Annelation of the thiazole ring to 1,2,4-triazines by tandem A_N—A_N or S_N^H—S_N^H reactions*

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The reactions of 3-aryl-1,2,4-triazines with aromatic thioamides and 4-arylthiosemicarbazides in acetic anhydride at room temperature afforded cyclic products of the tandem nucleophilic addition reactions, *viz.*, tetrahydrothiazolo[4,5-*e*]-annelated 1,2,4-triazines, in good yields. The latter underwent aromatization in the presence of potassium permanganate.

Key words: 3-aryl-1,2,4-triazines, tandem nucleophilic addition reactions, cyclic adducts, aromatic thioamides, 4-arylthiosemicarbazides, thiazole-annelated 1,2,4-triazines.

Tandem nucleophilic addition (A_N—A_N) of bifunctional reagents to azines, tandem substitutions (S_N^H—S_N^H), and their various combinations (A_N—S_N^{ipso}) find increasing use as convenient procedures for the synthesis of fused heterocyclic systems.[1—7]

Earlier,[1—8] we have reported that the reactions of 1,2,4-triazines and their quaternary salts with 1,3-*C*,*O*- and *C*,*N*-bifunctional reagents (acetoacetamides, ketene *N*,*N*-aminals, β-aminovinyl ketones, and ethyl β-aminocrotonate) proceed as nucleophilic diaddition (A_N—A_N) and provide an efficient approach to the synthesis of fused 1,2,4-triazines in which the tetrahydro-1,2,4-triazine ring is fused to the furan and pyrrole rings.[1,2,8—12]

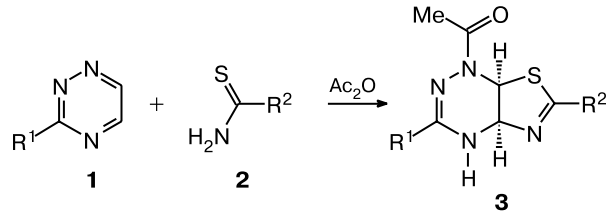
Recently, we have described the first successful example of tandem A_N—A_N reactions of 1,2,4-triazines with a 1,3-*S*,*N*-dinucleophile (thiobenzamide) involving the successive formation of two carbon—heteroatom bonds (for the preliminary communication, see Ref. 13).

The aim of the present study was to examine the possibility of performing S_N^H—S_N^H disubstitution of two *ortho*-arranged hydrogen atoms in 1,2,4-triazines under the action of aromatic thioamides and thiosemicarbazides, establish the three-dimensional structures of the cycloadducts, determine their stability, and reveal their further transformation pathways.

Results and Discussion

It was found that cyclizations of 3-aryl-1,2,4-triazines (**1**) with thioamides **2** in acetic anhydride occur smoothly and regioselectively at room temperature resulting in annelation of the thiazole ring to form 1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazines **3a—l** (Scheme 1).

Scheme 1



Compound **3**	R^1	R^2	Compound **3**	R^1	R^2
a	Ph	Ph	**g**	*p*-Me-C_6H_4	*p*-Cl-C_6H_4
b	*p*-MeO-C_6H_4	Ph	**h**	*p*-Cl-C_6H_4	*p*-Cl-C_6H_4
c	*p*-NO_2-C_6H_4	Ph	**i**	Ph	2-C_5H_4N
d	*p*-Cl-C_6H_4	Ph	**j**	*p*-Me-C_6H_4	2-C_5H_4N
e	*p*-Me-C_6H_4	Ph	**k**	*p*-Me-C_6H_4	4-C_5H_4N
f	Ph	*p*-Cl-C_6H_4	**l**	Ph	4-C_5H_4N

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The structures of compounds **3a—l** were established by elemental analysis, mass spectrometry, and ^{1}H and ^{13}C NMR spectroscopy, including HETCOR and HMBC experiments. The presence of molecular ion peaks $[M]^+$ in the mass spectra of compounds **3a—l** and the results of elemental analysis of these compounds confirm the formation of the 1 : 1 cyclic adducts of 1,2,4-triazines with thioamides (Table 1).

Table 1. Reaction conditions, yields, melting points, elemental analysis data, and mass spectra of 1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazines **3a—l**

Compound	R^1 (R^2)	Reaction conditions		Yield (%)	M.p. /°C	Found / Calculated (%)			Molecular formula (Molecular weight)	Mass spectrum, m/z (I_{rel} (%))
		Ac_2O /mL	τ /h			C	H	N		
3a	Ph (Ph)	0.6	8	58	206—207	64.27 64.27	4.93 4.79	16.87 16.65	$C_{18}H_{16}N_4OS$ (336.42)	337 $[M + 1]^+$ (19), 336 $[M]^+$ (83), 173 (33), 158 (22), 157 (43), 121 (34), 104 (100), 103 (23), 77 (28)
3b	*p*-$MeOC_6H_4$ (Ph)	0.7	6	51	172—173	62.56 62.28	4.88 4.95	15.16 15.29	$C_{19}H_{18}N_4O_2S$ (366.44)	366 $[M]^+$ (100), 221 (25), 220 (28), 203 (32), 188 (25), 187 (36), 134 (80), 133 (34), 121 (37)
3c	*p*-$NO_2C_6H_4$ (Ph)	11	3*	15	236—238	56.72 56.68	3.87 3.96	18.23 18.36	$C_{18}H_{15}N_5O_3S$ (381.42)	382 $[M + 1]^+$ (23), 381 $[M]^+$ (100), 339 (27), 236 (45), 218 (32), 203 (22), 202 (50), 149 (42), 121 (55), 104 (34), 103 (54)
3d	*p*-ClC_6H_4 (Ph)	2.9	4	44	213—214	58.21 58.30	4.12 4.08	15.13 15.11	$C_{18}H_{15}ClN_4OS$ (370.86)	372 $[M + 1]^+$ (39), 371 $[M]^+$ (23), 370 (100), 225 (39), 207 (39), 193 (34), 192 (26), 191 (55), 140 (30), 138 (91), 137 (39), 121 (51), 104 (28)
3e	*p*-MeC_6H_4 (Ph)	1.8	6	44	191—192	65.19 65.12	5.36 5.18	16.08 15.99	$C_{19}H_{18}N_4OS$ (350.45)	351 $[M + 1]^+$ (23), 350 $[M]^+$ (100), 205 (35), 204 (29), 187 (38), 172 (26), 171 (48), 121 (38), 118 (93), 117 (25), 91 (20)
3f	Ph (*p*-ClC_6H_4)	1.5	2*	54	245—247	58.27 58.30	4.19 4.08	15.15 15.11	$C_{18}H_{15}ClN_4OS$ (370.86)	372 $[M + 1]^+$ (26), 371 $[M]^+$ (15), 370 (68), 191 (28), 173 (48), 158 (27), 157 (59), 155 (25), 104 (100), 103 (26), 77 (24)
3g	*p*-MeC_6H_4 (*p*-ClC_6H_4)	1.5	9	64	248—249	59.33 59.29	4.49 4.45	14.61 14.56	$C_{19}H_{17}ClN_4OS$ (384.89)	386 $[M + 1]^+$ (24), 385 $[M]^+$ (14), 384 (60), 205 (28), 204 (23), 187 (41), 172 (26), 171 (50), 155 (25), 118 (100), 117 (27)
3h	*p*-ClC_6H_4 (*p*-ClC_6H_4)	2.8	8	47	>250	53.42 53.34	3.58 3.48	13.80 13.82	$C_{18}H_{14}Cl_2N_4OS$ (405.31)	406 $[M + 1]^+$ (60), 405 $[M]^+$ (18), 404 (84), 362 (22), 207 (48), 193 (35), 192 (27), 191 (54), 157 (14), 155 (37), 140 (33), 138 (100), 137 (33), 111 (17), 58 (27)
3i	Ph (2-C_5H_4N)	1.7	2*	17	171—172	60.57 60.52	4.65 4.48	20.79 20.76	$C_{17}H_{15}N_5OS$ (337.41)	338 $[M + 1]^+$ (18), 337 $[M]^+$ (82), 264 (42), 177 (34), 173 (100), 159 (20), 158 (21), 123 (31), 122 (20), 105 (30), 104 (79), 77 (25)
3j	*p*-MeC_6H_4 (2-C_5H_4N)	1.8	6	48	207—208	61.52 61.52	5.03 4.88	19.94 19.93	$C_{18}H_{17}N_5OS$ (351.43)	352 $[M + 1]^+$ (21), 351 $[M]^+$ (93), 278 (49), 205 (23), 187 (100), 177 (32), 172 (23), 123 (26), 118 (78), 105 (20)
3k	*p*-MeC_6H_4 (4-C_5H_4N)	4.6	4*	28	192—193	61.70 61.52	4.94 4.88	19.88 19.93	$C_{18}H_{17}N_5OS$ (351.43)	352 $[M + 1]^+$ (22), 351 $[M]^+$ (100), 309 (28), 187 (30), 172 (20), 171 (41), 118 (76), 117 (21), 91 (17)
3l	Ph (4-C_5H_4N)	17.5	5*	35	182—184	60.74 60.52	4.44 4.48	20.58 20.76	$C_{17}H_{15}N_5OS$ (337.41)	338 $[M + 1]^+$ (17), 337 $[M]^+$ (83), 295 (26), 173 (28), 158 (20), 157 (44), 105 (24), 104 (100), 103 (23), 77 (26)

