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Synthesis and Transformations of 2-R-5-Aryl-5,6-dihydro-7*H*-[1,2,4]-triazolo[5,1-*b*]-[1,3]thiazin-7-ones

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Abstract—A new procedure for preparation of 2-R-5-aryl-5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones by condensation of 5-R-1,2,4-triazole-3-thiones with 3-arylacryloyl chlorides was developed. The thiazine ring of the [1,2,4]triazolo-[5,1-*b*][1,3]thiazin-7-ones is easily cleaved by treating with ammonia and hydrazine affording amides and hydrazides of 3-aryl-3-(1H-1,2,4-triazol-5-ylsulfanyl)propanoic acids. The latter react with isothiocyanates furnishing carbamoyl thiohydrazides of 3-aryl-3-(1H-1,2,4-triazol-5-ylsulfanyl)propanoic acids that in alkaline media undergo cyclization into 4-aryl-5-[2-(4H-1,2,4-triazol-5-ylsulfanyl)-2-phenylethyl]-2,4-dihydro-3H-1,2,4-triazole-5-thiones.

Derivatives of 4*H*-1,3-thiazin-4-one possess antiphlogistic, analgesic, and tuberculocidal activity [1–3]. A 1,3-thiazine fragment is also included into the composition of 7-aminocephalosporanic acid whose structure underlies that of в-lactam antibiotics [4]. In fused heterocycles containing a 1,3-thiazine ring was recently revealed also antitumor [5] and anticonvulsant [6] activity. Therefore the synthesis and the study of properties of 1,3-thiazine derivatives is an urgent task.

1,2,4-Thiazole-3-thione is frequently used as an initial compound for the synthesis of 4*H*-1,3-thiazin-4-one derivatives [7–9]. It was shown formerly that the acylation of 1,2,4-triazoline-3-thione with acyl chlorides occurred as selective N-acylation into the position *2* [10, 11], and at the sacrifice of the mercapto group the 1,2,4-triazoline-3-thione readily added at 20°C to compounds containing an activated multiple bond, e.g., to propiolic and acrylic acids [9, 12], and to acrylonitrile [13]. We established [14] that the condensation of triazolinethione **Ia** with cinnamoyl chloride **IIa** gave rise to 5-aryl-5,6-dihydro-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]-thiazin-7-one **IVa**. In continuation of this research we established that in this reaction were also involved 5-aryl-2,4-dihydro-3*H*-1,2,4-triazole-3-thiones **Ib–g**, 3-arylacryloyl chlorides **IIb**, **c**, and 3-heterylacryloyl chlorides **IId–f**. Thus were obtained 2-R-5-aryl-5,6-dihydro-7*H*-[1,2,4]-triazolo[5,1-*b*]-[1,3]-thiazin-7-ones **IVb–k** (Scheme 1).

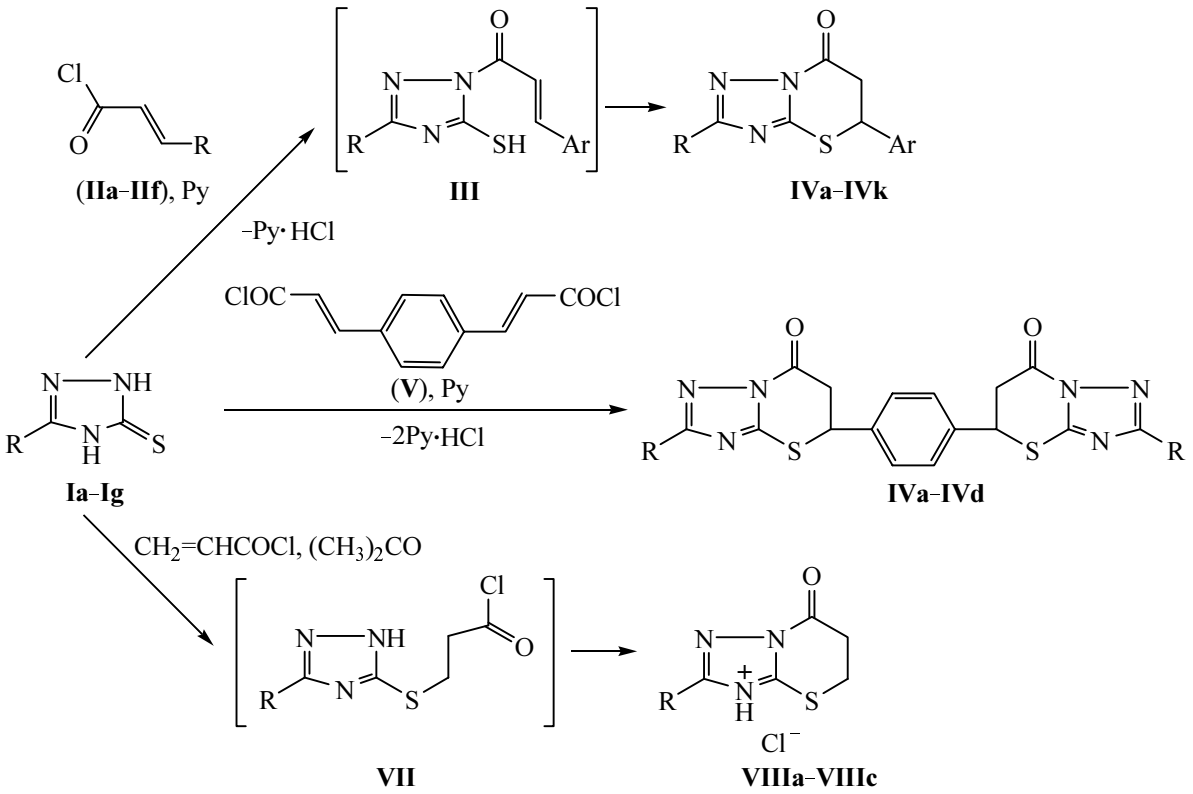
Triazolo[5,1-*b*][1,3]-thiazin-7-ones **IV** synthesized are colorless or yellowish substances well crystallizable from acetic acid. Yields, melting points, elemental analyses, ^{1}H and IR spectra are compiled in Tables 1–3.

