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SHORT COMMUNICATIONS

New Method of 5-Mercaptotetrazoles Functionalization

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Tetrazole derivatives containing a sulfur atom in the position *5* of the ring are promising as biologically active compounds and also as components of photomaterials [1–4]. At the same time the mercaptothiazoles are efficient reagents in the schemes of the total synthesis of natural substances [4].

A significant attention was paid to the development of efficient synthetic procedures for 5-(R-sulfanyl)tetrazoles (R = Alk, Bn) [1]. The traditional methods of preparation of these compounds are based on the alkylation of 5-mercaptotetrazoles with various electrophilic agents [1, 2].

The preparation methods of 5-(R-sulfanyl)tetrazoles (R = Ar) are poorly understood. A synthesis was reported of 5-arylsulfanyltetrazoles by the direct arylation of 5-mercaptotetrazoles by fluoro(chloro)nitrobenzenes [5], by the reaction of 5-mercaptotetrazoles with phenols under electrolysis conditions [6], and also by the reaction of 5-tosyltetrazoles with thiophenols [7]. These methods are not general for they make it possible to obtain 5-arylsulfanyltetrazoles only with definite substituents (R = Ar). Besides the necessity to use difficultly available reagents and special equipment, long reaction time and relatively low yield of target compounds reduce the efficiency of the cited methods.

Therefore the development of a general and efficient method of the synthesis of 5-арилsulfanyltetrazoles is an urgent problem.

At present one of the most promising methods of synthesis and functionalization of aromatic thioethers is their direct arylation with aryl halides catalyzed by palladium and copper complexes [6].

We found that the arylation of 1-phenyl-5-mercaptotetrazole (**I**) with iodobenzene catalyzed by CuI (10 mol%) in the presence of a ligand (2 equiv of ethylenediamine) and a base (2 equiv of Cs_2CO_3), made it possible to obtain 5-phenylsulfanyltetrazole (**II**) in a high yield (see the scheme).

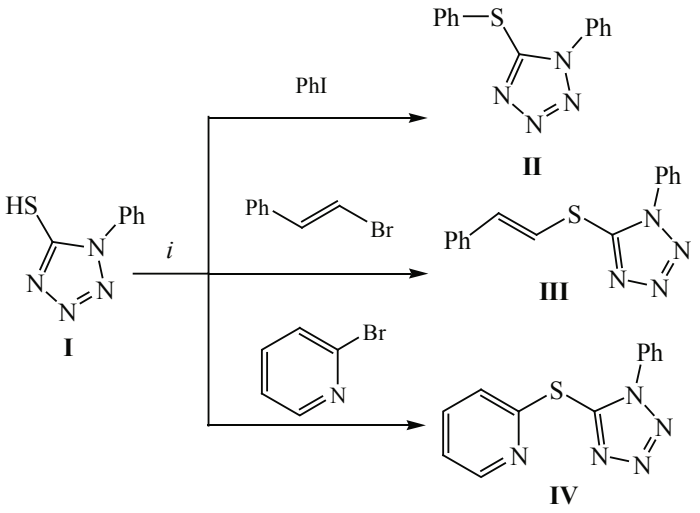
The developed method of the sysnthesis of 5-arylsulfanyl-tetrazoles can be used for the synthesis of 5-(R-sulfanyl)tetrazoles (R = Vin, Ht). By the Cu-catalyzed vinylation and hetarylation tetrazole **I** we obtained sulfanyltetrazoles **III** and **IV** in the yields of 92 and 85% respectively (see the scheme).

Note that in contrast to the method of direct arylation of mercaptotetrazoles [5] the Cu-catalyzed arylation allows the preparation also of the other 5-(R-sulfanyl) tetrazoles with R = Vin and Ht, and also does not require the use of rare reagents and additional equipment.

