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Some aspects of synthesis 3- (2-florphenyl) -6-r1- [1,2,4] triazol [3,4-b] [1,3,4] thiadiazoleand 3- (2-, 3-ftorphenyl) - 6-r2-7h [1,2,4] triazolo [3,4-b] [1,3,4] tiadiazines.

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ABSTRACT

Of particular note is the combination of 1,2,4-triazole with other structural fragments. The additional introduction of an amino group to the "structure" of fluorophenylderivatives 1,2,4-triazol-3-thiol and the production of a number of new substances on their basis can lead to the appearance of molecules with new types of biological activity. The aim of this work is synthesis and research of new substances of1,2,4-triazole with fluorophenyl derivatives, synthesize new 3- (2-fluorophenyl) -6-R1- [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazole and 3- (2-fluorophenyl, 3 -Fluorophenyl) -6-R2-7H [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazines, in some cases, the passage of the cyclization reaction. Using the compound 5- (2-fluorophenyl) -4-amino-1,2,4-triazol-3-thiol, we first investigated the reaction of its cyclization in the presence of the corresponding aryl, heterocarboxylic acids in $POCl_3$ medium.

Keywords: 3- (2-fluorophenyl) -6-R1- [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazole and 3- (2-fluorophenyl, 3-fluorophenyl) -6-R2-7H [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazines, synthesis, physicochemical properties, structure

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INTRODUCTION

In modern conditions, the development of the pharmaceutical industry regarding the introduction of new synthetic medicines requires constant monitoring of the quality and safety of their use. For many years, synthetic drugs remain a powerful tool in the prevention and control of diseases of various etiologies [1]. Safe, low-toxic and effective substances deserve attention among the other synthetic classes. Undisputed leaders among many heterocyclic compounds today are derivatives of 1,2,4-triazole which fully meet the requirements of broad biological activity and unconditional safety [2].

The original from our point of view, is the combination of 1,2,4-triazole with other structural fragments [3]. The molecules are formed contribute to the expansion of the arsenal of compounds not only for further synthesis, most of them are potentially active in the biological aspect and may be of interest for further introduction into various branches of life. Also worthy of attention is the successful attempt of domestic scientists to synthesize 1,2,4-triazole fluorophenyl derivatives, promising for the biologically active compounds search [4]. Theoretically, the additional introduction of an amino group to the "structure" of fluorophenyl derivatives of 1,2,4-triazole-3-thiol and the production of a number of new substances on their basis can lead to the appearance of molecules with new types of biological activity, and sometimes to an increase in known pharmacological effects [5].

Thus, the aim of our work was to synthesize new 3-(2-fluorophenyl)-6-R1-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazoleand 3-(2-fluorophenyl,3-fluorophenyl)-6-R2-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines, in some cases, the passage of the cyclization reaction, complex physic al and chemical analysis methods, confirm the structure of the obtained compounds.

MATERIALS AND METHODS

The chemical names of synthesized compounds are used according to the requirements of the IUPAC nomenclature (1979) and IUPAC recommendations (1993). Studies of the physical and chemical properties of 3-(2-fluorophenyl)-6-R1-[1,2,4] triazolo[3,4-b] [1,3,4] thiadiazole and 3-(2-fluorophenyl,3-fluorophenyl)-6-R2-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazinium were conducted on certified and licensed equipment of physico-chemical laboratories of the Zaporozhye State Medical University according to thestudy plans.

Earlier we have noted that the synthesis of the initial compound - 4-amino-5(3-fluorophenyl)-1,2,4-triazole-3-thiol (2, Fig. 1) can be carried out by the method described in the publication [5]. By synthesizing 4-amino-5(2-fluorophenyl)-1,2,4-triazole-3-thiol (1, Fig. 1), we used 2-fluorobenzoic acid hydrazide, which in a stepwise manner was transferred to starting compound 1 (figure 1).