* Days.

In the ^{1}H NMR spectra of compounds **3**, the signals for the bridgehead hydrogen atoms are easy to identify. The signal for the bridgehead H(4a) proton is observed at δ 6.07—6.18 as a doublet of doublets with the vicinal constants $^3J_{H(4a),H(7a)}$ = 7.4—7.9 and $^3J_{H(4a),N(4)H}$ = 2.3—2.7 Hz, whereas the signal for the bridgehead H(7a) proton is observed as a doublet at δ 6.25—6.46 with the constant $^3J_{H(7a),H(4a)}$ = 7.4—7.9 Hz (Table 2). The vicinal constants $^3J_{H(7a),H(4a)}$ = 7.4—7.9 Hz correspond to the *cis* orientation of the bridgehead protons and are indicative of annelation of the five-membered heterocycle to 1,2,4-triazine.[14]

This skeleton of the bicyclic system is confirmed by the fact that the HMBC spectra of compound **3b** (Fig. 1) show cross-peaks between the *ortho*-protons of the methoxyphenyl fragment and the C(3) atom, which, in turn, has a cross-peak with the bridgehead H(4a) atom. This allowed us to identify the bridgehead protons and the NH group. The long-range couplings in the HMBC spectra of compound **3b** are shown in Fig. 1.

The character of fusion of the thiazole and 1,2,4-triazine rings in compounds **3a—l** can be judged from the ^{13}C NMR spectra (Table 3). Earlier,[14] it has been demonstrated that in the ^{13}C NMR spectra of related systems,

Table 2. ^{1}H NMR spectroscopic data (DMSO-d_6) for 1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazines **3a—l**

Compound	δ (*J*/Hz)					
	COMe (s)	H(4a) (dd)	H(7a) (d)	Ar	N(4)H (d)	Other signals
3a	2.28	6.18 (*J* = 7.7, *J* = 2.5)	6.46 (*J* = 7.7)	7.44—7.57 (m, 6 H, Ph); 7.73—7.77, 7.84—7.87 (both m, 2 H each, Ph)	8.47 (*J* = 2.5)	—
3b	2.26	6.16 (*J* = 7.9, *J* = 2.6)	6.45 (*J* = 7.9)	7.01 (d, 2 H, *p*-MeOC$_6$H$_4$, *J* = 8.8); 7.45—7.56 (m, 3 H, Ph); 7.72—7.82 (m, 2 H, Ph); 7.80 (d, 2 H, *p*-MeOC$_6$H$_4$, *J* = 8.8)	8.38 (*J* = 2.6)	3.80 (s, 3 H, *p*-MeOC$_6$H$_4$)
3c	2.31	6.12 (*J* = 7.4, *J* = 2.3)	6.36 (*J* = 7.4)	7.40—7.51 (m, 3 H, Ph); 7.73—7.76 (m, 2 H, Ph); 8.11, 8.26 (both d, 2 H each, *p*-NO$_2$C$_6$H$_4$, *J* = 9.2)	8.64 (s)	—
3d	2.28	6.08 (*J* = 7.5, *J* = 2.3)	6.38 (*J* = 7.5)	7.39—7.53 (m, 5 H, Ph); 7.746 7.85 (both d, 2 H each, *p*-ClC$_6$H$_4$, *J* = 8.6)	8.32 (*J* = 2.3)	—
3e	2.27	6.07 (*J* = 7.8, *J* = 2.4)	6.38 (*J* = 7.8)	7.19 (d, 2 H, *p*-MeC$_6$H$_4$, *J* = 7.9); 7.38—7.52 (m, 3 H, Ph); 7.70—7.76 (m, 4 H, Ph, *p*-MeC$_6$H$_4$)	8.15 (*J* = 2.4)	2.36 (s, 3 H, *p*-MeC$_6$H$_4$)
3f	2.28	6.08 (*J* = 7.7, *J* = 2.5)	6.39 (*J* = 7.7)	7.38—7.46 (m, 5 H, Ph, *p*-ClC$_6$H$_4$); 7.73—7.85 (m, 4 H, Ph, *p*-ClC$_6$H$_4$)	8.25 (*J* = 2.5)	—
3g	2.27	6.08 (*J* = 7.6, *J* = 2.7)	6.38 (*J* = 7.6)	7.19 (d, 2 H, *p*-MeC$_6$H$_4$, *J* = 7.9); 7.44 (d, 2 H, *p*-ClC$_6$H$_4$, *J* = 8.6); 7.69—7.75 (m, 4 H, *p*-ClC$_6$H$_4$, *p*-MeC$_6$H$_4$)	8.18 (*J* = 2.7)	2.36 (s, 3 H, *p*-MeC$_6$H$_4$)
3h	2.27	6.10 (*J* = 7.7, *J* = 2.3)	6.40 (*J* = 7.7)	7.43—7.49 (m, 4 H, *p*-ClC$_6$H$_4$); 7.74, 7.85 (both d, 2 H each, *p*-ClC$_6$H$_4$, *J* = 8.6);	8.39 (*J* = 2.3)	—
3i	2.27	6.14 (*J* = 7.9, *J* = 2.4)	6.26 (*J* = 7.9)	7.38—7.43 (m, 3 H, Ph); 7.50 (ddd, 1 H, C$_5$H$_4$N, H(5′), *J* = 7.6, *J* = 4.9, *J* = 1.2); 7.82—7.86 (m, 2 H, Ph); 7.89 (dd, 1 H, C$_5$H$_4$N, H(4′), *J* = 7.6, *J* = 1.5); 8.02 (ddd, 1 H, C$_5$H$_4$N, H(3′), *J* = 7.6, *J* = 1.2, *J* = 0.9); 8.60 (ddd, 1 H, C$_5$H$_4$N, H(6′), *J* = 4.9, *J* = 1.5, *J* = 0.9)	8.32 (*J* = 2.4)	—
3j	2.25	6.13 (*J* = 7.9, *J* = 2.7)	6.25 (*J* = 7.9)	7.20 (d, 2 H, *p*-MeC$_6$H$_4$, *J* = 7.9); 7.49 (ddd, 1 H, C$_5$H$_4$N, H(5′), *J* = 7.6, *J* = 4.9, *J* = 1.2); 7.72 (d, 2 H, *p*-MeC$_6$H$_4$, *J* = 7.9); 7.87 (dd, 1 H, C$_5$H$_4$N, H(4′), *J* = 7.6, *J* = 1.5); 8.01 (ddd, 1 H, C$_5$H$_4$N, H(3′), *J* = 7.6, *J* = 1.2, *J* = 0.9); 8.60 (ddd, 1 H, C$_5$H$_4$N, H(6′), *J* = 4.9, *J* = 1.5, *J* = 0.9)	8.24 (*J* = 2.7)	2.60 (s, 3 H, *p*-MeC$_6$H$_4$)
3k	2.27	6.13 (*J* = 7.9, *J* = 2.7)	6.40 (*J* = 7.9)	7.20 (d, 2 H, *p*-MeC$_6$H$_4$, *J* = 7.9); 7.62 (d, 2 H, C$_5$H$_4$N, *J* = 4.6); 7.71 (d, 2 H, *p*-MeC$_6$H$_4$, *J* = 7.9); 8.65 (d, 2 H, C$_5$H$_4$N, *J* = 4.6)	8.28 (*J* = 2.7)	2.37 (s, 3 H, *p*-MeC$_6$H$_4$)
3l	2.28	6.15 (*J* = 7.6, *J* = 2.7)	6.40 (*J* = 7.6)	7.38—7.44 (m, 3 H, Ph); 7.62 (d, 2 H, C$_5$H$_4$N, *J* = 4.6); 7.81—7.85 (m, 2 H, Ph); 8.66 (d, 2 H, C$_5$H$_4$N, *J* = 4.6)	8.36 (*J* = 2.7)	—

