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The synthesis and physicochemical properties of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4H-1,2,4-triazole-3-yl) ethan(propan,benz)imidates

The synthesis of new biologically active compounds that will replace expensive foreign medicines at the pharmaceutical market of Ukraine is one of the most important directions in development of modern pharmacy and medicine. The synthesis, study of physicochemical and biological properties of new compounds containing 1,2,4-triazole and 1*H*-tetrazole cores are important tasks of modern synthetic chemistry.

Aim. To synthesize new highly efficient and low-toxic substances, namely alkil-2-((5-(1*H*-tetrazole-1-yl) methyl-4-R-1,2,4-triazole-3-yl)thio)etan(propan,benz)imidates, and study physicochemical properties of all compounds synthesized.

Results and discussion. Twelve new compounds have been obtained as a result of synthetic transformations, the structure of compounds synthesized has been confirmed by modern complex of physicochemical methods of analysis (IR-spectrophotometry, ^{1}H NMR-spectroscopy, elemental analysis), and their individuality has been proven on an Agilent 1260 Infinity HPLC high-performance liquid chromatograph equipped with an Agilent 6120 mass spectrometer.

Experimental part. As starting materials for the synthesis of alkil-2-((5-(1*H*-tetrazole-1-yl)methyl-4-R-1,2,4-triazole-3-yl)thio)etan(propan,benz)imidates the corresponding 2-((5-(1*H*-tetrazole-1-yl)methyl-4-R-1,2,4-triazole-3-yl)thio)aceto(propane,benzo)nitriles were used. The synthesis was carried out in the absolute alcohol medium (propanol, butanol, octanol or allyl alcohol) with chloroform.

Conclusions. During synthetic and physicochemical studies the preparative methods for the synthesis of alkil-2-((5-(1*H*-tetrazole-1-yl)methyl-4-R-1,2,4-triazole-3-yl)thio)etan(propan,benz)imidates have been developed, the structure of the compounds synthesized has been determined and finally confirmed.

Key words: 1,2,4-triazole; 1*H*-tetrazole; synthesis; physical-chemical properties

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Синтез та фізико-хімічні властивості алкіл-2-((5-(1*H*-тетразол-1-іл)метилен-4-R-1,2,4-триазол-3-іл)тіо)етан(пропан,бенз)імідатів

Одним із пріоритетних напрямків сучасної фармації та медицини є синтез нових вітчизняних біологічно активних сполук, які будуть замінювати дорогі закордонні аналоги на фармацевтичному ринку. На теперішній час актуальним є синтез, вивчення фізико-хімічних та біологічних властивостей нових сполук, які містять ядра 1,2,4-триазолу та 1*H*-тетразолу.

Мета. Цілеспрямований синтез сполук, що містять ядро 1,2,4-триазолу та ядро 1*H*-тетразолу, вивчення фізико-хімічних властивостей синтезованих сполук.

Результати та їх обговорення. В результаті синтетичних перетворень отримано 12 нових сполук, будову яких підтверджено за допомогою комплексу сучасних фізико-хімічних методів аналізу (ІЧ-спектрофотометрії, ^{1}Н ЯМР-спектроскопії, елементного аналізу), а їх індивідуальність підтвердили на рідинному хроматографі Agilent 1260 Infinity HPLC, обладнаного мас-спектрометром Agilent 6120.

Експериментальна частина. Для синтезу алкіл-2-((5-(1*H*-тетразол-1-іл)метилен-4-R-1,2,4-триазол-3-іл)тіо)етан(пропан,бенз)імідатів як вихідні речовини використали 2-((5-(1*H*-тетразол-1-іл)метил-4-R-1,2,4-триазол-3-іл)тіо)ацето(пропан,бензо)нітрили. Синтез проводили у середовищі відповідного абсолютного спирту (пропанолу, бутанолу, октанолу або алілового спирту) у присутності хлороформу.

Висновки. Під час синтетичних та фізико-хімічних досліджень розроблені препаративні методики синтезу алкіл-2-((5-(1*H*-тетразол-1-іл)метилен-4-R-1,2,4-триазол-3-іл)тіо)етан(пропан,бенз)імідатів, встановлено та остаточно підтверджено будову всіх синтезованих сполук.

