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# Synthesis, spectral characteristics, and molecular structure of N-(2,2,2-trichloro-1-((4-phenylthiazol-2-yl)amino)ethyl)carboxamides

**Yelyzaveta R. Lomynoha, Pavlo V. Zadorozhnii*, Pavlo V. Romanenko, Vadym V. Kiselev, Oxana V. Okhtina, Aleksandr V. Kharchenko**

UKRAINIAN STATE UNIVERSITY OF SCIENCE AND TECHNOLOGIES

**Department of Pharmacy, Chemistry and Technologies, Ukrainian State University of Science and Technologies, Lazariana St., 2, Dnipro, 49010, Ukraine**

***Correspondence: torfp@i.ua; Tel.: +38-067-425-2710**

DEPARTMENT OF PHARMACY, CHEMISTRY AND TECHNOLOGIES

## INTRODUCTION & AIM

Heterocyclic compounds occupy a leading position in modern organic and medicinal chemistry due to their structural diversity and wide spectrum of biological activity. Among them, 1,3-thiazoles are of particular interest, which combine Sulfur and Nitrogen atoms in their structure. This determines their unique electronic and physicochemical properties. The presence of a reactive 1,3-thiazole nucleus makes these compounds convenient platforms for synthetic modification and creation of new biologically active substances [1].

Many 1,3-thiazole derivatives exhibit various pharmacological properties, including anti-inflammatory, antimicrobial], antitumor], antifungal, and anticonvulsant. Some of them have already become the basis of medicines used in clinical practice, while others are actively studied as promising pharmacophores. In addition, 1,3-thiazoles have found application in agriculture as fungicides, insecticides, and plant growth regulators, as well as in materials science as components of new functional materials. Despite significant progress in the chemistry of 1,3-thiazole, further research into new derivatives with specific properties is an urgent task. A promising direction in the creation of new biologically active substances is the combination of the thiazole ring with other pharmacophoric groups [1]. In this study, we report the synthesis of amidoalkylated 1,3-thiazole derivatives. The alkylamide moiety is a well-known pharmacophore [2-5], and its combination with the 1,3-thiazole ring opens up prospects for the creation of compounds with potential pharmacological and pesticidal activity.

## METHOD

$^{1}$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra were measured for DMSO-$d_6$ solutions on a Varian Agilent VNMRS 400 MHz spectrometer. Residual solvent signals were used as a standard. Elemental analysis was performed on a LECO CHNS-900 instrument. The course of the reaction and the purity of the synthesized compounds were checked by TLC on Silufol UV-254 plates, using a mixture of chloroform and acetone (3:1) as the eluent. Melting points were determined in open capillaries and were not corrected.

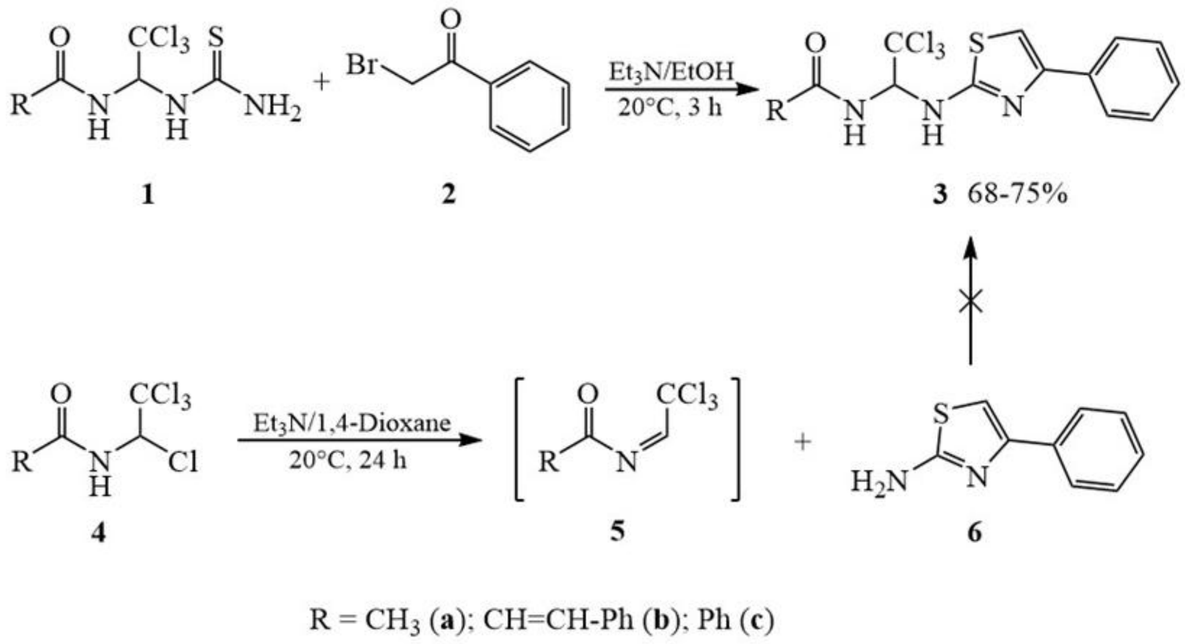
**Synthesis of *N*-(2,2,2-trichloro-1-((4-phenylthiazol-2-yl)amino)ethyl)carboxamides (3)**. A mixture of equimolar amounts (10 mmol) of monoamidoalkylated thiourea **1** [6,7], α-bromoacetophenone **2**, and triethylamine in ethanol was stirred at room temperature for 3 hours. During the reaction, the precipitate of thiourea **1** disappeared. The resulting solution was filtered, and the filtrate was evaporated at 20 ℃ and atmospheric pressure. After 24 hours, the crystalline product was collected and purified by recrystallization from an appropriate solvent.

