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Research Article

# CREATION, PHYSICAL AND CHEMICAL PROPERTIES OF ALKIL-2-((5-PHENETHYL-4-R-1,2,4-TRIAZOLE-3-YL)THIO)ACET(PROPAN,BENZ)IMIDATES

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**ABSTRACT**

**Objective:** The aim of this research was to synthesize and evaluate physical-chemical properties of 5-pheneyhyl-4-R-3-thio-1,2,4-triazole and to establish identity and structure of the synthesized compounds, namely alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz)imidates.

**Methods:** As starting materials for synthesis of alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz)imidates, the corresponding 2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)aceto(propane,benzo)nitrile have been used. Synthesis has been set in the absolute alcohol medium (propanol or butanol alcohol) with chloroform, using the saturation with dry hydrogen chloride.

**Results:** In this study, we have developed nine new compounds have been received as a result of synthetic transformations, the structure of synthesized compounds has been confirmed by modern complex of physical-chemical methods of analysis ($^1$H NMR-spectroscopy, elemental analysis), and their individuality has been conducted on gas-liquid chromatograph Agilent 1260 Infinity HPLC equipped with a mass spectrometer Agilent 6120.

**Conclusion:** As a result of the work, it was synthesized the new compounds of the series of alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio) acet(propan,benz)imidates and was characterized by elemental analysis and proton nuclear magnetic resonance spectroscopic analysis.

**Keywords:** 1,2,4-Triazole, Synthesis, Physical and chemical properties.

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## INTRODUCTION

In the past three decades, a pharmaceutical market of Ukraine has had significant problems. This problem consists of a shortage of cheap national medicines, which has not its own side effects. The literature analysis of the last years about 1,2,4-triazole derivatives shows the intensive growth of bibliographic sources number [1-7]. Currently, the works of azole nitrogen compounds have been progressively getting people's attention and have been published, owing to their functionality and the wide range of the practical application [8-10].

More recently, the number of publications with the research of compounds, which contain 1,2,4-triazole core remains to grow [1,11,12]. 1,2,4-Triazoles are one very significant class of compounds for treating many types of diseases. For example, voriconazole, itraconazole, fluconazole, saperconazole, and other medicines with different biological activity [1-8]. Based on this, it was synthesized 1,2,4-triazole derivatives as new potential biological active substances.

According to the results of previous research, the purpose of our experiment is the creation and the establishment of physical-chemical properties of new highly efficient and low-toxic substances, namely alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz)imidates.

## METHODS

Physical and chemical properties of the new compounds (6–15) were considered according to the methods described in the State Pharmacopeia of Ukraine [13,14]. Melting point was measured by the capillary method (2.2.14). Elemental composition of compounds was received on the elemental analyzer Elementar Vario L cube (CHNS) (standard – Sulfonamide). Proton nuclear magnetic resonance ($^1$H NMR) spectra of synthesized compounds are recorded in Varian Mercury VX-200 ($^1$H, 200 MHz). The solvent was used as DMSO-d6, the internal standart – as tetramethylsilane. Chromatography-mass spectrometry studies were conducted on gas-liquid chromatograph Agilent 1260 Infinity HPLC equipped with a mass spectrometer Agilent 6120 (in electrospray ionization).

### General procedure for the preparation of compounds 6–15: Alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz) imidates

The mixture of 2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio) aceto(propane,benzo)nitrile (0.01 mol), chloroform (10 ml) and absolute alcohol (25 ml) was added into Bunsen flask. It was equipped with calcium chloride tube. The mixture was cooled to the temperature of −5°C, and was saturated with dry hydrogen chloride. The 2 moles excess of dry hydrogen chloride was used for the saturation of 1 mole of 2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)aceto(propane,benzo)nitrile. Then, the mixture was left at 0°C for 24 h and the solvent was evaporated (Fig. 1).

Synthesized alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio) acet(propan,benz)imidates (compounds 5–15, Tables 1-3) are brown (6, 7, 8, 11, 15), white (9, 13), yellow (10, 14) or grey (12) amorphous substances, soluble in organic solvents and slightly soluble in water. Target compounds were recrystallized from ethanol for the analysis.

## RESULTS AND DISCUSSION

The individuality of alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz)imidates was confirmed by gas-liquid chromatography Agilent 1260 Infinity HPLC equipped with a mass spectrometer Agilent 6120. The melting point was determined by the capillary method (2.2.14) with the PTP (M) device (Table 1).

The structure of synthesized compounds (6–15) was confirmed by the complex using of elemental analysis. The elemental composition of new substances coincides within the limits of the calculated data error (Table 2).

