METHOD OF SYNTHESIS NOVEL N'-SUBSTITUTED-2-((5-(THIOPHEN-2-YLMETHYL)-4H-1,2,4-TRIAZOL-3-YL)THIO)ACETOHYDRAZIDES

YENİ N'-SÜBSTİTÜÊ-2-((5-TİYOFEN-2-İLMETİL)-4H-1,2,4-TRİAZOL-3-İL)TİYO)ASETOHİDRAZİTLERİNSENTEZ YÖNTEMİ

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ABSTRACT

Objective: The purpose of this work is to synthesize new series of N'-substituted-2-((5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-yl)thio)acetohydrazides.

Material and Method: The compound (3) (2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide) was synthesized by adding hydrazine hydrate to isopropyl 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetate (1) and refluxed for 3-4 h in propan-2-ol. Synthesis of (5a-s) (N'-substituted-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide) was carried out by adding aromatic or heterocyclic aldehyde to 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3) in acetic acid. The structure of synthesized compounds is confirmed using Elemental analysis (CHNS), ¹H-NMR and Chromatographic mass spectral analysis.

Result and Discussion: The compound (3) was synthesized by adding hydrazine hydrate to compound (1) and compound (3) characterized by ¹H-NMR peak, as a singlet due to (NH₂) at δ=2.01ppm. Synthesis of (5a-s) was carried out by adding aromatic or heterocyclic aldehyde to compound (3) in acetic acid. The signals of ¹H-NMR for (5a-s) are consented with the proposed structure. The elemental analysis (CHNS) was accomplished for synthesized compounds to confirm their basic chemical structures and revealed acceptable agreement with the calculated percentages.

Keywords: ¹H-NMR, heterocyclic compounds, synthesis, 1,2,4-triazole

ÖZ

Amaç: Bu çalışmanın amacı, bir seri yeni N'-sübstitüê-2-((5-티य운-2-일مر티)-4H-1,2,4-티리올-3-일)티요)아세토히드라질 시נטезlemektir.

Gereç ve Yöntem: Birleşik (3) (2-((3-(티य운-2-릴미티)-1H-1,2,4-티리올-5-일)티요)아세토히드라질), isopropil 2-((3-(티요운-2-릴미티)-1H-1,2,4-티리올-5-일)티요)에테etat (1)’e hidrazin hidrat ilave edilerek sentezlenmiş ve

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INTRODUCTION

The search for means to combat diseases was conducted throughout the history of human existence. However, if in the past medical preparations were made, as a rule, from substances of animal and vegetable origin, today the achievements in the field of synthetic organic chemistry are used for the production of medicines.

Modern science is linked to the creation of the necessary synthetic drugs [1, 2, 3]. As a result, it is possible to treat many diseases that were previously considered incurable or fatal [4, 5].

Synthetic drugs in modern medicine are an important, dominant group. Substances that receive synthetically contain less impurities than the extract from the plant material. Chemical preparations are subject to higher requirements than herbal preparations. A more rigorous assessment shall be made of their medicinal properties and the conditions of use.

Synthesis of 1,2,4-triazole derivatives is a promising direction for the creation of new substances [6, 7, 8] with different types of biological activity [9, 10, 11].

The aim of the work was to synthesize and to confirm structure of N'-substituted -2-((5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-ylthio)acetohydrazides.

MATERIAL AND METHOD

Chemicals

The initial compounds isopropyl 2-((3-thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-ylthio)acetate and (1) were synthesized at the Department of Toxicological and Inorganic Chemistry of the Zaporizhzhya State Medical University (Ukraine) and purified by recrystallization with content of the main component ≥ 98% [12]. The hydrazine hydrate (assay- 50-60%), acetic acid (99%), benzaldehyde (99.5%), 2-bromobenzaldehyde (98%), 2-chlorobenzaldehyde (99%), 4-chlorobenzaldehyde (97%), 4-fluorobenzaldehyde (98%), 2-hydroxybenzaldehyde (98%), 4-hydroxybenzaldehyde (98%), 3-methoxybenzaldehyde (98%), 2-nitrobenzaldehyde (98%), 3-nitrobenzaldehyde (98%), 4-
(dimethylamino)benzaldehyde (99%), 2,4-dimethylbenzaldehyde (90%), 2,3-dimethoxybenzaldehyde (98%), 3,4-dimethoxybenzaldehyde (99%), 3,5-dimethoxybenzaldehyde (98%), 3-bromo-4-fluorobenzaldehyde (98%), nicotinaldehyde (98%), thiophene-2-carbaldehyde (95%), 5-nitrofuran-2-carbaldehyde (90%) and 2-propanol (99.5%) were obtained from SIGMA-ALDRICH (Germany).