## RESULTS & DISCUSSION

The starting *N*-(2,2,2-trichloro-1-thioureidoethyl)carboxamides **1** were prepared previously [6,7]. These compounds readily reacted with α-bromoacetophenone **2** to give the corresponding *N*-amidoalkylated 1,3-thiazole derivatives **3** (Scheme 1). The reaction was carried out under stirring at 20 °C in ethanol with the addition of an equimolar amount of triethylamine to neutralize HBr. *N*-(2,2,2-trichloro-1-((4-phenylthiazol-2-yl)amino)ethyl)carboxamides **3** were obtained in 68-75% yield. Attempts to perform the countersynthesis of compounds **3** by amidoalkylation of 4-phenylthiazol-2-amine **6** were unsuccessful. In this case, strong tarring of the reaction mixture was observed, and the product could not be isolated.

The structures of compounds **3** and **5** were confirmed by $^{1}$H and $^{13}$C NMR spectroscopy, as well as by X-ray structural analysis. In the $^{1}$H NMR spectra, the characteristic doublet signals of two NH protons appeared in the region of 9.25-8.39 ppm. In addition, the signals of two CH protons were indicative, one of which appeared as a singlet at 7.24-7.19 ppm and belongs to the thiazole ring, and the other appeared as a doublet of doublets at 7.03-6.84 ppm and corresponds to the alkylamide fragment.

In the $^{13}$C NMR spectra, the signals of carbon atoms C=O, $CCl_3$, and CH of the alkylamide fragment were characteristic, appearing at approximately 167, 102, and 71 ppm, respectively. Also indicative were the signals of the three carbon atoms of the thiazole ring, which appeared at approximately 166 (C=N), 149 and 103 (C=C) ppm.




**Scheme 1**. Synthesis of *N*-(2,2,2-trichloro-1-((4-phenylthiazol-2-yl)amino)ethyl)carboxamides (**3a-c**).

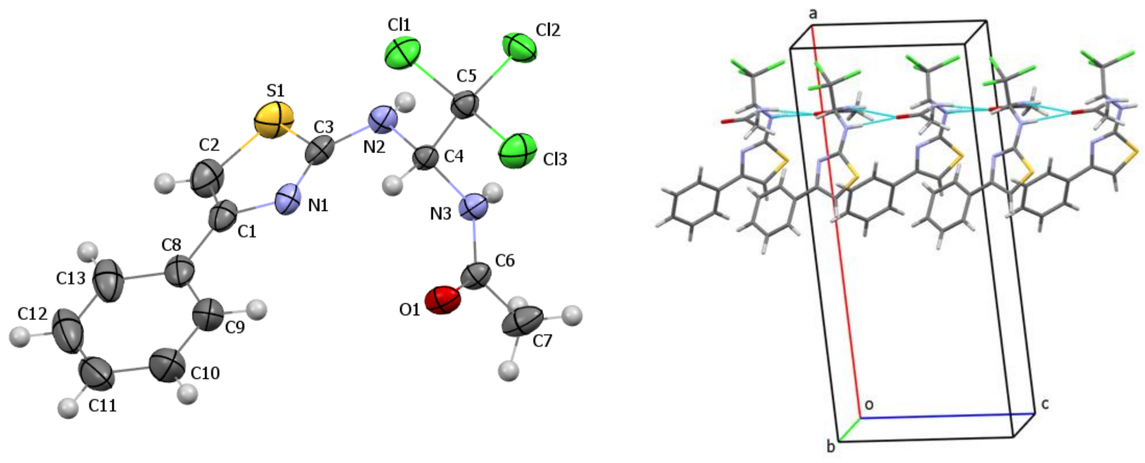



**Figure 1**. Molecular and crystal structure of compound **3a** according to XRD.

## CONCLUSION

We have developed a preparative method for the first time to synthesize *N*-amidoalkylated derivatives of 1,3-thiazole. The structure of the synthesized compounds has been reliably confirmed by $^{1}$H and $^{13}$C NMR spectroscopy and X-ray structural analysis. The obtained compounds are of interest as potential biologically active substances.

## FUTURE WORK / REFERENCES

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