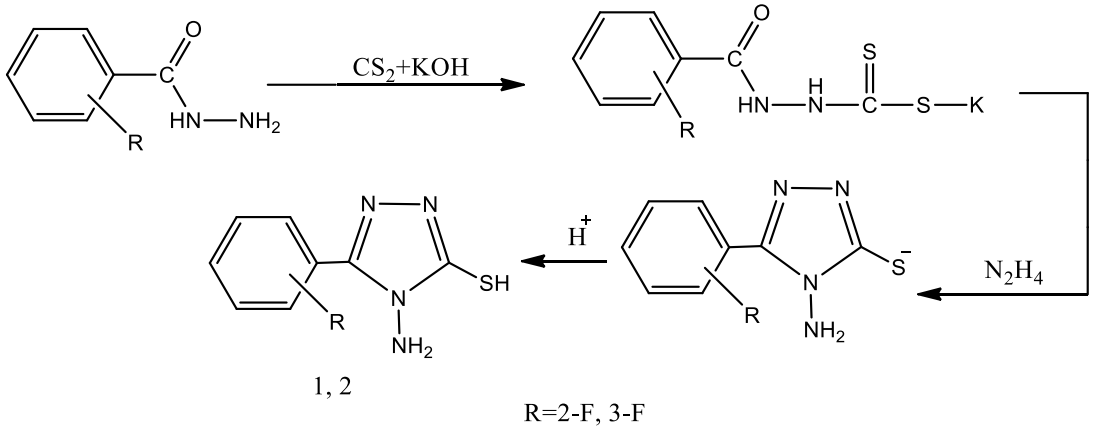

Fig: 1 Synthesis of 4-amino-5-(2-fluorophenyl,3-fluorophenyl)-1,2,4-triazole-3-thiol

The physical and chemical properties, the analysis constants, confirm the structure of 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol (2, Fig. 1) were described by us earlier and presented in [5]. 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol (1, Figure 1) is an individual, crystalline compound of white color

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(1, Fig. 1), which is soluble in organic solvents, insoluble in water. To analyze 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol recrystallized from a mixture of 1,4-dioxane and water in a 1: 1 ratio. The yield of 5-(2-fluorophenyl)-4-amino-1,2,4-triazol-3-thiol (1, Fig. 1) is 84%. M.p. = 144-146 °C. Found,%: C 45.77; H, 3.33; N, 26.61; S, 15.15. C8H7FN4S. Calculated: C, 45.70; H, 3.36; N, 26.65; S, 15.25.

Continuing the search for promising classes of compounds to expand the arsenal of biologically active substances based on fluorenyl derivatives of 1,2,4-triazole-3-thiol, we carried out that 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol (1, Fig. 1) in the presence of aromatic and fluorophenylide carboxylic acids in POCl3 medium (Fig. 2). It is well known that the passage of heterocyclization in this case passes through the intermediate stage of acylation of 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol (1) in the direction of reaction "a" and the formation of compounds 1.1- 1.3, which can exist in two tautomeric forms - "NH" and "OH" (Figure 2). Further heating of compounds 1.1-1.3 in POCl3 initiates the passage of reaction "c" (Figure 2) and the formation of the corresponding 3-(2-fluorophenyl)-6-R1-[1,2,4] triazolo [3,4-b] [1,3,4] Thiadiazole (3-14, Figure 2). We also investigated the possibility of passage of heterocyclization according to reaction scheme "b" to form a series of corresponding 3-(2-fluorophenyl)-6-R1-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (3-14, Figure 2).

We have proved that the peculiarity of the passage of the reactions "a", "b", "c" (Figure 2) is the fact that in each of the cases there are different reaction conditions. If the reaction is carried out in the presence of an excess of POCl3 under mild conditions, i.e., heating the reaction mixture in a water bath before the components are dissolved, followed by isolation of the products according to the generally known procedure [5], the process proceeds according to reaction scheme "a". In this case, when the initial components are mixed, the corresponding carboxylic acid chloride forms, which subsequently act as an acylating agent, resulting in the formation of intermediates (1.1-1.3, Figure 2), which, with further three-hour boiling in excess POCl3, are converted to bicyclic derivatives (3-14, figure) 2), fulfilling the requirements of the "c" reaction. Cyclization is accompanied by dehydration of one water molecule (Fig. 2). (3-14, figure 2).