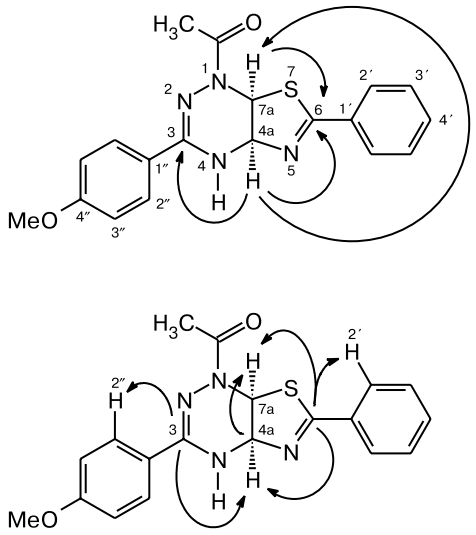


Fig. 1. Long-range couplings $^{n}J_{C,H}$ in the 2D HMBC spectra of compound **3b**.

viz., 3a,4,9,9a-tetrahydrothiazolo[4,5-*b*]quinoxalines, the bridgehead carbon atom located between the nitrogen and sulfur atoms resonates at higher field (δ = 67—70) and has the larger direct C—H coupling constant ($^{1}J_{C,H}$ = 164—167 Hz) compared to the tetrahydropyrazine carbon atom, which is bound to the C=N fragment of thioamide and resonates at lower field (δ = 93—97) with the smaller direct coupling constant $^{1}J_{C,H}$ = 154—157 Hz.

The bridgehead C(4a) and C(7a) atoms were reliably identified based on the HETCOR spectra of compounds **3a—c**. In complete agreement with the data published in the literature, the signals at δ 80.71—81.00 with the direct coupling constants $^{1}J_{C(4a),H(4a)}$ = 160.8—162.1 Hz were assigned to the bridgehead C(4a) atom and the signals at δ 61.29—62.06 with the constants $^{1}J_{C(7a),H(7a)}$ = 166.8—168.9 Hz were assigned to the C(7a) atom.

When studying cyclization of 1,2,4-triazines with 4-arylthiosemicarbazides, we took into account that the latter can exist in different tautomeric forms and exhibit properties of both 1,3- and 1,4-dinucleophilic reagents. Cyclization with 4-arylthiosemicarbazides can lead to annelation of both the imidazole (triazine) and thiazole (thiadiazine) rings. Earlier,[3] it has been demonstrated that cyclization of unsubstituted thiosemicarbazides with *N*(1)-alkyl-5-methoxy-1,2,4-triazines occurs as tandem addition—substitution (A_N—S_N^{ipso}) and gives rise to the imidazole ring.

We found that the reactions of 3-aryl-1,2,4-triazines (**1**) with 4-phenyl- and 4-(*p*-fluorophenyl)thiosemicarbazides (**4a,b**) in acetic anhydride at room temperature afford cyclic A_N—A_N-type products **5a,b** (Scheme 2).

The structures of cycloadducts **5** were established by one- and two-dimensional ^{1}H and ^{13}C NMR spectroscopy, including the nuclear Overhauser effect experiments (2D NOESY).

In the ^{1}H NMR spectra of compounds **5a,b**, the signals for the bridgehead H(7a) and H(4a) protons are observed at δ 6.12—6.22 as a doublet with the constant $^{3}J_{H(7a),H(4a)}$ = 6.4—6.8 Hz and at δ 5.50—5.60 as a doublet of doublets with the spin-spin coupling constants

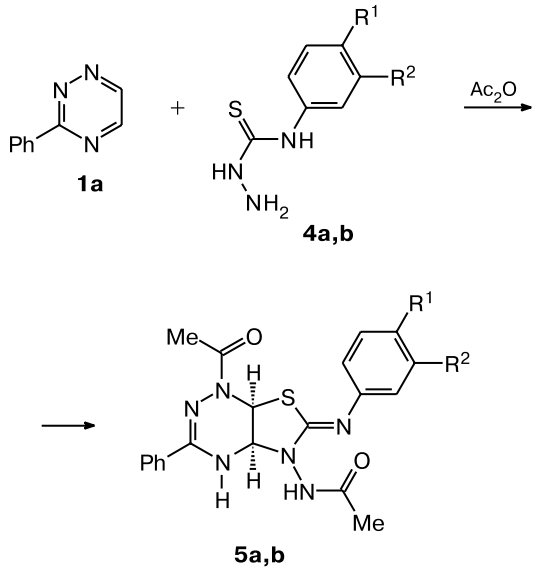
Table 3. ^{13}C NMR spectroscopic data (DMSO-d_6) for 1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazines **3a—c**

C atom	δ ($J_{C,H}$/Hz)		
	3a	**3b***	**3c**
CO<u>Me</u>	21.37 (q, *J* = 129.2)	21.22 (q, *J* = 129.6)	21.60 (q, *J* = 129.2)
<u>C</u>OMe	170.48 (q, *J* = 6.4)	171.62 (qd, *J* = 6.4, *J* = 0.9)	170.97 (d, *J* = 6.4)
C(3)	146.14 (m)	145.89 (dt, *J* = 3.7)	143.71 (m)
C(4a)	81.00 (d, *J* = 160.8)	80.71 (dd, *J* = 162.1, *J* = 0.9)	80.79 (d, *J* = 162.1)
C(6)	167.31 (dt, $J_d \approx J_t$ = 4.9)	171.38 (dt, $J_1 \approx J_2$ = 5.2)	167.25 (td, *J* = 5.4, *J* = 4.9)
C(7a)	62.06 (dd, *J* = 168.2, *J* = 4.0)	61.29 (ddd, *J* = 166.8, *J* = 4.4, *J* = 1.4)	61.95 (ddd, *J* = 168.9, *J* = 4.0, *J* = 1.0)
C(1´)	132.79 (t, *J* = 7.9)	132.55 (t, *J* = 7.8)	132.75 (t, *J* = 7.8)
C(1″)	133.08 (t, *J* = 6.9)	125.12 (t, *J* = 7.5)	139.09 (t, *J* = 7.7)
C(2´)	**	128.03 (ddd, *J* = 160.6, *J* = 7.4, *J* = 6.4)	128.29 (ddd, *J* = 159.8, *J* = 7.2)
C(3´)	**	128.49 (dd, *J* = 162.1, *J* = 7.9)	129.49 (dd, *J* = 161.6, *J* = 7.2)
C(4´)	**	132.01 (dt, *J* = 164.5, *J* = 7.2)	132.78 (dt, *J* = 162.9, *J* = 7.4)
C(2″)	**	127.20 (dd, *J* = 159.9, *J* = 7.0)	127.81 (dd, *J* = 168.4, *J* = 7.5)
C(3″)	**	113.88 (dd, *J* = 160.4, *J* = 5.1)	124.20 (dd, *J* = 172.4, *J* = 4.4)
C(4″)	**	161.35 (dqt, *J* = 4.8, *J* = 6.8, *J* = 2.4)	148.62 (tt, *J* = 9.5, *J* = 3.3)
OMe	—	55.27 (q, OMe, *J* = 144.2)	—

* In $CDCl_3$.

