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Studying Of Physico-Chemical Properties Of 5-(2-,3-Fluorophenyl)-4-((Aryl-, Geteryl) Yliden) Amino-1,2,4-Triazole-3-Thiols And Any Of Their Retrievalproducts.

Oleksii Bihdan[1]*, Volodymyr Parchenko[1], Volodymyr Zazharskyi[2], Tetyana Fotina[3], and Pavlo Davydenko[2].

[1]Zaporizhzhya State Medical University, Zaporizhzhya.
[2]Dnipro State Agrarian and Economics University.
[3]Sumy National Agrarian University.

ABSTRACT

The need for highly effective and low-toxic drugs is constantly increasing in the modern world. Therefore, the creation of new original molecules, which can turn into effective bioactive compounds, and then into drugs, is a topical issue of the modern pharmaceutical and medical industries. The purpose of the work is to study the physico-chemical properties of new 5-(2-,3-fluorophenyl)-4-((aryl,heteryl)ylidenes)amino-1,2,4-triazole-3-thiols and some products of their reduction. As the starting compounds, we used 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol and 5- (3-fluorophenyl) -4-amino-1,2,4 -triazole-3-thiol

Keywords: 2-, 3-fluorophenyl derivative 4-amino-1,2,4-triazole, physical and chemical properties, chemical transformations, regeneration

Corresponding author

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INTRODUCTION

Analyzing certain scientific achievements, it should be noted the special role of nitrogen-containing heterocyclic systems, which are very widely represented in modern organic chemistry [1, 2]. Special attention should be paid to compounds containing the heterocyclic system of 1,2,4-triazole in its composition [3, 4], since this is a very large group of substances that for many years attracts scientists of various fields of scientific activity [5, 6, 7]. The current trend is the possibility of combining 1,2,4-triazole and various representatives of pharmacophoric substituents, which are oriented according to the different positions of this heterocycle [8, 9]. Scientists confidently and reasonably argue this expediency [10]. A striking example of the successful introduction of 1,2,4-triazole derivatives is the achievement of the scientists of Zaporizhzhya State Medical University [11-13].In July 2018, the "Trifuzol 1%" veterinary medicine under the trademark "Trifuzol-Neo 1%" (RP No. AB-07793-01-18 dated 27.07.2018) was re-registered, the domestic fertilizer "Fortis Combi" is gaining popularity among users. Also, in our opinion, derivatives of 1,2,4-triazole, containing in their composition fluorophenyl radical in combination with other reactive substituents [14, 15], deserve attention. It is known that such combination is promising in various scientific aspects of the pharmaceutical field and, of course, creates favorable conditions for the search of new biologically active compounds [15].

Therefore, the purpose of the work is to study the physico-chemical properties of new 5-(2-,3-fluorophenyl)-4-((aryl,heteryl)ylidenes)amino-1,2,4-triazole-3-thiols and some products of their reduction , which can be promising objects for the creation of new biologically active molecules as potential drugs.

MATERIALS AND METHODS OF RESEARCH

The chemical names of compounds are given in accordance with the IUPAC nomenclature (1979) and the recommendations of the IUPAC (1993). The study of the physico-chemical properties of the obtained compounds was carried out according to the methods presented in the State Pharmacopoeia of Ukraine. The melting temperature was determined on the OptiMelt Stanford Research Systems MPA100 (US production) automatic melting device. Elemental composition of new compounds was established on elemental analyzer ElementarVario L cube (CHNS) (standard - sulfanilamide). Elemental analysis data is in line with the calculated ones. The ^{1}H NMR spectra of the compounds were recorded using the Mercury 400 spectrometer, as a solvent was used DMSO-d6, the internal standard - tetramethylsilane (TMS) and deciphered using the SpinWorks computer program.

Chromate-mass spectra were recorded on the Agilent 6890N/5973N/FID of the Agilent Technologies, with the Din microprobe switch. Column number 1 - quartz capillary HP-5MS 0.25 mm.h30 m., The output of the column is connected to the flame ionization detector, № 2 - quartz capillary DB-17MS 0.25 mmh30 m, the end of the column directly enters the mass spectrometer. The inlet temperature is 250 °C, the interface line of the mass transfer tube (Transfer line) is 280 °C, the ion source is 230 °C, the quadrupole is 150 °C. Ionization mode - electronic shock, electron energy - 70 eV, electric power amplifier voltage - 200 V more than at Autotune (automatic tuning scale mass). Scan range 40-750 a. at. m., threshold - 110, scanning speed - 2.11 scan / sec. Thermostat thermostat programming mode: 70 °C - 2 min, then rise to 210 °C at a rate of 45 °C / ab, then rise to 310 °C at a speed of - 06 °C / ab, and maintain at this temperature 18.22 min. Pressure of gas - carrier (helium) at the entrance to the first column - 26.00 psi, the second - 19.30 psi. Physico-chemical properties of synthesized compounds were investigated on certified and licensed equipment of physico-chemical laboratories of Zaporizhzhya State Medical University according to research plans.

As the starting compounds, we used 5-(2-fluorophenyl)-4-amino-1,2,4-triazole-3-thiol (1) and 5- (3-fluorophenyl) -4-amino-1,2,4 -triazole-3-thiol (2), the physicochemical properties of which are described earlier by us [16]. Using a well-known technique, we received a number of new aldimines (3-31, Fig. 1), some of them were subsequently restored (Fig. 1). In this case, the compounds (32-40, Fig. 1) were obtained.

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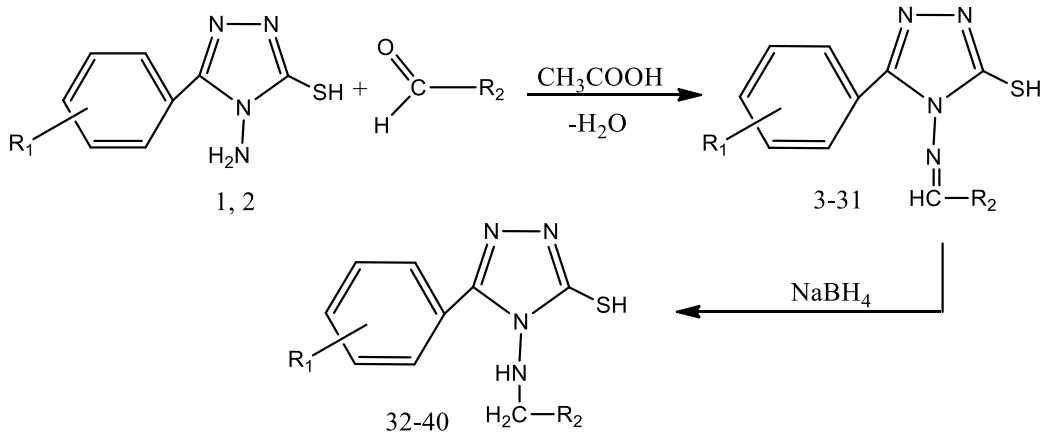