Ключові слова: 1,2,4-триазол; 1*H*-тетразол; синтез; фізико-хімічні властивості

Ю. С. Фролова, А. Г. Каплаушенко

Синтез и физико-химические свойства алкил-2-((5-(1*H*-тетразол-1-ил)метилен-4-R-1,2,4-триазол-3-ил)тио)этан(пропан,бенз)имидатов

Одним из приоритетных направлений современной фармации и медицины является синтез новых отечественных биологически активных соединений, которые будут заменять дорогие зарубежные аналоги на фармацевтическом рынке. Сегодня актуальным является синтез, изучение физико-химических и биологических свойств новых соединений, которые включают ядра 1,2,4-триазола и 1,2,3,4-тетразола.

Цель. Целенаправленный синтез соединений, содержащих ядро1,2,4-триазола и ядро 1*H*-тетразола, изучение физико-химических свойств синтезированных соединений.

Результаты и их обсуждение. В результате синтеза получено 12 новых соединений, строение которых подтверждено с помощью комплекса современных физико-химических методов анализа (ИК-спектрофотометрии, ^{1}Н ЯМР-спектроскопии, элементного анализа), а их индивидуальность подтверждена с помощью жидкостного хроматографа Agilent 1260 Infinity HPLC, оборудованного масс-спектрометром Agilent 6120.

Экспериментальная часть. Для синтеза алкил-2-((5-(1*H*-тетразол-1-ил)метилен-4-R-1,2,4-триазол-3-ил)тио)этан(пропан,бенз)имидатов в качестве исходных веществ использовали 2-((5-(1*H*-тетразол-1-ил) метил-4-R-1,2,4-триазол-3-ил)тио)ацето(пропан,бензо)нитрилы. Синтез проводили в среде соответствующего абсолютного спирта (пропанола, бутанола, октанола или аллилового спирта) в присутствии хлороформа.

Выводы. Во время синтетических и физико-химических исследований разработаны препаративные методики синтеза алкил-2-((5-(1*H*-тетразол-1-ил)метилен-4-R-1,2,4-триазол-3-ил)тио)этан(пропан,бенз)имидатов, установлено и окончательно подтверждено строение всех синтезированных соединений.

Ключевые слова: 1,2,4-триазол; 1*H*-тетразол; синтез; физико-химические свойства

The synthesis of new domestic biologically active compounds, which may replace expensive foreign medicines at the pharmaceutical market of Ukraine, is one of the priority directions in modern pharmacy and medicine. As it is known from the literature sources [1-6], the growth rate for the number of publications in the field of medicinal chemistry of the compounds, which contain such heterocycles as 1,2,4-triazole and 1*H*-tetrazole, is higher than for another representatives of the azole series. This fact indicates the interest to these compounds as potential objects of the pharmaceutical market, namely compounds, which contain both heterocycles.

Special attention is paid to the tetrazole cycle stability with regard to biodecomposition. This property of 1*H*-tetrazoles leads to the fact that medicines with tetrazole structures are less prone to destruction in the process of metabolism. As a result more reliable and long intercellular cooperation is ensured, thus, more accurate and targeted distribution of drug molecules to the corresponding receptor (a biological target) is provided [7, 8].

Therefore, the synthesis and study of physicochemical and biological properties of new compounds, which contain both 1,2,4-triazole and 1*H*-tetrazole rings are important tasks of modern synthetic chemistry.