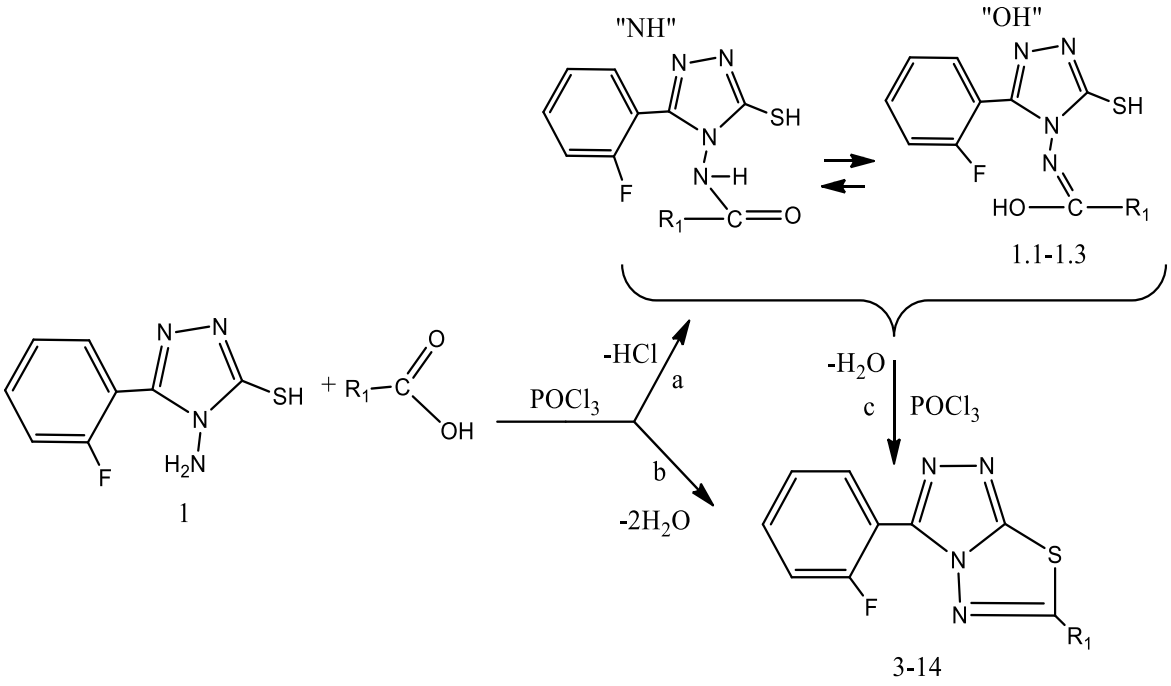

Fig 2: Synthesis of 3-(2-fluorophenyl)-6-R₁-[1,2,4]triazolo[3,4-b][1,3,4]Thiadiazoles

Reaction of the initial compound (1) and the corresponding carboxylic acids in the medium of excess POCl3 under more stringent conditions, that is, with a three-hour boiling of the components, followed by isolation of the products according to the well-known procedure [5], orientates cyclizationin a one-stage "b" (Fig. 2). The chemical process in this case is accompanied by dehydration of two water molecules. The

compounds are obtained by the two methods: "b" and "c" and do not give a depression of the melting point, which, together with other physical and chemical methods, confirm the structure of the obtained substances.