Fig 1: Synthesis of 5-(2-,3-fluorophenyl)-4-((aryl,heteryl)ylidene)amino-1,2,4-triazole-3-thiols and the restoration of some of them

The synthesized compounds (3-40, Table 1) are individual crystalline substances with white (3, 5, 6, 8, 18, 22, 23, 31, 35, 36, 37, 38, Table 1), light yellow (4, 7, 9-14, 17, 19, 21, 24, 26, Table 1), yellow (25, 27-30, 32, 33, 34, 39, 40), orange (16, 20, Table1) and brown (15, Table 1), soluble in organic solvents, insoluble in water. The compounds were recrystallized from butane-1-ol for analysis.

In the IR spectra of the 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl)ylidene)amino-1,2,4-triazole-3-thiols (3-31, Table 5) Oscillations of the groups characteristic of the 1,2,4-triazole core: -C = N-1690-1600 cm^{-1}. Also, there are bands of oscillation of groups -S-S- at 705-570 cm^{-1}. Available strips of oscillation are typical for the -SH group within the range of 2592-2353 cm^{-1}. The presence of characteristic vibrations of functional groups of the corresponding 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl) ylidene)amino-1,2,4-triazole-3-thiols can be traced by the IR spectrum 5-(3-fluorophenyl)-4-((2,4-dimethylphenyl)ylidene)amino-1,2,4-triazole-3-thiol (26, Fig. 2).

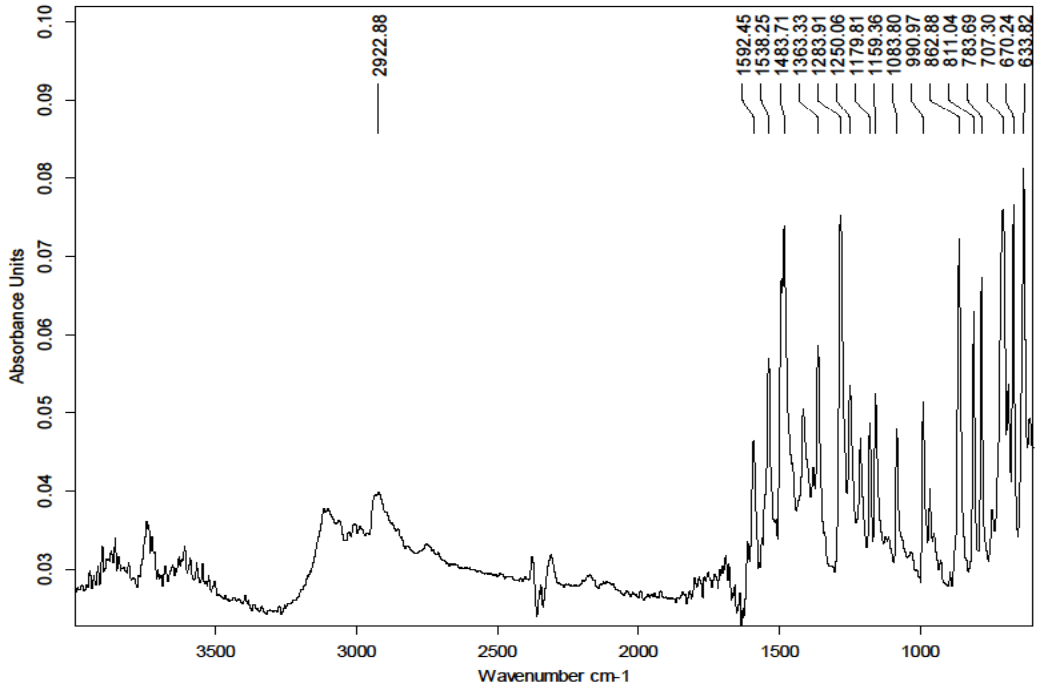

Fig 2: IR spectrum of 5-(3-fluorophenyl)-4-((2,4-dimethylphenyl)ylidene)amino-1,2,4-triazole-3-thiol (26).

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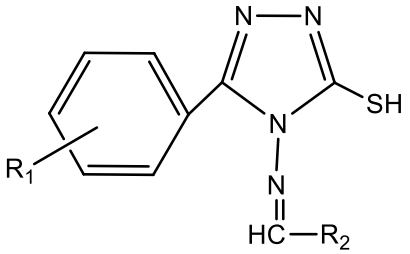
RESULTS OF THE EXPERIMENT

The structure of the molecules of all synthesized compounds was proved using modern physico-chemical methods of analysis (elemental analysis, ^1H NMR spectroscopy, chromatographic mass spectrometry), and their individuality was confirmed by chromatography. Physico-chemical constants of new 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl)ylidene)amino-1,2,4-triazole-3-thiols (3-31, fig. 1) and products The restoration of some of them (32-40, Fig. 1) is presented in Tables 1 and 2, respectively.

Table 1: Physico-chemical constants of 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl)ylidene)amino-1,2,4-triazole-3-thiols