** 126.41 (dt, *J* = 160.8, *J* = 6.7); 128.00 (dt, *J* = 161.2, *J* = 6.7); 128.45 (dd, *J* = 161.3, *J* = 7.5); 128.84 (dd, *J* = 161.8, *J* = 6.7); 130.30 (dt, *J* = 161.0, *J* = 8.3); 132.08 (dt, *J* = 161.5, *J* = 8.4) (signals for six aromatic CH carbon atoms of two phenyl groups).

Scheme 2



$R^1 = R^2 = H$ (**a**); $R^1 = F$, $R^2 = H$ (**b**).

$^3J_{H(4a),H(7a)} = 6.4—6.8$ Hz and $^3J_{H(4a),N(4)H} = 2.4—3.4$ Hz, respectively (Table 4). The vicinal constants $^3J_{H(7a),H(4a)} = 6.4—6.8$ Hz correspond to the *cis* orientation of the bridgehead protons and are indicative, as mentioned above, of the annelation of the five-membered heterocycle.[14] The low-field region of the ^{13}C NMR spectrum of **5** showing C=O signals of two acetyl fragments (at δ 169.25 and 170.19) (Table 5) is also informative. It should be noted that the ^{13}C NMR spectra have no signals for the carbon atom at δ 179—182 characteristic of the C=S fragments, which is evidence that the thiazole rather than imidazole ring is fused to the 1,2,4-triazine moiety. The

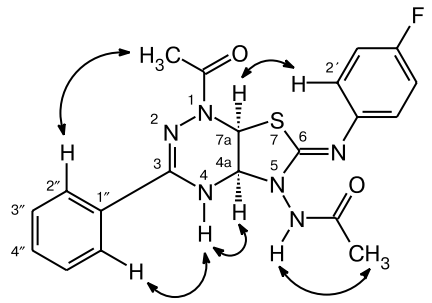


Fig. 2. Correlations in the $^1H—^1H$ NOESY spectra of compound **5b**.

2D HSQC spectrum of compound **5b** shows a signal for the C(4a) atom at δ 65.87 with $^1J_{C(4a),H(4a)} = 166.7$ Hz and a signal for the C(7a) atom at δ 52.39 with $^1J_{C(7a),H(7a)} = 172.8$ Hz. Therefore, in agreement with the earlier observations,[14] the bridgehead carbon atom located between the nitrogen and sulfur atoms also resonates at higher field and has the larger direct C—H coupling constant compared to the carbon atom bound to the C=N fragment of thioamide, which resonates at lower field and has the smaller direct coupling constant. The HMBC spectra of compound **5b** show cross-peaks between the labile proton of the NH group (at δ 10.22 in the ^1H NMR spectrum) and the carbon atom of the acetyl group, which makes it possible to distinguish the acetamide fragment. The mutual spatial orientation of the thiazole and 1,2,4-triazine rings is also evident from the 2D NOESY spectra of compound **5b** (Fig. 2). The presence of cross-peaks, which are associated with the nuclear Overhauser effect, between the H(2′) protons of the *p*-fluorophenyl substituent and the bridgehead H(7a) proton confirms the spatial orientation of the thiazole ring shown in Fig. 2.

Table 4. ^1H NMR spectroscopic data (DMSO-d_6) for compounds **5a—d**

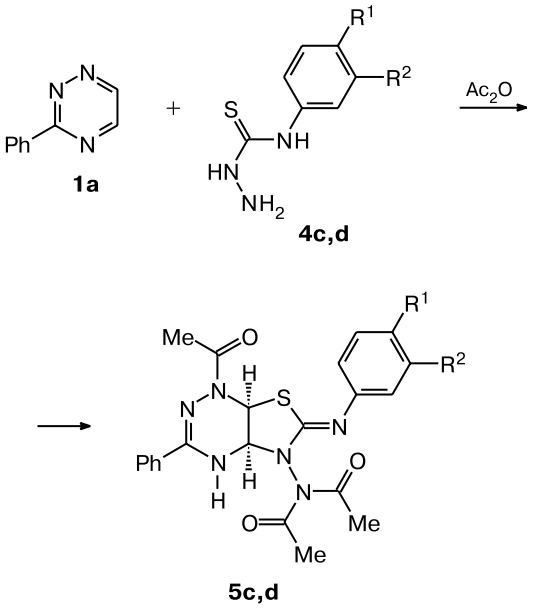
Compound	δ (*J*/Hz)					
	COMe (s)	H(4a) (dd)	H(7a) (d)	Ar	N(4)H (d)	Other signals
5a	2.01, 2.27	5.50 (*J* = 6.4, *J* = 2.4)	6.22 (*J* = 6.4)	6.75—6.83 (m, 2 H, Ph); 6.96 (t, 1 H, Ph, *J* = 7.3); 7.20 (t, 2 H, Ph, *J* = 7.6); 7.41—7.45 (m, 3 H, Ph); 7.82—7.86 (m, 2 H, Ph)	8.11 (*J* = 2.4)	10.13 (s, 1 H, NH)
5b	1.99, 2.26	5.60 (*J* = 6.8, *J* = 3.4)	6.12 (*J* = 6.8)	6.75 (dd, 2 H, *p*-FC_6H_4, *J* = 8.9, *J* = 5.0); 7.08 (dd, 2 H, *p*-FC_6H_4, *J* = 8.9, *J* = 8.8); 7.48—7.52 (m, 3 H, Ph); 7.87 (dd, 2 H, Ph, *J* = 7.7, *J* = 2.1)	8.40 (*J* = 3.4)	10.22 (s, 1 H, NH)
5c	2.04, 2.32, 2.56	5.76 (*J* = 7.0, *J* = 4.6)	5.91 (*J* = 7.0)	6.70 (ddd, 1 H, *m*-ClC_6H_4, *J* = 7.9, *J* = 2.0, *J* = 2.0); 6.76 (dd, 1 H, *m*-ClC_6H_4, *J* = 2.0, *J* = 2.0); 7.01 (ddd, 1 H, *m*-ClC_6H_4, *J* = 7.9, *J* = 2.0, *J* = 2.0); 7.23 (dd, 1 H, *m*-ClC_6H_4, *J* = 7.9, *J* = 7.9); 7.42—7.47 (m, 3 H, Ph); 7.75—7.79 (m, 2 H, Ph)	8.51 (*J* = 4.6)	—
5d	2.04, 2.27, 2.56	5.74 (*J* = 6.7, *J* = 4.3)	5.86 (*J* = 6.7)	6.64 (d, 2 H, *p*-$MeC_6\underline{H}_4$, *J* = 7.9); 7.02 (d, 2 H, *p*-$MeC_6\underline{H}_4$, *J* = 7.9); 7.43—7.47 (m, 3 H, Ph); 7.75—7.79 (m, 2 H, Ph)	8.46 (*J* = 4.3)	2.31 (c, 3 H, *p*-$\underline{Me}C_6H_4$)

Table 5. ^{13}C NMR spectroscopic data (DMSO-d_6) for coompounds **5b** and **5c**

C atom	δ ($J_{C,H}$/Hz, $J_{C,F}$/Hz)	
	5b	**5c**
N(1)COMe	170.19 (q, J = 6.4)	172.90
N(1)CO<u>Me</u>	20.99 (q, J = 129.2)	22.40
<u>C</u>OMe	169.25 (dq, J = 9.2, J = 6.2)	169.70
CO<u>Me</u>	20.87 (q, J = 128.6)	20.38
C(3)	144.19 (s)	141.86
C(4a)	65.87 (dd, J = 166.7, J = 1.0)	64.43 (d, J = 167.2)
C(6)	154.37 (m, $J_{C,F}$ = 1.3)	153.16
C(7a)	52.39 (dd, J = 172.8, J = 2.7)	52.12 (d, J = 174.7)
C(1´)	146.02 (tt, J = 8.7, J = 1.5, $J_{C,F}$ = 2.0)	132.70
C(2´)	122.61 (dd, J = 161.2, J = 7.4, $J_{C,F}$ = 8.1)	120.52
C(3´)	115.57 (dd, J = 163.3, J = 4.5, $J_{C,F}$ = 22.2)	149.48
C(4´)	158.58 (tt, J = 10.5, J = 5.5, $J_{C,F}$ = 239.8)	123.09
C(5´)	—	130.12
C(6´)	—	119.32
C(1″)	132.26 (t, J = 6.9)	130.21
C(2″)	126.50 (ddd, J = 160.9, J = 7.8, J = 6.5)	125.24
C(3″)	128.41 (ddd, J = 160.8, J = 6.9, J = 1.8)	128.18
C(4″)	130.44 (dt, J = 161.7, J = 7.9)	130.95
COMe	—	26.03 (CO<u>Me</u>); 168.69 (<u>C</u>OMe)

