chemistry proceedings

MDPI

*Proceedings Paper*

# Synthesis and Structure of (2*E*)-3-Aryl(hetaryl)-2-[5-bromo-4-aryl(hetaryl)-1,3-thiazol-2-yl]acrylonitriles †

**Nikolay Pakholka [2,*], Victor L. Abramenko [2], Victor V. Dotsenko [1,3] and S. G. Krivokolysko [2]**

[1] Kuban State University, 149 Stavropolskaya Str., 350040 Krasnodar, Russia; email1@gmail.com
[2] ChemEx Lab, Vladimir Dal' Lugansk National University, 20A/7 Molodezhny, 91034 Lugansk, Russia; email2@gmail.com (V.L.A.); email3@gmail.com (S.G.K.)
[3] Department of Chemistry, North Caucasus Federal University, 1a Pushkin St., 355009 Stavropol, Russia
* Correspondence: nikolaypaholka@yandex.ru
† Presented at the 25th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2021; Available online: https://ecsoc-25.sciforum.net/.

**Abstract:** Bromination of (2E)-3-aryl(hetaryl)-2-[4-aryl(hetaryl)-1,3-thiazol-2-yl]acrylonitriles proceeds regioselectively at the C5 atom of the thiazole ring with the formation of new (2E)-3-aryl(hetaryl)-2-[5-bromo-4-aryl(hetaryl)-1,3-thiazol-2-yl]acrylonitriles. The latter were alternatively obtained by the reaction of aldehydes, cyanothioacetamide, $\alpha$-bromoketones and bromine in the presence of triethylamine in DMF. Structure of the keycompounds was confirmed using 2D NMR spectroscopy and single crystal X-ray diffraction analysis.

**Keywords:** 1,3-thiazoles; 5-bromo-1,3-thiazoles; cyanothioacetamide; 2-cyanothioacrylamides; bromination

**Citation:** Pakholka, N.; Abramenko, V.L.; Dotsenko, V.V.; Krivokolysko, S.G. Synthesis and Structure of (2*E*)-3-Aryl(hetaryl)-2-[5-bromo-4-aryl(hetaryl)-1,3-thiazol-2-yl]acrylonitriles. **2021**, *3*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Julio A. Seijas