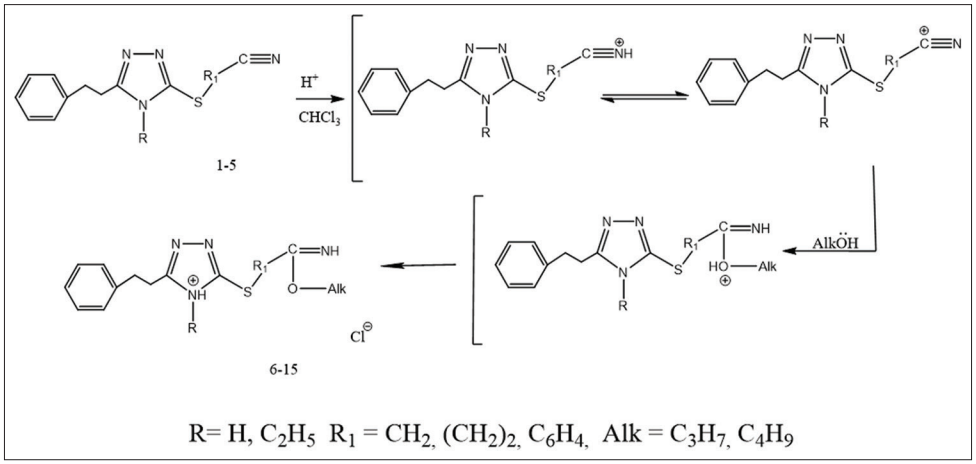



**Fig. 1: Scheme of synthesis of alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz)imidates**

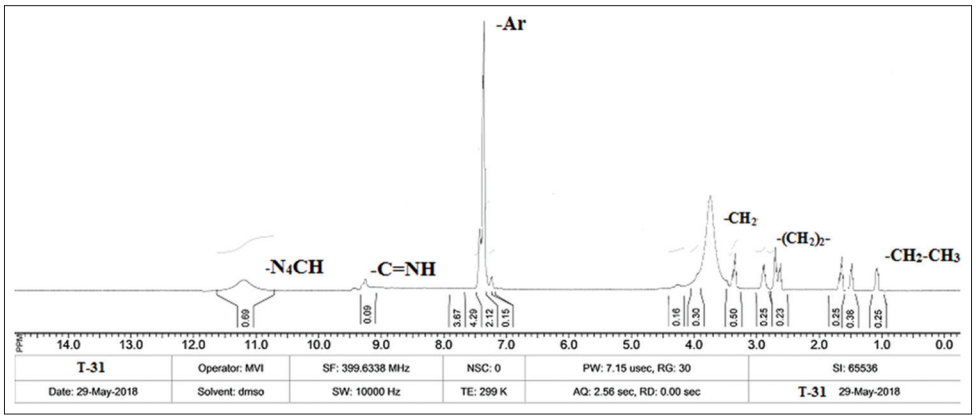
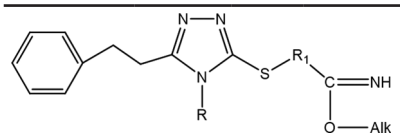



**Fig. 2: $^1$H NMR spectrum of propyl 2-((5-phenethyl-4*H*-1,2,4-triazole-3-yl)thio)acetimidate**

**Table 1: Physical-chemical properties of compounds 6-15**



| Compound | R | R1 | Alk | $M_p$, °C | Empirical formula | Yield (%) |
|---|---|---|---|---|---|---|
| 6 | H | $CH_2$ | $C_3H_7$ | 113–114 | $C_{15}H_{20}N_4OS$ | 85 |
| 7 | H | $CH_2$ | $C_4H_9$ | 115–117 | $C_{16}H_{22}N_4OS$ | 68 |
| 8 | Ethyl | $CH_2$ | $C_3H_7$ | <250 | $C_{17}H_{24}N_4OS$ | 55 |
| 9 | Ethyl | $CH_2$ | $C_4H_9$ | 138–139 | $C_{18}H_{26}N_4OS$ | 67 |
| 10 | Ethyl | $(CH_2)_2$ | $C_3H_7$ | 131–132 | $C_{18}H_{26}N_4OS$ | 58 |
| 11 | Ethyl | $(CH_2)_2$ | $C_4H_9$ | <250 | $C_{19}H_{28}N_4OS$ | 78 |
| 12 | H | $C_6H_4$ | $C_3H_7$ | 158–159 | $C_{20}H_{22}N_4OS$ | 23 |
| 13 | H | $C_6H_4$ | $C_4H_9$ | 138–139 | $C_{21}H_{24}N_4OS$ | 33 |
| 14 | Ethyl | $C_6H_4$ | $C_3H_7$ | <250 | $C_{22}H_{26}N_4OS$ | 40 |
| 15 | Ethyl | $C_6H_4$ | $C_4H_9$ | 130–132 | $C_{23}H_{28}N_4OS$ | 59 |

The results of proton nuclear magnetic resonance spectra of synthesized compounds are presented in Table 3. $^1$H NMR spectrum of propyl 2-((5-phenethyl-4*H*-1,2,4-triazole-3-yl)thio)acetimidate are presented in Fig. 2. All experimental values of $^1$H NMR-spectrophotometry of new alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz) imidates correspond to theoretical data [15,16].

## CONCLUSIONS

An effective method of new 1,2,4-triazole derivatives was developed. A series of alkil-2-((5-phenethyl-4-R-1,2,4-triazole-3-yl)thio)acet(propan,benz)imidates was successfully synthesized and characterized by elemental analysis and proton nuclear magnetic resonance spectroscopic analysis. These compounds can be used for modeling chemical molecules of new biologically active substances.