The compounds (1.1-1.3) are individual crystalline substances with light yellow color, which are soluble in organic solvents and insoluble in water. For physical and chemical analysis of compounds 1.1-1.3 they were recrystallized from 1,4-dioxane. The yield of the reaction product for compound 1.1, where R_1 = phenyl, (1.1, Fig. 2) is 53%. M.p. = 115-117 ° C. Found,%: C, 56.95; H, 3.49; N, 17.78; S, 10.17. $C_{15}H_{11}FN_4OS$. Calculated: C, 57.31; H, 3.53; N, 17.82; S, 10.20. The ^{1}H NMR spectra of the compound 1.1: 7.29 (t, 2H, Ar), 7.37 (t, 3H, Ar), 7.54 (m, 2H, Ar), 7.83 (d, 2H, Ar), 13.31 (s, 1H, SH). The yield of the reaction product forcompound 1.2, where R_1 = 2-methoxyphenyl, (1.2, Fig. 2) is 61%. M.p. = 102-104 ° C. Found, %: C 55.66; H, 3.77; N, 16.31; S, 9.29. $C_{16}H_{13}FN_4O2S$. Calculated: C, 55.80; H, 3.81; N, 16.27; S, 9.31. The ^{1}H NMR spectra of the compound 1.2: 3.88 (s, 3H, O-CH3), 7.18 (t, 2H, Ar), 7.36 (m, 4H, Ar), 7.55 (m, 2H , Ar), 13.35 (s, 1H, SH). The yield of the reaction product for compound 1.3, where R_1 = furan-2-yl, (1.3, Fig. 2) is 67%. M.p. = 157-159 ° C. Found,%: C 51.22; H, 2.95; N, 18.37; S, 10.58. C13H9FN4O2S. Calculated: C, 51.31; H, 2.98; N, 18.41; S, 10.54. The ^{1}H NMR spectra of compound 1.3: 6.52 (t, 1H, Fur), 7.12 (d, 1H, Fur), 7.29 (t, 1H, Ar), 7.32 (t, 1H, Ar), 7.74 (m, 2H, Ar, 1H, Fur), 13.48 (1H, s, SH).

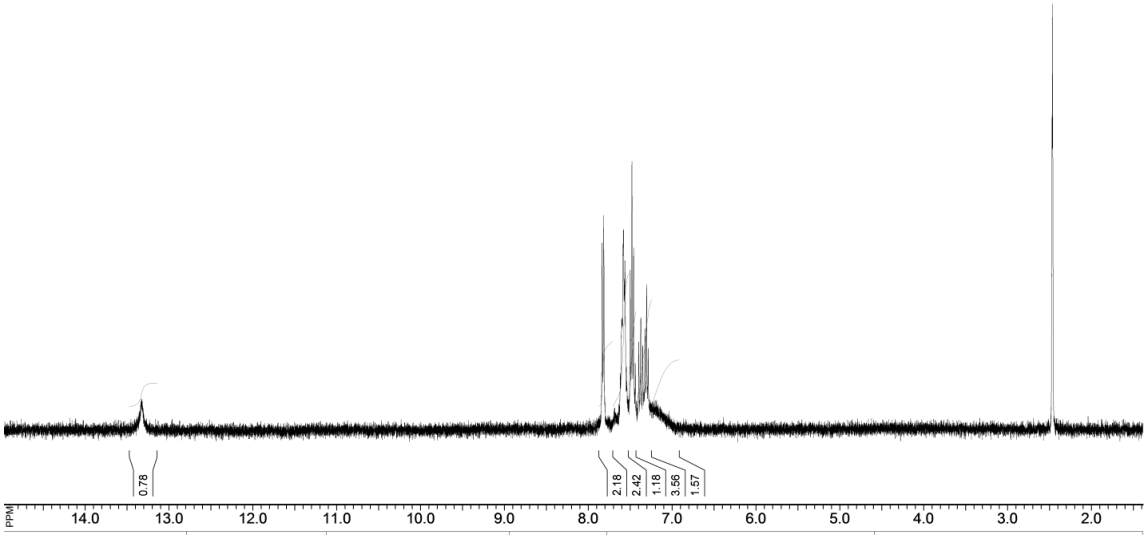

Fig 3: ^{1}H NMR spectrumof N-(3-(2-fluorophenyl)-5-mercapto-4H-1,2,4-triazole-4-yl)benzimidicacid (1.1)

In the ^{1}H NMR spectrum of N-(3-(2-fluorophenyl)-5-mercapto-4H-1,2,4-triazole-4-yl)benzimidoicacid (1.1) there are signals of aromatic cycle protons that are fixed in the form of two triplets at 7.29 (2H), 7.37 (3H) multiplet 7.54 (2H), doublet 7.83 (2H), the proton signals of the SH group are recorded as a singletat 13.31 (1H).