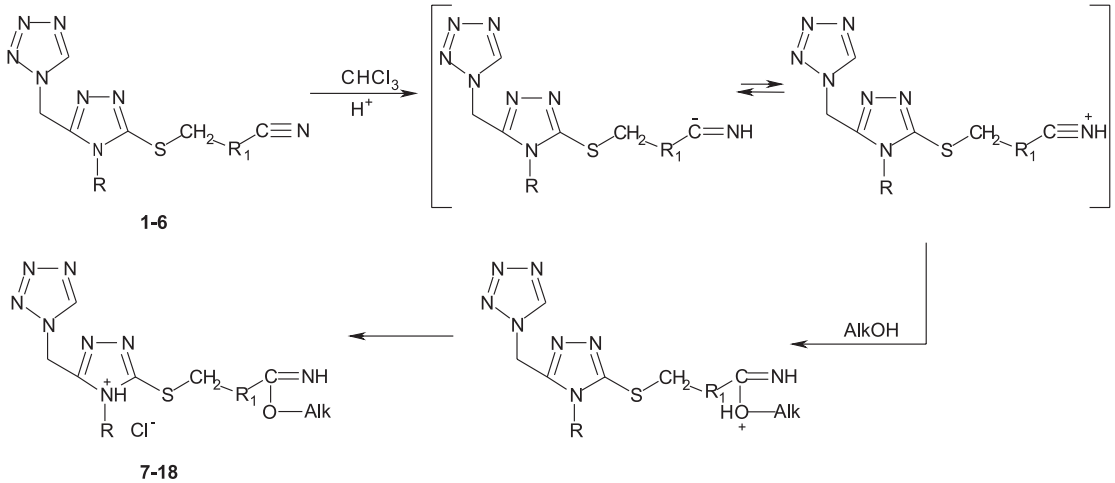
The aim of our study is the target synthesis of new highly efficient and low-toxic substances, which contain 1,2,4-triazole and 1*H*-tetrazole cycles, namely alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz)imidates, as well as determination of physicochemical properties of all compounds synthesized.

Results and discussion

For the purpose of our work, namely to obtain alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz)imidates as the initial substances for further research 2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)aceto(propano,benzo) nitrile (compounds **1-6**, Fig. 1) were used. The synthesis was carried out in the corresponding absolute alcoholic medium (propanol, butanol, octanol or allyl alcohol) in the presence of chloroform. The mixture was cooled to the temperature of -5 °C and saturated with the flow of dry hydrogen chloride till the weight increment of 2 Mole in relation to 2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)aceto(propano,benzo)nitriles **1-6.** Then the reaction mixture was evaporated.

Thus, alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz)imidates **7-18** was obtained with the yields of 42-80 %. The highest yields were fixed for propyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-phenyl-4*H*-1,2,4-triazole-3-yl) propanimidate (77 %) and propyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-phenyl-4*H*-1,2,4-triazole-3-yl)acetimidate (80 %).

The alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz)imi-

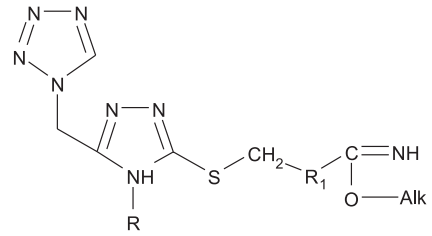


R = CH_3, C_6H_5; R_1 = CH_2, C_2H_4, C_6H_4; Alk = C_3H_7, C_4H_9, C_5H_{11}, C_8H_{17}

Fig. 1. The scheme of obtaining alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz)imidates

Table 1

Physical and chemical characteristics of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4H-1,2,4-triazole-3-yl) ethan(propan,benz)imidates



Compound	R	R_1	Alk	Melting point, °C	Gross formula	Yield, %
7	methyl	–	$-C_4H_9$	> 220	$C_{11}H_{18}N_8OS$	55
8	methyl	–	$-C_5H_{11}$	> 250	$C_{12}H_{20}N_8OS$	57
9	phenyl	–	$-C_3H_7$	138-140	$C_{15}H_{18}N_8OS$	80
10	phenyl	–	$-C_4H_9$	96-98	$C_{16}H_{20}N_8OS$	42
11	phenyl	$-CH_2$	$-C_3H_7$	177-179	$C_{16}H_{20}N_8OS$	77
12	phenyl	$-CH_2$	$-C_4H_9$	102-104	$C_{17}H_{22}N_8OS$	56
13	phenyl	$-C_6H_4$-2	$-C_3H_7$	> 250	$C_{21}H_{22}N_8OS$	42
14	phenyl	$-C_6H_4$-2	$-C_4H_9$	> 250	$C_{22}H_{24}N_8OS$	65
15	phenyl	$-C_6H_4$-3	$-C_4H_9$	134-136	$C_{22}H_{24}N_8OS$	65
16	phenyl	$-C_6H_4$-3	$-C_8H_{17}$	148-150	$C_{26}H_{32}N_8OS$	47
17	phenyl	$-C_6H_4$-4	$-C_3H_7$	> 250	$C_{21}H_{22}N_8OS$	68
18	phenyl	$-C_6H_4$-4	$-C_4H_9$	> 250	$C_{22}H_{24}N_8OS$	46

dates synthesized (compounds **7-18**, Tab. 1-4) are yellow (compounds **9, 10, 11, 12, 13, 14, 17, 18**), green (compound **16**) or brown (compounds **7, 8, 15**) amorphous substances, which are soluble in organic solvents and slightly soluble in water. For further analysis compounds **7 – 18** were recrystallized from ethanol.