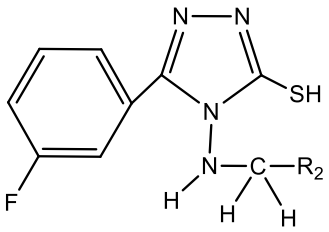
Compound	R_1	R_2	Tmel., °C	Grossformula	Exodus, %
1	2	3	4	5	6
3	2-fluorophenyl	phenyl	177-179	$C_{15}H_{11}FN_4S$	69
4	2-fluorophenyl	4-bromophenyl	205-207	$C_{15}H_{10}BrFN_4S$	82
5	2-fluorophenyl	3-fluorophenyl	206-208	$C_{15}H_{10}F_2N_4S$	78
6	2-fluorophenyl	4-fluorophenyl	182-184	$C_{15}H_{10}F_2N_4S$	72
7	2-fluorophenyl	2-hydroxyphenyl	207-209	$C_{15}H_{11}FN_4OS$	69
8	2-fluorophenyl	4-hydroxyphenyl	215-217	$C_{15}H_{11}FN_4OS$	72
9	2-fluorophenyl	2-nitrophenyl	191-193	$C_{15}H_{10}FN_5O_2S$	84
10	2-fluorophenyl	3-nitrophenyl	218-220	$C_{15}H_{10}FN_5O_2S$	81
11	2-fluorophenyl	4-nitrophenyl	231-233	$C_{15}H_{10}FN_5O_2S$	83
12	2-fluorophenyl	3-methoxyphenyl	171-173	$C_{16}H_{13}FN_4OS$	88
13	2-fluorophenyl	2,3-dimethoxyphenyl	182-184	$C_{17}H_{15}FN_4O_2S$	84
14	2-fluorophenyl	3,4-dimethoxyphenyl	198-200	$C_{17}H_{15}FN_4O_2S$	86
15	2-fluorophenyl	3,5-dimethoxyphenyl	204-206	$C_{17}H_{15}FN_4O_2S$	81
16	2-fluorophenyl	4-dimethylaminophenyl	196-198	$C_{17}H_{16}FN_5S$	79
17	2-fluorophenyl	2-carboxyphenyl	180-182	$C_{16}H_{11}FN_4O_2S$	76
18	2-fluorophenyl	3-bromo-4-fluorophenyl	215-217	$C_{15}H_9BrF_2N_4S$	84
19	2-fluorophenyl	2-chloro-6-fluorophenyl	178-180	$C_{15}H_9ClF_2N_4S$	78
20	2-fluorophenyl	5-nitrofuran-2-yl	219-221	$C_{13}H_8FN_5O_3S$	72
21	2-fluorophenyl	pyridine-3-yl	184-186	$C_{14}H_{10}FN_5S$	74
22	2-fluorophenyl	thiophene-2-yl	210-212	$C_{13}H_9FN_4S_2$	77
23	2-fluorophenyl	4-fluorophenyl	206-208	$C_{15}H_{10}F_2N_4S$	68
24	2-fluorophenyl	2-hydroxyphenyl	212-214	$C_{15}H_{11}FN_4OS$	75
25	2-fluorophenyl	4-methoxyphenyl	185-188	$C_{16}H_{13}FN_4OS$	82
26	2-fluorophenyl	2,4-dimethylphenyl	213-215	$C_{17}H_{15}FN_4S$	72
27	2-fluorophenyl	2,4-dimethoxyphenyl	217 decomp	$C_{17}H_{15}FN_4O_2S$	77
28	2-fluorophenyl	2,3-dimethoxyphenyl	173-175	$C_{17}H_{15}FN_4O_2S$	71
29	2-fluorophenyl	3,4-dimethoxyphenyl	205-207	$C_{17}H_{15}FN_4O_2S$	71
30	2-fluorophenyl	3-bromo-4-fluorophenyl	218-219	$C_{15}H_9BrF_2N_4S$	64
31	2-fluorophenyl	pyridine-3-yl	189-190	$C_{14}H_{10}FN_5S$	64

Compound	Found, %	Calculated, %

ISSN: 0975-8585

	C	H	N	S	C	H	N	S
1	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
3	60,15	3,69	17,66	10,78	60,39	3,72	18,70	10,79
4	47,71	2,66	14,82	8,85	47,76	2,67	14,85	8,90
5	57,03	3,11	17,66	10,12	56,95	3,10	17,71	10,14
6	56,78	3,15	17,54	10,13	56,95	3,19	17,71	10,14
7	57,33	3,55	17,74	10,17	57,31	3,53	17,82	10,20
8	57,33	3,55	17,87	10,15	57,31	3,53	17,82	10,20
9	52,44	2,93	20,36	9,31	52,47	2,94	20,40	9,34
10	52,42	2,97	20,37	9,31	52,47	2,94	20,40	9,34
11	52,41	2,88	20,35	9,33	52,47	2,94	20,40	9,34
12	58,49	3,92	17,02	9,81	58,52	3,99	17,06	9,77
13	57,02	4,26	15,71	8,94	56,97	4,22	15,63	8,95
14	56,92	4,19	15,67	8,92	56,97	4,22	15,63	8,95
15	56,88	4,21	16,63	8,96	56,97	4,22	15,63	8,95
16	59,88	4,70	20,48	9,37	59,81	4,72	20,51	9,39
17	56,06	3,27	16,33	9,32	56,13	3,24	16,37	9,37
18	49,55	2,33	14,12	8,06	49,58	2,30	14,18	8,11
19	51,23	2,61	15,88	9,15	51,36	2,59	15,97	9,14
20	46,84	2,41	20,95	9,55	46,85	2,42	21,01	9,62
21	56,06	3,31	23,33	10,66	56,18	3,37	23,40	10,71
22	51,03	2,95	18,36	20,93	51,30	2,98	18,41	21,07
23	57,09	3,20	17,67	10,11	56,95	3,19	17,71	10,13
24	57,19	3,54	17,78	10,22	57,32	3,53	17,82	10,20
25	58,64	3,98	17,09	9,74	58,53	3,99	17,06	9,76
26	62,56	4,63	17,17	9,82	62,56	4,63	17,17	9,82
27	56,84	4,23	15,60	8,97	56,97	4,22	15,63	8,95
28	56,85	4,21	15,66	8,97	56,97	4,22	15,63	8,95
29	56,84	4,21	15,67	8,93	56,97	4,22	15,63	8,95
30	45,48	2,29	14,15	8,13	45,59	2,30	14,18	8,11
31	56,06	3,38	23,35	10,73	56,18	3,37	23,40	10,71

Table 2: Physico-chemical constants of 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols



Compound	R_1	T mel., °C	Grossformula	Entrance, %
1	**2**	**3**	**4**	**5**
32	4-fluorophenyl	223-225	$C_{15}H_{12}F_2N_4S$	78
33	2-hydroxyphenyl	226-228	$C_{15}H_{13}FN_4OS$	63
34	4-methoxyphenyl	277 decomp	$C_{16}H_{15}FN_4OS$	64
35	2,4-dimethylphenyl	199-201	$C_{17}H_{17}FN_4S$	64
36	2,4-dimethoxyphenyl	168-170	$C_{17}H_{17}FN_4O_2S$	59
37	2,3-dimethoxyphenyl	194-196	$C_{17}H_{17}FN_4O_2S$	70
38	3,4-dimethoxyphenyl	174 decomp	$C_{17}H_{17}FN_4O_2S$	77
39	3-bromo-4-fluorophenyl	209-211	$C_{15}H_{11}BrF_2N_4S$	69
40	pyridine-3-yl	252-254	$C_{14}H_{12}FN_5S$	71