Compounds (3-14, Table 1) are individual crystalline substances, light yellow (3, 5, 8-14), white (4, 6), yellow (7), soluble inorganic solvents, in soluble in water. For physical and chemical analysis of the compound (3-14, Table 1) they were recrystallized with isopropanol.

The next step in our exploratory studies was the reaction of 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol (1) and 5-(3-fluorophenyl)-4-amino-1,2 4-triazol-3-thiol (2) with an equivalent amount of 2-bromo-1-aryletanone and 1-bromopropan-2-one in isopropanol. The reaction was carried out under analogous conditions described in the dissertation [2]. The final products (15-20, figure 4) were obtained by adding an aqueous solution of sodium bicarbonate (Figure 4).

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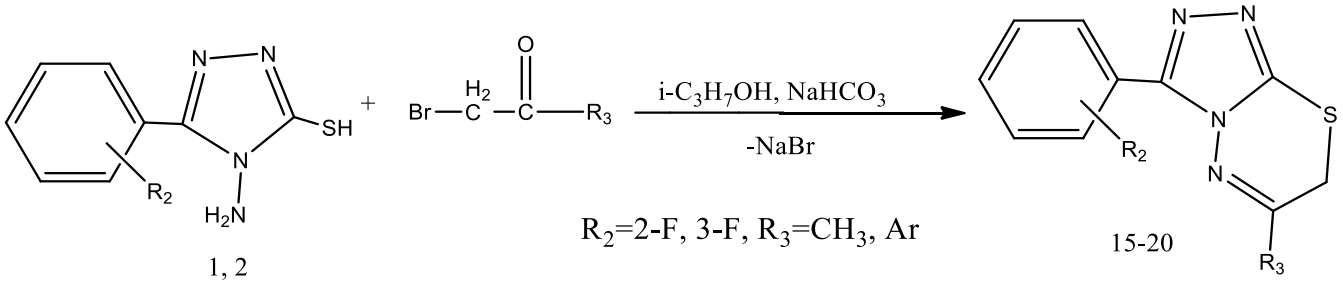


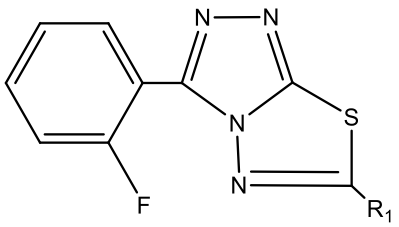
Fig 4: Synthesis of 3-(2-fluorophenyl,3-fluorophenyl)-6-R3-7H[1,2,4] triazolo [3,4-b][1,3,4]thiadiazine

In all cases, new individual crystalline compounds of light yellow (15, 16, 20 Table 3), yellow (17 Table 3), white (19 Table 3), orange (18 Table 3), soluble in organic solvents, insoluble in water. For physical and chemical analysis, 3(2-fluorophenyl, 3-fluorophenyl)-6-R3-7H [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazines recrystallized with isopropanol.

RESULTS AND DISCUSSION

The structure of the molecules of all synthesized compounds was proved using modern physical and chemical methods of analysis (elemental analysis, ^{1}H NMR spectroscopy, chromatography-mass spectrometry), and their individuality was confirmed by chromatography. Physicochemical constants of synthesized 3-(2-fluorophenyl) -6-R1-[1,2,4] triazolo[3,4-b] [1,3,4]thiadiazole(3-14, Table 1) and 3(2-fluorophenyl,3-fluorophenyl)-6-R3-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazinium (15-20, Table 3) are given in corresponding tables 2, 4.