The structure of compounds **7-18** was confirmed by the complex application of the elemental analysis, IR- and ^{1}H NMR-spectrophotometry. Individuality of the corresponding substances was proven by the method of HPLC/DAD-MS. Some of their physical and chemical properties and the elemental composition are presented in Tab. 1 and 2. The results of the elemen-

Table 2

Results of elemental analysis of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4H-1,2,4-triazole-3-yl) ethan(propan,benz)imidates

Compound	Found, %				Calculated, %			
	C	H	N	S	C	H	N	S
7	42.56	5.86	36.14	10.32	42.57	5.85	36.10	10.33
8	44.48	6.18	34.56	9.86	44.43	6.21	34.54	9.88
9	50.29	5.05	31.29	8.92	50.27	5.06	31.26	8.94
10	54.63	5.42	30.12	8.57	51.60	5.41	30.09	8.61
11	51.90	5.43	29.97	8.58	51.60	5.41	30.09	8.61
12	52.84	5.72	29.02	8.31	52.83	5.74	28.99	8.30
13	58.07	5.08	25.84	7.37	58.05	5.10	25.79	7.38
14	58.93	5.40	25.01	7.13	58.91	5.39	24.98	7.15
15	58.93	5.38	25.01	7.13	58.91	5.39	24.98	7.15
16	61.91	6.37	22.24	6.34	61.88	6.39	22.20	6.35
17	57.80	5.49	25.69	7.33	57.78	5.54	25.67	7.34
18	58.67	5.84	24.88	7.14	58.65	5.82	24.87	7.12

Table 3

Absorption maxima in IR-spectra of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4H-1,2,4-triazole-3-yl) ethan(propan,benz)imidates

Compound	Absorption frequency, cm^{-1}					
	$\nu_{C=Ncycle}$	ν_{C-O-C}	ν_{Ar}	ν_{C-S}	$\nu_{C=NH}$	$\nu^{s/as}_{CH_2}$
7	1085, 1600	948	1575	680	3338	2850, 2930
8	1070, 1605	940	1590	700	3335	2870, 2930
9	1085, 1598	940	1586	695	3320	2870, 2940
10	1055, 1660	950	1575	687	3318	2840, 2940
11	1030, 1535	940	1586	620	3340	2861, 2923
12	998, 1600	948	1575	700	3320	2870, 2923
13	1015, 1590	940	1565	697	3318	2870, 3000
14	1030, 1605	940	1575	685	3320	2870, 2970
15	1070, 1610	938	1586	708	3335	2870, 2940
16	1110, 1598	936	1570	700	3340	2840, 2920
17	1035, 1610	936	1585	700	3340	2840, 2917
18	1085, 1586	938	1570	705	3335	2840, 2935

tal composition determination indicate that the experimental data do not differ from the theoretical ones by more than 0.29 %.

In IR-spectra [11-13] of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl) ethan(propan,benz)imidates (Tab. 3) there are ab-

Table 4

^{1}H NMR spectra of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4H-1,2,4-triazole-3-yl)ethan(propan,benz) imidates