All chemicals and solvents used during synthesis were of analytical grade and used without further purification.

**Equipment**

The melting temperature was determined on an automatic melting device OptiMelt Stanford Research Systems MPA100 (US production). The elemental analysis of the compounds is installed on the elemental analyzer Elementar Vario L cube (CHNS) (Analysetypen) GmbH, Germany). Chromatographic mass spectral studies were performed on Agilent 1260 Infinity HPLC liquid chromatograph equipped with an Agilent 6120 mass spectrometer (ionization in an electric spray (ESI) (US production), $^1$H-NMR spectra were recorded on a Mercury 400 spectrometer (Umatek International Inc.), DMSO-d$_6$ solvent, internal standard - tetramethylsilane and deciphered using the ADVASP 143 computer program. The synthetic method is outlined in scheme 1 [13, 14, 15].

**Chemical Synthesis**

*General method for synthesis of 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3)*

A mixture of isopropyl 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetate (1) (0.1 mol) and hydrazine hydrate (0.15 mol) (2) were dissolved in 250 ml propan-2-ol in a round bottom flask and refluxed for 3-4 h. After completion of the reaction, the mixture was evaporated. The residue obtained was dried, recrystallized from propan-2-ol.

2-((3-(Thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3)

Bright yellow powder; yield 72%; m.p. 124-126°C; $^{1}$HNMR (400 MHz, DMSO-d$_6$, $\delta$=ppm): 13.51 (1H, s, NH); 8.02 (1H, s, NH); 7.31(1H, d, thiophen-H); 6.87 (1H, t, thiophen-H); 6.72 (1H, d, thiophen-H); 3.69 (2H, s, CH$_2$); 3.50 (2H, s, CH$_2$); 2.01 (2H, s, NH$_2$); CHNS elemental analysis Calcd. for (C$_9$H$_{11}$N$_5$OS$_2$): found C% 40.10, H% 4.10, N% 26.05, S% 23.79; calculated C% 40.13, H% 4.12, N% 26.00, S% 23.81. Peak of a pseudo-molecular ion [MH]+ 270.

*Synthesis of titled compounds (5a-5s)*

A mixture of 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3) (0.01 mol, 2.69g) and aromatic or heterocyclic aldehyde (4) (0.01 mol): benzaldehyde (1.06g) or 2-bromobenzaldehyde (1.85g) or 2-chlorobenzaldehyde (1.40g) or 4-chlorobenzaldehyde (1.40g) or 4-fluorobenzaldehyde (1.24g) or 2-hydroxybenzaldehyde (1.22g) or 4-hydroxybenzaldehyde (1.22g) or 3-
methoxybenzaldehyde (1.36g) or 2-nitrobenzaldehyde (1.51g) or 3-nitrobenzaldehyde (1.51g) or 4-(dimethylamino)benzaldehyde (1.49g) or 2,4-dimethylbenzaldehyde (1.34g) or 2,3-dimethoxybenzaldehyde (1.66g) or 3,4-dimethoxybenzaldehyde (1.66g) or 3,5-dimethoxybenzaldehyde (1.66g) or 3-bromo-4-fluorobenzaldehyde (2.01g) or nicotinaldehyde (1.07g) or thiophene-2-carbaldehyde (1.12g) or 5-nitrofuranylcarbaldehyde (1.41g) in concentrated acetic acid was heated until the solid was dissolved. After cooling the residue was formed and washed by diethyl ether, filtered and dried, then recrystallized from acetic acid.