The heterocylization occurs at heating at reflux a solution of initial compounds in a mixture benzene–pyridine, 1:1, for 1 h resulting in good yields (50–81%). The advantage of the procedure consists in the possibility to synthesize triazolo[5,1-*b*][1,3]thiazin-7-ones **IV** with various substituents (aryl, heteryl, and alkyl) in positions *2* and *5*. The best yields of compounds **IV** were obtained at R = H, C_6H_5, Ar = C_6H_5, 4-$CH_3OC_6H_4$, 3-$O_2NC_6H_4$ (65–81%), somewhat worse at R = alkyl, heteryl, Ar = heteryl (50–63%).

The data of ^{1}H NMR spectroscopy unambiguously prove the formation of a heterocycle. The signals of protons at the double bond of the initial 3-arylacryloyl chloride **II** in the ^{1}H NMR spectra are observed as two doublets in the region 6.80 and 7.50 ppm. The double C=C bond after heterocyclization becomes an ordinary bond in compounds **IV**. The signals of protons in positions *5* and *6* appear in the ^{1}H NMR spectra as ABX system, and their signals are present in the region 3.30–5.50 ppm The characteristic absorption bands in the IR spectra of compounds **IV** are those of C=O (1720–1750 cm^{-1}) and C=N (1590–1610 cm^{-1}) groups.

Notice that the attempt to carry out the cyclization of 1,2,4-triazole-3-thiones **I** with 3-arylacryloyl chlorides **II** in acetone or benzene failed. The reaction does not occur at room temperature, and at heating only tarring of the reaction mixture was observed. Therefore it is presumable

Scheme 1.



I, R = H (**a**), C_6H_5 (**b**), 4-FC_6H_4 (**c**), 1-naphthyl (**d**), 1-adamantyl (**e**), $(C_6H_5)_2CH$ (**f**), 1,3-benzodioxol-5-yl (**g**); **II**, Ar = C_6H_5 (**a**), 4-$CH_3OC_6H_4$ (**b**), 3-$O_2NC_6H_4$ (**c**), 1,3-benzodioxol-5-yl (**d**), 2-thienyl (**e**), 2-furyl (**f**); **IV**, R = H (**a–c**), C_6H_5 (**d**), 4-FC_6H_4 (**e, f**), 1-naphthyl (**g**), 1-adamantyl (**h, i**), $(C_6H_5)_2CH$ (**j**), 1,3-benzodioxol-5-yl (**k**); Ar = C_6H_5 (**a, e, g, h, j, k**), 4-$CH_3OC_6H_4$ (**b**), 3-$O_2NC_6H_4$ (**c**), -1,3-benzodioxol-5-yl (**d**), 2-thienyl (*f*), 2-furyl (i); **VI**, R = C_6H_5 (**a**), 4-$CH_3OC_6H_4$ (**b**), 4-$CH_3C_6H_4$ (**c**), 4-FC_6H_4 (**d**); **VIII**, R = C_6H_5 (**a**), 4-$CH_3OC_6H_4$ (**b**), 4-FC_6H_4 (**c**).

