric acid leads to the formation of 3-methyl-7-phenyl-[1,2,4]triazolo[3,4-*b*][1,3]thiazin-5-one (**IVb**).

Table 2. Bond lengths *d* in the molecule of 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (**IIIa**)

Bond	*d*, Å	Bond	*d*, Å
N^1–C^2	1.313(2)	C^6–C^7	1.446(2)
N^1–N^8	1.376(2)	C^7–O^7	1.209(2)
C^2–N^3	1.380(2)	C^7–N^8	1.420(2)
N^3–C^{3a}	1.313(2)	C^{51}–C^{56}	1.387(2)
C^{3a}–N^8	1.356(2)	C^{51}–C^{52}	1.389(2)
C^{3a}–S^4	1.721(2)	C^{52}–C^{53}	1.372(2)
S^4–C^5	1.747(2)	C^{53}–C^{54}	1.375(2)
C^5–C^6	1.344(2)	C^{54}–C^{55}	1.374(2)
C^5–C^{51}	1.486(2)	C^{55}–C^{56}	1.381(2)

EXPERIMENTAL

The electronic absorption spectra were measured from solutions in ethanol on an SF-2000 spectrophotometer. The IR spectra were recorded in KBr and in $CHCl_3$ on an FSM 1201 spectrometer with Fourier transform. The ^{1}H and ^{13}C NMR spectra of compounds **IIIb**–**IIIe**, **IIIg**, **IIIh**, and **IVb** in $CDCl_3$ and of **IIIf** and **IIIi** in DMSO-d_6 were obtained on a Bruker AM-500 spectrometer at 500.17 and 125 MHz, respectively. The ^{1}H, ^{13}C, and ^{1}H-^{15}N INEPT spectra of a solution of compound **IIIa** in $CDCl_3$ were measured on a Bruker DPX-300 instrument at 300.13, 75.48, and 30.41 MHz, respectively. While recording the ^{1}H–^{15}N INEPT spectrum, the pulse delay ($\tau = 1/2J$) was adjusted to a coupling constant J of 10 Hz. The ^{1}H and ^{13}C chemical shifts are given relative to tetramethylsilane, and the ^{15}N chemical shifts, relative to nitromethane. The mass

Scheme 3.

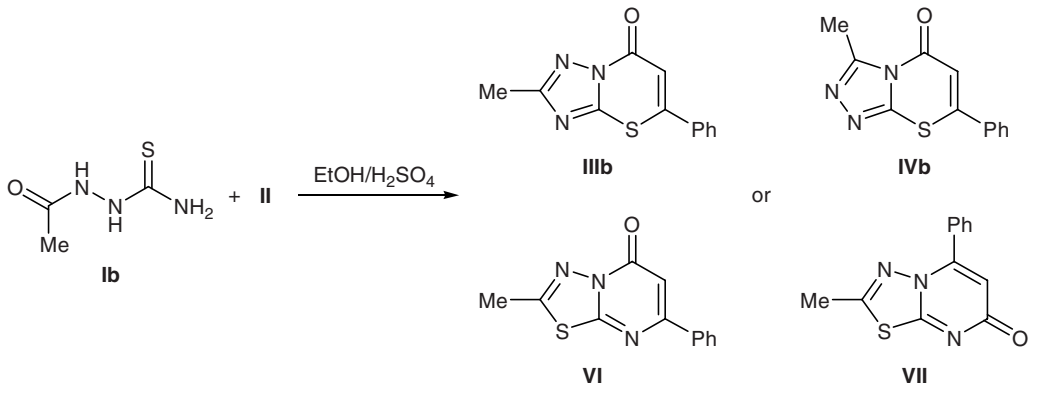


Table 3. Bond angles ω in the molecule of 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (**IIIa**)