Scheme 1: Synthesis of 1,2,4-triazole derivatives 3-5s

\[ \text{N'}-(2-Bromobenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5a) \]

Yellow powder; yield 70%; m.p. 56-580°C; 1HNMR (400 MHz, DMSO-d6, \( \delta = \text{ppm} \)): 13.52 (1H, s, NH); 8.81 (1H, s, CH), 8.04 (1H, s, NH); 7.81 (2H, d, Ar-H), 7.51 (3H, m, Ar-H), 7.30 (1H, d, thiophen-H); 6.86 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 3.78 (2H, s, CH2); 3.59 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H15N5OS2): found C% 53.70, H% 4.21, N% 19.56, S% 17.96; calculated C% 53.76, H% 4.23, N% 19.59, S% 17.94. Peak of a pseudo-molecular ion [MH]+ 358.

\[ \text{N'}-(2-Bromobenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5b) \]

Orange powder; yield 79%; m.p. 114-1160°C; 1HNMR (400 MHz, DMSO-d6, \( \delta = \text{ppm} \)): 13.50 (1H, s, NH); 8.75 (1H, s, CH), 8.06 (1H, s, NH); 7.81 (1H, d, Ar-H), 7.57 (1H, d, Ar-H), 7.34 (m, 1H, thiophen-H, 2H, Ar-H); 6.85 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 3.79 (2H, s, CH2); 3.61 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H14BrN5OS2): found C% 44.12, H% 3.25, N% 16.09, S% 14.72; calculated C% 44.04, H% 3.23, N% 16.05, S% 14.70. Peak of a pseudo-molecular ion [MH]+ 437.
N’-(2-Chlorobenzilidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5c)

Yellow powder; yield 74%; m.p. 161-163°C; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.51 (1H, s, NH); 8.72 (1H, s, CH), 8.02 (1H, s, NH); 7.80 (1H, d, Ar-H), 7.51 (1H, d, Ar-H), 7.30 (m, 1H, thiophen-H), 2H, Ar-H); 6.89 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 3.85 (2H, s, CH2); 3.58 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H14ClN5OS2) : found C% 49.12, H% 3.63, N% 17.91, S% 16.39; calculated C% 49.04, H% 3.60, N% 17.87, S% 16.36. Peak of a pseudo-molecular ion [MH]+ 393.

N’-(4-Chlorobenzilidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5d)

Bright yellow powder; yield 79%; m.p. 189-191°C; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.56 (1H, s, NH); 8.81 (1H, s, CH), 7.99 (1H, s, NH); 7.80 (2H, d, Ar-H), 7.52 (2H, d, Ar-H), 7.38 (d, 1H, thiophen-H); 6.86 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 3.65 (2H, s, CH2); 3.52 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H14ClN5OS2) : found C% 49.12, H% 3.62, N% 17.89, S% 16.38; calculated C% 49.04, H% 3.60, N% 17.87, S% 16.36. Peak of a pseudo-molecular ion [MH]+ 393.

N’-(4-Fluorobenzilidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5e)

Yellow powder; yield 76%; m.p. 166-1680°C; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.48 (1H, s, NH); 8.88 (1H, s, CH), 8.00 (1H, s, NH); 7.76 (2H, d, Ar-H), 7.48 (2H, d, Ar-H), 7.32 (d, 1H, thiophen-H); 6.80 (1H, t, thiophen-H); 6.62 (1H, d, thiophen-H); 3.71 (2H, s, CH2); 3.52 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H14FN5OS2): found C% 51.25, H% 3.78, N% 18.68, S% 17.12; calculated C% 51.19, H% 3.76, N% 18.65, S% 17.08. Peak of a pseudo-molecular ion [MH]+ 376.

N’-(2-Hydroxobenzilidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5f)

Yellow powder; yield 69%; m.p. 188-1900°C; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.53 (1H, s, NH); 8.78 (1H, s, CH), 7.96 (1H, s, NH); 7.68 (1H, d, Ar-H), 7.51 (1H, t, Ar-H), 7.34 (d, 1H, thiophen-H); 7.11 (2H, m, Ar-H), 6.89 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 5.41 (1H, s, OH); 3.95 (2H, s, CH2); 3.67 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H15N5O2S2): found C% 51.37, H% 4.03, N% 18.69, S% 17.13; calculated C% 51.46, H% 4.05, N% 18.75, S% 17.17. Peak of a pseudo-molecular ion [MH]+ 374.