Compound	^{1}H NMR (δ, mp, TMS)
7	0.9 (3H, t, $-CH_3$); 1.40-1.45 (4H, m, $(CH_2)_2$); 3.50 (3H, s, $-N-CH_3$); 3.65 (2H, t, $-O-CH_2$); 3.77 (2H, s, $-S-CH_2$); 5.16 (2H, s, $-N-CH_2$); 9.36 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
8	0.9 (3H, t, $-CH_3$); 1.40-1.50 (6H, m, $(CH_2)_3$); 3.53 (3H, s, $-N-CH_3$); 3.68 (2H, t, $-O-CH_2$); 3.80 (2H, s, $-S-CH_2$); 5.25 (2H, s, $-N-CH_2$); 9.56 (1H, s, HN=C); 9.90 (1H, s, N_4CH)
9	1.05 (3H, t, $-CH_3$); 1.74 (2H, m, CH_2); 3.58 (2H, t, $-O-CH_2$); 3.89 (2H, s, $-S-CH_2$); 4.58 (2H, s, $-N-CH_2$); 7.28-7.62 (5H, m, C_6H_5); 9.30 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
10	0.9 (3H, t, $-CH_3$); 1.40-1.45 (4H, m, $(CH_2)_2$); 3.40 (2H, t, $-O-CH_2$); 3.77 (2H, s, $-S-CH_2$); 4.99 (2H, s, $-N-CH_2$); 7.35-7.83 (5H, m, C_6H_5); 9.36 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
11	1.01 (3H, t, $-CH_3$);1.64 (2H, m, CH_2); 2.50-3.30 (4H, s, $-S-(CH_2)_2$); 3.56 (2H, t, $-O-CH_2$); 5.00 (2H, s, $-N-CH_2$); 7.38-7.62 (5H, m, C_6H_5); 8.45 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
12	0.9 (3H, t, $-CH_3$); 1.40-1.45 (4H, m, $(CH_2)_2$); 2.85-3.14 (4H, s, $-S-(CH_2)_2$); 3.65 (2H, t, $-O-CH_2$); 5.28 (2H, s, $-N-CH_2$); 7.38-7.62 (5H, m, C_6H_5); 9.55 (1H, s, HN=C); 10.15 (1H, s, N_4CH)
13	1.01 (3H, t, $-CH_3$); 1.64 (2H, m, CH_2); 3.58 (2H, t, $-O-CH_2$); 4.36 (2H, s, $-S-CH_2$); 4.99 (2H, s, $-N-CH_2$); 7.25-7.48 (4H, m, C_6H_4); 7.38-7.68 (5H, m, C_6H_5); 9.36 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
14	0.9 (3H, t, $-CH_3$); 1.40-1.45 (4H, m, $(CH_2)_2$); 3.60 (2H, t, $-O-CH_2$); 4.36 (2H, s, $-S-CH_2$); 4.99 (2H, s, $-N-CH_2$); 7.25-7.48 (4H, m, C_6H_4); 7.38-7.68 (5H, m, C_6H_5); 9.36 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
15	0.85 (3H, t, $-CH_3$); 1.40-1.45 (4H, m, $(CH_2)_2$); 3.60 (2H, t, $-O-CH_2$); 4.36 (2H, s, $-S-CH_2$); 4.89 (2H, s, $-N-CH_2$); 7.12-7.40 (4H, m, C_6H_4); 7.38-7.68 (5H, m, C_6H_5); 9.36 (1H, s, NH=C); 9.45 (1H, s, N_4CH)
16	0.88 (3H, t, $-CH_3$); 1.26-1.51 (12H, m, $(CH_2)_6$); 3.58 (2H, t, $-O-CH_2$); 4.36 (2H, s, $-S-CH_2$); 4.89 (2H, s, $-N-CH_2$); 7.12-7.40 (4H, m, C_6H_4); 7.38-7.68 (5H, m, C_6H_5); 9.36 (1H, s, HN=C); 9.45 (1H, s, N_4CH)
17	1.12 (3H, t, $-CH_3$); 1.64 (2H, m, CH_2); 3.68 (2H, t, $-O-CH_2$); 4.26 (2H, s, $-S-CH_2$); 4.89 (2H, s, $-N-CH_2$); 7.25-7.48 (4H, m, C_6H_4); 7.38-7.68 (5H, m, C_6H_5); 9.36 (1H, s, HN=C); 10.01 (1H, s, N_4CH)
18	0.78 (3H, t, $-CH_3$); 1.32-1.45 (4H, m, $(CH_2)_2$); 3.68 (2H, t, $-O-CH_2$); 4.26 (2H, s, $-S-CH_2$); 5.34 (2H, s, $-N-CH_2$); 7.25-7.48 (4H, m, C_6H_4); 7.38-7.68 (5H, m, C_6H_5); 9.36 (1H, s, HN=C); 10.01 (1H, s, N_4CH)

sorption bands of C=N-groups at 1660-1535 cm^{-1} and 1110-998 cm^{-1}, bands of aromatic rings at 1590-1565 cm^{-1}, C–S-groups at 708-620 cm^{-1}, C–O–C–groups at 950-936 cm^{-1}, and also symmetric and asymmetric absorption bands, which can be caused by the presence of CH_2-groups, – in the range 2870-240 cm^{-1} and 3000-2917 cm^{-1}, respectively.

