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LETTERS TO THE EDITOR

Modification of 2-Amino-4-phenylthiazole under Microwave Irradiation

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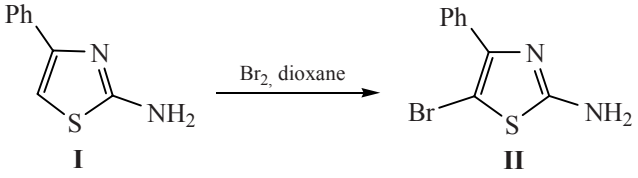
The high scientific interest attracted by the derivatives of 2-amino-4-phenylthiazole is due to the broad spectrum of biological activity exhibited by these compounds. For instance, in this series substances were found possessing antipyretic, antioxidative, analgesic, and some other types of biological activity [1–3]. The main disadvantage in the synthesis of 2-amino-4-phenylthiazole derivatives is the long reaction time [3]. We have studied the possibility of synthesis of 5-amino-containing 2-amino-4-phenyl-thiazole under the conditions of microwave irradiation.

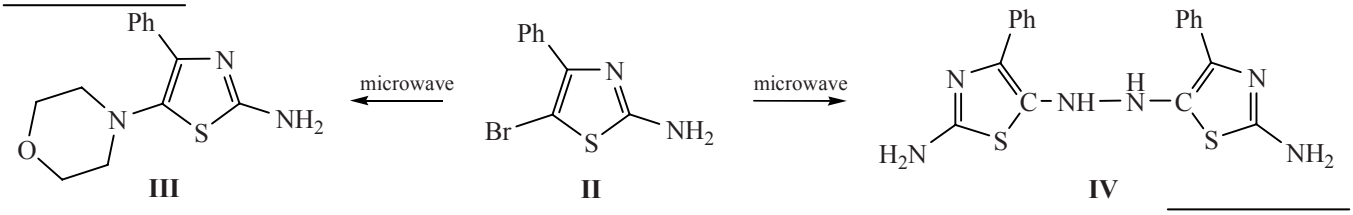
The starting substance, 2-amino-5-bromo-4-phenyl-thiazole, was obtained by bromination of 2-amino-4-phenylthiazole **I** with the molecular bromine in dioxane.



I **II**

Product **II** was a tar-like brown mass. It was used in further transformations without the additional purification.

2-Amino-5-morpholyl-4-phenylthiazole **III** and 1,2-*N,N*-bis(2-amino-4-phenylthiazolyl)hydrazine **IV** were prepared by treating compound **II** with an excess of morpholine or hydrazine under the conditions of microwave irradiation.



III **II** **IV**

The only product of the reaction of 2-amino-5-bromo-4-phenylthiazole with hydrazine hydrate under the conditions of the microwave irradiation is the product of symmetric alkylation of hydrazine, 1,2-bis (2-amino-4-phenylthiazolyl)hydrazine.

2-Amino-4-phenylthiazole was synthesized under the conditions of the microwave irradiation according to the procedure [4].

Synthesis of 2-amino-5-bromo-4-phenylthiazole (II). 2-Amino-4-phenylthiazole, 1 g, was dissolved in 10 ml of dioxane. The solution obtained was treated with a solution of 0.29 ml of bromine in 5 ml of dioxane in the course of 30 min. After the addition was complete the reaction mixture was stirred for 30 min, and dioxane was removed in a vacuum of a water-jet pump. The compound obtained was used without the additional purification.

Synthesis of 2-amino-5-*N*-morpholyl-4- phenyl-thiazole (III). 2-Amino-5-bromo-4-phenylthiazole (**II**), 1.50 g, was treated with 10 ml of morpholine, and

the resulting mixture was exposed to the microwave irradiation (70 W, 10 min). Morpholine was distilled off in a vacuum, and the residue was treated with chloroform. The solution obtained was washed with the saturated solution of sodium hydrogen carbonate, with the saturated solution of sodium chloride, and dried over sodium sulfate. The solvent was removed in a vacuum of a water-jet pump, and the residue was purified by column chromatography on silica gel, elution with 2:1 hexane–ethyl acetate. mp 205°C with decomposition, yield 37%. IR spectrum (KBr), ν, cm^{-1}: 3383, 3279, 3241, 2964, 2909, 2857, 2819, 1626, 1531, 1326, 1042, 848, 693. ^1H NMR spectrum (DMSO-d_6) δ, ppm: 2.72–2.75 t (4H, CH_2N), 3.71-3.73 t (4H, CH_2O), 6.8 s (2H, NH_2), 7.20-7.23 t (2H, Ph), 8.1 d (2H, Ph). Found, %: C 59.68, H 5.77. $C_{13}H_{15}N_3OS$. Calculated, %: C 59.74, H 5.79.

1,2-Bis(2-amino-4-phenylthiazolyl)hydrazine (IV). This compound was prepared under the conditions analogous to the previous synthesis, mp 105–107°C, yield 45%. IR spectrum (KBr) ν, cm^{-1}: 3443, 3375, 3230, 3172, 2857, 1623, 1508, 1336, 1069, 850, 695. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.3 m (3H, Ph), 7.7 m (2H, Ph). Mass spectrum, [*m*/*z*, (*I*, %)]: 51 (33), 60(40), 77(55), 89(100), 104(50), 121(45), 133 (40), 165(50), 176(47), $[M]^+$ 382(15). Found, %: C 56.79, H 4.45. $C_{18}H_{10}N_6S_2$. Calculated, %: C 56.82, H 4.24.

IR spectra were recoded on a NICOLET AVATAR-320 Fourier spectrometer in KBr pellets. ^1H NMR spectra were taken on a Bruker DRX-500 (500 MHz) spectrometer in DMSO-d_6 against internal TMS. Mass spectra were measured on a MX-1321 device with the direct injection system and the ionizing electron energy 70 eV. Melting points were measured on a Boetius installation. Experiments were carried out in a LG MS2022H microwave stove.

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