[15] that the reaction of 1,2,4-triazole-3-thiones **I** with 3-arylacryloyl chlorides in pyridine proceeds first as the N-acylation of triazoline-3-thione to give intermediate adduct **III** that then converts into triazolo[5,1-*b*]-[1,3]-thiazin-7-one **IV**.

In the same fashion 1,2,4-triazole-3-thiones **I** react with 3-{4-[2-(chlorocarbonyl)ethenyl]phenyl-}acryloyl chloride **V** in pyridine. As a result of this condensation form benzene-1,4-diylbis-2-R-5-aryl-5,6-dihydro-7*H*-[1,2,4]triazolo[5,1-*b*]-[1,3]-thiazin-7-ones **VIa–d** in 61–72% yield.

Yet 1,2,4-triazole-3-thiones **I** do not react with acryloyl -chloride in pyridine The reaction of 1,2,4-triazole-3-thiones **I** with acryloyl -chloride takes place in acetone giving rise to triazolo[5,1-*b*][1,3]-thiazin-7-ones hydrochlorides **VIII** (yield 60–71%). This reaction apparently occurs [16] first as an addition of 1,2,4-triazoline-3-thione by its thioxo group to the double bond of the acryloyl -chloride via intermediate **VII**, and then it undergoes an intramolecular acylation affording compound **VIII**.

In the ^{1}H NMR spectra of compounds **VIIIa–c** as characteristic signals should be mentioned two triplets from the protons of the thiazine ring (д 2.82–2.87 and 3.33–3.38 ppm), and the broadened singlet from the proton of the NH group (д 6.80–7.40 ppm).

Different conditions required by reactions of 5-aryl-1,2,4-triazole-3-thione with 3-arylacryloyl chlorides (in pyridine) and with acryloyl -chloride (in acetone) although both processes afford [1,2,4]triazolo-[5,1-*b*][1,3]thiazines are apparently due to unequal reactivity of the double bonds in 3-arylacryloylchlorides and acryloylchloride.

In the same fashion 1,2,4-triazole-3-thiones **I** react with 3-{4-[2-(chlorocarbonyl)ethenyl]phenyl-}acryloyl chloride **V** in pyridine. As a result of this condensation form benzene-1,4-diylbis-2-R-5-aryl-5,6-dihydro-7*H*-

Table 1. Yields, melting points, and elemental analyses of 5,6-dihydro-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **IVa–k**, **VIa–d,** and **VIIIa–c**, propanamides **IXa, b**, propanehydrazides **Xa, b**, hydrazones **XIa, b**, thiosemicarbazides **XIIa, b**, and 1,2,4-triazole-3-thione **XIII**

Compd. no.	Yield, %	mp, °C[a]	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IVa	70	161–163	56.86	3.95	18.20	$C_{11}H_9N_3OS$	57.14	3.92	18.18
IVb	72	143–145	55.12	4.10	16.12	$C_{12}H_{11}N_3O_2S$	55.17	4.24	16.09
IVc	81	202–205	47.85	2.90	20.60	$C_{11}H_8N_4O_3S$	47.83	2.92	20.29
IVd	70	190–192	61.77	3.61	12.12	$C_{18}H_{13}N_3O_3S$	61.53	3.73	11.96
IVe	68	193–195	62.55	3.86	13.05	$C_{17}H_{12}FN_3OS$	62.76	3.72	12.91
IVf	61	188–190	54.14	2.91	12.80	$C_{15}H_{10}FN_3OS_2$	54.37	3.04	12.68
IVg	57	137–139	70.41	4.52	11.89	$C_{21}H_{15}N_3OS$	70.57	4.23	11.76
IVh	69	220–222	69.30	6.21	11.69	$C_{21}H_{23}N_3OS$	69.01	6.34	11.50
IVi	67	217–220	64.09	6.13	12.02	$C_{19}H_{21}N_3O_2S$	64.20	5.95	11.82
IVj	50	163–165	72.38	4.98	10.71	$C_{24}H_{19}N_3OS$	72.52	4.82	10.57
IVk	52	190–192	61.75	3.89	12.15	$C_{18}H_{13}N_3O_3S$	61.53	3.73	11.96
VIa	54	277–280	62.84	3.97	15.44	$C_{28}H_{20}N_6O_2S_2$	62.67	3.76	15.66
VIb	68	330–335	60.04	4.19	14.22	$C_{30}H_{24}N_6O_4S_2$	60.39	4.05	14.08
VIc	57	316–320	63.97	4.41	14.70	$C_{30}H_{24}N_6O_2S_2$	63.81	4.28	14.88
Vid	51	310–315	58.65	3.33	14.78	$C_{28}H_{18}F_2N_6O_2S_2$	58.73	3.17	14.68
VIIIa	67	137–140	49.48	3.68	15.77	$C_{11}H_{10}ClN_3OS$	49.35	3.76	15.69
VIIIb	55	141–143	48.62	4.17	14.25	$C_{12}H_{12}ClN_3O_2S$	48.41	4.06	14.11
VIIIc	61	120–122	46.09	3.34	14.83	$C_{11}H_9ClFN_3OS$	46.24	3.17	14.71
IXa	77	143–145	53.42	5.08	22.37	$C_{11}H_{12}N_4OS$	53.21	4.87	22.56
IXb	71	153–155	51.60	5.29	20.29	$C_{12}H_{14}N_4O_2S$	51.79	5.07	20.13
Xa	83	163–165	50.32	5.13	26.78	$C_{11}H_{13}N_5OS$	50.18	4.98	26.60
Xb	75	170–172	49.27	5.28	24.06	$C_{12}H_{15}N_5O_2S$	49.13	5.15	23.87
XIa	68	204–207	61.57	5.06	20.14	$C_{18}H_{17}N_5OS$	61.52	4.88	19.93
XIb	59	185–187	53.61	4.10	19.78	$C_{16}H_{15}N_5OS_2$	53.76	4.23	19.59
XIIa	83	190–194	54.29	4.31	21.25	$C_{18}H_{18}N_6OS_2$	54.25	4.55	21.09
XIIb	75	187–190	46.30	4.93	25.20	$C_{13}H_{16}N_6OS_2$	46.41	4.79	24.98
XIII	63	145–147	56.87	4.13	21.91	$C_{18}H_{16}N_6S_2$	56.82	4.24	22.09