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Compound	Found, %				Calculated, %			
	C	H	N	S	C	H	N	S
1	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
32	56,72	3,81	17,56	10,05	56,59	3,80	17,60	10,07
33	57,08	4,13	17,75	10,12	56,95	4,14	17,71	10,14
34	58,03	4,59	16,92	9,72	58,17	4,58	16,96	9,70
35	62,31	5,23	17,02	9,74	62,17	5,22	17,06	9,76
36	56,76	4,74	15,58	8,88	56,65	4,75	15,55	8,90
37	56,49	4,76	15,51	8,92	56,65	4,75	15,55	8,90
38	56,79	4,74	15,59	8,88	56,65	4,75	15,55	8,90
39	45,23	2,78	14,14	8,09	45,35	2,79	14,10	8,07
40	55,90	4,00	23,28	10,62	55,80	4,01	23,24	10,64

Analysis of the ^{1}H NMR spectra of the synthesized compounds (3-31, Table 3) indicates the passage of the reaction and the formation of a number of new 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl)ylidene)amino-1,2,4-triazole-3-thiols. The protons of methoxy groups resonate in the strong part of the field at 3.85 and 3.89 mph, forming singles that are located adjacent (14). The analysis of signals in the spectra of NMR 1 H in the region of aromatic protons allowed us to conclude that the presence in molecules is 13-15. two fragments of a substituted phenyl radical. Protons of the 3,4-methoxyphenyl substituent form a set of signals in the form of a doublet and multiplets at 6.90 mph, 7.27-7.30 mph. and at 7.35-7.38 mph in accordance. Protons of the 3-fluorophenyl substituent form a triplet at 7.52-7.55 mph., doublets in the region of 7.19-7.21 mph, 7.70 mph. and 8.03-8.05 mph It is necessary to note the presence of a single themal proton azamethine fragment which forms a characteristic singlet signal, for example, at 9.90 mph. (Compound 26). The proton of the thiol substituent forms a singlet in the weak part of the spectrum at 14.3 mph. (Compound 26)

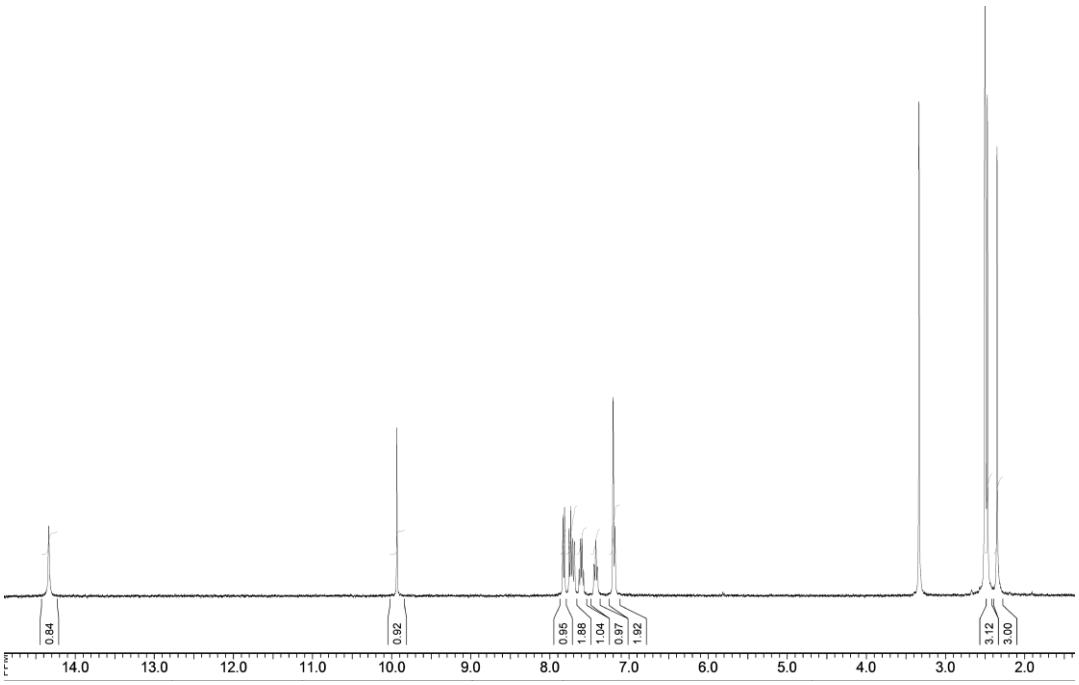

Fig 3: ^{1}H NMR spectrum of 4-(2,4-dimethylbenzylideneamino)-5-(3-fluorophenyl)-4H-1,2,4-triazole-3-thiol (26)

Table 3: Constituentsofthe^{1}H NMR spectraof 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl)ylidene)amino-1,2,4-triazole-3-thiols and 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols

№ compounds	^{1}H NMR DMSO-d_6, δ ppm

3	14.34 (s, 1H, SH), 8.89 (s, 1H, -N=CH-), 8.05-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.56-7.64 (m, 3H, 2-F-$C_6\underline{H_4}$, $C_6\underline{H_5}$), 7.35-7.30 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.16-7.10 (m, 1H, 2-F-$C_6\underline{H_4}$,), 6.89 – 6.82 (m, 2H, $C_6\underline{H_5}$).
4	14.26 (s, 1H, SH), 10.89 (s, 1H, -N=CH-), 8.06-7.93 (d, 1H, 2-F-$C_6\underline{H_4}$), 7.75-7.69 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.53-7.44 (m, 1H, 4-Br-$C_6\underline{H_4}$), 7.39-7.32 (dd, 2H, 4-Br-$C_6\underline{H_4}$), 7.19-7.10 (dd, 2H, 4- Br -$C_6\underline{H_4}$).
5	14.35 (s, 1H, SH), 10.81 (s, 1H, -N=CH-), 8.05-7.93 (d, 1H, 2-F-$C_6\underline{H_4}$), 7.75-7.70 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.64-7.57 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.44-7.38 (dd, 2H, 3-F-$C_6\underline{H_4}$), 7.22-7.18 (dd, 2H, 3-F-$C_6\underline{H_4}$).
6	14.35 (s, 1H, SH), 10.89 (s, 1H, -N=CH-), 8.06-7.93 (d, 1H, 2-F-$C_6\underline{H_4}$), 7.75-7.69 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.64-7.55 (m, 1H, 4-F-$C_6\underline{H_4}$), 7.43-7.38 (dd, 2H, 4-F-$C_6\underline{H_4}$), 7.23-7.17 (dd, 2H, 4-F-$C_6\underline{H_4}$).
7	14.34 (s, 1H, SH), 11.05 (s, 1H, 2-O$\underline{H}$-C_6H_4), 8.89 (s, 1H, -N=CH-), 8.05-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.56-7.64 (m, 3H, 2-F-$C_6\underline{H_4}$, 2-OH-C_6H_4), 7.35-7.30 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.15-7.09 (m, 1H, 2-F-$C_6\underline{H_4}$,), 6.94 – 6.85 (m, 2H, 2-OH-$C_6\underline{H_4}$).
8	14.34 (s, 1H, SH), 11.05 (s, 1H, 4-O$\underline{H}$-C_6H_4), 8.89 (s, 1H, -N=CH-), 8.05-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.56-7.64 (m, 3H, 2-F-$C_6\underline{H_4}$, 4-OH-C_6H_4), 7.35-7.30 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.15-7.09 (m, 1H, 2-F-$C_6\underline{H_4}$,), 6.94 – 6.85 (m, 2H, 2-OH-$C_6\underline{H_4}$).
9	14.21 (s, 1H, SH), 8.89 (s, 1H, -N=CH-), 8.31 (д, 1H, 2-NO_2-$C_6\underline{H_4}$), 8.05-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.56-7.64 (m, 1H, 2-F-$C_6\underline{H_4}$,), 7.35-7.29 (m, 3H, 2-NO_2-C_6H_4, 2-F-$C_6\underline{H_4}$), 7.15-7.09 (m, 1H, 2-F-$C_6\underline{H_4}$,), 6.94 – 6.85 (m, 2H, 2-NO_2-$C_6\underline{H_4}$).
10	14.18 (s, 1H, SH), 8.78 (s, 1H, -N=CH-), 8.33 (д, 1H, 3-NO_2-$C_6\underline{H_4}$), 8.05-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.56-7.64 (m, 1H, 2-F-$C_6\underline{H_4}$,), 7.35-7.29 (m, 3H, 3-NO_2-C_6H_4, 2-F-$C_6\underline{H_4}$), 7.15-7.09 (m, 1H, 2-F-$C_6\underline{H_4}$,), 6.96- 6.84 (m, 2H, 3-NO_2-$C_6\underline{H_4}$).
11	14.22 (s, 1H, SH), 8.82 (s, 1H, -N=CH-), 8.35 (д, 1H, 4-NO_2-$C_6\underline{H_4}$), 8.05-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.56-7.65 (m, 1H, 2-F-$C_6\underline{H_4}$,), 7.32-7.26 (m, 3H, 4-NO_2-C_6H_4, 2-F-$C_6\underline{H_4}$), 7.16-7.11 (m, 1H, 2-F-$C_6\underline{H_4}$,), 6.91- 6.87 (m, 2H, 4-NO_2-$C_6\underline{H_4}$).
12	14.32 (s, 1H, SH), 9.64 (s, 1H, -N=CH-), 7.98-8.05 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.65-7.55 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.59 – 7.54 (dd, 2H, 3-OCH_3-$C_6\underline{H_4}$), 7.20-7.18 (m, 1H, 2-F-$C_6\underline{H_4}$), 6.97 – 6.90 (dd, 2H, 3-OCH_3-$C_6\underline{H_4}$), 3.81 (s, 3H, 3-OC$\underline{H_3}$-C_6H_4).
13	14.28 (s, 1H, SH), 9.51 (s, 1H, -N=CH-), 8.05 – 7.93 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.75-7.61 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.22-7.18 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.05-6.91 (m, 2H, 2,3-OCH_3-$C_6\underline{H_4}$), 3.94(s, 3H, 2,3-OC$\underline{H_3}$-C_6H_4), 3.82 (s, 3H, 2,3-OC$\underline{H_3}$-C_6H_4).