N’-(4-Hydroxobenzilidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5g)
Orange powder; yield 73%; m.p. 180-1820C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.54 (1H, s, NH); 8.38 (1H, s, CH); 8.03 (1H, s, NH); 7.74 (2H, d, Ar-H), 7.34 (d, 1H, thiophen-H); 6.89 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 6.59 (2H, m, Ar-H), 5.34 (1H, s, OH); 3.86 (2H, s, CH2); 3.59 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H15N5O2S2) : found C% 51.52, H% 4.08, N% 18.81, S% 17.19; calculated C% 51.46, H% 4.05, N% 18.75, S% 17.17. Peak of a pseudo-molecular ion [MH]+ 374.

\[ N'-(3-Methoxybenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide \] (5h)

Yellow powder; yield 76%; m.p. 85-870C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.51 (1H, s, NH); 8.54 (1H, s, CH); 8.05 (1H, s, NH); 7.57 (1H, s, Ar-H), 7.38 (m, 1H, thiophen-H, 2H, Ar-H); 7.06 (1H, d, Ar-H), 6.89 (1H, t, thiophen-H); 6.71 (1H, d, thiophen-H); 6.59 (2H, m, Ar-H), 5.34 (1H, s, OH); 3.86 (2H, s, CH2); 3.64 (3H, s, CH3) 3.59 (2H, s, CH2); CHNS elemental analysis Calcd. for (C17H17N5O2S2) : found C% 52.72, H% 4.45, N% 18.09, S% 16.57; calculated C% 52.69, H% 4.42, N% 18.07, S% 16.55. Peak of a pseudo-molecular ion [MH]+ 388.

\[ N'-(2-Nitrobenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide \] (5i)

Yellow powder; yield 72%; m.p. 124-1260C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.50 (1H, s, NH); 8.54 (1H, s, CH), 8.09 (1H, s, NH); 7.94 (3H, m, Ar-H), 7,52 (1H, t, Ar-H), 7.35 (d, 1H, thiophen-H); 6.87 (1H, t, thiophen-H); 6.75 (1H, d, thiophen-H); 3.84 (2H, s, CH2); 3.53 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H14N6O3S2) : found C% 47.99, H% 3.52, N% 20.84, S% 15.98; calculated C% 47.79, H% 3.53, N% 20.90, S% 15.91. Peak of a pseudo-molecular ion [MH]+ 403.

\[ N'-(3-Nitrobenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide \] (5j)

Orange powder; yield 70%; m.p. 98-1000C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.52 (1H, s, NH); 8.61 (1H, d, Ar-H), 8.49 (1H, s, CH), 8.14 (2H, m, Ar-H), 8.00 (1H, s, NH); 7.74 (1H, t, Ar-H), 7.34 (d, 1H, thiophen-H); 6.87 (1H, t, thiophen-H); 6.72 (1H, d, thiophen-H); 3.88 (2H, s, CH2); 3.51 (2H, s, CH2); CHNS elemental analysis Calcd. for (C16H14N6O3S2) : found C% 47.70, H% 3.53, N% 20.89, S% 15.93. Peak of a pseudo-molecular ion [MH]+ 403.

\[ N'-(4-Dimethylaminobenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide \] (5k)

Orange powder; yield 78%; m.p. 121-1230C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.54 (1H, s, NH); 8.55 (1H, s, CH), 8.08 (1H, s, NH); 7.45 (2H, d, Ar-H), 7.38 (d, 1H, thiophen-H); 6.89 (1H, t, thiophen-H); 6.81 (2H, d, Ar-H), 6.72 (1H, d, thiophen-H); 3.65 (2H, s, CH2); 3.48 (2H, s, CH2);
3.02 (6H, s, 2CH3); CHNS elemental analysis Calcd. for (C18H20N6OS2) : found C% 53.91, H% 5.05, N% 20.99, S% 16.03; calculated C% 53.98, H% 5.03, N% 20.98, S% 16.01. Peak of a pseudo-molecular ion [MH]+ 401.

*N'-((2,4-Dimethylbenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5l)

Yellow powder; yield 68%; m.p. 106-1080C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.45 (1H, s, NH); 8.88 (1H, s, CH); 8.00 (1H, s, NH); 7.78 (1H, d, Ar-H); 7.38 (d, 1H, thiophen-H); 7.05 (2H, s, Ar-H), 6.89 (1H, t, thiophen-H); 6.75 (1H, d, thiophen-H); 3.70 (2H, s, CH2); 3.50 (2H, s, CH2); 2.41 (3H, s, CH3); 2.24 (3H, s, CH3); CHNS elemental analysis Calcd. for (C18H19N5OS2) : found C% 56.12, H% 4.99, N% 18.20, S% 16.61; calculated C% 56.08, H% 4.97, N% 18.17, S% 15.36. Peak of a pseudo-molecular ion [MH]+ 386.