Table 1: Physicochemicalconstantsof 3(2-fluorophenyl)-6-R1-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole



Compound	R_1	Tмр ,°C	Gross formula	Output,%
1	**2**	**3**	**4**	**5**
3	fenil	137-139	$C_{15}H_9FN_4S$	67
4	2-Fluorophenol	169-171	$C_{15}H_{18}F_2N_4S$	78
5	4-Fluorophenyl	151-153	$C_{15}H_{18}F_2N_4S$	72
6	4-i-Butylphenyl	189-191	$C_{19}H_{17}FN_4S$	71
7	2-methoxyphenyl	118-120	$C_{16}H_{11}FN_4OS$	72
8	2-Brom-4-fluorophenyl	160-162	$C_{15}H_7BrF_2N_4S$	58
9	2-Chloro-4-nitrophenol	183-185	$C_{15}H_7ClFN_5O_2S$	74
10	2-Chloro-5-nitrophenol	216-218	$C_{15}H_7ClFN_5O_2S$	64
11	2-Bromo-5-methoxyphenyl	92-94	$C_{16}H_{10}BrFN_4OS$	62
12	furan-2-yl	181-183	$C_{13}H_7FN_4OS$	69
13	pyridine-2-yl	158-160	$C_{14}H_8FN_5S$	78
14	pyridine-4-yl	121-123	$C_{14}H_8FN_5S$	72

Continued table 1

Compound	Found,%				Calculated,%			
	C	H	N	S	C	H	N	S
1	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**

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3	60,69	3,08	18,88	10,76	60,80	3,06	18,91	10,82
4	57,21	2,56	17,86	10,18	57,32	2,57	17,83	10,20
5	57,33	2,55	17,78	10,23	57,32	2,57	17,83	10,20
6	64,77	4,88	15,84	9,11	64,75	4,86	15,90	9,10
7	58,82	3,38	17,14	9,77	58,89	3,40	17,17	9,82
8	45,77	1,76	14,22	8,14	45,82	1,79	14,25	8,15
9	47,91	1,90	18,87	8,55	47,95	1,88	18,84	8,53
10	47,87	1,88	18,82	8,54	47,95	1,88	18,84	8,53
11	47,41	2,51	13,85	7,89	47,42	2,49	13,83	7,91
12	54,49	2,47	19,55	11,18	54,54	2,46	19,57	11,20
13	56,55	2,69	23,59	10,77	56,56	2,71	23,56	10,79
14	56,48	2,66	23,51	10,72	56,56	2,71	23,56	10,79

The signals of the aromatic protons 3(2-fluorophenyl)-6-phenyl[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (3, Table 2) in the ^{1}H NMR spectrum were recorded in a triplet and multiplets with corresponding chemical shifts. Thus, the proton signals of the 2-fluorophenyl radical were fixed in a stronger field as a tripletat 7.25 pm and multiplet at 7.70 - 8.09 m.ch. Other proton signals of 2-fluorophenyl radicals were observed in a weaker field and produced a multiplet with signals of protons of the phenyl radical at 7.41 ppm. In addition, according to the ^{1}H NMR spectra of compounds (3-14, Table 2), in all cases there are no signals of protons of NH_2 and SH groups, in combination with other physicochemical methods, confirms the formation of precisely these bicyclic derivatives.

Table 2: Constant^{1}H NMR Spectrum 3-(2-Fluorophenyl)-6-R1-[1,2,4]triazole[3,4-b][1,3,4]thiadiazolethe 3-(2-,3-fluorophenyl)-6-R2-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine

№ Compound	^{1}H NMP DMSO-d_6, δ ppm
3	8.09 (m, 2H, Phenyl), 7.70 (m, 2H, Phenyl), 7.41 (m, 4H, Phenyl), 7.25 (t, 2H, Phenyl)
4	7.70 (m, 4H, Phenyl), 7.49 (m, 2H, Phenyl), 7.21 (m, 2H, Phenyl)
5	7.68 (m, 4H, Phenyl), 7.47 (t, 2H, Phenyl), 7.25 (m, 3H, Phenyl)
6	7.66 (m, 4H, Phenyl), 7.43 (t, 2H, Phenyl), 7.31 (m, 2H, Phenyl), 7.24 (t, 1H, Phenyl), 2.51 (m, 1H, -CH-(i-butyl)), 1.58 (m, 2H, -CH_2-(i-butyl)), 1.25 (d, 3H, -CH_3(i-butyl)), 0.95 (t, 3H, -CH_3(i-butyl)).
7	7.69 (m, 2H, Phenyl), 7.39 (t, 1H, Phenyl), 7.29 (t, 1H, Phenyl), 7.15 (m, 2H, Phenyl), 7.01 (m, 2H, Phenyl), 3.81(s, 3H, -OCH_3).
8	7.81 (m, 3H, Phenyl), 7.44 (m, 2H, Phenyl), 7.24 (m, 2H, Phenyl)
9	8.41 (s, 1H, Phenyl), 8.20 (d, 1H, Phenyl), 7.99 (d, 1H, Phenyl), 7.69 (m, 2H, Phenyl), 7.46 (t, 1H, Phenyl), 7.28 (m, 1H, Phenyl)
10	8.60 (s, 1H, Phenyl), 8.00 (d, 1H, Phenyl), 7.81 (m, 3H, Phenyl), 7.48 (m, 1H, Phenyl), 7.25 (t, 1H, Phenyl)
11	7.68 (m, 2H, Phenyl), 7.49 (m, 2H, Phenyl), 7.25 (m, 2H, Phenyl), 6.94 (d, 1H, Phenyl), 3.84(s, 3H, -OCH_3).
12	7.90 (d, 1H, Furan),7.69 (m, 2H, Phenyl), 7.48 (t, 1H, Phenyl),7.28 (t, 1H, Phenyl),7.07 (d, 1H, Furan), 6.65 (t, 1H, Furan)
13	8.59 (d, 1H, Pyridine), 8.03 (d, 1H, Pyridine), 7.95 (m, 1H, Pyridine),7.70 (m, 2H, Phenyl),7.40 (t, 1H, Phenyl), 7.32 (t, 1H, Pyridine),7.21 (m, 1H, Phenyl)
14	8.75 (d, 2H, Pyridine), 7.98 (d, 2H, Pyridine),7.72 (m, 2H, Phenyl),7.42 (m, 1H, Phenyl),7.23 (t, 1H, Phenyl)
15	7.75 (m, 2H, Phenyl), 7.48 (m, 1H, Phenyl), 7.27 (m, 1H, Phenyl), 3.87 (s, 2H, -S-CH_2-), 2.35(s, 3H, -CH_3), 8.75 (d, 2H, Pyridine), 7.98 (d, 2H, Pyridine), 7.72 (m, 2H, Phenyl), 7.42 (m, 1H, Phenyl), 7.23 (t, 1H, Phenyl)
16	8.00 (d, 2H, Phenyl), 7.70 (m, 2H, Phenyl),7.51 (m, 4H, Phenyl),7.21 (t, 1H, Phenyl), 4.41 (s, 2H, -S-CH_2-)
17	7.91 (m, 2H, Phenyl),7.69 (m, 2H, Phenyl),7.40 (t, 1H, Phenyl),7.30 (t, 1H, Phenyl),7.21 (t, 1H,

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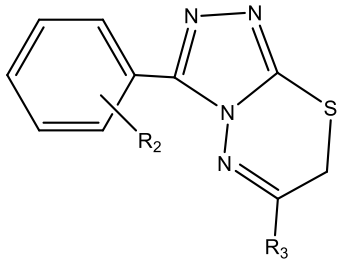
	Phenyl), 4.45 (s, 2H, -S-CH_2-)
18	7.95 (d, 2H, Phenyl),7.74 (m, 2H, Phenyl),7.41 (t, 1H, Phenyl),7.28 (t, 1H, Phenyl), 7.06 (d, 2H, Phenyl), 4.40 (s, 2H, -S-CH_2-), 3.83(s, 3H, -CH_3)
19	8.05 (m, 1H, Phenyl), 7.55 (m, 2H, Phenyl), 7.20 (t, 1H, Phenyl), 3.89 (s, 2H, -S-CH_2-), 2.39(s, 3H, -CH_3)
20	8.07 (m, 1H, Phenyl), 7.91 (m, 2H, Phenyl),7.53 (m, 2H, Phenyl),7.23 (t, 1H, Phenyl), 7.07 (d, 2H, Phenyl), 4.49 (s, 2H, -S-CH_2-), 3.89(s, 3H, -OCH_3)