14	14.31 (s, 1H, SH), 9.57 (s, 1H, -N=CH-), 8.03-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.76-7.69 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.40-7.33 (m, 2H, 3,4-OCH_3-$C_6\underline{H_4}$), 7.22-7.16 (m, 1H, 2-F-$C_6\underline{H_4}$), 6.94 (d, 1H, 3,4-OCH_3-$C_6\underline{H_4}$), 3.92 (s, 3H, 3,4-OC$\underline{H_3}$-C_6H_4), 3.87 (s, 3H, 3,4-OC$\underline{H_3}$-C_6H_4).
15	14.31 (s, 1H, SH), 9.57 (s, 1H, -N=CH-),), 8.03-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.76-7.69 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.42-7.34 (m, 2H, 3,5-OCH_3-$C_6\underline{H_4}$), 7.25-7.14 (m, 1H, 2-F-$C_6\underline{H_4}$), 6.97-6.99 (d, 1H, 3,5-OCH_3-$C_6\underline{H_4}$), 3.90 (s, 3H, 3,5-OC$\underline{H_3}$-C_6H_4), 3.87 (s, 3H, 3,5-OC$\underline{H_3}$-C_6H_4).
16	14.30 (s, 1H, SH), 9.61 (s, 1H, -N=CH-),), 8.01-7.95 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.75-7.69 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.57-7.43 (m, 3H, $C_6\underline{H_5}$), 7.40-7.33 (dd, 2H, $C_6\underline{H_5}$), 7.25-7.19 (m, 1H, 2-F-$C_6\underline{H_4}$), 3.42 (s, 3H, CH_3), 3.35 (s, 3H, CH_3).
17	14.33 (s, 1H, SH), 13,54 (1H, c, COOH),9.04 (s, 1H, -N=CH-), 8.02 – 7.95 (m, 2H, 2-F-$C_6\underline{H_4}$, $C_6\underline{H_5}$COOH), 7.65– 7.58 (m, 3H, 2-F-$C_6\underline{H_4}$, $C_6\underline{H_5}$COOH), 7.28 – 7.18 (m, 3H, 2-F-$C_6\underline{H_4}$, $C_6\underline{H_5}$COOH).
18	14.30 (s, 1H, SH), 9.04 (s, 1H, -N=CH-), 8.02 – 7.95 (m, 2H, 2-F-$C_6\underline{H_4}$, 3-Br-4-F-$C_6\underline{H_4}$), 7.65– 7.58 (m, 2H, 2-F-$C_6\underline{H_4}$, 3-Br-4-F-$C_6\underline{H_4}$), 7.28 – 7.18 (m, 2H, 2-F-$C_6\underline{H_4}$, 3-Br-4-F-$C_6\underline{H_4}$).
19	14.32 (s, 1H, SH), 8.91 (s, 1H, -N=CH-), 8.03-7.96 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.66-7.54 (m, 3H, 2-F-$C_6\underline{H_4}$, 2-Cl-6-F-$C_6\underline{H_3}$), 7.37-7.34 (dd, 2H, 2-Cl-6-F-$C_6\underline{H_3}$), 7.21-7.17 (m, 1H, 2-F-$C_6\underline{H_4}$)
20	14.30 (s, 1H, SH), 9.22 (s, 1H, -N=CH-), 7.98-8.05 (m, 1H, 2-F-$C_6\underline{H_4}$), 7.88 (d, 1H, furan-2-yl), 7.65-7.55 (m, 2H, 2-F-$C_6\underline{H_4}$), 7.42 (d, 1H, furan-2-yl),7.20-7.18 (m, 1H, 2-F-$C_6\underline{H_4}$).
21	14.27 (s, 1H, SH), 9.90 (s, 1H, -N=CH-), 8.15-8.03 (m, 2H, C_6H_5, Pyr), 7.78-7.67 (m, 2H, C_6H_5, Pyr), 7.62-7.54 (m, 2H, C_6H_5, Pyr), 7.46-7.42 (t, 1H, 2-F-$C_6\underline{H_4}$), 7.26-7.20 (d, 1H, 2-F-$C_6\underline{H_4}$).
22	14.30 (s, 1H, SH), 10.05 (s, 1H, -N=CH-), 7.78 (t, 1H, thiophen), 7.46-7.38 (m, 3H, 2-F-$C_6\underline{H_4}$), 7.26-7.20 (d, 1H, 2-F-$C_6\underline{H_4}$), 7.05-7.03 (d, 1H, thiophen), 6,87 (d, 1H, thiophen).
23	14.32 (s, 1H, SH), 10.85 (s, 1H, -N=CH-), 8.04-7.95 (d, 1H, 3-F-$C_6\underline{H_4}$), 7.75-7.68 (m, 2H, 3-F-$C_6\underline{H_4}$), 7.63-7.55 (m, 1H, 4-F-$C_6\underline{H_4}$), 7.45-7.37 (dd, 2H, 4-F-$C_6\underline{H_4}$), 7.24-7.19 (dd, 2H, 4-F-$C_6\underline{H_4}$).
24	14.30 (s, 1H, SH), 11.00 (s, 1H, 2-O$\underline{H}$-C_6H_4), 8.88 (s, 1H, -N=CH-), 8.05-7.99 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.56-7.64 (m, 3H, 3-F-$C_6\underline{H_4}$,2-OH-C_6H_4), 7.35-7.31 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.18-7.15 (m, 1H, 3-F-$C_6\underline{H_4}$,), 6.94 – 6.87 (m, 2H, 2-OH-$C_6\underline{H_4}$).
26	14.30 (s, 1H, SH), 9.62 (s, 1H), 7.98-8.05 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.65-7.55 (m, 2H, 3-F-$C_6\underline{H_4}$), 7.58 –