Interestingly, cyclization of 3-phenyl-1,2,4-triazine (**1a**) with 4-(*m*-chlorophenyl)- and 4-(*p*-tolyl)thiosemicarbazides (**4c,d**) afforded cyclic adducts **5c,d** containing the *N*,*N*-diacetylated hydrazone fragment (Scheme 3). The mass spectra of cycloadducts **5c,d** have molecular ion peaks $[M]^+$ (Table 6). The ^1H NMR spectra show signals of three acetyl fragments.

Scheme 3



R^1 = H, R^2 = Cl (**c**); R^1 = Me, R^2 = H (**d**).

The ^1H NMR spectra of compounds **5c,d** have characteristic signals for the bridgehead H(7a) (a doublet at

Table 6. Reactions times (τ), yields, melting points, elemental analysis data, and mass spectra of compounds **5a—d**, **6a,b**, and **7**

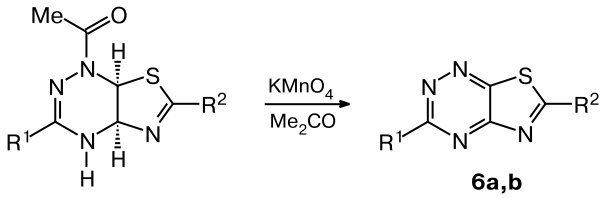
Compound	R^1 (R^2)	τ /days	Yield (%)	M.p. /°C	Found / Calculated (%)			Molecular formula (Molecular weight)	MS, m/z (I_{rel} (%))
					C	H	N		
5a	H (H)	1	47	194—195	<u>58.49</u> 58.81	<u>4.99</u> 4.94	<u>20.88</u> 20.57	$C_{20}H_{20}N_6O_2S$ (408.49)	408 $[M]^+$ (10), 201 (11), 175 (10), 158 (100), 135 (11), 104 (35), 103 (23), 77 (18)
5b	F (H)	1	30	222—223	<u>56.42</u> 56.33	<u>4.61</u> 4.49	<u>19.48</u> 19.71	$C_{20}H_{19}FN_6O_2S$ (426.49)	426 $[M]^+$ (7), 201 (10), 159 (54), 158 (100), 111 (9), 103 (20), 74 (14)
5c	H (Cl)	1	18	142—143	<u>54.68</u> 54.49	<u>4.67</u> 4.36	<u>17.58</u> 17.33	$C_{22}H_{21}ClN_6O_3S$ (484.97)	486 $[M + 1]^+$ (40), 485 $[M]^+$ (28), 484 (100), 444 (6), 442 (14), 358 (5)
5d	Me (H)	1	51	203—205	<u>59.23</u> 59.47	<u>5.29</u> 5.21	<u>18.54</u> 18.09	$C_{23}H_{24}N_6O_3S$ (464.55)	466 $[M + 1]^+$ (1), 465 $[M]^+$ (4), 464 (14), 206 (14), 205 (13), 201 (16), 190 (11), 159 (58), 158 (100), 149 (25), 107 (10), 104 (38)
6a	Ph (Ph)	5	7	216—217	<u>66.12</u> 66.19	<u>3.37</u> 3.47	<u>18.59</u> 19.30	$C_{16}H_{10}N_4S$ (290.35)	290 $[M]^+$ (5), 262 (12), 159 (100), 77 (34)
6b	Ph (p-ClC_6H_4)	7	47	225—227	<u>59.25</u> 59.17	<u>2.90</u> 2.79	<u>17.25</u> 17.25	$C_{16}H_9N_4SCl$ (324.79)	326 $[M + 1]^+$ (2), 324 (4), 296 (12), 195 (15), 193 (42), 159 (100), 111 (9), 77 (31)
7	—	14	6	202—203 (decomp.)	<u>59.84</u> 59.66	<u>4.12</u> 3.89	<u>23.02</u> 23.19	$C_{18}H_{14}N_6OS$ (362.42)	363 $[M + 1]^+$ (23), 362 $[M]^+$ (100), 320 (41), 217 (98), 160 (12), 159 (37), 104 (57), 103 (24), 86 (34), 77 (81), 70 (50)

δ 5.86—5.91 with the spin-spin coupling constant $^3J_{H(7a),H(4a)}$ = 6.7—7.0 Hz) and H(4a) (a doublet of doublets at δ 5.74—5.76 with the spin-spin coupling constants $^3J_{H(4a),H(7a)}$ = 6.7—7.0 Hz and $^3J_{H(4a),N(4)H}$ = 4.3—4.6 Hz) protons. The vicinal constants between the protons at the bridgehead atoms ($^3J_{H(7a),H(4a)}$ = 6.7—7.0 Hz) are indicative of annelation the five-membered ring to 1,2,4-triazine (see Table 4).[14] The structures of cycloadducts **5c,d** were established based on the ^{13}C NMR spectra (HSQC, HMBC, NOESY), which show the same characteristic features as those observed in the spectra of hydrogenated thiazolotriazines **5a,b** (see Table 5).

Cyclic adducts produced in tandem addition A_N—A_N reactions of bifunctional nucleophilic reagents to 1,2,4-triazines are, as a rule, susceptible to dissociation. With the aim of retaining the bicyclic core and preparing aromatic fused systems, we studied oxidation of partially hydrogenated thiazole-annelated 1,2,4-triazines. Potassium permanganate proved to be highly efficient in dehydrogenation of dihydro- and tetrahydroazines.[15—17]

Actually, oxidation of 1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazines (**3a,e**) with potassium permanganate in acetone at room temperature resulted in double dehydrogenation accompanied by elimination of the *N*-acetyl group to give compounds **6a,b** (Scheme 4).

Scheme 4



3a,f **6a,b**

$R^1 = R^2$ = Ph (**3a**, **6a**); R^1 = Ph, R^2 = *p*-Cl-C_6H_4 (**3f**, **6b**).

The structures of oxidation products **6a,b**, which can be considered as products of the tandem S_N^H—S_N^H reactions (nucleophilic substitution of two hydrogen atoms in the triazine ring), are consistent with the results of elemental analysis, ^{1}H NMR spectroscopy, and mass spectrometry (see Table 6). The fact that the ^{1}H NMR spectra have neither signals at δ 5—7, where the methine protons at the bridgehead atoms of their hydrogenated precursors **3a,f** resonate, nor signals of the acetyl and NH groups is indicative of aromatization of the 1,2,4-triazine ring (see the Experimental section).

Table 7. Selected bond lengths (*d*) in the structure of **6b**

Bond	*d*/Å	Bond	*d*/Å
C(l1)—C(17)	1.722(6)	C(l21)—C(217)	1.732(6)
S(7)—C(6)	1.765(5)	S(27)—C(26)	1.763(5)
S(7)—C(7a)	1.717(6)	S(27)—C(27a)	1.747(6)
N(1)—N(2)	1.357(7)	N(21)—N(22)	1.357(7)
N(1)—C(7a)	1.347(8)	N(21)—C(27a)	1.314(7)
N(2)—C(3)	1.334(7)	N(22)—C(23)	1.330(6)
N(4)—C(3)	1.364(8)	N(24)—C(23)	1.365(7)
N(4)—C(4a)	1.342(8)	N(24)—C(24a)	1.323(7)
N(5)—C(4a)	1.366(8)	N(25)—C(24a)	1.381(7)
N(5)—C(6)	1.292(7)	N(25)—C(26)	1.300(7)
C(3)—C(8)	1.468(8)	C(23)—C(28)	1.478(8)
C(4a)—C(7a)	1.384(7)	C(24a)—C(27a)	1.397(7)
C(6)—C(14)	1.487(8)	C(26)—C(214)	1.491(8)

The structure of compound **6b** in the crystal was established by X-ray diffraction analysis (Fig. 3, Tables 7 and 8).