Table 3: Physical and chemical constants of 3- (2-fluorophenyl,3-fluorophenyl)-6-R_3-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines



Compound	R_2	R_3	Tмр ,°C	Gross formula	Output,%
1	**2**	**3**	**4**	**5**	**6**
15	2-fluorophenyl	methyl	202-204	$C_{11}H_9FN_4S$	78
16	2-fluorophenyl	phenyl	218-220	$C_{16}H_{11}FN_4S$	82
17	2-fluorophenyl	4-fluorophenyl	207-209	$C_{16}H_{10}F_2N_4S$	82
18	2-fluorophenyl	4-Methoxyphenyl	184-186	$C_{17}H_{13}FN_4OS$	80
19	3-fluorophenyl	methyl	198-200	$C_{11}H_9FN_4S$	66
20	3-fluorophenyl	4-Methoxyphenyl	163-165	$C_{17}H_{13}FN_4OS$	64

Continued tabl. 3

Compound	Found,%				Calculated,%			
	C	H	N	S	C	H	N	S
1	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
15	53,17	3,67	22,60	12,87	53,21	3,65	22,57	12,91
16	61,88	3,58	18,02	10,31	61,92	3,57	18,05	10,33
17	58,49	3,05	16,95	9,71	58,53	3,07	17,06	9,77
18	59,88	3,84	16,47	9,45	59,99	3,85	16,46	9,42
19	40,19	2,75	17,03	9,72	40,26	2,76	17,07	9,77
20	60,06	3,88	16,47	9,41	59,99	3,85	16,46	9,42

Analyzing the values of the peaks constants of pseudomolecular ions of 3(2-fluorophenyl)-6-R_1-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole, their intermediates and 3-(2-fluorophenyl,3-fluorophenyl)-6-R_2-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines (1.1-20, Table 4), it can be stated with confidence the correspondence between the calculated values of the masses found during the analysis.

Table 4: The peaks of the pseudomolecular ion peaks of 3(2-fluorophenyl)-6-R_1-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole, their intermediates and 3-(2-fluorophenyl,3-fluorophenyl)-6-R_2-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines

№ compounds	Exactmass	[MH] m/z	№ compounds	Exactmass	[MH] m/z
1.1	314	315	***11***	405	406
1.2	344	345	***12***	286	287
1.3	304	305	***13***	297	298
3	296	297	***14***	297	298
4	314	315	***15***	248	249

5	314	315	***16***	310	311
6	352	353	***17***	328	329
7	326	327	***18***	340	341
8	393	394	***19***	248	249
9	375	376	***20***	340	341
10	375	376			

CONCLUSION

1. Using 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol as the starting compound, we first investigated its cyclization in the presence of the corresponding aryl, heteryl carboxylic acids in $POCl_3$ medium. It is proved that the reaction takes place in different ways, depending on the conditions of its conduct. A number of new 3-(2-fluorophenyl)-6-R_1-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole and their intermediates were obtained. It has also been proved that the reaction of 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol and 5-(3-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol with the equivalent amount of 2-bromo-1-aryletanone and 1-bromopropan-2-one in the isopropanol medium, the corresponding 3-(2-fluorophenyl,3-fluorophenyl)-6-R_2-7H[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines.
2. The passage of cyclization and the formation of intermediate products in all cases is confirmed by complex modern physical and chemical methods of analysis (elemental analysis, $_1$H NMR spectroscopy, chromatography-mass spectrometry), in some cases counter-synthesis was used. Individuality of the compounds is proved chromatographically.

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