Angle	ω, deg	Angle	ω, deg
$C^2N^1N^8$	101.31(15)	$N^8C^7C^6$	114.38(19)
$N^1C^2N^3$	116.64(18)	$C^{3a}N^8N^1$	109.34(13)
$C^{3a}N^3C^2$	101.28(16)	$C^{3a}N^8C^7$	127.84(18)
$N^3C^{3a}N^8$	111.44(15)	$N^1N^8C^7$	122.82(18)
$N^3C^{3a}S^4$	123.99(16)	$C^{56}C^{51}C^{52}$	117.48(17)
$N^8C^{3a}S^4$	124.57(15)	$C^{56}C^{51}C^5$	121.74(18)
$C^{3a}S^4C^5$	101.33(10)	$C^{52}C^{51}C^5$	120.78(18)
$C^6C^5C^{51}$	124.02(15)	$C^{53}C^{52}C^{51}$	120.66(18)
$C^6C^5S^4$	122.39(15)	$C^{52}C^{53}C^{54}$	120.96(18)
$C^{51}C^5S^4$	113.59(14)	$C^{55}C^{54}C^{53}$	119.6(2)
$C^5C^6C^7$	129.38(18)	$C^{54}C^{55}C^{56}$	119.3(2)
$O^7C^7N^8$	120.2(2)	$C^{55}C^{56}C^{51}$	122.0(2)
$O^7C^7C^6$	125.40(19)		

Table 4. Torsion angles φ in the molecule of 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (**IIIa**)

Angle	φ, deg	Angle	φ, deg
$N^8N^1C^2N^3$	–0.2(2)	$C^2N^1N^8C^7$	179.44(16)
$N^1C^2N^3C^{3a}$	–0.2(3)	$O^7C^7N^8C^{3a}$	–178.00(18)
$C^2N^3C^{3a}N^8$	0.5(2)	$C^6C^7N^8C^{3a}$	2.0(3)
$C^2N^3C^{3a}S^4$	179.77(13)	$O^7C^7N^8N^1$	3.3(3)
$N^3C^{3a}S^4C^5$	177.77(16)	$C^6C^7N^8N^1$	–176.76(16)
$N^8C^{3a}S^4C^5$	–3.07(17)	$C^6C^5C^{51}C^{56}$	–173.36(19)
$C^{3a}S^4C^5C^6$	2.34(16)	$S^4C^5C^{51}C^{56}$	5.8(2)
$C^{3a}S^4C^5C^{51}$	–176.88(14)	$C^6C^5C^{51}C^{52}$	6.4(3)
$C^{51}C^5C^6C^7$	179.5(2)	$S^4C^5C^{51}C^{52}$	–174.44(15)
$S^4C^5C^6C^7$	0.3(3)	$C^{56}C^{51}C^{52}C^{53}$	0.4(3)
$C^5C^6C^7O^7$	177.17(19)	$C^5C^{51}C^{52}C^{53}$	–179.35(17)
$C^5C^6C^7N^8$	–2.8(3)	$C^{51}C^{52}C^{53}C^{54}$	–0.6(3)
$N^3C^{3a}N^8N^1$	–0.7(2)	$C^{52}C^{53}C^{54}C^{55}$	0.2(3)
$S^4C^{3a}N^8N^1$	–179.95(13)	$C^{53}C^{54}C^{55}C^{56}$	0.5(3)
$N^3C^{3a}N^8C^7$	–179.54(16)	$C^{54}C^{55}C^{56}C^{51}$	–0.7(3)
$S^4C^{3a}N^8C^7$	1.2(3)	$C^{52}C^{51}C^{56}C^{55}$	0.3(3)
$C^2N^1N^8C^{3a}$	0.52(19)	$C^5C^{51}C^{56}C^{55}$	–179.98(17)

spectra (electron impact, 70 eV) were run on an MKh-1321 mass spectrometer with direct sample admission into the ion source (batch inlet temperature 140–300°C). The progress of reactions and the purity of products were monitored by TLC on Sorbfil plates using hexane–acetone (2:1 for **IIIa–IIIh** and **IVb**; 1:1 for **IIIi**) as eluent.

Methyl 3-phenylprop-2-ynoate [22], 1-acylthiosemicarbazides **Ia**, **Ib** [23], and **Ic–Ii** [24], and 1,2,4-triazole-3-thiols **Va** and **Vb** [23] were prepared according to known procedures.

Crystals of compound **IIIa** suitable for X-ray analysis were obtained by crystallization from ethanol via slow evaporation at 18–20°C. The X-ray diffraction data were acquired on a Bruker SMART 1000 CCD diffractometer (MoK_α irradiation). $C_{11}H_7N_3OS$; monoclinic crystal system, space group $P2_1/n$; unit cell parameters: a = 7.0563(8), b = 10.5306(12), c = 13.7171(16) Å; Z = 4; d_{calc} = 1.536 g/cm^3; 2102 of non-zero independent reflections were measured; R_1 = 0.0267 [$I > 2\sigma(I)$], wR_2 = 0.0367. The complete set of crystallographic data for compound **IIIa** was deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 655791).