Synthesis of tetrazoles II–IV. General procedure. A dispersion of 2.8 mmol of tetrazole **I**, 0.28 mmol of CuI, 5.9 mmol of ethylenediamine, 5.9 mmol of Cs_2CO_3,[1] 3.4 mmol of halide, and 2 ml of DMF was stirred for 1 h (TLC monitoring of conversion) at 85°C in an argon atmosphere. The reaction mixture was cooled to 20°C and poured into 20 ml of water. The obtained solution was extracted with ethyl acetate (2 × 8 ml). The combine extract was washed with brine (2 × 8 ml), dried with anhydrous Na_2SO_4, the solvent was removed in a vacuum. The residue obtained was dispersed in 30 ml of hexane, and the dispersion was filtered. The precipitate, sulfanyltetrazole **II–IV**, was dried in an air flow.

[1] The application of K_2CO_3 as base gave worse results.

Scheme.



i, CuI (10 mol%), $H_2N(CH_2)_2NH_2$ (2 equiv), Cs_2CO_3 (2 equiv), DMF, 85°C, under argon.

1-Phenyl-5-(phenylsulfanyl)tetrazole (II). Yield 0.67 g (94%), colorless crystals, mp 129–130°C, R_f 0.3 (hexane–ethyl acetate, 7:3). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.41–7.46 m (3H, Ph, Ph–S), 7.53–7.56 m (2H, Ph, Ph–S), 7.64–7.70 m (5H, Ph, Ph–S). ^{13}C NMR spectrum, δ, ppm: 125.16, 127.40 (Ph), 129.63 (Ph–S), 129.76 (Ph), 129.86 (Ph–S), 130.76 (Ph), 133.02 (PhS), 153.20 (CN_4). Mass spectrum: *m*/*z* 255.37 [M + H]$^+$. Calculated M 254.31.

1-Phenyl-5-(*E*)-(styrylsulfanyl)tetrazole (III). Yield 0.72 g(92%), colorless crystals, mp 92–93°C, R_f 0.25 (hexane–ethyl acetate, 7 : 3). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.07 d (1H, Ph–C<u>H</u>=CH, J 15.67 Hz), 7.26–7.40 m (4H, Ph, $C_6\underline{H}_4$CH=CH), 7.49–7.51 m (2H, Ph, $C_6\underline{H}_4$–CH=CH), 7.66–7.72 m (5H, Ph–CH=C<u>H</u>, Ph). ^{13}C NMR spectrum, δ, ppm: 115.57 (Ph–CH=<u>C</u>H), 124.87 (Ph), 126.58 (<u>C</u>$_6$H$_4$–CH=CH), 128.66 (Ph), 128.81 (<u>C</u>$_6$H$_4$–CH=CH), 129.99 (Ph), 130.81, 132.94 (<u>C</u>$_6$H$_4$–CH=CH), 135.13 (Ph), 135.56 (Ph–<u>C</u>H=CH), 152.61 (CN_4). Mass spectrum: *m*/*z* 281.39 [M + H]$^+$. Calculated M 280.34.

2-(1-Phenyltetrazol-5-yl)pyridine (IV). Yield 0.6 g (85%), colorless crystals, mp 88–89°C, R_f 0.4 (hexane–ethyl acetate, 7:3). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.24 m (1H, C_6H_4N), 7.45–7.75 m (7H, Ph, C_6H_4N), 8.34 m (1H, C_6H_4N). ^{13}C NMR spectrum, δ, ppm: 122.45, 123.47 (C_6H_4N), 125.23, 129.50, 130.67, 133.32 (Ph), 138.08 (C_6H_4N), 149.46 (CN_4), 150.15, 152.98 (C_6H_4N). Mass spectrum: *m*/*z* 256.41 [M + H]$^+$. Calculated M 255.3.

^{1}H, ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-300 at operating frequencies 300.1 and 75.5 MHz respectively. The signals of the solvent DMSO-d_6 (δ_H, 2.50, δ_C 39.52 ppm) served as internal references. Mass spectra were obtained on a liquid chromato-mass spectrometer Thermo Scientific TSQ Quantum Access MAX. The melting points were measured on a PTP device at the heating rate of 1 deg min^{-1} in the range of the melting point. The homogeneity of compounds obtained was checked by TLC on Merck Kieselgel 60F_{245} plates, development under UV irradiation (λ 254 nm).

The characteristics of 1-phenyl-5-mercaptotetrazole (**I**) were consistent with the published data [9].

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