[a] Compounds **IVa–IVk**, **XIa, XIb**, and **XIII** were recrystallized from acetic acid, **VIa–VId** from benzonitrile, **VIIIa–VIIIc** from ethanol, **IXa, IXb** and **Xa, b** Xfrom a mixture ethanol–water, 1:1.

[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **VIa–VId** in 61–72% yield.

Triazolo[5,1-*b*][1,3]-thiazin-7-ones are poorly studied compounds whose chemical properties are hardly described. We found that the CO–N bond of the 1,3-thiazine ring was weak, and triazolo[5,1-*b*][1,3]-thiazin-7-ones **IV** readily reacted with ammonia and hydrazine. After these reactions we isolated from the reaction mixtures 3-aryl-3-(1*H*-1,2,4-triazol-5-ylsulfanyl)propanoic acids amides **IXa, IXb** and hydrazides **Xa, Xb**.

Hydrazides **X** possess high reactivity and form hydrazones **XIa, XIb** with aldehydes and with isothiocyanates afford thiosemicarbazide derivatives **XIIa, XIIb**. In a boiling water solution of sodium hydroxide compound **XIIa** converted into 5-[2-(1*H*-1,2,4-triazol-5-ylsulfanyl)-2-phenylethyl]-4-phenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione **XIII** (Scheme 2).

In the ^{1}H NMR spectra of compounds **IXa, IXb** and **Xa, Xb** the following signals are characteristic: peaks of CH_2–CH groups (*ABX* system, δ 2.76–2.90 and 4.97–

Table 2. ^{1}H NMR spectra of 5,6-dihydro-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **IVa–IVk**, **VIa–VId,** and **VIIIa–VIIIc**, propanamides **IXa, IXb**, propanehydrazides **Xa, Xb**, hydrazones **XIa, XIb**, thiosemicarbazides **XIIa, XIIb**, and 1,2,4-triazole-3-thione **XIII**