In molecule **6b**, the deviations of the atoms from the mean plane passing through all nonhydrogen atoms are no larger than 0.14(1) Å. The bicyclic system is planar within 0.017(8) Å. The benzene ring at the C(6) atom lies virtually in the plane of the bicyclic fragment (the N(5)C(6)C(14)C(19) torsion angles are no larger than −1.6(9)°). The twist of the phenyl substituent at the C(3) atom is somewhat larger (the N(2)C(3)C(8)C(13) torsion angles in molecules **1** and **2** are −7.3(9) and 4.7(8)°, respectively). Therefore, the aromatic substituents in molecules **6b** are conjugated with the heteroaromatic bicyclic π system, which is consistent with the distribution of the bond lengths in the molecules.

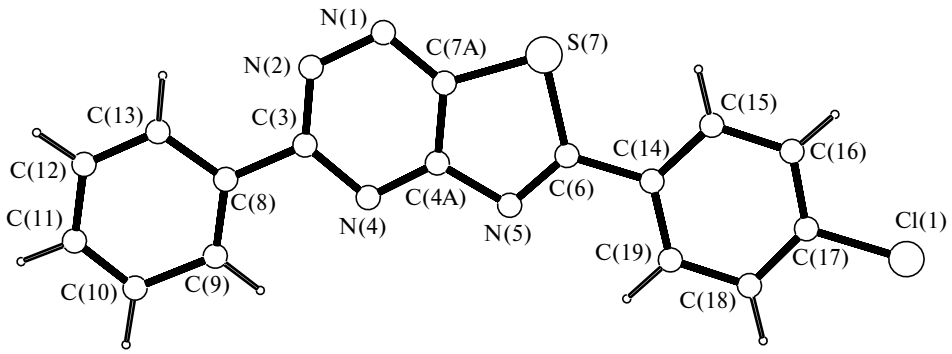


Fig. 3. Geometry of one of two independent molecules of compound **6b** in the crystal.

Table 8. Selected bond angles (ω) in the structure of **6b**

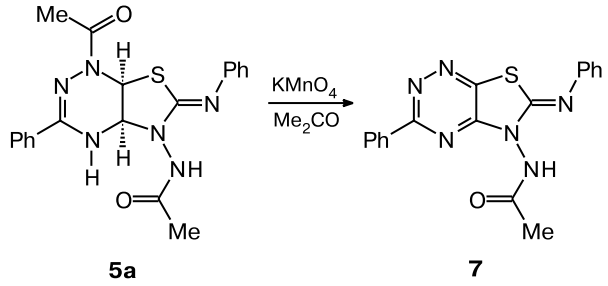
Angle	ω/deg	Angle	ω/deg
C(6)—S(7)—C(7a)	86.6(3)	C(26)—S(27)—C(27a)	87.5(3)
N(2)—N(1)—C(7a)	116.2(4)	N(22)—N(21)—C(27a)	114.1(4)
N(1)—N(2)—C(3)	119.2(5)	N(21)—N(22)—C(23)	120.0(5)
C(3)—N(4)—C(4a)	114.2(4)	C(23)—N(24)—C(24a)	112.7(4)
C(4a)—N(5)—C(6)	108.3(4)	C(24a)—N(25)—C(26)	109.0(4)
N(2)—C(3)—N(4)	126.4(5)	N(22)—C(23)—N(24)	127.1(5)
N(2)—C(3)—C(8)	117.3(5)	N(22)—C(23)—C(28)	117.1(5)
N(4)—C(3)—C(8)	116.3(5)	N(24)—C(23)—C(28)	115.8(4)
N(4)—C(4a)—N(5)	123.0(5)	N(24)—C(24a)—N(25)	123.1(4)
N(4)—C(4a)—C(7a)	120.5(5)	N(24)—C(24a)—C(27a)	120.5(5)
N(5)—C(4a)—C(7a)	116.5(5)	N(25)—C(24a)—C(27a)	116.5(5)
S(7)—C(6)—N(5)	117.8(4)	S(27)—C(26)—N(25)	117.4(4)
S(7)—C(6)—C(14)	119.0(4)	S(27)—C(26)—C(214)	119.7(4)
N(5)—C(6)—C(14)	123.1(5)	N(25)—C(26)—C(214)	122.8(5)
S(7)—C(7a)—N(1)	125.7(4)	S(27)—C(27a)—N(21)	124.8(4)
S(7)—C(7a)—C(4a)	110.8(4)	S(27)—C(27a)—C(24a)	109.5(4)
N(1)—C(7a)—C(4a)	123.5(5)	N(21)—C(27a)—C(24a)	125.6(5)

The planar conformation of the molecules is favorable for their stacking in crystal structures. Actually, molecules **6b** in the crystal are parallel to each other and there are numerous contacts corresponding to stacking interactions between the aromatic systems (Fig. 4).

Oxidation of *N*-(1-acetyl-3-phenyl-6-phenylimino-1,4a,7,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazin-5-yl)acetamide (**5a**) occurs analogously and affords product **7** (Scheme 5).

The structure of compound **7**, in particular, the character of annelation of the thiazole and 1,2,4-triazine rings, was established by X-ray diffraction analysis (Fig. 5, Tables 9 and 10). The results of X-ray diffraction

Scheme 5



5a **7**

studydemonstrate that the tandem addition of 4-arylthiosemicarbazides to 3-aryl-1,2,4-triazine (**1a**) occurs regioselectively to give thiazolo[4,5-*e*]-annelated tetrahydro1,2,4-triazines **5**, which are subjected to aromatization under oxidative conditions to give thiazolo[4,5-*e*][1,2,4]triazines **7**.

In molecule **7**, the thiazolotriazine fragment is planar (the average deviation from the plane is 0.033 Å). The NHC(=O)Me group bound to this fragment is rotated about the N(1)—N(6) bond by 84.3°. The planar phenyl group C(5)—C(10) (0.003 Å) is almost coplanar to the thiazolotriazine system (the angle of rotation about the C(4)—C(5) bond is 6.5°). In the crystal structure, the second phenyl group is disordered over two positions with occupancies of ~0.65 and ~0.35, respectively, which differ in the angle of rotation about the N(5)—C(11) bond by 37.5°. The dihedral angles between the disordered phenyl group in two positions and the central thiazolotriazine core are 62.9° (C(11)—C(16)) and 79.9° (C(11)C(12a)C(13a)C(14)C(15a)C(16a)).

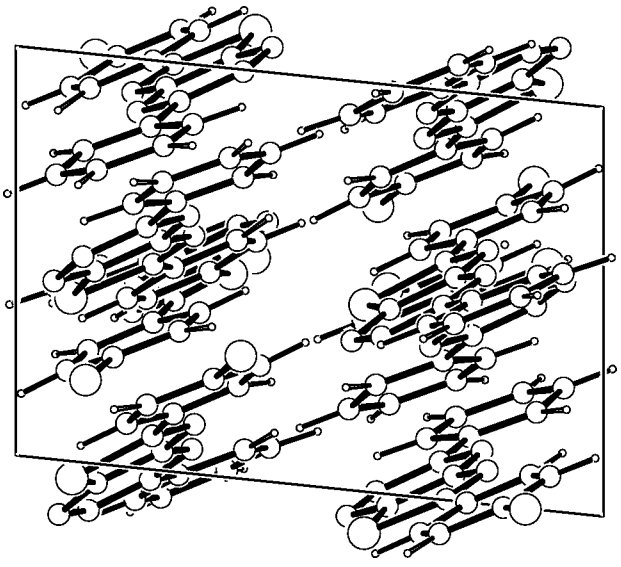


Fig. 4. Molecular packing in the crystal of **6b** projected along the *OY* axis.