*N'-((2,3-Dimethoxybenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5m)

Yellow powder; yield 75%; m.p. 131-1320C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.51 (1H, s, NH); 8.80 (1H, s, CH), 8.10 (1H, s, NH); 7.40 (1H, d, thiophen-H); 7.26 (1H, d, Ar-H); 7.08 (1H, d, Ar-H): 6.87 (m, 1H, thiophen-H, 1H, Ar-H); 6.71 (1H, d, thiophen-H); 3.74 (2H, s, CH2); 3.52 (2H, s, CH2); 3.44 (6H, s, CH3); CHNS elemental analysis Calcd. for (C18H19N5O3S2) : found C% 51.84, H% 4.57, N% 16.79, S% 15.40; calculated C% 51.78, H% 4.59, N% 16.77, S% 15.36. Peak of a pseudo-molecular ion [MH]+ 418.

*N'-((3,4-Dimethoxybenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5n)

Yellow powder; yield 79%; m.p. 167-1690C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.56 (1H, s, NH); 8.72 (1H, s, CH); 8.02 (1H, s, NH); 7.59 (1H, s, Ar-H); 7.40 (1H, d, thiophen-H); 7.28 (1H, d, Ar-H); 6.87 (m, 1H, thiophen-H, 1H, Ar-H); 6.72 (1H, d, thiophen-H); 3.74 (2H, s, CH2); 3.52 (2H, s, CH2); 3.49 (6H, s, CH3); CHNS elemental analysis Calcd. for (C18H19N5O3S2) : found C% 51.87, H% 4.62, N% 16.81, S% 15.38; calculated C% 51.78, H% 4.59, N% 16.77, S% 15.36. Peak of a pseudo-molecular ion [MH]+ 418.

*N'-((3,5-Dimethoxybenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5o)

Yellow powder; yield 74%; m.p. 140-1420C ; 1HNMR (400 MHz, DMSO-d6, δ=ppm): 13.41 (1H, s, NH); 8.64 (1H, s, CH); 8.05 (1H, s, NH); 7.40 (1H, d, thiophen-H); 7.09 (2H, s, Ar-H): 6.87 (1H, t, thiophen-H); 6.72 (1H, d, thiophen-H); 6.53(s, 1H, Ar-H); 3.78 (2H, s, CH2); 3.54 (2H, s, CH2); 3.41 (6H, s, CH3); CHNS elemental analysis Calcd. for (C18H19N5O3S2) : found C% 51.74, H% 4.56, N% 16.76, S% 15.40; calculated C% 51.78, H% 4.59, N% 16.77, S% 15.36. Peak of a pseudo-molecular ion [MH]+ 418.
N’-(3-Bromo-4-fluorobenzylidene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5p)

Bright orange powder; yield 68%; m.p. 148-150°C; 1H NMR (400 MHz, DMSO-d6, δ=ppm): 13.48 (1H, s, NH); 8.39 (1H, s, CH); 8.12 (1H, s, NH); 7.94 (1H, d, Ar-H); 7.74 (1H, m, Ar-H); 7.40 (1H, d, thiophen-H); 7.21 (1H, t, Ar-H); 6.83 (1H, t, thiophen-H); 6.70 (1H, d, thiophen-H); 3.84 (2H, s, CH2); 3.69 (2H, s, CH2); CHNS elemental analysis Calcld. for (C16H13BrFN5OS2) : found C% 42.36, H% 2.86, N% 15.44, S% 14.09; calculated C% 42.30, H% 2.88, N% 15.41, S% 14.11. Peak of a pseudo-molecular ion [MH]+ 455.