	7.52 (dd, 2H, 4-OCH_3-$C_6\underline{H_4}$), 7.20-7.18 (m, 1H, 3-F-$C_6\underline{H_4}$), 6.98 – 6.92 (dd, 2H, 4-OCH_3-$C_6\underline{H_4}$), 3.81 (s, 3H, 4-$OC\underline{H_3}$-C_6H_4).
27	14.30 (s, 1H, SH), 10.05 (s, 1H, -N=CH-), 7.85 (d, 1H, C_6H_5), 7.78-7.67 (m, 2H, C_6H_5), 7.64-7.56 (m, 1H, C_6H_5), 7.45-7.38 (t, 1H, C_6H_5), 7.22-7.17 (d, 1H, C_6H_5), 7.18 (m, 2H, C_6H_5), 3.33 (s, 3H, CH_3), 2.35 (s, 3H, CH_3).
28	14.30 (s, 1H, SH), 8.98 (s, 1H, -N=CH-), 8.05-7.99 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.67-7.55 (m, 3H, 3-F-$C_6\underline{H_4}$, 2,4-OCH_3-$C_6\underline{H_4}$), 7.21-7.17 (m, 1H, 3-F-$C_6\underline{H_4}$), 6.61-6.54 (m, 2H, 2,4-OCH_3-$C_6\underline{H_4}$), 3.86 (s, 3H, 2,4-$OC\underline{H_3}$-C_6H_4), 3.81 (s, 3H, 2,4-$OC\underline{H_3}$-C_6H_4).
29	14.30 (s, 1H, SH), 9.01 (s, 1H, -N=CH-), 8.00 – 7.93 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.75-7.62 (m, 2H, 3-F-$C_6\underline{H_4}$), 7.20-7.17 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.02-6.92 (m, 2H, 2,3-OCH_3-$C_6\underline{H_4}$), 3.92 (s, 3H, 2,3-$OC\underline{H_3}$-C_6H_4), 3.87 (s, 3H, 2,3-$OC\underline{H_3}$-C_6H_4).
30	14.30 (s, 1H, SH), 9.61 (s, 1H, -N=CH-), 8.01-7.95 (m, 1H, 3-F-$C_6\underline{H_4}$), 7.75-7.69 (m, 2H, 3-F-$C_6\underline{H_4}$), 7.53 (t, 1H), 7.40-7.33 (m, 2H, 3,4-OCH_3-$C_6\underline{H_4}$), 7.22-7.16 (m, 1H, 3-F-$C_6\underline{H_4}$), 6.91 (d, 1H, 3,4-OCH_3-$C_6\underline{H_4}$), 3.89 (s, 3H, 3,4-$OC\underline{H_3}$-C_6H_4), 3.85 (s, 3H, 3,4-$OC\underline{H_3}$-C_6H_4).
32	14.30 (s, 1H, SH), 9.04 (s, 1H, -N=CH-), 8.00 – 7.92 (m, 2H, 3-F-$C_6\underline{H_4}$, 3-Br-4-F- $C_6\underline{H_4}$), 7.67– 7.55 (m, 2H, 3-F-$C_6\underline{H_4}$, 3-Br-4-F- $C_6\underline{H_4}$), 7.23 – 7.13 (m, 2H, 3-F-$C_6\underline{H_4}$, 3-Br-4-F- $C_6\underline{H_4}$).
33	14.29 (s, 1H, SH), 9.95 (s, 1H, -N=CH-), 8.15-8.05 (m, 2H, C_6H_5, Pyr), 7.78-7.69 (m, 2H, C_6H_5, Pyr), 7.64-7.55 (m, 2H, C_6H_5, Pyr), 7.47-7.42 (t, 1H, C_6H_5), 7.25-7.19 (d, 1H, 3-F-$C_6\underline{H_4}$).
34	14.03 (s, 1H, SH), 7.50-7.39 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.27-7.24 (t, 1H, 3-F-$C_6\underline{H_4}$), 7.27-7.20 (dd, 2H, 4-F-$C_6\underline{H_4}$), 7.16-7.09 (dd, 2H, 4-F-$C_6\underline{H_4}$), 4.54 (s, 2H, -CH_2-).
35	14.03 (s, 1H, SH), 11.19 (s, 1H, -OH), 7.88 (d, 1H, 2-OH-$C_6\underline{H_4}$),7.52-7.41 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.32-7.26 (m, 2H, 3-F-$C_6\underline{H_4}$, 2-OH-$C_6\underline{H_4}$), 7.04-6.97 (m, 2H, 2-OH-$C_6\underline{H_4}$), 4.41 (s, 2H, -CH_2-).
36	14.03 (s, 1H, SH), 7.50-7.39 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.27-7.24 (t, 1H, 3-F-$C_6\underline{H_4}$), 7.16 – 7.09 (dd, 2H, 4-OCH_3- $C_6\underline{H_4}$), 6.90 – 6.83 (dd, 2H, 4-OCH_3- $C_6\underline{H_4}$), 4.50 (s, 2H, -CH_2-), 3.78 (s, 2H, -OCH_3).
37	14.03 (s, 1H, SH), 7.50-7.39 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.27-7.24 (t, 1H, 3-F-$C_6\underline{H_4}$), 6.81-6.73 (dd, 2H, 2,4-CH_3-$C_6\underline{H_3}$), 6.69-6.64 (d, 1H, 2,4-CH_3-$C_6\underline{H_3}$), 6.50-6.45 (d, 1H), 4.15 (s, 2H, -CH_2-), 2.12 (s, 3H, -CH_3), 2.00 (s, 3H, -CH_3).
38	13.96 (s, 1H, SH), 7.53-7.38 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.25-7.23 (t, 1H, 3-F-$C_6\underline{H_4}$), 6.80-6.77 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 6.74-6.68 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 6.65-6.59 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 4.08 (s, 2H, -CH_2-), 3.52 (s, 3H, -OCH_3), 3.48 (s, 3H, -OCH_3).
39	14.02 (s, 1H, SH), 7.53-7.40 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.25-7.22 (t, 1H, 3-F-$C_6\underline{H_4}$), 6.80-6.77 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 6.74-6.68 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 6.65-6.59 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 4.08 (s, 2H, -CH_2-), 3.39 (s, 3H, -OCH_3), 3.36 (s, 3H, -OCH_3).
40	14.07 (s, 1H, SH), 7.50-7.39 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.27-7.24 (t, 1H, 3-F-$C_6\underline{H_4}$), 6.80-6.77 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 6.74-6.68 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 6.65-6.59 (d, 1H, 2,4-OCH_3-$C_6\underline{H_3}$), 4.02 (s, 2H, -CH_2-).
41	14.09 (s, 1H, SH), 7.59-7.44 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.31-7.27 (t, 1H, 3-F-$C_6\underline{H_4}$), 7.27-7.20 (m, 2H, 3-Br-4-F-$C_6\underline{H_3}$), 7.16 (d, 1H, 3-Br-4-F-$C_6\underline{H_3}$), 4.53 (s, 2H, -CH_2-).
42	14.01 (s, 1H, SH), 7.70 (t, 1H, Py), 7.62 (d, 1H, Py), 7.53 (d, 1H, Py), 7.50-7.39 (m, 3H, 3-F-$C_6\underline{H_4}$), 7.29-7.24 (m, 2H, 3-F-$C_6\underline{H_4}$, Py), 4.61 (s, 2H, -CH_2-).