It has been found by the method of HPLC/DAD-MS that the higher is the yield of the compound synthesized, the cleaner it is. The lower is the yield of the compound, the more intensive peak of the impurity of unreacted initial 2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)aceto(propano,benzo)nitrile is observed on the chromatograms (Fig. 2).

The results of ^{1}H NMR-spectroscopy [11, 12, 14] are presented in Tab. 4. The ^{1}H NMR-spectra of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz) imidates are characterized by the intensive singlets fixed in the range of 9.45-10.15 mp and 4.58-5.34 mp, which are the evidence of the presence of protons of tetrazolemethylene groups in the structure of all compounds. The signals of aromatic ring protons for the compounds with the phenyl radical are interpreted by multiplets in the range of 7.28-7.83 mp. One-proton singlets in the range of 8.45-9.56 mp are present in the ^{1}H NMR-spectra and attributed to the imino groups. The signals of protons of thiomethylene groups are fixed in the range of 3.77-3.89 mp for ethanimidates, unlike signals in the range of 4.26-4.36 mp for benzimidates and 2.50-3.30 for propanimidates. The triplet signals in the range of 0.78-1.12 mp and 3.40-3.68 mp, and multiplet signals in the range of 1.26-1.74 mp confirm the presence of alcohol residues in iminoethers.

Experimental part

Alkyl-2-(3-thio-5-(1H-tetrazole-1-yl)methyl-4-R-4H-1,2,4-triazole-3-yl)ethan(propan,benz) imidates 7-18. Place the solution of 0.01 Mole of 2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)aceto(propano,benzo)nitrile **1-6** in 15 mL of chloroform and 25 mL of the corresponding absolute alcohol into a Bunsen flask with the calcium chloride tube bound to its side tube. Close the flask with a stopper with the glass tube to the bottom of the flask connected to the drainage beakers. Cool the mixture in a desiccator filled with ice to the temperature of -5 °C, and pass a flow of dry hydrogen chloride through the mixture, ultimately increment of hydrogen chloride is 2 Mole with the excess of 1 Mole related to the corresponding 2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl) aceto(propano,benzo)nitrile **1-6**. After saturation with hydrogen chloride leave the reaction mixture in the refrigerator at the temperature of 0 °C. In 24 h evaporate the solution.

The compounds synthesized are soluble in organic solvents and slightly soluble in water. Wash the substance with diethyl ether and dry. For further analysis recrystallize these substances from ethanol.

The study of some physical and chemical characteristics of the compounds synthesized was conducted according to the methods specified in the State Pharmacopoeia of Ukraine (SPhU) [9, 10]. The temperature of the melting point was determined by the capillary method (2.2.14) [9, 10] using a PTP (M) device produced in Ukraine.

The elemental composition of new compounds was determined using an "ELEMENTAR vario EL cube" ana-