Compd. no.	^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz)[a]
IVa	3.42 m (1H, H^6), 3.90 m (1H, H^6), 5.45 (1H, H^5), 7.40–7.62 m (5H, C_6H_5), 8.31 s (1H, H^2)
IVb	3.41 m (1H, H^6), 3.78 m (1H, H^6), 3.83 c (3H, CH_3O), 5.36 m (1H, H^5), 7.00 d (2H, H arom, *J* 8.1), 7.53 d (2H, H arom, *J* 8.1), 8.06 s (1H, H^2)
IVc	3.41 m (1H, H^6), 3.99 m (1H, H^6), 5.60 m (1H, H^5), 7.76 t (1H, H arom, *J* 8.7), 7.95 d (1H, H arom, *J* 8.7), 8.25 d (1H, H arom, *J* 8.7) 8.30 c (1H, H^2), 8.38 d (1H, H arom, *J* 8.7)
IVd	3.38 m (1H, H^6), 3.91 m (1H, H^6), 5.41 m (1H, H^5), 6.07 s (2H, OCH_2O), 6.98 m (2H, H arom), 7.13 s (1H, H arom), 7.55 m 3H, C_6H_5), 8.09 m (2H, C_6H_5)
IVe	3.46 m (1H, H^6), 3.89 m (1H, H^6), 5.51 m (1H, H^5), 7.31–7.59 m (7H, H arom), 8.13 m (2H, H arom)
IVf	3.66 m (1H, H^6), 3.83 m (1H, H^6), 5.76 m (1H, H^5), 7.04 d.d (1H, H^4 thiophene, J_1 4.8, J_2 3.1), 7.21 d (1H, H^3 thiophene, *J* 3.1), 7.40 m (2H, H arom), 7.57 d (1H, H^3 thiophene, *J* 4.8), 8.11 m (2H, H arom)
IVg	3.49 m (1H, H^6), 3.99 m (1H, H^6), 5.55 m (1H, H^5), 7.42–7.70 m (8H, H arom), 8.06 d (1H, $C_{10}H_7$, *J* 9.0), 8.15 d (1H, $C_{10}H_7$, *J* 9.0), 8.30 d (1H, $C_{10}H_7$, *J* 9.0), 9.14 d (1H, $C_{10}H_7$, *J* 9.0)
IVh	1.73 s (6H, $C_{10}H_{15}$), 1.93 s (6H, $C_{10}H_{15}$), 2.03 s (3H, $C_{10}H_{15}$), 3.22 m (1H, H^6), 3.83 m (1H, H^6), 5.40 m (1H, H^5), 7.42 m (5H, C_6H_5)
IVi	1.72 s (6H, $C_{10}H_{15}$), 1.92 s (6H, $C_{10}H_{15}$), 2.02 s (3H, $C_{10}H_{15}$), 3.58 d (2H, H^6, *J* 6.0), 5.44 t (1H, H^5, *J* 6.0), 6.43 m (2H, furan), 7.69 d (1H, H^5 furan, *J* 2.9)
IVj	3.29 m (1H, H^6), 3.87 m (1H, H^6), 5.47 m (1H, H^5), 5.68 s [1H, $(C_6H_5)_2\underline{CH}$], 7.03–7.69 m (15H, $3C_6H_5$)
IVk	3.40 m (1H, H^6), 3.85 m (1H, H^6), 5.51 m (1H, H^5), 6.13 s (2H, OCH_2O), 7.05 d (1H, H arom, *J* 7.6), 7.40–7.65 m (7H, H arom)
VIa	2.98–3.68 m (4H, $2CH_2CO$), 5.13 m (2H, 2SCH), 7.03 s (4H, H arom), 7.32–7.71 m (10H, $2C_6H_5$)
VIb	3.20–3.61 m (4H, $2CH_2CO$), 3.79 s (6H, $2CH_3O$), 5.39 m (2H, 2SCH), 6.96 d (4H, H arom, *J* 8.0), 7.52 d (4H, H arom, *J* 8.1), 7.79 d (4H, H arom, *J* 8.1)
VIc	2.24 s (6H, $2CH_3$), 3.42–3.83 m (4H, $2CH_2CO$), 5.32 m (2H, 2SCH), 7.18 d (4H, H arom, *J* 6.9), 7.46 s (4H, Harom), 7.61 d (4H, H arom, *J* 6.9)
VId	3.45–3.89 m (4H, $2CH_2CO$), 5.35 m (2H, 2SCH), 7.05 s (4H, H arom), 7.49 s (4H, H arom), 7.81 s (4H, H arom)