Regarding the analysis of the ^{1}H NMR spectra of 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols (32-40, Table 3), the presence of peculiarities in the signals of the corresponding protons . In the ^{1}H NMR spectrum of compound 37, the protons of aromatic substituents are manifested in the range 7.50-6.45, namely: the protons of the 3-fluorophenyl substituent form the triproton multiplet at 7.50-7.39 m.ch. and triplet at 7.27-7.24 mph; the aromatic protons of the 2,4-dimethylphenyl substituent in positions 5 and 6 form a doublet doublet region at 6.81-6.73 mph. Proton -SH group is a widespread singlet at 14.03 mph. The pronounced two-proton singlet of the -CH_2 fragment at 4.15 mph. confirms the successful course of restoration of azomethine group to azomethylene. The presence of two methyl substituents is confirmed by singlet signals at 2.12 mph. and at 2.00 mph(Fig. 4).

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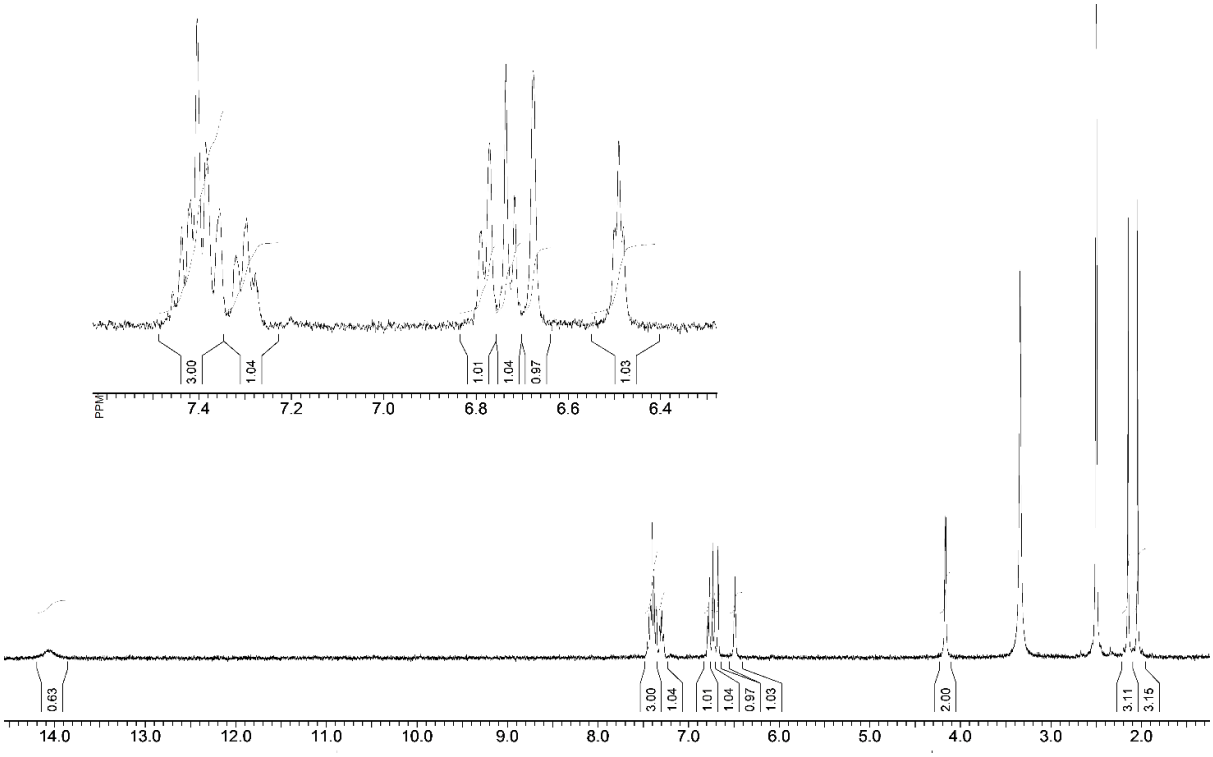

Fig 4: ^{1}H NMR spectrum of 4-((2,4-dimethylbenzylamino)-5-(3-fluorophenyl)-4H-1,2,4-triazole-3-thiol (37)

An integrated approach to the analysis of peak constants of pseudomolecular ions of 5-(2-,3-fluorophenyl)-4-((aryl-,heteryl)ylidene)amino-1,2,4-triazole-3-thiolsand 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols (3-40, Table 4), we can confidently assert the conformity of the calculated mass values to those found during the analysis.

Table 4: Theconstantsofthepeaksofthepseudomolecularionsof 5-(2-,3-fluorophenyl)-4-((aryl-, heteryl)ylidene) amino-1,2,4-triazole-3-thiols and 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols

№ compounds	Exactmass	[MH] m/z	№ compounds	Exactmass	[MH] m/z
3	298	299	**24**	314	315
4	377	378	**25**	328	329
5	316	317	**26**	326	327
6	316	317	**27**	358	359
7	314	315	**28**	358	359
8	314	315	**29**	358	359
9	343	344	**30**	395	396
10	343	344	**31**	299	300
11	343	344	**32**	318	319
12	328	329	**33**	316	317
13	358	359	**34**	330	331
14	358	359	**35**	328	329
15	358	359	**36**	360	361
16	341	342	**37**	360	361
17	342	343	**38**	360	361
18	395	396	**39**	397	398
19	350	351	**40**	301	302
20	333	334			
21	299	300			
22	304	305			

ISSN: 0975-8585

23	316	317

In the IR spectra of the 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols (32-40, Table 5), the available fluctuation bands are characteristic for C = N in the cycle , C = C groups within the limits of 1571-1606 cm^{-1} and the band of NH-group fluctuations within the limits of 3213-3393 cm^{-1}. A feature is the fact that there is no fluctuation band that is characteristic of the C = N group.

Table 5: The maximums of absorption in the infrared spectra of 5-(2-,3-fluorophenyl)-4-((aryl-, heteryl)ylidene) amino-1,2,4-triazole-3-thiols

Compound	Absorptionrate, cm^{-1}						
	vC=N cycle	vC-S	vF	$v_{феніл}$	vC=N	vNO_2	v_{NH}
1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
3	1599	697	1109	3021	1690	–	–
4	1601	705	1009	3039	1655	–	–
5	1605	700	1050	3040	1665		–
6	1610	685	1069	3047	1678	–	–
7	1608	703	1086	3019	1682	–	–
8	1607	699	1054	3024	1652	–	–
9	1589	696	1078	3031	1647	3089	–
10	1604	704	1087	3025	1663	3085	–
11	1582	691	1067	3021	1674	3092	–
12	1601	679	1083	3028	1684	–	–
13	1644	688	1096	3036	1690	–	–
14	1635	689	1090	3034	1682	–	–
15	1644	691	1093	3042	1685	–	–
16	1635	694	1069	3005	1677	–	–
17	1617	683	1070	3029	1650	–	–
18	1619	693	1100	3016	1688	–	–
19	1602	687	1099	3012	1641	3090	–
20	1614	703	1095	3028	1648	3084	–
21	1621	700	1001	3021	1671	–	–
22	1615	699	1033	3013	1689	–	–
23	1584	684	1055	3018	1655	–	–
24	1599	689	1088	3029	1669	–	–
25	1617	693	1057	3033	1677	–	–
26	1619	690	1066	3024	1650	–	–
27	1610	705	1091	3041	1662	–	–
28	1589	701	1058	3027	1685	–	–
29	1584	699	1077	3030	1657	–	–
30	1598	698	1084	3011	1683	–	–
31	1590	696	1049	3017	1670	–	–
32	1586	677	1069	3034	–	–	3214
33	1571	685	1057	3042	–	–	3222
34	1581	686	1066	3005	–	–	3214
35	1590	695	1091	3029	–	–	3393
36	1606	691	1058	3016	–	–	3213
37	1603	687	1077	3012	–	–	3275
38	1596	699	1074	3028	–	–	3382
39	1587	693	1078	3021	–	–	3225
40	1590	702	1087	3013	–	–	3220

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CONCLUSIONS

1. Using 5-(2-,3-fluorophenyl)-4-amino-1,2,4-triasole-3-thiol as starting compounds, we studied the formation of 5-(2-,3-fluorophenyl)-4-((aryl,heteryl) ylidene)amino-1,2,4-triazole-3-thiols. Further restoration of some of them leads to the formation of a number of 4-(R_2-amino)-5-(3-fluorophenyl)-1,2,4-triazole-3-thiols.

2. Passage of reactions and formation of the corresponding products in all cases is confirmed by complex modern physico-chemical methods of analysis (elemental analysis, IR, ^{1}H NMR spectroscopy, chromatographic mass spectrometry). The identity of the compounds is proved chromatographically.

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