2-Substituted 5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*]-[1,3]thiazin-7-ones IIIa–IIIi. *a*. Methyl 3-phenylprop-2-ynoate (**II**), 3 mmol, was added to a solution or suspension of 3 mmol of 1-acylthiosemicarbazide **Ia–Ii** in 15 ml of glacial acetic acid. The mixture was heated for 15 h under reflux, cooled, poured into water (70 ml), and left to stand for 20 h at 18–20°C. The precipitate was filtered off, washed with water, and recrystallized from butan-1-ol (**IIIa–IIIe**, **IIIg**, **IIIi**) or butan-1-ol–DMF (4:1) (**IIIf**, **IIIh**). Before recrystallization, compounds **IIIc**, **IIIe**, and **IIIg** were purified from unreacted acylthiosemicarbazides by treatment with chloroform (2×15 ml); the solvent was removed, and the residue was recrystallized from butan-1-ol.

b. Ester **II**, 3 mmol, was added to a suspension of 3 mmol of 1-acylthiosemicarbazide **Ia–Ii** in 15 ml of methanol containing 0.1 ml of a 1 M solution of NaOMe in MeOH. The mixture was heated for 15 h under reflux and evaporated to 1/4 of the initial volume, and the precipitate was filtered off, washed with 5 ml of ethanol, and recrystallized from butan-1-ol.

c. Ester **II**, 3 mmol, was added to a solution or suspension of 3 mmol of 1,2,4-triazole-3-thiol **Va** or **Vb** in 15 ml of glacial acetic acid. The mixture was heated for 15 h under reflux and was then treated as described above in *a*.

d. Ester **II**, 3 mmol, was added to a suspension of 3 mmol of 1,2,4-triazole-3-thiol **Va** or **Vb** in 15 ml of MeOH containing 0.1 ml of a 1 M solution of MeONa in MeOH. The mixture was heated for 15 h under reflux and was then treated as described above in *b*.

e. Ester **II**, 3 mmol, was added to a suspension of 3 mmol of 1,2,4-triazole-3-thiol **Va** or **Vb** in 15 ml of

ethanol containing 0.01 ml of concentrated sulfuric acid. The mixture was heated for 15 h under reflux and was then treated as described above in *b*.

5-Phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIa). Yield 58 (*a*), 52 (*b*), 63 (*c*), 60 (*d*), 30% (*e*); mp 193–195°C, R_f 0.25. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 210 (1.74), 250 (1.39), 284 (1.42). IR spectrum, ν, cm^{-1}: 3115, 3075, 2700, 1690, 1645, 1560, 1500, 1485. ^1H NMR spectrum, δ, ppm: 7.0 s (1H, 5-H), 7.5–7.6 m (5H, H_{arom}), 8.3 s (1H, 7-H). Mass spectrum, *m/z* (I_{rel}, %): 229 (100) $[M]^+$, 201 (41), 174 (4), 146 (10), 134 (3), 129 (26), 102 (74). Found, %: C 57.3; H 3.2; N 18.6; S 14.5. $C_{11}H_7N_3OS$. Calculated, %: C 57.6; H 3.1; N 18.3; S 14.0. *M* 229.26.

2-Methyl-5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIb). Yield 64 (*a*), 36 (*b*), 68 (*c*), 53 (*d*), 18% (*e*); mp 182–184°C, R_f 0.27. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 210 (1.73), 251 (1.51), 284 (1.45). IR spectrum, ν, cm^{-1}: 3049, 2931, 1702, 1654, 1581, 1566, 1518, 1808, 1491. ^1H NMR spectrum, δ, ppm: 2.5 s (3H, CH_3), 6.9 s (1H, 5-H), 7.5–7.6 m (5H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 243 (100) $[M]^+$, 215 (22), 174 (4), 146 (8), 134 (40), 129 (41), 102 (68). Found, %: C 59.6; H 3.2; N 17.1; S 13.8. $C_{12}H_9N_3OS$. Calculated, %: C 59.2; H 3.7; N 17.3; S 13.2. *M* 243.29.