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**Table 2: The results of elemental composition determination of compounds 6-15**

| Compound | Found (%) | | | | Calculated (%) | | | |
|---|---|---|---|---|---|---|---|---|
| | C | H | N | S | C | H | N | S |
| 6 | 51.19 | 6.64 | 18.42 | 10.54 | 51.18 | 6.62 | 18.41 | 10.53 |
| 7 | 60.37 | 6.97 | 17.57 | 10.09 | 60.35 | 6.96 | 17.59 | 10.07 |
| 8 | 61.44 | 7.29 | 16.85 | 9.62 | 61.42 | 7.28 | 16.85 | 9.64 |
| 9 | 62.42 | 7.54 | 16.19 | 9.23 | 62.40 | 7.56 | 16.17 | 9.25 |
| 10 | 62.42 | 7.58 | 16.15 | 9.26 | 62.40 | 7.56 | 16.17 | 9.25 |
| 11 | 63.32 | 7.84 | 15.52 | 8.90 | 63.30 | 7.83 | 15.54 | 8.89 |
| 12 | 65.57 | 6.07 | 15.27 | 8.76 | 65.55 | 6.05 | 15.29 | 8.75 |
| 13 | 66.31 | 6.37 | 14.73 | 8.44 | 66.29 | 6.36 | 14.72 | 8.43 |
| 14 | 66.96 | 6.62 | 14.22 | 8.11 | 66.98 | 6.64 | 14.20 | 8.13 |
| 15 | 67.63 | 6.92 | 13.72 | 7.86 | 67.62 | 6.91 | 13.71 | 7.85 |

**Table 3: $^1$H NMR spectra of compounds 6-15**

| Compound | $^1$H NMR (δ, ppm, TMS) |
|---|---|
| 6 | 1.05–1.70 (5H, m, $CH_2$–$CH_3$); 2.80–2.95 (4H, m, $(CH_2)_2$); 3.60–3.85 (4H, s, $CH_2$); 7.25–7.30 (5H, m, $C_6H_5$); 9.45 (1H, s, NH=C); 11.20 (1H, s, $N_4CH$) |
| 7 | 0.85–1.55 (7H, m, $CH_2$–$CH_2$–$CH_3$); 2.85–2.90 (4H, m, $(CH_2)_2$); 3.60–3.80 (4H, s, $CH_2$); 7.27–7.33 (5H, m, $C_6H_5$); 9.40 (1H, s, NH=C); 11.15 (1H, s, $N_4CH$) |
| 8 | 1.10–1.40 (6H, m, $CH_3$); 1.80 (2H, m, $CH_2$); 2.85–2.90 (4H, m, $(CH_2)_2$); 3.64–4.15 (6H, m, $CH_2$); 7.15–7.20 (5H, m, $C_6H_5$); 9.30 (1H, s, NH=C) |
| 9 | 1.07–1.35 (6H, m, $CH_3$); 1.45–2.90 (8H, m, $(CH_2)_2$); 3.45–4.18 (6H, m, $CH_2$); 7.23–7.42 (5H, m, $C_6H_5$); 9.46 (1H, s, NH=C) |
| 10 | 0.75–1.25 (6H, m, $CH_3$); 1.75–4.10 (14H, m, $CH_2$); 7.10–7.24 (5H, m, $C_6H_5$); 9.40 (1H, s, NH=C) |
| 11 | 0.75–1.45 (6H, m, $CH_3$); 1.50–4.15 (16H, m, $CH_2$); 7.21–7.50 (5H, m, $C_6H_5$); 9.43 (1H, s, NH=C) |
| 12 | 1.35 (3H, m, $CH_3$); 1.70–3.60 (8H, m, $CH_2$); 7.15–7.35 (4H, m, $C_6H_4$); 7.40–7.50 (5H, m, $C_6H_5$); 9.50 (1H, s, NH=C); 11.20 (1H, s, $N_4CH$) |
| 13 | 0.95 (3H, m, $CH_3$); 1.45–3.55 (10H, m, $CH_2$); 7.10–7.40 (4H, m, $C_6H_4$); 7.15–7.20 (5H, m, $C_6H_5$); 9.45 (1H, s, NH=C); 11.20 (1H, s, $N_4CH$) |
| 14 | 1.10–1.35 (6H, m, $CH_3$); 1.50–4.24 (10H, m, $CH_2$); 7.15–7.30 (4H, m, $C_6H_4$); 7.20–7.35 (5H, m, $C_6H_5$); 9.55 (1H, s, NH=C) |
| 15 | 1.05–1.35 (6H, m, $CH_3$); 1.45–4.20 (10H, m, $CH_2$); 7.20–7.45 (4H, m, $C_6H_4$); 7.25–7.30 (5H, m, $C_6H_5$); 9.45 (1H, s, NH=C) |

## AUTHORS' CONTRIBUTIONS

The article is a product of the intellectual environment of the whole team and that all members have contributed in various degrees to the synthesis, physical-chemical methods used, to the research concept, and to the experiment design.

## CONFLICTS OF INTEREST

All authors have none to declare.

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