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Synthesis and Regiospecific Bromination of (2E, 4E) -5-Aryl-2-(4-arylthiazol-2-yl) penta-2,4-dienenitriles †

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Abstract: In the reaction of (2E, 4E) -5-phenyl-2-cyano-2,4-pentadientioamide or (E) -3- (2-nitrophenyl) acrolein and cyanothioacetamide with α-bromoketones received new (2E, 4E) -5-aryl-2- (4-arylthiazol-2-yl) penta-2,4-dienenitriles. Direct bromination of the latter by the action of Br2 in DMF proceeds regiospecifically at the C5 position of the thiazole ring without affecting the diene system and leads to the formation of previously undescribed (2E, 4E) -5-aryl-2- (5-bromo-4-arylthiazol-2-yl) penta-2,4-diennitriles. The structure of the reaction products was established using 2D NMR spectroscopy and X-ray diffraction analysis.

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

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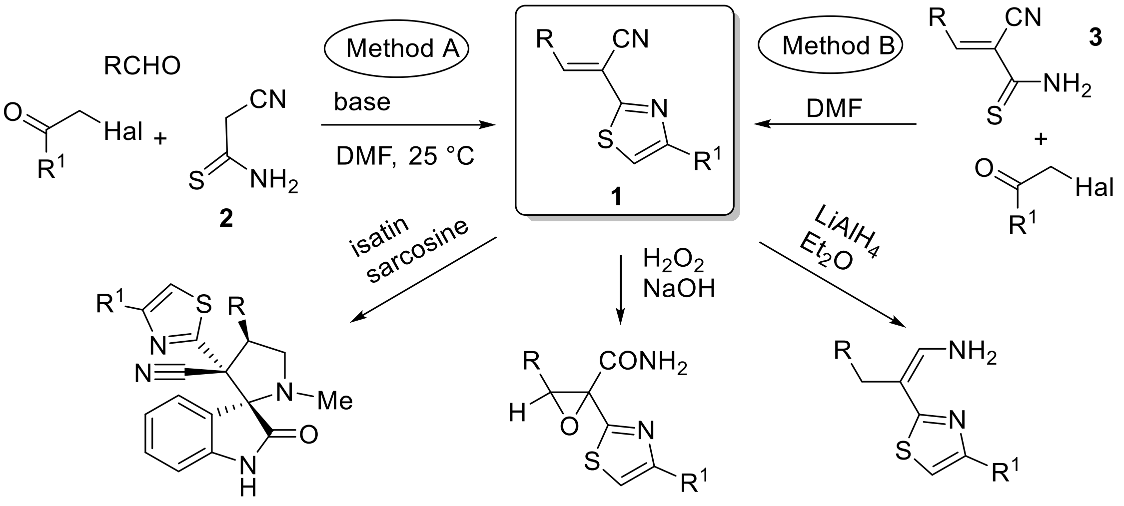
1. Introduction

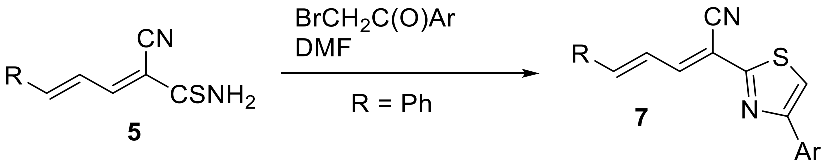
Thiazole and its derivatives are valuable reagents for organic synthesis and have wide pharmacological applications. 3-R-2-(Thiazol-2-yl)acrylonitriles **1** can be easily obtained by the reaction of aldehydes with cyanothioacetamide **2** and α-bromo(chloro)ketones (method A, Scheme 1) or by the Hantzsch method from (2*E*)-3-R-2-cyanothioacrylamides **3** and haloketones (method B, Scheme 1). Compounds **1** have been successfully used as activated electron-deficient substrates in the [3+2] dipolar cycloaddition reactions, Radzishevsky oxidation reaction with the formation of oxirane-2-carboxamides, as well as in the synthesis of functionally substituted 2-(β aminovinyl) thiazoles(Scheme1). Herein we reported the synthesis of new 2-(4-arylthiazol-2-yl)penta-2,4-dienenitriles **7**. Their structure was studied using two-dimensional NMR spectroscopy methods. In addition, in continuing our previous studies, we examined regioselectivity of the bromination of the obtained compounds **7**.



Scheme 1.

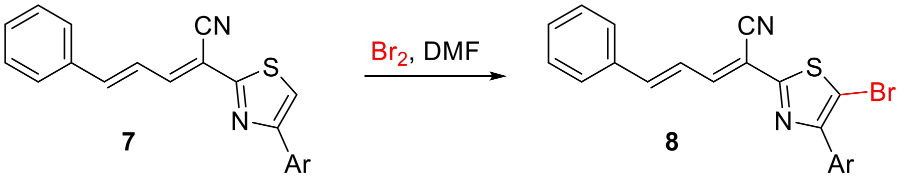
2. Results and Discussion

The reaction of (2E,4E)-5-phenyl-2-cyano-2,4-pentadienethioamide (5, R = Ph) with α-bromoketones upon short-term heating in DMF furnished a series of 2-(4-arylthiazol-2-yl)penta-2,4-dienenitriles7.



Scheme 2.

Single examples demonstrate the reactivity of thiazoles **7**. The presence of activated rings and aconjugated diene system makes compounds **7** attractive objects for studying halogenation reactions. We found that the action of an equimolar amount or excess of bromine in DMF does not affect the diene fragment of compounds 7. Bromination proceeded regiospecifically at the C5 position of the thiazole ring with the formation of 5-bromothiazoles **8** (Scheme 3).



Scheme 3. **7**,**8**: Ar = 2,4-$Me_2C_6H_3$ (**a**); Ar = 4-BrC_6H_4 (**b**).

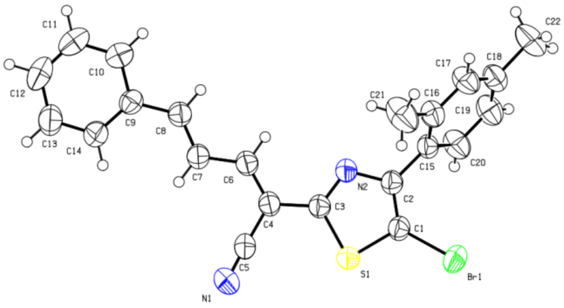
3. Experimental

General procedure for the synthesis (2*E*,4*E*)-2-(4-Arylthiazol-2-yl)penta-2,4-dienenitriles 7:

A mixture of 1.07 g (5 mmol) of (2*E*,4*E*)-5-phenyl-2-cyano-2,4- pentadienethioamide **5**, 5 mmol of the corresponding α-bromoacetophenone in 10 mL of DMF was refluxed. The mixture was filtered through a folded filter paper. After 12 h, the crystalline precipitate of thiazole **7** was filtered off, washed with ethanol and hexane, and dried at 60 °C for 3 h.

General procedure for the synthesis of 5-bromothiazoles 8a, 8b:

To a solution of 5 mmol of thiazole 7a or 7b in 10 mL of DMF was added dropwise 0.31 mL (6 mmol) of bromine, then the mixture was immediately filtered through a folded paper filter. After 12 h, the precipitate was filtered off, washed with ethanol and hexane, and dried at 60 °C for 3 h.



General view of the molecule of compound 8a in the crystal.

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