2-Benzyl-5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIc). Yield 52% (*a*), mp 124–126°C, R_f 0.29. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 210 (1.77), 252 (1.10), 287 (1.05). IR spectrum, ν, cm^{-1}: 3055, 2933, 1700, 1660, 1610, 1584, 1572, 1520, 1491. ^1H NMR spectrum, δ, ppm: 4.25 s (2H, CH_2), 7.0 s (1H, 5-H), 7.2–7.6 m (10H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 319 (100) $[M]^+$, 291 (22), 174 (3), 146 (11), 134 (40), 129 (34), 102 (50). Found, %: C 67.1; H 4.1; N 13.2; S 9.8. $C_{18}H_{13}N_3OS$. Calculated, %: C 67.7; H 4.1; N 13.2; S 10.0. *M* 319.38.

2,5-Diphenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIId). Yield 48% (*a*), mp 210–213°C, R_f 0.45. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 207 (2.30), 301 (2.25). IR spectrum, ν, cm^{-1}: 3055, 1699, 1655, 1605, 1583, 1567, 1520, 1481, 1445. ^1H NMR spectrum, δ, ppm: 7.0 s (1H, 5-H), 7.5–8.3 m (10H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 305 (100) $[M]^+$, 277 (57), 174 (4), 146 (10), 134 (3), 129 (48), 102 (70). Found, %: C 67.2; H 3.7; N 13.8; S 10.2. $C_{17}H_{11}N_3OS$. Calculated, %: C 66.9; H 3.6; N 13.8; S 10.5. *M* 305.35.

2-(4-Methylphenyl)-5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIe). Yield 50% (*a*), mp 209–211°C, R_f 0.50. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 208 (2.18), 250 (1.53), 300 (1.44). IR spectrum, ν, cm^{-1}: 3027, 1707, 1662, 1625, 1587, 1543, 1490, 1449. ^1H NMR spectrum, δ, ppm: 2.4 s (3H, CH_3), 7.0 s (1H, 5-H), 7.3 d (2H, H_{arom}, J = 8.3 Hz), 7.5 m (3H, H_{arom}), 7.6 d (2H, H_{arom}, J = 7.2 Hz), 8.2 d (2H, H_{arom}, J = 7.2 Hz). Mass spectrum, *m/z* (I_{rel}, %): 319 (100) $[M]^+$, 277 (57), 174 (4), 146 (10), 134 (3), 129 (48), 102 (70). Found, %: C 67.2; H 4.4; N 13.5; S 9.8. $C_{18}H_{13}N_3OS$. Calculated, %: C 67.7; H 4.1; N 13.2; S 10.0. *M* 319.38.

2-(4-Methoxyphenyl)-5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIf). Yield 45% (*a*), mp 250–252°C, R_f 0.44. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 207 (1.11), 255 (0.83), 307 (0.69). IR spectrum, ν, cm^{-1}: 3052, 2839, 1702, 1654, 1613, 1583, 1567, 1483. ^1H NMR spectrum, δ, ppm: 3.8 s (3H, OCH_3), 7.3 s (1H, 5-H), 7.1 d (2H, H_{arom}, J = 8.6 Hz), 7.6 m (3H, H_{arom}), 7.9 d (2H, H_{arom}, J = 7.6 Hz), 8.1 d (2H, H_{arom}, J = 8.6 Hz). Mass spectrum, *m/z* (I_{rel}, %): 335 (100) $[M]^+$, 307 (35), 174 (2), 146 (5), 134 (10), 129 (42), 102 (40). Found, %: C 64.6; H 3.7; N 12.3; S 9.4. $C_{18}H_{13}N_3O_2S$. Calculated, %: C 64.5; H 3.9; N 12.5; S 9.6. *M* 335.38.