VIIIa	2.85 t (2H, CH_2CO, *J* 6.5), 3.37 t (2H, CH_2S, *J* 6.5), 6.03 br.s (1H, HCl), 7.51 m (3H, C_6H_5), 8.02 m (2H, C_6H_5)
VIIIb	2.83 t (2H, CH_2CO, *J* 6.2), 3.34 t (2H, CH_2S, *J* 6.2), 3.81 s (3H, CH_3O), 6.80 br.s (1H, HCl), 7.12 d (2H, H arom, *J* 8.5), 8.02 d (2H, H arom, *J* 8.5)
VIIIc	2.87 t (2H, CH_2CO, *J* 6.7), 3.37 t (2H, CH_2S, *J* 6.7), 7.01 br.s. (1H, HCl), 7.40 m (2H, H arom), 8.09 m (2H, Harom)
IXa	2.81 d (2H, CH_2CO, *J* 5.5), 5.01 t (1H, SCH, *J* 5.5), 6.92 br.s (1H, CONH), 7.20 m (5H, C_6H_5), 7.33 br.s (1H, CONH), 8.53 s (1H, CH triazole), 14.07 br.s (1H, NH triazole)
IXb	2.78 d (2H, CH_2CO, *J* 6.2), 3.75 s (3H, CH_3O), 4.98 t (1H, SCH, *J* 6.2), 6.98 br.s (1H, CO–NH), 6.79 d (2H, H arom, *J* 8.5), 7.25 d (2H, H arom, *J* 8.5), 7.31 br.s (1H, CO–NH), 8.38 s (1H, CH triazole), 13.91 br.s (1H, NH triazole)
Xa	2.81 d (2H, CH_2CO, *J* 6.7), 3.80 br.s (2H, NH_2), 5.11 t (1H, SCH, *J* 6.7), 7.26 m (5H, C_6H_5), 8.42 s (1H, CH triazole), 9.06 br.s (1H, CONH), 13.91 br.s (1H, NH triazole)
Xb	2.76 d (2H, CH_2CO, *J* 6.6), 3.65 br.s (2H, NH_2), 3.78 s (3H, CH_3O), 5.01 t (1H, SCH, *J* 6.6), 6.81 d (2H, Harom, *J* 7.7), 7.26 d (2H, Harom, *J* 7.7), 8.40 s (1H, CH triazole), 9.03 br.s (1H, CONH), 13.52 br.s (1H, NH triazole)
XIa[b]	3.10 m (1H, CH_2CO), 3.53 m (1H, CH_2CO), 5.24 m (1H, SCH), 7.10–7.82 m (10H, $2C_6H_5$), 8.07 s and. 8.24 s (1H, CH=N), 8.60 s (1H, CH triazole), 11.32 s and 11.51 s (1H, CONH), 14.14 br.s (1H, NH triazole)
XIb[b]	3.26 m (1H, CH_2CO), 3.51 m (1H, CH_2CO), 5.13 m (1H, SCH), 7.05–7.76 m (8H, C_6H_5 + C_4H_3S), 8.22 s and 8.32 s (1H, CH=N), 8.59 s (1H, CH triazole), 11.28 s and 11.33 s (1H, CONH), 14.12 br.s (1H, NH triazole)
XIIa	3.05 m (2H, CH_2CO), 5.12 m (1H, SCH), 7.03–7.96 m (10H, $2C_6H_5$), 8.57 s (1H, CH triazole), 9.41 br.s (1H, $C_6H_5\underline{NH}CS$), 9.59 br.s (1H, $NH\underline{NH}CS$), 10.04 br.s (1H, CONH), 14.03 br.s (1H, NH triazole)
XIIb	2.71 d (3H, CH_3, *J* 3.8), 3.02 m (2H, CH_2CO), 5.06 m (1H, SCH), 7.05–7.60 m (6H, C_6H_5 + $\underline{NH}CH_3$), 8.59 s (1H, CH triazole), 9.23 br.s (1H, $NH\underline{NH}CS$), 9.82 br.s (1H, CONH), 14.13 уш.с (1H, NH triazole)
XIII	3.21 m (2H, CH_2CO), 4.77 m (1H, SCH), 7.04–7.80 m (11H, $2C_6H_5$ + NHC=S), 8.42 s (1H, CH triazole), 13.71 br.s (1H, NH triazole)