Published: 15 November 2021

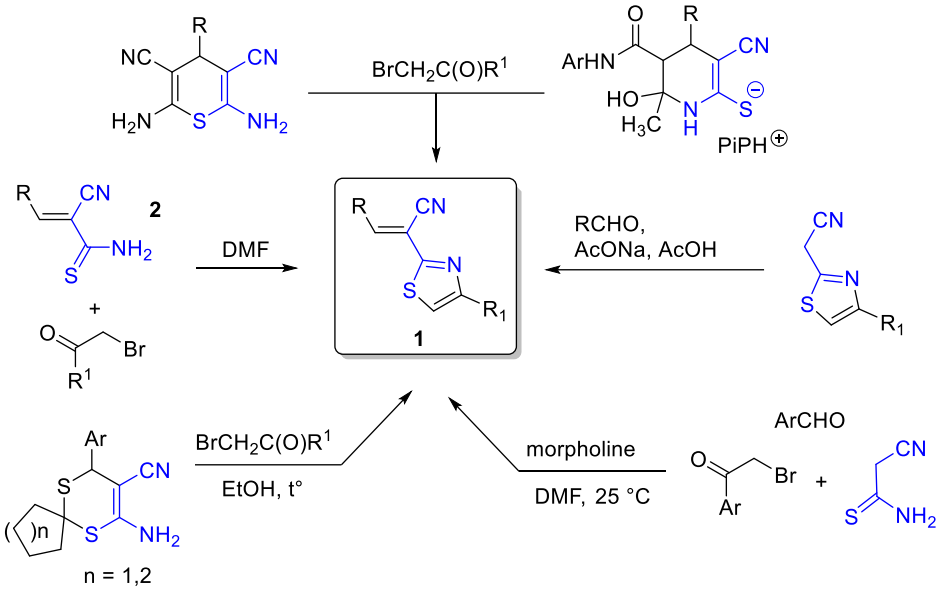


## 1. Introduction

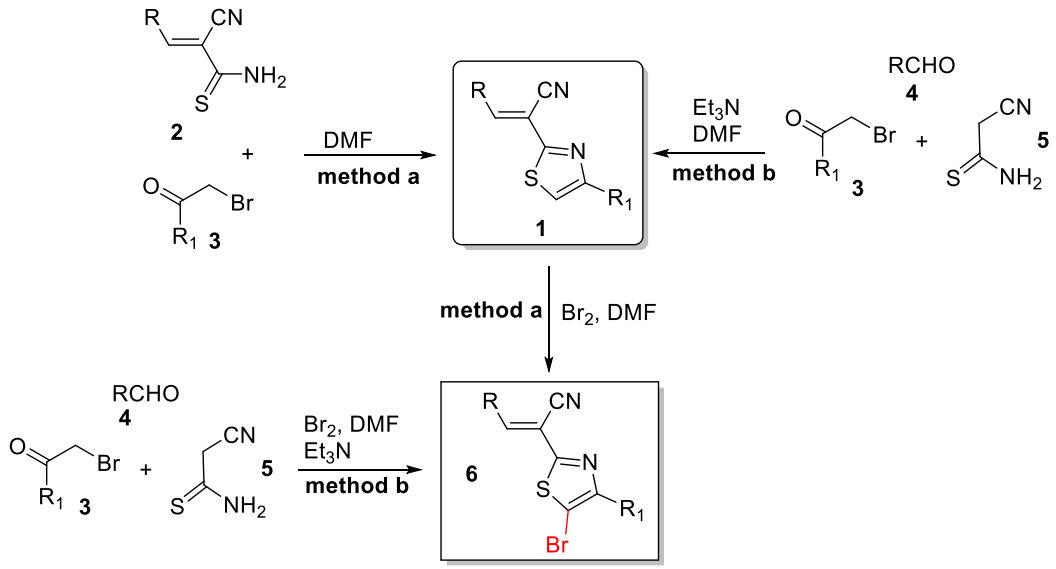
Functionally substituted thiazoles are important reactants for fine organic synthesis. They also exhibit a broad spectrum of biological activity and have different practical applications. Numerous thiazole derivatives exhibiting antibacterial, antifungal, anti-inflammatory, antitumor, anti-tuberculosis, antidiabetic, antiviral and antioxidant and other practically useful properties have been reported. Among the most significant representatives of this class of compounds, it is worth mentioning vitamin B1 (thiamine), nizatidine, penicillin, fanetizole, meloxicam, ritonavir. In this regard, the development of available approaches to the synthesis of new 1,3-thiazole derivatives seems to be a very urgent task.

## 2. Results and discussion.

We synthesized a small library of starting 2-thiazolylacrylonitriles **1**. It was shown that the bromination of compounds **1** in DMF or alcohols (methanol, ethanol, n-butanol) under the action of an equimolar or two-foldamount of bromine both at room temperature and upon heating does not affect the C=C bond of the acrylonitrile fragment. The reaction resulted in regioselective bromination at the C5-position of the thiazole ring to give5-bromothiazoles 6 in high yields (75–92%) (Scheme 2, method a). The choice of DMF as the preferred solvent is due to the fact that the starting 2-thiazolylacrylonitriles1 are very poorly soluble in alcohols. In these cases, the reaction with bromine has to be carried out at reflux and/or in a heterogeneous medium, which affects the purityand yields of the target products **6**.




**Scheme 1.**



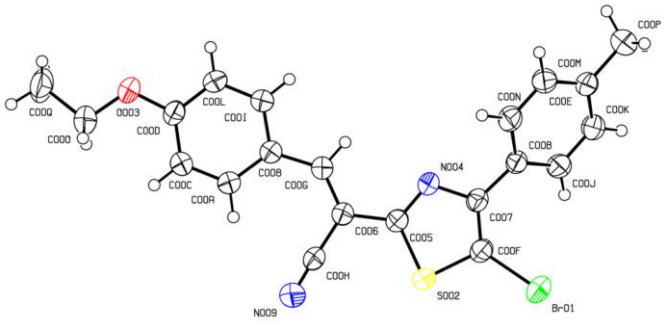

**Scheme 2.**

## 3. Experimental.

General procedure for the synthesis of (2*E*)-3- aryl(hetaryl)-2-[4-aryl(hetaryl)-1,3-thiazol-2-yl]-acrylonitriles:

*Method a.* A mixture of 5 mmol of 2-cyanothioacrylamide **2**, 5 mmol of $\alpha$-bromoketone **3** in 10 mL of DMF was brought to a boil and filtered through a folded paper filter. After 12 h, the precipitate was filtered off, washed with ethanol and hexane, and dried for 3 h at 60 °C.

*Method b.* A mixture of 0.46 mL (5 mmol) of thiophene-2-carbaldehyde **1**, 0.5 g (5 mmol) of cyanothioacetamide **5**, and 1 drop of triethylamine in 10 mL of DMF was stirred for 5 min, then 5 mmol of $\alpha$-bromoketone **3** were added. The resulting mixture was brought to a boil, filtered through a folded paper filter. After 12 h, the precipitate was filtered off, washed with ethanol and hexane, and dried for 3 h at 60°C.




General view of the molecule of compound **6h** in the crystal.

**Institutional Review Board Statement:**

**Informed Consent Statement:**

**Data Availability Statement:**

## References

1. Paladhi, S.; Jana, B.; Pathak, S.; Mannab, S.K. *Arkivoc* **2019**, 256.
2. Alneyadi, S.S. *Heterocycles* **2018**, *96*, 803.
3. Metwally, M.A.; Farahat, A.A.; Abdel-Wahab, B.F. *J. Sulfur Chem.* **2010**, *31*, 315.
4. Song, Y.X.; Du, D.M. *Org. Biomol. Chem*. **2020**, *18*, 6018.
5. Rouf, A.; Tanyeli, C. *Eur. J. Med. Chem*. **2015**, *97*, 911.
6. Tawfik, S.S.; Liu, M.; Farahat, A.A. *Arkivoc* **2020**, 180.