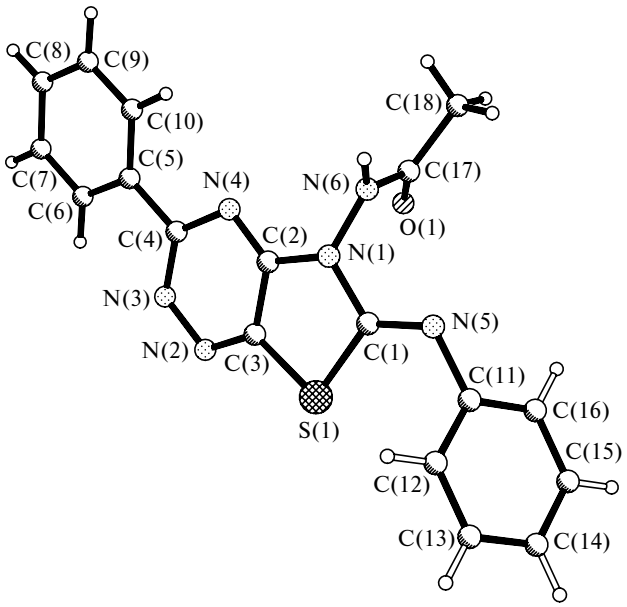


Fig. 5. Geometry of molecule **7** in the crystal.

Table 9. Selected bond lengths (*d*) in the structure of **7**

Bond	*d*/Å	Bond	*d*/Å
S(1)—C(1)	1.771(4)	N(5)—C(11a)	1.388(4)
S(1)—C(3)	1.743(4)	N(5)—C(11)	1.437(4)
O(1)—C(17)	1.198(4)	N(6)—C(17)	1.371(5)
N(1)—C(1)	1.409(4)	C(2)—C(3)	1.420(5)
N(1)—C(2)	1.365(5)	C(4)—C(5)	1.481(5)
N(1)—N(6)	1.389(4)	C(5)—C(6)	1.361(7)
N(2)—C(3)	1.284(5)	C(5)—C(10)	1.358(7)
N(2)—N(3)	1.366(4)	C(6)—C(7)	1.386(7)
N(3)—C(4)	1.326(5)	C(7)—C(8)	1.369(8)
N(4)—C(2)	1.297(4)	C(8)—C(9)	1.333(8)
N(4)—C(4)	1.363(5)	C(9)—C(10)	1.380(7)
N(5)—C(1)	1.260(5)	C(17)—C(18)	1.502(6)

Table 10. Selected bond angles (ω) in the structure of **7**

Angle	ω/deg	Angle	ω/deg
C(3)—S(1)—C(1)	89.65(17)	N(2)—C(3)—S(1)	125.1(3)
C(2)—N(1)—N(6)	122.0(3)	C(2)—C(3)—S(1)	113.0(3)
C(2)—N(1)—C(1)	115.0(3)	N(3)—C(4)—N(4)	126.2(3)
N(6)—N(1)—C(1)	118.6(3)	N(3)—C(4)—C(5)	116.5(3)
C(3)—N(2)—N(3)	117.6(3)	N(4)—C(4)—C(5)	117.3(3)
C(4)—N(3)—N(2)	118.6(3)	C(10)—C(5)—C(6)	117.9(4)
C(2)—N(4)—C(4)	113.4(3)	C(10)—C(5)—C(4)	121.8(4)
C(1)—N(5)—C(11a)	115.5(3)	C(6)—C(5)—C(4)	120.3(4)
C(1)—N(5)—C(11)	116.7(3)	C(5)—C(6)—C(7)	120.5(5)
C(17)—N(6)—N(1)	116.0(3)	C(8)—C(7)—C(6)	120.7(5)
N(5)—C(1)—N(1)	122.1(3)	C(9)—C(8)—C(7)	118.5(5)
N(5)—C(1)—S(1)	127.6(3)	C(8)—C(9)—C(10)	121.1(6)
N(1)—C(1)—S(1)	110.4(2)	C(5)—C(10)—C(9)	121.4(5)
N(4)—C(2)—N(1)	126.5(3)	O(1)—C(17)—N(6)	122.0(3)
N(4)—C(2)—C(3)	122.2(3)	O(1)—C(17)—C(18)	124.9(3)
N(1)—C(2)—C(3)	111.3(3)	N(6)—C(17)—C(18)	113.0(3)
N(2)—C(3)—C(2)	121.9(3)		

The molecule contains one active proton at the N(6) atom, which can be involved in hydrogen bonding. Actually, molecules **1** in the crystal are linked in chains extended along the *b* axis by the intermolecular N(6)—H...O(1) hydrogen bond (*x*, *y* + 1, *z*) (H...O, 2.035 Å; N...O, 2.775 Å; N—H...O, 141.02°).

To summarize, the tandem A_N—A_N reactions of 3-aryl-1,2,4-triazines with aromatic thioamides and thiosemicarbazides in acetic anhydride at room temperature provide a convenient approach to the synthesis of thiazolo[4,5-*e*]-annelated tetrahydrotriazines, which undergo aromatization under the action of potassium permanganate to give thiazolo[4,5-*e*][1,2,4]triazines, thus completing the tandem S_N^H—S_N^H reactions.

Experimental

The ^{1}H and ^{13}C NMR spectra in DMSO-d_6 and $CDCl_3$ were recorded on Bruker DRX-400 and Bruker WP-250 spectrometers (operating at 400.13 and 250.13 for ^{1}H and at 100.61 MHz for ^{13}C) with Me_4Si as the internal standard. The mass spectra were obtained on a Varian MAT-311A spectrometer with direct inlet of the sample into the ion source; the accelerating voltage was 3 kV; the energy of ionizing electrons was 70 eV. The course of the reactions and purity of the products were monitored by TLC on Silufol UV-254 plates.

The reaction conditions, yields, melting points, elemental analysis data, and spectroscopic characteristics of the compounds synthesized are given in Tables 1—6.

3-Aryl-1,2,4-triazines **1**,[18] aromatic thioamides **2**, and 4-arylthiosemicarbazides **4** were synthesized according to known procedures.[19,20]

Synthesis of 1-acetyl-3,6-diaryl-1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazines (3a—l) (general procedure). Thioamide (1 mmol) was added to a solution of 3-aryl-1,2,4-triazine **1** (1 mmol) in acetic anhydride (see Table 1). The reaction mixture was stirred at room temperature. The precipitate that formed was filtered off, washed successively with a small amount of acetic anhydride and diethyl ether (in the case of compounds **3a,b**, with hexane; in the case of **3c**, with propan-2-ol), and dried in air. To isolate compound **3l**, the reaction mixture was kept at ~20 °C for 5 days and then concentrated on a rotary evaporator to 1/5 of the initial volume. The precipitate that formed was filtered off and washed successively with a small amount of acetic anhydride and diethyl ether.

***N*-(1-Acetyl-3-phenyl-6-phenylimino-1,4a,7,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]-triazin-5-yl)acetamide (5a).** 4-Phenylthiosemicarbazide **(4a)** (406 mg, 2.43 mmol) was added to a solution of 3-phenyl-1,2,4-triazine (**1a**) (382 mg, 2.43 mmol) in acetic anhydride (4.8 mL). The reaction mixture was stirred at ~20 °C for one day. The precipitate that formed was filtered off and washed successively with a small amount of acetic anhydride and diethyl ether.

***N*-{(1-Acetyl-6-(4′-fluorophenylimino)-3-phenyl-1,4a,7,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazin-5-yl)}acetamide (5b).** 4-(4-Fluorophenyl)thiosemicarbazide (**4b**) (373 mg, 2.37 mmol) was added to a solution of 3-phenyl-1,2,4-triazine (**1a**) (439 mg, 2.37 mmol) in acetic anhydride (4 mL). The reaction mixture was stirred at ~20 °C for one day. The precipitate that formed was filtered off and washed successively with a small amount of acetic anhydride and diethyl ether. The colorless finely crystalline precipitate was recrystallized from acetic anhydride.