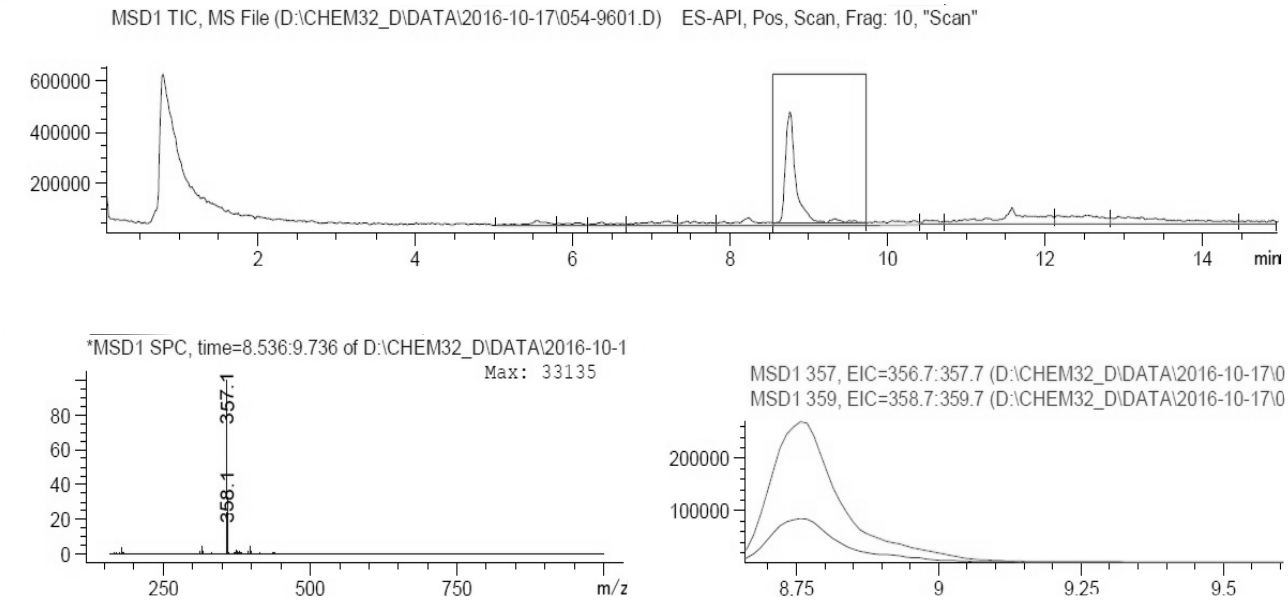


Fig. 2. The HPLC/DAD-MS-chromatogram of propil-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-phehyl-4*H*-1,2,4-triazole-3-yl)ethanimidate, yield 80 % (Compound **9**)

lyser (Germany) (the reference compound was sulphanilamide).

IR-spectra were registered for pellets of potassium bromide (the substance concentration was 1 %) using a SPECORD 200 spectrophotometer (Germany) in the range of frequencies of 4000-500 cm^{-1} (scanning conditions: target program 3.0, time constant τ was 3 sec, scanning time was 33 min). Pellets were prepared in the way of combined grinding of 200 mg of potassium bromide and 2 mg of the compound studied with further pressing.

^{1}H NMR-spectra were recorded on a Varian Mercury VX-200 (^{1}H, 200 MHz) spectrophotometer (USA) of nuclear magnetic resonance (DMSO-D_6 as a solvent, tetramethylsilane as the internal standard); the data were decoded with the SpinWorks 3.1.8 software.

The molecular mass of substances and the presence of impurities were determined by the method of high-performance liquid chromatography under the following conditions:

- device – Agilent 1260 Infinity HPLC System;
- software – OpenLAB CDS;
- column – ∅4.6 × 30 mm, reversible phase Zorbax SB C18, 1.8 mm;
- column temperature – 40 °C;
- eluent A – H_2O – 0.1 % HCOOH;
- eluent B – CH_3CN – 0.1 % HCOOH;
- flow rate – 400 mL/min;
- gradient – linear from 5 % to 100 % of eluent B for 15 min;
- detector: 1) diode array ($л_1$ = 210 nm; $л_2$ = 254 nm); 2) Agilent 6120 single-quadrupole mass-spectrometer: ion source – API-ES; positive polarity; SIM mode; fragmentator – 10 V; drying gas – nitrogen (temperature – 300 °C, rate – 10 L/min); nebulizer pressure 40 psig; scanning in the range of m/z 160-1000.

Conclusions

1. The preparative method for the synthesis of alkyl-2-(3-thio-5-(1*H*-tetrazole-1-yl)methyl-4-R-4*H*-1,2,4-triazole-3-yl)ethan(propan,benz)imidates, which can be used for modeling the chemical molecules of new biologically active compounds, has been developed, and 12 new compounds previously non-registered have been obtained.

2. The structure, individuality and physical and chemical constants have been determined for all compounds synthesized using modern methods of physical and chemical analysis.

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