N’-(Pyridin-3-ylmethylene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5q)

Yellow powder; yield 71%; m.p. 101-103°C; 1H NMR (400 MHz, DMSO-d6, δ=ppm): 13.61 (1H, s, NH); 9.09 (1H, s, Pyr-H); 8.74 (1H, d, Pyr-H); 8.53 (1H, s, CH); 8.30 (1H, d, Pyr-H); 8.01 (1H, s, NH); 7.54 (1H, t, Pyr-H); 7.32 (1H, d, thiophen-H); 6.87 (1H, t, thiophen-H); 6.72 (1H, d, thiophen-H); 3.98 (2H, s, CH2); 3.69 (2H, s, CH2); CHNS elemental analysis Calcld. for (C15H14N6OS2) : found C% 50.29, H% 3.91, N% 23.48, S% 17.92; calculated C% 50.26, H% 3.94, N% 23.43, S% 17.89. Peak of a pseudo-molecular ion [MH]+ 359.

2-((3-(Thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)-N’-(thiophen-2-ylmethylene)acetohydrazide (5r)

Bright brown powder; yield 67%; m.p. 111-113°C; 1H NMR (400 MHz, DMSO-d6, δ=ppm): 13.50 (1H, s, NH); 8.24 (1H, s, CH); 8.09 (1H, s, NH); 7.84 (1H, d, thiophen-H); 7.59 (1H, d, thiophen-H); 7.34 (1H, d, thiophen-H); 7.11 (1H, t, thiophen-H); 6.82 (1H, t, thiophen-H); 6.70 (1H, d, thiophen-H); 3.71 (2H, s, CH2); 3.53 (2H, s, CH2); CHNS elemental analysis Calcld. for (C14H13N5OS3) : found C% 46.31, H% 3.61, N% 19.29, S% 26.49; calculated C% 46.26, H% 3.60, N% 19.27, S% 26.46. Peak of a pseudo-molecular ion [MH]+ 364.

N’-(5-Nitrofuran-2-yl)methylene)-2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (5s)

Brown powder; yield 74%; m.p. 158-1600C; 1H NMR (400 MHz, DMSO-d6, δ=ppm): 13.55 (1H, s, NH); 8.44 (1H, s, CH); 7.92 (1H, s, NH); 7.59 (1H, d, Fur-H); 7.30 (1H, d, thiophen-H); 7.08 (1H, d, Fur-H); 6.80 (1H, t, thiophen-H); 6.68 (1H, d, thiophen-H); 3.84 (2H, s, CH2); 3.62 (2H, s, CH2); CHNS elemental analysis Calcld. for (C14H12N6O4S2): found C% 42.92, H% 3.07, N% 21.47, S% 16.36; calculated C% 42.85, H% 3.08, N% 21.44, S% 16.39. Peak of a pseudo-molecular ion [MH]+ 394.
RESULT AND DISCUSSION

The compound (3) (2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide) was synthesized by adding hydrazine hydrate to compound (1) and refluxed for 3-4 h in propan-2-ol. Compound (3) characterized by $^1$H-NMR peak, as a singlet due to (NH$_2$) at δ=2.01ppm.

Synthesis of (5a-s) was carried out by adding aromatic or heterocyclic aldehyde to compound (3) in acetic acid. It is known, that this reaction proceeds by the mechanism of nucleophilic attachment of an amine to an aldehyde or ketone carbon. The attachment of the nucleophile to the carbonyl compound proceeds through the bipolar ion, as a result unstable heme amino alcohol is synthesized, which dehydrates to the final product. The signals of $^1$H-NMR for (5a-s) are consented with the proposed structure.

Analyzing the LS/MS chromatogram in the MS spectrum there are molecular peaks with a value of 270 and 403 (m/z), which corresponds to the calculated theoretical value of 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3) (left) and 3-nitrobenzylidene-2-((5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-yl)thio)acetohydrazide (5j) (right) (Fig. 1)

![Mass spectrum of 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3) (left) and 3-nitrobenzylidene-2-((5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-yl)thio)acetohydrazide (5j) (right).](image)

**Fig. 1.** Mass spectrum of 2-((3-(thiophen-2-ylmethyl)-1H-1,2,4-triazol-5-yl)thio)acetohydrazide (3) (left) and 3-nitrobenzylidene-2-((5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-yl)thio)acetohydrazide (5j) (right).

The elemental analysis (CHNS) was accomplished for synthesized compounds to confirm their basic chemical structures and revealed acceptable agreement with the calculated percentages.

The novel $N'$-substituted-2-((5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-yl)thio)acetohydrazides were synthesized and characterized.

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