***N*-Acetyl-*N*-{1-acetyl-6-(3′-chlorophenylimino)-3-phenyl-1,4a,7,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazin-5-yl}acetamide (5c).** 4-(3-Chlorophenyl)thiosemicarbazide (**4c**) (475 mg, 3.02 mmol) was added to a solution of 3-phenyl-1,2,4-triazine (**1a**) (610 mg, 3.02 mmol) in acetic anhydride (5 mL). The reaction mixture was stirred at ~20 °C for one day. Then the solution was concentrated on a rotary evaporator. The residue was suspended in propan-2-ol. The precipitate that formed was filtered off and washed with a small amount of diethyl ether.

***N*-Acetyl-*N*-{1-acetyl-6-(4′-methylphenylimino)-3-phenyl-1,4a,7,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazin-5-yl}acetamide (5d).** 3-Phenyl-1,2,4-triazine (**1a**) (324 mg, 2.06 mmol) was dissolved in acetic anhydride (4 mL) and 4-(4-methylphenyl)thiosemicarbazide (**4d**) (374 mg, 2.06 mmol) was added. The reaction mixture was stirred at ~20 °C for one day. The precipitate that formed was filtered off and washed successively with a small amount of acetic anhydride and diethyl ether.

3,6-Diphenylthiazolo[4,5-*e*][1,2,4]triazine (6a). 1-Acetyl-3,6-diphenyl-1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazine (**3a**) (1.3 g, 3.86 mmol) was added to a solution of potassium permanganate (1.8 g, 11.6 mmol) in acetone (430 mL). The reaction mixture was stirred at ~20 °C for 5 days and filtered off from MnO_2 through a paper filter with a thin layer of silica gel. The filtrate was concentrated on a rotary evaporator. The product was purified by gravitational column chromatography (silica gel, $CHCl_3$). Yellow crystalline product **6a** (R_f 0.63) and a mixture of the product and the starting compound (R_f 0.10) were obtained in yields of 75 mg (7%) and 230 mg, respectively. ^{1}H NMR (DMSO-d_6), δ: 7.57—7.78 (m, 6 H, Ph); 8.27—8.30 (m, 2 H, Ph); 8.55—8.59 (m, 2 H, Ph).

6-(4´-Chlorophenyl)-3-phenylthiazolo[4,5-*e*][1,2,4]triazine (6b). 1-Acetyl-6-(4´-chlorophenyl)-3-phenyl-1,4,4a,7a-tetrahydrothiazolo[4,5-*e*][1,2,4]triazine (**3f**) (1 g, 2.7 mmol) was added to a solution of potassium permanganate (1.3 g, 8.09 mmol) in acetone (400 mL). The reaction mixture was stirred at ~20 °C for one day. Then an additional amount of potassium permanganate (1.3 g, 8.09 mmol) was added. The reaction mixture was kept under the same conditions for 6 days and filtered off from MnO_2 through a paper filter with a thin layer of silica gel. The filtrate was concentrated to dryness on a rotary evaporator. The precipitate was crystallized from acetonitrile. The yield was 410 mg (47%). ^{1}H NMR (DMSO-d_6), δ: 7.64—7.67 (m, 3 H, Ph); 7.79 (d, 2 H, *p*-ClC_6H_4, J = 6.7 Hz); 8.37 (d, 2 H, *p*-ClC_6H_4, J = 6.7 Hz); 8.55—8.59 (m, 2 H, Ph).

X-ray diffraction analysis. Crystals of **6b**, $C_{16}H_9N_4SCl$, m.p. 225—227 °C, are monoclinic, at 20 °C a = 7.724(2), b = 32.959(9), c = 11.138(2) Å, β = 95.93(2)°, V = 2820(1) Å^3, Z = 8, d_{calc} = 1.53 g cm^{-3}, space group $P2_1/n$ (two independent molecules in the unit cell).

The unit cell parameters and intensities of 6303 reflections, of which 3205 reflections were with $I \geq 3\sigma$, were measured on an automated four-circle Enraf—Nonius CAD-4 diffractometer (λ(CuKα), graphite monochromator, ω scanning technique, θ ≤ 76°). The intensities of three check reflections showed no decrease in the course of X-ray data collection. The empirical absorption correction was applied (μ(Cu) 37.93 cm^{-1}).

The structure was solved by direct methods using the SIR program[21] and refined first isotropically and then anisotropically. All hydrogen atoms were revealed from difference electron density syntheses and included in the refinement with fixed positional and isotropic thermal parameter in the final stage. The final reliability factors were as follows: R = 0.068, R_w = 0.076 based on 2613 reflections with $F^2 \geq 3\sigma$. All calculations were carried out using the MOLEN program package[22] on an AlphaStation 200 computer. The hydrogen bonds and the conformation of molecule **6b** were analyzed with the use of the PLATON program.[23]

The atomic coordinates of the structure of **6b** were deposited with the Cambridge Structural Database. The geometry of the molecule is shown in Fig. 3. The geometric parameters are given in Tables 7 and 8.

The X-ray diffraction study was carried out at the Department of X-ray Diffraction Studies of the Spectral and Analytical Center of the Collaborative Use of the Russian Foundation for Basic Research based on the A. E. Arbuzov Institute of Organic and Physical Chemistry of the Kazan Research Center of the Russian Academy of Sciences.

***N*-{3-Phenyl-6-(phenylimino)thiazolo[4,5-*e*][1,2,4]triazin-5-yl}acetamide (7).** 2-(1-Acetyl-3,5-diphenyl-4,4a,7,7a-tetrahydro-1*H*-thiazolo[4,5-*e*][1,2,4]triazin-6-ylidene)hydrazide of acetic acid (**5a**) (400 mg, 0.979 mmol) was added to a solution of potassium permanganate (1.39 g, 8.81 mmol) in acetone (450 mL). The reaction mixture was stirred at ~20 °C for 14 days and filtered off from MnO_2 through a paper filter with a thin layer of silica gel. The filtrate was concentrated on a rotary evaporator. The product was purified by gravitational column chromatography (silica gel, ethyl acetate—hexane, 2 : 1). Yellow crystalline product **7** (R_f 0.44) was obtained in a yield of 20 mg (6%). ^{1}H NMR (DMSO-d_6), δ: 2.20 (s, 3 H, NHCO<u>Me</u>); 7.04—7.07 (m, 2 H, Ph); 7.23—7.27 (m, 1 H, Ph); 7.45—7.62 (m, 5 H, Ph); 8.34—8.37 (m, 2 H, Ph); 11.49 (s, 1 H, N<u>H</u>COMe).

X-ray diffraction analysis. Crystals of **7**, $C_{18}H_{14}N_6OS$, m.p. 202—203 °C (decomp.), at 120(2) K are monoclinic, a = 14.847(5), b = 4.7230(10), c = 23.795(7) Å, β = 91.600(10)°, V = 1667.9(8) Å^3, crystal dimensions 0.56×0.32×0.13 mm, space group $P2_1/n$, Z = 4, d_{calc} = 1.442 g cm^{-3}, F(000) = 752, μ = 0.215 mm^{-1}.

X-ray diffraction data were collected on a Bruker AXS SMART 1000 diffractometer equipped with a CCD detector (λ(Mo), graphite monochromator, 120 K, ω scanning technique, the scan step was 0.3°, frames were exposed for 15 s, $2\theta_{max}$ = 60°) using a standard procedure.[24] A total of 7808 reflections were collected, of which 3164 reflections were independent. The semiempirical absorption correction was applied.[25] The structure was solved by direct methods using the SHELXS97 program package[26] and refined by the full-matrix least-squares method using the SHELXL97 program package[27] (the positions of the H atoms were kept fixed with U_H = 0.08 Å^2) to R_1 = 0.0826, wR_2 = 0.1116 based on 2386 reflections with $F^2 > 2\sigma(I)$.

The atomic coordinates and thermal parameters for the structure of **7** and complete tables of the bond lengths and bond angles were deposited with the Cambridge Structural Database. Selected bond lengths and bond angles are given in Tables 9 and 10, respectively.

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