[a] Spectrum of compound **IVb** was registered in acetone-d_6, spectra of compounds **VIa–VId** were recorded in CF_3COOD.

[b] Hydrazones **XIa, XIb** form as a mixture of (*Z*)- and (*E*)-form in a ratio approximately 1:1.

Table 3. IR spectra of 5,6-dihydro-7*H*-[1,2,4]triazolo[5,1-*b*]-[1,3]thiazin-7-ones **IVa–IVk**, **VIa–VId,** and **VIIIa–VIIIc**, propanamides **IXa, IXb**, propanehydrazides **Xa, Xb**, hydrazones **XIa, XIb**, thiosemicarbazides **XIIa, XIIb**, and 1,2,4-triazole-3-thione **XIII**

Compd. no.	IR spectrum, ν, cm^{-1}
IVa	3100–3000, 1730, 1600, 1510, 1450, 1410
IVb	3100–3000, 1720, 1600, 1480, 1420
IVc	3100–3000, 1730, 1590, 1540, 1510, 1400
IVd	3100–2900, 1740, 1610, 1480, 1440
IVe	3100–2900, 1750, 1600, 1490, 1410
IVf	3150–3000, 1740, 1600, 1480, 1420
IVg	3100–3000, 1740, 1610, 1500, 1480, 1450
IVh	3000–2800, 1730, 1600, 1500, 1450
IVi	3000–2800, 1720, 1620, 1500, 1450, 1410
IVj	3100–2900, 1730, 1590, 1520, 1490, 1450
IVk	3100–3000, 1720, 1600, 1490, 1440
VIa	3100–3000, 1740, 1600, 1590, 1470, 1410
VIb	3100–3000, 1750, 1600, 1580, 1480, 1420
VIc	3100–3000, 1730, 1610, 1530, 1490, 1410
VId	3150–3000, 1750, 1600, 1490, 1410
VIIIa	3250–2700, 1730, 1610, 1580, 1500, 1440, 1410
VIIIb	3250–2700, 1720, 1610, 1590, 1520, 1480, 1430
VIIIc	3250–2700, 1710, 1610, 1510, 1490, 1410
IXa	3200–2800, 1660, 1610, 1490, 1440, 1400
IXb	3200–2800, 1650, 1600, 1510, 1440, 1410
Xa	3200–2800, 1630, 1590, 1550, 1480, 1450, 1430
Xb	3200–2800, 1680, 1610, 1520, 1460
XIa	3200–2800, 1660, 1600, 1490, 1450, 1400
XIb	3200–2800, 1670, 1590, 1550, 1490, 1430, 1400
XIIa	3200–2800, 1680, 1540, 1500, 1450
XIIb	3200–2800, 1670, 1560, 1510, 1440
XIII	3100–2900, 2500, 1600, 1510

5.11 ppm), of $CO–NH_2$ groups (δ 6.92–6.98 and 7.31–7.33 ppm), of $CO–NH–NH_2$ groups (δ 3.65–3.80 and 9.03–9.06 ppm), and of CH and NH protons of the triazole ring (δ 8.38–8.53 and 14.12–14.23 ppm). In the IR spectra appear characteristic absorption bands of NH groups (2800–3200 cm^{-1}), C=O groups (1630–1680 cm^{-1}), and C=N bonds (1590–1610 cm^{-1}). In the ^{1}H NMR spectra of compounds **XIa, XIb** and **XIIa, XIIb** are present signals from protons of CH_2–CH groups (*ABX* system, δ 3.02–3.53 and 5.06–5.24 ppm), of CH=N group (δ 8.07–8.32 ppm), of CO–NH (δ 9.82–11.51 ppm), of CH and NH protons of triazole ring (δ 8.57–8.60 ppm and 14.03–14.14 ppm), NH–CS (δ 9.41 ppm), and NH–NH–CS group (δ 9.23–9.59 ppm). The ^{1}H NMR spectrum of compound **XIII** is simpler than the spectra of initial compounds, and it contains signals of protons from CH_2–CH group (δ 3.21– 4.77 ppm), from aromatic rings (δ 7.04–7.80 ppm), and from protons of CH and NH groups of the triazole ring (δ 8.42 and 13.71 ppm).

And so the reaction of 5-R-1,2,4-triazole-3-thiones with acryloyl chloride, 3-arylacryloyl chlorides, and benzene-1,4-diylbisacryloyl chloride possesses a general character and is a new convenient one-stage synthetic procedure for preparation of [1,2,4]triazolo[5,1-*b*]-[1,3]thiazin-7-ones interesting as potential physiologically active substances. Being highly reactive they are promising for preparation of other heterocyclic compounds.

EXPERIMENTAL

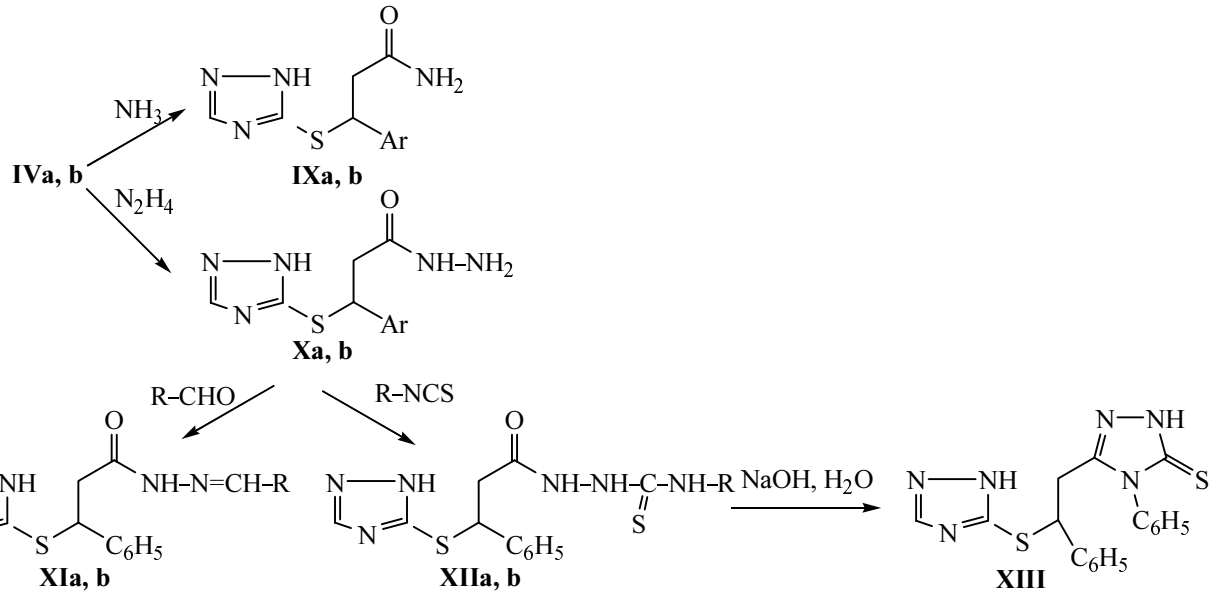
^{1}H NMR spectra were registered on spectrometer Varian VXR-300 (operating frequency 300 MHz) from solutions of compounds in DMSO-d_6, acetone-d_6, or CF_3COOD, internal reference TMS. IR spectra from samples of compounds pelletized with KBr were recorded on spectriphotometer UR-20.