2-(4-Chlorophenyl)-5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIg). Yield 65% (*a*), mp 204–206°C, R_f 0.71. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 208 (2.58), 251 (1.89), 297 (1.83). IR spectrum, ν, cm^{-1}: 3374, 3065, 1699, 1649, 1598, 1578, 1562, 1524, 1481. ^1H NMR spectrum, δ, ppm: 7.0 s (1H, 5-H), 7.4 d (2H, H_{arom}, J = 8.3 Hz), 7.6 m (3H, H_{arom}) 7.7 d (2H, H_{arom}, J = 7.2 Hz), 8.2 d (2H, H_{arom}, J = 8.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 339 (100) $[M]^+$, 311 (25), 174 (4), 146 (8), 134 (15), 129 (51), 102 (48). Found, %: C 60.1; H 3.3; Cl 10.8; N 12.6; S 9.1 $C_{17}H_{10}ClN_3O_2S$. Calculated, %: C 60.1; H 3.0; Cl 10.4; N 12.4; S 9.4. *M* 339.80.

2-(4-Nitrophenyl)-5-phenyl-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (IIIh). Yield 25% (*a*), mp 248–250°C, R_f 0.56. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 210 (3.42), 231 (2.92), 249 (2.84), 293 (2.68). IR spectrum, ν, cm^{-1}: 3059, 1703, 1606, 1582, 1567, 1524, 1490, 1473. ^1H NMR spectrum, δ, ppm: 7.1 s (1H, 5-H), 7.6 m (3H, H_{arom}), 7.7 d (2H, H_{arom}, J = 8.3 Hz), 8.3 d (2H, H_{arom}, J = 8.3 Hz), 8.5 d (2H_{arom}, J = 8.3 Hz). Mass spectrum, *m/z* (I_{rel}, %): 350 (56) $[M]^+$, 322 (22), 174 (2), 146 (8), 134 (6), 129 (81), 102 (100). Found, %: C 58.0; H 3.2; N 16.4; S 9.6. $C_{17}H_{10}N_4O_3S$. Calculated, %: C 58.3; H 2.9; N 16.0; S 9.2. *M* 350.35.

5-Phenyl-2-(pyridin-4-yl)-7*H*-[1,2,4]triazolo-[5,1-*b*][1,3]thiazin-7-one (IIIi). Yield 58% (*a*), mp 235–237°C, R_f 0.16. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 207 (3.22), 233 (2.72), 285 (2.68). IR spectrum, ν, cm^{-1}: 3055, 2933, 1700, 1660, 1610, 1584, 1572, 1520, 1491. ^1H NMR spectrum, δ, ppm: 7.4 s (1H, 5-H), 7.6 m (3H, H_{arom}), 7.9 d (2H, H_{arom}, J = 6.8 Hz), 8.1 d (2H_{arom}, J = 4.6 Hz), 8.8 d (2H, H_{arom}, J = 4.6 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 306 (100) $[M]^+$, 278 (29), 174 (3), 146 (7), 134 (9), 129 (43), 102 (67). Found, %: C 62.4; H 3.5; N 18.7; S 10.4. $C_{16}H_{10}N_4OS$. Calculated, %: C 62.7; H 3.3; N 18.3; S 10.5. *M* 306.34.

3-Methyl-7-phenyl[1,2,4]triazolo[3,4-*b*][1,3]thiazin-5-one (IVb). Ester **II**, 7 mmol, was added to a suspension of 7 mmol of 1-acetylthiosemicarbazide (**Ib**) in 30 ml of methanol containing 0.1 ml of concentrated sulfuric acid. The mixture was heated to maintain it slightly boiling until compound **Ib** dissolved completely and was then left to stand for 72 h at 18–20°C. Unreacted thiosemicarbazide **Ib** separated from the solution as transparent star-like crystals. The mixture was repeatedly heated for five times, the solvent was removed under reduced pressure, and the residue consisting mainly of unreacted compound **Ib** was treated with chloroform (2×15 ml). The extracts were evaporated under reduced pressure, and the residue was recrystallized from ethanol. Yield 7%, mp 205–208°C, R_f 0.16. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-4}$): 210 (1.63), 223 (1.49), 252 (1.36). IR spectrum, ν, cm^{-1}: 3055, 3030, 1696, 1568, 1500, 1451. ^1H NMR spectrum, δ, ppm: 2.9 s (3H, CH_3), 6.7 s (1H, 5-H), 7.5–7.6 m (5H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 243 (100) $[M]^+$, 215 (38), 174 (4), 146 (11), 134 (43), 129 (36), 102 (97). Found, %: C 58.9; H 3.2; N 17.6; S 14.9. $C_{12}H_9N_3OS$. Calculated, %: C 59.2; H 3.7; N 17.3; S 13.2. *M* 243.29.

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