2-R-5-Aryl-5,6-dihydro-7*H*-[1,2,4]triazolo-[5,1-*b*]-[1,3]thiazin-7-ones (IVa–k), and benzene-1,4-diylbis(2-R-5-aryl-5,6-dihydro-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones (VIa–d). To a solution of 10 mmol of 5-R-2,4-dihydro-3*H*-1,2,4-triazole-3-thione **I** in 5 ml of pyridine at 20°C was added a solution of 10 mmol of 3-arylacryloyl -chloride **II** or 5 mmol of benzene-1,4-diylbisacryloyl chloride **V** in 5 ml of benzene. The solution was heated at reflux for 1 h, cooled, and diluted with 50 ml of water. The separated precipitate was filtered off, washed with ether, and dried.

2-R-5,6-Dihydro-7*H*-[1,2,4]triazolo[5,1-*b*][1,3]-thiazin-7-ones hydrochlorides (VIIIa–c). To a dispersion of 10 mmol of 5-R-2,4-dihydro-3*H*-1,2,4-triazole-3-thione **I** in 30 ml of acetone at 25°C was added 11 mmol of acryloyl -chloride, and the mixture was stirred for 4 h. The separated precipitate of compound **VIII** was filtered off, washed with acetone, and dried.

3-Aryl-3-(1*H*-1,2,4-triazol-5-ylsulfanyl)-propanamides (IXa, b), and 3-aryl-3-(1*H*-1,2,4-triazol-5-ylsulfanyl)propanehydrazides (Xa, b). Into a solution of 5 mmol of triazolo[5,1-*b*][1,3]thiazin--7-one **IV** in 10 ml of ethanol at 25°C for 1 h was passed a flow of 30 mmol of gaseous ammonia or was added dropwise

Scheme 2.



IV, IX, X, Ar = C_6H_5 (**a**), 4-$CH_3OC_6H_4$ (**b**); **XI**, R = C_6H_5 (**a**), 2-thienyl (**b**); **XII**, R = C_6H_5 (a), CH_3 (**b**).

10 mmol of hydrazine hydrate. The reaction mixture was left standing for 24 h at room temperature, then it was heated for 3 h at 60°C. The reaction product **IX** or **X** precipitated on cooling was filtered off and dried.

N[1]-(R-Methylene)-3-(1*H*-1,2,4-triazol-5-ylsulfanyl)-3-phenylpropanehydrazides (XIa, b). To a solution of 2.5 mmol of hydrazide **X** in 4 ml of acetic acid was added at 40°C 2.6 mmol of an appropriate aldehyde , and the reaction mixture was left standing for 24 h at the above temperature. On cooling the separated precipitate of compound **XI** was filtered off, washed with ethanol, and dried.

4R-1-[3-(1*H*-1,2,4-triazol-5-ylsulfanyl)-3-phenylpropanoyl]thiosemicarbazides (XIIa, b). To a solution of 2.5 mmol of hydrazide **X** in 4 ml of ethanol at 20°C was added 2.6 mmol of an appropriate isothiocyanate. The reaction mixture was boiled for 2 h, then it was cooled, the separated precipitate of compound **XII** was filtered off and dried.

5-[2-(1*H*-1,2,4-triazol-5-ylsulfanyl)-2-phenylethyl]-4-phenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione (XIII). A solution of 1.5 mmol of thiosemicarbazide XIIa and 3 mmol of sodium hydroxide in 5 ml of water was boiled for 2 h, then cooled, and acidified with 0.6 ml of 30% hydrochloric acid. The separated precipitate of compound **XIII** was filtered off and dried.

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